Equipment, procedures, and experimental data

for the manuscript

Two photons are better than one: continuous flow synthesis of b-lactones through a doubly photochemically-activated Paternò Büchi reaction

List of contents

1. General remarks

NMR spectra were recorded at 400 MHz (1H) and 101 MHz (13C) and the chemical shifts (δ) are expressed in parts per million relative to tetramethylsilane (TMS) as internal standard (0.00 ppm). Coupling constants are reported in hertz. NMR acquisitions were performed at 300 K and CDCl3 was used as solvent.

GC−MS analyses were carried out on Shimadzu GC−MS-QP2010 SE with an AOC-20i Plus auto-injector mounting an Avantor Hichrom HI-5 MS column (internal diameter 0.25 mm, film thickness 0.25 mm, length 30 m). Samples were prepared upon dilution 1:100 in Et_2O of a mother solution of an estimated 1000 ppm concentration. Run parameters: V_{inj} = 6 mL, T_{inj} = 250°C, T_{ramp} = 3 min@120°C, then 10°C/min up to 300°C, then 4 min@300°C, total run time 25 min, He carrier gas, column flow 1 mL/min, split ratio 1:10, MS acquisition (TIC, m/z range 35−250) from 3 to 25 min.

HR-MS analyses were carried out on a Synapt G2 QToF mass spectrometer. MS signals were acquired from 50 to 1200 m/z in ESI positive ionization mode.

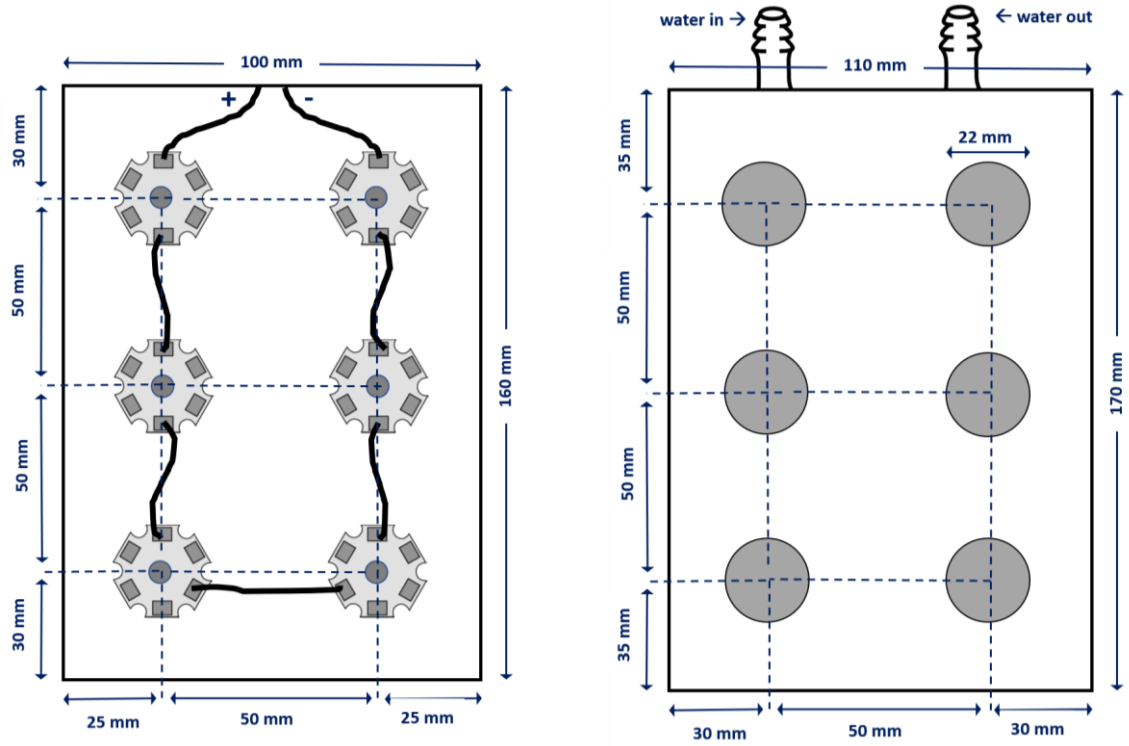
Reactions were monitored by TLC. TLC analyses were carried out on silica gel plates (thickness = 0.25 mm), viewed at UV (λ = 254 nm) and developed with Hanessian stain (dipping into a solution of (NH4)4MoO4•4H2O (21 g) and Ce(SO4)2•4H2O (1 g) in H2SO4 (31 mL) and H2O (469 mL) and warming).

Column chromatographies were performed with the “flash” methodology alternatively using 220-400 mesh silica, grade I alumina or 60-100 mesh Florisil. Solvents employed as eluents and for all other routinary operations, as well as anhydrous solvents and all reagents used were purchased from commercial suppliers and employed without any further purification.

2. Photochemical equipment

Batch Photoreactor

Batch reactions were conducted in a dedicated apparatus consisting of an aluminum cooling plate (LWH 160x100x25 mm) with 6 OSRAM® Oslon SSL 80 LDCQ7P (nominal 450 nm, royal blue) LEDs mounted in series powered by a MeanWell® LPC-20-700 constant current power supply (700 mA) and a water-cooled aluminum vessel holder. The vessel holder (LWH 170x110x38 mm) holds the sealed vials 10 mm over the LEDs in a fixed position while cooling both the LED plate and the vial, keeping the temperature of the latter below 20°C. Both the LED plate and the water-cooled vessel were custom built, while the vials were purchased from Wicom International Co. (WIC43005, 5 mL crimp top vial 38.5x22.0 mm; WIC44510 20 mm crimp caps with 3.0 mm PTFE septum).



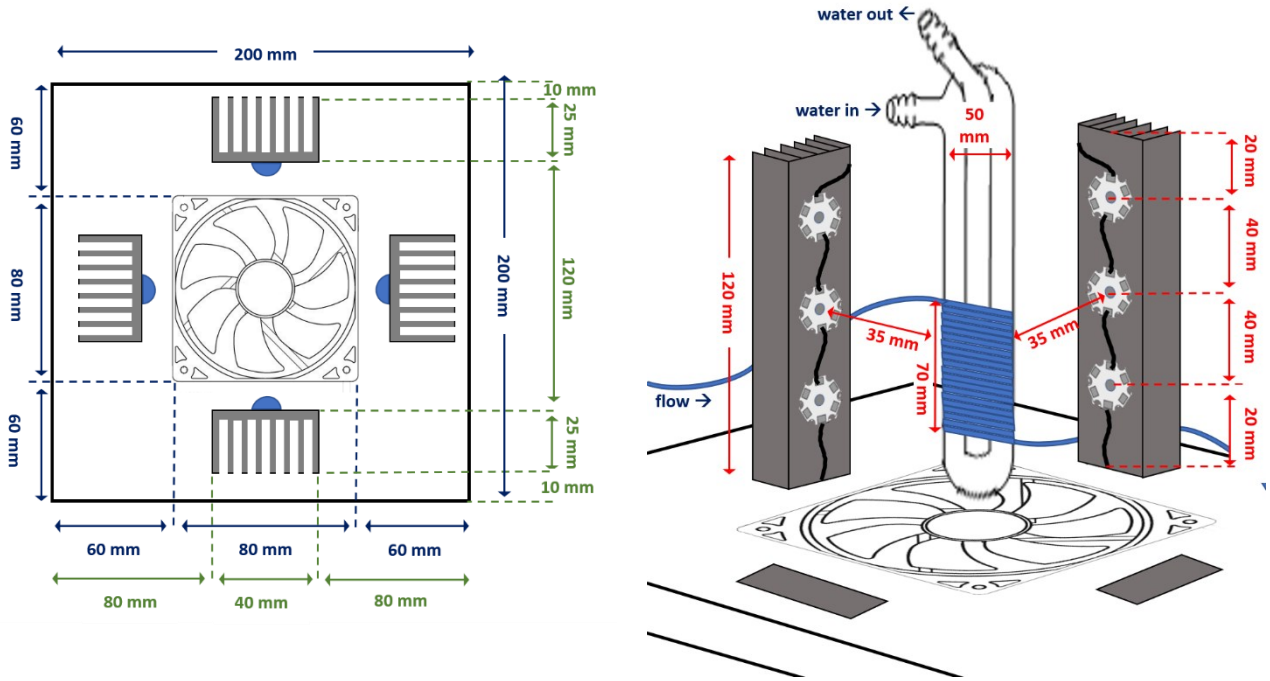
Flow Photoreactor

Flow reactions were conducted in a custom-built flow system consisting of:

- A programmable syringe pump (World Precision Instrument AL-1000);
- 25 mL air-tight syringes (purchased from SGE Analytical);
- Loading loops (6 mL) in FEP tubing (ID 1.6 mm, OD 3.2 mm);
- Reaction coil (3 mL) in FEP tubing (ID 0.8 mm, OD 1.6 mm);
- Irradiation system with 12 x OSRAM® Oslon SSL 80 LDCQ7P (nominal 450 nm, royal blue) LEDs mounted in series powered by an EA Elektro-Automatik EA-PS 2042-06 B Digital Bench Power Supply.
- A light-shielded collecting flask

All tubing was purchased from BOLA (Bohlender GmbH) and after mounting was shielded with aluminum foil to prevent undesired light exposure (except for the reaction coil). The reaction coil (height 70 mm) consists of FEP tubing for a total volume of 3 mL wrapped around a 50 mm cylindrical glass water jacket to ensure proper cooling, keeping the reaction mixture below 20°C during the irradiation. The reaction coil is clamped to a support and is placed in the middle of the irradiation system, with the tubing spacing 35 mm from the nearest LEDs plate. The irradiation system consists of 4 aluminum LEDs plates connected in series and mounted on a 200x200 mm wooden support. Each aluminum cooling plate (HWD 130x40x25 mm) bears 3 blue LEDs (40 mm apart) and is placed in the middle of each side of the square wooden

support. To ensure proper heat dispersion of the LEDs plates, an 80 mm fan (powered independently with a 12V DC power supply) is placed in the middle of the wooden support in a hollow cavity to grant air circulation.



Modulation of LEDs intensity

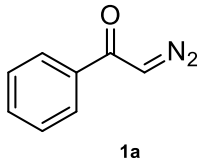
To regulate the LED intensity, we used a benchtop power supply and a photodiode connected to a tester. Once set on the benchtop the erogated current to the maximum for our measurements, we modified the applied voltage until the emitted radiant power detected by photodiode was equal to a predefined value (a preliminary calibration of the system was necessary).

Photodiodes (FD11A – 320-110 nm, active area 1.21 mm^2) were purchased from Thorlabs and a 3D-print of a proper support case was realized (cylinder in PLA of ID 4 mm, OD 18 mm, and 70 mm tall). A calibration curve was carried out, collecting points every 50 mW in a suitable range of values (from 0 to the maximum voltage tolerated by the LEDs of the plate, usually 1000 mA). To establish the reference value for the regulation of LEDs intensity, we estimated the emitted power (mW) from the photodiode reading (measured current in mA) when the LEDs were powered by a MeanWell® LPC-35-700 constant current power supply (700 mA). Once defined the desired proportional emitted power, we calculate the expected photodiodes reading (mA). We always considered the same LED to regulate the emitted intensity of each experiment.

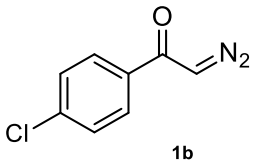
3. Synthetic procedures

Overview of the synthesized compounds

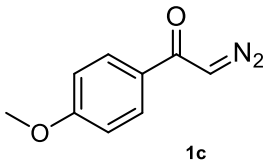
Diazoketones



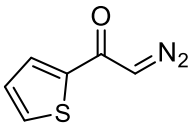
1a



1b

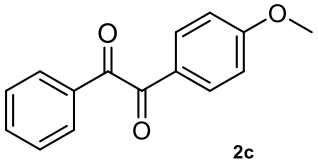


1c



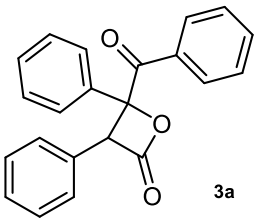
1d

Benzil-type compound

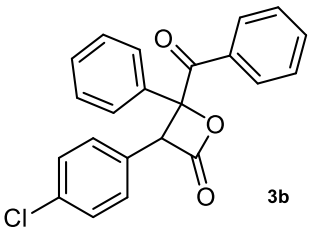


2c

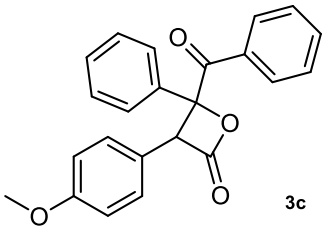
β-Lactones



3a



3b



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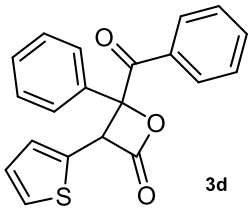
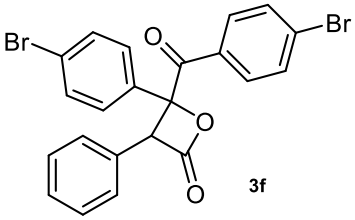
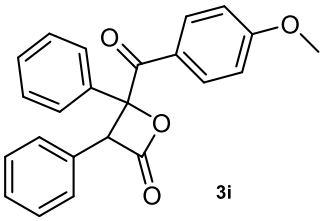


3d

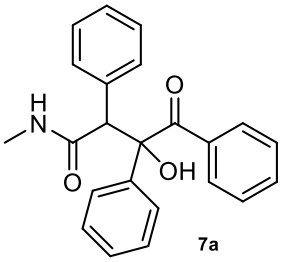


3f

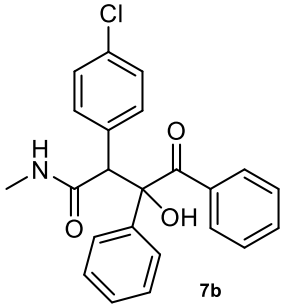


3i

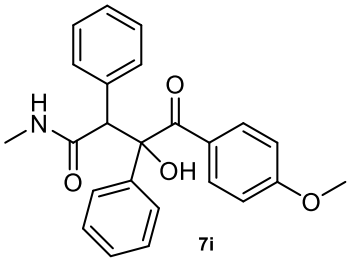
β-Hydroxy amides



7a



7b



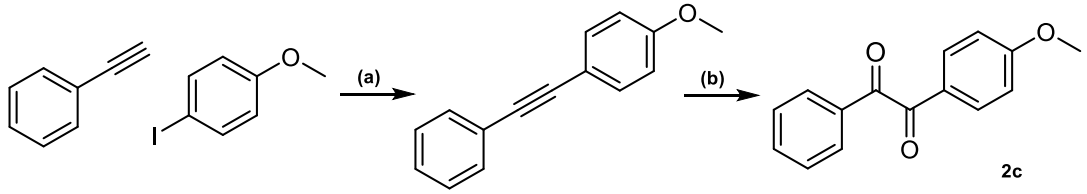
7i

*Synthesis of diazoketones **1a-d***

Diazoketones were prepared according to the procedure reported in ref. 10b.

A solution of diazomethane (14.3 mmol, 1.1 eq., 0.22 M, 65 mL) was added to a suspension of CaO (18.2 mmol, 1.4 eq.) in Et_2O (80 mL) in a 250 mL flask. The flask was chilled to 0°C in ice bath and then a solution of the acyl chloride (13 mmol, 1 eq.) in Et_2O (40 mL) was slowly added through a dripping funnel. The reaction was left proceeding overnight and checked by TLC (PE: EA 8:2, UV/Hanessian stain). The solution was filtered under vacuum over Celite, the solvent removed under reduced pressure and the crude purified by flash chromatography (SiO_2, PE: EA 8:2 → 7:3).

*Synthesis of benzil **2c***



a) 4-Iodoanisole (1.6 mmol, 1 eq.) was dissolved in diethylamine (0.7 M) under inert atmosphere (Ar), and $(PPh_3)_2PdCl_2$ (0.032 mmol, 0.02 eq.), CuI (0.064 mmol, 0.04 eq.) and phenylacetylene (1.9 mmol, 1.2 eq.) were added. The reaction was left proceeding for 4 hours and checked by TLC (Hexane, UV/Hanessian stain). The solution was extracted with NH_4Cl and diethylether, dried with Na_2SO_4. The solvent was removed under reduce pressure and the crude purified by flash chromatography (SiO_2, PE: Et_2O 100:1).

b) The substrate (1.5 mmol,1 eq.) was dissolved in 60 mL of acetone. $KMnO_4$ (4 eq.), $NaHCO_3$ (1.5 eq.), $MgSO_4$ (2 eq.), and 30 mL of water were added. The reaction was left proceeding for 24 hours and checked by TLC (Hexane, UV/Hanessian stain). To the reaction mixture were added 80 mL of EA and the solution was extracted with brine and water. The organic phase was dried with Na_2SO_4, and the solvent was removed under reduce pressure.

*Synthesis of product **3a** in batch*

The phenyl diazoketone (0.1 mmol, 1 eq., 0.04M) and the benzil (0.1 mmol, 1 eq., 0.04M) were added to a vial. The vial was sealed and degassed with argon for 5 minutes. The solvent (dry DCM, 2.5 mL) was added. The mixture was then irradiated at constant temperature (below 20°C) at 450 nm (blue LEDs) under magnetic stirring until complete consumption of the diazoketone (24h) upon TLC analysis (PE: EA 8:1, UV/Hanessian stain). The reaction yield was determined through a GC-MS analysis using an internal standard (benzyl phenyl sulfide).

*Synthesis of products **3a-i** under flow conditions*

Prior to irradiation, the flow apparatus was flushed with nitrogen and conditioned with dry DCM (including the air-tight syringe). The solution of reactants (see batch conditions above) was loaded into the loading loop and then eluted at 1 mL h^{-1} (residence time 3h) for a total of 12h to ensure complete collection of the irradiated solution. The products were then purified as previously described for the batch conditions. The solvent was removed under reduced pressure and the crude analysed at NMR.

*Synthesis of product **7a***

The crude of **3a** (0.1 mmol, 1 eq.) was dissolved il dichloromethane (0.1 M) and methylamine (25 µL, 2 eq., solution 33% wt in ethanol) was added. The reaction was left proceeding for 30 minutes and checked by TLC (PE: EA 2:1, UV/Hanessian stain). The solvent was removed under reduce pressure and the crude purified by flash chromatography (SiO_2, PE: EA 4:1).

Determination of the reaction yield

During the screening design, the determination of the reaction yield was carried out using an internal standard (benzyl phenyl sulfide). A solution of benzyl phenyl sulfide (0.2 M in diethyl ether, 500 µL, 1 eq.) was added to the reaction crude. Aliquot (20 µL) of the solution were sampled, diluted, and analysed via GC-MS. Integration of signals of products with respect to that of the internal standard allowed to calculate the reaction yield.

In the case of reactions performed in a continuous flow system, the determination of the reaction yield through a ^{1}H-NMR analysis was preferred to the internal standard procedure. Integration of selected signals of products (CH lactone, for **3a** s 5.17 ppm and s 5.83 ppm, value of integration 1 and 0.4 respectively) with respect to all aromatic signals allowed to calculate the reaction yield, given by the following equation:

$$reaction\ yiled\ \% = \frac{(integration\ signals\ of\ products \cdot number\ of\ aromatic\ protons\ of\ product)}{integration\ of\ all\ aromatic\ signals} \cdot 100$$

4. Design of Experiments

Screening Design

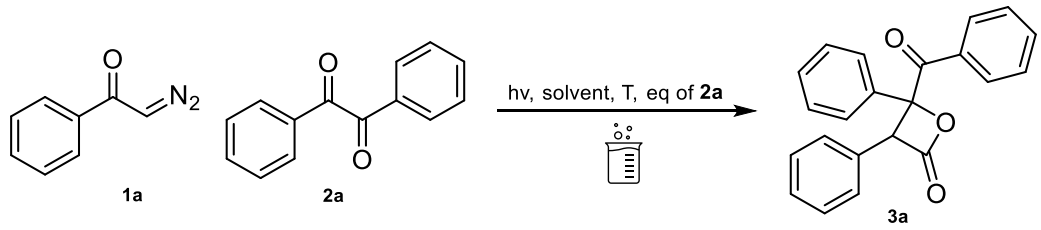


Table 1*. Variables with the corresponding levels.*

Var. ID	Variable	Levels					
X1	Wavelength	365 nm	385 nm	405 nm	450 nm*	470 nm	
X2	Temperature	-15°C	0°C	rt*			
X3	Solvent	MeCN	DCM*	Et_2O	MeOH	THF	$HC(OMe)_3$
X4	Equiv. of **2a**	1	1.5	2			

**implicit level.*

The experiments were conducted on three parallel thermostated plates, each requiring a specific operating temperature for a set of experiments. Each plate can accommodate up to six distinct reactions in separate locations, with independent LEDs emitting at different wavelengths, as illustrated in Table 1.1. As a result, the three plates available in our laboratory did not share the same wavelengths, necessitating the identification of the best combination of variables at different levels to maximize the capacity of each plate, thereby saving time and reducing experimental effort.

Table 1.1*. Details of the three plates, each equipped with six independent LEDs per position.*

Position	Plate #1	Plate #2	Plate #3
1	365 nm	450 nm	470 nm
2	365 nm	450 nm	470 nm
3	385 nm	450 nm	470 nm
4	385 nm	450 nm	470 nm
5	405 nm	450 nm	470 nm
6	405 nm	450 nm	470 nm

The postulated model consists of 14 terms, including 1 constant, 12 linear terms, and 1 quadratic term. The model matrix was built using "dummy coding" by creating *levels - 1* dummy variable for the selected factors, listed in Table 1a. They were coded as 1 if it belongs to the corresponding level or as 0 if it does not. The reference level (or implicit level) was taken as 450 nm for Wavelength, DCM dry for Solvent, and room temperature for Temperature. The factor Equivalent was coded in the range of -1 to +1.

All elaborations of obtained data were performed using the chemometric software CAT (*R. Leardi. C. Melzi. G. Polotti. CAT (Chemometric Agile Tool),* freely downloadable from *http://gruppochemiometria.it/index.php/software*).

Step 1

Variables: wavelength, solvent, temperature, equivalents of 2a.

Experimental matrix:

365nm	***385nm***	***405nm***	***470nm***	***T-15***	***T0***	***Et_2O***	***$HC(OMe)_3$***	***MeCN***	***MeOH***	***THF***	***Eq***	***Yield (%)***
1	0	0	0	1	0	0	0	1	0	0	-1	2.6
1	0	0	0	1	0	0	0	0	0	0	0	8.4
0	1	0	0	1	0	1	0	0	0	0	1	3.9

0	1	0	0	1	0	0	0	0	1	0	-1	2.1
0	0	1	0	1	0	0	0	0	0	1	0	3.9
0	0	1	0	1	0	0	1	0	0	0	1	14.4
0	0	0	0	0	0	0	0	1	0	0	1	3.5
0	0	0	0	0	0	0	0	0	0	0	-1	33.3
0	0	0	0	0	0	1	0	0	0	0	0	10.3
0	0	0	0	0	0	0	0	0	1	0	1	0
0	0	0	0	0	0	0	0	0	0	1	-1	3.8
0	0	0	0	0	0	0	1	0	0	0	0	11.2
0	0	0	1	0	0	0	0	1	0	0	0	5.8
0	0	0	1	0	0	0	0	0	0	0	1	38.1
0	0	0	1	0	0	1	0	0	0	0	-1	9
1	0	0	0	0	0	1	0	0	0	0	1	2.8
1	0	0	0	0	0	0	0	0	1	0	0	0
0	1	0	0	0	0	0	0	0	0	1	1	0
0	1	0	0	0	0	0	1	0	0	0	-1	2.9
0	0	1	0	0	0	0	0	1	0	0	0	8.9
0	0	1	0	0	0	0	0	0	0	0	-1	35.4
0	0	0	0	0	1	0	0	1	0	0	-1	3.8
0	0	0	0	0	1	0	0	0	0	0	1	38.3
0	0	0	0	0	1	1	0	0	0	0	-1	17.1
0	0	0	0	0	1	0	0	0	1	0	0	0
0	0	0	0	0	1	0	0	0	0	1	0	2.9
0	0	0	0	0	1	0	1	0	0	0	1	18.9
0	0	0	1	0	0	0	0	0	1	0	-1	0
0	0	0	1	0	0	0	0	0	0	1	1	0
0	0	0	1	0	0	0	1	0	0	0	0	5.7

Experimental plan:

λ (nm)	***T (°C)***	***Solvent***	***Eq***	***Yield (%)***
365	-15	MeCN	1	2.6
365	-15	DCM	1.5	8.4
385	-15	Et_2O	2	3.9
385	-15	MeOH	1	2.1
405	-15	THF	1.5	3.9
405	-15	$HC(OMe)_3$	2	14.4
450	rt	MeCN	2	3.5
450	rt	DCM	1	33.3
450	rt	Et_2O	1.5	10.3
450	rt	MeOH	2	0
450	rt	THF	1	3.8
450	rt	$HC(OMe)_3$	1.5	11.2
470	rt	MeCN	1.5	5.8
470	rt	DCM	2	38.1
470	rt	Et_2O	1	9
365	rt	Et_2O	2	2.8
365	rt	MeOH	1.5	0
385	rt	THF	2	0

385	rt	$HC(OMe)_3$	1	2.9
405	rt	MeCN	1.5	8.9
405	rt	DCM	1	35.4
450	0	MeCN	1	3.8
450	0	DCM	2	38.3
450	0	Et_2O	1	17.1
450	0	MeOH	1.5	0
450	0	THF	1.5	2.9
450	0	$HC(OMe)_3$	2	18.9
470	rt	MeOH	1	0
470	rt	THF	2	0
470	rt	$HC(OMe)_3$	1.5	5.7

$$Y = 28.3 - 7.1\ X_{1,365} - 4.2\ X_{1,385} + 5.3\ X_{1,405} - 0.6\ X_{1,470} - 2.5\ X_{2,T\text{-}15} + 3.2\ X_{2,T0} - 20.2\ X_{3,Et2O}\ (***) - 20.1\ X_{3,HCOMe3}\ (***) - 25.0\ X_{3,MeCN}\ (***) - 27.7\ X_{3,MeOH}\ (***) - 28.6\ X_{3,THF}\ (***) + 0.3\ X_4 + 3.4\ X_4^2$$

Equation S1. Explained variance by the model: 80.1%; standard deviation of the residuals: 5.3 (16 degrees of freedom).

Step 2

Variables: wavelength, temperature, equivalents of 2a.

Experimental plan:

λ (nm)	***T (°C)***	***Eq***	***Yield (%)***
365	-15	1.5	8.4
450	rt	1	33.3
470	rt	2	38.1
405	rt	1	35.4
450	0	2	38.3
450	rt	1	32
450	rt	1.5	34.3
450	rt	2	32.9
450	rt	1	32.2
450	rt	1.5	35.6
450	rt	2	36.7
365	0	1	14.1
365	0	2	14.6
385	0	1	28.8
385	0	2	21.3
405	0	1.5	37.5
405	0	2	34.7
470	rt	1	38.6
470	rt	1.5	35.8
470	rt	2	39
450	-15	1	41.9
450	-15	1.5	43.4
450	-15	2	43.9
450	-15	1	41.4
450	-15	1.5	38.8
450	-15	2	43.4
365	rt	1	25.8

365	rt	2	21.3
385	rt	1	19
385	rt	1.5	33.7
405	rt	1.5	39.8
405	rt	2	40.7
470	rt	1	42.7
470	rt	1.5	42
470	rt	2	42.8

$Y = 35.6 - 19.5\ X_{1,365}$ (***) $- 9.4\ X_{1,385}$ (**) $+ 2.2\ X_{1,405} + 3.7\ X_{1,470} + 4.1\ X_{2,T\text{-}15} - 1.7\ X_{2,T0} + 0.6\ X_3 + 0.7\ X_3^2$

Equation S2. Explained variance by the model: 74.9%; standard deviation of the residuals: 4.6 (21 degrees of freedom).

Excluding all the experiments performed at 365 nm and 385 nm, another experimental matrix was realized:

λ (nm)	***T (°C)***	***Eq***	***Yield (%)***
450	rt	1	33.3
470	rt	2	38.1
405	rt	1	35.4
450	0	2	38.3
450	rt	1	32
450	rt	1.5	34.3
450	rt	2	32.9
450	rt	1	32.2
450	rt	1.5	35.6
450	rt	2	36.7
405	0	1.5	37.5
405	0	2	34.7
470	rt	1	38.6
470	rt	1.5	35.8
470	rt	2	39
450	-15	1	41.9
450	-15	1.5	43.4
450	-15	2	43.9
450	-15	1	41.4
450	-15	1.5	38.8
450	-15	2	43.4
405	rt	1.5	39.8
405	rt	2	40.7
470	rt	1	42.7
470	rt	1.5	42
470	rt	2	42.8

$Y = 34.4 + 3.1\ X_{1,405}$ (*) $+ 5.3\ X_{1,470}$ (**) $+ 7.7\ X_{2,T\text{-}15}$ (***) $- 0.3\ X_{2,T0} + 0.9\ X_3 + 0.0\ X_3^2$

Equation S3. Explained variance by the model: 58.6%; standard deviation of the residuals: 2.4 (23 degrees of freedom).

Step 3

Variables: wavelength, temperature, equivalents of 2a.

Experimental matrix:

λ (nm)	***T (°C)***	***Eq***	***Yield (%)***

-1	1	-1	33.3
1	1	1	38.1
-1	1	-1	32
-1	1	0	34.3
-1	1	1	32.9
-1	1	-1	32.2
-1	1	0	35.6
-1	1	1	36.7
1	1	-1	38.6
1	1	0	35.8
1	1	1	39
-1	-1	-1	41.9
-1	-1	0	43.4
-1	-1	1	43.9
-1	-1	-1	41.4
-1	-1	0	38.8
-1	-1	1	43.4
1	1	-1	42.7
1	1	0	42
1	1	1	42.8
1	-1	-1	44.9
1	-1	0	40.2
1	-1	1	41.8

Y = 39.0 + 1.5 lambda - 2.6 T + 0.1 Eq + 1.4 lambda*T – 1.0 lambda*Eq + 0.3 T*Eq + 0.9 Eq^2

Equation S4. Explained variance by the model: 71.8%; standard deviation of the residuals: 2.2 (15 degrees of freedom).

Central Composite Design

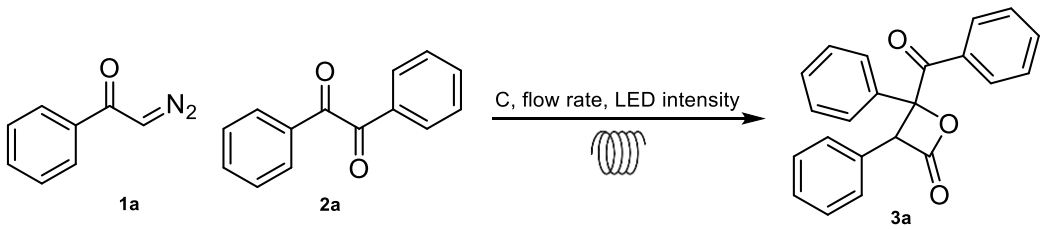


Table 3*. Variables of the system in Central Composite Design.*

		Levels		
Var. ID	Variable	-1	0	1
X_1	Concentration (M)	0.02	0.04	0.06
X_2	Flow rate (mL/h)	0.5	0.75	1
X_3	LED intensity (mA)	0.36	0.54	0.73

The postulated model consists of 10 terms, including 1 constant, 3 linear terms, 3 interactions and 3 quadratic terms. The model matrix was built using a Faced Central Composite Design. They were coded in the range of -1 to +1.
All elaborations of obtained data were performed using the chemometric software CAT (*R. Leardi. C. Melzi. G. Polotti. CAT (Chemometric Agile Tool),* freely downloadable from *http://gruppochemiometria.it/index.php/software*).

Variables: concentration, flow rate, LED intensity.

Experimental matrix:

C (M)	*Flow rate (mL/h)*	*Intensity (mA)*	*NMR Yield*
-1	-1	-1	57
1	-1	-1	60
-1	1	-1	56
1	1	-1	56
-1	-1	1	61
1	-1	1	65
-1	1	1	60
1	1	1	64
-1	0	0	66
1	0	0	65
0	-1	0	62
0	1	0	65
0	0	-1	57
0	0	1	63
0	0	0	63
0	0	0	65
0	0	0	60
0	0	0	60

Y = 64.6 + 1.0 Conc – 0.4 Flow + 2.7 Int – 0.4 Conc*Flow + 0.6 Conc*Int + 0.4 Flow*Int + 0.9 Conc^2 – 1.1 Flow^2 – 4.6 Int^2

Equation S5. Explained variance by the model: 69.5%; standard deviation of the residuals: 2 (4 degrees of freedom).

5. Single crystal studies of product 3f

A translucent light colourless, plate-like single crystal was selected from a freshly prepared powder sample with the aid of an optical microscope, then it was embedded in grease and glued to a loop pin. The sample turned out to be stable for the whole data collection time (overnight); after several days it was checked one more time and its deterioration was clear from the poor quality of diffraction.

The X-ray diffraction measurements were performed on a three-circle Bruker D8 QUEST diffractometer (using Mo Kα radiation) equipped by a PHOTON III 14 photon counting detector and by an Oxford Cryostream 1000. Temperature dependent screening measurements were obtained in a routine fashion; a complete dataset was finally collected at 100 K. The measurement strategy, consisting of five ω- and two φ-scans, was chosen using the APEX4 software[1] guaranteeing good data completeness, redundancy, and resolution limit. Data were collected over the reciprocal space up to ~ 31° in θ (achieving a resolution of ca. 0.7 Å) with exposures of 15 s per frame. The softwares SAINT[2] and XPREP[3] were used for data reduction. Lorentz, polarization, and absorption effects (Multi-Scan methods) were corrected by SADABS[4]; the crystal structure was solved and refined with the aid of SHELXTL[5].

The integration of the data using a monoclinic unit cell yielded a total of 90569 reflections, 5635 of which are independent (average redundancy 16.073, completeness = 99.6%, Rint = 5.49%, Rsig = 2.99%). The refined cell parameters are a = 6.6352(2) Å, b = 10.7113(3) Å, c = 25.8904(8) Å, β = 92.3460(10)°. The structure was solved by intrinsic phasing algorithm and refined in the space group $P2_1/n$ (N. 14) with Z=4 for the formula unit, $C_{22}H_{14}Br_2O_3$. All atoms were refined anisotropically, except hydrogen ones, added by geometrical constraints. The final anisotropic full-matrix least-squares refinement on F^2 with 247 variables converged at R1 = 4.79% and wR2 = 12.36%. The largest peak in the final difference electron density synthesis was 1.738 e-/Å^3 and the largest hole was -0.591 e-/Å^3. The corresponding CIF file, available as supplementary material, was deposited at the Cambridge Database.

Details of data collection and structure refinement are summarized in Table S1 together with selected crystal data; atomic coordinates and equivalent displacement parameters are listed in Table S2; bond lengths and angles are listed in Table S3 and S4, respectively. Reconstructed intensity profiles are shown in Figure S1. The structure is depicted in Figure S2.

1. Bruker. APEX4 v2022.10-0. (2022).
2. Bruker. SAINT v8.30A. (2012).
3. Bruker. XPREP v2014/2. (2014).
4. Bruker. SADABS v2016/2. (2016).
5. Sheldrick, G. M. SHELXL-2019/1. (2019).

Table S1. Selected crystallographic data and structure refinement parameters for $C_{22}H_{14}Br_2O_3$ single crystal.

CSD code	2250935
Chemical formula	$C_{22}H_{14}Br_2O_3$
Formula weight	486.15 g/mol
Crystal size	0.030 x 0.120 x 0.130 mm
Crystal system	monoclinic
Space group, Z	$P2_1/n$, 4
Unit cell dimensions	a = 6.6352(2) Å
	b = 10.7113(3) Å
	c = 25.8904(8) Å
	β = 92.3460(10)°
Volume	1838.53(9) $Å^3$
Density (calculated)	1.756 g/cm^3
Absorption coefficient	4.429 mm^{-1}
Theta range for data collection	2.47 to 30.61°
Index ranges	$-9 \le h \le 9$, $-15 \le k \le 15$, $-36 \le l \le 36$
Reflections collected	90569
Independent reflections	5635 [R(int) = 0.0549]
Coverage of independent reflections	99.6%
Data / restraints / parameters	5635 / 0 / 247
Goodness-of-fit on F^2	1.050
Final R indices	4372 data; $I>2\sigma(I)$ R1 = 0.0479, wR2 = 0.1143
	all data R1 = 0.0677, wR2 = 0.1236
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0630P)^2+3.2783P]$ where $P=(F_o^2+2F_c^2)/3$
Largest diff. peak and hole	1.738 and -0.591 $eÅ^{-3}$

Table S2. Atomic coordinates and equivalent displacement parameters (U_{eq}) for the $C_{22}H_{14}Br_2O_3$ single crystal.

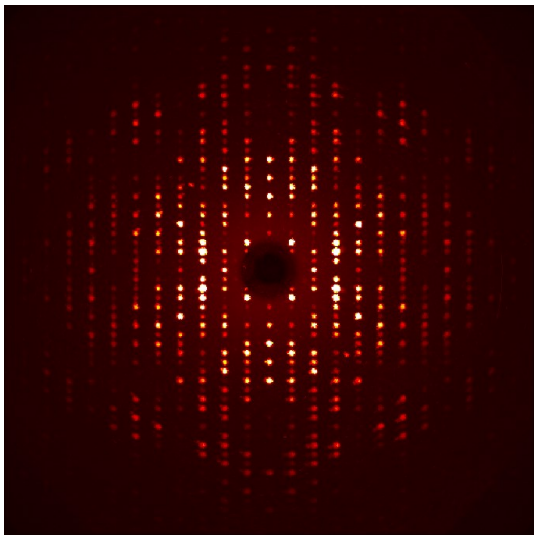
Atom	**Site**	**x/a**	**y/b**	**z/c**	**U(eq)**
Br1	4*e*	0.94008(6)	0.41948(3)	0.05849(2)	0.03630(12)
Br2	4*e*	0.02327(5)	0.16625(3)	0.46826(2)	0.03317(11)
O1	4*e*	0.6591(3)	0.4919(2)	0.25486(8)	0.0224(4)
O2	4*e*	0.7800(4)	0.6715(2)	0.29261(10)	0.0320(5)
O3	4*e*	0.2609(3)	0.2899(2)	0.29302(8)	0.0215(4)
C1	4*e*	0.3258(4)	0.4521(3)	0.21239(10)	0.0184(5)
C2	4*e*	0.1257(4)	0.4906(3)	0.20982(11)	0.0228(6)
C3	4*e*	0.0100(5)	0.4795(3)	0.16401(12)	0.0241(6)
C4	4*e*	0.0974(5)	0.4305(3)	0.12097(11)	0.0238(6)
C5	4*e*	0.2967(5)	0.3914(3)	0.12246(12)	0.0263(6)
C6	4*e*	0.4112(5)	0.4020(3)	0.16855(12)	0.0235(6)
C7	4*e*	0.4457(4)	0.4603(3)	0.26283(10)	0.0180(5)
C8	4*e*	0.6469(5)	0.5996(3)	0.28348(12)	0.0240(6)
C9	4*e*	0.4257(4)	0.5845(3)	0.29471(11)	0.0220(6)
C10	4*e*	0.4209(4)	0.3445(3)	0.29670(10)	0.0173(5)
C11	4*e*	0.5772(4)	0.3079(3)	0.33731(10)	0.0171(5)
C12	4*e*	0.5091(4)	0.2829(3)	0.38676(11)	0.0201(5)
C13	4*e*	0.6409(5)	0.2428(3)	0.42609(11)	0.0216(6)
C14	4*e*	0.8411(4)	0.2222(3)	0.41490(11)	0.0216(6)
C15	4*e*	0.9108(4)	0.2419(3)	0.36597(12)	0.0224(6)
C16	4*e*	0.7797(4)	0.2883(3)	0.32715(11)	0.0194(5)
C17	4*e*	0.3675(5)	0.5790(3)	0.35049(11)	0.0231(6)
C18	4*e*	0.5035(5)	0.6045(3)	0.39134(13)	0.0278(6)
C19	4*e*	0.4440(6)	0.5962(3)	0.44217(13)	0.0324(7)
C20	4*e*	0.2488(6)	0.5631(3)	0.45274(13)	0.0360(8)
C21	4*e*	0.1120(6)	0.5378(3)	0.41264(13)	0.0328(7)
C22	4*e*	0.1691(5)	0.5462(3)	0.36153(12)	0.0272(6)
Hydrogen atoms added by geometrical considerations					
H2		0.0674	0.5248	0.2396	0.027000
H3		-0.1271	0.5052	0.1624	0.029000
H5		0.3544	0.3579	0.0925	0.032000
H6		0.5477	0.3751	0.1702	0.028000
H9		0.3415	0.6471	0.2750	0.026000
H12		0.3704	0.2937	0.3934	0.024000
H13		0.5956	0.2296	0.4600	0.026000
H15		1.0471	0.2239	0.3589	0.027000
H16		0.8279	0.3064	0.2939	0.023000
H18		0.6380	0.6278	0.3845	0.033000
H19		0.5385	0.6135	0.4698	0.039000
H20		0.2091	0.5577	0.4875	0.043000
H21		-0.0221	0.5145	0.4199	0.039000
H22		0.0733	0.5297	0.3341	0.033000

Table S3. Bond lengths (Å) for $C_{22}H_{14}Br_2O_3$

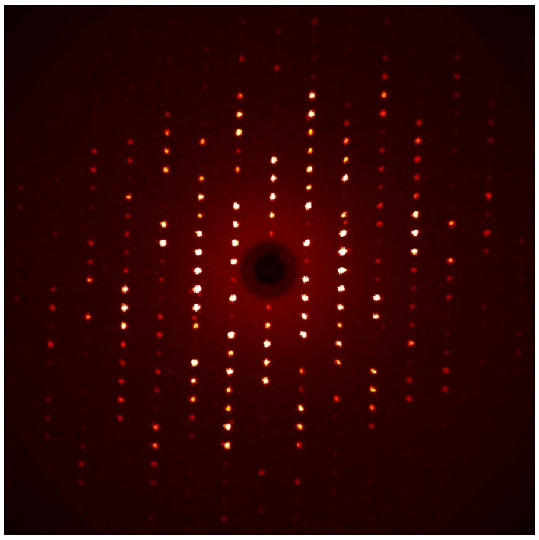
Atoms	Bond length	Atoms	Bond length
Br1-C4	1.892(3)	Br2-C14	1.896(3)
O1-C8	1.375(4)	O1-C7	1.479(3)
O2-C8	1.189(4)	O3-C10	1.212(3)
C1-C2	1.389(4)	C1-C6	1.396(4)
C1-C7	1.503(4)	C2-C3	1.391(4)
C3-C4	1.380(4)	C4-C5	1.386(5)
C5-C6	1.393(4)	C7-C10	1.532(4)
C7-C9	1.573(4)	C8-C9	1.516(4)
C9-C17	1.511(4)	C10-C11	1.498(4)
C11-C16	1.396(4)	C11-C12	1.401(4)
C12-C13	1.384(4)	C13-C14	1.388(4)
C14-C15	1.382(4)	C15-C16	1.393(4)
C17-C18	1.389(4)	C17-C22	1.404(5)
C18-C19	1.392(5)	C19-C20	1.381(6)
C20-C21	1.378(5)	C21-C22	1.394(5)

Table S4. Bond angles (°) for $C_{22}H_{14}Br_2O_3$

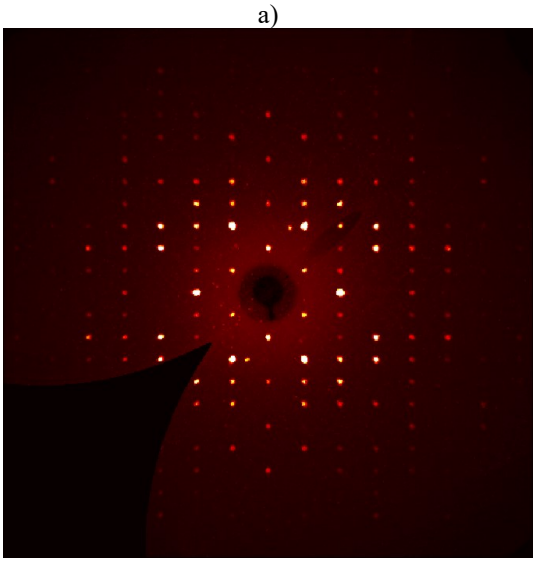
Atoms	Bond angle	Atoms	Bond angle
C8-O1-C7	92.2(2)	C2-C1-C6	119.6(3)
C2-C1-C7	119.7(2)	C6-C1-C7	120.7(3)
C1-C2-C3	120.6(3)	C4-C3-C2	119.0(3)
C3-C4-C5	121.6(3)	C3-C4-Br1	118.6(2)
C5-C4-Br1	119.8(2)	C4-C5-C6	119.0(3)
C5-C6-C1	120.2(3)	O1-C7-C1	111.6(2)
O1-C7-C10	113.0(2)	C1-C7-C10	112.6(2)
O1-C7-C9	89.0(2)	C1-C7-C9	116.9(2)
C10-C7-C9	111.8(2)	O2-C8-O1	126.2(3)
O2-C8-C9	138.4(3)	O1-C8-C9	95.3(2)
C17-C9-C8	118.3(2)	C17-C9-C7	119.9(2)
C8-C9-C7	83.5(2)	O3-C10-C11	120.5(2)
O3-C10-C7	117.4(2)	C11-C10-C7	121.8(2)
C16-C11-C12	119.5(2)	C16-C11-C10	123.5(2)
C12-C11-C10	116.8(2)	C13-C12-C11	120.9(3)
C12-C13-C14	118.5(3)	C15-C14-C13	121.7(3)
C15-C14-Br2	119.3(2)	C13-C14-Br2	119.0(2)
C14-C15-C16	119.5(3)	C15-C16-C11	119.7(3)
C18-C17-C22	118.7(3)	C18-C17-C9	122.5(3)
C22-C17-C9	118.9(3)	C17-C18-C19	120.5(3)
C20-C19-C18	120.5(3)	C21-C20-C19	119.7(3)
C20-C21-C22	120.5(3)	C21-C22-C17	120.2(3)



a)



b)



c)

Figure S1. Intensity profiles for 0*kl* (a), *h*0*l* (b) and *hk*0 (c) zones for $C_{22}H_{14}Br_2O_3$

6. Computational Details

All the calculations were carried out using the Gaussian16 program package, revision C.01 installed on the HPC infrastructure Galileo100 at CINECA facility (Italy).[*] In our investigation, the level of theory chosen for the optimization of the reported stationary points was DFT (Density Functional Theory) by using the B3LYP functional and the 6-311+G(d,p) basis set in the gas phase. When appropriate, an unrestricted formalism (U prefix) has been adopted via the UB3LYP/6-311+G(d,p) keyword. No symmetry constraint was applied to the structures investigated and a thorough conformers search has been performed to locate the absolute minimum for each species. The structures and data used for this work correspond to those of the absolute minima. Frequency calculations were performed in the gas phase to check that minima and transition states (TS) had 0 or 1 imaginary frequencies, respectively.

Solvent effect was included by single-point calculations at the same level of theory (B3LYP/6-311+G(d,p)) adopting the standard implicit solvent model implemented in Gaussian16 via the keyword SCRF=(SOLVENT=DICHLOROMETHANE) on the optimized geometries obtained in vacuo.

The DFT Gibbs free energies mentioned in the text (see also Tables S5-S8) have been calculated by means of Eq. S6 reported below:

$$G_{DFT} = E_{0(DFT,DCM)} + \Delta G_{CORR(vacuo)} \qquad (S6)$$

Where:

- $E_{0(DFT,DCM)}$ is the total electronic energy calculated at the SCRF-B3LYP/6-311+G(d,p) level (dichloromethane bulk);
- $\Delta G_{CORR(vacuo)}$ is the unscaled thermal correction to Gibbs Free Energy as from the output of the frequency calculation in vacuo, also including the zero-point vibrational energy (ZPVE).

Further notice that the two terms from Eq. S6 have been reported in blue color for all the stationary points reported below.

As for TSs, Intrinsic Reaction Coordinate (IRC) calculations were performed in both directions (40 steps each) at the same level of theory adopted for optimizations (B3LYP/6-311+G(d,p) in the gas phase) in order to investigate the process in detail and to confirm the nature of the TS itself. The "LQA" option for the IRC keyword has been specified, in order to adopt the local quadratic approximation for the predictor step.

When structures not corresponding to stationary points have been considered (e.g. along IRC profiles), energies have been expressed simply by considering the first term of Eq. S6, that is $E_{0(DFT,DCM)}$, since frequency calculations (needed for determining $\Delta G_{CORR(vacuo)}$) were carried out exclusively on stationary points. These data have been obtained through single-point calculations at the SCRF-B3LYP/6-311+G(d,p) level of theory in dichloromethane bulk performed on selected geometries resulting from IRC calculations in the gas phase. This solvation procedure has been performed every ten steps along the IRC and then further refined around the highest points along the reaction profiles (five steps in both directions). These data have been used for Figure 6 in the main text (see also Table S7, S8 for further details).

Optimized geometry listed in cartesian format (coordinates are given in Å), minimum energies and thermochemical data (in Hartree; the default options were adopted in the latter case, *viz.* temperature: 298.150 K and pressure: 1.00000 atm) are reported below.

The conversion factor between Hartree and kcal mol^{-1} has been: 1 Hartree = 627.509 kcal mol^{-1}.

[*] Gaussian 16, Revision C.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2016.

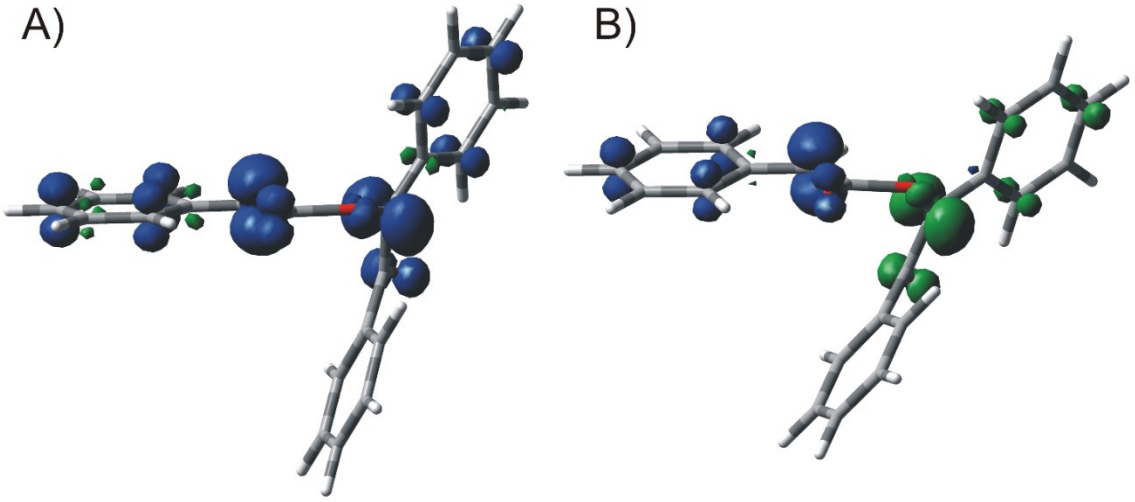


Figure S3. Spin density plots for 1,4-diradical species: **^{3}Int** (a) and **^{1}Int** (b).

Table S5. Computational data obtained for the modelling of the reaction between benzil **2a** and ketene **Ket**, as from calculations at the B3LYP/6-311+G(d,p) level of theory in dichloromethane (DCM) bulk.

Overall reaction profile		
Situation	**Gibbs free-energy, G** [kcal·mol^{-1}]	**Additional data** [kcal·mol^{-1}]
Benzil (**2a**) + ketene (**Ket**)	0.00[a]	
Benzil (^{3}**2a**) + ketene (**Ket**)	48.09	Triplet energy for **2a**: 48.09
TS-1	55.53	$\Delta G^{\ddagger}$(**TS-1** vs ^{3}**2a** + **Ket**) = 7.44
^{3}**Int**	33.70	ΔG(^{3}**Int** vs ^{3}**2a** + **Ket**) = -14.40
^{1}**Int**	32.22	DG(^{3}**Int** vs ^{1}**Int**) = 1.48
^{3}**TS-2**^{trans}	81.59	$\Delta G^{\ddagger}$(^{3}**TS-2**^{trans} vs ^{3}**Int**) = 47.89 $\Delta G^{\ddagger}$(^{3}**TS-2**^{cis} vs ^{3}**Int**) = 49.41
^{3}**TS-2**^{cis}	83.11	ΔG(^{3}**TS-2**^{trans} vs ^{3}**TS-2**^{cis}) = -1.52
Product **3a**^{trans}	7.93	ΔG(**3**^{trans} vs **2a** + **Ket**) = 7.93
Product **3a**^{cis}	6.11	ΔG(**3**^{cis} vs **2a** + **Ket**) = 6.11 ΔG(**3**^{trans} vs **3**^{cis}) = 1.82
IRC for TS-2		
Situation	**Electronic energy, E** [kcal·mol^{-1}]	**Additional data** [kcal·mol^{-1}]
^{3}**TS-2**^{trans}	48.55[b]	ΔE(^{3}**TS-2**^{trans} vs ^{3}**TS-2**^{cis}) = -0.97
^{3}**TS-2**^{cis}	49.52[b]	
^{1}**TS-2**^{trans}	13.44[c]	ΔE(^{1}**TS-2**^{trans} vs ^{1}**TS-2**^{cis}) = -0.89
^{1}**TS-2**^{cis}	14.33[c]	

[a] This situation has been taken as the reference and has been arbitrarily assigned with a value of 0; [b] the electronic energy of ^{3}**Int** has been taken as the reference; [c] the electronic energy of ^{1}**Int** has been taken as the reference.

Table S6. Gibbs *free energies (shown in Hartree) of the species optimized to study the profile of our model reaction between benzil 2a and ke*tene Ket, as determined from B3LYP/6-311+G(d,p) calculations in bulk dichloromethane.

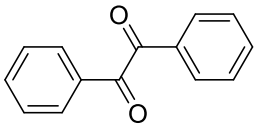
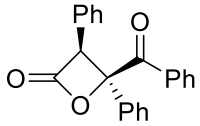
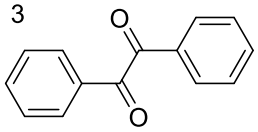
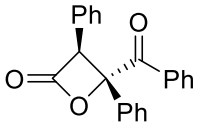
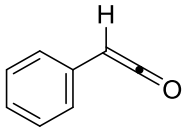
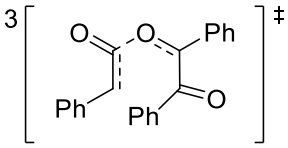
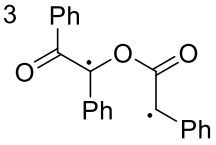
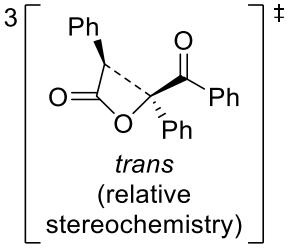
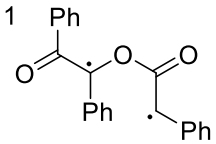
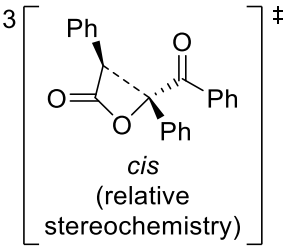
SPECIES	G_{DFT} [Hartree]	SPECIES	G_{DFT} [Hartree]
 **2a**	-689.985392	 *trans* (relative stereochemistry) **3a^{trans}**	-1073.658186
 (triplet excited state) **^{3}2a**	-689.908752	 *cis* (relative stereochemistry) **3a^{cis}**	-1073.661076
 **Ket**	-383.685426	 **TS-1**	-1073.582329
 (triplet diradical) **^{3}Int**	-1073.617118	 *trans* (relative stereochemistry) **TS-2^{trans}**	-1073.540801
 (singlet diradical) **^{1}Int**	-1073.619465	 *cis* (relative stereochemistry) **TS-2^{cis}**	-1073.538376

Table S7. IRC profile for the transition state describing the cyclization of **Int** to deliver the *trans*-cycloadduct product *trans*-**3a**, as determined from B3LYP/6-311+G(d,p) calculations in bulk dichloromethane. The point characterized by the highest energy value for both spin manifold has been been highlighted with a **bold** character.

IRC step[a]	**IRC value**	**$E_{0(DFT,DCM)}$ for TRIPLET manifold**	**$E_{0(DFT,DCM)}$ for SINGLET manifold**
Optimized structure of **Int**		-1073.878636	-1073.883102
-40	-12.99319	-1073.867329	-1073.869986
-30	-12.67089	-1073.865057	-1073.866958
-20	-12.35062	-1073.862559	-1073.864291
-16	-5.28431		-1073.863349
-15	-4.95553		-1073.863000
-14	-4.62622		-1073.862530
-13	-4.29642		-1073.862163
-12	-3.96629		-1073.861850
-11	-3.63620		**-1073.861691**
-10	-3.30781	-1073.855163	-1073.861862
-9	-2.97801		-1073.862406
-8	-2.64784		-1073.863675
-7	-2.31721		-1073.865702
-6	-1.98623		-1073.868794
-5	-1.65525	-1073.838296	
-4	-1.32417	-1073.832151	
-3	-0.99319	-1073.825078	
-2	-0.66227	-1073.817254	
-1	-0.33122	-1073.809149	
0	0.00000	**-1073.801268**	-1073.895913
1	0.33122	-1073.801673	
2	0.66053	-1073.80444	
3	0.99077	-1073.807097	
4	1.32126	-1073.808822	
5	1.64896	-1073.809686	
10	3.24216	-1073.811136	-1073.907192
20	6.44576	-1073.812458	-1073.909371
30	9.67460	-1073.813544	-1073.910471
40	12.85634	-1073.814591	-1073.910812

[a] The steps count along the IRC has been arbitrarily assigned so as to set the TS as the point "zero"; the forward and reverse directions assume therefore positive and negative values, respectively.

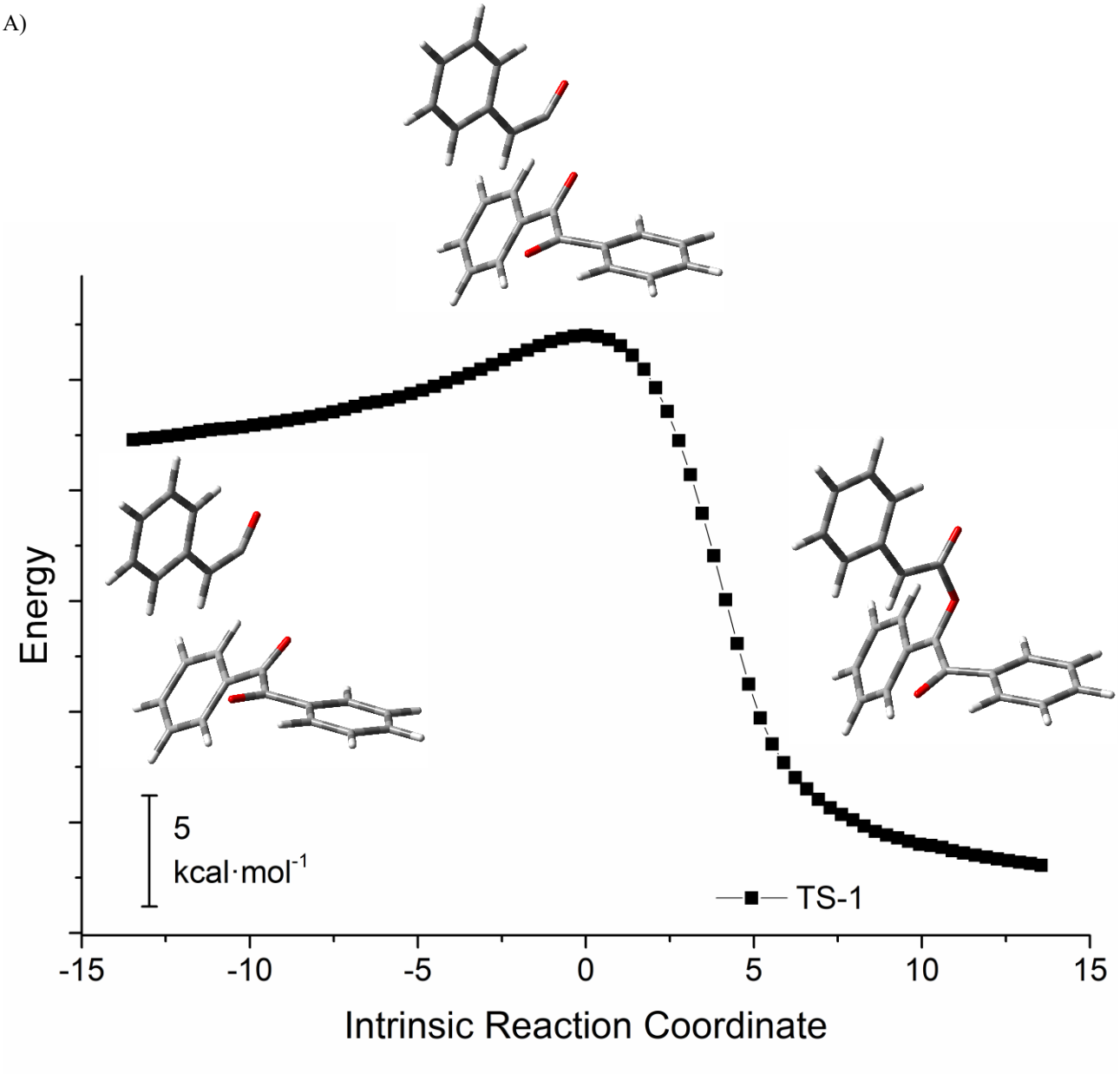
Table S8. IRC profile for the transition state describing the cyclization of **Int** to deliver the *cis*-cycloadduct product *cis*-**3a**, as determined from B3LYP/6-311+G(d,p) calculations in bulk dichloromethane. The point characterized by the highest energy value for both spin manifold has been been highlighted with a **bold** character.

IRC step[a]	**IRC value**	**$E_{0(DFT,DCM)}$ for TRIPLET manifold**	**$E_{0(DFT,DCM)}$ for SINGLET manifold**
Optimized structure of **Int**		-1073.878636	-1073.883102
-40	-11.88091	-1073.866982	-1073.869149
-30	-11.58872	-1073.864286	-1073.866722
-20	-11.29508	-1073.860219	-1073.863735
-16	-4.79255		-1073.862190
-15	-4.49402		-1073.861699
-14	-4.19491		-1073.861289
-13	-3.89520		-1073.860826
-12	-3.59559		-1073.860488
-11	-3.29579		**-1073.860260**
-10	-2.99613	-1073.850930	-1073.860337
-9	-2.69636		-1073.860735
-8	-2.39706		-1073.861672
-7	-2.09816		-1073.863213
-6	-1.79990		-1073.865809
-5	-1.50046	-1073.835584	
-4	-1.20039	-1073.830039	
-3	-0.90053	-1073.823422	
-2	-0.60040	-1073.815370	
-1	-0.30037	-1073.805819	
0	0.00000	**-1073.799719**	-1073.879816
1	0.30037	-1073.800577	
2	0.59959	-1073.802499	
3	0.89954	-1073.804627	
4	1.19972	-1073.806613	
5	1.49967	-1073.808164	
10	2.98098	-1073.811634	-1073.901813
20	5.85850	-1073.813074	-1073.903640
30	8.74305	-1073.814028	-1073.902909
40	11.57199	-1073.814818	-1073.902909

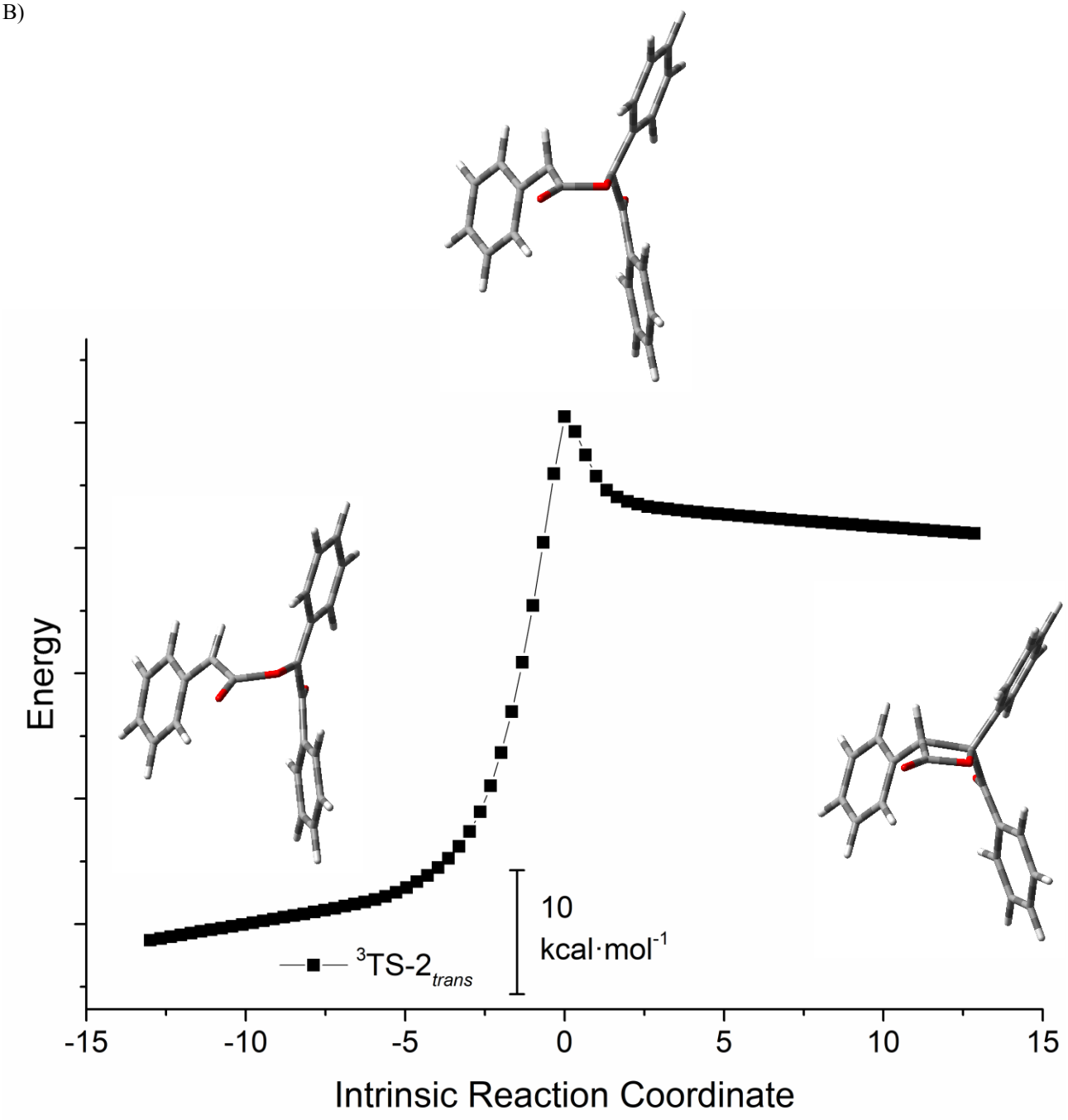
[a] The steps count along the IRC has been arbitrarily assigned so as to set the TS as the point "zero"; the forward and reverse directions assume therefore positive and negative values, respectively.

IRC Plots.

A)


Energy
5
kcal·mol-1
TS-1
-15
-10
-5
0
5
10
15
Intrinsic Reaction Coordinate

B)


Energy
-15
-10
-5
0
5
10
15
Intrinsic Reaction Coordinate
10
kcal·mol-1
3TS-2trans

C)

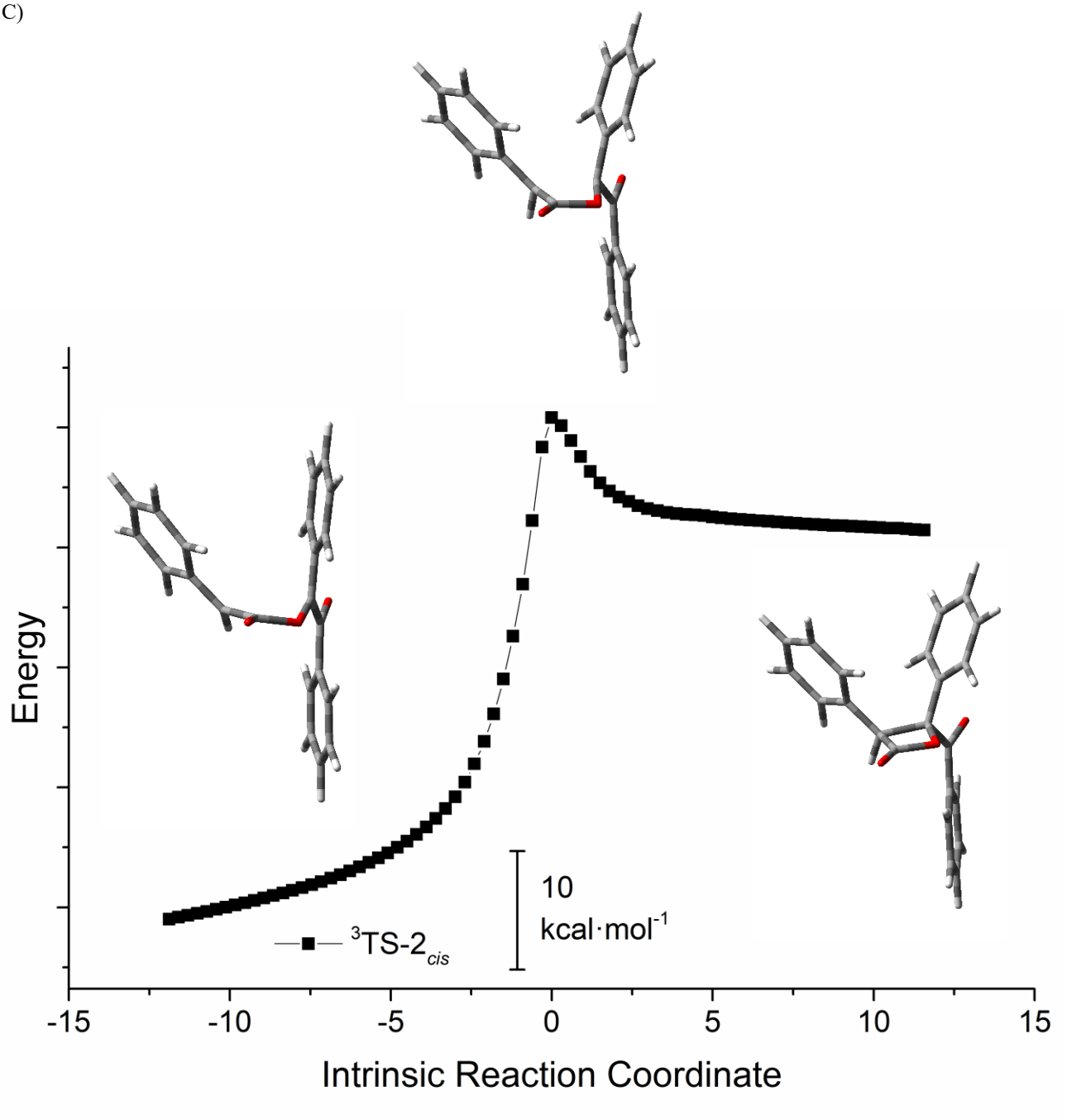
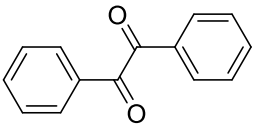


Figure S4. IRC plots of the transition states (top to bottom): **TS1** (A), **^{3}TS-2**$_{trans}$ (B) and **^{3}TS-2**$_{cis}$ (C), as from calculations at the wB97xD/def2TZVP level of theory in the gas phase (total electronic energy values have been reported). The three structures reported in the graph refer, respectively, to those of the first point (left), the transition state (center) and the last point (right) along the reaction coordinate. The LQA option has been adopted for all the reported IRC traces.

Optimized Structures



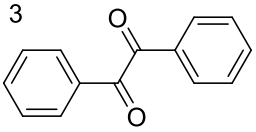
2a

C	0.23045400	4.35775200	-0.96302800
C	1.19749100	3.35768600	-1.04805400
C	0.97271700	2.11726600	-0.45720800
C	-0.22804400	1.87086300	0.22318800
C	-1.19749100	2.88241300	0.30187500
C	-0.96803000	4.11887900	-0.28604000
H	0.40928500	5.32370600	-1.42212400
H	2.12873000	3.54500600	-1.56990700
H	1.73572400	1.35178700	-0.51138900
H	-2.12077600	2.67592400	0.82946000
H	-1.71871500	4.89808700	-0.22013900
C	-0.53815400	0.55331000	0.83868600
O	-1.58877600	0.31377100	1.40470000
C	0.53815400	-0.55331000	0.83868600
O	1.58877600	-0.31377100	1.40470000
C	0.22804400	-1.87086300	0.22318800
C	1.19749100	-2.88241300	0.30187500
C	-0.97271700	-2.11726600	-0.45720800
C	0.96803000	-4.11887900	-0.28604000
H	2.12077600	-2.67592400	0.82946000
C	-1.19749100	-3.35768600	-1.04805400
H	-1.73572400	-1.35178700	-0.51138900
C	-0.23045400	-4.35775200	-0.96302800
H	1.71871500	-4.89808700	-0.22013900
H	-2.12873000	-3.54500600	-1.56990700
H	-0.40928500	-5.32370600	-1.42212400

E(B3LYP, vacuo) -690.135846
Zero-point correction= 0.199925
Thermal correction to Energy= 0.212819
Thermal correction to Enthalpy= 0.213763
Thermal correction to Gibbs Free Energy= **0.158855**

E(B3LYP, DCM) **-690.144247**

3



(triplet excited state)

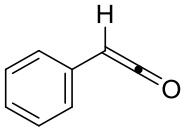
^{3}2a

C	0.00000000	0.00000000	0.00000000
C	0.00000000	0.00000000	1.39354610
C	1.19922345	0.00000000	2.10159115
C	2.41954767	-0.01050297	1.41186584
C	2.41381444	0.01406127	0.00433307
C	1.21285031	0.00774211	-0.69133589
H	-0.93759076	-0.00058853	-0.54427578
H	-0.93740684	0.01061501	1.93765141
H	1.18148057	0.01347673	3.18194932
H	3.35781976	0.01954798	-0.52544911
H	1.22163748	0.00500098	-1.77546060
C	3.74407440	-0.00210419	2.08645758

O	4.75717289	0.34907223	1.45423424
C	3.87895508	-0.45931829	3.50982500
O	2.88795366	-0.92206485	4.10411583
C	5.19505147	-0.40835395	4.19888854
C	5.35611365	-1.21718841	5.33977878
C	6.24843645	0.42403471	3.79573632
C	6.55878625	-1.21949552	6.03251492
H	4.53613912	-1.84891806	5.65664584
C	7.44876240	0.41846811	4.50188880
H	6.13436179	1.07611697	2.94166026
C	7.61127544	-0.40207525	5.61645994
H	6.67796509	-1.86286659	6.89696918
H	8.25539337	1.06815258	4.18227743
H	8.54884592	-0.40138436	6.16077052

E(B3LYP, vacuo) -690.058572
Zero-point correction= 0.197219
Thermal correction to Energy= 0.210097
Thermal correction to Enthalpy= 0.211042
Thermal correction to Gibbs Free Energy= **0.155167**

E(B3LYP, DCM) **-690.0639193**

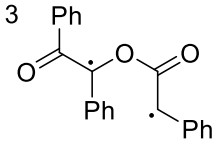


Ket

C	-1.47111100	0.86764900	0.00014500
H	-1.66042800	1.93554400	-0.00001400
C	-2.55040200	0.11160000	0.00006300
O	-3.50672300	-0.54794300	-0.00017200
C	-0.08876500	0.37165900	0.00007600
C	0.22390700	-0.99800300	0.00009000
C	0.96770400	1.29524800	-0.00001600
C	1.54721900	-1.42366200	0.00002500
H	-0.57142700	-1.73674100	0.00015300
C	2.29121200	0.86390200	-0.00007700
H	0.74815000	2.35755700	-0.00003600
C	2.59037700	-0.49691100	-0.00005800
H	1.76500000	-2.48593200	0.00004000
H	3.09079300	1.59642300	-0.00014400
H	3.62084600	-0.83220000	-0.00010900

E(B3LYP, vacuo) -383.762604
Zero-point correction= 0.113962
Thermal correction to Energy= 0.121337
Thermal correction to Enthalpy= 0.122281
Thermal correction to Gibbs Free Energy= **0.081357**

E(B3LYP, DCM) **-383.766783**



(triplet diradical)

^{3}Int

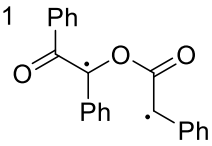
C	-0.99921900	1.05244800	0.11087300
C	1.53978700	-0.20827500	0.14675600
C	-0.50707100	0.45157800	1.33541000

O	0.81253500	-0.03618500	1.30026000
C	1.10092200	-1.24258600	-0.80124500
O	1.48700500	-1.21539200	-1.97285100
C	0.16168400	-2.32734400	-0.35665800
C	-0.64745900	-2.91790100	-1.33873300
C	0.12834600	-2.83567100	0.94959900
C	-1.48992100	-3.97515700	-1.01791500
H	-0.59550100	-2.53723000	-2.35137100
C	-0.70217000	-3.90874100	1.26295400
H	0.75095300	-2.40221000	1.72069800
C	-1.51782500	-4.47469000	0.28515400
H	-2.12065600	-4.41475800	-1.78237000
H	-0.71370400	-4.29928900	2.27404200
H	-2.17098500	-5.30319000	0.53576000
C	2.72725000	0.59647900	0.03617700
C	3.00364700	1.56544100	1.03575500
C	3.66191200	0.44706600	-1.02143700
C	4.14614000	2.34688600	0.97247200
H	2.31577700	1.68228600	1.86207500
C	4.80062800	1.23658900	-1.06872900
H	3.47084000	-0.28004500	-1.79579400
C	5.05186800	2.19104600	-0.07985100
H	4.33606000	3.08016600	1.74810600
H	5.50147000	1.10759000	-1.88580900
H	5.94493900	2.80375700	-0.12641700
H	-0.30932000	1.10899200	-0.72215200
C	-2.29862800	1.58487200	-0.09218600
C	-3.32829500	1.58573000	0.89012100
C	-2.59277600	2.15372100	-1.36423900
C	-4.56964400	2.12646700	0.60088900
H	-3.12414800	1.15933400	1.86153200
C	-3.83706700	2.69140600	-1.63743400
H	-1.82039900	2.15960500	-2.12570400
C	-4.83480100	2.68142900	-0.65608900
H	-5.34406900	2.11886700	1.35951700
H	-4.03870000	3.11956000	-2.61257600
H	-5.81080100	3.10187700	-0.86982800
O	-1.08149100	0.36032000	2.39264400

E(B3LYP, vacuo) -1073.867670
Zero-point correction= 0.315949
Thermal correction to Energy= 0.336702
Thermal correction to Enthalpy= 0.337646
Thermal correction to Gibbs Free Energy= **0.261518**

E(B3LYP, DCM) **-1073.878636**

1



(singlet diradical)

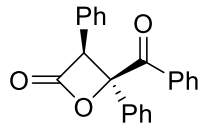
^{1}Int

C	-0.77282900	1.30016100	0.43819000
C	1.48981000	-0.16525700	0.17948800
C	-0.42440600	0.36788200	1.47985600
O	0.94465100	-0.02498600	1.41306500
C	0.77364900	-0.94249600	-0.85973800
O	1.00046000	-0.72660100	-2.04973400
C	-0.17591400	-2.03556700	-0.46307200
C	-1.14105600	-2.42100800	-1.40520100

C	-0.07246700	-2.74790700	0.73908600
C	-1.99761000	-3.48234500	-1.14222200
H	-1.19799500	-1.87882900	-2.34091600
C	-0.92139900	-3.82275000	0.99179300
H	0.66767900	-2.47169400	1.47852600
C	-1.88769700	-4.18815800	0.05751900
H	-2.74841700	-3.76412600	-1.87187100
H	-0.82910700	-4.37041700	1.92254100
H	-2.55268600	-5.02007200	0.26136900
C	2.81128200	0.38725800	0.02427800
C	3.35528100	1.17501900	1.06981600
C	3.60993900	0.15147900	-1.12262500
C	4.63434900	1.69998500	0.96976400
H	2.76078000	1.35906900	1.95442200
C	4.88716400	0.68380100	-1.20743900
H	3.21127100	-0.43663700	-1.93549300
C	5.40729200	1.45964100	-0.16830000
H	5.03243100	2.30024500	1.77990100
H	5.48474600	0.49367800	-2.09163200
H	6.40655500	1.87299500	-0.24493400
H	0.04866800	1.76823000	-0.08960500
C	-2.08903400	1.75099400	0.13358800
C	-3.25955200	1.23895300	0.75345700
C	-2.24549100	2.74913700	-0.86478400
C	-4.50944500	1.70951500	0.38437500
H	-3.15938300	0.48793400	1.52433100
C	-3.50037600	3.20743600	-1.22686800
H	-1.36150700	3.14805500	-1.35057700
C	-4.64076400	2.69073500	-0.60347500
H	-5.39389200	1.31143900	0.86881300
H	-3.59771800	3.96781100	-1.99327500
H	-5.62369400	3.05141500	-0.88438100
O	-1.08662300	-0.05068300	2.39515300

E(B3LYP, vacuo)	-1073.871689
Zero-point correction=	0.316203
Thermal correction to Energy=	0.336841
Thermal correction to Enthalpy=	0.337785
Thermal correction to Gibbs Free Energy=	**0.263637**

E(B3LYP, DCM) **-1073.883102**



trans
(relative
stereochemistry)

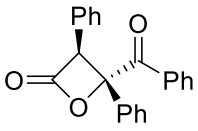
3a^{trans}

C	-1.01260200	1.16484200	0.82978900
C	0.36844500	0.54178400	0.35698800
C	-0.58490100	0.62177700	2.19147100
O	0.60852900	0.10528500	1.74770500
C	0.26304600	-0.62153600	-0.64813900
O	-0.36445800	-0.40525100	-1.66685600
C	0.92676300	-1.93683100	-0.40999900
C	0.50122500	-3.01450000	-1.20376900
C	1.97125400	-2.13120400	0.50504400
C	1.09669500	-4.26200500	-1.07562000
H	-0.29789900	-2.84954300	-1.91576300
C	2.57843300	-3.37941500	0.61587400

H	2.31522500	-1.31785200	1.12692600
C	2.13991800	-4.44603600	-0.16604600
H	0.75383000	-5.09038000	-1.68495200
H	3.39167900	-3.51917300	1.31862300
H	2.60914600	-5.41869300	-0.06822200
C	1.41233200	1.55166000	-0.09182700
C	2.44585200	1.93619000	0.76734200
C	1.32889900	2.13135900	-1.36481900
C	3.38107500	2.88757700	0.35997900
H	2.51703800	1.49564600	1.75321400
C	2.26343800	3.08232700	-1.76375500
H	0.53855200	1.83040400	-2.04137400
C	3.29343800	3.46372800	-0.90398700
H	4.17807000	3.17581100	1.03614300
H	2.18768900	3.52403200	-2.75097500
H	4.02091900	4.20323600	-1.21868300
H	-0.93878200	2.25420300	0.82221100
C	-2.34346900	0.73441600	0.27493700
C	-2.92168700	-0.49086600	0.62340700
C	-3.03059900	1.57837800	-0.60303800
C	-4.15277700	-0.86832100	0.09380400
H	-2.41997500	-1.15151100	1.32249200
C	-4.26032000	1.20141700	-1.13572700
H	-2.59757300	2.53543200	-0.87438700
C	-4.82423600	-0.02499300	-0.78961300
H	-4.59029800	-1.81882900	0.37733300
H	-4.77892100	1.86638600	-1.81706100
H	-5.78380000	-0.31869900	-1.19978000
O	-1.01234800	0.58509500	3.29921100

E(B3LYP, vacuo) -1073.914228
Zero-point correction= 0.319230
Thermal correction to Energy= 0.339243
Thermal correction to Enthalpy= 0.340187
Thermal correction to Gibbs Free Energy= **0.267362**

E(B3LYP, DCM) **-1073.925548**



cis
(relative stereochemistry)

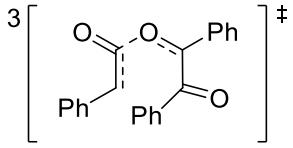
3a^{cis}

C	-0.99195300	-1.45822400	0.22410800
C	0.19876900	-0.42531600	0.23025500
C	-0.57535100	-1.68162300	1.67409200
H	-0.70727000	-2.32453400	-0.37631600
O	0.51595200	-0.84100100	1.61375600
C	1.32432000	-0.79916000	-0.76127000
O	0.99290600	-1.30398500	-1.81882300
C	2.75260400	-0.50733900	-0.44891100
C	3.71342100	-0.92222800	-1.38559800
C	3.17136500	0.16315000	0.70915300
C	5.06169200	-0.67367800	-1.16881800
H	3.37839000	-1.43765600	-2.27701200
C	4.52404400	0.41551800	0.91982000
H	2.45221600	0.48263400	1.44899300
C	5.46968900	-0.00215500	-0.01450900
H	5.79603100	-1.00029100	-1.89615900

H	4.83932200	0.93554000	1.81692800
H	6.52261700	0.19329600	0.15563000
C	-0.14504600	1.04645800	0.13882300
C	-0.20156600	1.84806900	1.28208000
C	-0.42737100	1.61384100	-1.10983700
C	-0.53552800	3.19758700	1.17735500
H	0.01601000	1.41766500	2.25124700
C	-0.76204200	2.96106500	-1.20884000
H	-0.38902900	1.00245000	-2.00367600
C	-0.81610300	3.75799000	-0.06611600
H	-0.57554400	3.80924100	2.07168200
H	-0.98112500	3.38797700	-2.18089000
H	-1.07515200	4.80762400	-0.14554700
C	-2.40128400	-1.05216300	-0.10712900
C	-2.88169300	-1.25956500	-1.40542500
C	-3.24547200	-0.46403800	0.83991500
C	-4.17465300	-0.87742100	-1.75327800
H	-2.23548300	-1.72037000	-2.14508600
C	-4.54064700	-0.08514100	0.49318800
H	-2.90109800	-0.31490600	1.85674400
C	-5.00781000	-0.28777900	-0.80377000
H	-4.53281000	-1.04572500	-2.76273200
H	-5.18593600	0.36406100	1.23962400
H	-6.01681000	0.00526800	-1.07111500
O	-0.94143700	-2.30618300	2.61581300

E(B3LYP, vacuo) -1073.918047
Zero-point correction= 0.319312
Thermal correction to Energy= 0.339361
Thermal correction to Enthalpy= 0.340305
Thermal correction to Gibbs Free Energy= **0.267562**

E(B3LYP, DCM) **-1073.928638**



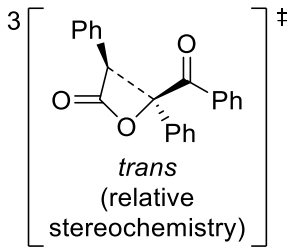
^{3}TS-1

C	-1.89779400	0.03804900	0.34900500
C	1.30803800	0.64138600	0.34530100
C	-1.37247600	-0.00568800	1.67099600
O	0.85958800	0.25521600	1.44484300
C	1.56753700	-0.41310200	-0.72382500
O	1.16349400	-0.22433100	-1.86466200
C	2.25945200	-1.68024600	-0.34354600
C	2.32407700	-2.70477300	-1.30087600
C	2.88404200	-1.86428200	0.89877900
C	2.99098800	-3.89019600	-1.02076400
H	1.84523900	-2.54697100	-2.25953300
C	3.55689400	-3.05186700	1.17375100
H	2.83479100	-1.08802100	1.64975200
C	3.60988300	-4.06575400	0.21883000
H	3.03258000	-4.67755900	-1.76495700
H	4.03719300	-3.18654100	2.13616500
H	4.13232700	-4.99046100	0.43805000
C	1.48758200	2.07635300	0.04766600
C	1.10257200	3.00602700	1.03255800
C	2.05925400	2.55444900	-1.14628100
C	1.27400400	4.36862700	0.82586100
H	0.67873800	2.63400500	1.95706900
C	2.23438300	3.91989500	-1.34319500

H	2.35272700	1.86004500	-1.92139100
C	1.84111600	4.83178700	-0.36294100
H	0.97113600	5.07262900	1.59305000
H	2.67645100	4.27492200	-2.26742600
H	1.97817700	5.89544700	-0.52288300
H	-1.20568900	0.34061400	-0.42909400
C	-3.23444400	-0.27866800	-0.02526000
C	-4.22398300	-0.68823300	0.90837300
C	-3.59976100	-0.18012000	-1.39587200
C	-5.50831200	-0.97854100	0.48211400
H	-3.96311000	-0.77057900	1.95549300
C	-4.88742200	-0.47339400	-1.80763600
H	-2.85013000	0.12738300	-2.11645800
C	-5.84823900	-0.87344400	-0.87190000
H	-6.25555600	-1.28985100	1.20283700
H	-5.15149100	-0.39420300	-2.85582300
H	-6.85672600	-1.10328000	-1.19605000
O	-1.75070700	-0.26678100	2.76161500

E(B3LYP, vacuo)	-1073.826772
Zero-point correction=	0.313091
Thermal correction to Energy=	0.334549
Thermal correction to Enthalpy=	0.335493
Thermal correction to Gibbs Free Energy=	**0.255553**

E(B3LYP, DCM)	**-1073.837882**



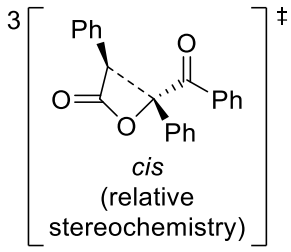
^{3}TS-2^{trans}

C	-0.53376900	-1.24962400	1.05701800
C	-0.87596300	0.45478100	0.23923900
C	-0.22854000	-0.26276100	2.15108500
O	-0.62550200	0.92233900	1.56842300
C	0.17639400	0.77248900	-0.75616900
O	0.02108200	0.29006900	-1.93467700
C	1.38672900	1.56388700	-0.49595000
C	2.44204500	1.44660100	-1.43513800
C	1.54005300	2.48745200	0.56193500
C	3.60240100	2.19294200	-1.29970400
H	2.33433300	0.74772500	-2.25489600
C	2.71260500	3.22247900	0.68711500
H	0.74740000	2.63678700	1.27850900
C	3.75215700	3.08407300	-0.23486700
H	4.39841700	2.07665200	-2.02728400
H	2.80911600	3.92075700	1.51123400
H	4.66019000	3.66618900	-0.12869000
C	-2.29670500	0.56118800	-0.14886000
C	-3.27755900	0.68651000	0.86061400
C	-2.72729300	0.49486200	-1.49106500
C	-4.62609100	0.70205200	0.54060800
H	-2.97178700	0.77171400	1.89498100
C	-4.08260200	0.48799100	-1.80028900
H	-1.99169700	0.47633100	-2.28420500
C	-5.03823900	0.59260500	-0.79128100
H	-5.36261100	0.79759400	1.33023900

H	-4.39132600	0.43238000	-2.83774500
H	-6.09363800	0.61047500	-1.03801600
H	-1.52941300	-1.67515400	1.16367100
C	0.45634500	-2.14787800	0.49893000
C	1.83928100	-1.88400000	0.59873300
C	0.04059200	-3.28840700	-0.22413600
C	2.76270500	-2.72881700	-0.00169600
H	2.18512400	-1.02367800	1.15890100
C	0.96736100	-4.12747700	-0.82123700
H	-1.01939800	-3.50272000	-0.30982000
C	2.33440700	-3.84991900	-0.71580200
H	3.82172900	-2.51533100	0.08716700
H	0.63158000	-4.99950100	-1.37068300
H	3.05946000	-4.50607200	-1.18346600
O	0.19875000	-0.35994900	3.25820500

E(B3LYP, vacuo) -1073.789831
Zero-point correction= 0.313130
Thermal correction to Energy= 0.333398
Thermal correction to Enthalpy= 0.334342
Thermal correction to Gibbs Free Energy= **0.260467**

E(B3LYP, DCM) **-1073.801268**



^{3}TS-2^{cis}

C	-0.31645000	-1.20869900	0.49734200
C	0.38356300	0.63147600	0.34588000
C	-0.00043400	-0.81234900	1.90322600
H	0.52209700	-1.72153000	0.02943300
O	0.68591800	0.37248800	1.71778700
C	1.50047100	0.77848900	-0.53398600
O	1.28348100	1.33642200	-1.71001400
C	2.84498700	0.20619900	-0.38552500
C	3.54075500	-0.20307900	-1.54662300
C	3.49668900	0.10813000	0.86244900
C	4.82497900	-0.72417600	-1.45390500
H	3.05430400	-0.11925400	-2.50977900
C	4.77552700	-0.42722600	0.94007700
H	2.99921800	0.45054300	1.75796600
C	5.44835200	-0.84440100	-0.21215800
H	5.33951100	-1.04218900	-2.35375000
H	5.25694700	-0.51098500	1.90797200
H	6.44985200	-1.25257900	-0.14035500
C	-0.76437600	1.53712700	0.10116100
C	-1.30004200	2.32532000	1.12662500
C	-1.29802400	1.63985700	-1.19527400
C	-2.31045000	3.23895400	0.84394700
H	-0.89814000	2.24485900	2.12867700
C	-2.29542500	2.57479500	-1.47545600
H	-0.97396200	0.95363800	-1.96841700
C	-2.80533000	3.37305000	-0.45791100
H	-2.70339300	3.86380700	1.63814300
H	-2.69185800	2.65073200	-2.48116900
H	-3.59263400	4.08784000	-0.66805700

C	-1.62805100	-1.66698700	0.06858700
C	-1.75465800	-2.38928300	-1.13610100
C	-2.80083500	-1.36920900	0.79150800
C	-2.99963800	-2.79528500	-1.59900500
H	-0.86216800	-2.63358800	-1.70323300
C	-4.04304200	-1.78115800	0.32662600
H	-2.73123100	-0.82892200	1.72798600
C	-4.15129900	-2.49243700	-0.87036400
H	-3.07409500	-3.35392400	-2.52535100
H	-4.93317800	-1.55016500	0.90100100
H	-5.12307600	-2.81244000	-1.22840500
O	-0.23462500	-1.28647300	2.97230400

E(B3LYP, vacuo)	-1073.789275
Zero-point correction=	0.313835
Thermal correction to Energy=	0.334099
Thermal correction to Enthalpy=	0.335043
Thermal correction to Gibbs Free Energy=	**0.261343**

E(B3LYP, DCM)	**-1073.799719**

7. Characterization of compounds

Analytical data for *diazoketones* are in accordance with the literature.

1a, 1d Capurro P., Lambruschini C., Lova P., Moni L., Basso A. (2021). Into the blue: ketene multicomponent reactions under visible light. J. Org. Chem., 86(8), 5845-5851. https://doi.org/10.1021/acs.joc.1c00278.

1b, 1c Minuto F., Lambruschini C., Basso A. (2021). Ketene 3-Component Staudinger Reaction (K-3CSR) to β-Lactams: A New Entry in the Class of Photoinduced Multicomponent Reactions. Eur. J. Org. Chem., 2021(22), 3270-3273. https://doi.org/10.1002/ejoc.202100577.

Analytical data for *1-(4-Methoxyphenyl)-2-phenylethane-1,2-dione* ***2c*** are in accordance with the literature.
Rao G.N., Sekar G. (2023). Stable and reusable Pd-nanoparticle catalyzed synthesis of symmetrical and unsymmetrical 1, 2-dicarbonyl compounds. NJC, 47(6), 3167-3177.

4-benzoyl-3,4-diphenyloxetan-2-one ***3a***

[major diasteroisomer] R_f = 0.27 (PE/EA 8:1); colorless oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.81 – 7.65 (m, 4H, Ar), 7.56 – 7.45 (m, 3H, Ar), 7.45 – 7.38 (m, 1H, Ar), 7.38 – 7.29 (m, 5H, Ar), 7.17 (dd, J = 6.6, 2.9 Hz, 2H, Ar), 5.17 (s, 1H, CH lactone).

^{13}C NMR (101 MHz, Chloroform-d) δ 194.73 (CO-Ph), 168.15 (CO lactone), 137.30 (Cq Ar), 135.21 (Cq Ar), 133.61 (Ar), 130.69 (Cq Ar), 129.71 (Ar x2), 129.32 (Ar x3), 129.13 (Ar x4), 128.98 (Ar), 128.45 (Ar x2), 125.45 (Ar x2), 88.00 (Cq lactone), 70.36 (CH lactone).

HRMS (ESI): m/z calcd for $C_{22}H_{16}O_3$+H^+: 329.1173 $[M+H]^+$; found: 329.1161.

[minor diasteroisomer] R_f = 0.37 (PE/EA 8:1); colorless oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 8.05 – 7.94 (m, 2H, Ar), 7.56 – 7.49 (m, 1H, Ar), 7.40 (t, J = 7.7 Hz, 2H, Ar), 7.28 (d, J = 2.0 Hz, 1H, Ar), 7.22 – 7.11 (m, 7H, Ar), 7.06 (dd, J = 6.8, 3.0 Hz, 2H, Ar), 5.83 (s, 1H, CH lactone).

^{13}C NMR (101 MHz, Chloroform-d) δ 194.93 (CO-Ph), 168.53 (CO lactone), 134.24 (Ar), 133.22 (Cq Ar), 132.75 (Cq Ar), 130.70 (Ar x2), 129.92 (Cq Ar), 129.13 (Ar x2), 128.82 (Ar), 128.75 (Ar x2), 128.69 (Ar x2), 128.56 (Ar x2), 128.24 (Ar), 125.41 (Ar x2), 88.04 (Cq lactone), 65.49 (CH lactone).

HRMS (ESI): m/z calcd for $C_{22}H_{16}O_3$+H^+: 329.1173 $[M+H]^+$; found: 329.1159.

4-benzoyl-3-(4-chlorophenyl)-4-phenyloxetan-2-one ***3b***

[major diasteroisomer] R_f = 0.47 (PE/EA 8:1); colorless oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.72 (ddd, J = 8.2, 2.0, 1.2 Hz, 4H, Ar), 7.56 – 7.30 (m, 8H, Ar), 7.14 – 7.07 (m, 2H, Ar *a*), 5.12 (s, 1H, CH lactone).

^{13}C NMR (101 MHz, Chloroform-d) δ 194.54 (CO-Ph), 167.67 (CO lactone), 137.07 (Cq Ar *b*), 135.03 (Cq Ar *c*), 134.98 (Cq Ar), 133.87 (Ar), 130.42 (Ar *a* x2), 129.76 (Ar x2), 129.46 (Ar), 129.42 (Ar x2), 129.38 (Ar x2), 129.27 (Cq Ar *a*), 128.58 (Ar x2), 125.26 (Ar x2), 87.84 (Cq lactone), 69.76 (CH lactone).

HRMS (ESI): m/z calcd for $C_{22}H_{15}ClO_3$+H^+: 363.0783 $[M+H]^+$; found: 363.0778.

[minor diasteroisomer] R_f = 0.61 (PE/EA 8:1); δ 5.79 (s, CH lactone). The compound was not characterized due to coelution with unreacted benzil (R_f = 0.59). After treatment with methylamine, the resulting amide **7b** was fully characterized.

4-benzoyl-3-(4-methoxyphenyl)-4-phenyloxetan-2-one ***3c***

[major diasteroisomer] R_f = 0.41 (PE/EA 8:2); colorless oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.72 (ddt, J = 7.0, 5.9, 1.5 Hz, 4H, Ar), 7.53 – 7.44 (m, 3H, Ar), 7.44 – 7.38 (m, 1H, Ar), 7.38 – 7.30 (m, 2H, Ar), 7.12 – 7.03 (m, 2H, Ar-OCH_3), 6.91 – 6.80 (m, 2H, Ar-OCH_3), 5.13 (s, 1H, CH lactone), 3.80 (s, 3H, CH_3).

^{13}C NMR (101 MHz, Chloroform-d) δ 194.99 (CO-Ph), 168.63 (CO lactone), 159.95 (Cq-OCH_3), 137.41 (Cq Ar), 135.33 (Cq Ar), 133.57 (Ar), 130.37 (Ar x2), 129.73 (Ar x2), 129.28 (Ar x2), 129.25 (Ar), 128.45 (Ar x2), 125.45 (Ar x2), 122.69 (Cq Ar-OCH_3), 114.54 (Ar x2), 88.16 (Cq lactone), 69.89 (CH lactone), 55.41 (CH_3).

HRMS (ESI): m/z calcd for $C_{23}H_{18}O_4+H^+$: 359.1278 $[M+H]^+$; found: 359.1281.

[minor diasteroisomer] R_f = 0.53 (PE/EA 8:2); colorless oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 8.03 – 7.95 (m, 2H, Ar), 7.52 (ddt, J = 7.8, 6.9, 1.3 Hz, 1H, Ar), 7.42 – 7.35 (m, 2H, Ar), 7.31 – 7.23 (m, 2H, Ar), 7.22 – 7.12 (m, 3H, Ar), 6.99 – 6.92 (m, 2H, Ar), 6.68 – 6.61 (m, 2H, Ar), 5.76 (s, 1H, CH lactone), 3.70 (s, 3H, CH_3).

^{13}C NMR (101 MHz, Chloroform-d) δ 195.14 (CO-Ph), 169.01 (CO lactone), 159.45 (Cq-OCH_3), 134.18 (Ar), 133.37 (Cq Ar), 132.88 (Cq Ar), 130.68 (Ar x2), 130.44 (Ar x2), 128.80 (Ar x3), 128.68 (Ar x2), 125.47 (Ar x2), 122.01 (Cq Ar), 113.98 (Ar x2), 88.24 (Cq lactone), 65.08 (CH lactone), 55.28 (CH_3).

HRMS (ESI): m/z calcd for $C_{23}H_{18}O_4+H^+$: 359.1278 $[M+H]^+$; found: 359.1275.

4-benzoyl-4-phenyl-3-(thiophen-2-yl)oxetan-2-one ***3d***

[major diasteroisomer] R_f = 0.40 (PE/EA 8:1); colorless oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.76 – 7.68 (m, 4H, Ar), 7.57 – 7.40 (m, 4H, Ar), 7.40 – 7.31 (m, 3H, Ar), 6.99 (dd, J = 5.1, 3.6 Hz, 1H, Ar), 6.93 (dt, J = 3.7, 0.9 Hz, 1H, Thioph), 5.40 (d, J = 0.7 Hz, 1H, CH lactone).

^{13}C NMR (101 MHz, Chloroform-d) δ 194.41 (CO-Ph), 167.21 (CO lactone), 136.81 (Cq Ar), 135.07 (Cq Ar), 133.67 (Ar), 131.34 (Cq Ar), 129.73 (Ar x2), 129.45 (Ar), 129.34 (Ar x2), 128.47 (Ar x3), 127.59 (Ar), 127.45 (Ar), 125.45 (Ar x2), 88.29 (Cq lactone), 64.50 (CH lactone).

HRMS (ESI): m/z calcd for $C_{20}H_{14}O_3S+H^+$: 335.0737 $[M+H]^+$; found: 335.0732.

Minor diastereoisomer was not detected in the chromatographic eluate.

4-(4-bromobenzoyl)-4-(4-bromophenyl)-3-phenyloxetan-2-one ***3f***

[major diasteroisomer] R_f = 0.45 (PE/Et_2O 8:1); white solid.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.65 – 7.48 (m, 8H, Ar), 7.40 – 7.31 (m, 3H, Ar), 7.16 – 7.09 (m, 2H, Ar), 5.12 (s, 1H, CH lactone).

^{13}C NMR (101 MHz, Chloroform -D) δ 193.65 (CO-Ph), 167.36 (CO lactone), 136.03 (Cq Ar), 133.67 (Cq Ar), 132.59 (Ar x2), 131.98 (Ar x2), 131.16 (Ar x2), 130.17 (Cq Ar), 129.38 (Cq Ar), 129.28 (Ar x2), 129.26 (Ar), 128.98 (Ar x2), 127.07 (Ar x2), 123.97 (Cq Ar), 87.40 (Cq lactone), 70.81 (CH lactone).

HRMS (ESI): m/z calcd for $C_{22}H_{14}Br_2O_3+H^+$: 486.9362 $[M+H]^+$; found: 486.9369.

[minor diasteroisomer] R_f = 0.54 (PE/EA 8:2); colorless oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.86 – 7.78 (m, 2H, Ar), 7.59 – 7.49 (m, 2H, Ar), 7.35 – 7.28 (m, 2H, Ar), 7.17 (dt, J = 4.4, 1.7 Hz, 3H, Ar), 7.14 – 7.08 (m, 2H, Ar), 7.08 – 7.01 (m, 2H, Ar), 5.81 (s, 1H, CH lactone).

^{13}C NMR (101 MHz, Chloroform-d) δ 193.72 (CO-Ph), 167.75 (CO lactone), 132.23 (Ar x2), 132.13 (Cq Ar), 132.10 (Ar x2), 132.02 (Ar x2), 131.29 (Cq Ar), 130.07 (Cq Ar), 129.43 (Cq Ar), 129.02 (Ar x2), 128.87 (Ar x2), 128.66 (Ar), 127.09 (Ar x2), 123.51 (Cq Ar), 87.50 (Cq lactone), 65.62 (CH lactone).

HRMS (ESI): m/z calcd for $C_{22}H_{14}Br_2O_3+H^+$: 486.9362 $[M+H]^+$; found: 486.9363.

4-(4-methoxybenzoyl)-3,4-diphenyloxetan-2-one ***3i***

[major diastereoisomer] R_f=0.20 (PE/EA 8:1); colorless oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.82 – 7.75 (m, 2H, Ar), 7.75 – 7.69 (m, 2H, Ar), 7.4- - 7.43 (m, 2H, Ar), 7.43 – 7.37 (m, 1H, Ar), 7.37 – 7.28 (m, 3H, Ar), 7.21 – 7.12 (m, 2H, Ar), 6.86 – 6.78 (m, 2H, Ar), 5.15 (s, 1H, CH lactone), 3.82 (s, 3H, CH_3).

^{13}C NMR (101 MHz, Chloroform-d) δ 192.54 (CO-Ph), 168.37 (CO lactone), 163.95 (Cq Ar-OCH_3), 137.70 (Cq Ar), 132.42 (Ar x2), 130.96 (Cq Ar), 129.23 (Ar x2), 129.20 (Ar), 129.13 (Ar x2), 129.05 (Ar x2), 128.88 (Ar), 127.99 (Cq Ar), 125.45 (Ar x2), 113.77 (Ar x2), 88.09 (Cq), 70.30 (CH lactone), 55.62 (CH_3).

HRMS (ESI): m/z calcd for $C_{23}H_{18}O_4+H^+$: 359.1278 $[M+H]^+$; found: 359.1281.

[minor diasteroisomer] R_f = 0.30 (PE/EA 8:1); δ 5.84 (s, CH lactone). The compound was not characterized due to coelution with unreacted starting materials and impurities. After treatment with methylamine, the resulting amide **7i** was fully characterized.

*3-hydroxy-N-methyl-4-oxo-2,3,4-triphenylbutanamide **7a***

[major diastereoisomer] R_f=0.55 (PE/EA 2:1); colorless oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.98 – 7.90 (m, 2H, Ar), 7.44 – 7.32 (m, 1H, Ar), 7.32 – 7.24 (m, 2H, Ar), 7.24 – 7.19 (m, 2H, Ar), 7.19 – 7.12 (m, 4H, Ar), 7.09 (ddt, J = 8.4, 6.4, 1.6 Hz, 2H, Ar), 6.94 – 6.87 (m, 2H, Ar), 6.85 (s, 1H, OH), 5.64 (d, J = 5.2 Hz, 1H, NH), 4.44 (s, 1H, CH), 2.82 (d, J = 4.8 Hz, 3H, CH_3).

^{13}C NMR (101 MHz, Chloroform-d) δ 202.28 (CO-Ph), 175.73 (CO-$NHCH_3$), 138.65 (Cq Ar), 135.04 (Cq Ar), 134.67 (Cq Ar), 132.57 (Ar), 131.03 (Ar x2), 129.85 (Ar x2), 128.35 (Ar x2), 127.94 (Ar x2), 127.90 (Ar x2), 127.64 (Ar), 127.43 (Ar), 125.20 (Ar x2), 85.32 (Cq), 59.01 (CH), 26.68 (CH_3).

HRMS (ESI): m/z calcd for $C_{23}H_{21}NO_3+H^+$: 360.1595 $[M+H]^+$; found: 360.1589.

[minor diastereoisomer] R_f=0.50 (PE/EA 2:1); colorless oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.71 – 7.57 (m, 4H, Ar), 7.50 – 7.41 (m, 2H, Ar), 7.41 – 7.30 (m, 4H, Ar), 7.30 – 7.19 (m, 5H, Ar), 6.88 (s, 1H, OH), 5.96 (s, 1H, NH), 4.47 (s, 1H, CH), 2.63 (d, J = 4.8 Hz, 3H, CH_3).

^{13}C NMR (101 MHz, Chloroform-d) δ 199.94 (CO-Ph), 173.74 (CO-$NHCH_3$), 141.21 (Cq Ar), 135.67 (Cq Ar), 135.19 (Cq Ar), 132.53 (Ar), 130.57 (Ar x2), 130.11 (Ar x2), 128.73 (Ar x2), 128.48 (Ar x2), 128.08 (Ar), 127.93 (Ar x2), 127.82 (Ar), 126.06 (Ar x2), 85.65 (Cq), 59.91 (CH), 26.47 (CH_3).

HRMS (ESI): m/z calcd for $C_{23}H_{21}NO_3+H^+$: 360.1595 $[M+H]^+$; found: 360.1591.

*2-(4-chlorophenyl)-3-hydroxy-N-methyl-4-oxo-3,4-diphenylbutanamide **7b***

[minor diastereoisomer] R_f=0.54 (PE/EA 2:1); colorless oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.72 – 7.57 (m, 4H, Ar), 7.46 – 7.32 (m, 5H, Ar), 7.32 – 7.17 (m, 5H, Ar), 6.82 (s, 1H, OH), 5.90 (s, 1H, NH), 4.45 (s, 1H, CH), 2.61 (d, J = 4.8 Hz, 3H, CH_3).

^{13}C NMR (101 MHz, Chloroform-d) δ 199.53 (CO-Ph), 173.37 (CO-$NHCH_3$), 140.84 (Cq Ar), 135.37 (Cq Ar), 133.87 (Cq Ar), 133.72 (Cq Ar), 132.76 (Ar), 131.87 (Ar x2), 130.18 (Ar x2), 128.85 (Ar x2), 128.59 (Ar x2), 128.24 (Ar), 128.02 (Ar x2), 125.89 (Ar x2), 85.56 (Cq), 59.13 (CH), 26.49 (CH_3).

HRMS (ESI): m/z calcd for $C_{23}H_{20}ClNO_3+H^+$: 394.1205 $[M+H]^+$; found: 394.1211.

*3-hydroxy-4-(4-methoxyphenyl)-N-methyl-4-oxo-2,3-diphenylbutanamide **7i***

[major diastereoisomer] R_f=0.55 (PE/EA 2:1); colorless oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 8.04 – 7.94 (m, 2H, Ar), 7.22 – 7.02 (m, 8H, Ar), 6.95 (s, 1H, OH), 6.92 – 6.84 (m, 2H, Ar), 6.79 – 6.70 (m, 2H, Ar), 5.66 (d, J = 5.0 Hz, 1H, NH), 4.38 (s, 1H, CH), 3.76 (s, 3H, OCH_3), 2.80 (d, J = 4.9 Hz, 3H, CH_3).

^{13}C NMR (101 MHz, Chloroform-d) δ 200.21 (CO-Ar), 175.84 (CO-NHCH$_3$), 163.01 (Cq Ar), 139.09 (Cq Ar), 134.76 (Cq Ar), 133.57 (Ar x2), 129.76 (Ar x2), 128.22 (Ar x2), 127.83 (Ar x2), 127.54 (Cq Ar), 127.45 (Ar), 127.28 (Ar), 125.03 (Ar x2), 113.09 (Ar x2), 85.27 (Cq), 58.71 (CH), 55.40 (Ar-OCH$_3$), 26.61 (CH$_3$).

HRMS (ESI): m/z calcd for $C_{24}H_{23}NO_4$+H$^+$: 390.1700 [M+H]$^+$; found: 390.1708.

[minor diastereoisomer] R_f=0.52 (PE/EA 2:1); colorless oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.82 – 7.70 (m, 2H, Ar), 7.59 (d, J = 7.8 Hz, 2H, Ar), 7.40 (s, 2H, Ar), 7.32 (t, J = 7.1 Hz, 2H, Ar), 7.21 (dd, J = 4.9, 1.9 Hz, 4H, Ar), 6.91 – 6.80 (m, 1H, OH), 6.76 – 6.69 (m, 2H, Ar), 6.19 (s, 1H, NH), 4.48 (s, 1H, CH), 3.77 (s, 3H, OCH$_3$), 2.65 (d, J = 4.8 Hz, 3H, CH$_3$).

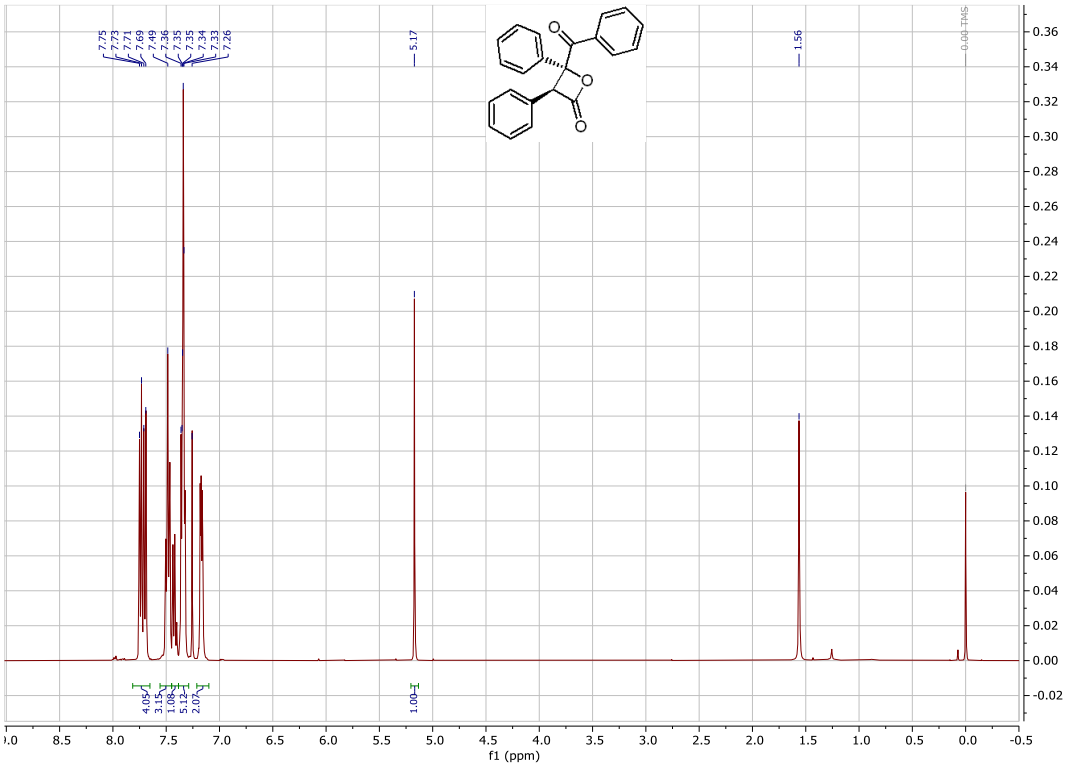
^{13}C NMR (101 MHz, Chloroform-d) δ 197.55 (CO-Ar), 173.77 (CO-NHCH$_3$), 163.12 (Cq Ar), 141.16 (Cq Ar), 139.87 (Cq Ar), 135.11 (Cq Ar), 132.89 (Ar x2), 130.48 (Ar), 128.71 (Ar x2), 128.43 (Ar x2), 128.02 (Ar), 127.76 (Ar x2), 126.09 (Ar x2), 113.31 (Ar x2), 85.19 (Cq), 59.50 (CH) 55.48 (Ar-OCH$_3$), 26.48 (CH$_3$).

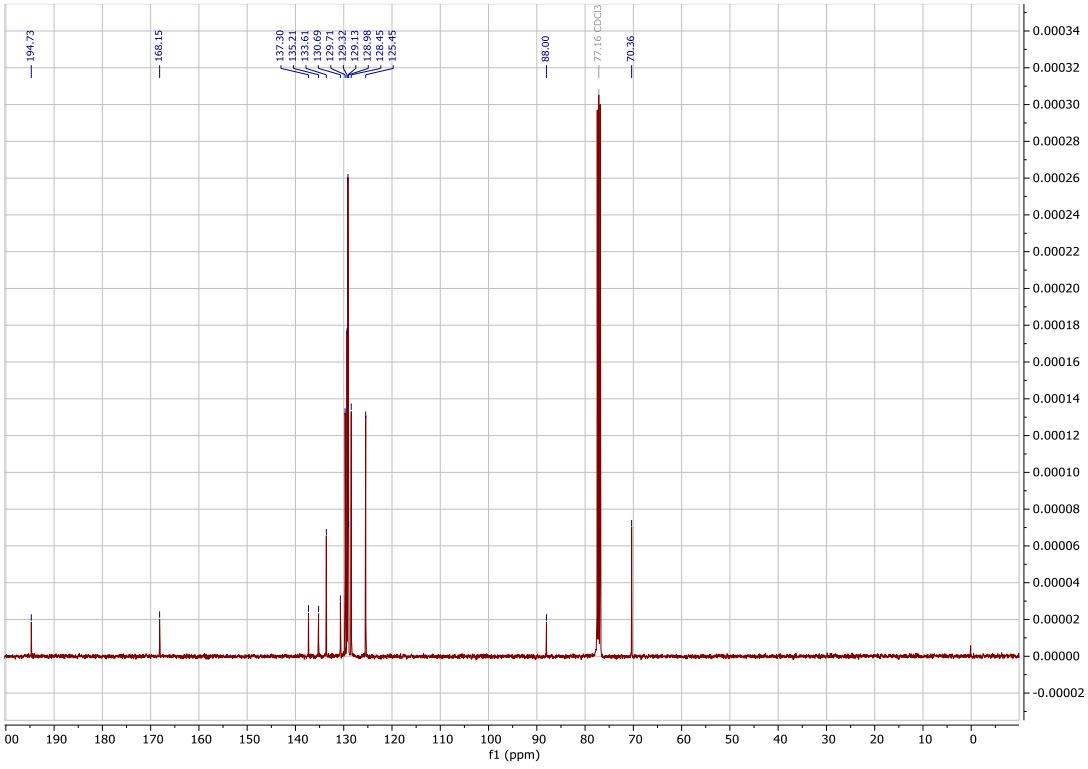
HRMS (ESI): m/z calcd for $C_{24}H_{23}NO_4$+H$^+$: 390.1700 [M+H]$^+$; found: 390.1715.

8. NMR Spectra of characterized compounds

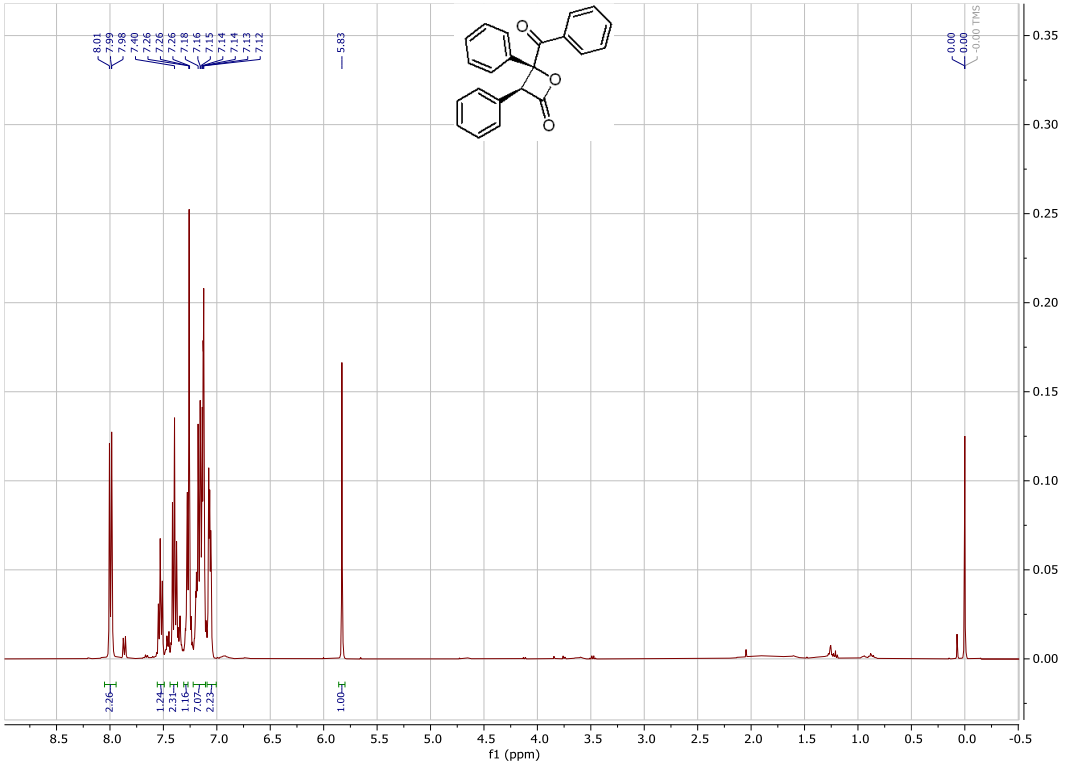
Compound 3a

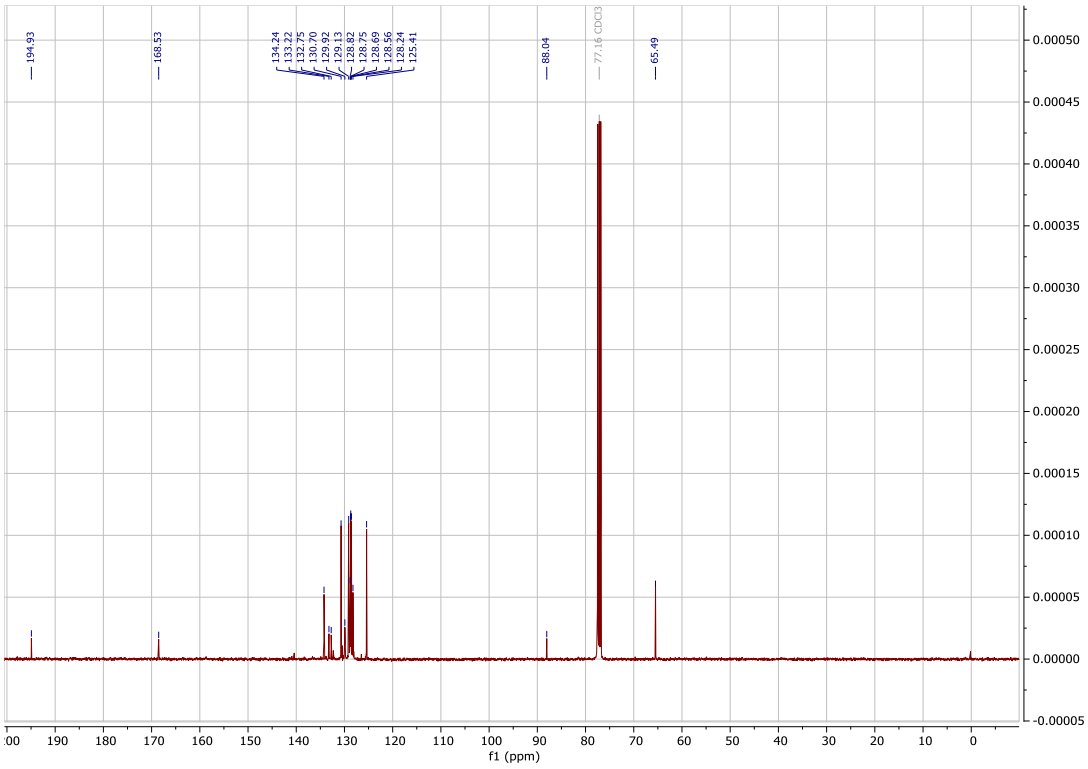
Major diastereoisomer





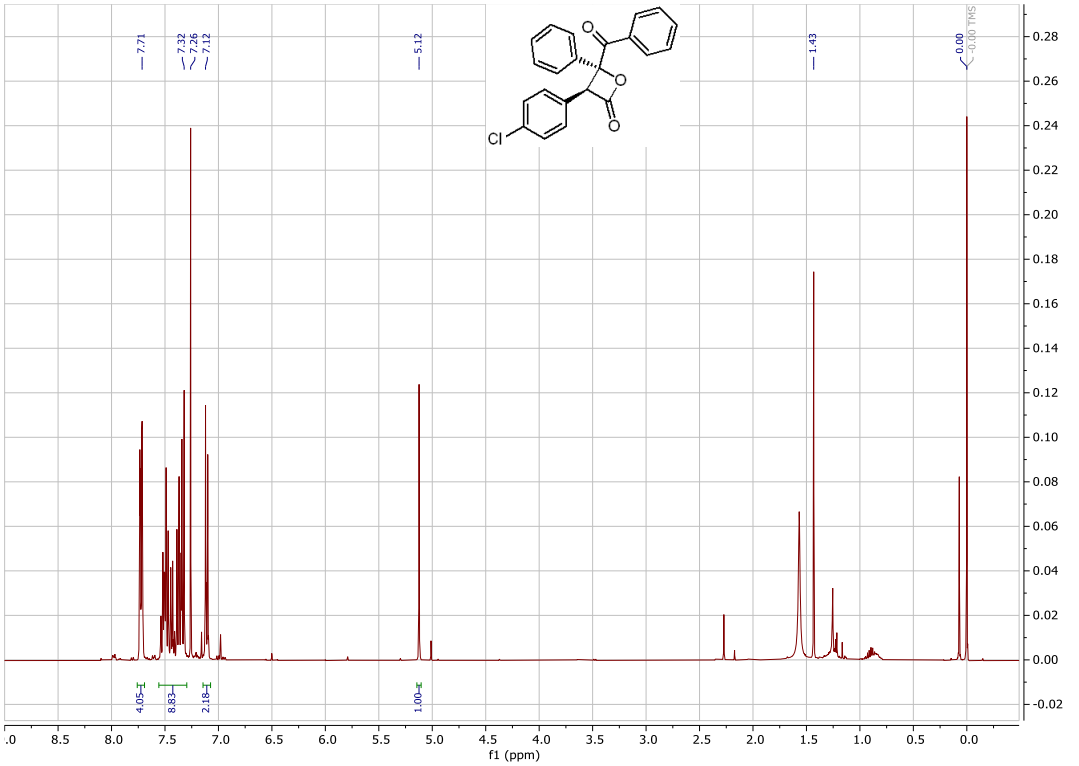
Minor diastereoisomer

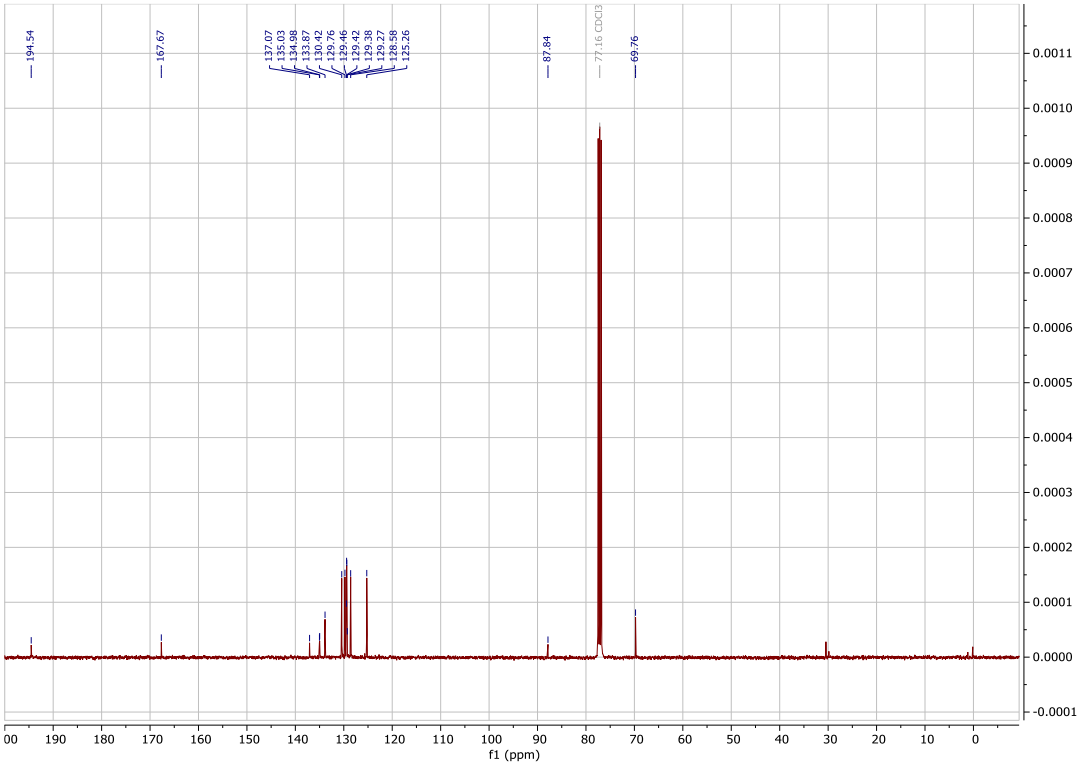




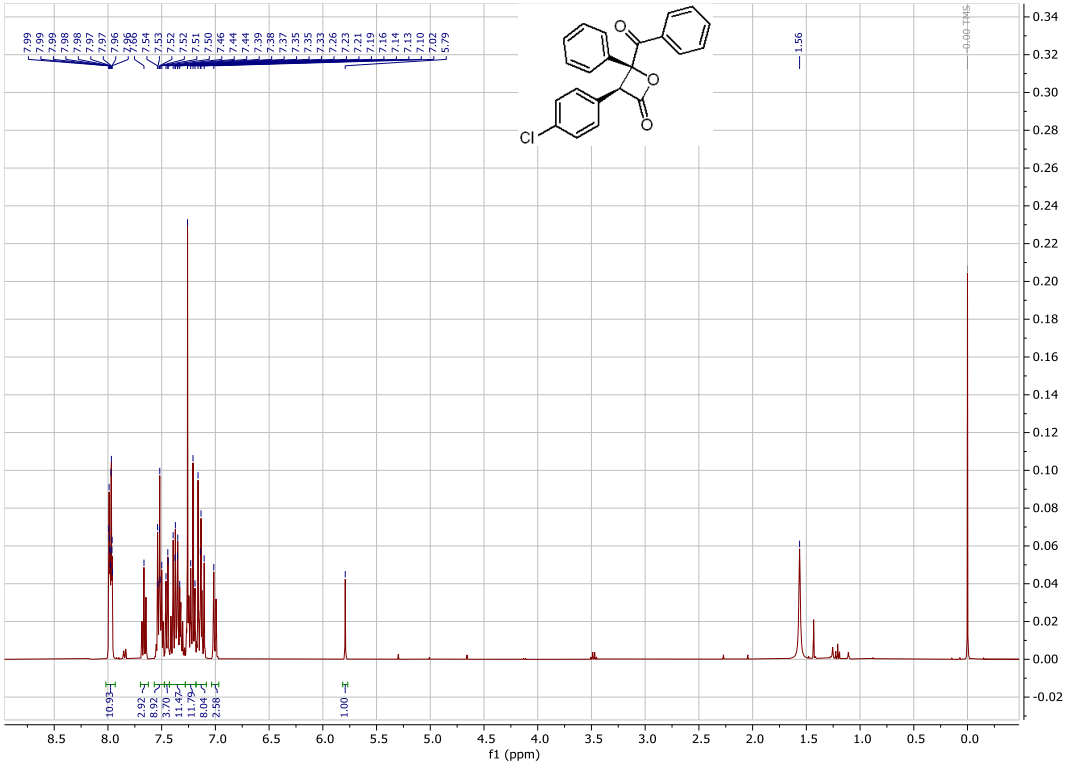
Compound 3b

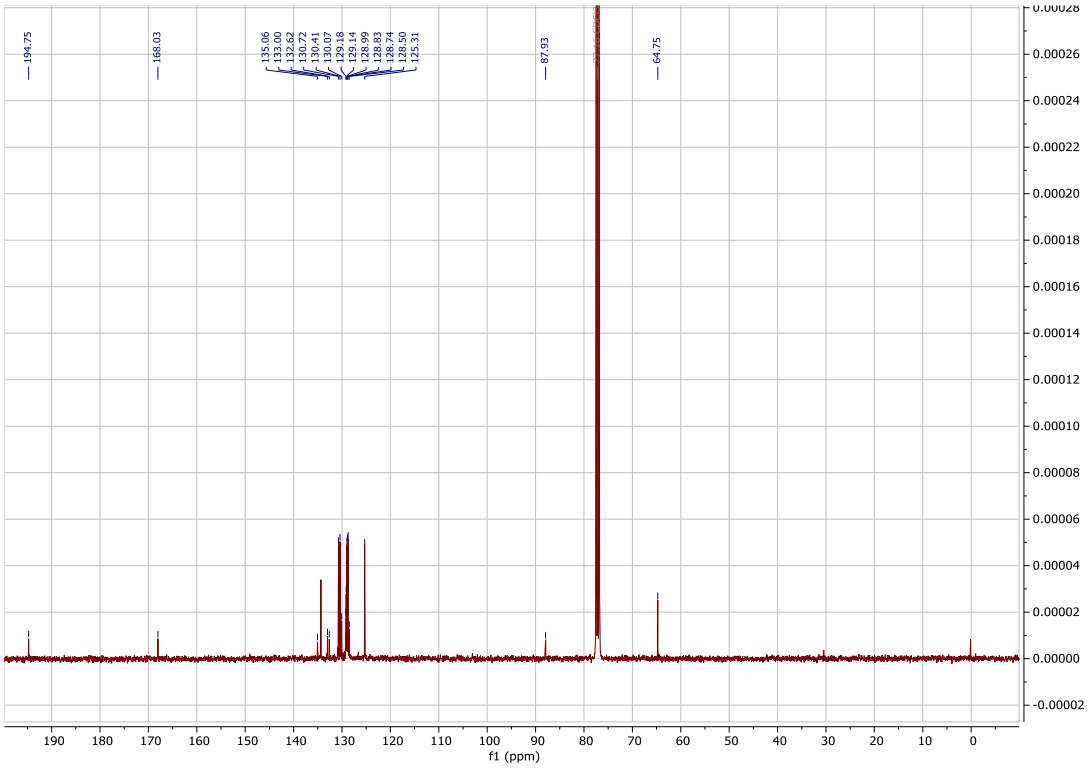
Major diastereoisomer





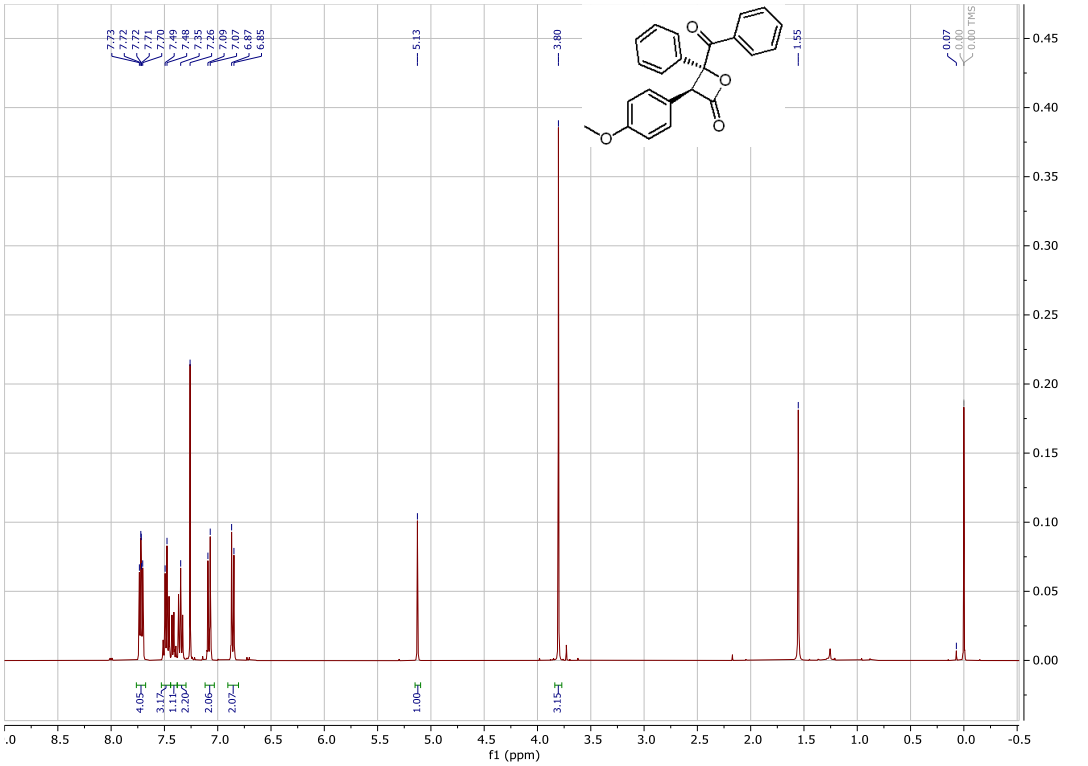
Minor diastereoisomer

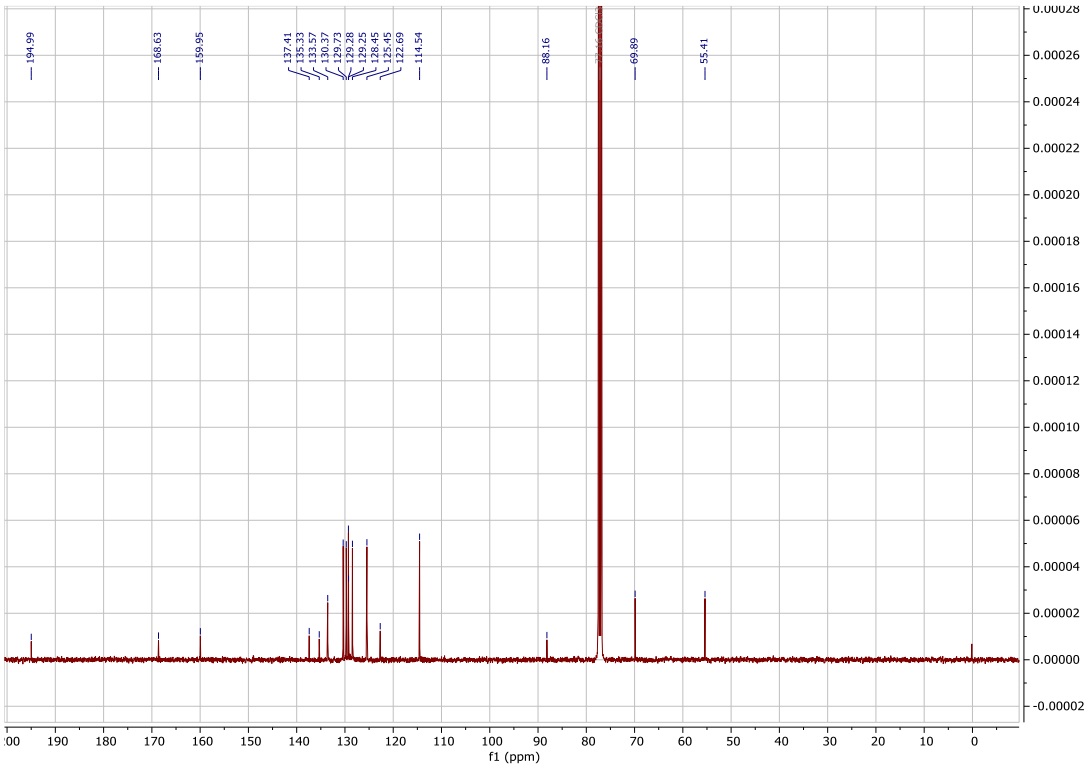




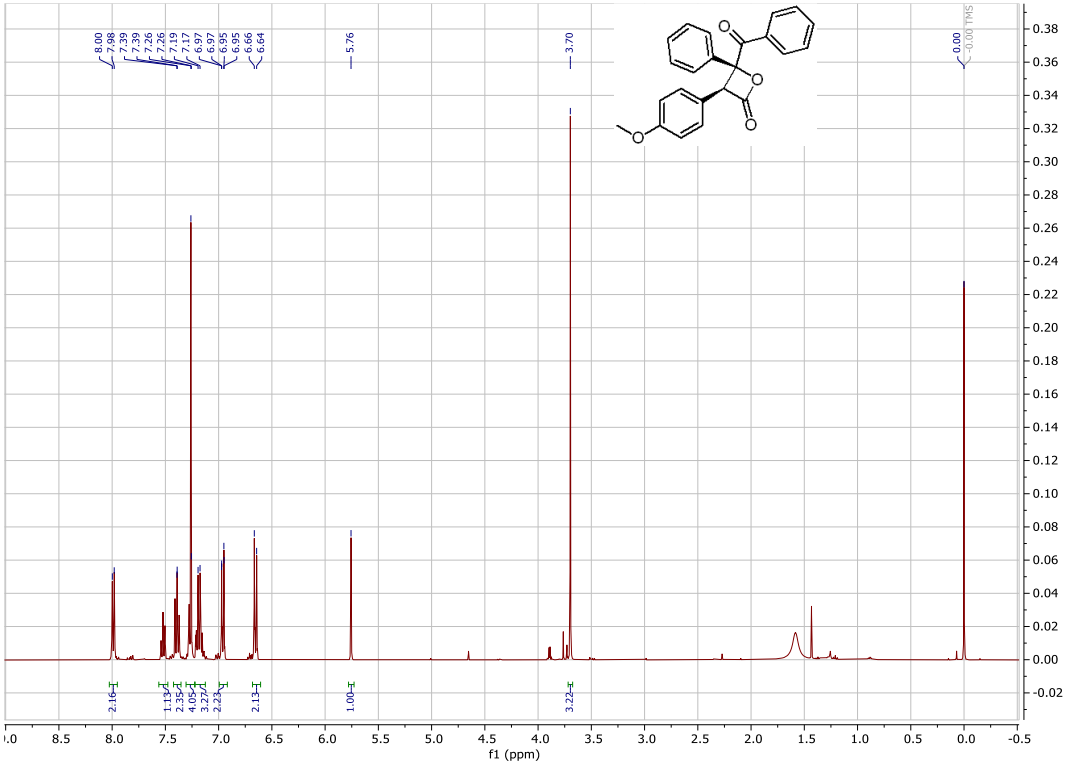
Compound 3c

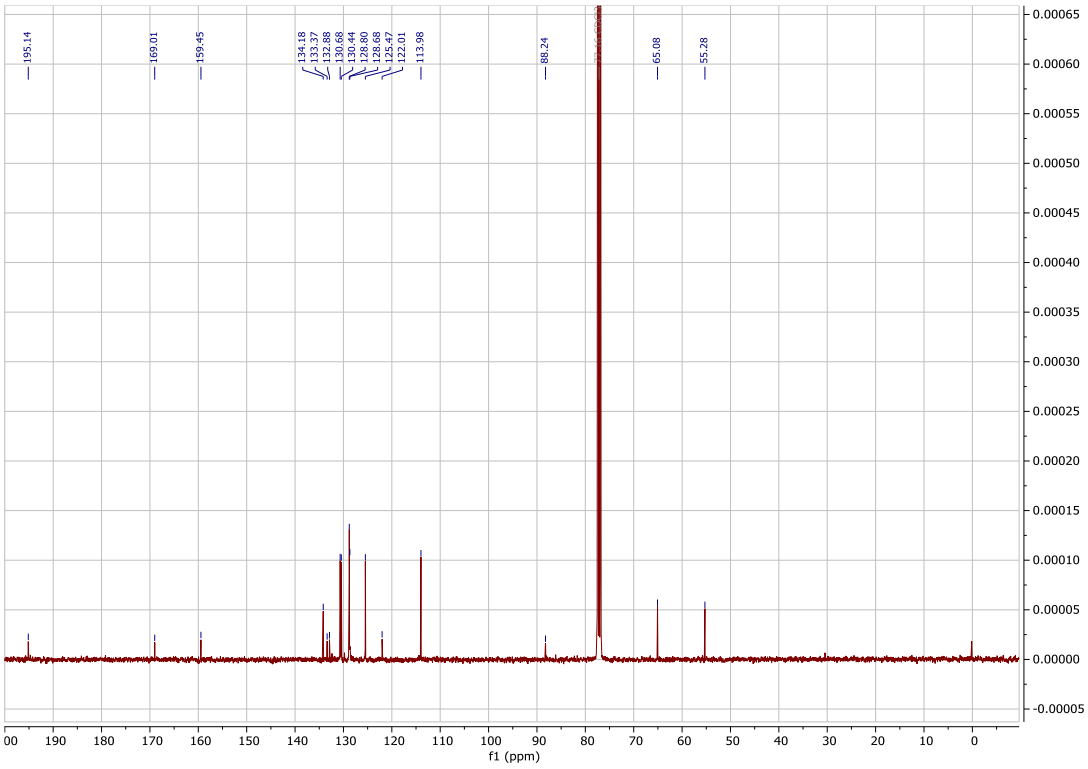
Major diastereoisomer





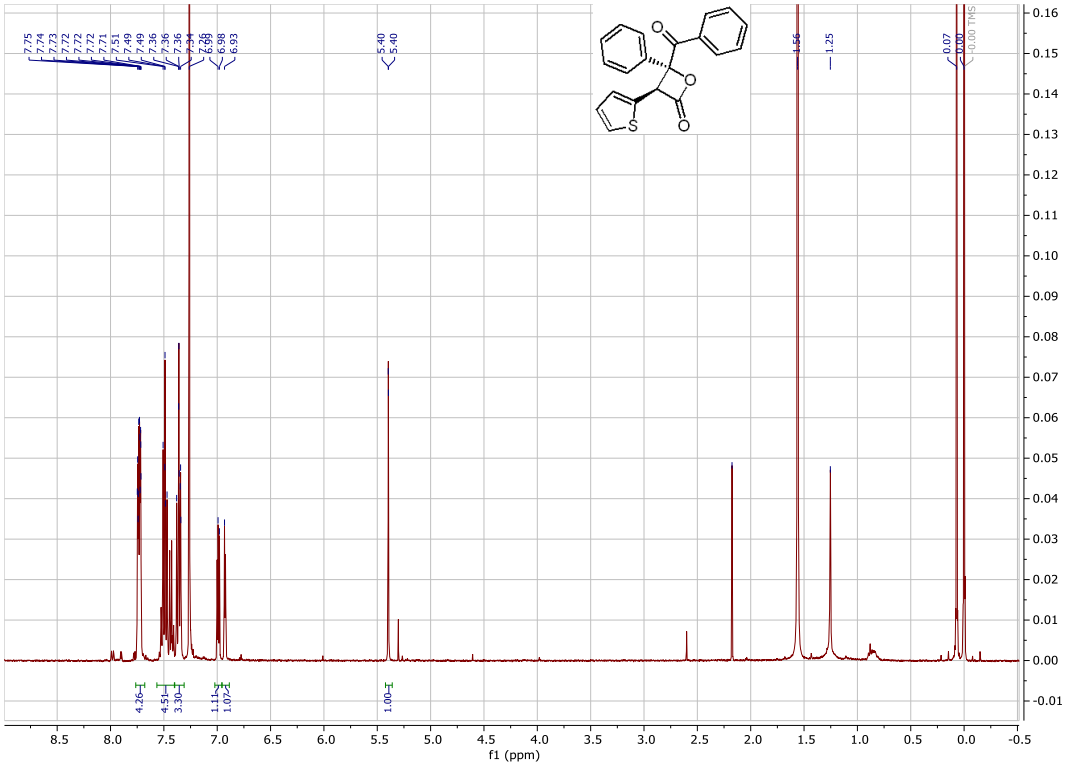
Minor diastereoisomer

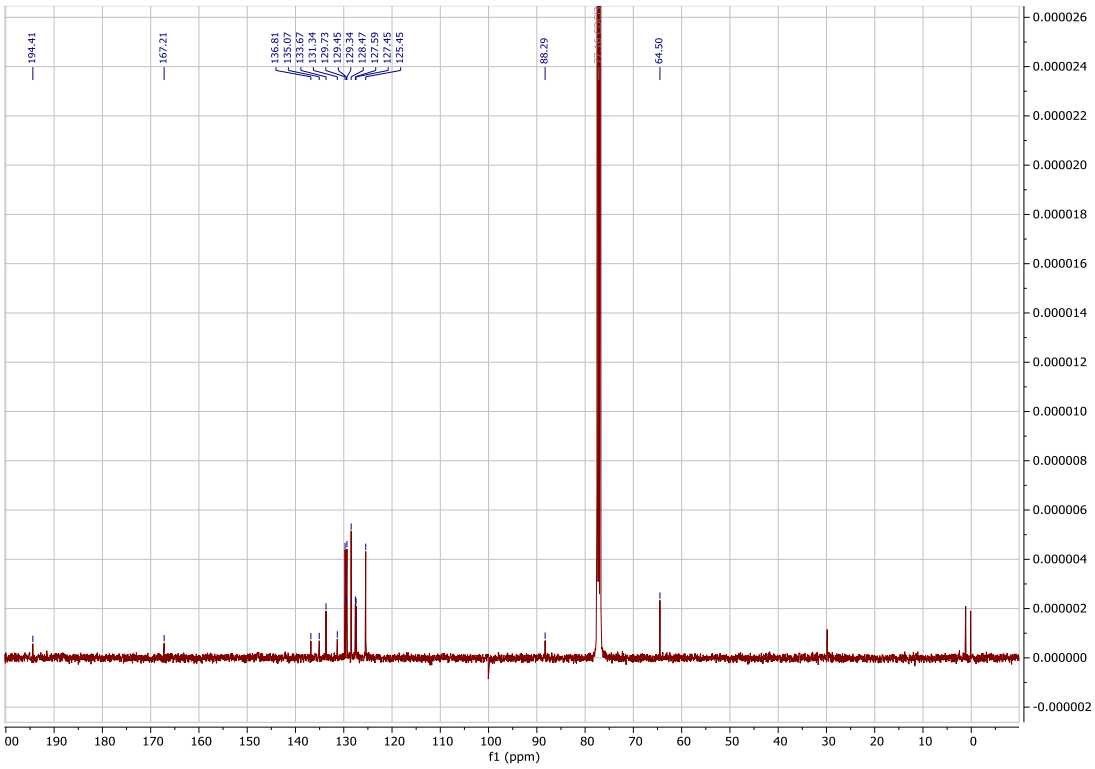




Compound 3d

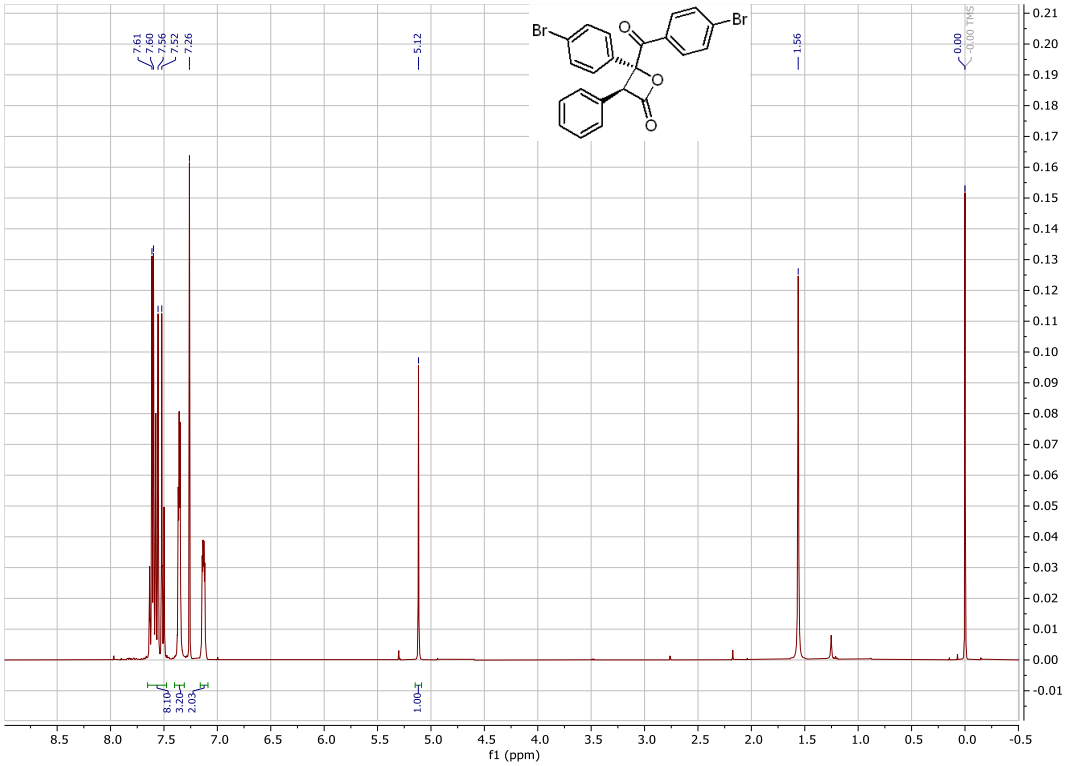
Major diastereoisomer

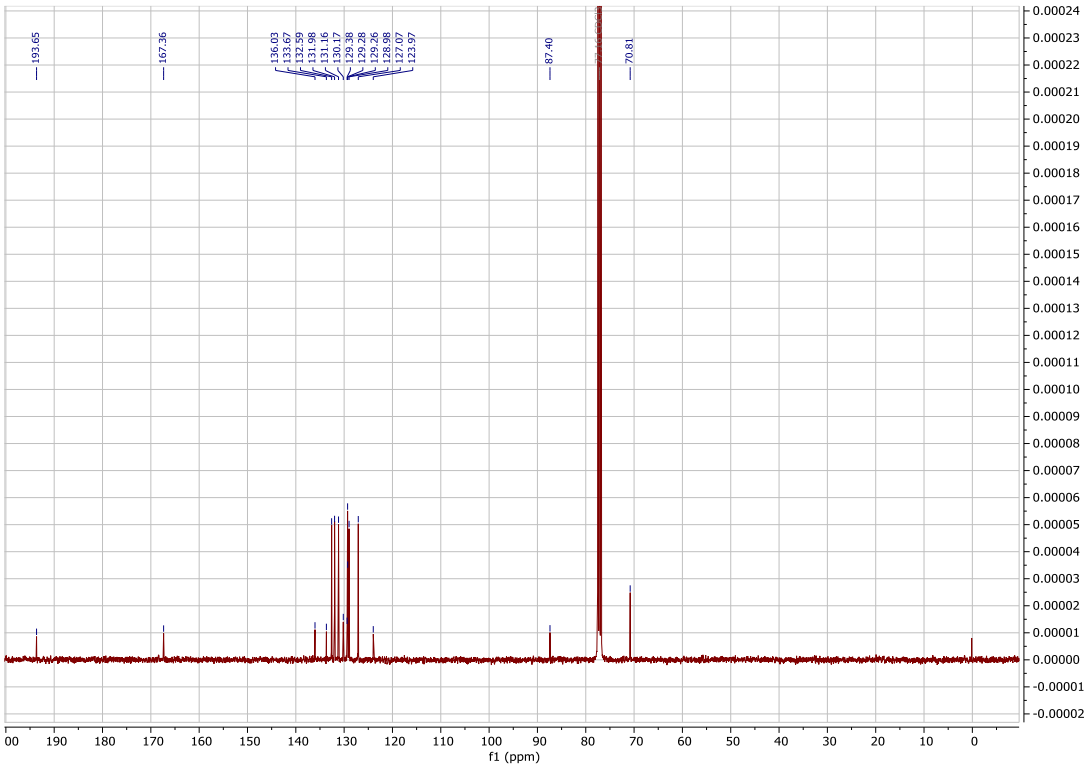




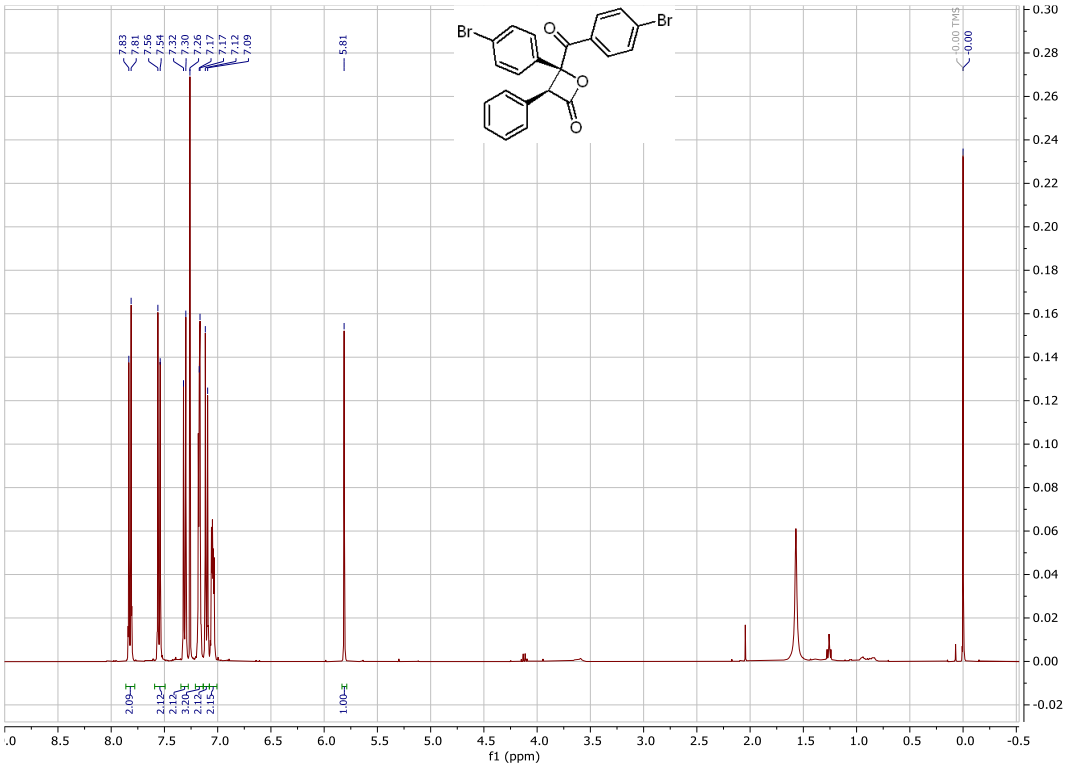
Compound 3f

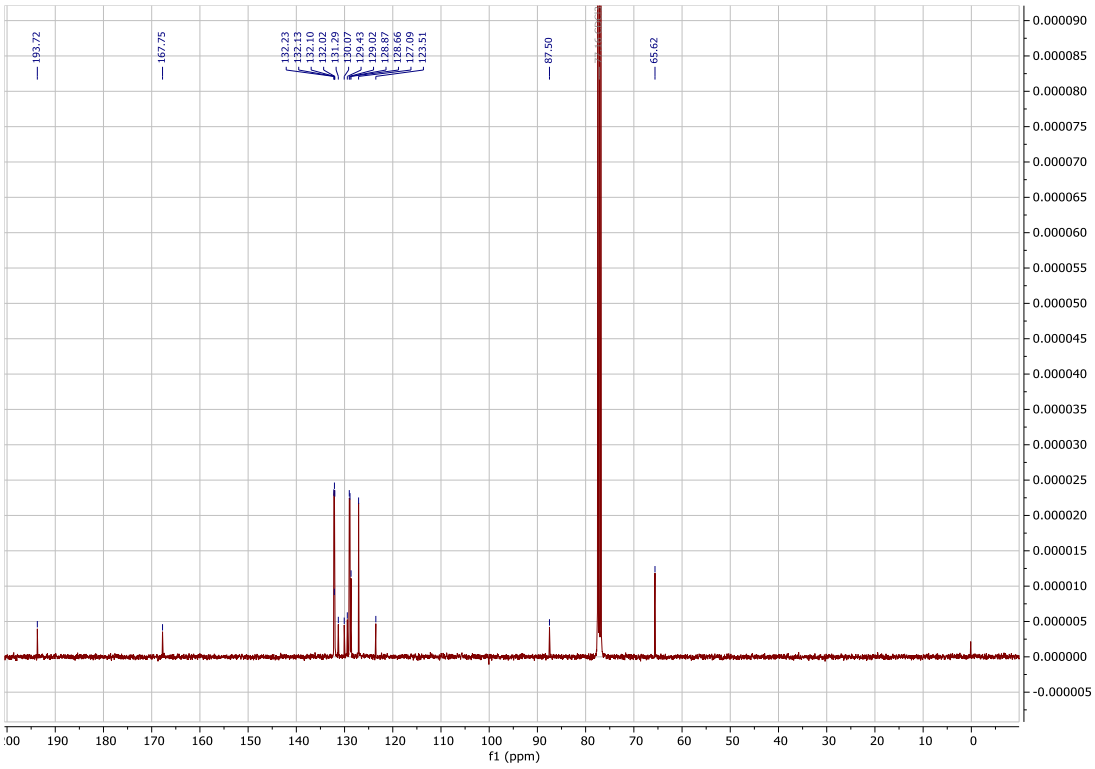
Major diastereoisomer





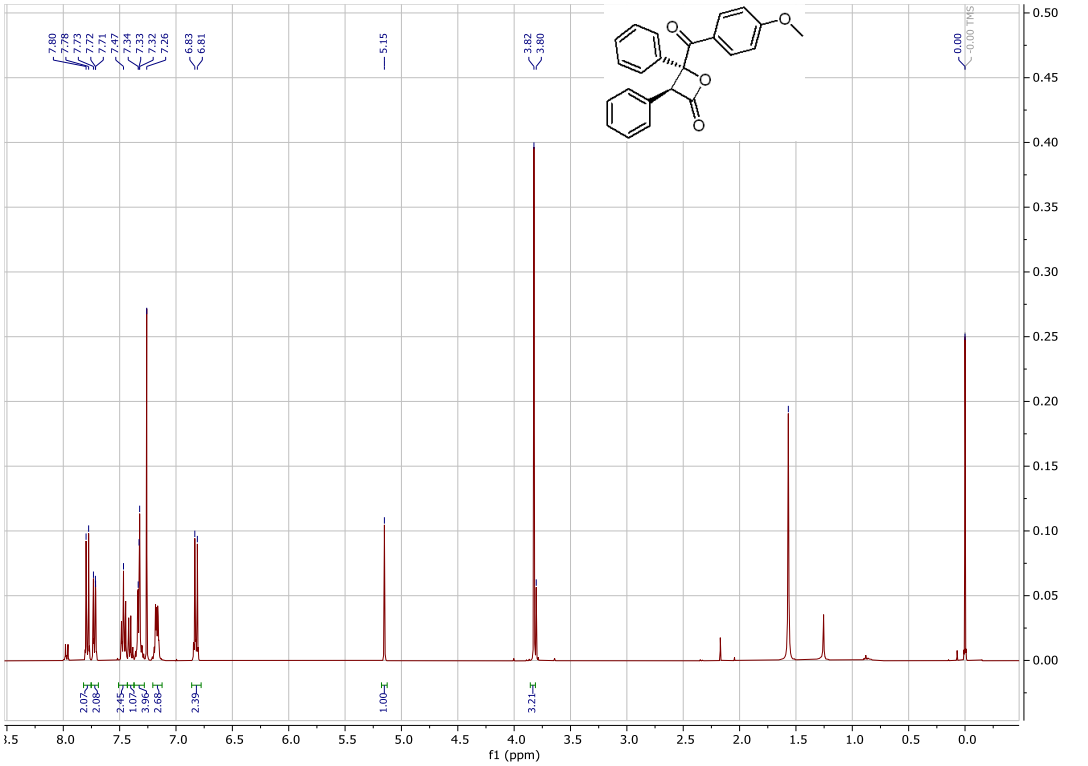
Minor diastereoisomer

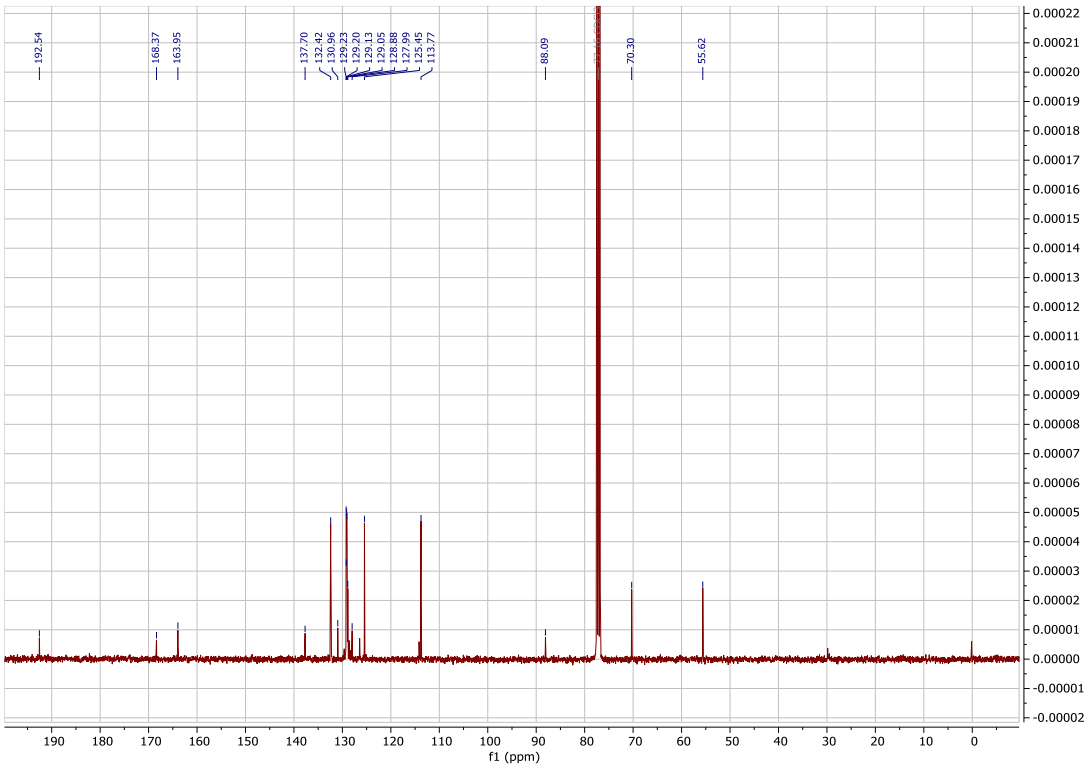




Compound 3i

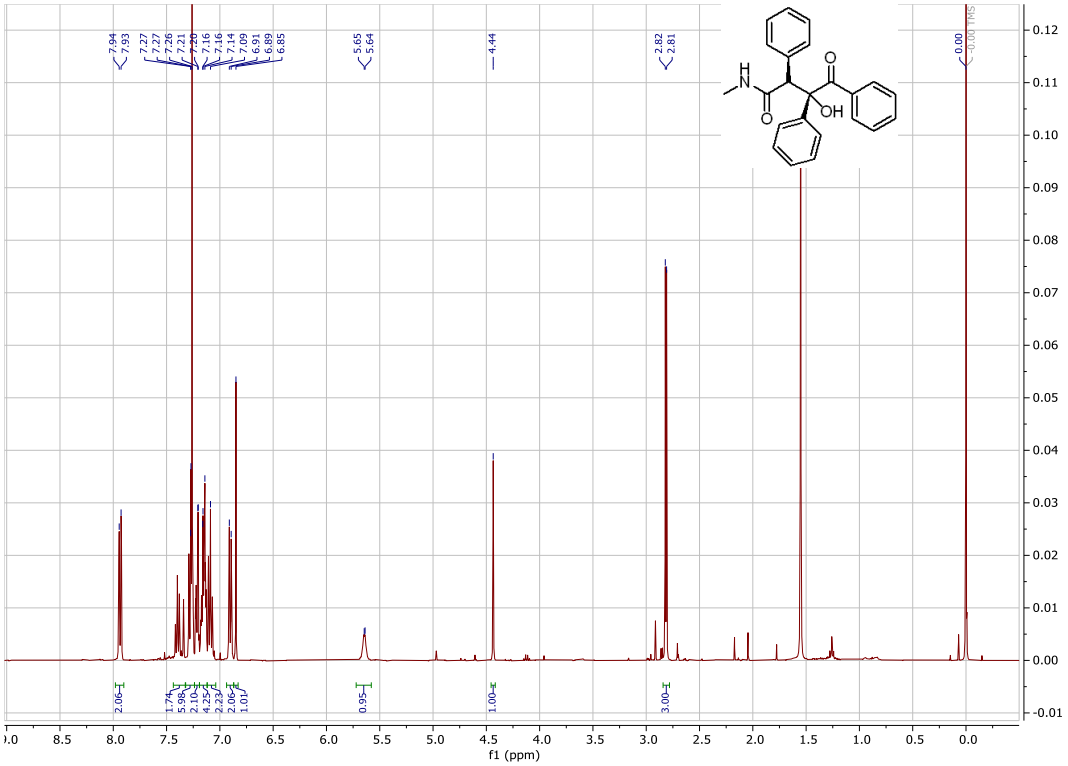
Major diastereoisomer

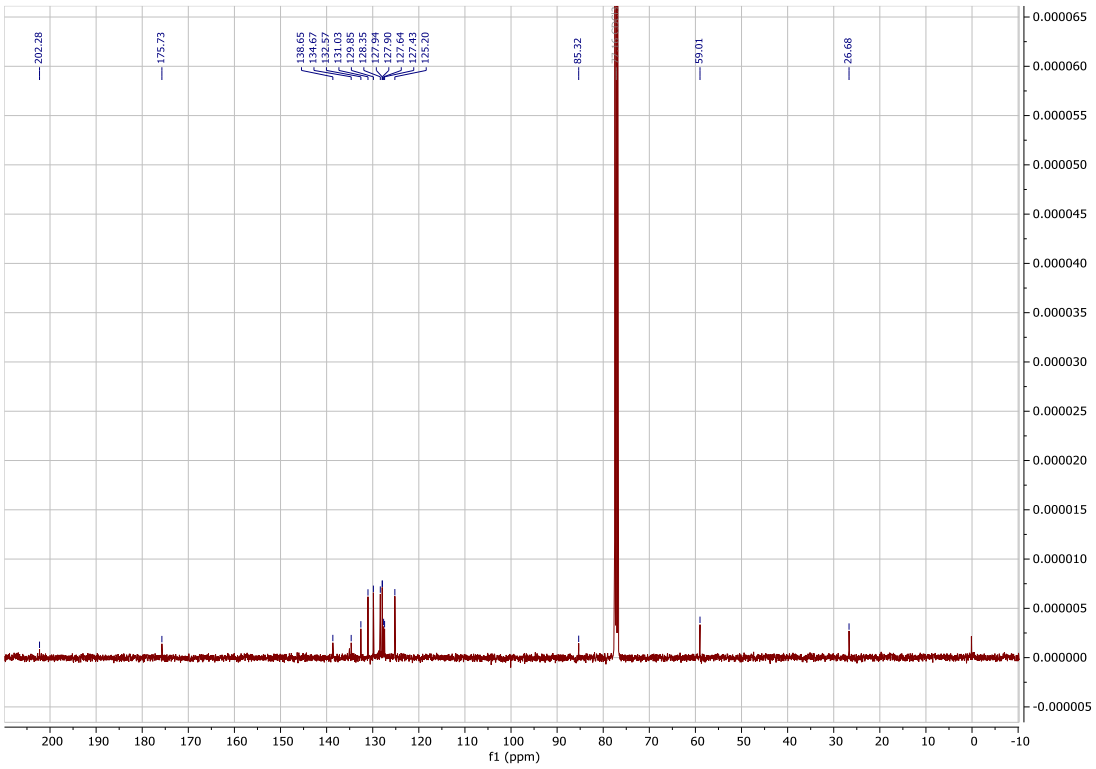




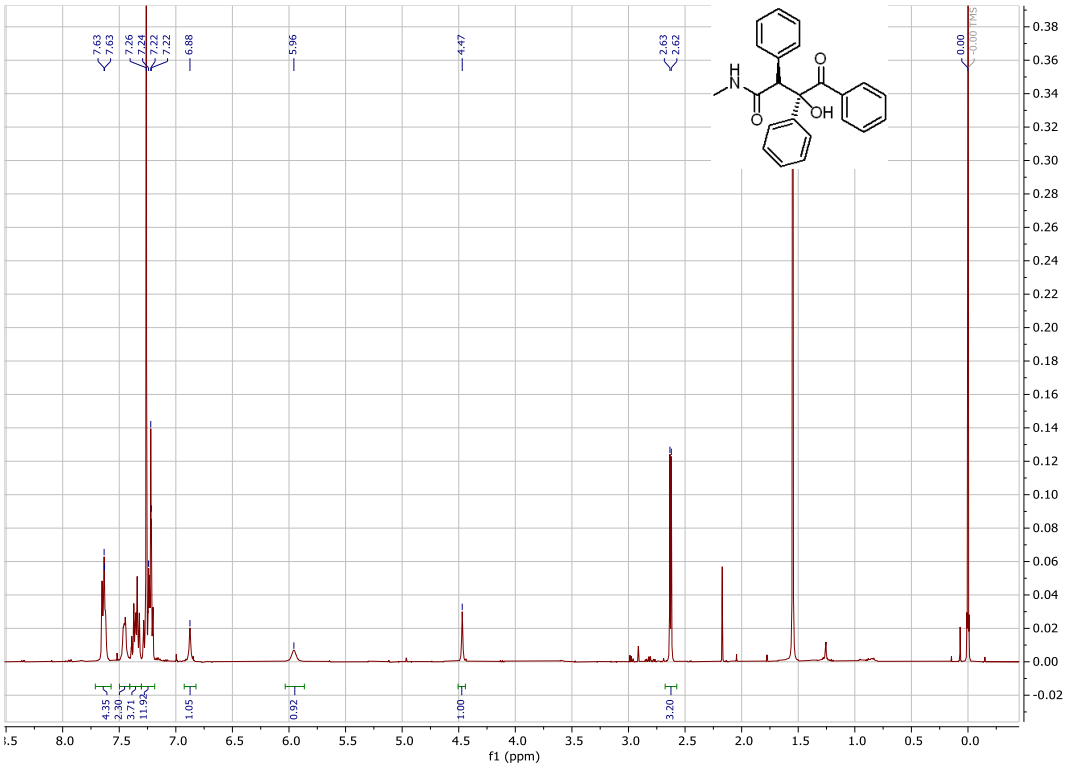
Compound 7a

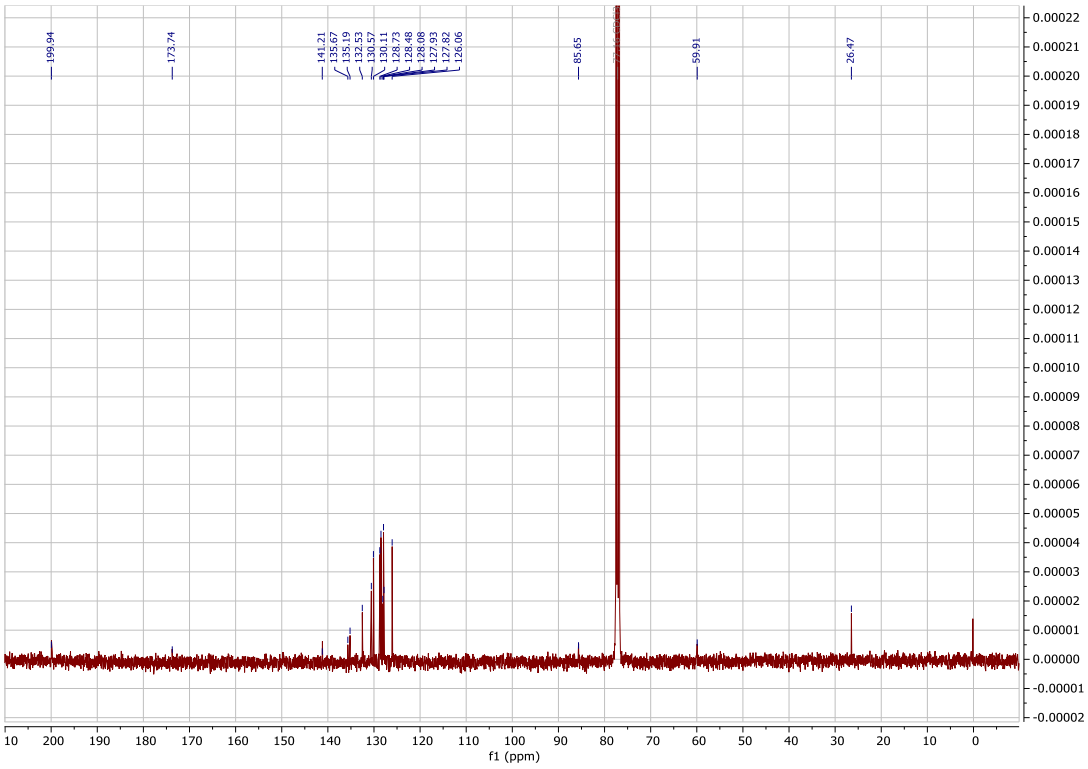
Major diastereoisomer





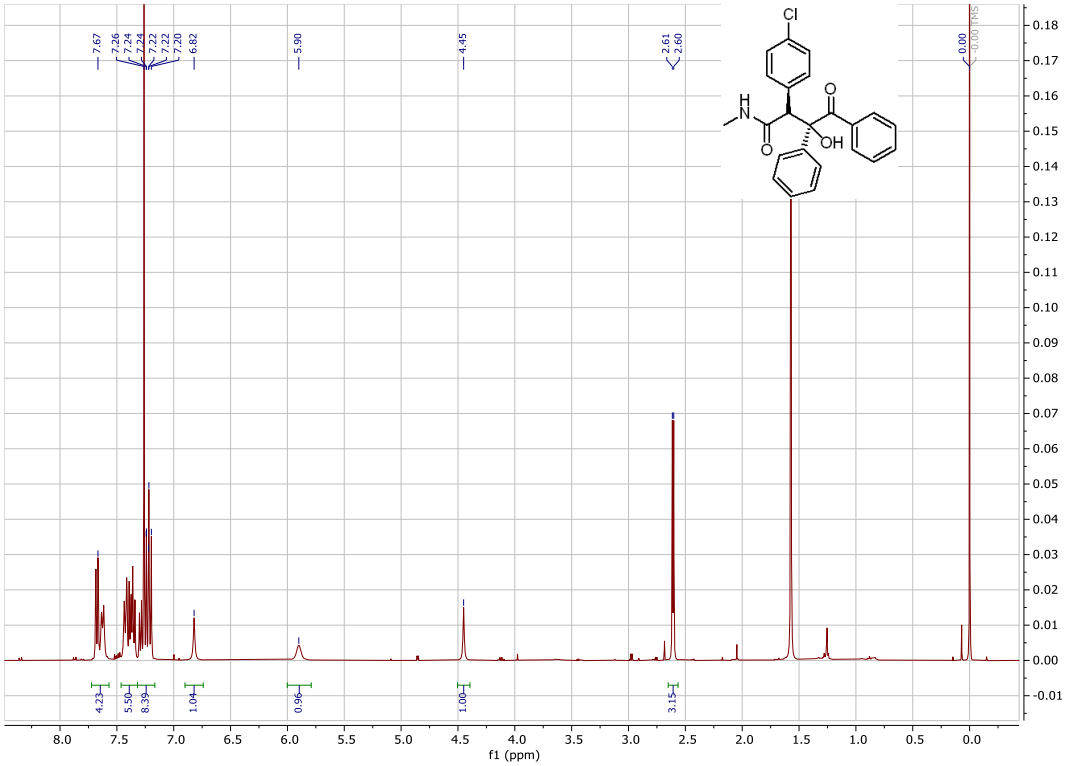
Minor diastereoisomer

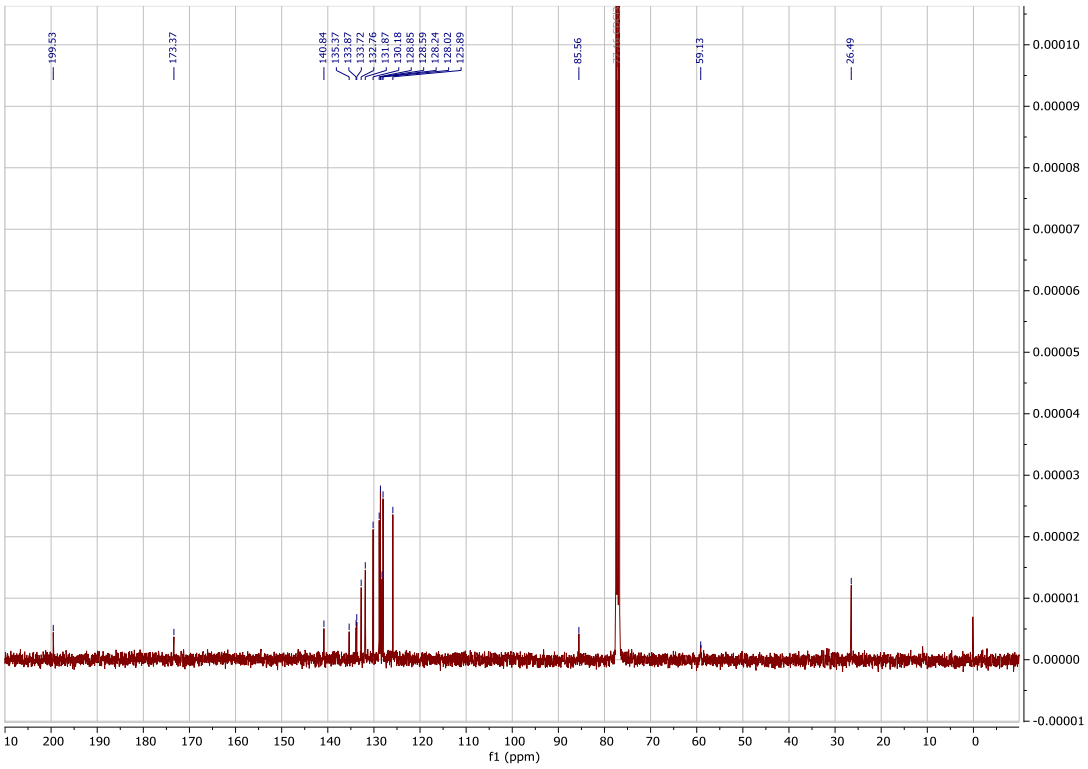




Compound 7b

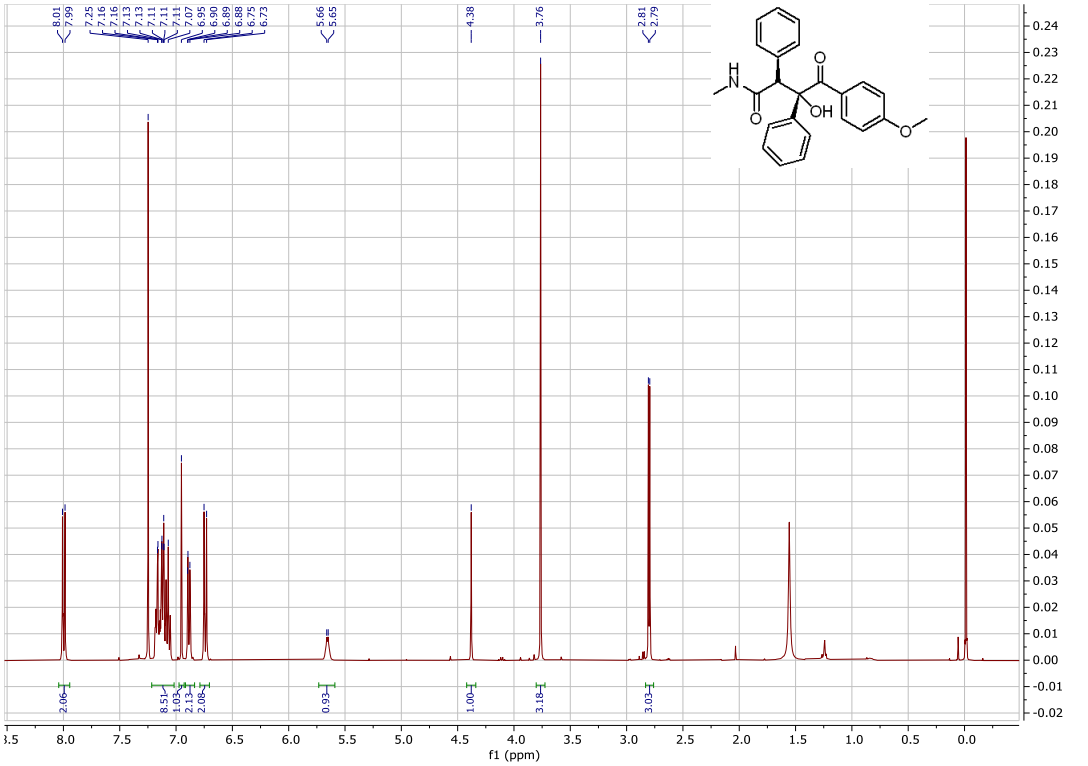
Minor diastereoisomer

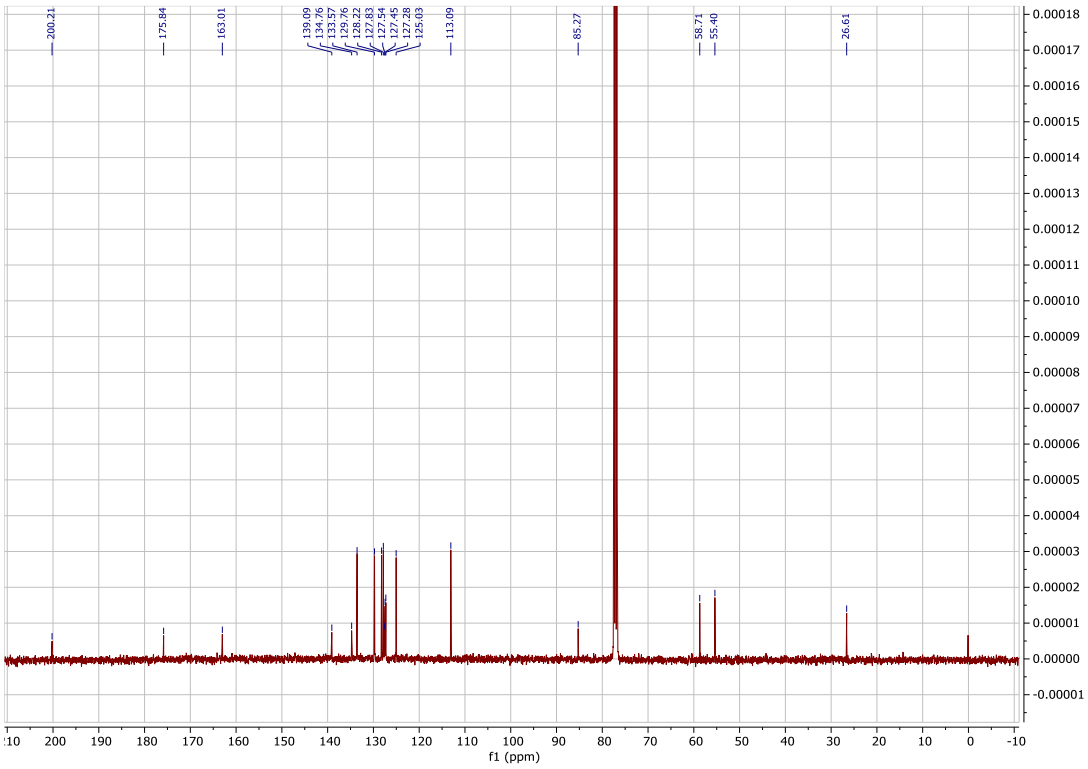




Compound 7i

Major diastereoisomer





Minor diastereoisomer