Electronic Supplementary Material (ESI) for Chemical Communications.

Electronic Supporting Information

Microfluidic Photoreactor Enables 2-Methylbenzophenone Light-Driven Reactions with Superior Performance

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TABLE OF CONTENTS

A. General Information

The continuous flow reactions were carried out using capillary reactors made with PTFE tubing (0.75 mm I.D., 1.58 mm O.D.) and fitting connections purchased from Sigma-Aldrich. Reagents were pumped using a Syrris Asia pump (https://syrris.com/modules/asia-syringe-pump/). LEDs were purchased from Roithner LaserTechnik GmbH (model LED365-06Z 5.5 mW http://www.roithner-laser.com/index.html). 26 W black bulb and 9W 365 nm bulb lamps were purchased from Amazon (https://www.amazon.it/Foxnovo-sostituzione-lampadina-essiccatore-lampada/dp/B00JKE1T70).

NMR spectra were recorded on Bruker 400 Avance III HD equipped with a BBI-z grad probehead 5mm, Bruker 500 Avance III equipped with a BBI-ATM-z grad probehead 5mm and Bruker DMX 600 equipped with a BBI z-grad probehead 5mm. The chemical shifts (δ) for ^{1}H and ^{13}C are given in ppm relative to residual signals of the solvents ($CHCl_3$ @ 7.26 ppm ^{1}H NMR, 77.16 ppm ^{13}C NMR). Coupling constants are given in Hz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad signal. NMR yields were calculated by using trichloroethylene as internal standard.
High-Resolution Mass Spectra (HRMS) were obtained using Waters GCT gas chromatograph coupled with a time-of-flight mass spectrometer (GC/MS-TOF) with electron ionization (EI) or MicroTOF II (Bruker Daltonics): HPLC-MS-TOF (ESI).
Chromatographic purification of products was accomplished using flash chromatography on silica gel (SiO_2, 0.04-0.063 mm) purchased from Machery-Nagel, with the indicated solvent system according to the standard techniques. Thin-layer chromatography (TLC) analysis was performed on pre-coated Merck TLC plates (silica gel 60 GF254, 0.25 mm). Visualization of the developed chromatography was performed by checking UV absorbance (254nm) as well as with aqueous ceric ammonium molybdate and potassium permanganate solutions. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator.

The authors are grateful to the research support area at Department of Chemical Sciences (DiSC) of the University of Padova. Prof. Tricia Naicker is thanked for proofreading the manuscript.

Determination of Diastereomeric Ratio: The diastereomeric ratio of products **3a**-**p** was determined by ^{1}H-NMR analysis of the crude reaction mixture through integration of diagnostic signals.

Materials: Commercial grade reagents and solvents were purchased at the highest commercial quality from Sigma Aldrich, Alfa Aesar or Fluka and used as received, unless otherwise stated. Carbon dioxide gas was purchased in 18.4 L bottle from Rivoira with a 99.998% purity. 2- Methylbenzophenone **1a**, maleimdes **2a** and **2b**, diethylfumarate **2c**, 3,3-dimethyl-1-(trifluoromethyl)-1,2-benziodoxole **2e**, ethyl-3-coumarincarboxylate **2g,** coumarin 3-carboxylic acid **2n** as well as coumarin **2k** were purchased from Sigma-Aldrich and used as received. Diethyl acetylenedicarboxylate **2d**, was purchased from Fluka. 2-MBP **1b-f** as well as coumarins **2h** and **2i** were synthesised as described previously in literature.[2]

B. SUPPLEMENTARY TABLES

Table S1. Screened reaction partners **2** of 2-methylbenzophenone **1a**, under the developed MFP method.

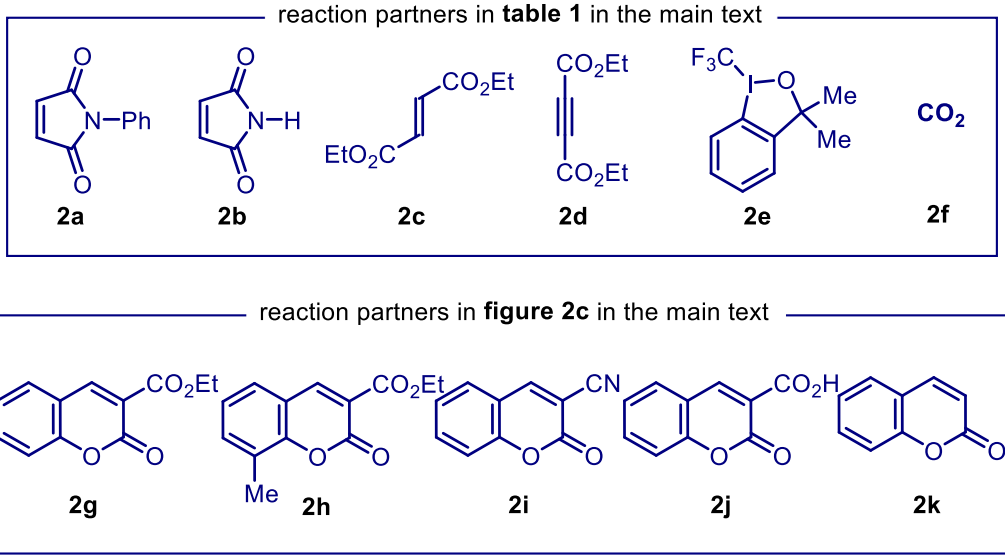


Table S2. Screened 2-methylbenzophenones **1**, under the developed MFP method.

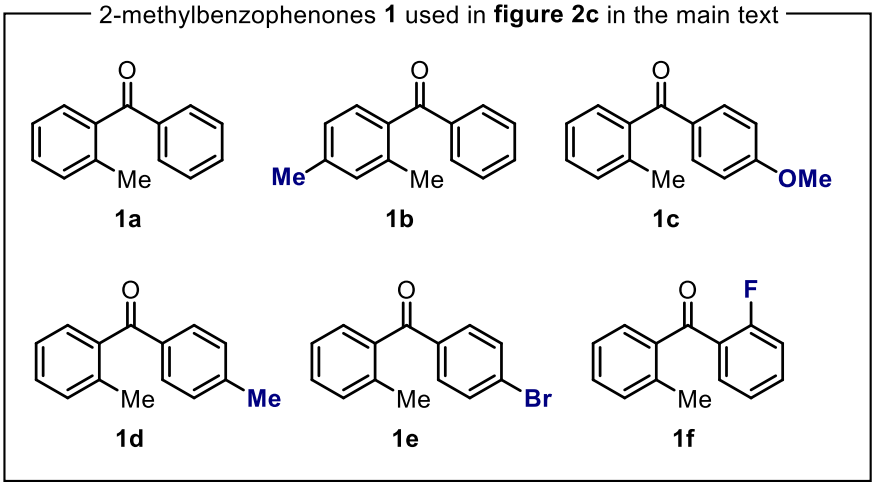


Table S3. Reported procedures for the light-driven reactions of 2-methylbenzophenone **1a** with different acceptors.

Entry	3	reaction conditions	light source	yield (%)	produced mmol/h	reference
1	**3b**	**Solvent**: CyH/PhMe (1mL) **Conc.**: 0.1 mmol/mL **Reaction time**: 24 h *3 equiv. of **1a** used*	Single black LED plate (365 nm)	72	0.003	*Angew. Chem. Int. Ed.*, 2016, **55**, 3313.
2	**3c**	**Solvent:** Benzene (120 mL) **Conc.:** 0.17 mmol/mL **Reaction time**: 24 h	Hanovia 8A-1 high-pressure quartz lamp	58	0.493	*J. Chem. Soc. Perkin Trans.* 1973, **1**, 308.
3	**3d**	**Solvent**: Benzene **Conc**.: not given **Reaction time**: 2 h *1.7 equiv. of **1a** used*	450 Watt Hanovia medium pressure mercury lamp	82	nd	*Can. J. Chem.*, 1995, **73**, 1454.
4	**3e**	**Solvent**: DMSO (1 mL) **Conc**.: 0.03 mmol/mL **Reaction time**: 1 h *3 equiv. of **1a** used*	Relyon LED lamp (3 W, 365 nm)	98	0.029	*Org. Lett.*, 2017, **19**, 4452.
5	**3f**	**Solvent**: DMSO (5 mL) **Conc**.: 0.04 mmol/mL **Reaction time**: 2 h *1 atm of CO_2 used*	CCS, 8332A AC8361 (lamp formed by 100 365 nm LEDs)	89	0.089	*J. Am. Chem. Soc.*, 2015, **137**, 14063.

C. MICROFLUIDIC PHOTO-REACTION SETUP AND BATCH REACTION SETUP

1. MICROFLUIDIC PHOTOREACTOR (MFP) SETUP

Figure S1 (below) shows a schematic representation of the microfluidic reactor employed for the photo-reactions of 2-MBP **1**. In this setup, the solution containing **1a-f** and the acceptor **2a-k** (0.1 M in Toluene or DMSO) was first degassed by bubbling nitrogen for 15 min. Subsequently, the solution under nitrogen atmosphere, was introduced in continuous-flow into the microreactor via double syringe pump (Syrris Asia, see general information). The microfluidic reactor consists of a transparent PTFE capillary (Supelco; internal diameter: 750 µm; inner volume: 400 µL); a 9 W 365 nm bulb lamp (**Figure S2**) or 12x3 W LEDs (**Figure S3**). In both cases, aluminium foil was used to avoid undesired irradiation of the tubing. To maintain a stable reaction temperature, two fans were placed in close proximity to the reactor and the temperature was controlled by a thermometer (25±2 °C).

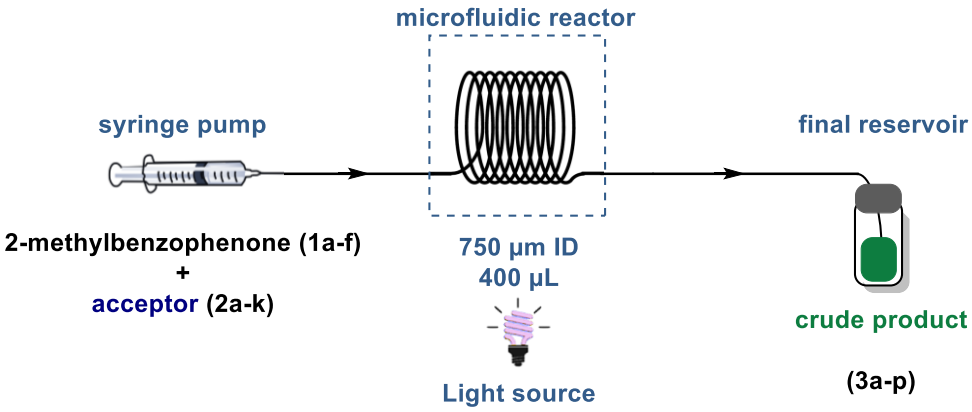


Figure S1. Schematic representation of the MFP setup. ID = internal diameter.

0.1 mL of product solution were introduced into an NMR tube, diluted with $CDCl_3$ and analysed by ^1H NMR in order to calculate the reaction conversion at different flow rates for each reaction. To determine the NMR yields, 0.2 mL of the same solution were introduced into an NMR tube, using trichloroethylene as internal standard.

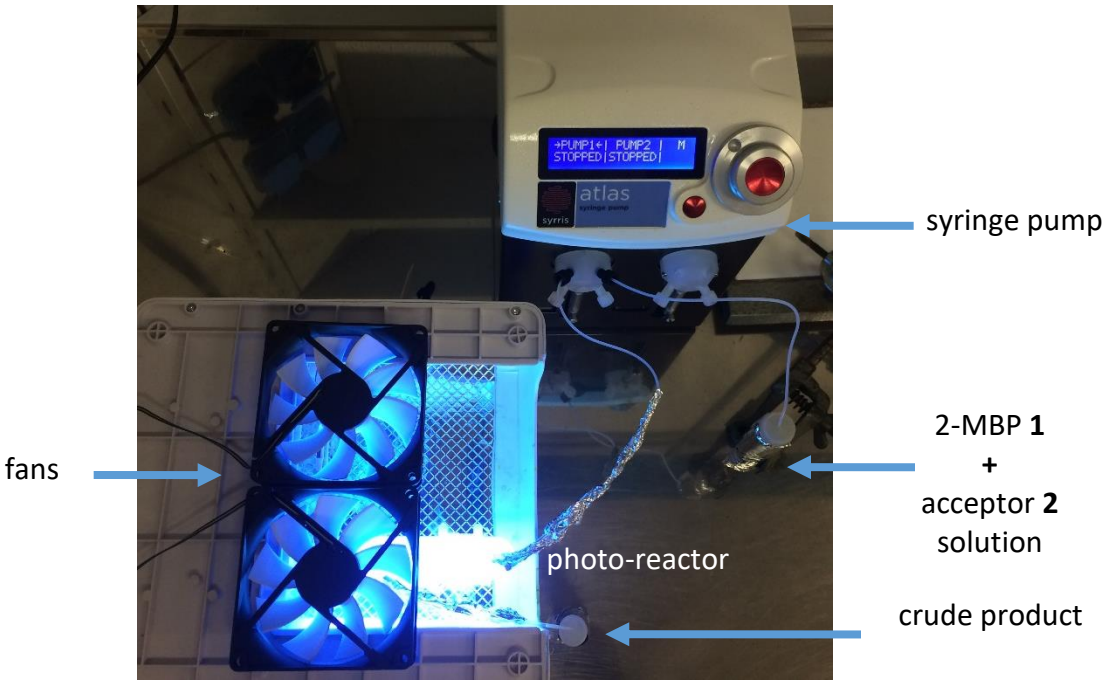


Figure S2. 9W 365 nm bulb MFP setup.

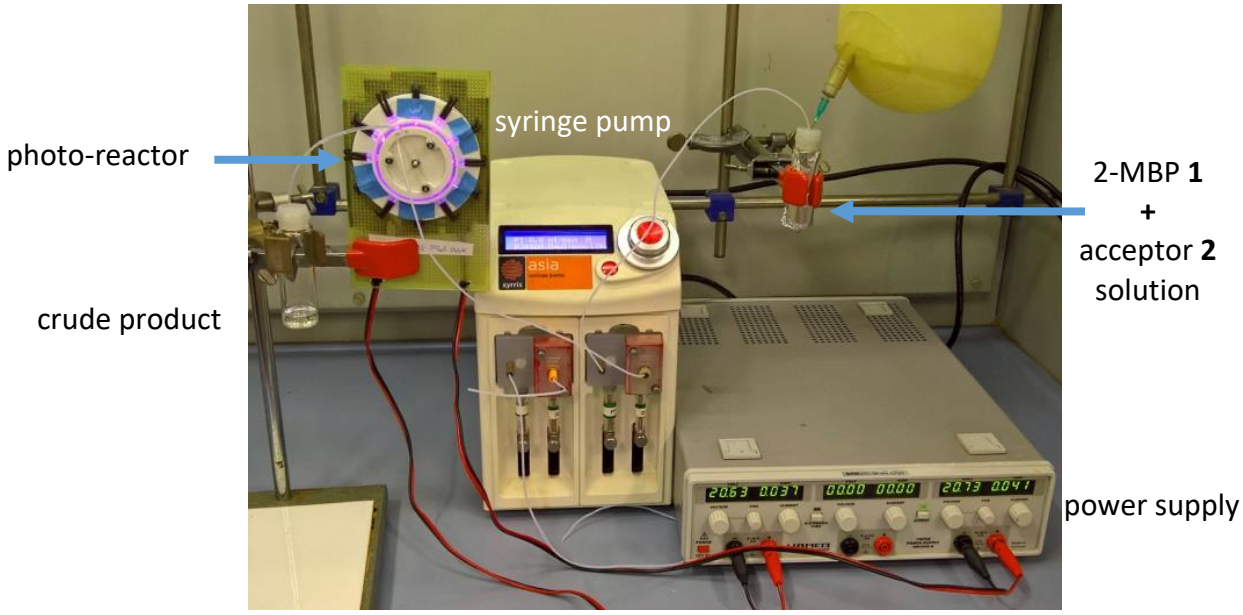


Figure S3. LED ring MFP setup.

The photoreactor shown in figure S3 was formed by a 3D-printed PLA support holding a ring of 12 LEDs pointing toward a PTFE tubing reactor wrapped around a cylindrical support. The distance between the LEDs and the PTFE tubing is 2 mm.

2. BATCH PHOTO-REACTION SETUP

Figure S4 (below) shows the general setup for the batch reactions. Two reaction vials containing the same degassed solution under N_2 atmosphere were placed in front of the 9 W 365 nm bulb (approximatively 1.5 cm distance). The reactions were stirred vigorously until full conversion was detected by ^{1}H-NMR analysis of the crude reaction mixture. To maintain a stable reaction temperature two fans were placed in close proximity to the reaction vials (25±2 °C) and the temperature was controlled by a thermometer.

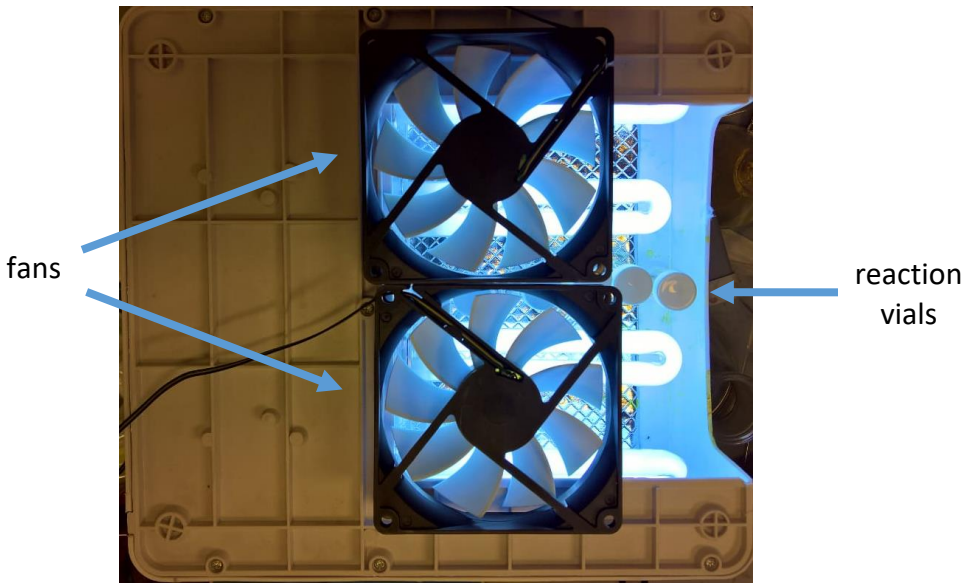


Figure S4. Batch photo-reactions setup.

0.1 mL of product solution were introduced into an NMR tube, diluted with $CDCl_3$ and analysed by ^{1}H NMR in order to calculate the reaction conversion at different flow rates for each reaction. To determine the NMR yields, 0.2 mL of the same solution were introduced into an NMR tube, using trichloroethylene as internal standard.

D. LIGHT SOURCES AND EMISSION SPECTRA

The following spectra were recorded by an AvaSpec ULS3648 high-resolution fiber-optic spectrometer which was placed at a fixed distance of 0.5 cm from the light source.

(more info at: https://www.avantes.com/products/spectrometers/starline/item/209-avaspec-uls3648-high-resolution-spectrometer).

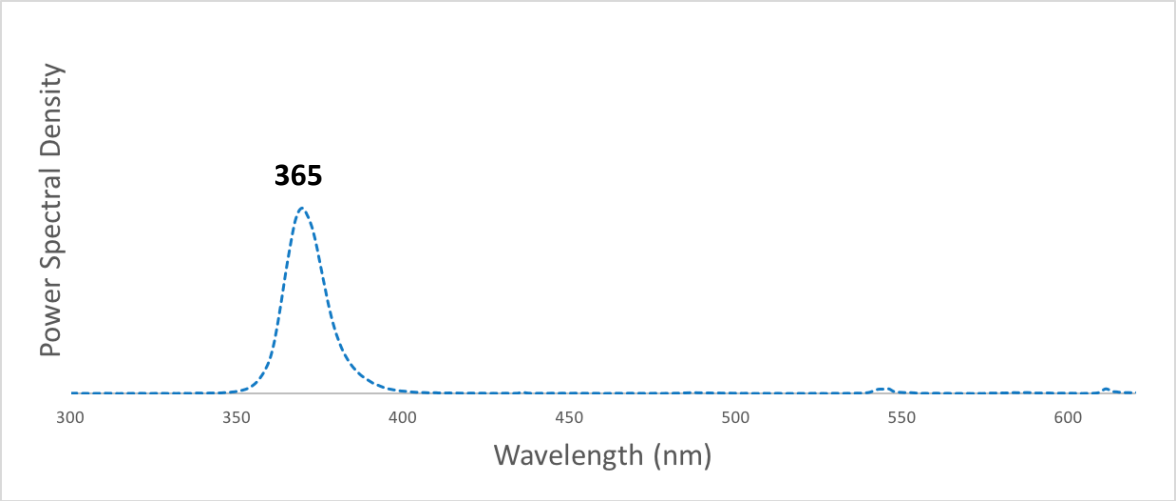


Figure S5. Emission spectra of the LEDs used in this study.

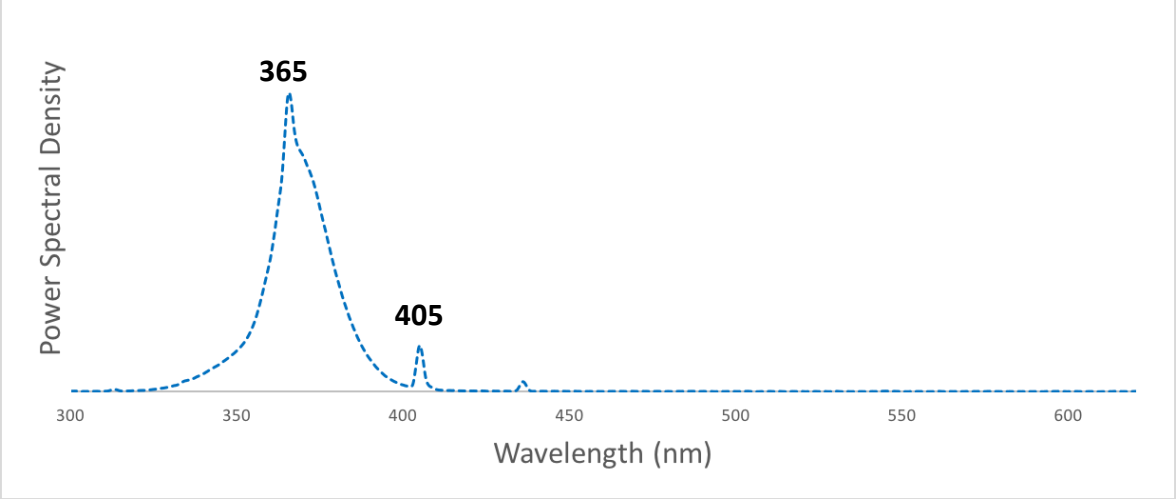


Figure S6. Emission spectra of the 9W 365nm bulb light used in this study.

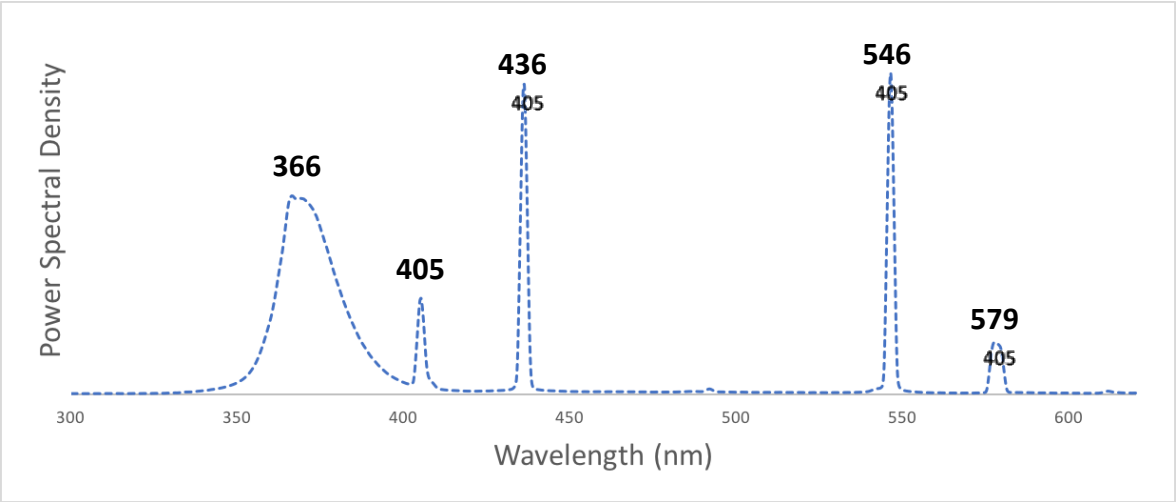
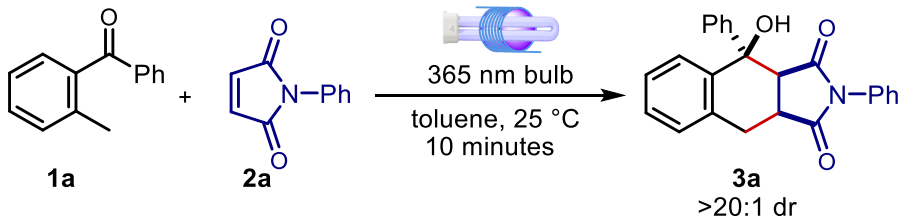


Figure S7. Emission spectra of the 23 W black light bulb (BLB) used in this study.

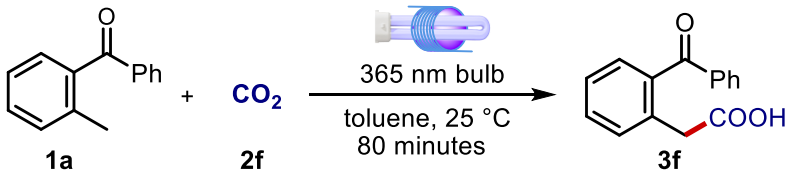
E. GENERAL PROCEDURES FOR THE MICROFLUIDIC LIGHT-DRIVEN REACTIONS

1. GENERAL PROCEDURE



N-Phenylmaleimide **2a** (173.2mg, 1 equivalent, 1.0 mmol) was introduced into a 12 mL vial under nitrogen atmosphere and dissolved with 10 mL of degassed toluene. Then, 2-methylbenzophenone **1a** (196.2 mg, 1 equivalent, 1.0 mmol) was added in one portion and the solution was further bubbled with nitrogen for 5 minutes. The resultant solution was pumped into the MFP irradiated by a 9W 365nm bulb with a residence time of 10 minutes. The product solution was collected into a round bottom flask. Subsequently, the solvent was removed by rotary evaporation furnishing **3a** (white solid) as a single diastereoisomer in >98% yield (365.7 mg, 0.989 mmol).

2. PROCEDURE FOR THE REACTION WITH CO_2

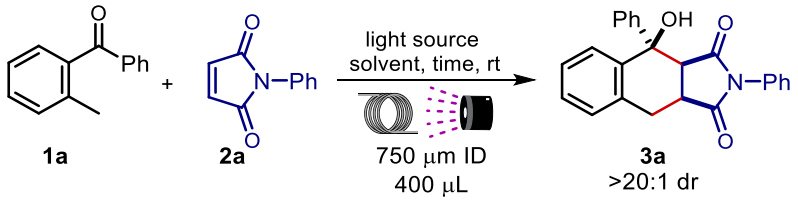


DMSO (5 mL) was bubbled with carbon dioxide **2f** in a 12 mL vial for 10 minutes. Then, 2-methylbenzophenone **1a** (39.2 mg, 0.2 mmol) was added in one portion and the solution was bubbled again with carbon dioxide for 5 minutes. The resultant solution was pumped into the MFP with a residence time of 80 minutes. The product solution was collected into a round bottom flask. The crude reaction mixture was diluted with EtOAc (5 mL) and poured into a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with EtOAc (x3). The combined organic layers were dried with anhydrous $MgSO_4$ and the solvent was removed under rotary evaporation to afford the pure product **3f** as a white solid in >98% of yield (47.5 mg, 0.197 mmol).

F. REACTION OPTIMIZATIONS AND KINETICS PROFILES

For all the microfluidic photo-reactions investigated in the present work, different reaction conditions were tested in function of the light source and power, solvent, reagent concentration, flow rate and residence time. The results obtained were compared to the results of the reactions performed in batch.

Table S4. Exploratory studies of the microfluidic light-driven reaction between 2-methylbenzophenone **1a** and N-Phenylmaleimide **2a** in MFP conditions.



entry	light source	solvent	**1a** (equiv.)	residence time (min)	conversion[a] (%)	yield (%)[b]
1	LED (x12)	toluene	10	8	20	-
2	LED (x12)	toluene	10	80	>99	94
3	LED (x12)	toluene	2	8	26	-
4	LED (x6)	toluene	2	80	56	51
5	LED (x12)	toluene	2	80	>99	95
6	LED (x12)	toluene	1	8	20	-
7	LED (x12)	toluene	1	80	>99	95
8	BLB	toluene	2	80	27	-
9	365nm bulb	toluene	2	5.33	>99	95
10	**365nm bulb**	**toluene**	**1**	**10**	**>99**	**>98[d]**
11	365nm bulb	ClPh	1	10	93	89[e]
12	365nm bulb	*o*-Cl_2Ph	1	10	97	93[e]
13	365nm bulb	DMSO	1	10	89	86[e]
14	365nm bulb	MeCN	1	10	66	-

entry	light source	solvent	**1a** (equiv.)	residence time (min)	conversion[a] (%)	yield (%)[b]
15	365nm bulb	*n*-hexane	1	10	88	nd
16	batch[c]	toluene	1	10	-	-
17	batch[c]	toluene	1	60	5	-
18	batch[c]	toluene	1	120	17	-
19	batch[c]	toluene	1	480	>99	95
20[f]	batch[c]	toluene	1	480	55	52[e]
21[g]	batch[c]	toluene	1	480	7	<5[e]
22	OFF	toluene	1	480	-	-

[a] Inferred by ^{1}H-NMR analysis of the crude mixture. [b] Isolated yield after flash chromatography. [c] The reactions performed in batch were irradiated by a 9W 365 nm bulb as reported in figure S4, section C2. [d] Isolated yield after solvent evaporation. [e] NMR yield calculated using trichloroethylene as internal standard. [f] The reaction was setup at 0.2 mmol scale. [g] The reaction was setup at 0.5 mmol scale.

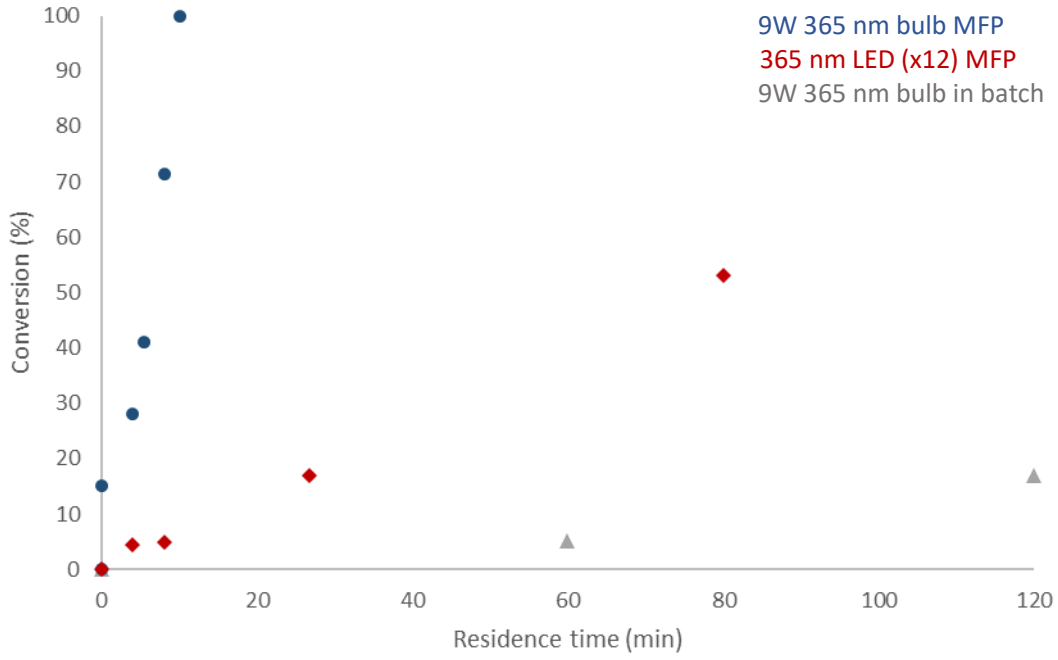
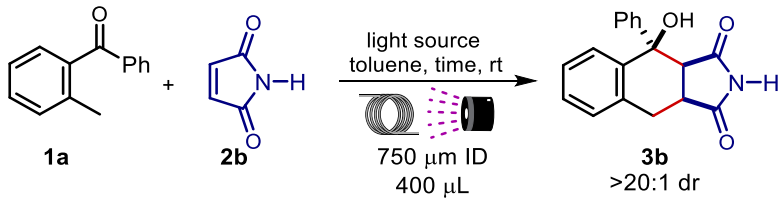


Figure S8. Kinetic profiles of the reactions between **1a** and **2a** in toluene using different light sources and setups. Reactions performed under the 9W 365 nm bulb MFP setup (blue circles); reactions performed under the 365 nm LEDs (x12) MFP setup (red diamonds), reactions performed under the 9W 365 nm bulb in batch (grey triangles).

Table S5. Exploratory studies of the microfluidic light-driven reaction between 2-methylbenzophenone **1a** and maleimide **2b** in MFP conditions.



1a **2b** **3b** >20:1 dr

Entry	Light source	**1a** (equiv.)	Residence time (min)	Conversion[a] (%)	Yield (%)[b]
1	LED (x12)	1	8	13	-
2	LED (x12)	1	80	>99	>98[d]
3	365 nm bulb	1	8	90	86[e]
4	**365 nm bulb**	**1**	**16**	**>99**	**>98[d]**
5	batch[c]	1	16	<5	-
6	batch[c]	1	240	63	57[e]
7	batch[c]	1	500	>99	92

[a] Inferred by ^{1}H-NMR analysis of the crude mixture. [b] Isolated yield after flash chromatography. [c] The reactions performed in batch were irradiated by a 9W 365 nm bulb as reported in figure S4, section C2. [d]Isolated yield after solvent evaporation. [e]NMR yield calculated using trichloroethylene as internal standard.

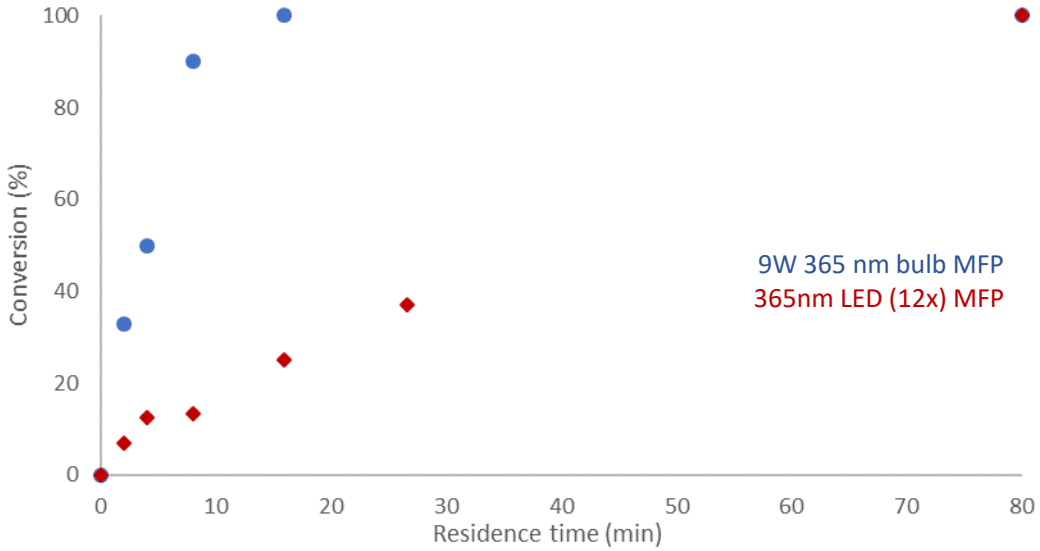
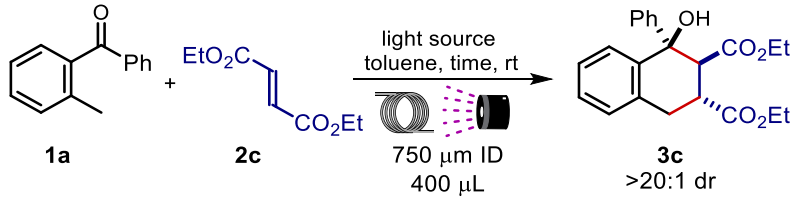


Figure S9. Kinetic profiles of the reaction between **1a** and **2b** using different light sources and setup. Reactions performed under the 9W 365 nm bulb MFP setup (blue circles); reactions performed under the 365 nm LEDs (x12) MFP setup (red diamonds).

Table S6. Exploratory studies of the microfluidic light-driven reaction between 2-methylbenzophenone **1a** and diethyl fumarate **2c** in MFP conditions.



1a **2c** **3c** >20:1 dr

Entry	Light source	**1a** (equiv.)	Residence time (min)	Conversion[a] (%)	Yield (%)[b]
1	365nm bulb	1	8	42	[40e]
2	365nm bulb	1	15	63	58
3	**365nm bulb**	**1**	**26.66**	**>99**	**>98**[d]
4	365nm bulb	1	40	>99	90
5	batch[c]	1	30	-	-
6	batch[c]	1	350	53	42[e]
7	batch[c]	1	600	>99	60[e]

[a] Inferred by ^{1}H-NMR analysis of the crude mixture. [b] Isolated yield after flash chromatography. [c] The reactions performed in batch were irradiated by a 9W 365 nm bulb as reported in figure S4, section C2. [d]Isolated yield after solvent evaporation. [e]NMR yield calculated using trichloroethylene as internal standard.

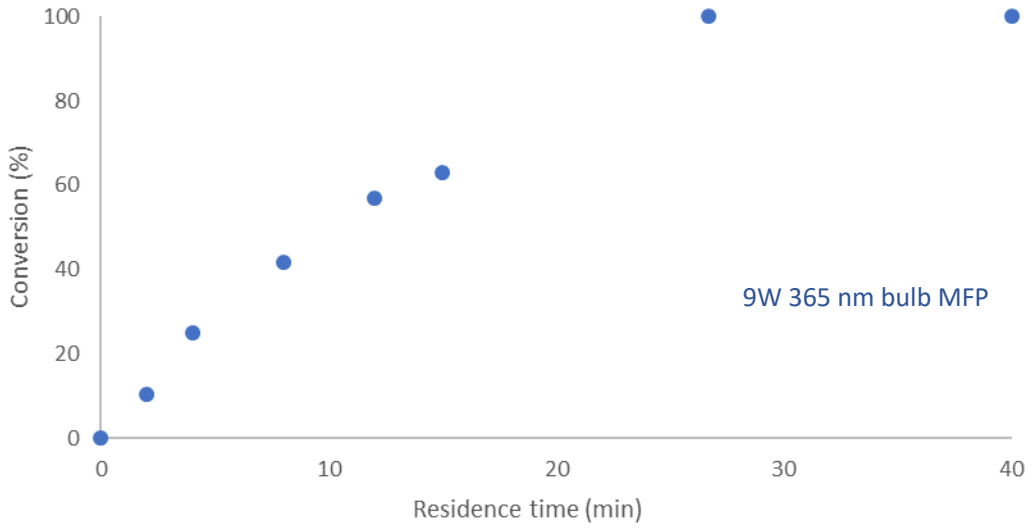
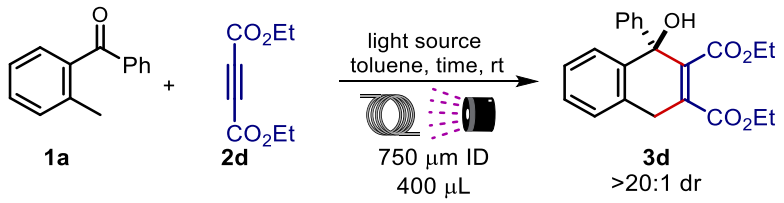


Figure S10. Kinetic profiles of the microfluidic photo-reaction between **1a** and **2c** performed in toluene under the 9W 365 nm bulb in the MFP setup.

Table S7. Exploratory studies of the microfluidic light-driven reaction between 2-methylbenzophenone **1a** and diethyl acetylenedicarboxylate **2d** in MFP conditions.



Entry	Light source	**1a** (equiv.)	Residence time (min)	Conversion[a] (%)	Yield (%)[b]
1	365 nm bulb	1	8	61	57
2	365 nm bulb	1	26.66	90	86
3	**365 nm bulb**	**1**	**40**	**>99**	**>98[d]**
4	365 nm bulb	1	40	<5	-
5	365 nm bulb	1	600	52	43[e]
6	batch[c]	1	1200	95	45

[a] Inferred by ^{1}H-NMR analysis of the crude mixture. [b] Isolated yield after flash chromatography. [c] The reactions performed in batch were irradiated by a 9W 365 nm bulb as reported in figure S4, section C2. [d]Isolated yield after solvent evaporation. [e]NMR yield calculated using trichloroethylene as internal standard.

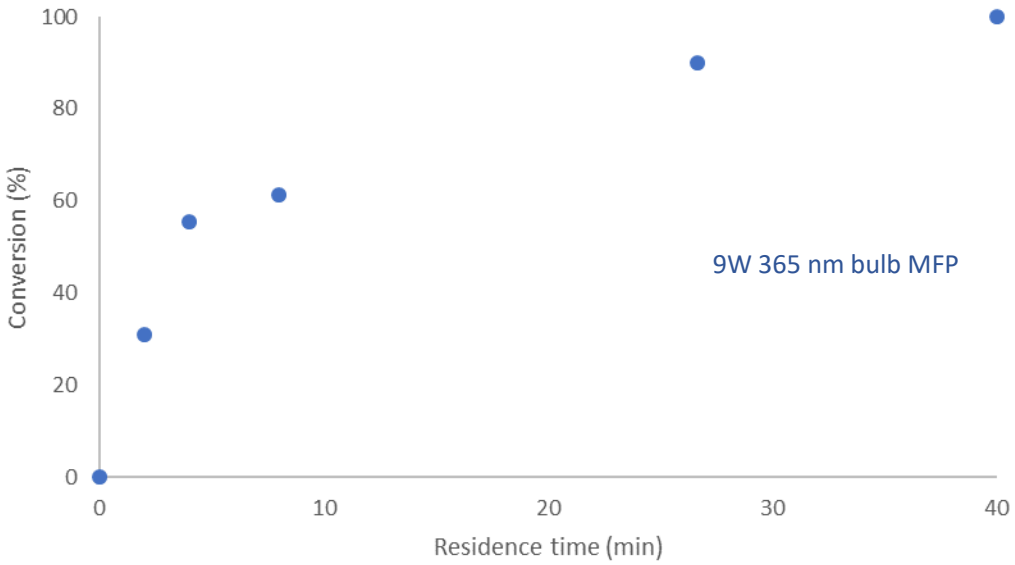
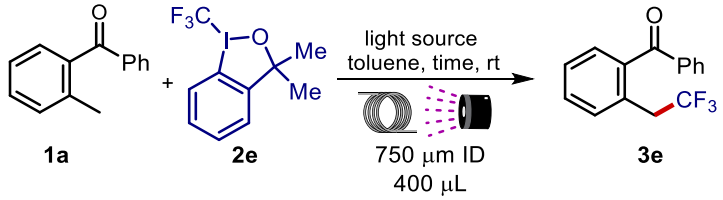


Figure S11. Kinetic profiles of the microfluidic photo-reaction between **1a** and **2d** performed in toluene under 9W 365 nm bulb in the MFP setup.

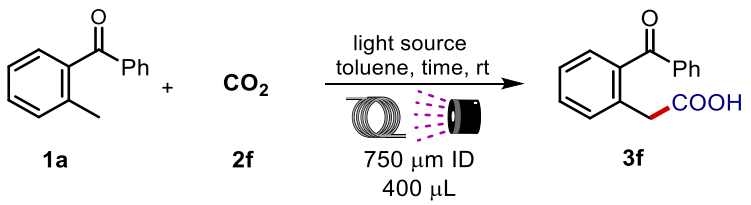
Table S8. Exploratory studies of the light-driven reaction between 2-methylbenzophenone **1a** and 3,3-dimethyl-1-(trifluoromethyl)-1,2-benziodoxole **2e** in MFP conditions.



Entry	Light source	**1a** (equiv.)	Residence time (min)	Conversion[a] (%)	Yield (%)[b]
1	LED (x12)	2	4	52	-
2	LED (x12)	2	8	>99	90
3	**365nm bulb**	**1**	**8**	**>99**	**95[d]**
4	batch[c]	1	8	<5	-
5	batch[c]	1	60	55	52[e]
6	batch[c]	1	120	>99	70

[a] Inferred by ^{1}H NMR analysis of the crude mixture. [b] Isolated yield after flash chromatography. [C] The reactions performed in batch were irradiated by a 9W 365 nm bulb as reported in figure S4, section C2. [d]Isolated yield after solvent evaporation. [e] NMR yield calculated using trichloroethylene as internal standard.

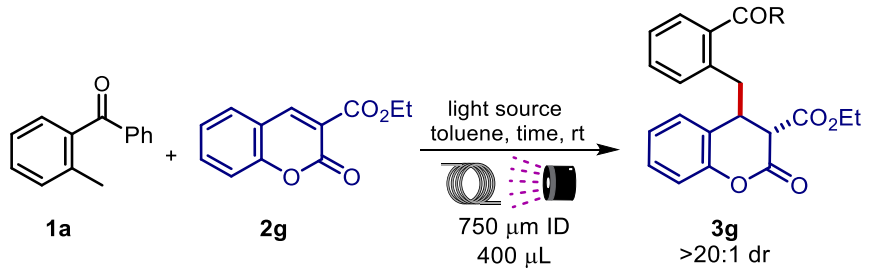
Table S9. Exploratory studies of the light-driven reaction between 2-methylbenzophenone **1a** and carbon dioxide **2f** in MFP conditions.



Entry	Light source	**1a** (equiv.)	Residence time (min)	Conversion[a] (%)	Yield (%)[b]
1	365nm bulb	1	8	17	-
2	365nm bulb	1	27	54	-
3	**365nm bulb**	**1**	**80**	**>99**	**98**
4	LED (x12)	1	80	82	-
5	batch[c]	1	1400	79	75

[a] Inferred by ^{1}H NMR analysis of the crude mixture. [b] Isolated yield after flash chromatography. [C] The reactions performed in batch were irradiated by a 9W 365 nm bulb as reported in figure S4, section C2.

Table S10. Exploratory studies of the light-driven reaction between 2-methylbenzophenone **1a** and ethyl-3-coumarincarboxylate **2g** in MFP conditions.



Entry	Light source	**1a** (equiv.)	Residence time (min)	NMR yield[a] (%)	Isolated Yield (%)[b]
1	LED (x12)	2	8	<5	-
2	LED (x12)	2	26.66	66	48
3	365nm bulb	2	8	17	-
4	365nm bulb	2	26.66	95	76
5	365nm bulb	1.5	18	80	67
6	**365nm bulb**	**1.5**	**26.66**	**90**	**75**
7	365nm bulb	1.5	55	80	-
8	365nm bulb	1.5	80	68	-
9	365nm bulb	1	26.66	81	68

10	LED (x12)	1.5	26.66	72	61
11	batch[c]	1	26.66	-	-
12	batch[c]	1	80	5	-
13	batch[c]	1	600	29	17
14	batch[c]	1	1200	45	32

[a] Inferred by ^{1}H NMR analysis of the crude mixture using trichloroethylene as internal standard. [b] Isolated yield after flash chromatography. [c] The reactions performed in batch were irradiated by a 9W 365 nm bulb as reported in figure S4, section C2.

In order to calculate the isolated yields reported in table S10 and in figure 2c in the main text, 1 mL of the product solutions were collected, analysed by ^{1}H-NMR and GC mass and subsequently subjected to flash chromatography.

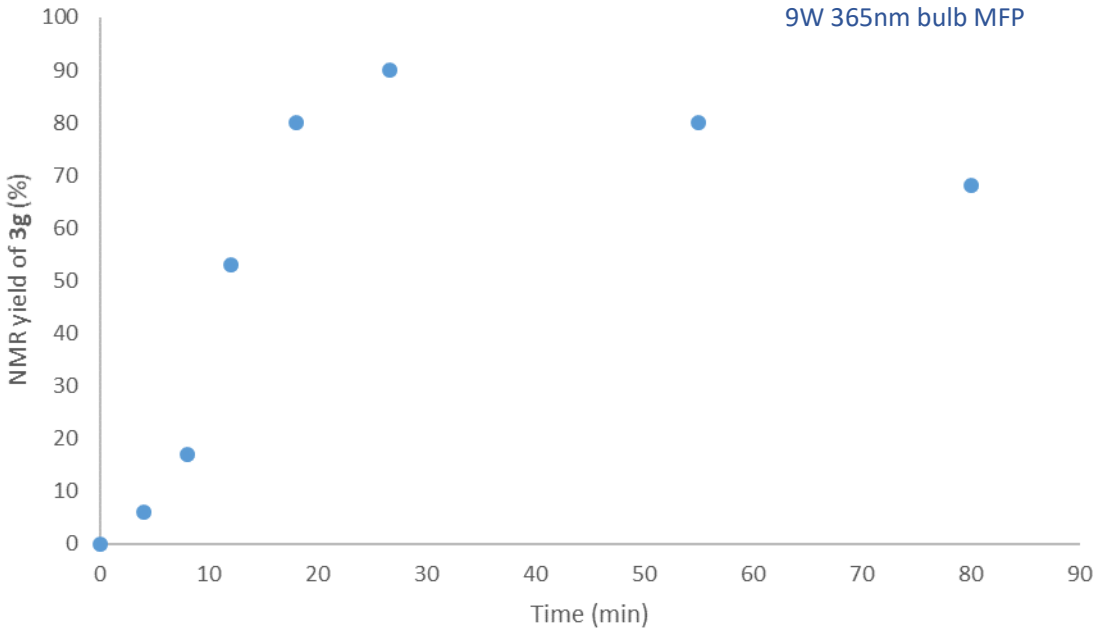


Figure S12. Kinetic profiles of the microfluidic photo-reaction between **1a** (1.5 equiv.) and **2g** (1 equiv.) performed in toluene using 9W 365 nm bulb MFP.

*As shown in figure S12, over irradiation of the crude reaction mixture provides lower values of NMR yield of the benzylated product **3g**, indicating that a light-mediated decomposition process is operative.*

G. SPECTROSCOPIC INVESTIGATIONS

1. NMR STUDIES

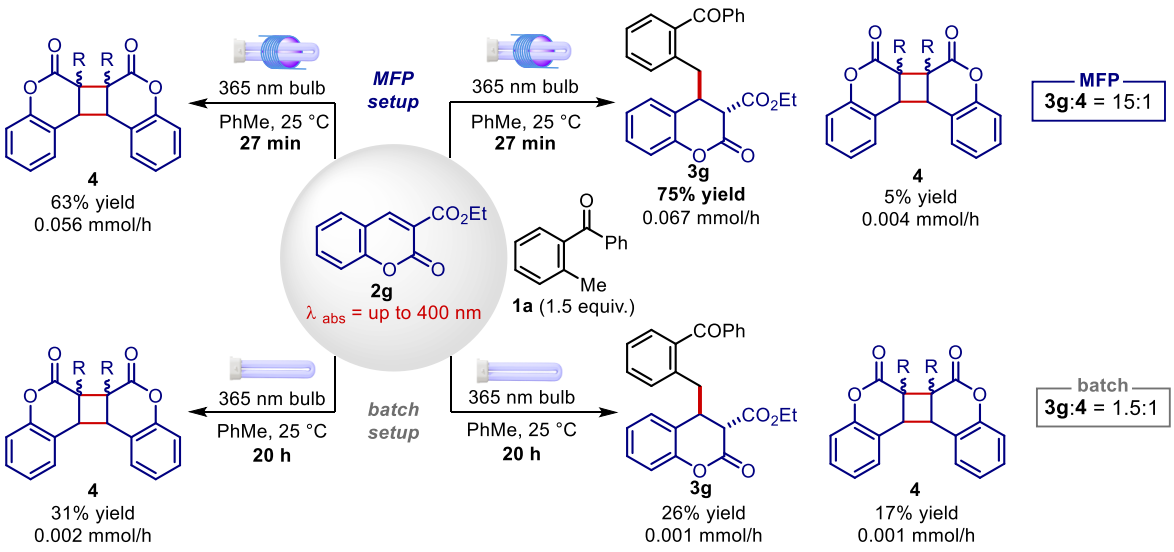


Figure S13. Comparison between the photo-reactions of ethyl-3-coumarincarboxylate **2g** under the developed MFP (top equations) vs in batch (bottom equations), in the absence (left) and in the presence of 2-methylbenzophenone **1a** (right).

In order to rationalize the superior performances observed for the MFP setup compared to batch setup a series of control experiments were performed under NMR tubes and analysed by ^{1}H-NMR at subsequent intervals of time.

*The fates of 2-methylbenzophenone **1a**, ethyl 3-coumarincarboxylate **2g** and product **3g** under light irradiation in batch conditions were evaluated by ^{1}H-NMR analysis.*

0.075 mmol of 2-methylbenzophenone **1a**, 0.05 mmol of ethyl-3-coumarincarboxylate **2g**, and 0.05 mmol of the product **3g** were independently introduced into NMR tubes, dissolved with 0.5 mL of toluene_d_8 (0.1 M) degassed with nitrogen (10 minutes) and irradiated with a 9W 365nm bulb, in an analogous manner compared to the batch reactions. NMR spectra of each sample were recorded in subsequent intervals of time.

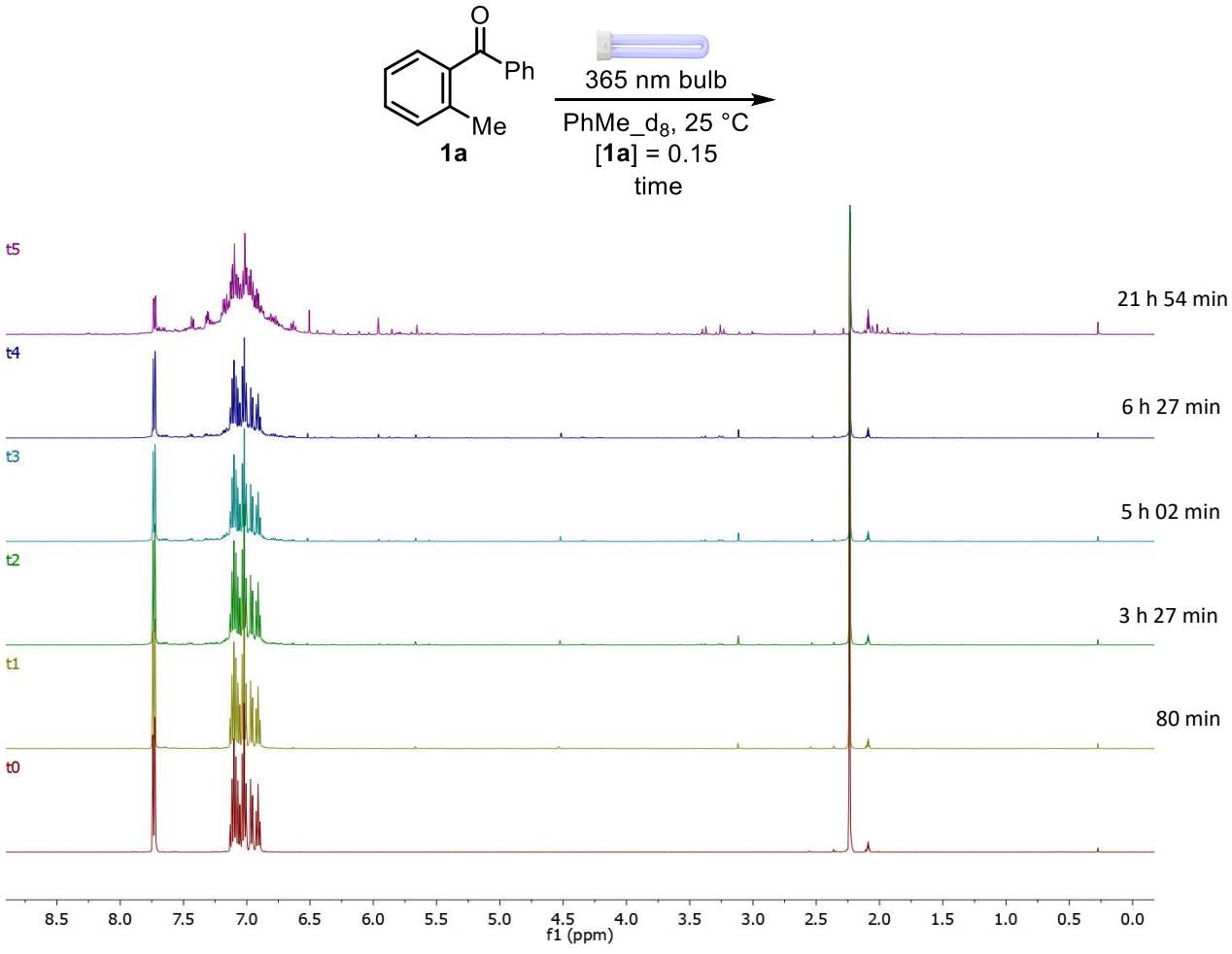


Figure S14. NMR spectra of 2-methylbenzophenone **1a** in toluene_d_8 (0.15 M) irradiated with 9W 365nm bulb lamp over time.

*As shown in figure S14 2-methylbenzophenone **1a** is not affected by extensive light-irradiation. Even after more than 29 h **1a** is still the major compound present in the solution.*

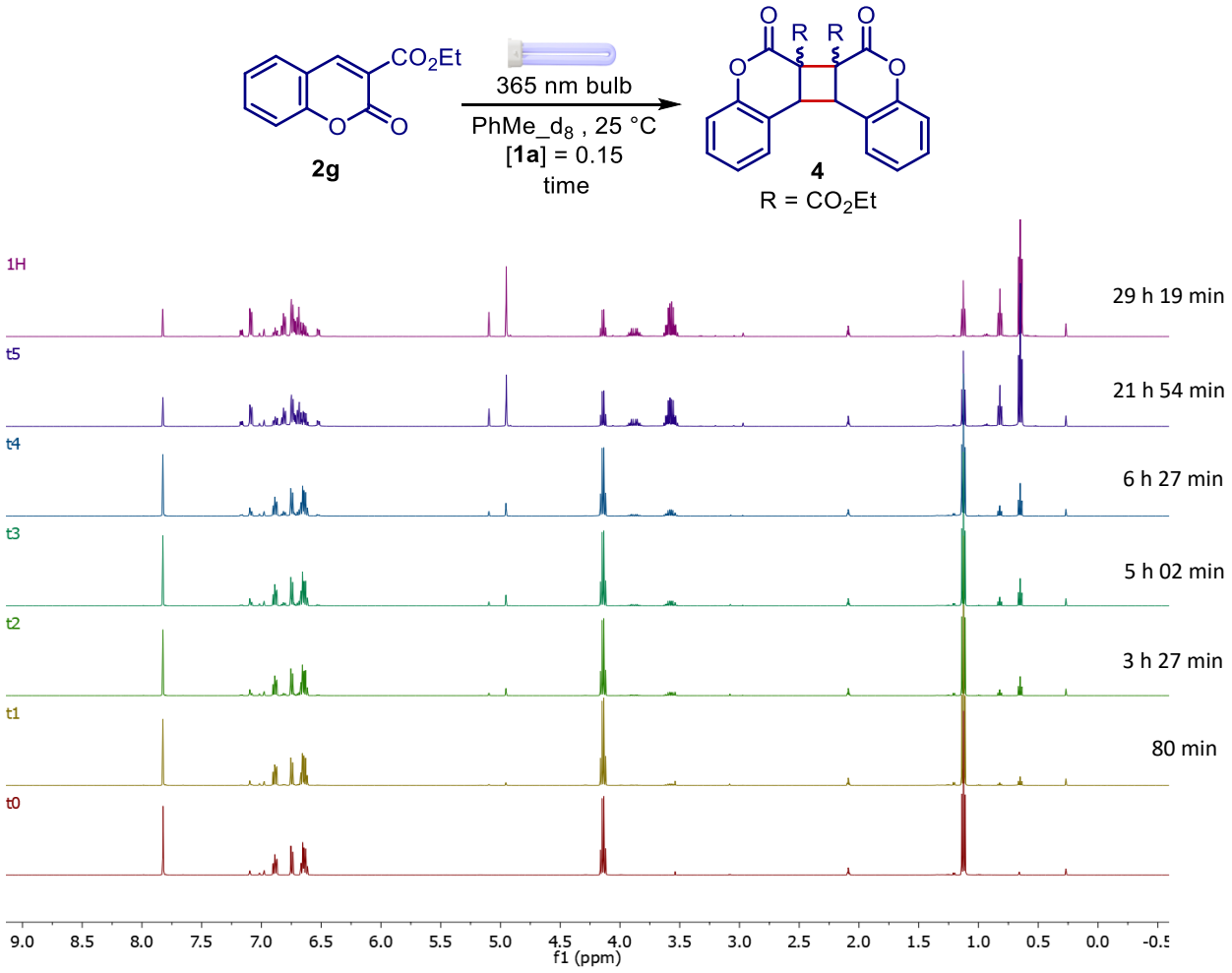


Figure S15. NMR spectra of ethyl-3-coumarincarboxylate **2g** in toluene_d_8 (0.1 M) irradiated with 9W 365nm bulb over time.

*As shown in figure S15, under light-irradiation, ethyl 3-coumarincarboxylate **2g** is converted into a diastereomeric mixture of the dimer **4** by means of light-driven [2+2]-cycloaddition (see reference 19 in the main text).*

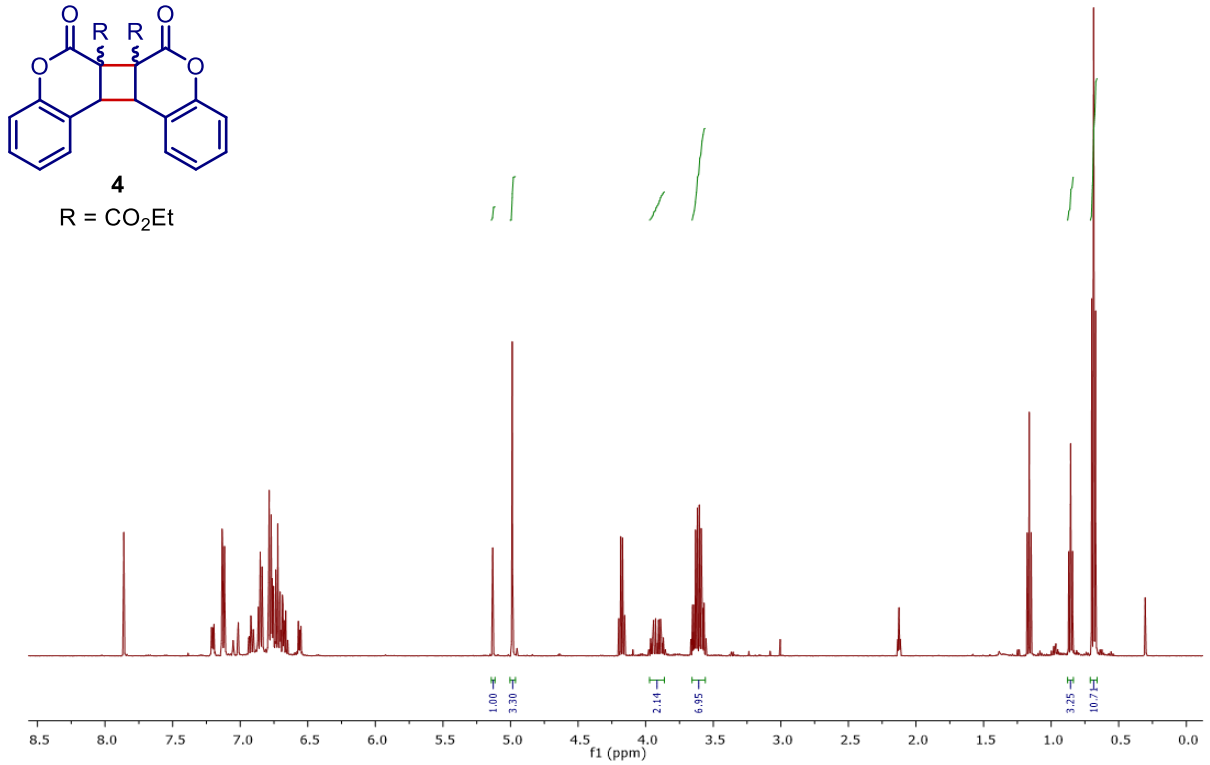


Figure S16. Crude NMR spectrum of **2g** in toluene_d_8 (0.1 M) irradiated with 9W 365 nm bulb lamp for 29h 19 min. Formation of two diastereoisomers of **4** with 80% conversion in 3.3:1 ratio.

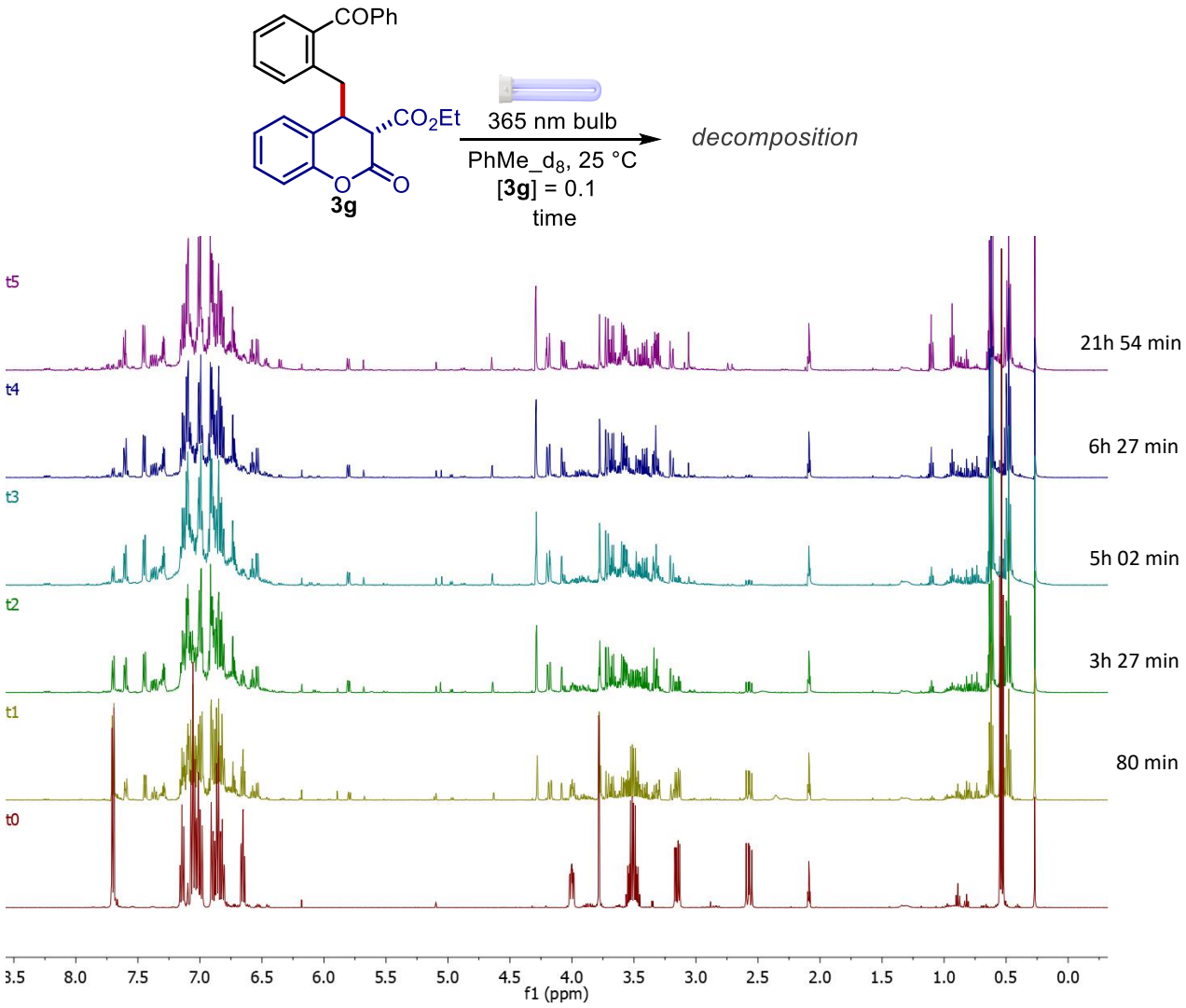


Figure S17. NMR spectra of the product **3g** in toluene_d_8 (0.1 M) irradiated with 9W 365nm bulb over the indicated time.

*As shown in figure S17, under light-irradiation, product **3g** rapidly decomposes into a complex mixture of undefined compounds. After 6h, only traces of the starting **3g** are observed.*

2. ABSORPTION SPECTRA STUDIES

All the absorption spectra were recorded using an Agilent Cary 100 UV-Vis spectrophotometer. The spectra were recorded in toluene using the same concentrations as in the reaction conditions.

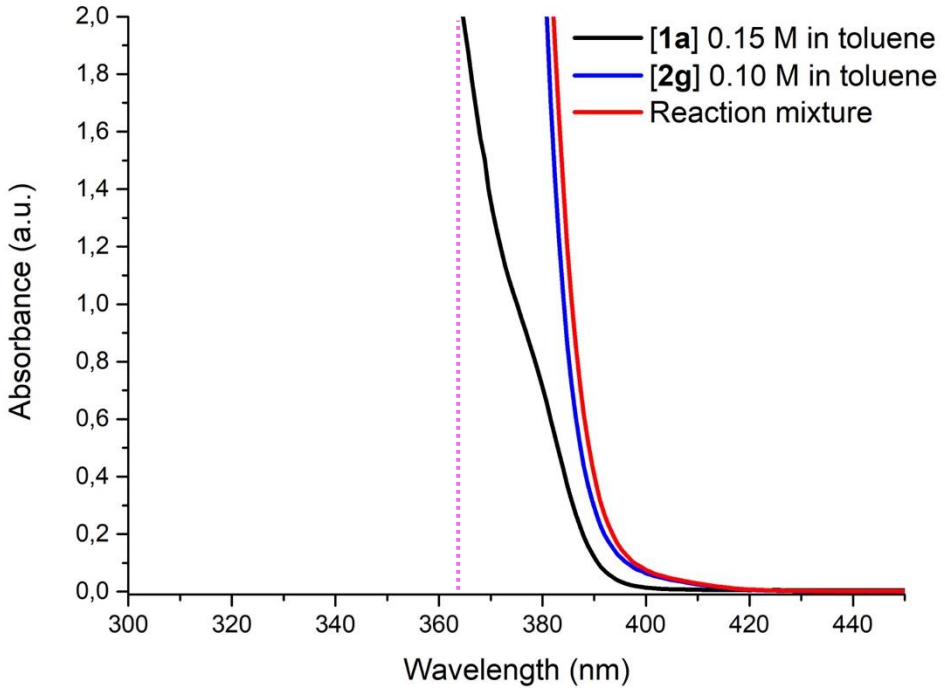


Figure S18. Comparison of the absorption spectra of 2-methylbenzophenone **1a** (black line, [**1a**] = 0.15 M), ethyl-3-coumarincarboxylate **2g** (blue line, [**2g**] = 0.1 M), and the reaction mixture (red line, [**1a**] = 0.15 M, [**2g**] = 0.1 M). The operative wavelength in the present work (365 nm) is showed as a dotted pink line.

*Due to the high concentration of the solutions, short light path cuvettes (1 mm Hellma Quartz SUPRASIL®) were employed to avoid fast signal saturation. As shown in figure S18 both 2-methylbenzophenone **1a** and ethyl-3-coumarincarboxylate **2g** are able to absorb the 365 nm light emitted by the 9W 365 nm bulb used in this study.*

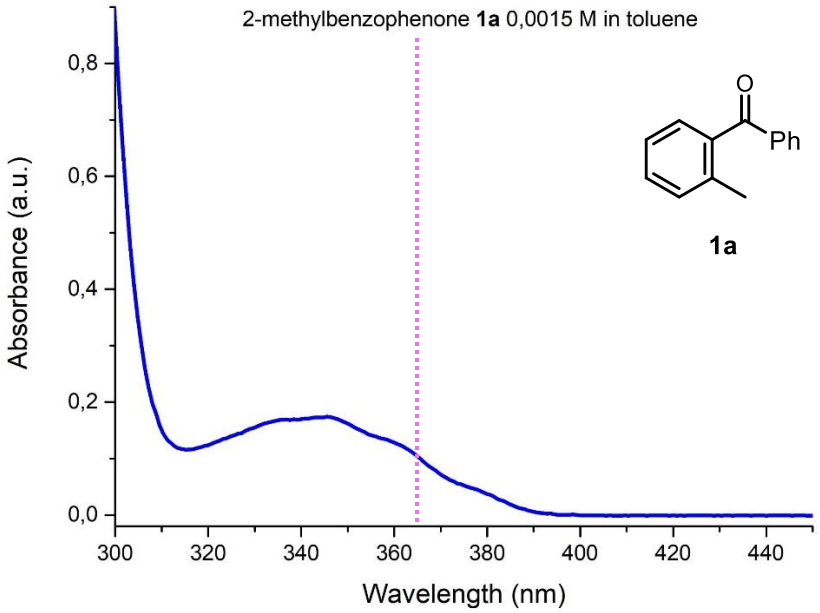


Figure S19. Absorption spectrum of 2-MBP **1a**. The spectrum was recorded for a degassed solution of toluene [**1a**] = 1.5 x 10^{-3}M into a 10 mm quartz cuvette. The operative wavelength in the present work (365 nm) is showed as a dotted pink line.

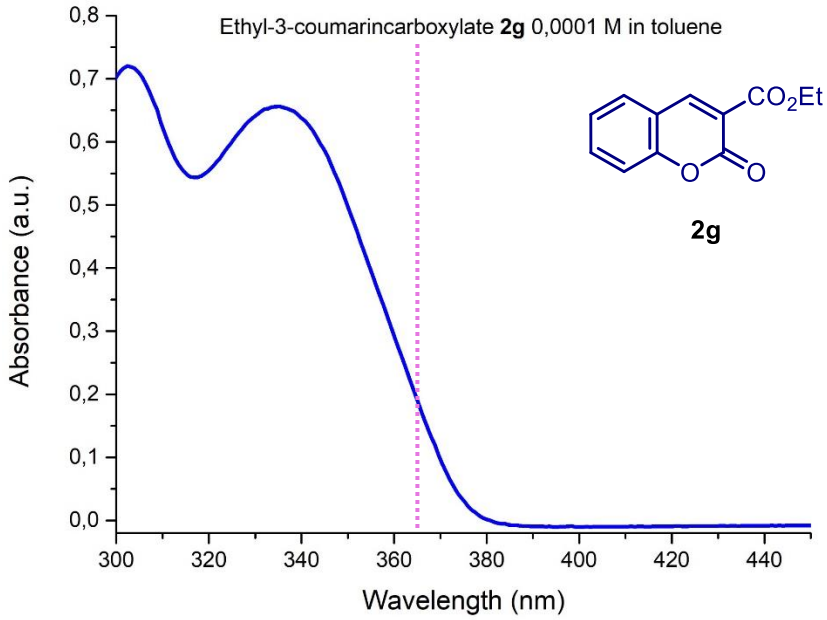


Figure S20. Absorption spectrum of ethyl-3-coumarincarboxylate **2g**. The spectrum was recorded for a degassed solution of toluene [**2g**] = 1.0 x 10^{-4} M into a 10 mm quartz cuvette. The operative wavelength in the present work (365 nm) is showed as a dotted pink line.

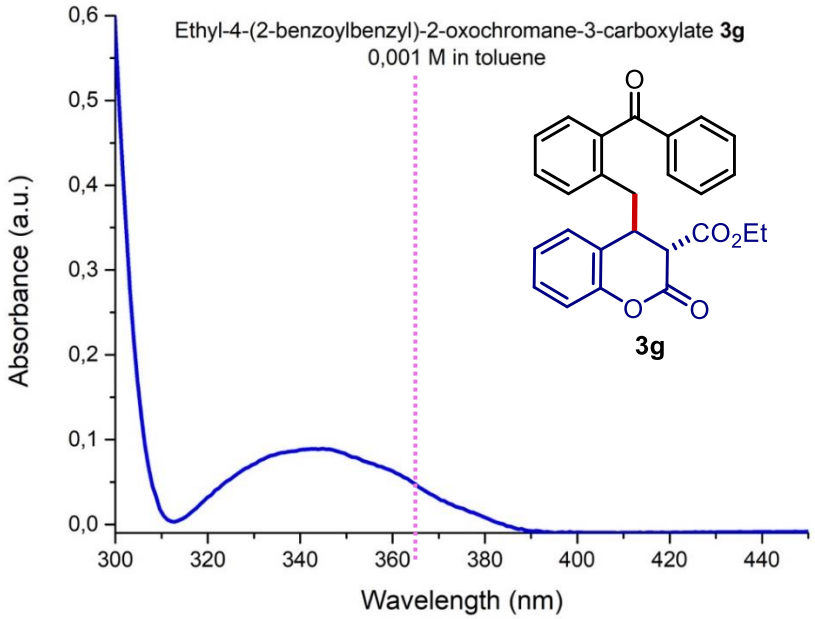


Figure S21. Absorption spectrum of ethyl-4-(2-benzoylbenzyl)-2-oxochromane-3-carboxylate **3g**. The spectrum was recorded for a degassed solution of toluene [**3g**] = 1.0 x 10^{-3} M into a 10 mm quartz cuvette. The operative wavelength in the present work (365 nm) is showed as a dotted pink line.

3. EMISSION SPECTRA STUDIES

The emission spectra were recorded using an Agilent Cary Eclipse Fluorescence Spectrophotometer. The spectra were recorded in degassed toluene irradiating at 340 nm wavelength.

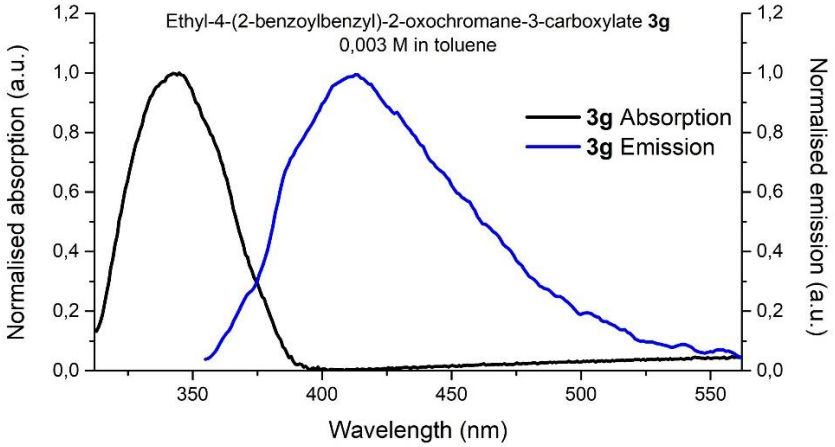


Figure S22. Normalised absorption spectrum (black line) and emission spectrum (blue line; excitation λ = 340 nm) of ethyl-4-(2-benzoylbenzyl)-2-oxochromane-3-carboxylate **3g** in toluene. The spectra were recorded for a degassed solution of [**3g**] = 3.5 x 10^{-3} M in toluene into a 10x10 mm quartz Hellma® fluorescence cuvette in an Agilent Cary Eclipse Fluorescence Spectrophotometer.

*The excitation wavelength (340 nm) was selected as the maximum absorbance of product **3g**. The concentration of the solution of **3g** was chosen in order to reach 0.3 units of absorbance at 340 nm. In order to avoid any presence of O_2, the solution was degassed by bubbling argon for 5 min prior the measurements.*

4. PHOTON FLOW MEASUREMENTS

As reported by Giménez et al., the photon flow of a photochemical reactions (φ) can be measured through the use of a 2-nitrobenzaldehyde (NBA) chemical actinometer.[6]
The actinometry experiments were conducted under the setups described in Figure S2 and Figure S4 and using an XS Instruments® pH 80 pH-meter.

Following the reported procedure, a solution of 0.1 M NBA and 0.005 M NaOH in H_2O/EtOH 1:1 was prepared and irradiated for the indicated time under both MPF and batch setups.
During all the actinometry experiments, the pH of the irradiated actinometric solution was measured at different residence times. Plotting the pH against time, a titration curve was obtained. The equivalence point was determined as where $\Delta^2pH/\Delta t^2$ crosses the y=0 axis.

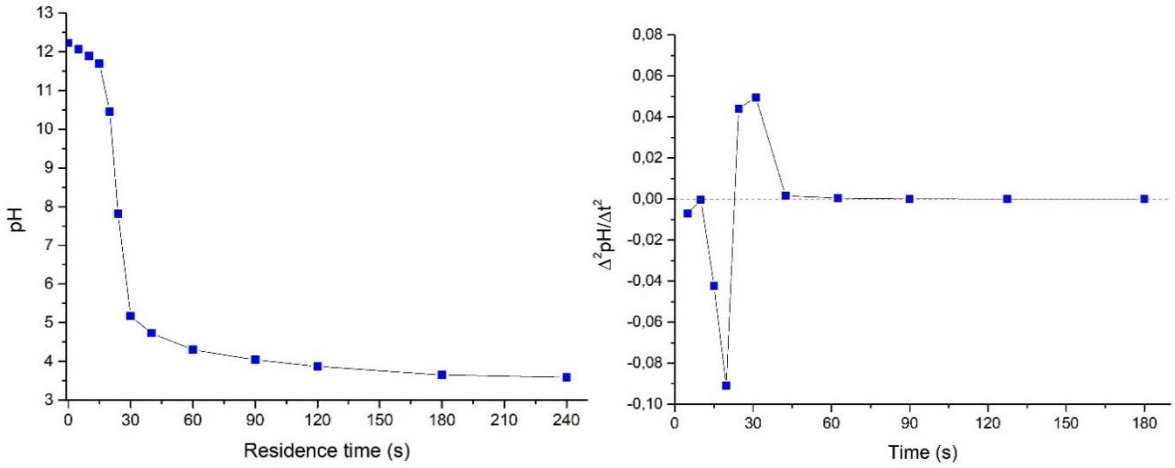


Figure S23. Plot of the pH of the reaction solution at different residence times in MFP setup (left) and plot of its second derivative (right). The equivalence point is estimated at t = 22.9 seconds. Note that every point represents the average of 3 runs.

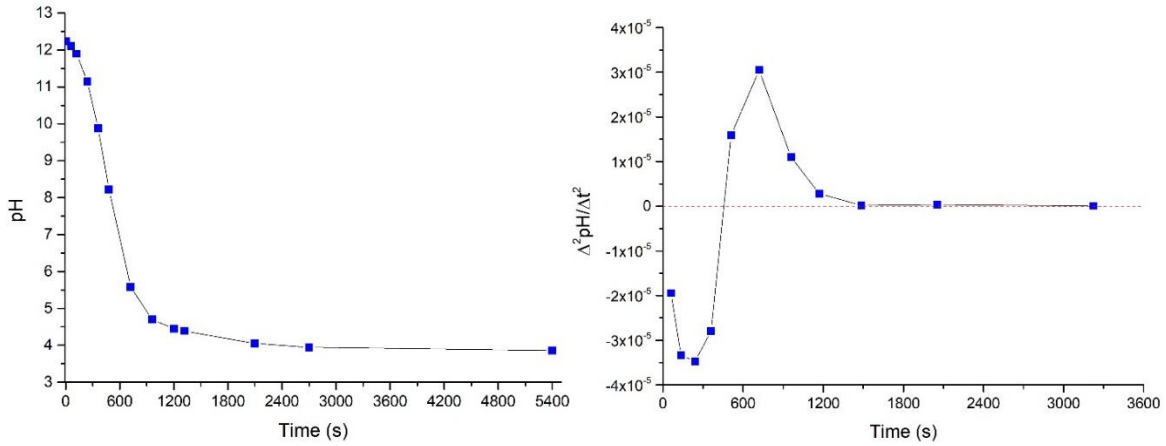


Figure S24. Plot of the pH of the reaction solution at different times in the batch reactor (left) and plot of its second derivative (right). The equivalence point is estimated at t = 455.6 seconds. Note that every point represents the average of 3 runs.

Following the reported procedure, the time to reach the equivalence point of the titration was chosen as the parameter to compare the two systems.[6] As detailed in section X of the ESI, the microfluidic photoreactor has a total volume of 0.4 mL. Contrary, a volume of 1.5 mL was used for the actinometric experiments for the batch setup (instead of 1 mL volume reported in section X) in order to facilitate the measurements in the *XS Instruments® pH 80* pH-meter.

The equivalence point for the MFP setup was found at 23 sec, corresponding to $2.0 \cdot 10^{-6}$ moles of HNB produced. While the equivalence point was found at 456 sec for the batch setup, corresponding to $7.5 \cdot 10^{-6}$ moles of HNB produced. The NBA actinometer has a previously described quantum yield (ϕ) of 0.5 under 290-400 nm irradiation. Thus, the photon flow (φ) was calculated as reported below in Eq. (S1) and Eq. (S2) for the MFP and the batch setups, respectively.

$$\varphi = \frac{moles\ of\ HNB\ produced}{\phi \cdot \mathrm{t(end\ point)}} = \frac{2.0 \cdot 10^{-6}\ mol}{0.5\ mol\ Einstein^{-1} \cdot 23\ s} = 1.74 \cdot 10^{-7}\ Einstein\ s^{-1} \qquad \text{(S1)}$$

$$\varphi = \frac{moles\ of\ HNB\ produced}{\phi \cdot \mathrm{t(end\ point)}} = \frac{7.5 \cdot 10^{-6}\ mol}{0.5\ mol\ Einstein^{-1} \cdot 456\ s} = 3.29 \cdot 10^{-8}\ Einstein\ s^{-1} \qquad \text{(S2)}$$

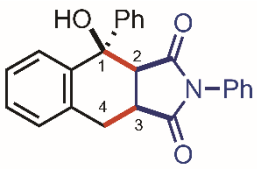
In order to estimate the accuracy of the used methods under the present setups, the obtained values of photon flows were normalized in respect to the reaction volumes. The photon flow in Einstein s^{-1} was then converted to W m^{-2}. Using the Planck equation $E = hv$, assuming a monochromatic irradiation wavelength of 365 nm has an energy of $5.45 \cdot 10^{-19}$ J $photon^{-1}$, equivalent to $3.28 \cdot 10^{5}$ J $Einstein^{-1}$. The cross-section of the MFP was calculated to be 7.5 cm^2 (the product of length, 1.00 m, times the width of the tubing, 0.75 mm). The cross-section of the batch vial was 1.4 cm^2 (the product of its width, 1.0 cm, times 1.4 cm, the height of 1.5 mL of reaction mixture). The photon flow in W m^{-2} was calculated following equations (S3) and (S4) for the microreactor and the batch respectively.

$$\frac{1.74 \cdot 10^{-7}\ Einstein\ s^{-1} \cdot 3.28 \cdot 10^{5}\ J\ Einstein^{-1}}{7.5 \cdot 10^{-4}\ m^2} = 76\ W\ m^{-2} \qquad \text{(S3)}$$

$$\frac{3.29 \cdot 10^{-8}\ Einstein\ s^{-1} \cdot 3.28 \cdot 10^{5}\ J\ Einstein^{-1}}{1.4 \cdot 10^{-4}\ m^2} = 77\ W\ m^{-2} \qquad \text{(S4)}$$

We were pleased to note that the two values of photon flow are very similar. This indicates a high accuracy of the used method for the two different setups.

H. CHARACTERIZATION DATA

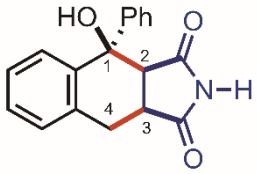


4-hydroxy-2,4-diphenyltetrahydro-1H-benzo[*f*]isoindole-1,3(2H)-dione (3a).

Synthesised following the general procedure 1 described in section **D**. **3a** was obtained as a white solid (>98% yield) after solvent evaporation.

^{1}H-NMR (400 MHz, $CDCl_3$): 7.90 (d, *J* = 7.4 Hz, 1H, Ar), 7.45 (t, *J* = 7.6 Hz, 1H, Ar), 7.37–7.32 (m, 7H, Ar), 7.28–7.26 (m, 2H, Ar), 7.15 (d, *J* = 7.4 Hz, 1H, Ar), 6.81-6.79 (m, 2H, Ar), 5.46 (s, 1H, OH), 4.18 (d, *J* = 9.0 Hz, 1H, H2), 3.40 (td, J = 8.8, 1.3 Hz, 1H, H3), 3.01 (d, *J* = 15.2 Hz, 1H, H4α), 2.64 (dd, *J* = 15.2, 8.7 Hz, 1H, H4ß) ppm. **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 179.6, 178.4, 141.0, 140.9, 134.2, 132.8, 131.1, 129.2, 129.0, 128.8, 128.5, 128.4, 128.2, 128.0, 126.9, 126.3, 126.1, 125.3, 48.3, 39.4, 30.4 ppm. **HRMS** calculated for $[C_{24}H_{19}NO_3+H]^+$: 370.1365, found: 370.1415.

4-hydroxy-4-phenyltetrahydro-1H-benzo[*f*]isoindole-1,3(2H)-dione (3b).

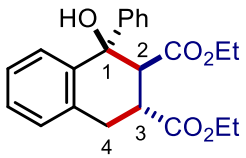


Synthesised following the general procedure 1 described in section **D. 3b** was obtained as a white solid after solvent evaporation (1mL of the product solution) in >98% yield, 29.3 mg, 0.1 mmol.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.22 (br s, 1H, NH), 7.83 (d, *J* = 7.4 Hz, 1H, Ar), 7.41 (t, *J* = 7.6 Hz, 1H, Ar), 7.35–7.28 (m, 4H, Ar), 7.21–7.17 (m, 2H, Ar), 7.12 (d, *J* = 7.4 Hz, 1H, Ar), 5.25 (s, 1H, OH), 4.01 (d, *J* = 9.0 Hz, 1H, H2), 3.23 (td, *J* = 8.8, 1.3 Hz, 1H, H3), 2.92 (d, *J* = 15.2 Hz, 1H, H4α), 2.54 (dd, *J* = 15.2, 8.7 Hz, 1H, H4ß) ppm. **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 180.3, 179.1, 140.9, 140.7, 132.8, 128.7, 128.4, 128.4 (x2), 127.9, 126.8, 125.3, 76.2, 49.3, 40.2, 29.6 ppm.

These spectra are in accordance with the previously described in literature.[1]

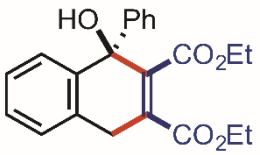
Diethyl-1-hydroxy-1-phenyltetrahydronaphthalene-2,3-dicarboxylate (3c).



Synthesised following the general procedure 1 described in section **D**. **3c** was obtained as a white solid after solvent evaporation (1mL of the product solution) in >98% yield, 36.7 mg, 0.1 mmol.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.40 (t, *J* = 7.4 Hz, 2H, Ar), 7.36 (d, *J* = 7.4 Hz, 2H, Ar), 7.33-7.30 (m, 1H, Ar), 7.24–7.21 (m, 2H, Ar), 7.11 (t, *J* = 7.4 Hz, 1H, Ar), 6.84 (d, *J* = 7.4 Hz, 1H, Ar), 4.29-4.15 (m, 2H, $COO\underline{CH_2}CH_3$), 4.01-3.84 (m, 2H, $COO\underline{CH_2}CH_3$), 3.71 (td, *J* = 12.0, 5.4 Hz, 1H, H3), 3.43 (d, *J* = 11.9 Hz, 1H, H2), 3.39 (dd, *J* = 15.9 Hz, 5.4 Hz, 1H, H

H4α), 3.23 (dd, *J* = 16.5, 12.1 Hz, 1H, H4ß), 1.32 (t, *J* = 7.1 Hz, 3H, $COOCH_2\underline{CH_3}$), 0.88 (t, *J* = 7.1 Hz, 3H, $COOCH_2\underline{CH_3}$) ppm. **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 174.1, 173.81,145.0, 139.9, 133.9, 129.7, 128.6, 128.2, 127.8, 127.8, 127.2, 126.8, 126.6, 126.6, 76.1, 61.1, 60.83, 54.41, 39.66, 32.41, 14.16, 13.58 ppm. *These spectra are in accordance with the previously described in literature.*[2]

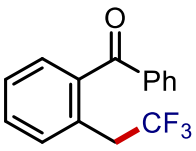


Diethyl-1-hydroxy-1-phenyltetrahydronaphthalene-2,3-dicarboxylate (3d).

Synthesised following the procedure 1 described in section **D**. **3d** was obtained as a white solid after solvent evaporation (1mL of the product solution) in >98% yield, 36.6 mg, 0.1 mmol.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.44-7.40 (m, 3H, Ar), 7.31 (t, *J* = 7.4 Hz, 2H, Ar), 7.27-7.21 (m, 4H, Ar), 4.32 (qd, *J* = 7.1, 1.9 Hz, 2H, $COO\underline{CH_2}CH_3$), 4.24 (br s, 1H, OH), 4.19-4.05 (m, 2H, $COO\underline{CH_2}CH_3$), 3.91 (s, 2H, CH_2), 1.37 (t, *J* = 7.1 Hz, 3H, $COOCH_2\underline{CH_3}$), 1.09 (t, *J* = 7.1 Hz, 3H, $COOCH_2\underline{CH_3}$) ppm. **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 167.5, 167.7, 145.1, 138.8, 131.9, 130.0, 128.1, 127.8, 127.5, 127.5, 127.3, 127.2, 125.7, 74.2, 61.6, 30.8, 14.0, 13.6 ppm. *These spectra are in accordance with the previously described in literature*.[3]

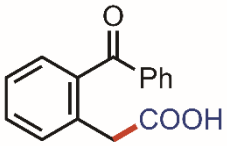
Phenyl[2-(trifluoroethyl)phenyl]methanone (3e).



Synthesised using DMSO instead of toluene following the general procedure described in section **D. 3e** was obtained as a white solid after purification by extraction (EtOAc x3) and subsequent filtration on a celite® pad.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.80 (m, 2H, Ar), 7.57 (m, 1H, Ar), 7.51 (m, 1H, Ar), 7.47 (m, 3H, Ar), 7.40 (m, 2H, Ar), 3.74 (q, *J* = 10.9 Hz, 2H, CH_2) ppm. **^{13}C-NMR (150 MHz, $CDCl_3$):** δ 197.7, 139.5, 137.4, 133.3, 132.4, 130.7, 130.4, 129.8, 129.5 (q, *J*= 2.4 Hz), 128.4, 127.4, 125.7 (q, *J* = 277.1 Hz), 36.1 ppm (q, *J* = 29.4 Hz). **^{19}F-NMR (376 MHz, $CDCl_3$):** δ -65.0 ppm (t, *J* = 10.9 Hz). *These spectra are in accordance with the previously described in literature*.[4]

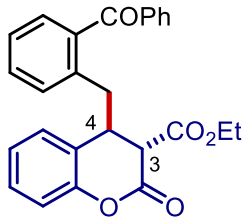
2-(2-benzoylphenyl)acetic acid (3f)



Synthesised following the general procedure 2 described in section **D. 3f** was obtained as a white solid (>98% yield) after DMSO removal by extraction with EtOAc (x3).

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.81 (m, 2H, Ar), 7.61 (1H, Ar), 7.48 (m, 5H, Ar), 7.35 (m, 1H, Ar), 3.83 (s, 2H) ppm. **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 199.1, 174.6, 137.5, 137.2, 133.9, 133.5, 131.9, 131.7, 130.7, 128.4, 126.7, 39.7 ppm. *These spectra are in accordance with the previously described in literature*. [5]

Ethyl-4-(2-benzoylbenzyl)-2-oxochromane-3-carboxylate (3g).

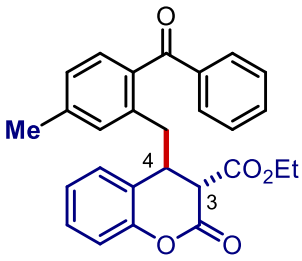


Synthesised following the general procedure 1 described in section **D**, using 1.5 equivalents of **1a** and a residence time of 26.6 minutes**.** In order to calculate the isolated yield, 1 mL of the product solution of **3g** was collected and subjected to flash column chromatography on silica gel (85:15 Hexane/EtOAc) yielding pure **3g** as a single diastereoisomer (white solid), in 75% yield, 31.1 mg, 0.075 mmol.

^{1}H-NMR (400 MHz, $CDCl_3$): 7.77 (d, *J* = 8.5 Hz, 2H, Ar), 7.60 (t, *J* = 7.4 Hz, 1H, Ar), 7.47 (t, *J* = 7.4 Hz, 2H, Ar), 7.43–7.40 (m, 2H, Ar), 7.35-7.31 (m, 1H, Ar), 7.24–7.20 (m, 1H, Ar), 7.10 (d, *J* = 7.6 Hz,1H, Ar), 7.04 (d, *J* = 8.1 Hz, 1H, Ar), 7.01 (m, 2H, Ar), 4.01-3.90 (m, 2H, $COO\underline{CH_2}CH_3$), 3.82-3.79 (m, 2H, C_3H & C_4H), 3.16 (dd, *J* = 13.6 Hz, 6.7 Hz, 1H, $CH_2\alpha$), 2.77 (dd, *J* = 13.9 Hz, 8.8 Hz, 1H, $CH_2ß$), 0.96 (t, *J* = 7.2 Hz, $COOCH_2\underline{CH_3}$) ppm. **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 198.0, 166.8, 166.4, 164.4, 137.1, 133.2, 132.0, 120.8, 130.3, 130.2, 128.9, 128.5, 126.5, 124.7, 123.3, 116.8, 62.0, 50.8, 41.5, 38.6, 13.7 ppm. **HRMS** calculated for $[C_{26}H_{22}O_5+H]^+$: 415.1467, found: 415.1460.

*By using two MFPs in a parallel setup, 664 mg of **3g** were obtained in 12 h.*

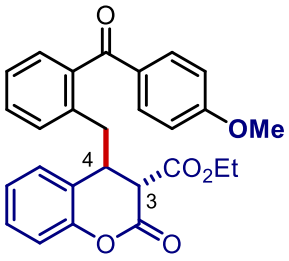
Ethyl-4-(2-benzoyl-5-methylbenzyl)-2-oxochromane-3-carboxylate (3h).



Synthesised following the general procedure 1 described in section **D** using 2 equivalents of **1b** and a residence time of 80 min**.** In order to calculate the isolated yield, 1 mL of the product solution of **3h** was collected and subjected to flash column chromatography on silica gel (85:15 Hexane/EtOAc) yielding pure **3h** as a single diastereoisomer (yellowish oil), in 83% yield, 35.5 mg, 0.083 mmol.

^{1}H-NMR (400 MHz, $CDCl_3$): 7.76 (d, *J* = 8.5 Hz, 2H, Ar), 7.58 (t, *J* = 7.6 Hz, 1H, Ar), 7.46 (t, *J* = 7.4 Hz, 2H, Ar), 7.33 (d, *J* = 7.8 Hz, 1H, Ar), 7.21 (m, 2H, Ar), 7.12 (d, *J* = 7.7 Hz, 1H, Ar), 7.07-7.00 (m, 3H, Ar), 6.90 (s, 1H, Ar), 4.21-3.92 (m, 2H, $COO\underline{CH_2}CH_3$), 3.82-3.79 (m, 2H, C_3H & C_4H), 3.21 (dd, *J* = 13.6 Hz, 6.7 Hz, 1H, $CH_2\alpha$), 2.74 (dd, *J* = 13.9 Hz, 8.8 Hz, 1H, $CH_2ß$), 2.37 (s, 3H, Ar-$\underline{CH_3}$), 0.96 (t, *J* = 7.2 Hz, $COOCH_2\underline{CH_3}$) ppm. **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 198.2, 167.1, 164.7, 164.4, 150.8, 141.7, 138.6, 137.7, 135.2, 131.2, 130.3, 129.1, 128.5, 127.2, 124.9, 124.1, 116.9, 62.2, 50.9, 41.6, 38.9, 21.6, 14.4 ppm. **HRMS** calculated for $[C_{27}H_{24}O_5+H]^+$: 429.1624, found: 429.1623.

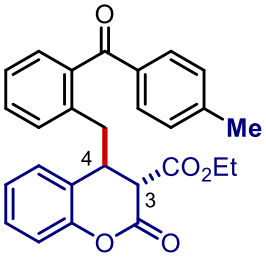
Ethyl-4-[2-(4-methoxybenzoyl)benzyl]-2-oxochromane-3-carboxylate (3i).



Synthesised following the general procedure 1 described in section **D** using 1.5 equivalents of **1c** and a residence time of 80 min**.** In order to calculate the isolated yield, 1 mL of the product solution of **3i** was collected and subjected to flash column chromatography on silica gel (85:15 Hexane/EtOAc) yielding pure **3i** as a single diastereoisomer (yellowish oil), in 50% yield, 22.2 mg, 0.050 mmol.

^{1}H-NMR (400 MHz, $CDCl_3$): 7.77 (d, *J* = 8.5 Hz, 2H, Ar), 7.41-7.37 (m, 2H, Ar), 7.34-7.28 (m, 2H, Ar), 7.24–7.19 (m, 2H, Ar), 7.08-6.98 (m, 3H, Ar), 6.93 (d, *J* = 7.6 Hz, 1H, Ar), 4.01-3.91 (m, 2H, COO$\underline{CH_2}CH_3$), 3.88 (s, 3H, O$\underline{CH_3}$), 3.80-3.75 (m, 2H, C_3H & C_4H), 3.10 (dd, *J* = 13.6 Hz, 6.7 Hz, 1H, $CH_2\alpha$), 2.74 (dd, *J* = 13.9 Hz, 8.8 Hz, 1H, $CH_2ß$), 0.95 (t, *J* = 7.2, $COOCH_2\underline{CH_3}$) ppm. **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 196.8, 167.0, 164.6, 163.9, 150.8, 139.0, 136.7, 132.7, 131.9, 130.7, 130.4, 129.0, 126.6, 124.8, 124.0, 116.9, 113.9, 62.2, 55.7, 51.0, 45.4, 41.6, 38.7, 13.8 ppm. **HRMS** calculated for $[C_{27}H_{24}O_6+H]^+$: 445.1573, found: 445.1576.

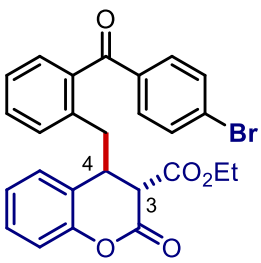
Ethyl-4-[2-(4-methylbenzoyl)benzyl]-2-oxochromane-3-carboxylate (3j).



Synthesised following the general procedure 1 described in section **D** using 1.5 equivalents of **1d** and a residence time of 80 min**.** In order to calculate the isolated yield, 1 mL of the product solution of **3j** was collected and subjected to flash column chromatography on silica gel (85:15 Hexane/EtOAc) yielding pure **3j** as a single diastereoisomer (white solid), in 87% yield, 37.3 mg, 0.087 mmol.

^{1}H-NMR (400 MHz, $CDCl_3$): 7.71 (d, *J* = 8.5 Hz, 2H, Ar), 7.41 (d, *J* = 7.4 Hz, 2H, Ar), 7.36 (d, *J* = 7.4 Hz, 1H, Ar), 7.30–7.23 (m, 3H, Ar), 7.12-7.03 (m, 4H, Ar), 4.04-3.94 (m, 2H, COO$\underline{CH_2}CH_3$), 3.82-3.79 (m, 2H, C_3H & C_4H), 3.16 (dd, *J* = 13.6 Hz, 6.7 Hz, 1H, $CH_2\alpha$), 2.79 (dd, *J* = 13.9 Hz, 8.8 Hz, 1H, $CH_2ß$), 2.46 (s, 3H, Ar-$\underline{CH_3}$), 0.98 (t, *J* = 7.2, $COOCH_2\underline{CH_3}$) ppm. **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 197.9, 167.0, 164.6, 150.8, 144.4, 138.7, 137.0, 135.4, 132.0, 130.7, 130.6, 130.3, 129.3, 129.0, 126.6, 124.9, 124.0, 116.9, 62.2, 51.0, 41.6, 38.8, 21.9, 13.9 ppm. **HRMS** calculated for $[C_{27}H_{24}O_5+H]^+$: 429.1624, found: 429.1629.

Ethyl-4-[2-(4-bromobenzoyl)benzyl]-2-oxochromane-3-carboxylate (3k).

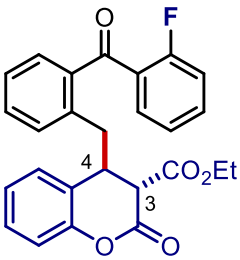


Synthesised following the general procedure 1 described in section **D** using 1.5 equivalents of **1e** and a residence time of 80 min**.** In order to calculate the isolated yield, 1 mL of the product solution of **3k** was collected and subjected to flash column chromatography

on silica gel (85:15 Hexane/EtOAc) yielding pure **3k** as a single diastereoisomer (yellowish oil), in 70% yield, 34.4 mg, 0.070 mmol.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.66–7.58 (m, 4H, Ar), 7.44 (td, *J* = 7.4, 1.5 Hz, 1H, Ar), 7.40–7.31 (m, 2H, Ar), 7.22 (td, *J* = 7.6, 2.2 Hz, 1H, Ar), 7.13 (d, *J* = 7.5 Hz, 1H, Ar), 7.07–6.97 (m, 3H, Ar), 4.06–3.90 (m, 2H, $COO\underline{CH_2}CH_3$), 3.82–3.74 (m, 2H, C_3H & C_4H), 3.16 (dd, *J* = 13.7, 6.8 Hz, 1H, $CH_2\alpha$), 2.79 (dd, *J* = 13.7, 9.2 Hz, 1H, $CH_2ß$), 0.96 (t, *J* = 7.1 Hz, 3H, $COOCH_2\underline{CH_3}$) ppm. **^{13}C-NMR (125 MHz, $CDCl_3$)**: δ 196.80, 166.79, 164.35, 150.71, 137.61, 137.28, 136.59, 132.08, 131.78, 131.67, 131.06, 130.18, 128.92, 128.85, 126.55, 124.74, 123.66, 116.86, 62.09, 50.86, 41.52, 38.51, 29.69, 13.71 ppm. **HRMS** m/z calculated for $[C_{26}H_{21}BrO_5+H]^+$: 493.0645, found: 493.0644.

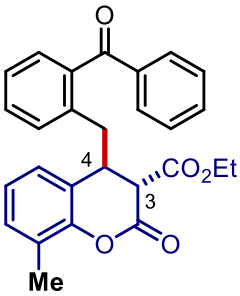
Ethyl-4-[2-(2-fluorobenzoyl)benzyl]-2-oxochromane-3-carboxylate (3l).



Synthesised following the general procedure 1 described in section **D** using 1.5 equivalents of **1f** and a residence time of 80 min**.** In order to calculate the isolated yield, 1 mL of the product solution of **3l** was collected and subjected to flash column chromatography on silica gel (85:15 Hexane/EtOAc) yielding pure **3l** as a single diastereoisomer (yellowish oil), in 93% yield, 40.2 mg, 0.093 mmol.

^{1}H-NMR (400 MHz, $CDCl_3$): 7.63 (t, *J* = 7.3 Hz, 1H, Ar), 7.56 (q, *J* = 6.9 Hz, 1H, Ar), 7.45 (m, 2H, Ar), 7.33–7.24 (m, 3H, Ar), 7.15 (d, *J* = 7.4 Hz, 2H, Ar), 7.11–7.03 (m, 3H, Ar), 4.04-3.93 (m, 2H, $COO\underline{CH_2}CH_3$), 3.87 (t, *J* = 7.8 Hz, 1H, C_3H), 3.80 (s, 1H, C_4H), 3.36 (dd, *J* = 13.6 Hz, 6.7 Hz, 1H, $CH_2\alpha$), 2.91 (dd, *J* = 13.9 Hz, 8.8 Hz, 1H, $CH_2\beta$), 0.98 (t, *J* = 7.2, $COOCH_2\underline{CH_3}$) ppm. **NMR (100 MHz, $CDCl_3$)**: δ 193.4, 167.1, 164.8, 150.9, 138.0, 134.1, 132.7, 132.1, 131.8, 131.4, 129.2, 129.0, 127.2, 125.0, 124.6, 124.5, 124.2, 117.0, 62.2, 51.0, 41.4, 39.2, 14.1 ppm**. HRMS** calculated for $[C_{26}H_{21}FO_5+H]^+$: 433.1373, found: 433.1361.

Ethyl-4-(2-benzoylbenzyl)-8-methyl-2-oxochromane-3-carboxylate (3m).

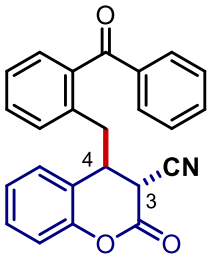


Synthesised following the general procedure 1 described in section **D** using 1.5 equivalents of **1a** and a residence time of 80 min**.** In order to calculate the isolated yield, 1 mL of the product solution of **3m** was collected and subjected to flash column chromatography on silica gel (85:15 Hexane/EtOAc) yielding pure **3m** as a single diastereoisomer (yellowish oil), in 67% yield, 28.7 mg, 0.067 mmol.

^{1}H-NMR (400 MHz, $CDCl_3$): 7.76 (d, *J* = 7.5 Hz, 2H, Ar), 7.59 (t, *J* = 7.4 Hz, 1H, Ar), 7.48-7.39 (m, 4H, Ar), 7.33 (t, *J* = 7.5 Hz, 1H, Ar), 7.13 (d, *J* = 7.5 Hz, 1H, Ar), 7.05 (d, *J* = 7.5 Hz, 1H, Ar), 6.90 (t, *J* = 7.5 Hz, 1H, Ar), 6.81 (d, *J* = 7.5 Hz, 1H, Ar), 4.01-3.90 (m, 2H, $COO\underline{CH_2}CH_3$),

3.76-3.73 (m, 2H, C_3H & C_4H), 3.16 (dd, *J* = 13.6 Hz, 6.7 Hz, 1H, $CH_2\alpha$), 2.77 (dd, *J* = 13.9 Hz, 8.8 Hz, 1H, $CH_2ß$), 2.28 (s, 3H, Ar$\underline{CH_3}$) 0.94 (t, *J* = 7.2, $COOCH_2\underline{CH_3}$). **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 198.0, 166.9, 164.7, 149.0, 138.2, 137.9, 137.2, 133.2, 132.0, 130.8, 130.3, 130.2, 128.4, 126.4, 126.4, 124.3, 123.5, 61.9, 50.8, 41.6, 38.5, 15.6 13.7. **HRMS** calculated for $[C_{27}H_{24}O_5+H]^+$: 429.1624, found: 429.1627.

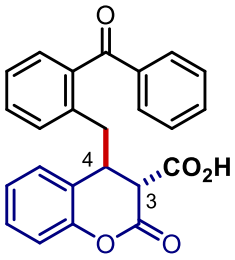
4-(2-benzoylbenzyl)-2-oxochromane-3-carbonitrile (3n).



Synthesised following the general procedure 1 described in section **D** using 1.5 equivalents of **1a** and a residence time of 80 min in a 7:3 toluene /DMSO mixture**.** In order to calculate the isolated yield, 1 mL of the product solution of **3n** was collected and subjected to flash column chromatography on silica gel (8:2 Hexane/EtOAc) yielding a 4:1 mixture of **3n** (transparent oil), in 58% yield, 21.3 mg, 0.058 mmol.

^{1}H-NMR (400 MHz, $CDCl_3$): 7.73 (d, *J* = 8.1 Hz, 2H, Ar), 7.60 (t, *J* = 7.6 Hz, 1H, Ar), 7.47-7.38 (m, 5H, Ar), 7.34–7.30 (m, 2H, Ar), 7.07 (d, *J* = 8.2 Hz, 1H, Ar), 6.94 (t, *J* = 7.6 Hz, 1H, Ar), 6.86-6.84 (m, 1H, Ar), 6.63 (d, *J* = 7.4 Hz, 1H, Ar), 4.03 (d, *J* = 5.1 Hz, 1H, C_3H), 3.91 (dt, *J* = 9.8 Hz, 5.6 Hz, 1H, C_4H), 3.39 (dd, *J* = 13.2 Hz, 5.8 Hz, 1H, $CH_2\alpha$), 2.90 (dd, *J* = 13.4 Hz, 10.2 Hz, 1H, $CH_2ß$) ppm. **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 198.0, 160.9, 151.9, 150.4, 138.7, 137.5, 135.8, 135.7, 133.6, 132.4, 130.5, 130.0, 129.8, 128.9, 128.6, 126.9, 125.8, 125.0, 122.8, 117.3, 113.5, 40.5, 38.8, 35.8 ppm. **HRMS** calculated for $[C_{24}H_{17}NO_3+H]^+$: 368.1208, found: 368.1268.

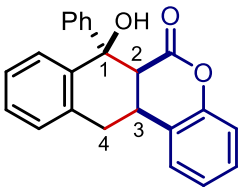
4-(2-benzoylbenzyl)-2-oxochromane-3-carboxylic acid (3o).



Synthesised following the general procedure 1 described in section **D** using 1.5 equivalents of **1a** and a residence time of 80 min in a 9:1 toluene /DMSO solvent mixture. In order to calculate the isolated yield, 1 mL of the product solution of **3o** was collected and subjected to extraction (EtOAc x3) and flash column chromatography on silica gel (8:2 Hexane/EtOAc) yielding pure **3o** as a single diastereoisomer (yellowish oil), in 77% yield, 29.7 mg, 0.077 mmol.

^{1}H-NMR (400 MHz, $CDCl_3$): 7.77 (d, *J* = 8.5 Hz, 2H, Ar), 7.60 (t, *J* = 7.4 Hz, 1H, Ar), 7.48–7.40 (m, 5H, Ar), 7.33 (d, *J* = 7.5 Hz, 1H, Ar), 7.10–6.99 (m, 4H, Ar), 3.86-3.82 (m, 2H, C_3H & C_4H), 3.13 (dd, *J* = 13.6 Hz, 6.7 Hz, 1H, $CH_2\alpha$), 2.77 (dd, *J* = 13.9 Hz, 8.8 Hz, 1H, $CH_2ß$). **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 198.1, 169.3, 164.4, 150.7, 138.2, 137.9, 137.1, 133.2, 132.0, 130.8, 130.3, 130.2, 129.0, 128.9, 128.5, 127.4, 126.5, 124.7, 123.7, 117.0, 50.6, 41.2, 38.9, 29.7. **HRMS** calculated for $[C_{24}H_{18}O_5+H]^+$: 387.1154, found: 387.1244.

7-hydroxy-7-phenyltetrahydro-6H-naphtho[2,3-*c*]chromenone (3p).



Synthesised following the general procedure 1 described in section **D** using 1.5 equivalents of **1a** and a residence time of 26.6 min**.** In order to calculate the isolated yield, 1 mL of the product solution of **3p** was collected and subjected to flash column chromatography on silica gel (8:2 Hexane/EtOAc) yielding pure **3p** (transparent oil), in 71% yield, 24.3 mg, 0.071 mmol.

^{1}H-NMR (400 MHz, $CDCl_3$): 7.67 (d, *J* = 7.5 Hz, 1H, Ar), 7.33-7.26 (m, 6H, Ar), 7.15 (t, *J* = 7.5 Hz, 2H, Ar), 7.12–7.07 (m, 4H, Ar), 5.43 (br s, 1H, OH), 3.31 (d, *J* = 4.4 Hz, 1H, CH), 3.19 (m, 2H, CH_2), 2.92-2.83 (m, 1H, CH). **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 170.3, 149.8, 145.5, 136.7, 132.5, 128.0, 127.3, 127.0, 126.7, 126.6, 126.4, 124.0, 116.2, 75.5, 49.9, 32.7, 32.5. **HRMS** calculated for $[C_{23}H_{18}O_3+H]^+$: 343.1256, found: 343.1258.

I. X-RAY STRUCTURE DETERMINATION AND REFINEMENT OF COMPOUND 3G

Colourless, block-shaped single crystals of compound **3g** were grown from a Et_2O/hexane solution by slow evaporation. An X-ray quality crystal with approximate dimensions 0.65 x 0.40 x 0.30 mm was chosen under the microscope for the measurement. Diffraction data for **3g** were collected at room temperature (296 K) with an Oxford Diffraction Gemini E diffractometer, equipped with a 2 K x 2 K EOS CCD area detector and sealed-tube Enhance (Mo) and (Cu) X-ray sources. Mo-Ka (λ = 0.71073 Å) radiation was used. Data collection, reduction and finalization were carried out through the CrysAlisPro software. The structures were resolved by direct methods and subsequently completed by Fourier recycling using the SHELXTL-2013 software package [7,8] and refined by the full-matrix least-squares refinements based on F^2 with all observed reflections. All non-hydrogen atoms were refined anisotropically; hydrogen atoms were included at geometrically calculated positions and refined using a riding model. The pendant atom of the ethyl group was modelled over two positions, named C13 and C13A; the relative occupancies of these two sites were refined freely within SHELXL while constraining their sum to unit and they reached values of ca. 0.60:0.40 at convergence, respectively. The disorder was refined using similarity restraints on 1,2- and 1,3-distances. Rigid-bond restraints were applied to the whole molecule.[9] The compound is racemic, and it crystallizes in the centrosymmetric triclinic space group P-1. The X-ray diffractometric analysis unequivocally established **3g** to be the (3RS,4SR) diastereoisomer. Figure S22 shows the content of the asymmetric unit as the 3R,4S enantiomer; the choice is arbitrary as the 3S,4R enantiomer is generated by inversion (see Figure S23). The final geometrical calculations and graphical manipulations were performed by using the XP utility within SHELX1. A summary of the crystallographic data and structure refinement for **3g** is given in Table S11. Bond distances and angles are fully listed in Table S12. Crystallographic data have been deposited at the Cambridge Crystallographic Data Centre (CCDC reference number 1811483). The data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures/.

Table S11. Summary of crystal data and structure refinement for **3g**.

Formula	$C_{26}H_{22}O_5$	
fw	414.43	
Crystal system	Triclinic	
Space group	*P*-1	
Unit cell dimensions	a = 8.58811(15) Å	a= 89.0458(13)°
	b = 9.78515(16) Å	b= 80.7673(14)°
	c = 13.2312(2) Å	g = 86.3224(14)°
V	1095.21(3) Å^3	
Z	2	
Density (calculated)	1.257 g/cm^3	
Absorption coefficient	0.087 mm^{-1}	
F(000)	436	
Crystal size	0.650 x 0.400 x 0.300 mm^3	
Reflections collected	24550	
Independent reflections	5384 [*R*(int) = 0.0218]	
Completeness to theta = 25.242°	99.9 %	
Data / restraints / parameters	5384 / 467 / 292	
Goodness-of-fit on F^2	1.047	
Final *R* indices [$I>2\sigma(I)$][a,b]	R_1 = 0.0452, wR_2 = 0.1117	
R indices (all data)[a,b]	R_1 = 0.0602, wR_2 = 0.1220	
$\Delta\rho_{max,\ min}$	0.161/-0.185 e Å^{-3}	

[a] $R_1 = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $wR_2 = \{\sum w(F_o^2 - F_c^2)^2/\sum[w(F_o^2)^2\}^{1/2}$ and $w = 1/[\ \sigma^2(F_o)^2 + (mP)^2 + nP]$ with $P = (F_o^2 + 2F_c^2)/3$, $m = 0.0513$ and $n = 0.1878$.

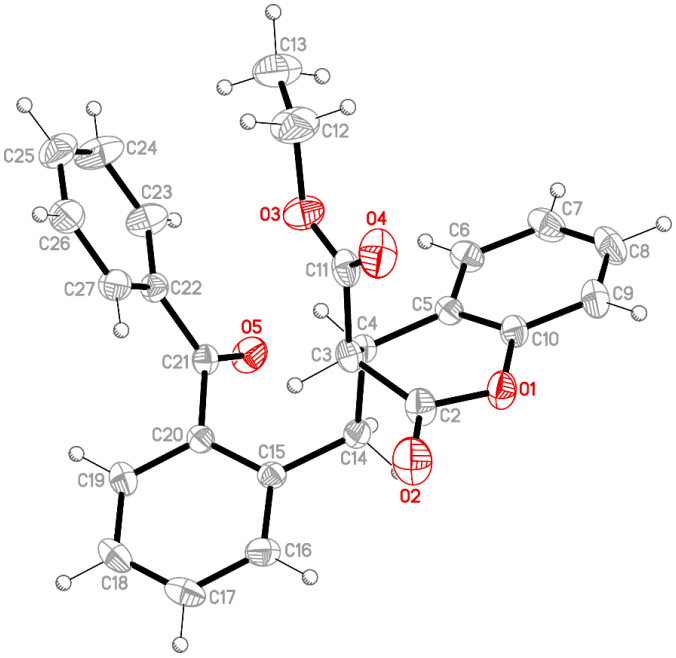


Figure S22. Molecular structure of **3g** with atom numbering. Thermal ellipsoids are drawn at the 30% probability level. Only one of the two disordered sites for the pendant atom of the ethyl group (C13) is shown for clarity. The 3R,4S enantiomer depicted here has been arbitrarily chosen to define the asymmetric unit content.

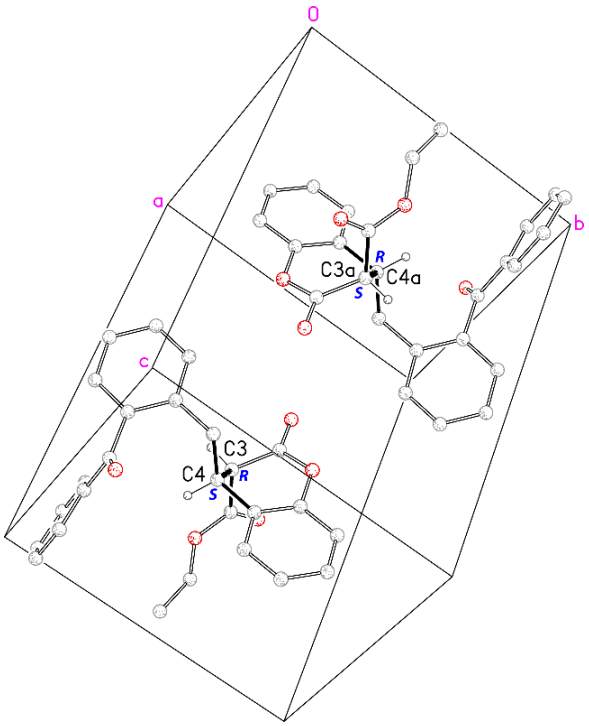


Figure S23. A view of the unit cell content for compound **3g**, showing both the 3*S*,4*R* and the 3*R*,4*S* enantiomers with only selected H atoms and atom labels. Again, only one of the two sites for atom C13 is shown, for clarity. Symmetry code: (a) -*x*+1, -*y*+1, -*z*+1.

Table S12. Bond distances (Å) and angles (°) for **3g**.

O(1)-C(2)	1.3642(16)	C(12)-C(13A)	1.426(6)
O(1)-C(10)	1.4004(15)	C(12)-C(13)	1.452(4)
O(2)-C(2)	1.1912(16)	C(14)-C(15)	1.5114(16)
O(3)-C(11)	1.3161(18)	C(15)-C(16)	1.3873(17)
O(3)-C(12)	1.4571(19)	C(15)-C(20)	1.3969(16)
O(4)-C(11)	1.1970(16)	C(16)-C(17)	1.386(2)
O(5)-C(21)	1.2183(14)	C(17)-C(18)	1.370(2)
C(2)-C(3)	1.5047(19)	C(18)-C(19)	1.374(2)
C(3)-C(11)	1.5175(18)	C(19)-C(20)	1.3957(16)
C(3)-C(4)	1.5327(16)	C(20)-C(21)	1.4936(16)
C(4)-C(5)	1.5053(15)	C(21)-C(22)	1.4898(17)
C(4)-C(14)	1.5376(16)	C(22)-C(23)	1.3823(18)
C(5)-C(10)	1.3770(18)	C(22)-C(27)	1.3874(18)
C(5)-C(6)	1.3879(17)	C(23)-C(24)	1.383(2)
C(6)-C(7)	1.384(2)	C(24)-C(25)	1.374(3)
C(7)-C(8)	1.373(2)	C(25)-C(26)	1.363(2)
C(8)-C(9)	1.375(2)	C(26)-C(27)	1.380(2)
C(9)-C(10)	1.3840(18)		
C(2)-O(1)-C(10)	120.52(10)	C(13A)-C(12)-O(3)	109.2(3)
C(11)-O(3)-C(12)	117.53(14)	C(13)-C(12)-O(3)	108.1(2)
O(2)-C(2)-O(1)	117.99(13)	C(15)-C(14)-C(4)	114.34(9)
O(2)-C(2)-C(3)	125.59(13)	C(16)-C(15)-C(20)	117.96(11)
O(1)-C(2)-C(3)	116.42(11)	C(16)-C(15)-C(14)	119.90(11)
C(2)-C(3)-C(11)	107.95(11)	C(20)-C(15)-C(14)	122.13(10)
C(2)-C(3)-C(4)	110.43(10)	C(17)-C(16)-C(15)	121.29(14)
C(11)-C(3)-C(4)	112.67(10)	C(18)-C(17)-C(16)	120.44(13)
C(5)-C(4)-C(3)	107.00(9)	C(17)-C(18)-C(19)	119.39(13)
C(5)-C(4)-C(14)	110.52(9)	C(18)-C(19)-C(20)	120.87(13)
C(3)-C(4)-C(14)	112.78(10)	C(19)-C(20)-C(15)	120.03(11)
C(10)-C(5)-C(6)	117.88(11)	C(19)-C(20)-C(21)	118.42(11)
C(10)-C(5)-C(4)	118.64(10)	C(15)-C(20)-C(21)	121.52(10)
C(6)-C(5)-C(4)	123.48(11)	O(5)-C(21)-C(22)	120.88(11)
C(7)-C(6)-C(5)	120.65(14)	O(5)-C(21)-C(20)	120.58(11)
C(8)-C(7)-C(6)	119.99(13)	C(22)-C(21)-C(20)	118.54(10)
C(7)-C(8)-C(9)	120.62(13)	C(23)-C(22)-C(27)	118.71(12)
C(8)-C(9)-C(10)	118.62(14)	C(23)-C(22)-C(21)	119.61(12)
C(5)-C(10)-C(9)	122.23(12)	C(27)-C(22)-C(21)	121.65(11)
C(5)-C(10)-O(1)	120.97(10)	C(22)-C(23)-C(24)	120.00(15)
C(9)-C(10)-O(1)	116.75(12)	C(25)-C(24)-C(23)	120.37(16)
O(4)-C(11)-O(3)	125.34(14)	C(26)-C(25)-C(24)	120.17(15)
O(4)-C(11)-C(3)	123.28(15)	C(25)-C(26)-C(27)	119.89(15)
O(3)-C(11)-C(3)	111.38(11)	C(26)-C(27)-C(22)	120.79(14)

J. REFERERNCES

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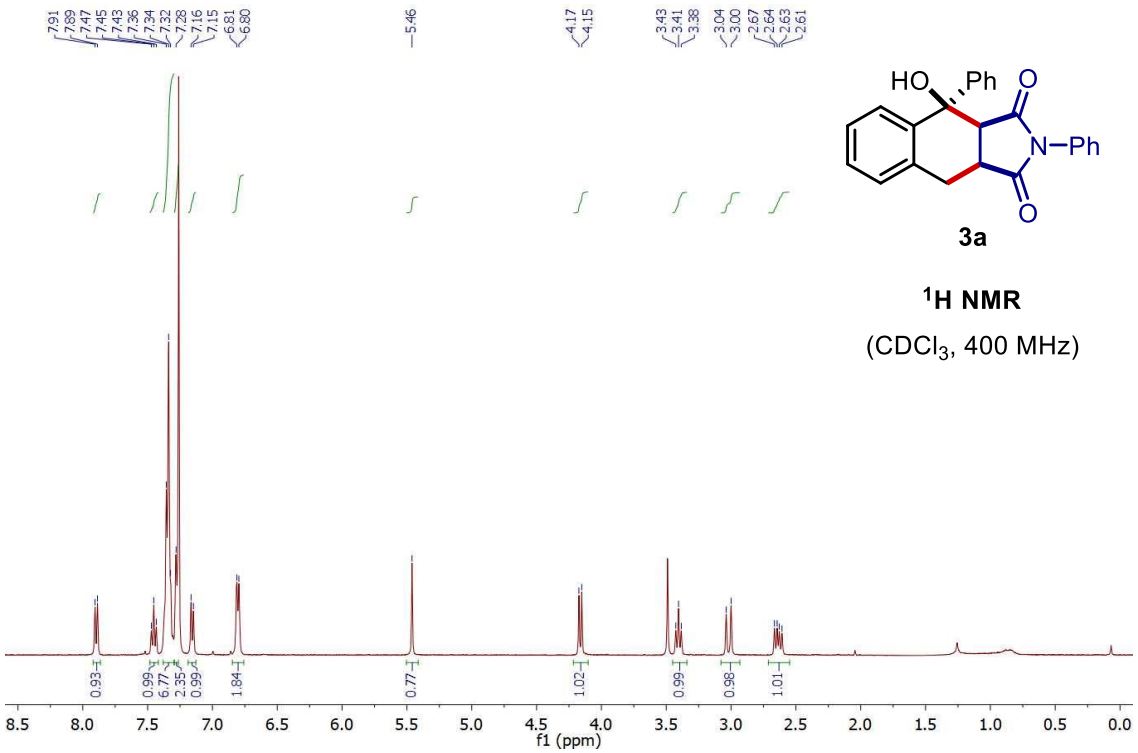
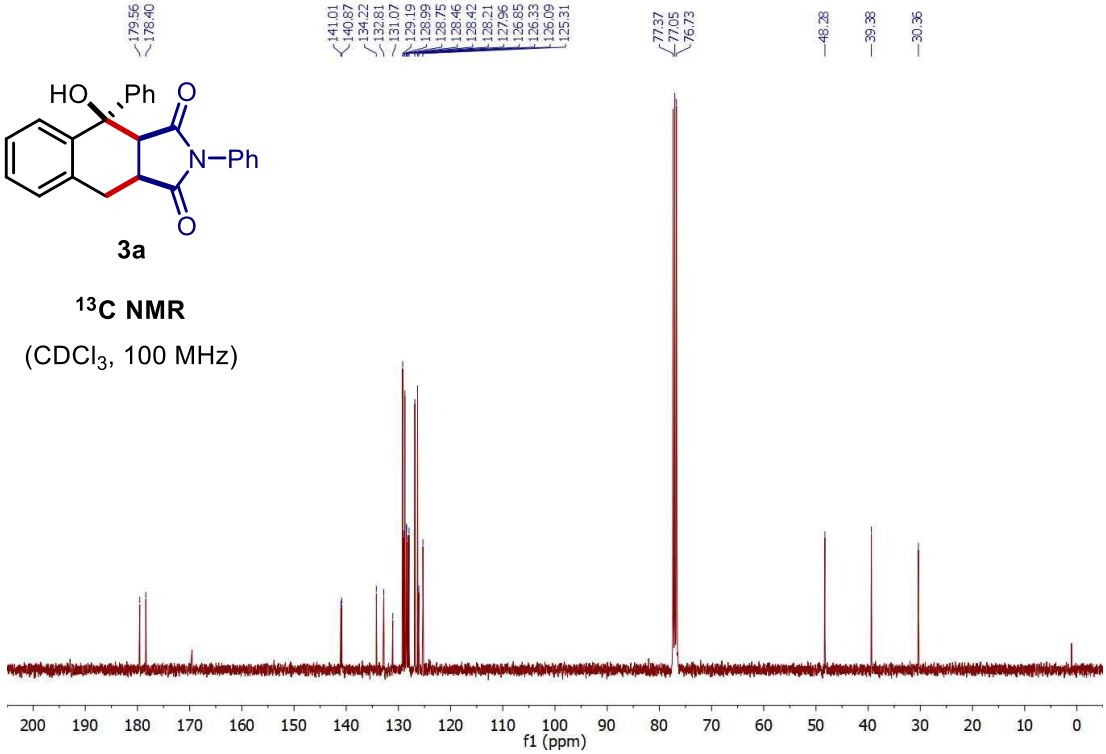
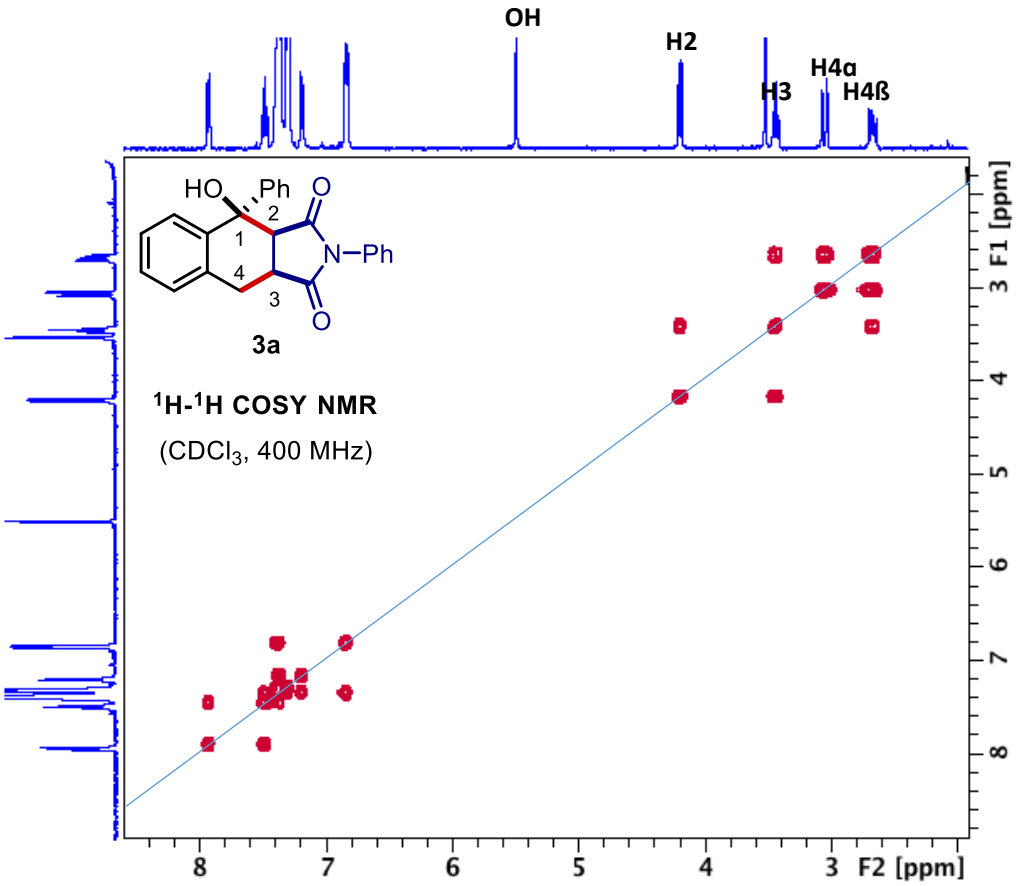
K. NMR SPECTRA



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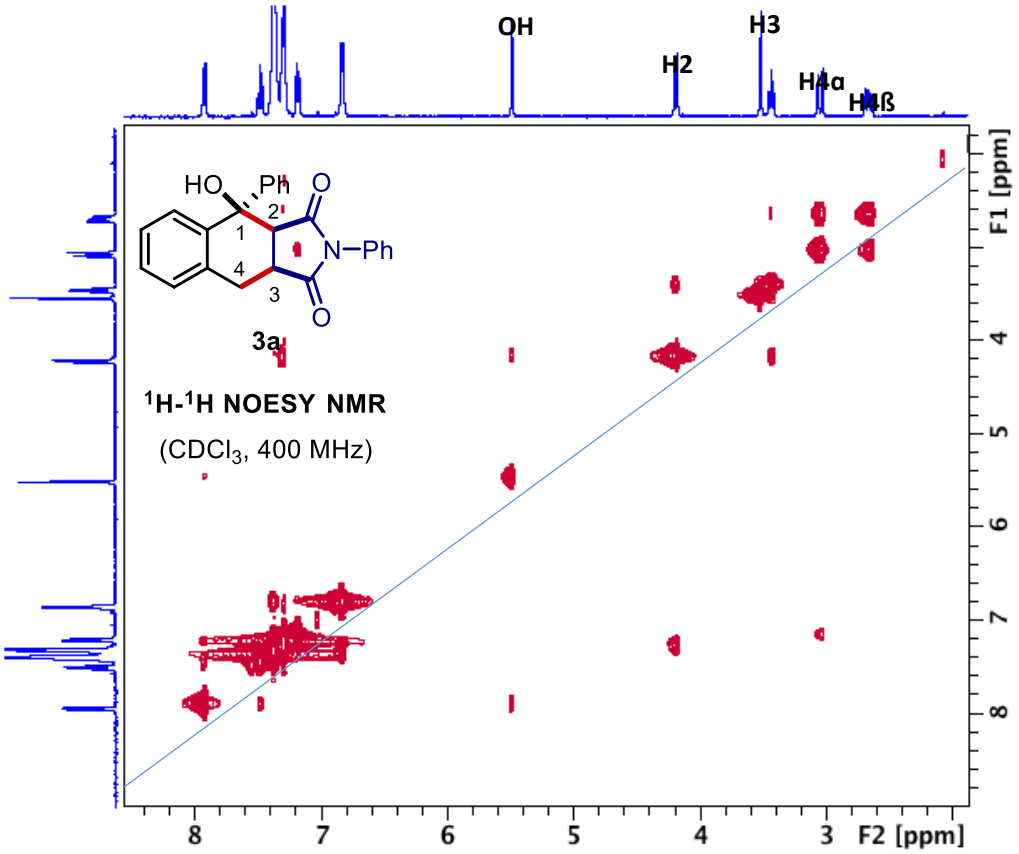
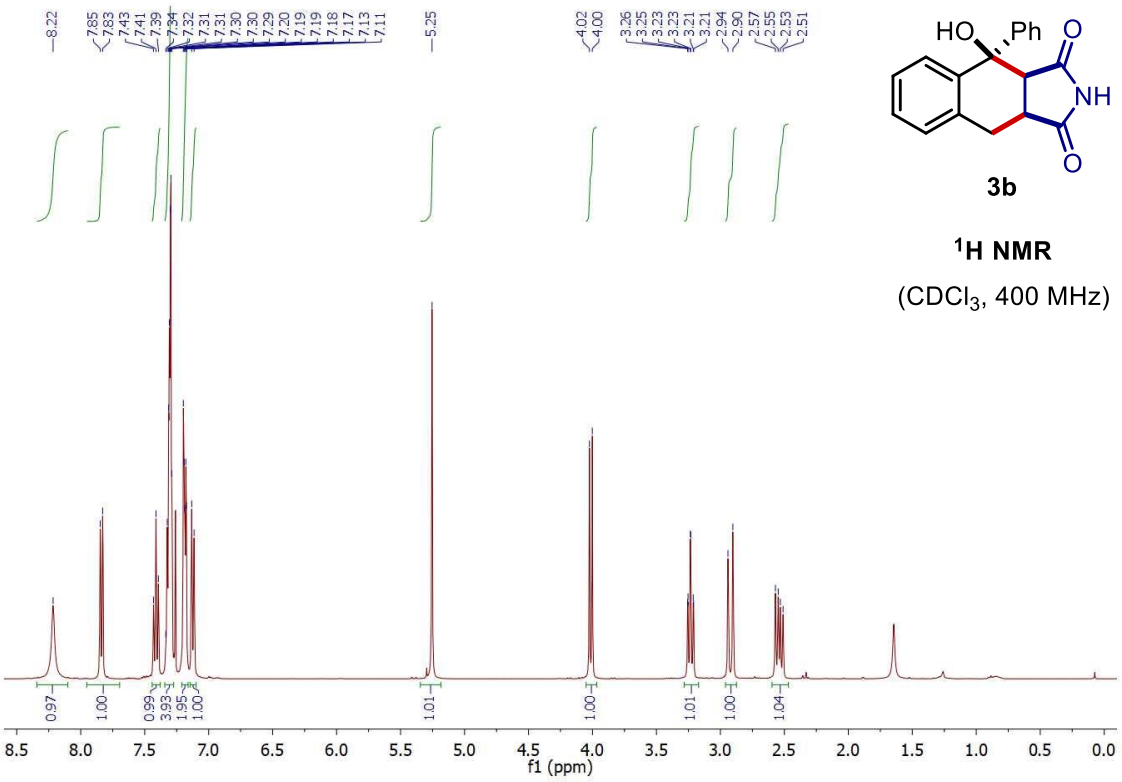
H2
H3
H4α
H4ß
HO
Ph
O
N–Ph
1
2
3
4
3a
^{1}H-^{1}H COSY NMR
(CDCl$_3$, 400 MHz)
F1 [ppm]
F2 [ppm]

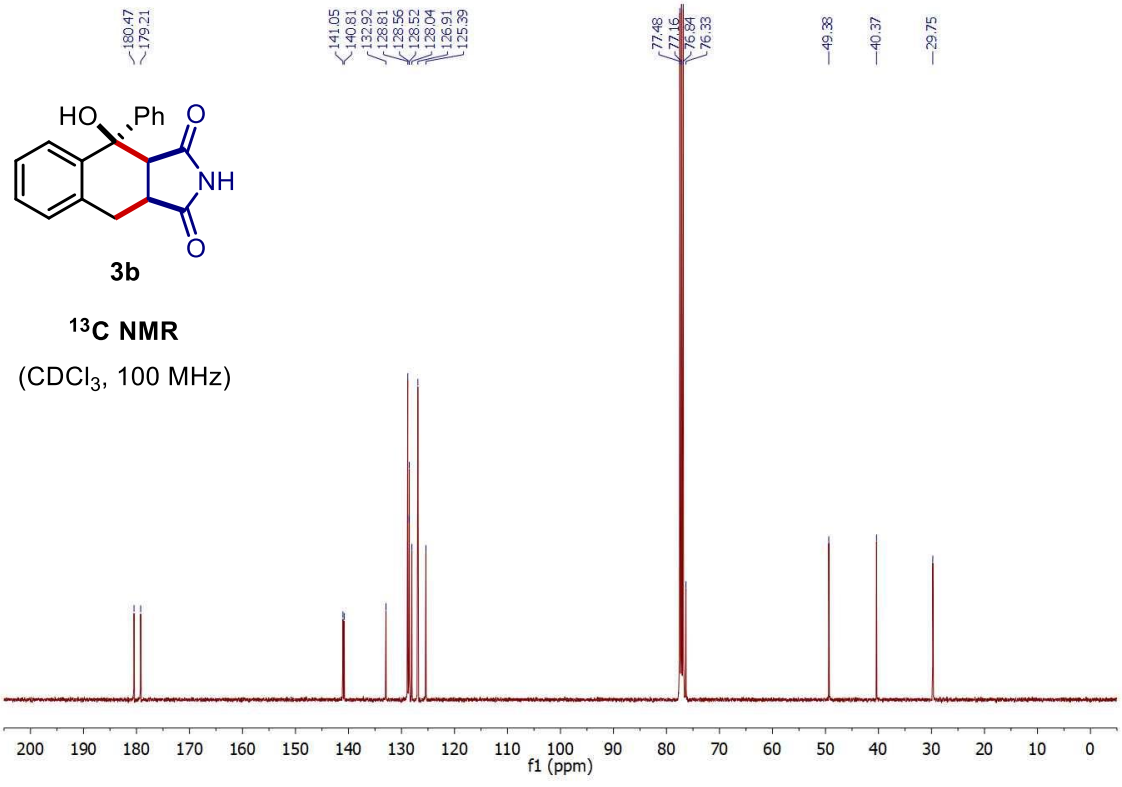

OH
H2
H3
H4α
H4ß
HO
Ph
O
N–Ph
1
2
3
4
3a
^{1}H-^{1}H NOESY NMR
(CDCl$_3$, 400 MHz)
F1 [ppm]
F2 [ppm]



3b

^{1}H NMR

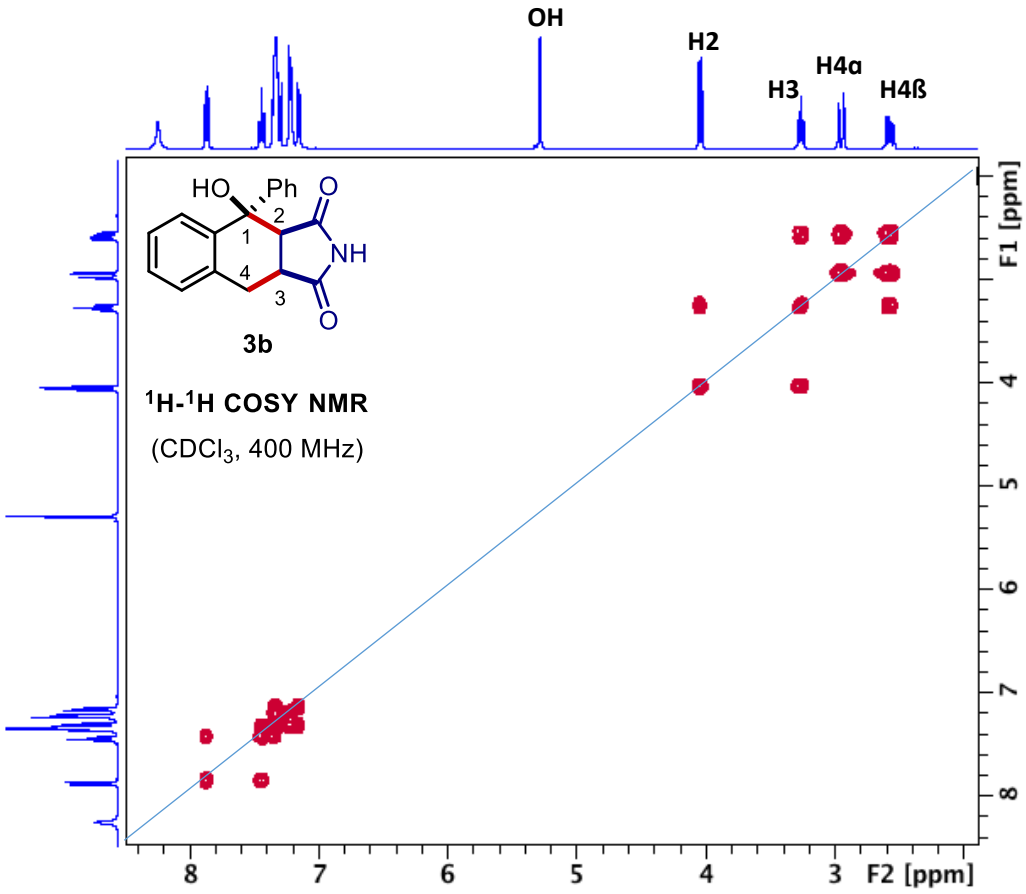
($CDCl_3$, 400 MHz)

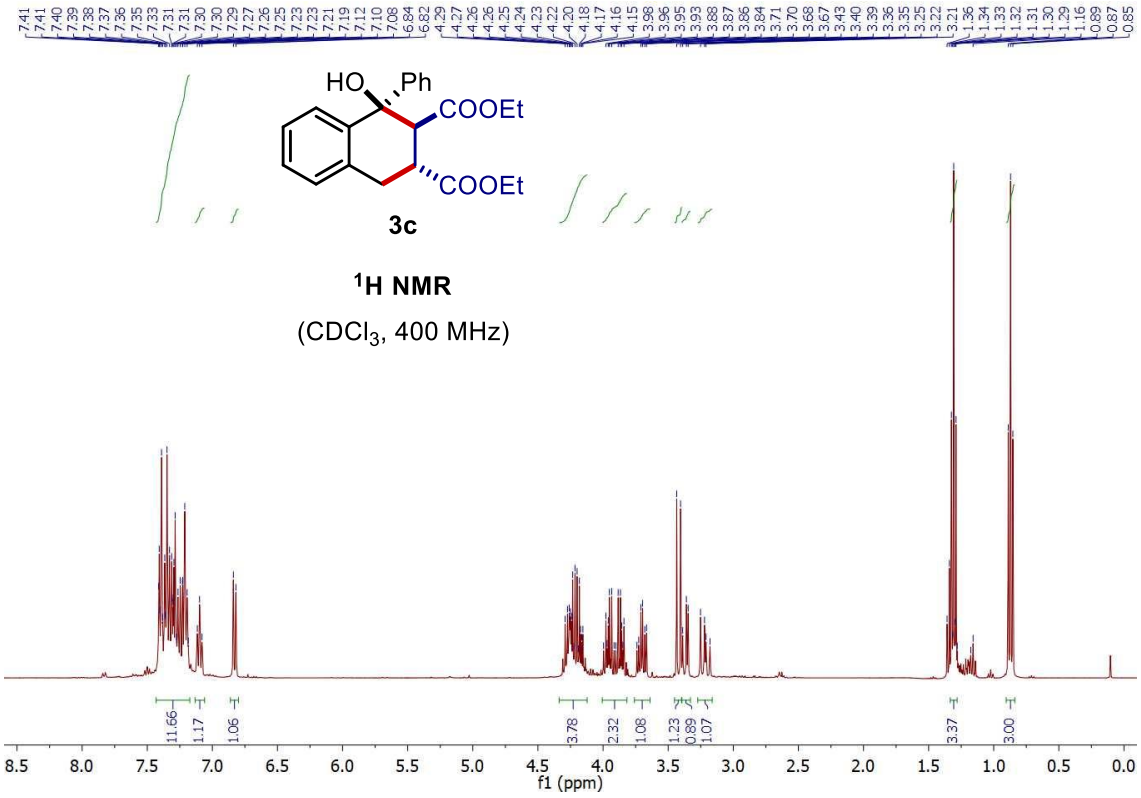


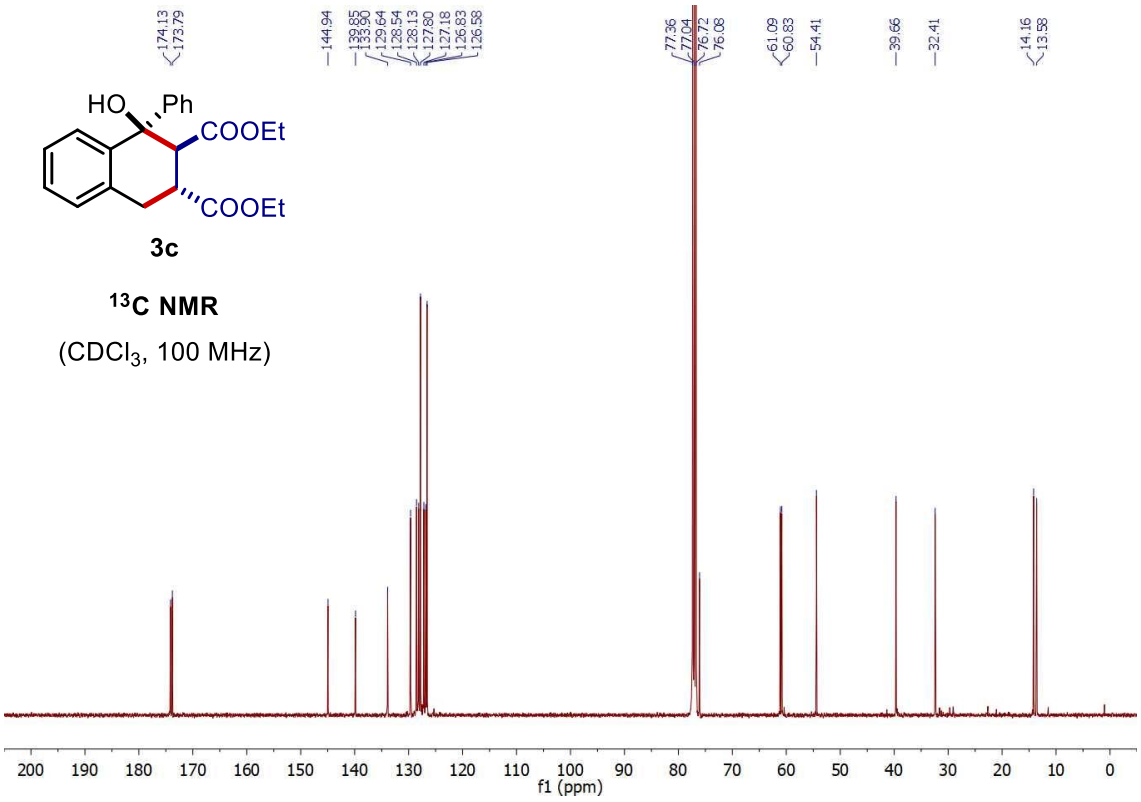
3b

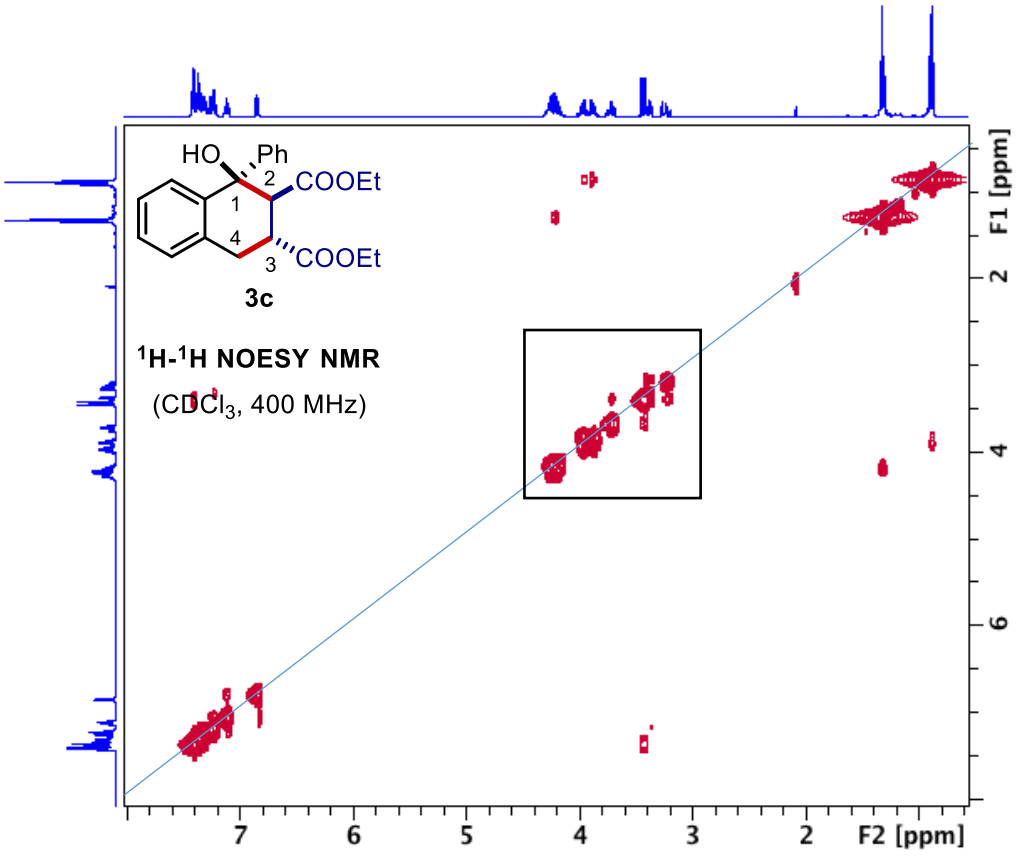
^{13}C NMR

($CDCl_3$, 100 MHz)

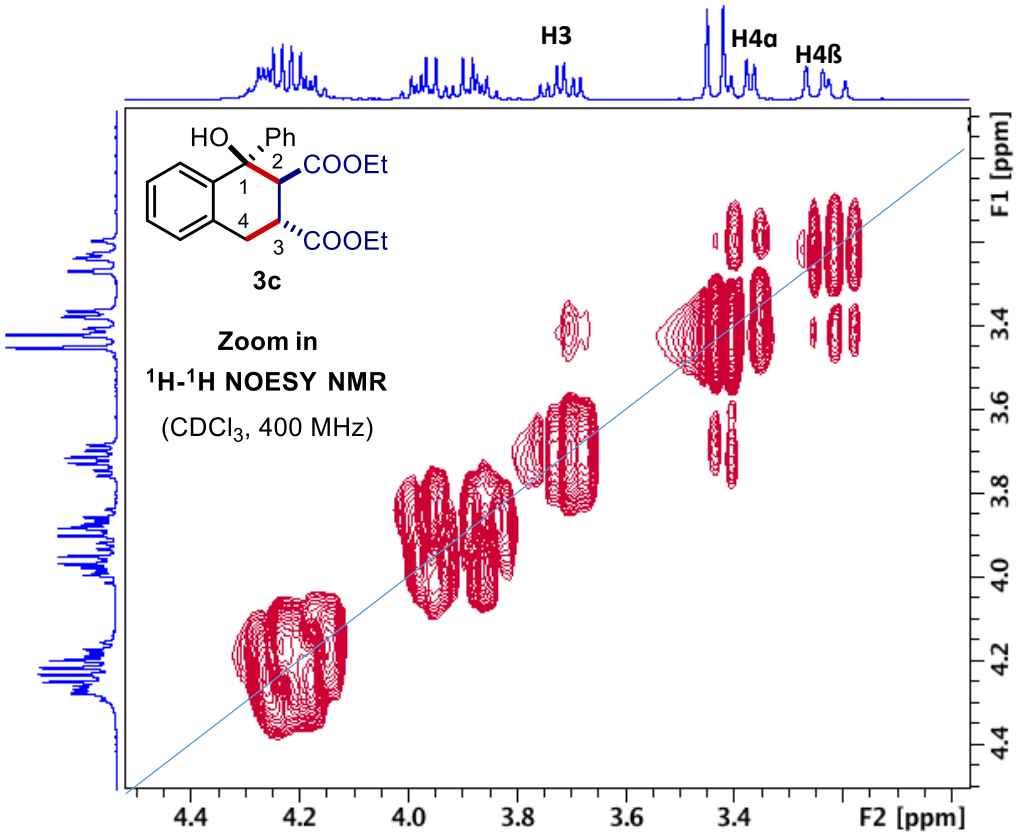

OH
H2
H3
H4a
H4ß
HO
Ph
O
NH
O
1
2
3
4
3b
^{1}H-^{1}H COSY NMR
(CDCl$_3$, 400 MHz)
F1 [ppm]
F2 [ppm]
8
7
6
5
4
3

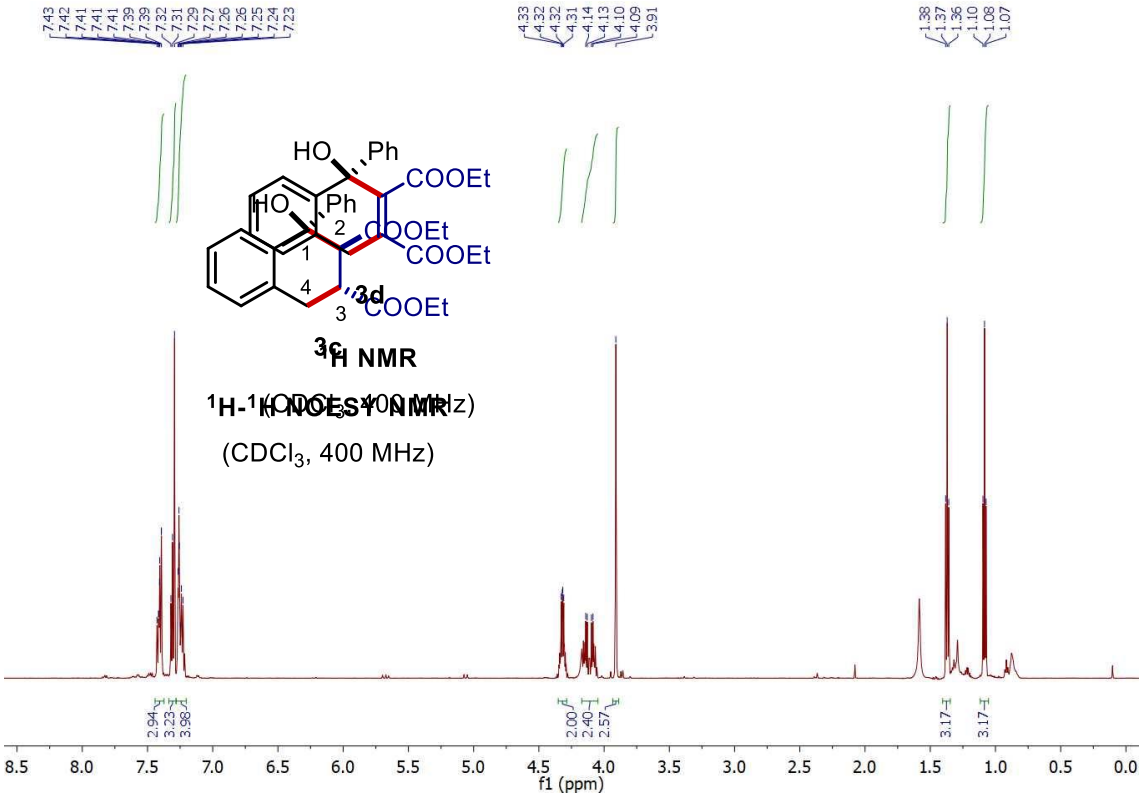

HO
Ph
COOEt
COOEt
3c
1H NMR
(CDCl3, 400 MHz)
f1 (ppm)

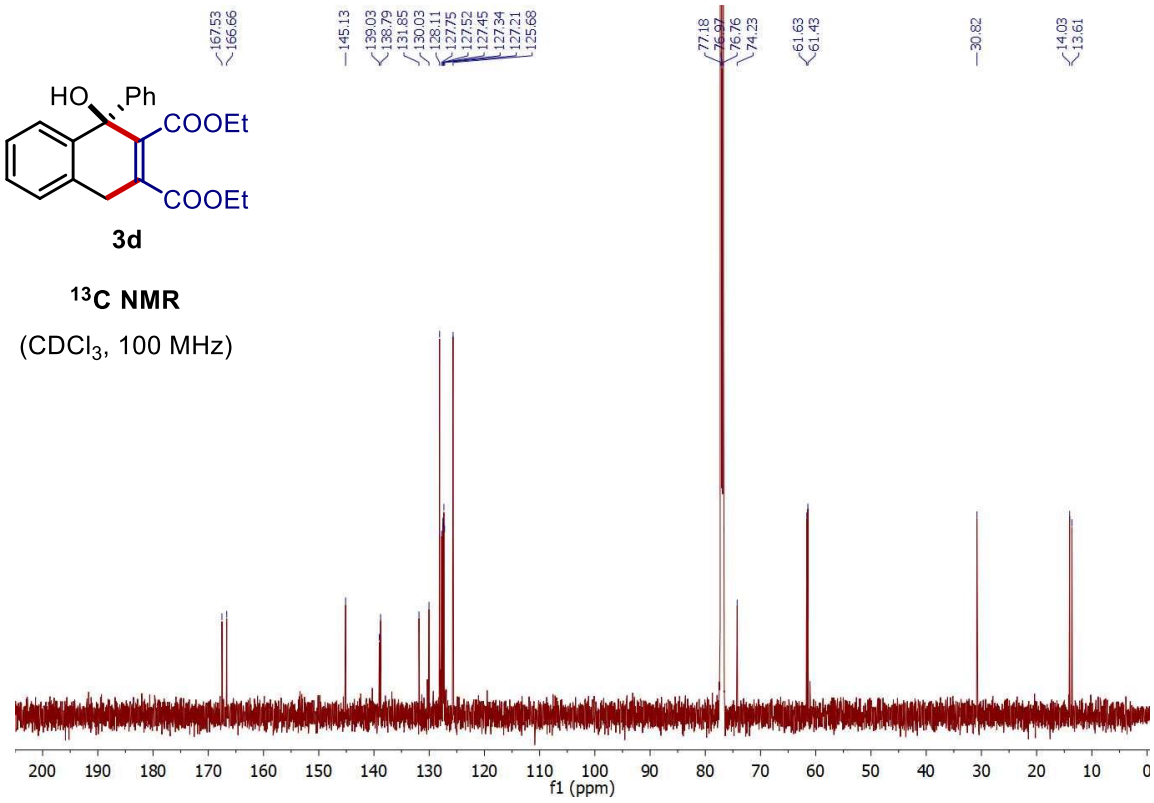

HO
Ph
COOEt
COOEt
3c
13C NMR
(CDCl3, 100 MHz)
f1 (ppm)

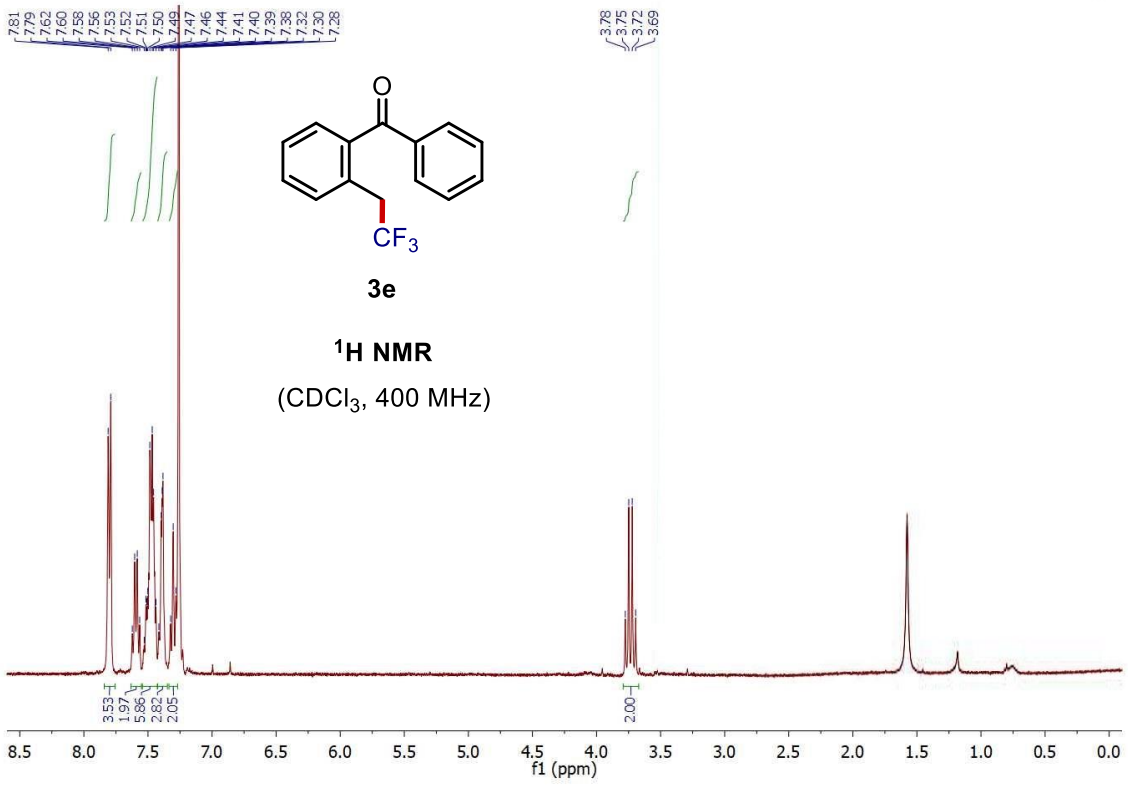

HO
Ph
2
COOEt
1
4
3
COOEt
3c
1H-1H NOESY NMR
(CDCl3, 400 MHz)
F1 [ppm]
F2 [ppm]
7
6
5
4
3
2
2
4
6

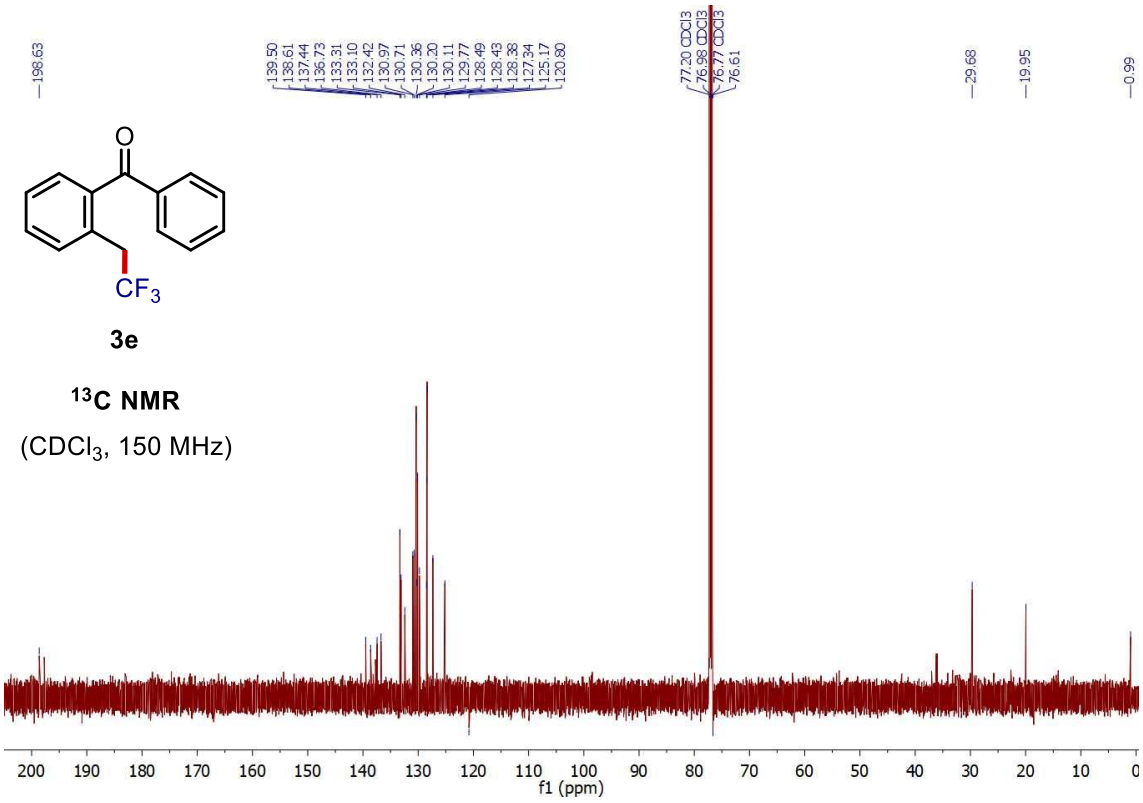
H2


H3
H4α
H4ß
HO
Ph
2
COOEt
1
4
3
COOEt
3c
Zoom in
^{1}H-^{1}H NOESY NMR
(CDCl$_3$, 400 MHz)
F1 [ppm]
4.4
4.2
4.0
3.8
3.6
3.4
F2 [ppm]


HO
Ph
COOEt
HO
Ph
2
COOEt
COOEt
1
4
3
COOEt
3d
3c
^{1}H NMR
^{1}H-^{1}H NOESY NMR
(CDCl$_3$, 400 MHz)
f1 (ppm)


HO
Ph
COOEt
COOEt
3d
13C NMR
(CDCl3, 100 MHz)
f1 (ppm)

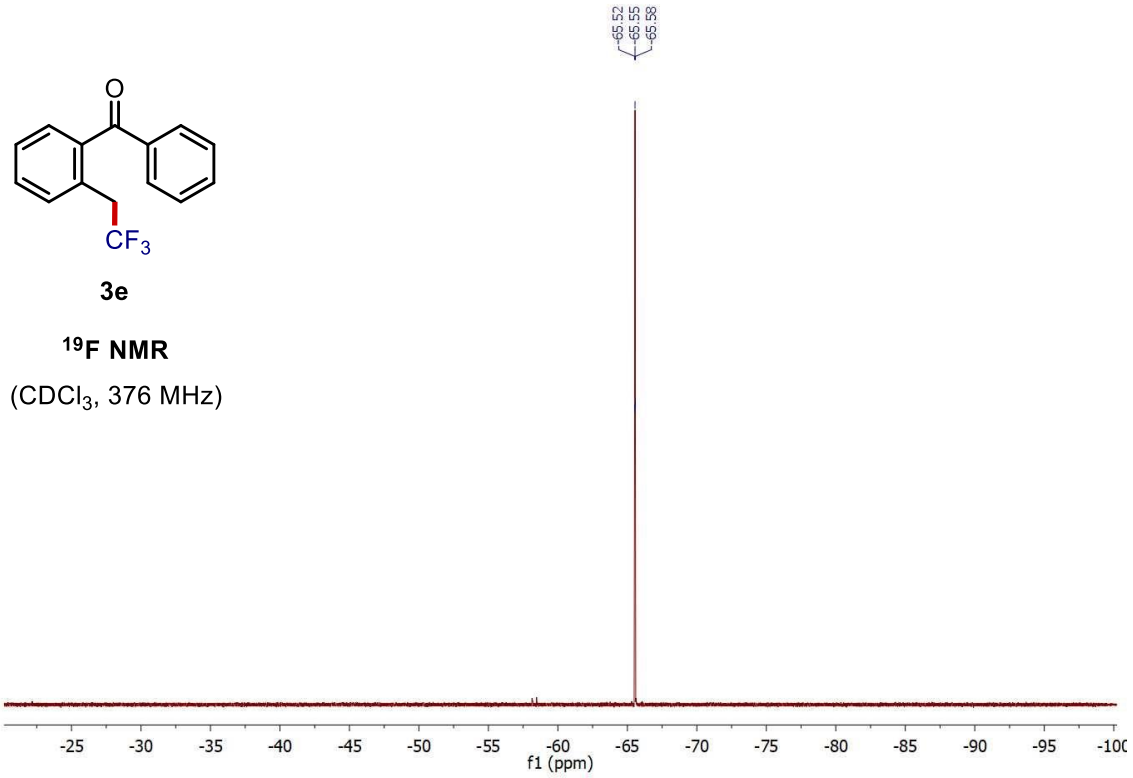

O
CF3
3e
1H NMR
(CDCl3, 400 MHz)
f1 (ppm)



3e

^{13}C NMR

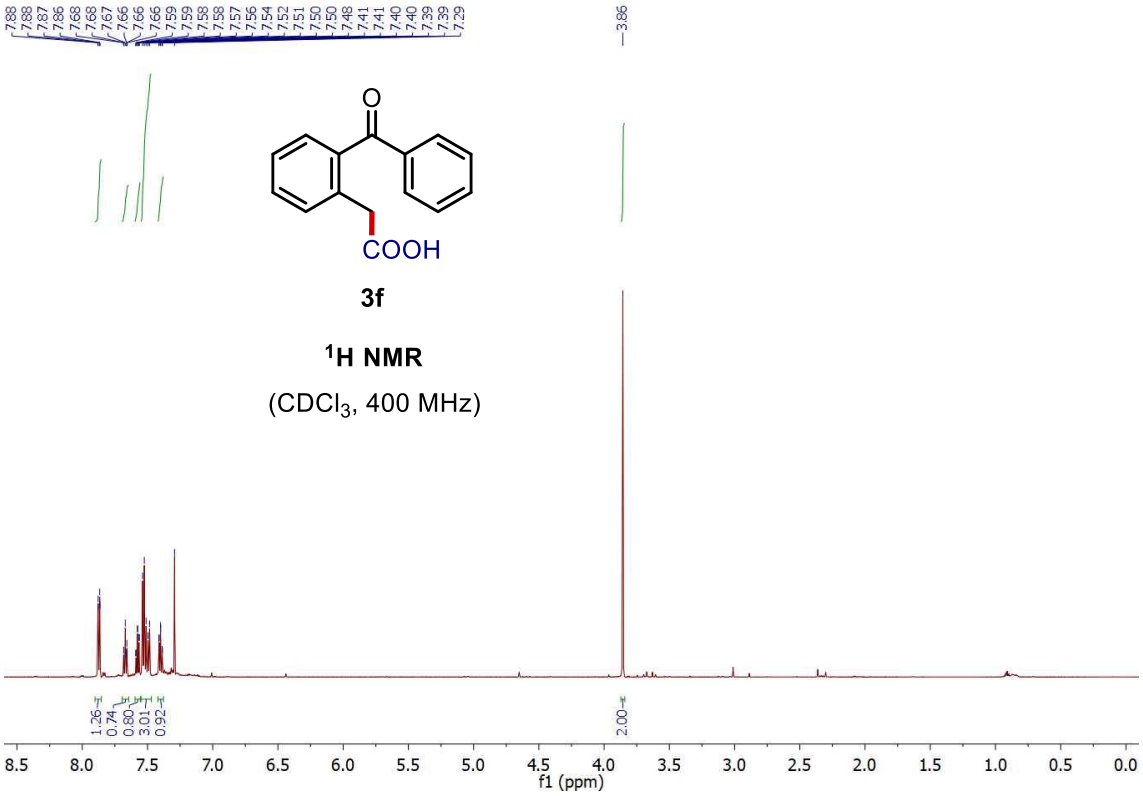
($CDCl_3$, 150 MHz)



3e

^{19}F NMR

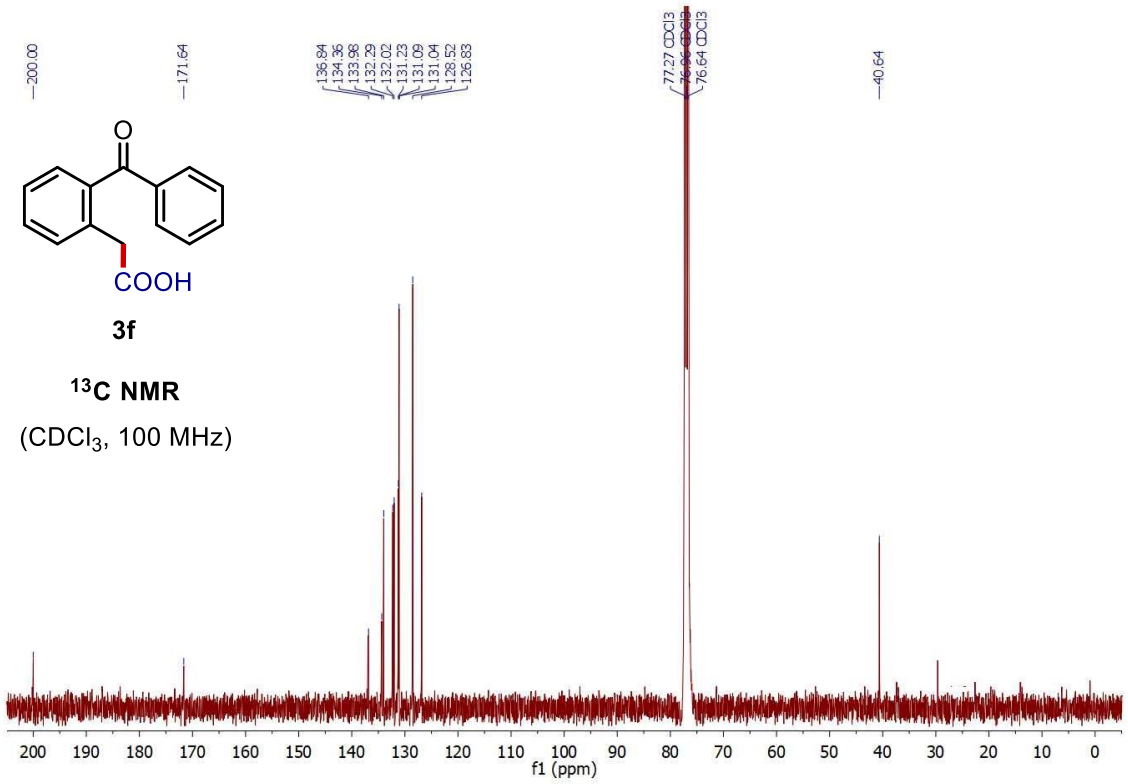
($CDCl_3$, 376 MHz)



3f

^{1}H NMR

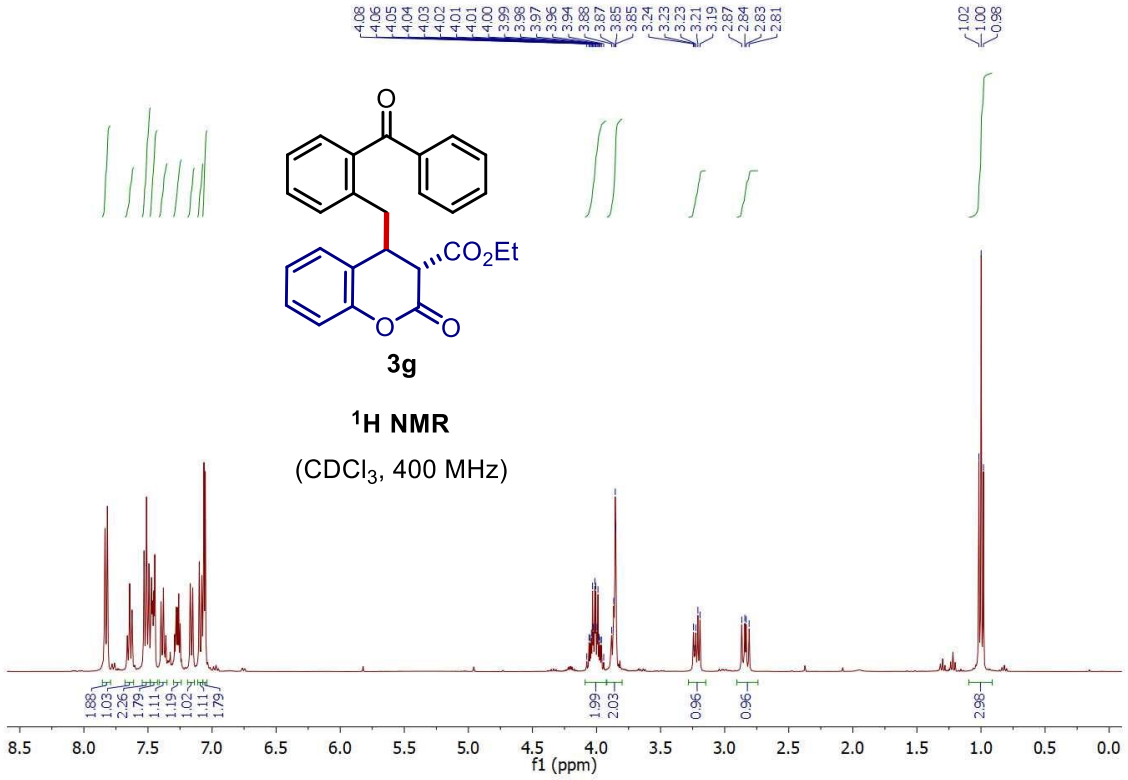
($CDCl_3$, 400 MHz)



3f

^{13}C NMR

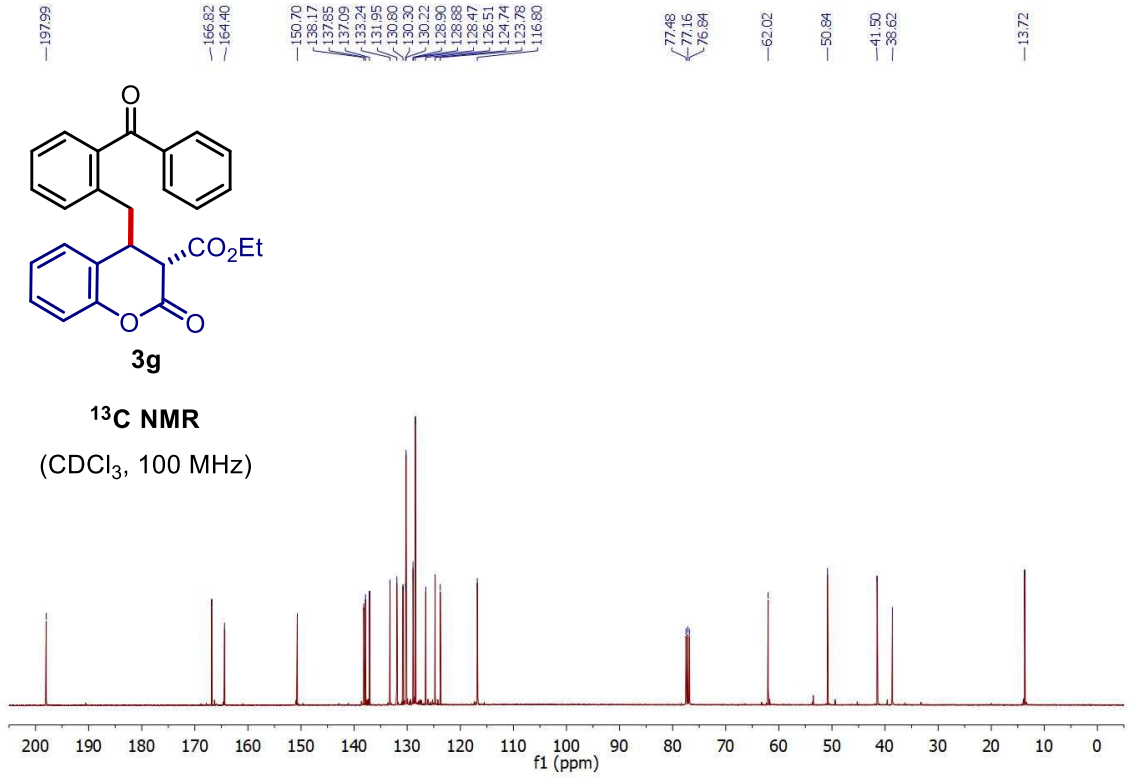
($CDCl_3$, 100 MHz)



3g

^{1}H NMR

($CDCl_3$, 400 MHz)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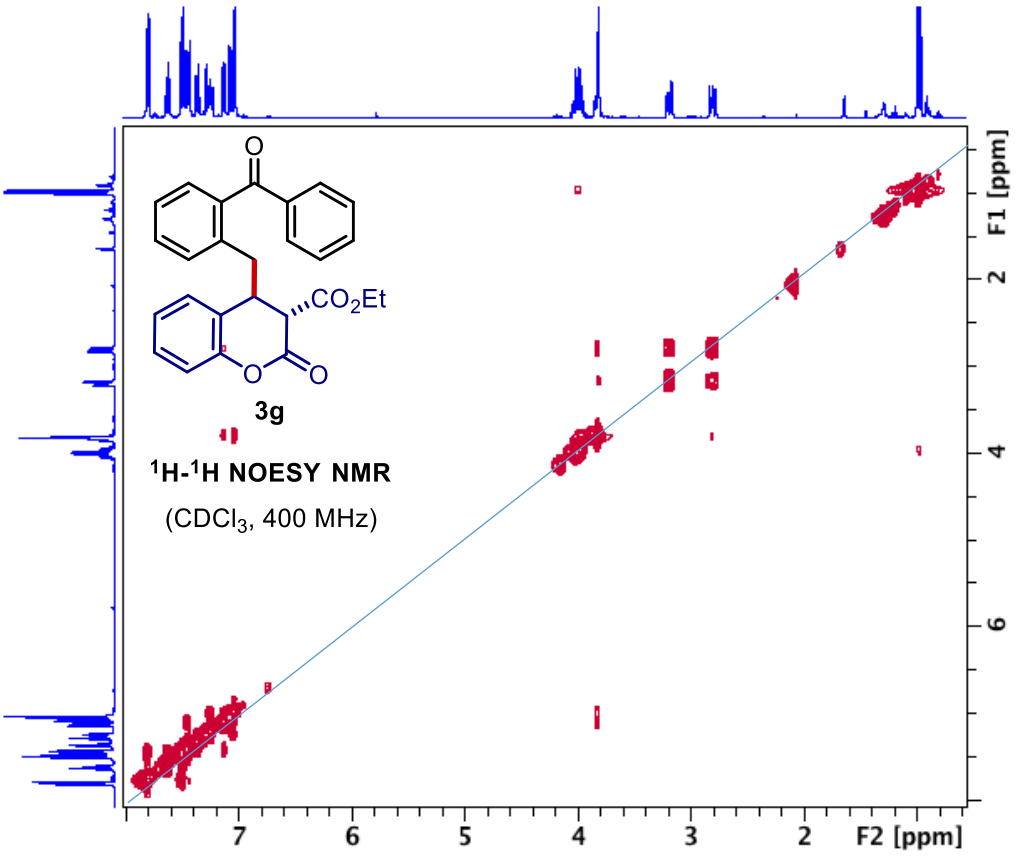
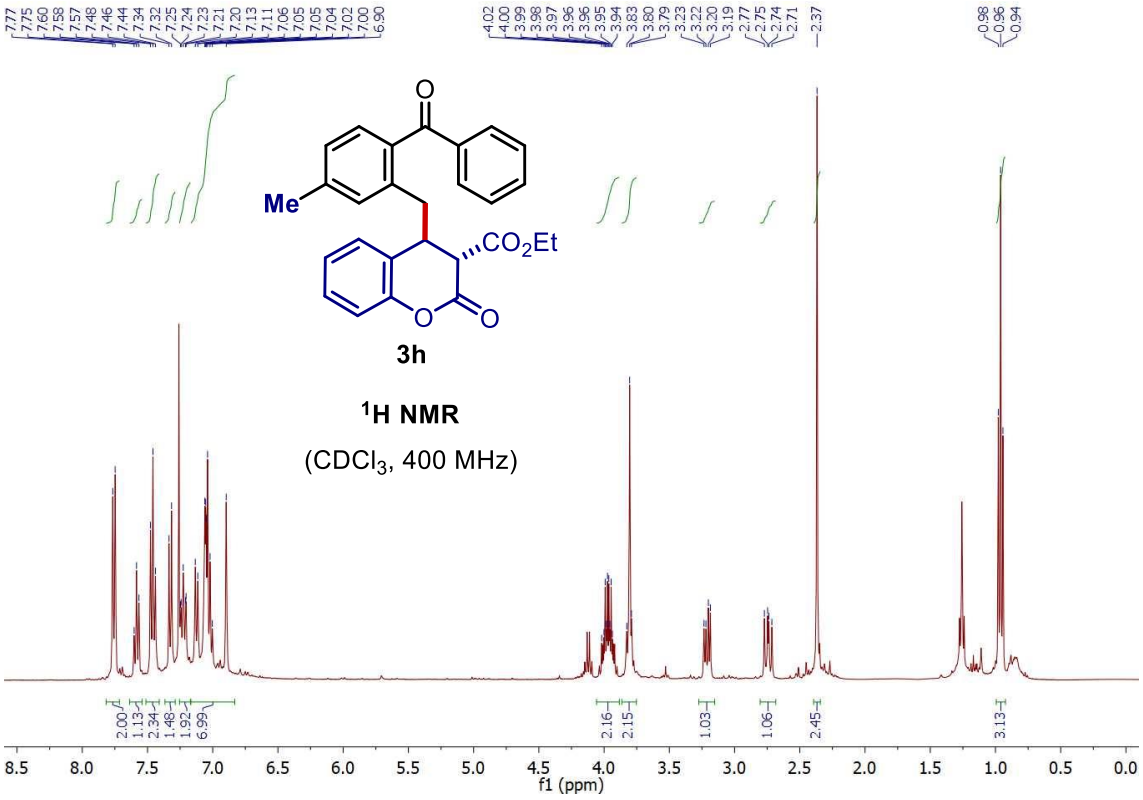
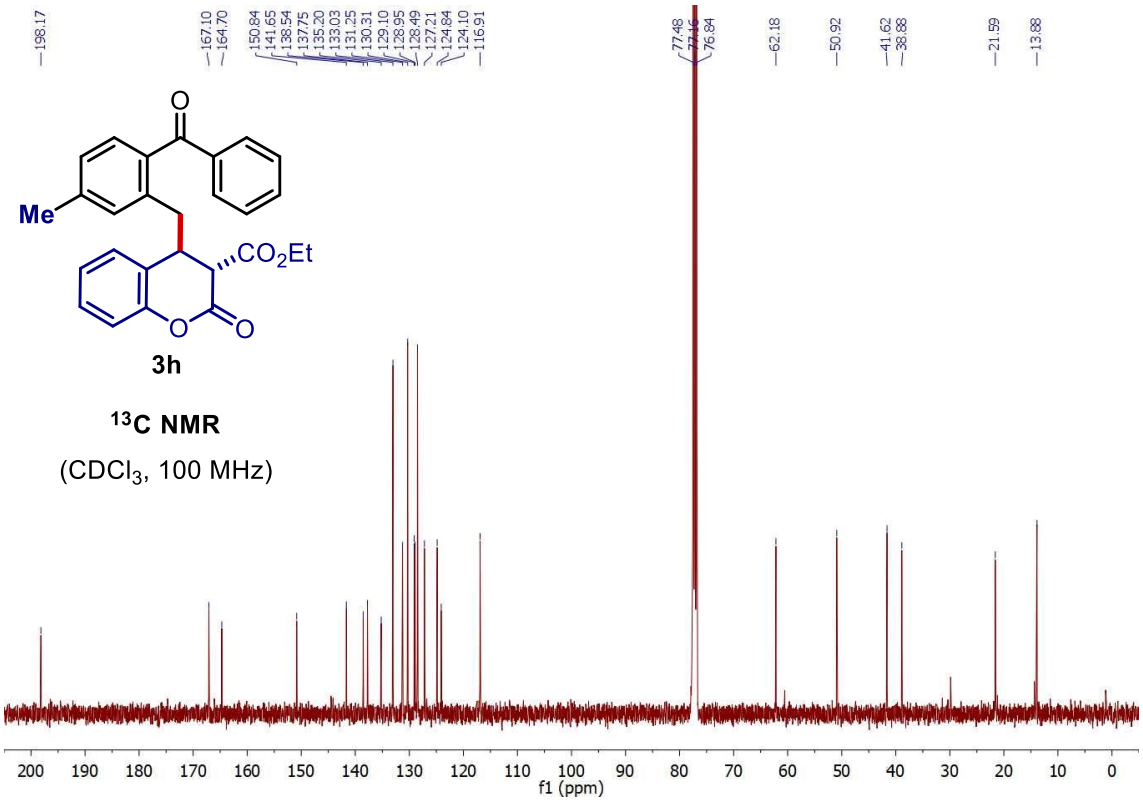
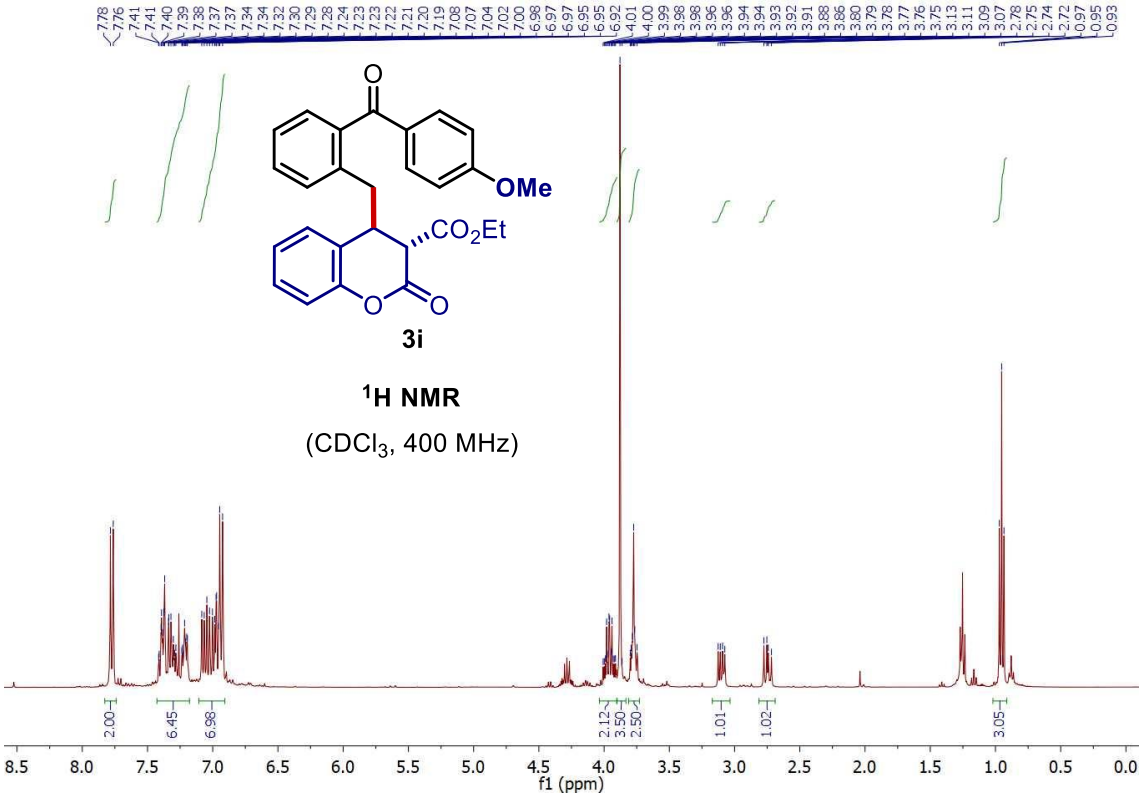
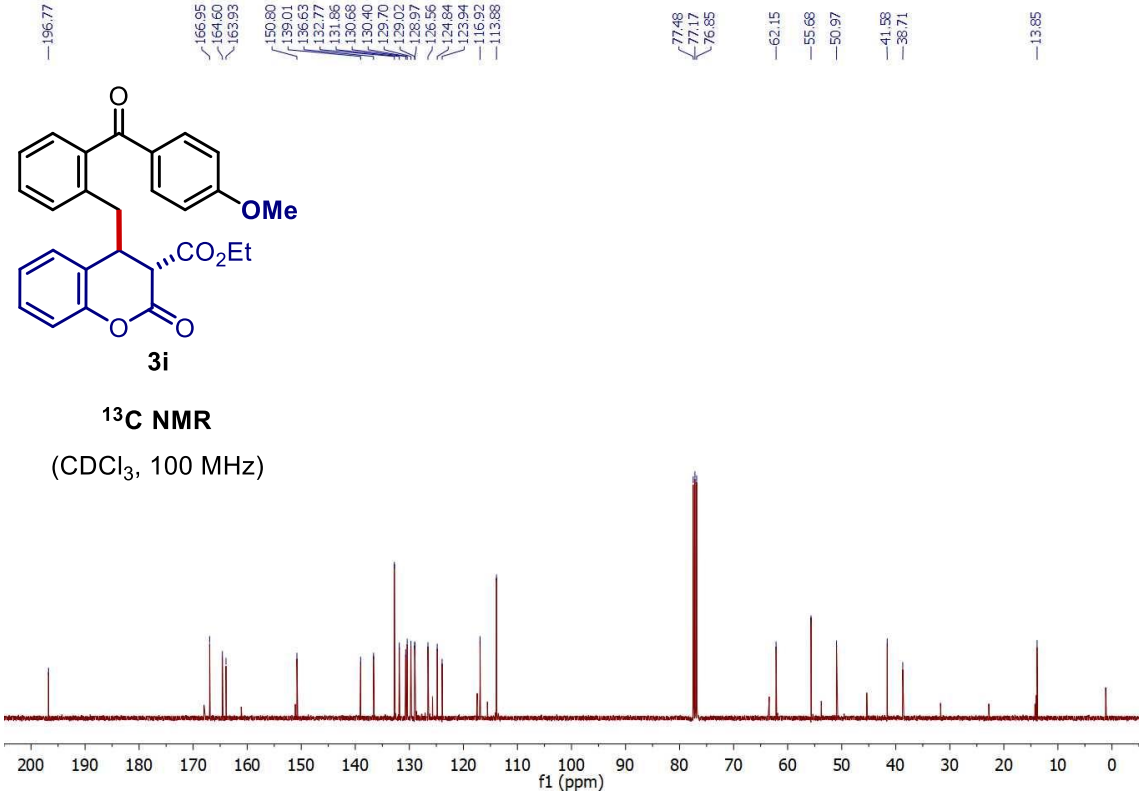
166.82
164.40
150.70
138.17
137.85
137.09
133.24
131.95
130.80
130.30
130.22
128.90
128.88
128.47
126.51
124.74
123.78
116.80
77.48
77.16
76.84
62.02
50.84
41.50
38.62
13.72
CO2Et
O
O
O
3g
13C NMR
(CDCl3, 100 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


CO2Et
O
O
O
3g
1H-1H NOESY NMR
(CDCl3, 400 MHz)
F1 [ppm]
2
4
6
7
6
5
4
3
2
F2 [ppm]


Me
CO2Et
O
O
O
3h
1H NMR
(CDCl3, 400 MHz)
f1 (ppm)


198.17
167.10
164.70
150.84
141.65
138.54
137.75
135.20
133.03
131.25
130.31
129.10
128.95
128.49
127.21
124.84
124.10
116.91
77.48
77.16
76.84
62.18
50.92
41.62
38.88
21.59
13.88
Me
CO2Et
O
O
O
3h
13C NMR
(CDCl3, 100 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

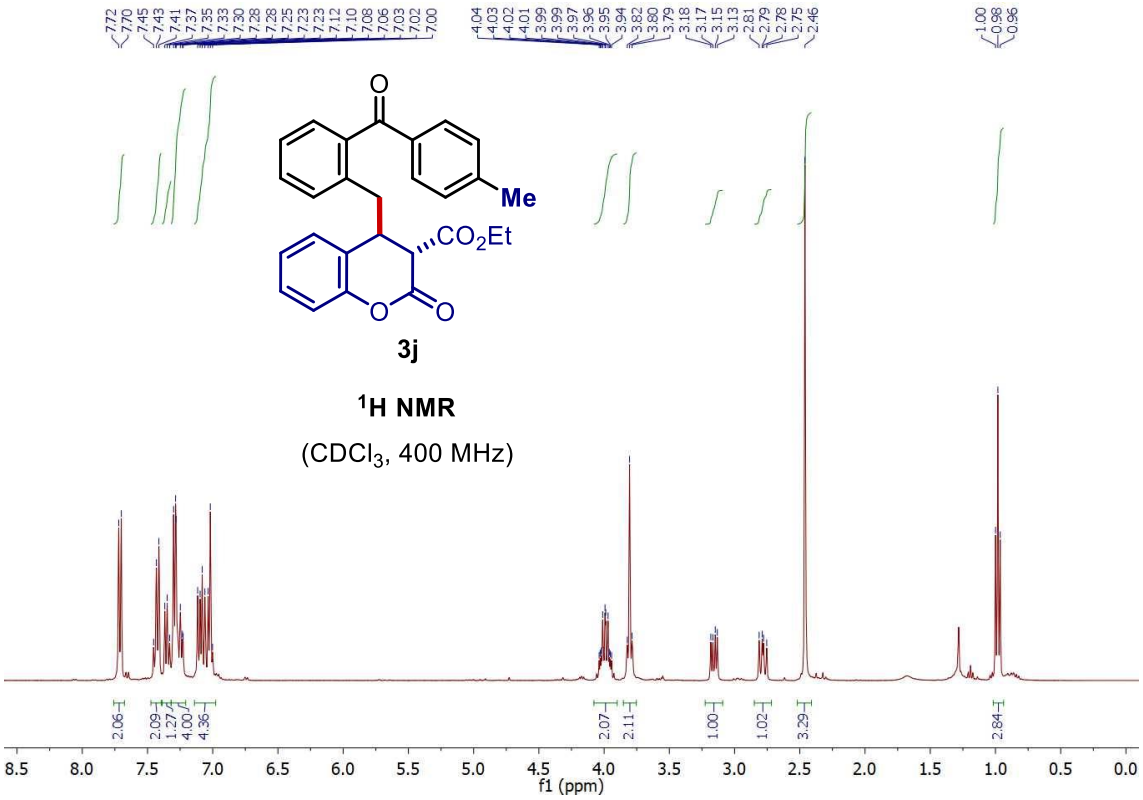

7.78
7.76
7.41
7.41
7.40
7.39
7.38
7.37
7.37
7.34
7.34
7.32
7.30
7.29
7.28
7.24
7.23
7.23
7.22
7.21
7.20
7.19
7.08
7.07
7.04
7.02
7.00
6.98
6.97
6.97
6.95
6.95
6.92
4.01
4.00
3.99
3.98
3.98
3.96
3.96
3.94
3.94
3.93
3.92
3.91
3.88
3.86
3.80
3.79
3.78
3.77
3.76
3.75
3.13
3.11
3.09
3.07
2.78
2.75
2.74
2.72
0.97
0.95
0.93
OMe
CO2Et
O
O
O
3i
1H NMR
(CDCl3, 400 MHz)
2.00
6.45
6.98
2.12
3.50
2.50
1.01
1.02
3.05
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



3i

^{13}C NMR

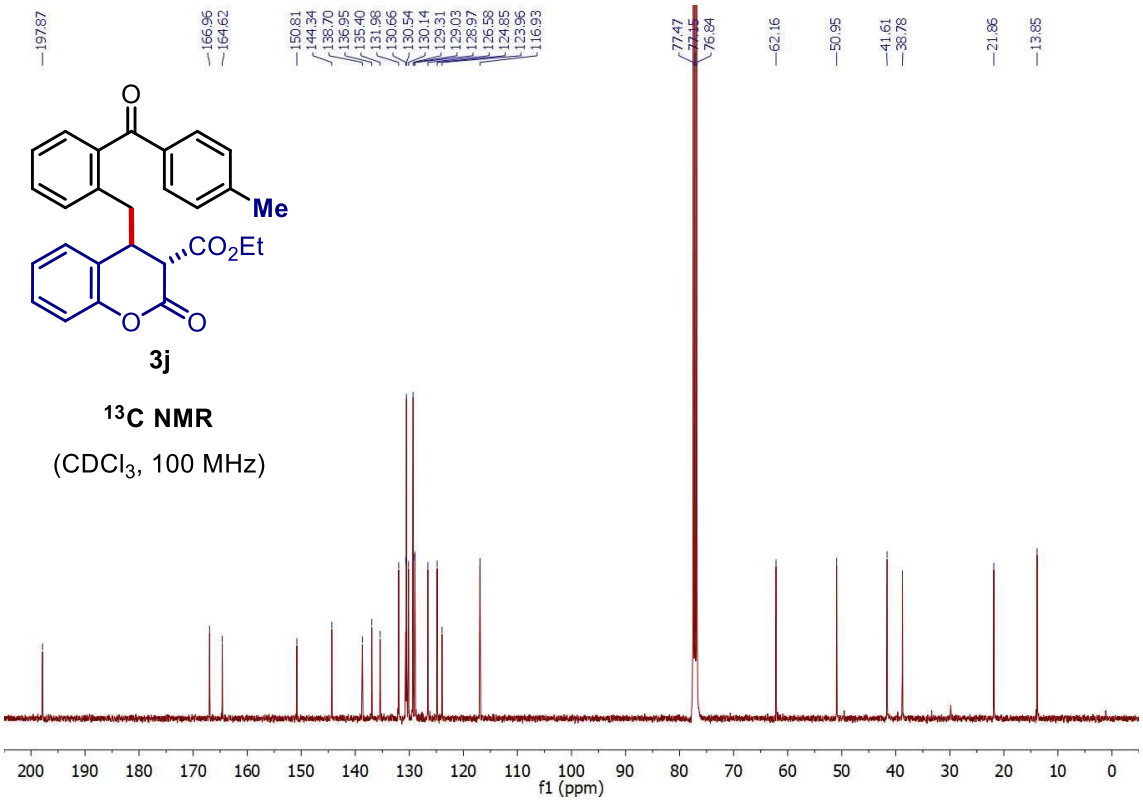
($CDCl_3$, 100 MHz)



3j

^{1}H NMR

($CDCl_3$, 400 MHz)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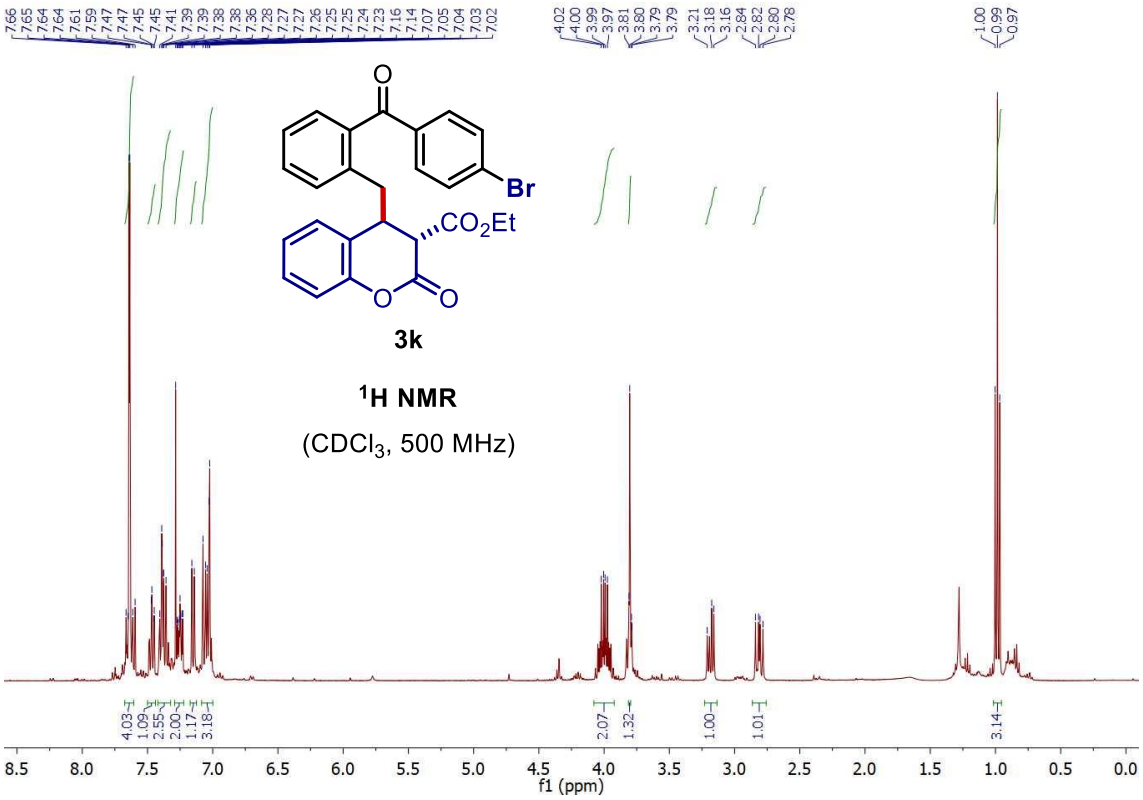
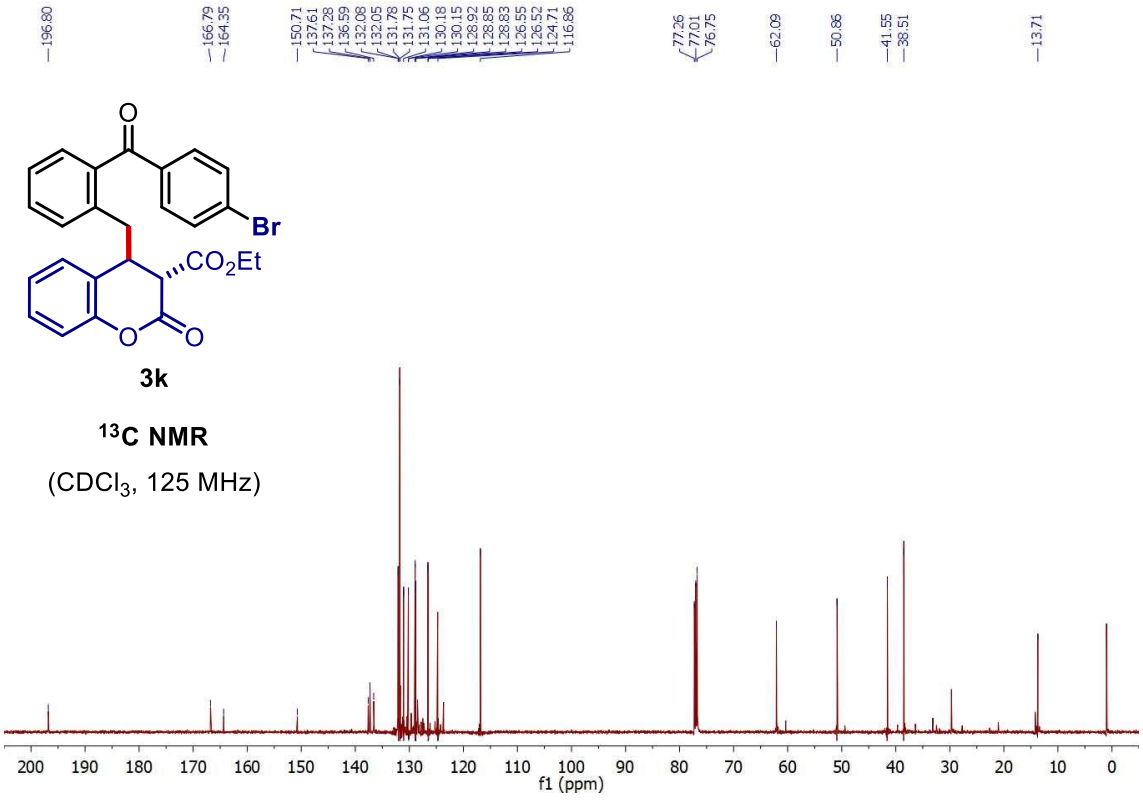
166.96
164.62
150.81
144.34
138.70
136.95
135.40
131.98
130.66
130.54
130.14
129.31
129.03
128.97
126.58
124.85
123.96
116.93
77.47
77.15
76.84
62.16
50.95
41.61
38.78
21.86
13.85
Me
CO2Et
O
O
O
3j
13C NMR
(CDCl3, 100 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

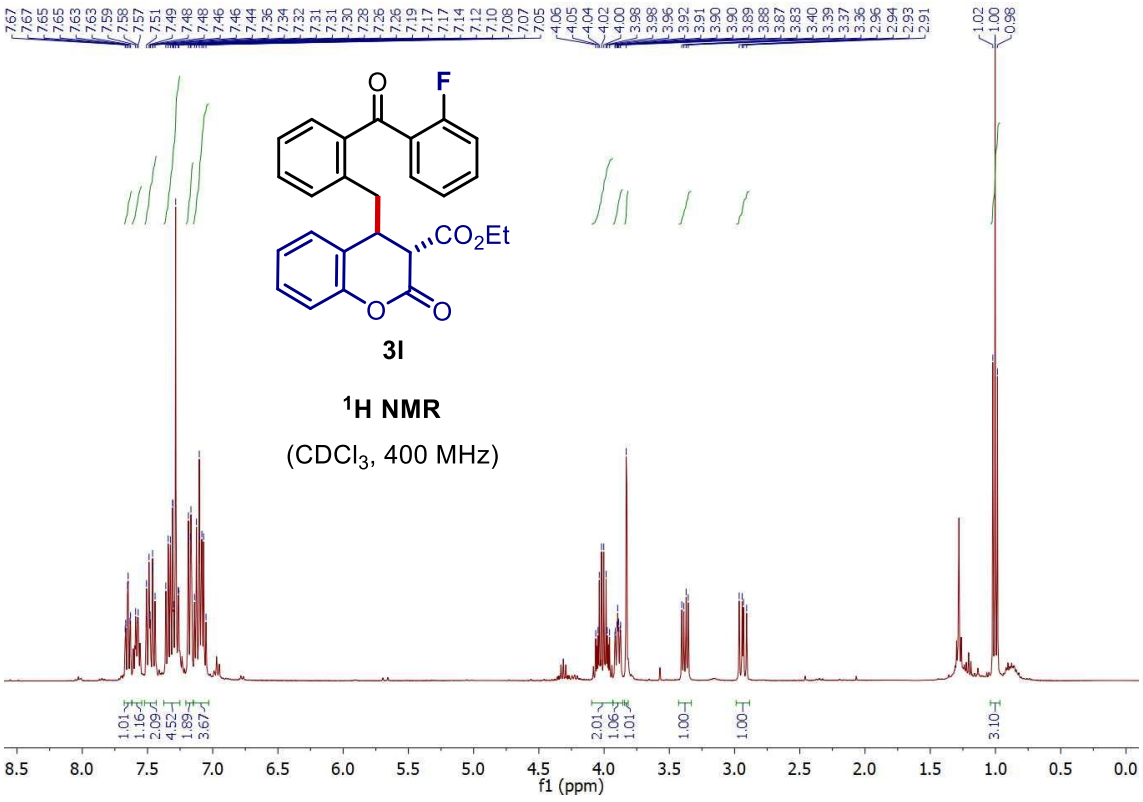

7.66
7.65
7.64
7.64
7.61
7.59
7.47
7.47
7.45
7.45
7.41
7.39
7.39
7.38
7.38
7.36
7.28
7.27
7.27
7.26
7.25
7.25
7.24
7.23
7.16
7.14
7.07
7.05
7.04
7.03
7.02
4.02
4.00
3.99
3.97
3.81
3.80
3.79
3.79
3.21
3.18
3.16
2.84
2.82
2.80
2.78
1.00
0.99
0.97
Br
CO2Et
O
O
O
3k
1H NMR
(CDCl3, 500 MHz)
4.03
1.09
2.55
2.00
1.17
3.18
2.07
1.32
1.00
1.01
3.14
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



3k

^{13}C NMR

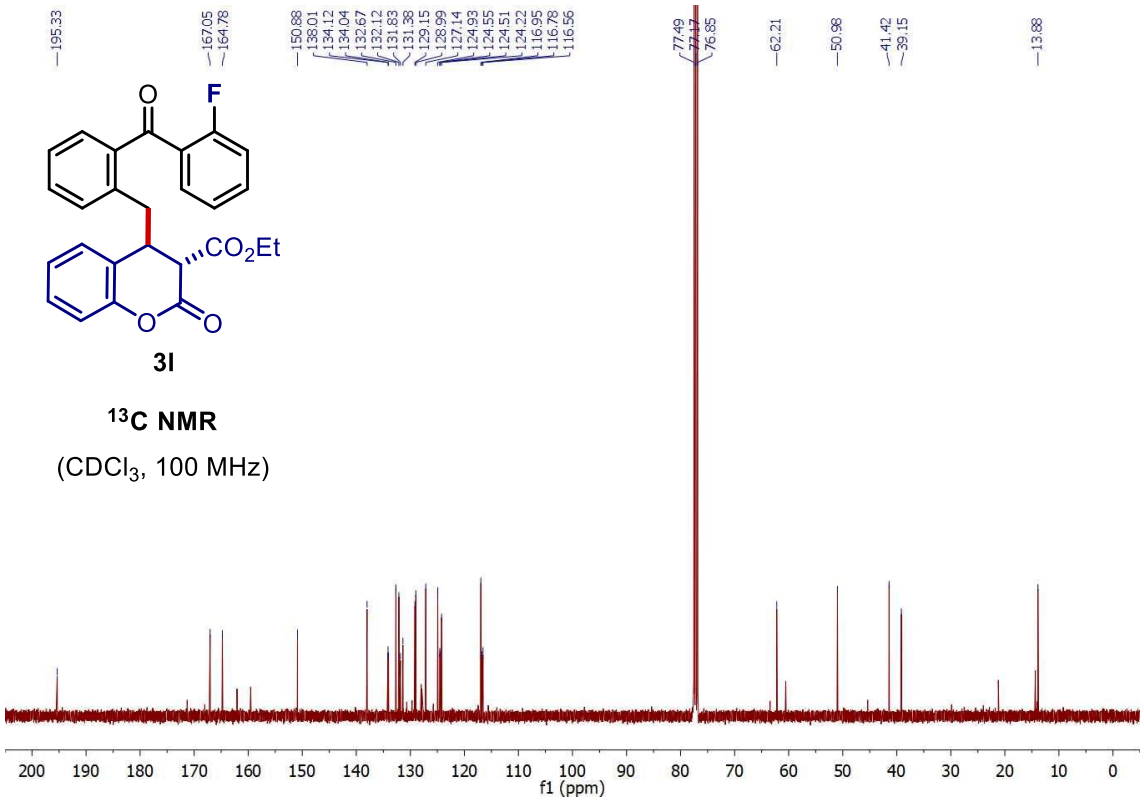
($CDCl_3$, 125 MHz)



3l

^{1}H NMR

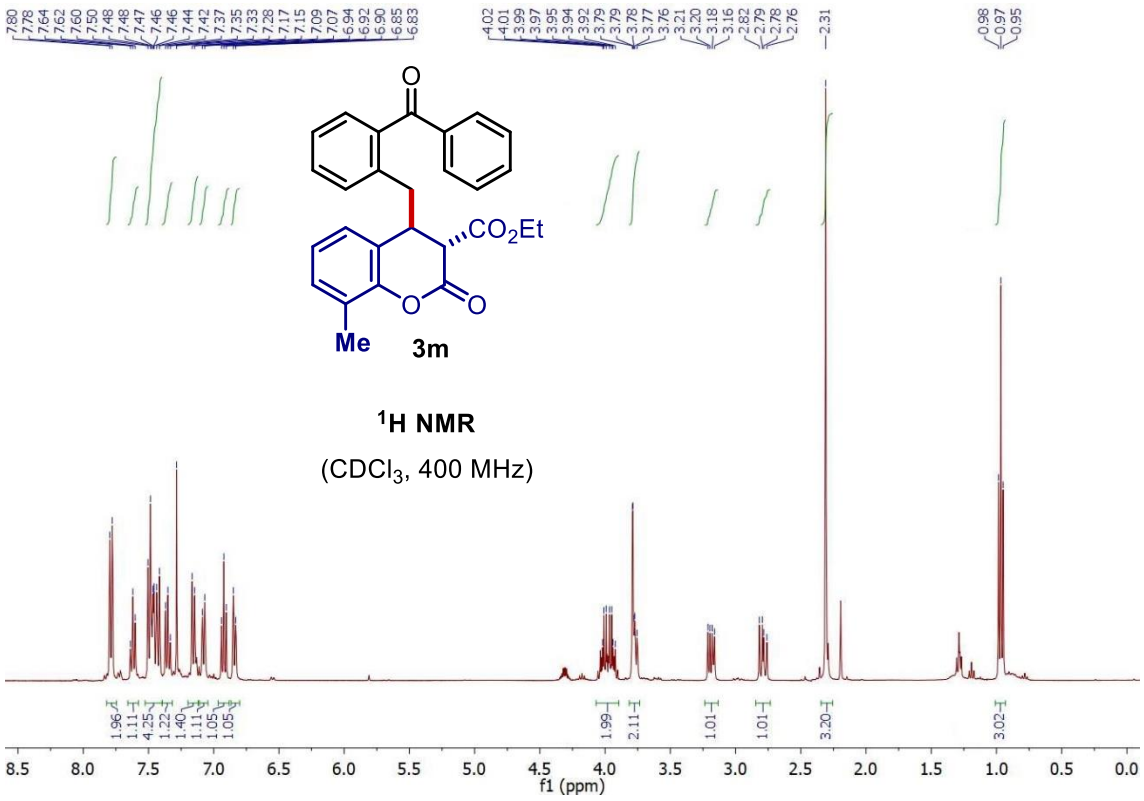
($CDCl_3$, 400 MHz)



3l

^{13}C NMR

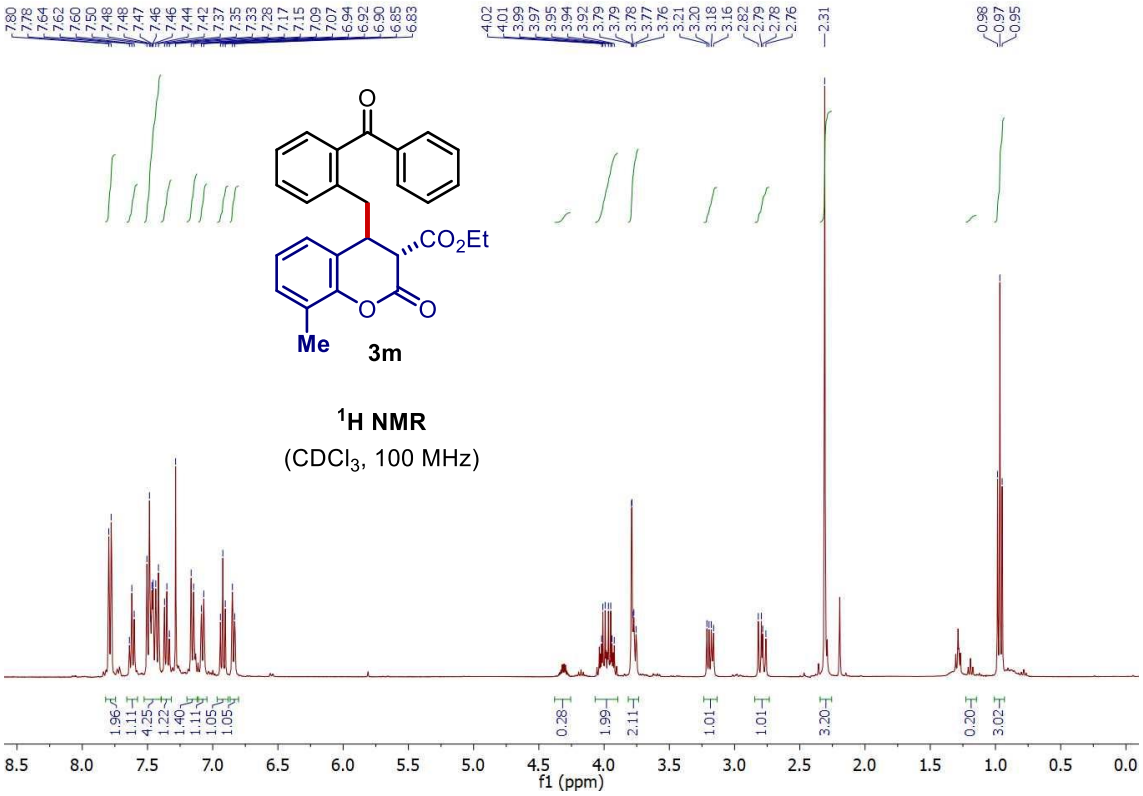
($CDCl_3$, 100 MHz)

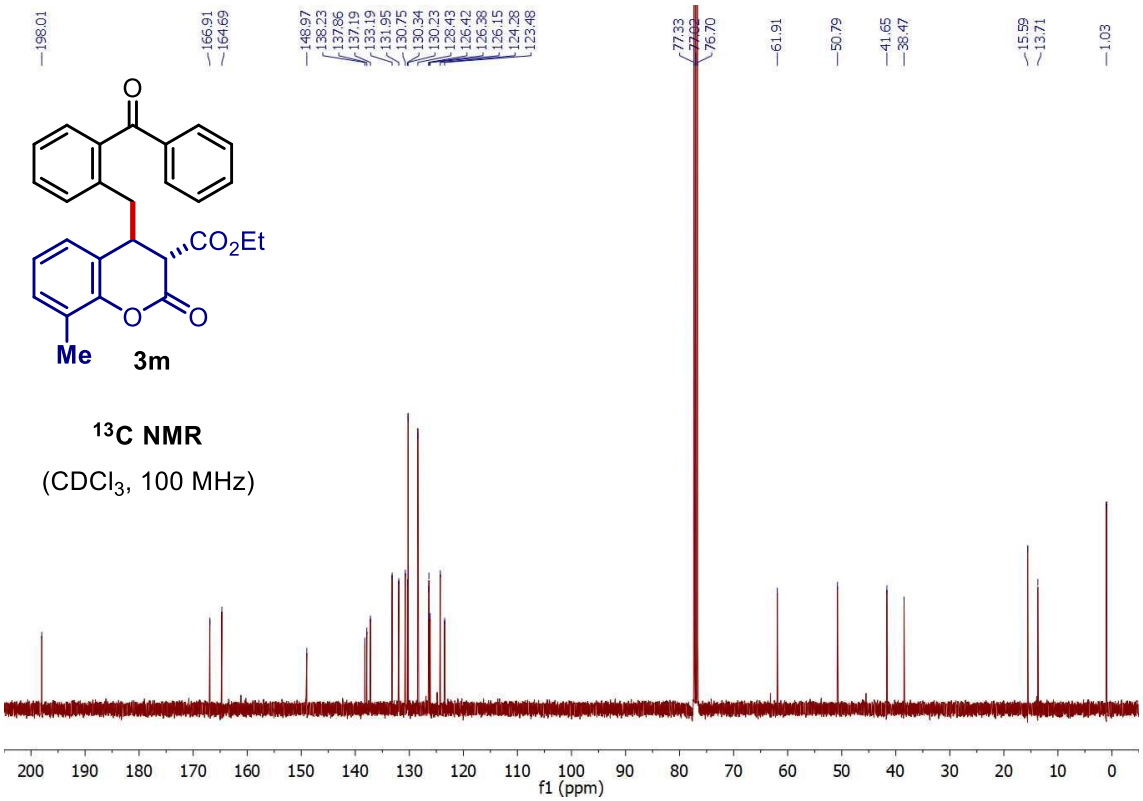


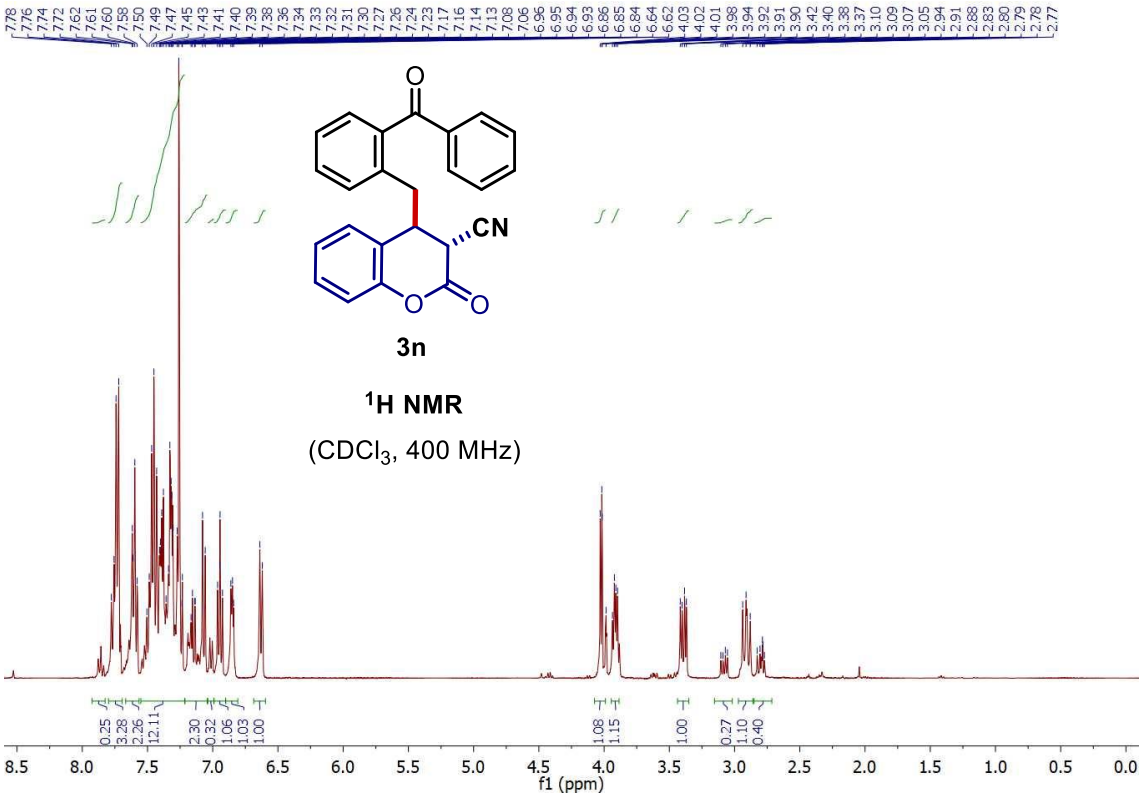
3m

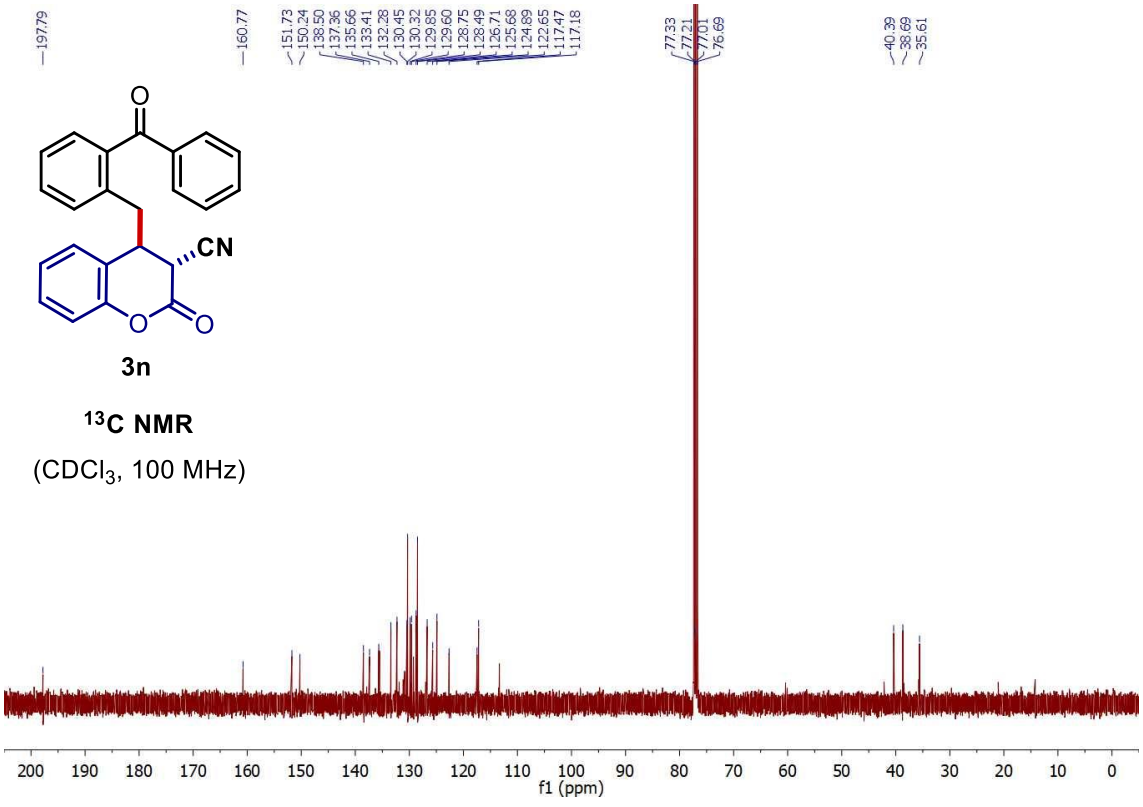
^{1}H NMR

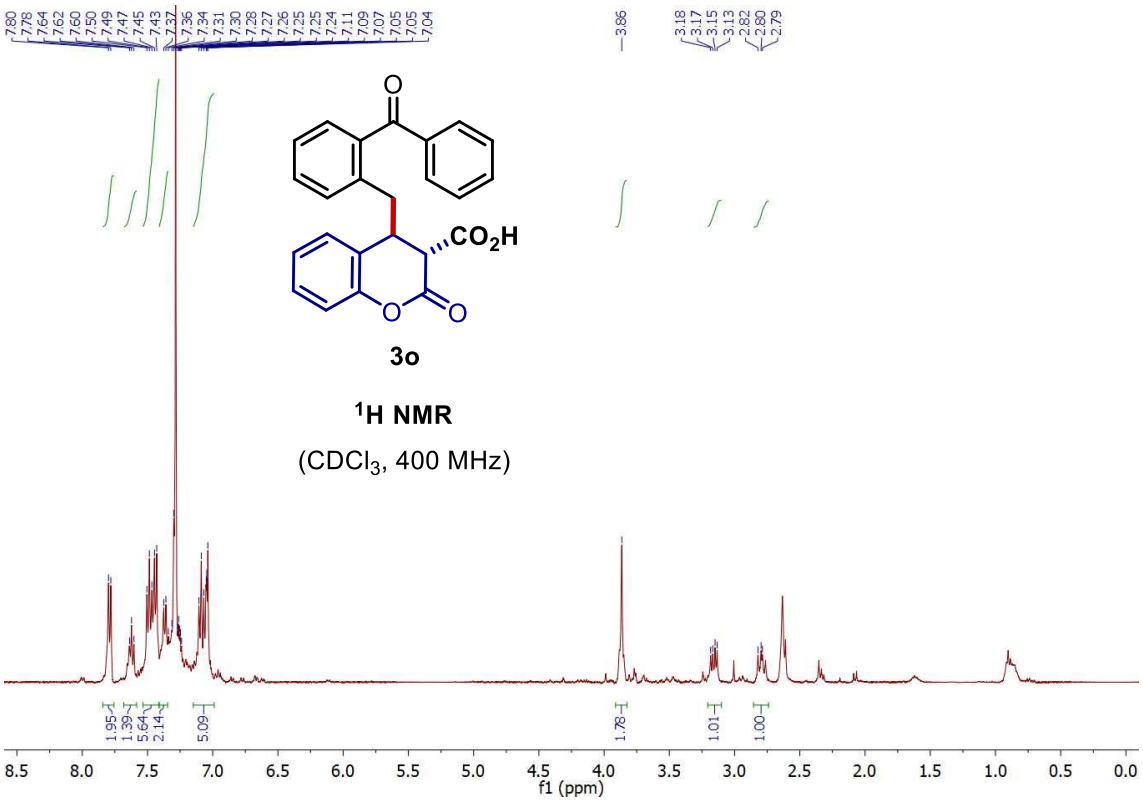
($CDCl_3$, 400 MHz)


7.80
7.78
7.64
7.62
7.60
7.50
7.48
7.48
7.47
7.46
7.46
7.44
7.42
7.37
7.35
7.33
7.28
7.17
7.15
7.09
7.07
6.94
6.92
6.90
6.85
6.83
4.02
4.01
3.99
3.97
3.95
3.94
3.92
3.79
3.79
3.78
3.77
3.76
3.21
3.20
3.18
3.16
2.82
2.79
2.78
2.76
2.31
0.98
0.97
0.95
O
CO2Et
O
O
Me
3m
1H NMR
(CDCl3, 100 MHz)
1.96
1.11
4.25
1.22
1.40
1.11
1.05
1.05
0.28
1.99
2.11
1.01
1.01
3.20
0.20
3.02
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


198.01
166.91
164.69
148.97
138.23
137.86
137.19
133.19
131.95
130.75
130.34
130.23
128.43
126.42
126.38
126.15
124.28
123.48
77.33
77.00
76.70
61.91
50.79
41.65
38.47
15.59
13.71
1.03
O
CO2Et
O
O
Me
3m
13C NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


CN
O
O
O
3n
1H NMR
(CDCl3, 400 MHz)
f1 (ppm)

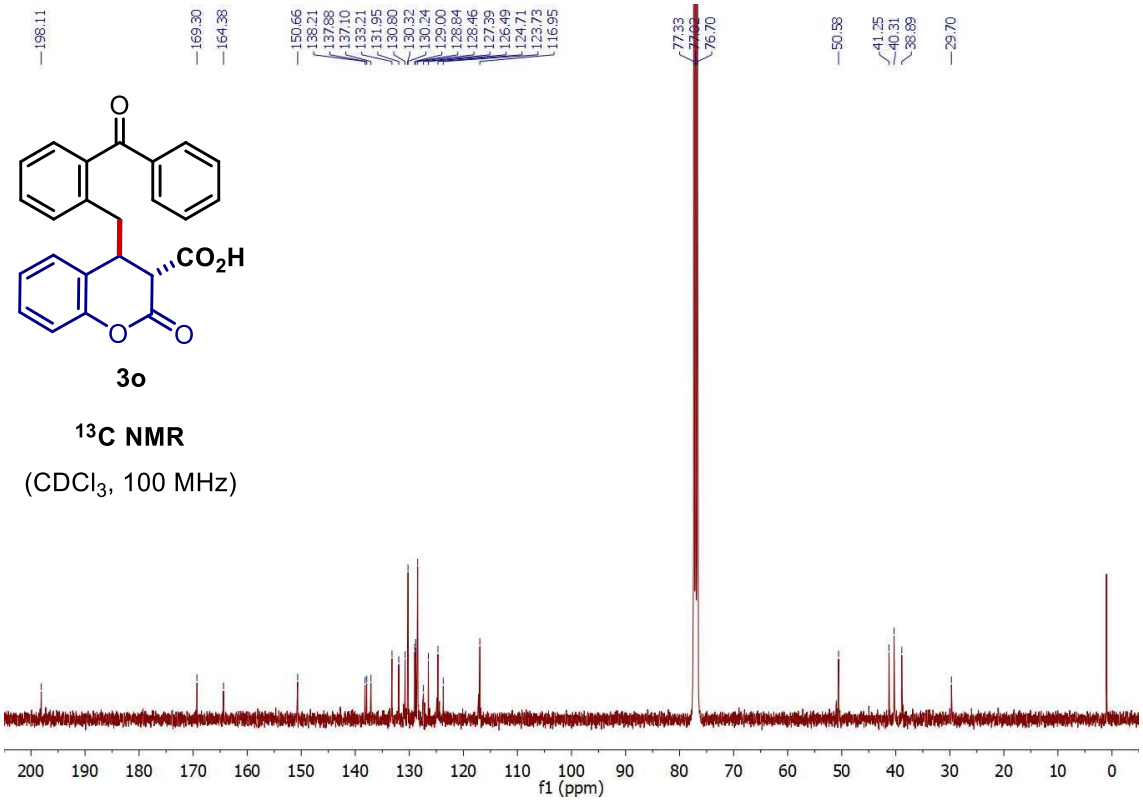

CN
O
O
O
3n
13C NMR
(CDCl3, 100 MHz)
f1 (ppm)



3o

^{1}H NMR

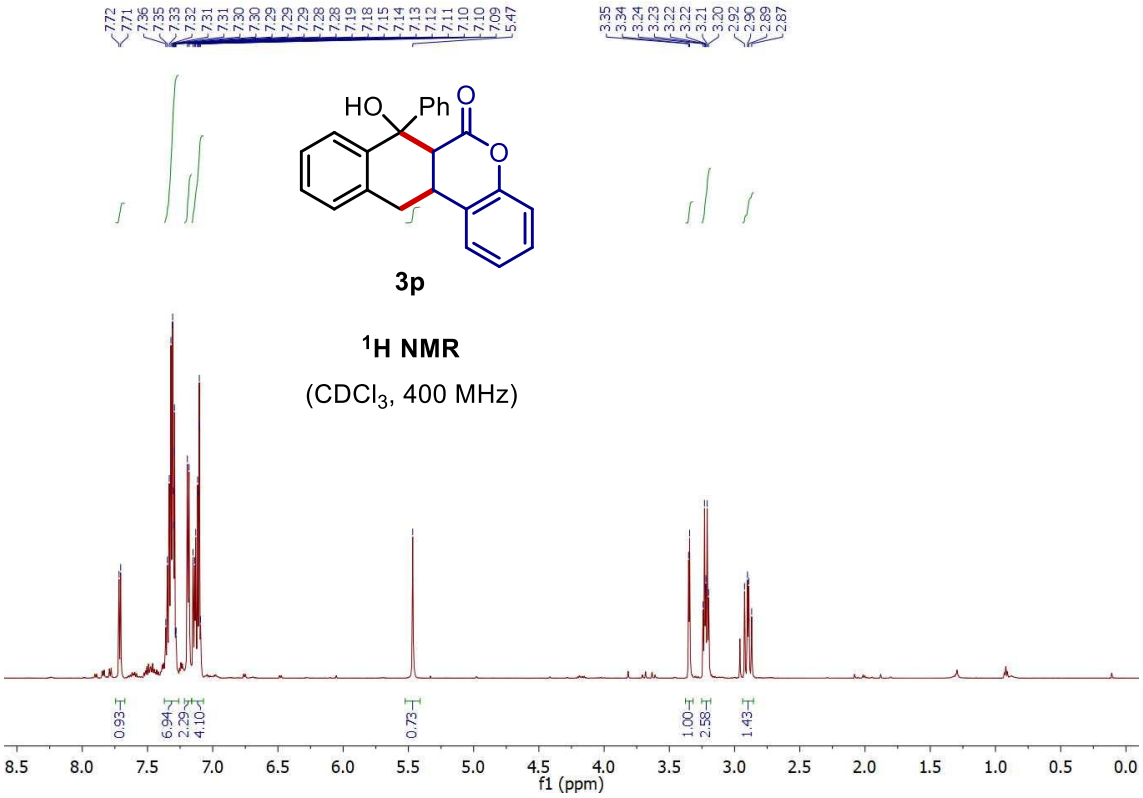
($CDCl_3$, 400 MHz)

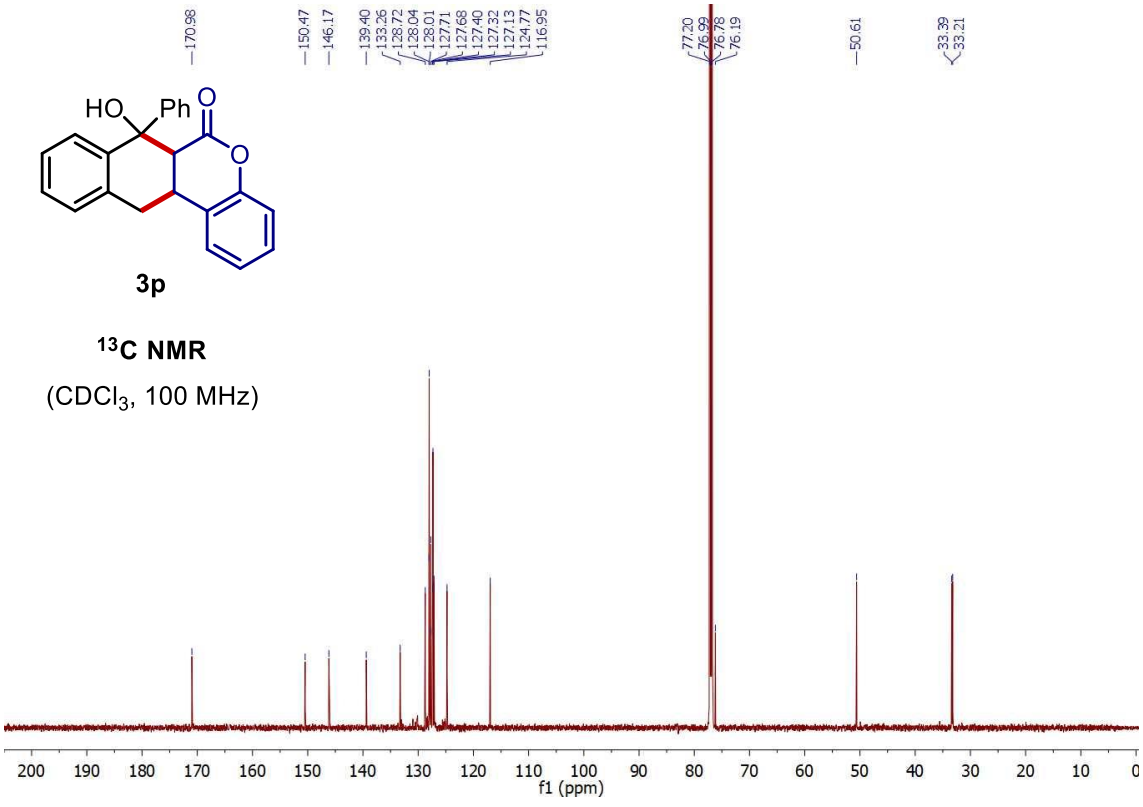


3o

^{13}C NMR

($CDCl_3$, 100 MHz)


HO
Ph
O
O
3p
1H NMR
(CDCl3, 400 MHz)
f1 (ppm)


HO
Ph
O
O
3p
13C NMR
(CDCl3, 100 MHz)
f1 (ppm)