Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Photocatalytic 1,2-oxo-alkylation reaction of styrenes with diazoacetates

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General Information

Unless otherwise noted, all commercially available compounds were used as provided without further purification. Chemicals used in this manuscript were purchased from Sigma Aldrich, Alfa Aesar, Chempur, Fluorochem and Carl Roth. Solvents used in reactions were p.A. grade. Solvents for chromatography were technical grade and distilled prior to use. Analytical thin-layer chromatography (TLC) was performed on Macherey-Nagel silica gel aluminium plates with F-254 indicator, visualized by irradiation with UV light. Column chromatography was performed using silica gel Merck 60 (particle size 0.063 – 0.2 mm). Solvent mixtures are understood as volume/volume. ^{1}H-NMR, ^{19}F-NMR and ^{13}C-NMR were recorded on a Varian AV600/AV400 or an Agilent DD2 400 NMR spectrometer in $CDCl_3$. Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated br (broadened singlet), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet); coupling constants (*J*) are in Hertz (Hz). HRMS data were recorded on a ThermoFisher Scientific LTQ Orbitrap XL using ESI ionization or on a Finnigan MAT 95 using EI ionization at 70 eV. GC/MS were recorded on a Shimadzu GCMS-QP2010 SE Gas chromatograph mass spectrometer. GC column: Optima 5 MS column, 30 m. Carrier gas: Helium. UV-VIS spectra were measured on a Shimadzu UV-2600 UV-VIS spectrophotometer. LEDs used in this manuscript were purchased from LUMITRONIX: Blue LED (470 nm) Module: rigid strips of 12 LEDs at 25 W and 30 lm, 2 single LEDs of this strip were used for each reaction. UV LEDs (375 nm, 25 W for 12 LEDs) used in this manuscript were purchased from LUMITRONIX and 2 single LEDs were used for each reaction. Reactions were irradiated from 1.5 cm, temperature maintained at room temperature by cooling with a fan. Fluorescence quenching experiments were performed on a Varian Cary Eclipse Fluorescence Spectrophotometer.

Important Safety Note

Handling of diazo compounds should only be done in a well-ventilated fume cupboard using an additional blast shield. No incidents occurred handling of diazoalkanes during the preparation of this manuscript, yet the reader should be aware of carcinogenicity and explosiveness of the herein described diazo compounds. General safety precautions when working with diazomethane and its derivatives should be followed. Any reactions described in this manuscript should not be performed without strict risk assessment and proper safety precautions.

General Procedures

General Procedure for Preparation of Diazoacetate Compounds – GP 1

All the diazoacetates compounds were prepared according to the literature procedure.[1]
The corresponding alcohol (1.0 mmol) and $NaHCO_3$ (3.0 mmol) were dissolved in dry, degassed MeCN and bromoacetyl bromide (1.5 mmol) was added slowly at 0 °C. After stirring 10 min, the reaction was quenched with H_2O and the solution was extracted with DCM three times. The organic phase was washed with brine and dried over $MgSO_4$. The solvent was evaporated under reduced pressure, and the residue was used in the next reaction without further purification. The bromoacetate and *N,N'*-ditosylhydrazine (2.0 mmol) were dissolved in dry, degassed THF and cooled to 0 °C. DBU (5.0 mmol) was added dropwise and the reaction mixture was stirred for 10 minutes. The reaction was quenched by adding saturated $NaHCO_3$ solution and extracted with Et_2O three times. The organic phase was washed with brine, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The diazoacetate was purified by silica column chromatography.

General Procedure for Photocatalytic 1,2-oxo-alkylation Reaction of Styrenes with Diazoacetates – GP 2

To a reaction tube equipped with a magnetic stir bar DABCO (45.0 mg, 0.4 mmol, 2.0 equiv.) and $(Ir[dF(CF_3)ppy]_2(dtbbpy))PF_6$ (2.0 mg, 1.0 mol%) were added. The tube was capped. After evacuation and backfilling with argon three times, anhydrous MeCN (0.5 mL) was added via a syringe, followed by the addition of styrene **2** (0.2 mmol, 1.0 equiv.), TBHP (0.6 mmol, 3.0 equiv.) and the corresponding diazo compound (0.4 mmol, 2.0 equiv.). The resulting solution was irradiated with blue LEDs (4 W) a distance of ~ 1.5 cm at room temperature (cooling with a fan) for 15 h. The product mixture was purified by column chromatography on silica gel with *n*-hexane / ethyl acetate as eluent to give the corresponding products.

General Procedure for Photocatalytic 1,2-oxo-alkylation Reaction of Styrenes with 2,2,2-Trifluorodiazoethane – GP 3

The 2,2,2-Trifluorodiazoethane was prepared according to the literature procedure.[2] The concentration of the obtained solution was determined to be 0.45 M in DCM by ^{19}F NMR analysis.
To a reaction tube equipped with a magnetic stir bar DABCO (45.0 mg, 0.4 mmol, 2.0 equiv.) and $(Ir[dF(CF_3)ppy]_2(dtbbpy))PF_6$ (2.0 mg, 1.0 mol%) were added. The tube was capped. After evacuation and backfilling with argon three times, styrene **2** (0.2 mmol, 1.0 equiv.), TBHP (0.6 mmol, 3.0 equiv.) were dissolved in 0.5 mL of dry and degassed MeCN in a separate tube under argon atmosphere and the resulting solution was added to the reaction tube by syringe. Then 2,2,2-Trifluorodiazoethane (0.45 M in DCM, 2.0 equiv.) was added via a syringe. The resulting solution was irradiated with blue LEDs (4 W) a distance of ~ 1.5 cm at room temperature (cooling with a fan) for 15 h. The product mixture

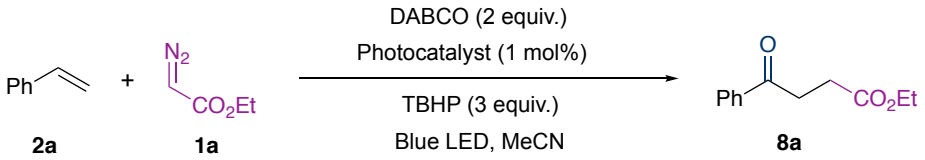
was purified by column chromatography on silica gel with *n*-hexane / ethyl acetate as eluent to give the corresponding products.

Scale Up Experiment

To a 10 mL reaction vessel DABCO (448 mg, 4 mmol, 2.0 equiv.) and ($Ir[dF(CF_3)ppy]_2(dtbbpy))PF_6$ (22 mg) were added. Then a magnet stirring bar was added to a reaction vessel, and the reaction vessel was capped. After evacuation and backfilling with argon three times, anhydrous MeCN (5 mL) was added via a syringe, followed by the addition of styrene **2a** (2 mmol, 1.0 equiv.), TBHP (6 mmol, 3.0 equiv.), and the ethyl diazoacetate **1a** (4 mmol, 2.0 equiv.). The resulting solution was irradiated with blue LEDs (4 W) at a distance of ~ 1.5 cm (cooling was realized by a fan) at room temperature for 15 h. After completion of the reaction, the solvent was removed under reduced pressure, and the product was purified by column chromatography on silica gel with *n*-hexane / ethyl acetate mixtures (60:1 → 20:1) as eluent to give the product **8a** as a colorless oil (81%, 333.7 mg).

Reaction Optimization

Table S1. Photocatalyst Screening

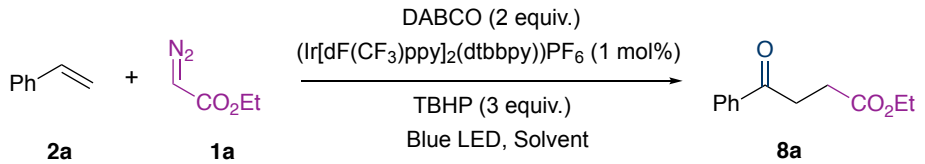


2a **1a** **8a**

Entry[a]	Photocat.	**8a** (%)[b]	Entry[a]	Photocat.	**8a** (%)[b]
1	$Ru(bpy)_3Cl_2$	50	4	$(Ir[dF(CF_3)ppy]_2(dtbbpy))PF_6$	90
2	Fluorescein	10	5	$MesAcr^+ ClO_4^-$	*traces*
3	Eosin Y	21	6	2,4,6-Triphenylpyrylium BF_4	15

[a]*Reaction conditions:* Reactions were carried out (**1a**/**2a**/photocat./DABCO/TBHP = 0.4/0.2/0.002/0.4/0.6 mmol) in 2.0 mL MeCN under argon at room temperature under irradiation with blue LEDs (4 W). [b]Yield of **8a** was determined by ^1H NMR spectroscopic analyses of the crude reaction mixture using mesitylene as internal standard.

Table S2. Solvent Screening

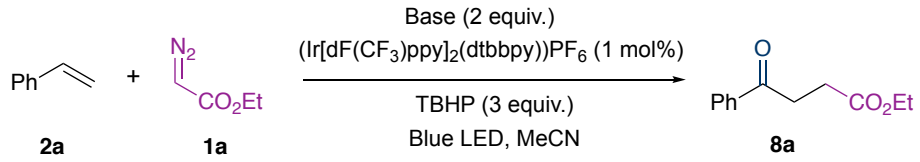


2a **1a** **8a**

Entry[a]	Solvent	**8a** (%)[b]	Entry[a]	Solvent	**8a** (%)[b]
1	THF	15	6	Acetone	60
2	DCM	26	7	DMSO	24
3	1,2-DCE	18	8	Toluene	25
4	1,4-Dioxane	30	9	$CHCl_3$	10
5	MeCN	90	10	$PhCF_3$	13

[a]*Reaction conditions:* Reactions were carried out (**1a**/**2a**/photocat./DABCO/TBHP = 0.4/0.2/0.002/0.4/0.6 mmol) in 2.0 mL solvent under argon at room temperature under irradiation with blue LEDs (4 W). [b]Yield of **8a** was determined by ^1H NMR spectroscopic analyses of the crude reaction mixture using mesitylene as internal standard.

Table S3. Base Screening

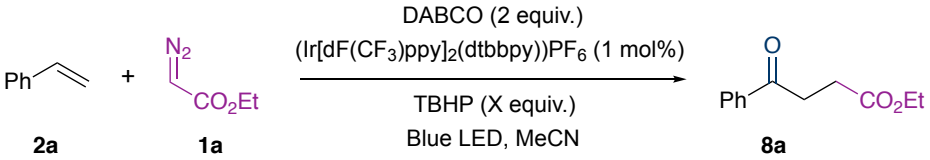


2a **1a** **8a**

Entry[a]	Base	**8a** (%)[b]	Entry[a]	Base	**8a** (%)[b]
1	DBU	15	6	$KHCO_3$	*not observed*
2	DIPEA	*trace*	7	K_2CO_3	*not observed*
3	DMAP	*trace*	8	Cs_2CO_3	*trace*
4	DABCO	90	9	K_2HPO_4	*trace*
5	*N'N*-Dimethylaniline	32	10	4-Chloro-*N*-methylpiperidine	12

[a]*Reaction conditions:* Reactions were carried out (**1a**/**2a**/photocat./base/TBHP = 0.4/0.2/0.002/0.4/0.6 mmol) in 2.0 mL MeCN under argon at room temperature under irradiation with blue LEDs (4 W). [b]Yield of **8a** was determined by ^{1}H NMR spectroscopic analyses of the crude reaction mixture using mesitylene as internal standard.

Table S4. Stoichiometry Screening

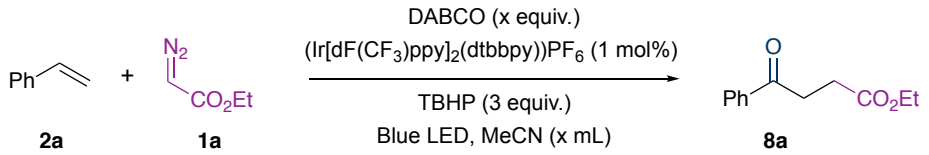


2a **1a** **8a**

Entry[a]	**2a**/**1a**/TBHP (equiv.)	**8a** (%)[b]	Entry[a]	**2a**/**1a**/TBHP (equiv.)	**8a** (%)[b]
1	1:1:1	47	4	1:2:2	70
2	1:1:2	50	5	1:2:3	90
3	1:1:3	60	6	2:1:3	77

[a]*Reaction conditions:* Reactions were carried out in 2.0 mL MeCN under argon at room temperature under irradiation with blue LEDs (4 W). [b]Yield of **8a** was determined by ^{1}H NMR spectroscopic analyses of the crude reaction mixture using mesitylene as internal standard.

Table S5. Base Loading and Concentration Screening

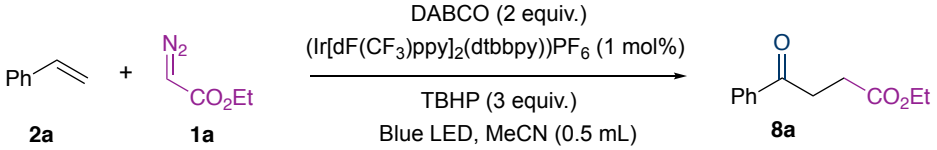


2a **1a** **8a**

Entry[a]	DABCO (equiv.)	**8a** (%)[b]	Entry[a]	Concentration (M)	**8a** (%)[b]
1	1	45	5	0.4	91
2	2	90	6	0.2	85
3	3	82	7	0.1	90
4	4	75	8	0.05	70

[a]*Reaction conditions:* Reactions were carried out (**1a**/**2a**/photocat./DABCO/TBHP = 0.4/0.2/0.002/X/0.6 mmol) in MeCN under argon at room temperature under irradiation with blue LEDs (4 W). [b]Yield of **8a** was determined by ^{1}H NMR spectroscopic analyses of the crude reaction mixture using mesitylene as internal standard.

Table S6. Control Reactions



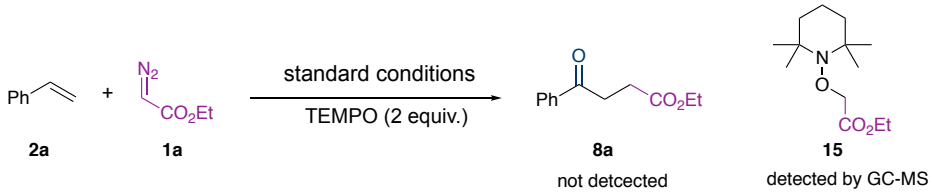
2a **1a** **8a**

Entry[a]	Change	**8a** (%)[b]	Entry[a]	Change	**8a** (%)[b]
1	none	91	4	no light	*no reaction*
2	no photocatalyst	*not detected*	5	UV light	40
3	air atmosphere	45			

[a]*Reaction conditions:* Reactions were carried out (**1a**/**2a**/photocat./DABCO/TBHP = 0.4/0.2/0.002/0.4/0.6 mmol) in 0.5 mL MeCN under argon at room temperature under irradiation with blue LEDs (4 W). [b]Yield of **8a** was determined by ^{1}H NMR spectroscopic analyses of the crude reaction mixture using mesitylene as internal standard.

Control Experiments

Radical Trapping Experiment with TEMPO



2a **1a** **8a** not detcected **15** detected by GC-MS

To a reaction tube equipped with a magnetic stir bar were added DABCO (45.0 mg, 0.4 mmol, 2.0 equiv.), ($Ir[dF(CF_3)ppy]_2(dtbbpy))PF_6$ (1.0 mg, 1.0 mol%) and TEMPO (2.0 equiv.). The tube was capped. After evacuation and backfilling with argon three times, anhydrous MeCN (0.5 mL) was added via a syringe, followed by the addition of styrene **2a** (0.2 mmol, 1.0 equiv.), TBHP (0.6 mmol, 3.0 equiv.) and the ethyl diazoacetate **1a** (0.4 mmol, 2.0 equiv.). The resulting solution was irradiated with blue LEDs (4 W) at a distance of ~ 1.5 cm (cooling with a fan) for about 15 h. The crude reaction mixture was analyzed by ^1H NMR and GC/MS.

Analysis of the crude reaction mixture by GC/MS.

Method: 60 °C/5 min, 20 K/min, 300 °C/13 min.

Compound **15** was observed using GC/MS.

MS: *m/z*: calcd. for $[M]^+$= 243.1, found: 243, calcd for $[M\text{-}CH_3]^+$ = 228.2, found:228, calcd. for $[M\text{-}C_4H_7O_2]^+$ = 156.1, found: 156, calcd. for $[M\text{-}C_4H_7O_3]^+$ = 140.1, found: 140.

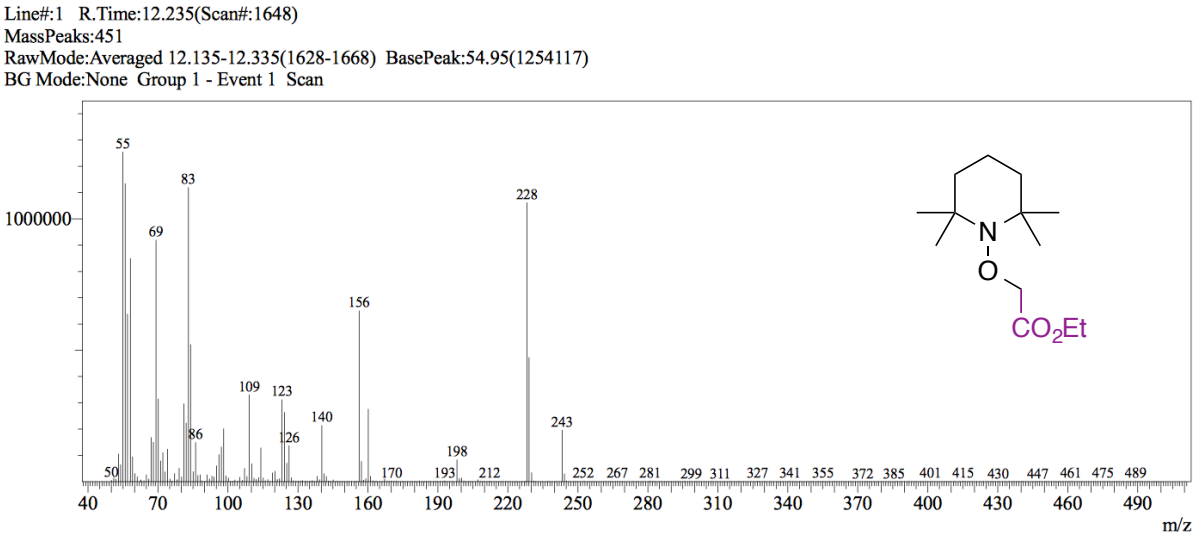
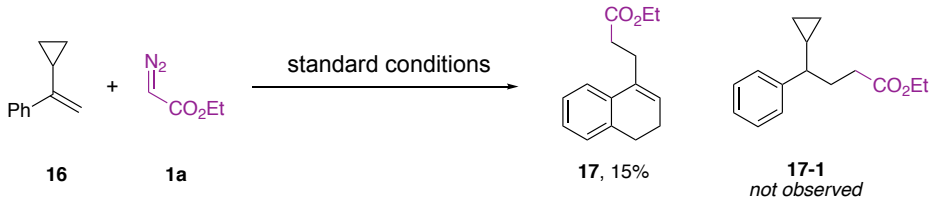


Figure S1. MS spectrum of compound **15**

Radical Clock Experiment



16 **1a** **17**, 15% **17-1** *not observed*

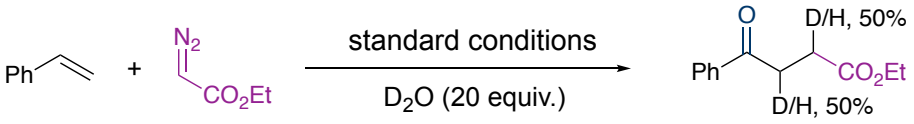
In accordance to **GP2** (1-cyclopropylvinyl)benzene **16** (28.8 mg, 0.2 mmol) was used as substrate. The crude reaction mixture was analyzed by ^{1}H NMR. The product was purified by column chromatography on silica gel (*n*-hexane / ethyl acetate 20:1) to give **17** (7.0 mg, 15%).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.19 – 7.16 (m, 1H), 7.15 – 7.12 (m, 1H), 7.09 – 7.05 (m, 2H), 5.82 (tt, *J* = 4.6, 1.3 Hz, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 2.74 – 2.69 (m, 2H), 2.66 (t, *J* = 8.0 Hz, 2H), 2.51 – 2.40 (m, 2H), 2.22 – 2.11 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H) ppm.

The data is in accordance with the literature.[3]

Deuterium Labelling Experiments

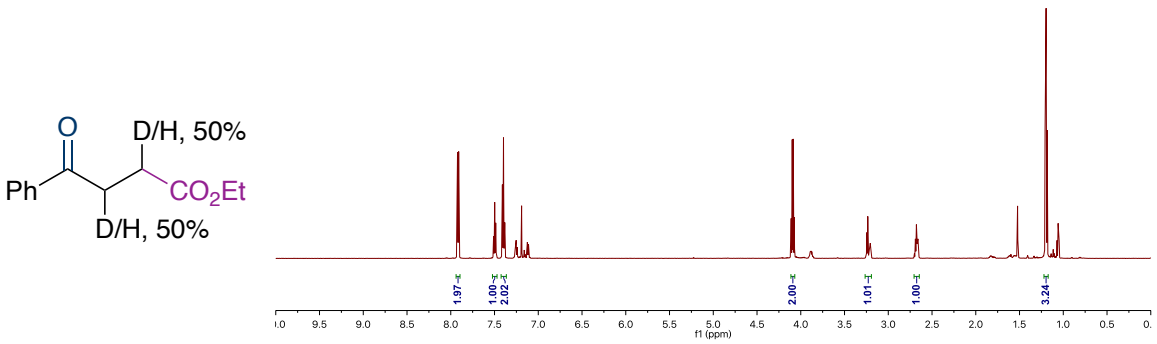
Reaction in the presence of an external deuterium source



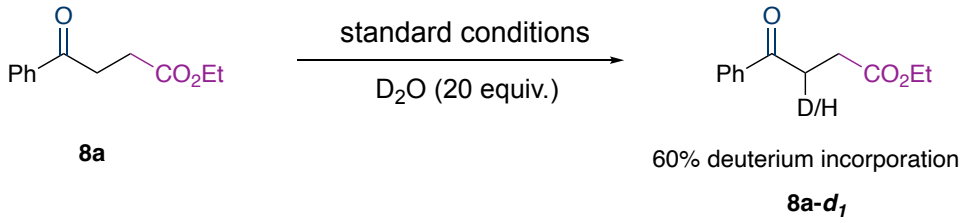
2a **1a** **8a-*d*$_2$**, 52 %

Prepared according to the General Procedure **GP2** using D_2O (20.0 equiv.). ^{1}H NMR analysis showed 50 % deuterium incorporation.

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.97 – 7.82 (m, 2H), 7.56 – 7.46 (m, 2H), 7.40 (t, *J* = 7.6 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.32 – 3.19 (m, 1.01H), 2.79 – 2.54 (m, 1H), 1.20 (t, *J* = 7.1 Hz, 3H) ppm.



Probing the keto-enol tautomerism

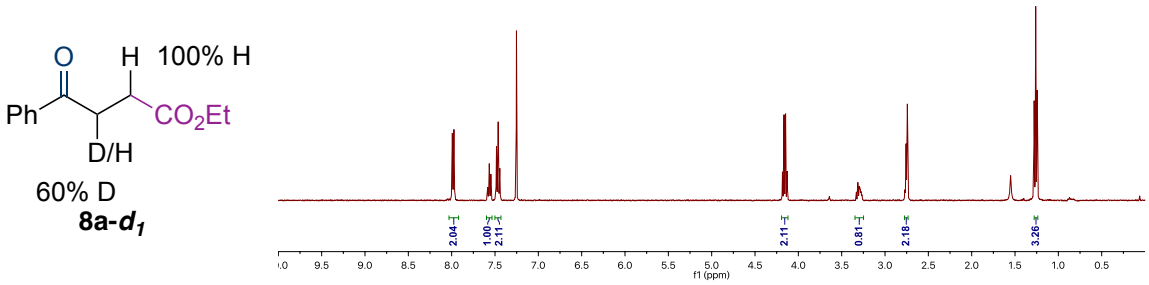


8a

60% deuterium incorporation

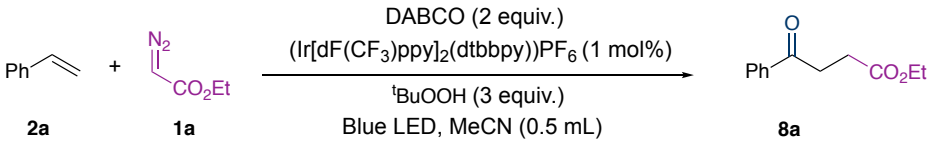
8a-*d*$_1$

Prepared according to the General Procedure **GP2** using D_2O (20.0 equiv.) without addition of EDA. ^{1}H NMR analysis showed 60 % deuterium incorporation.



On-Off Experiment

Several reactions following General Procedure (GP-2) were set up at the same time and irradiation with blue LEDs was started for all reactions at the same time. Every two hours, one reaction analyzed by ^{1}H NMR using mesitylene as internal standard to determine the yield of **8a**.



2a **1a** **8a**

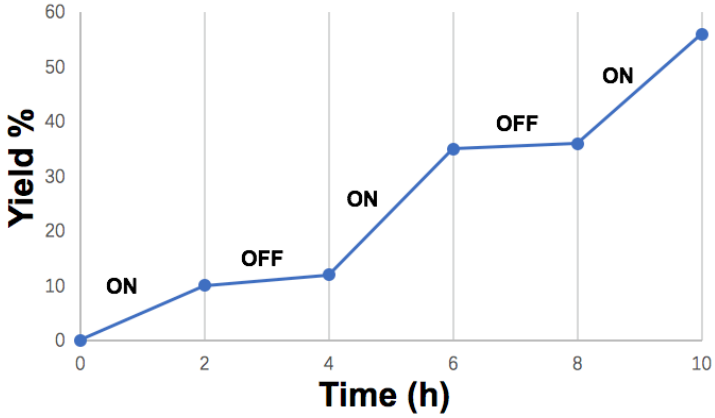


Figure S2. On-off experiment

Fluorescence Quenching Studies

Fluorescence quenching experiments were performed on a Varian Cary Eclipse Fluorescence Spectrophotometer. All $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ solutions were excited at 390 nm and emission intensity at 476 nm were collected. All the measurements were carried out mixing a solution of 4.5×10^{-6} M solution of in dry, degassed acetonitrile and appropriate amount of quencher in a screw top 1.0 cm quartz cuvette. Samples were degassed three times then the emission spectra of the samples were collected. I_0 is the intensity without quencher and I is the intensity with quencher. Plots were drawn according to the Stern-Volmer equation.

Stern-Volmer equation

$$I_0/I = 1 + k_q[Q]$$

Emission Quenching Studies with DABCO, TBHP, Styrene and Ethyl diazoacetate

Increasing amount of quencher were added to a solution of $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ in MeCN. After each addition emission spectra were recorded.

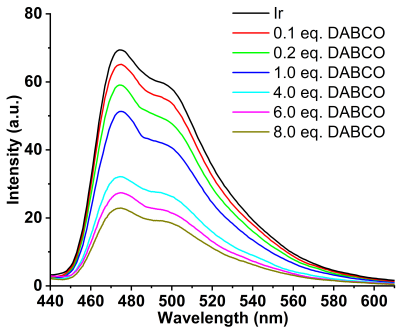


Figure S3. Fluorescence quenching of DABCO

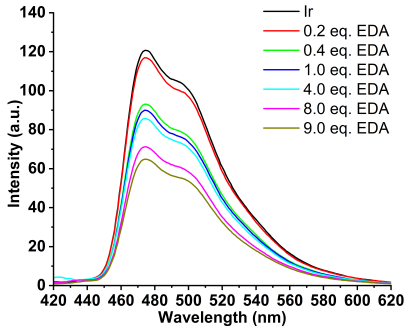


Figure S4. Fluorescence quenching of EDA

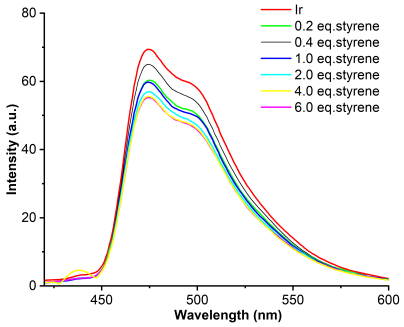


Figure S5. Fluorescence quenching of styrene

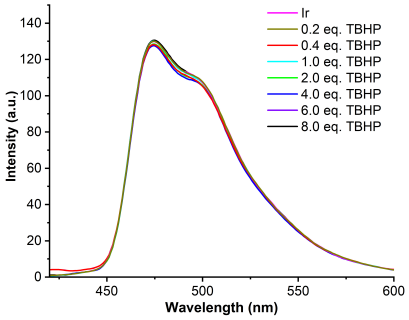


Figure S6. Fluorescence quenching of TBHP

Stern-Volmer Plots

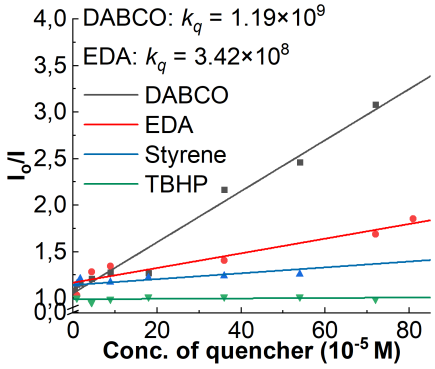


Figure S7. Stern-Volmer Plot of [Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$

The reported excited-state lifetime for [Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$ in MeCN (2300 ns) was used for k_q calculations.[4]

quencher	k_q ($M^{-1}s^{-1}$)
DABCO	1.19×10^9
EDA	3.42×10^8

Table S7. k_q of the DABCO and EDA

Experiment of time vs. yield of peroxy ether 20 and product 8a

A set of experiments were performed according to the general procedure (GP-2) to understand the rate of formation and consumption of **20** in the reaction medium. Reaction mixtures were irradiated with blue LED for the mentioned time and analyzed by ^{1}H NMR using mesitylene as internal standard.[5] Yields of **20** and **8a** were recorded from the ^{1}H NMR and plotted against the reaction time.

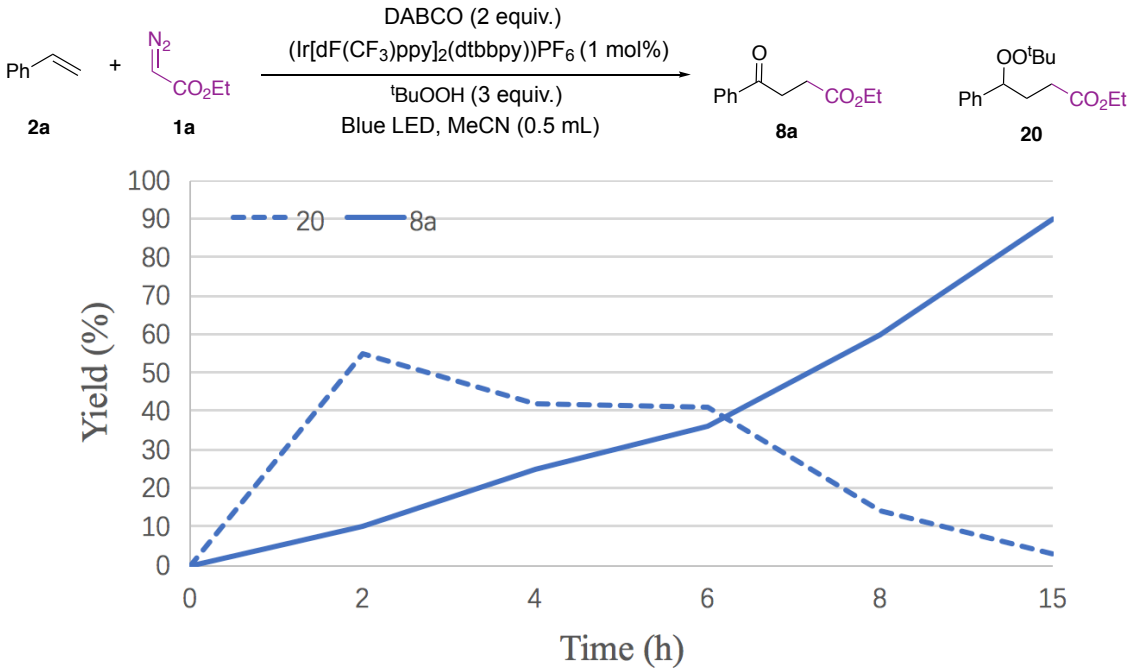
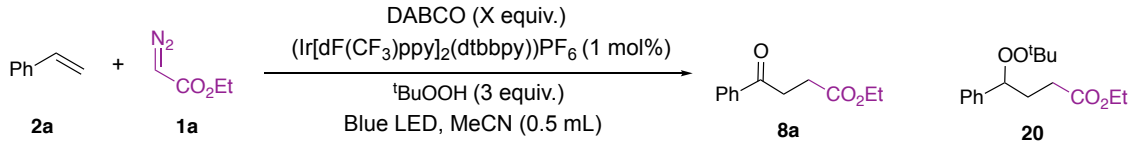


Table S8. Time/Yield Plot of **20** and **8a**

Experiments in the presence of catalytic amounts of DABCO

Two experiments were performed according to the general procedure (GP-2) in the presence of 5 mol% and 25 mol% of DABCO, respectively. Reaction mixtures were analyzed by ^{1}H NMR using mesitylene as internal standard to determine the yield of **8a** and **20**.

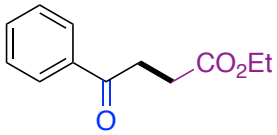


Catalytic loading of DABCO	**8a** (yield %)	**20** (yield %)
5 mol%	trace	13
25 mol%	9	42

Table S9. Yields of **20** and **8a** at different catalytic loading of DABCO

Physical Data

Ethyl 4-oxo-4-phenylbutanoate (8a)



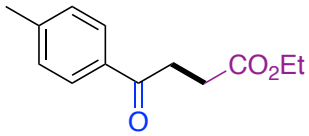
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (90%, 37.6 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.92 (d, *J* = 7.7 Hz, 2H), 7.56 – 7.44 (m, 1H), 7.45 – 7.31 (m, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.25 (t, *J* = 6.6 Hz, 2H), 2.69 (t, *J* = 6.6 Hz, 2H), 1.20 (t, *J* = 7.1 Hz, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 198.1, 172.9, 136.6, 133.2, 128.6, 128.0, 60.6, 33.4, 28.3, 14.2 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{12}H_{14}O_3Na^+$: 229.0835; Found: 229.0831.

Ethyl 4-oxo-4-(*p*-tolyl)butanoate (8b)



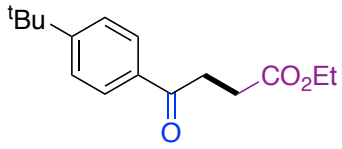
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (87%, 38.2 mg).

^{1}H NMR (400 MHz, Chloroform-*d*): δ = δ 7.98 – 7.73 (m, 2H), 7.37 – 7.06 (m, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.28 (t, *J* = 6.7 Hz, 2H), 2.74 (t, *J* = 6.7 Hz, 2H), 2.40 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H) ppm.

^{13}C NMR (101 MHz, Chloroform-*d*): δ = 197.7, 172.9, 143.9, 134.1, 129.2, 128.1, 60.6, 33.2, 28.3, 21.6, 14.1 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{13}H_{16}O_3Na^+$: 243.0991; Found: 243.0990.

Ethyl 4-(4-(*tert*-butyl)phenyl)-4-oxobutanoate (8c)



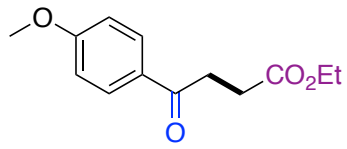
The titled compound was synthesized according to the general procedure GP-2, and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (74%, 38.8 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 8.16 – 7.75 (m, 2H), 7.48 (d, *J* = 8.5 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.29 (t, *J* = 6.7 Hz, 2H), 2.75 (t, *J* = 6.7 Hz, 2H), 1.34 (s, 9H), 1.26 (t, *J* = 7.1 Hz, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 197.7, 172.9, 156.9, 134.0, 127.9, 125.5, 60.6, 35.1, 33.2, 31.0, 28.3, 14.1 ppm.

HRMS (ESI): *m/z*: $[M + K]^+$ Calcd. for $C_{16}H_{22}O_3K^+$: 301.1200; Found: 301.1195.

Ethyl 4-(4-methoxyphenyl)-4-oxobutanoate (8d)



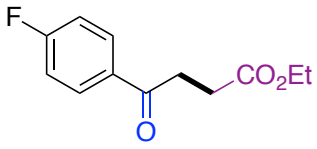
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 40:1 → 10:1) as a colorless oil (91%, 43.2 mg).

^{1}H NMR (400 MHz, Chloroform-*d*): δ = 8.14 – 7.64 (m, 2H), 7.06 – 6.69 (m, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 3.26 (t, *J* = 6.7 Hz, 2H), 2.73 (t, *J* = 6.7 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H) ppm.

^{13}C NMR (101 MHz, Chloroform-*d*): δ = 196.6, 173.0, 163.5, 130.2, 129.6, 113.7, 60.6, 55.4, 32.9, 28.3, 14.1 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{13}H_{16}O_4Na^+$: 259.0940; Found: 259.0940.

Ethyl 4-(4-fluorophenyl)-4-oxobutanoate (8e)



The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (81%, 36.5 mg).

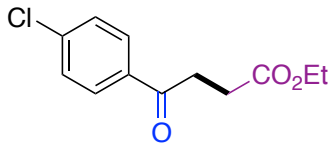
^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.98 – 7.90 (m, 2H), 7.06 (t, *J* = 8.6 Hz, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.21 (t, *J* = 6.6 Hz, 2H), 2.68 (t, *J* = 6.6 Hz, 2H), 1.22 – 1.14 (m, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 196.5, 172.8, 165.8 (d, *J* = 254.8 Hz), 133.07 (d, *J* = 3.0 Hz), 130.6 (d, *J* = 9.4 Hz), 115.7 (d, *J* = 21.9 Hz), 60.7, 33.2, 28.2, 14.1 ppm.

^{19}F NMR (565 MHz, Chloroform-*d*): δ = -105.11 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{12}H_{13}O_3FNa^+$: 247.0740; Found: 247.0731.

Ethyl 4-(4-chlorophenyl)-4-oxobutanoate (8f)



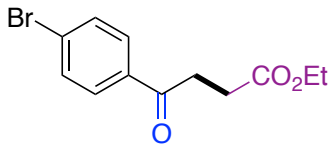
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (83%, 40.1 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 8.00 – 7.70 (m, 2H), 7.54 – 7.27 (m, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.20 (t, *J* = 6.6 Hz, 2H), 2.69 (t, *J* = 6.6 Hz, 2H), 1.20 – 1.19 (m, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 196.9, 172.7, 139.6, 134.9, 129.4, 128.9, 60.7, 33.3, 28.2, 14.2 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{12}H_{13}O_3ClNa^+$: 263.0445; Found: 263.0444.

Ethyl 4-(4-bromophenyl)-4-oxobutanoate (8g)



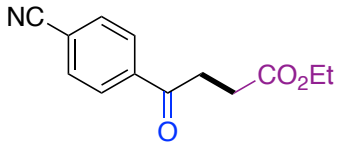
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (75%, 42.9 mg).

^{1}H NMR (400 MHz, Chloroform-*d*): δ = 8.09 – 7.78 (m, 2H), 7.68 – 7.47 (m, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.26 (t, *J* = 6.6 Hz, 2H), 2.75 (t, *J* = 6.6 Hz, 2H), 1.27 – 1.23 (m, 3H) ppm.

^{13}C NMR (101 MHz, Chloroform-*d*): δ = 197.1, 172.7, 135.2, 131.9, 129.5, 128.3, 60.7, 33.3, 28.1, 14.1 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{12}H_{13}O_3BrNa^+$: 306.9940; Found: 306.9940.

Ethyl 4-(4-cyanophenyl)-4-oxobutanoate (8h)



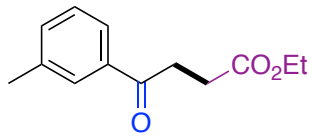
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 40:1 → 10:1) as a colorless oil (89%, 41.2 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 8.26 – 7.95 (m, 2H), 7.95 – 7.62 (m, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.30 (t, *J* = 6.5 Hz, 2H), 2.78 (t, *J* = 6.4 Hz, 2H), 1.26 (t, *J* = 7.2 Hz, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 196.9, 172.5, 139.5, 132.5, 128.4, 117.8, 116.4, 60.8, 33.6, 28.0, 14.1 ppm.

HRMS (APCI): *m/z*: $[M + H]^+$ Calcd. for $C_{13}H_{14}NO_3^+$: 232.0968; Found: 232.0967.

Ethyl 4-oxo-4-(*m*-tolyl)butanoate (8i)



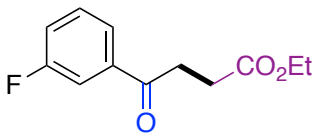
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (63%, 27.8 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.75 – 7.69 (m, 2H), 7.34 – 7.25 (m, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.23 (t, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 6.7 Hz, 2H), 2.34 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 198.3, 172.9, 138.4, 136.6, 133.9, 128.5, 128.4, 125.2, 60.6, 33.4, 28.3, 21.3, 14.2 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{13}H_{16}O_3Na^+$: 243.0991; Found: 243.0988.

Ethyl 4-(3-fluorophenyl)-4-oxobutanoate (8j)



The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (80%, 36.0 mg).

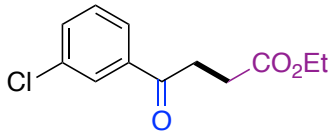
^{1}H NMR (400 MHz, Chloroform-*d*): δ = δ 7.74 – 7.67 (m, 1H), 7.63 – 7.55 (m, 1H), 7.42 – 7.33 (m, 1H), 7.25 – 7.15 (m, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.21 (t, *J* = 6.6 Hz, 2H), 2.69 (t, *J* = 6.6 Hz, 2H), 1.20 (t, *J* = 7.1 Hz, 3H) ppm.

^{13}C NMR (101 MHz, Chloroform-*d*): δ = 196.9 (d, *J* = 2.3 Hz), 172.7, 162.8 (d, *J* = 248.0 Hz), 138.6 (d, *J* = 6.2 Hz), 130.3 (d, *J* = 7.7 Hz), 123.8 (d, *J* = 3.0 Hz), 120.2 (d, *J* = 21.5 Hz), 114.8 (d, *J* = 22.2 Hz), 60.7, 33.5, 28.2, 14.1 ppm.

^{19}F NMR (565 MHz, Chloroform-*d*): δ = -111.83 ppm.

HRMS (ESI): *m/z*: $[M + K]^+$ Calcd. for $C_{12}H_{13}O_3FK^+$: 263.0480; Found: 263.0475.

Ethyl 4-(3-chlorophenyl)-4-oxobutanoate (8k)



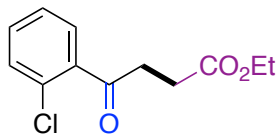
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (76%, 36.7 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.88 (t, *J* = 1.9 Hz, 1H), 7.81 – 7.76 (m, 1H), 7.49 – 7.44 (m, 1H), 7.34 (t, *J* = 7.9 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.21 (t, *J* = 6.6 Hz, 2H), 2.69 (t, *J* = 6.6 Hz, 2H), 1.20 (t, *J* = 7.2 Hz, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 196.9, 172.6, 138.1, 135.0, 133.1, 129.9, 128.2, 126.1, 60.7, 33.5, 28.2, 14.2 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{12}H_{13}O_3ClNa^+$: 263.0445; Found: 263.0446.

Ethyl 4-(2-chlorophenyl)-4-oxobutanoate (8l)



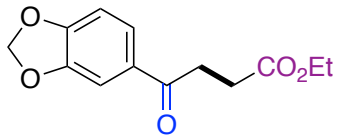
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (10%, 5.0 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.50 – 7.47 (m, 1H), 7.37 – 7.29 (m, 2H), 7.28 – 7.24 (m, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.19 (t, *J* = 6.6 Hz, 2H), 2.69 (t, *J* = 6.6 Hz, 2H), 1.20 (t, *J* = 7.1 Hz, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 201.2, 172.5, 138.9, 131.8, 130.9, 130.5, 129.2, 126.9, 60.7, 37.6, 28.5, 14.2 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{12}H_{13}O_3ClNa^+$: 263.0445; Found: 263.0441.

Ethyl 4-(benzo[*d*][1,3]dioxol-5-yl)-4-oxobutanoate (8m)



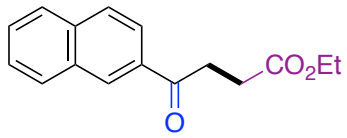
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 40:1 → 10:1) as a colorless oil (41%, 20.7 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.53 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.38 (d, *J* = 1.7 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 5.97 (s, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.16 (t, *J* = 6.7 Hz, 2H), 2.66 (t, *J* = 6.7 Hz, 2H), 1.20 (t, *J* = 7.1 Hz, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 196.1, 172.9, 151.8, 148.1, 131.5, 124.3, 107.9, 107.8, 101.8, 60.6, 33.1, 28.4, 14.2 ppm.

HRMS (ESI): *m/z*: $[M + H]^+$ Calcd. for $C_{13}H_{15}O_5^+$: 251.0914; Found: 251.0910.

Ethyl 4-(naphthalen-2-yl)-4-oxobutanoate (8n)



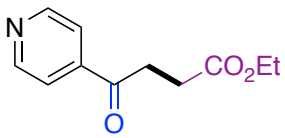
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (43%, 22.1 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 8.44 (d, *J* = 1.8 Hz, 1H), 7.97 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.81 (dd, *J* = 12.8, 8.4 Hz, 2H), 7.55 – 7.51 (m, 1H), 7.51 – 7.46 (m, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.39 (t, *J* = 6.7 Hz, 2H), 2.75 (t, *J* = 6.7 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 198.09, 172.9, 135.6, 133.9, 132.5, 129.7, 129.6, 128.5, 128.4, 127.8, 126.8, 123.7, 60.7, 33.5, 28.4, 14.2 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{16}H_{16}O_3Na^+$: 279.0991; Found: 279.0990.

Ethyl 4-oxo-4-(pyridin-4-yl)butanoate (8o)



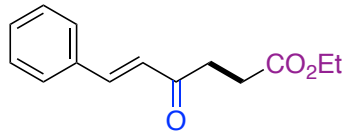
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 20:1 → 4:1) as a colorless oil (76%, 31.6 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 8.90 – 8.68 (m, 2H), 7.70 (d, *J* = 4.9 Hz, 2H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.22 (t, *J* = 6.5 Hz, 2H), 2.71 (t, *J* = 6.5 Hz, 2H), 1.20 (t, *J* = 7.1 Hz, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 197.8, 172.4, 151.01, 142.3, 121.1, 60.8, 33.6, 28.0, 14.1 ppm.

HRMS (ESI): *m/z*: $[M + H]^+$ Calcd. for $C_{11}H_{14}O_3N^+$: 208.0968; Found: 208.0966.

Ethyl (*E*)-4-oxo-6-phenylhex-5-enoate (8p)



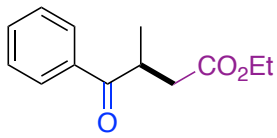
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (21%, 9.8 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.53 (d, *J* = 16.3 Hz, 1H), 7.50 – 7.46 (m, 2H), 7.36 – 7.27 (m, 3H), 6.70 (d, *J* = 16.2 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 2.95 (t, *J* = 6.7 Hz, 2H), 2.62 (t, *J* = 6.7 Hz, 2H), 1.27 – 1.13 (m, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 198.0, 172.9, 142.9, 134.4, 130.5, 128.9, 128.3, 125.9, 60.6, 35.2, 28.2, 14.2 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{14}H_{16}O_3Na^+$: 255.0991; Found: 255.0984.

Ethyl -3-methyl-4-oxo-4-phenylbutanoate (8q)



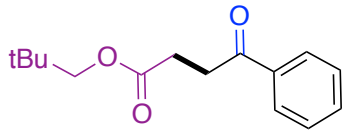
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (39%, 17.2 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.95 – 7.88 (m, 2H), 7.53 – 7.47 (m, 1H), 7.40 (t, *J* = 7.7 Hz, 2H), 4.07 – 3.99 (m, 2H), 3.93 – 3.81 (m, 1H), 2.88 (dd, *J* = 16.7, 8.4 Hz, 1H), 2.38 (dd, *J* = 16.7, 5.7 Hz, 1H), 1.18 – 1.13 (m, 6H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 202.8, 172.3, 135.9, 133.0, 128.6, 128.4, 60.5, 37.5, 37.2, 17.8, 14.1 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{13}H_{16}O_3Na^+$: 243.0991; Found: 243.0990.

Neopentyl 4-oxo-4-phenylbutanoate (12a)



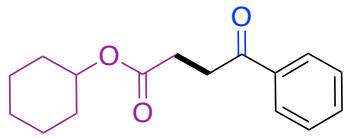
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (69%, 34.5 mg).

^{1}H NMR (400 MHz, Chloroform-*d*): δ = 8.01 – 7.95 (m, 2H), 7.61 – 7.52 (m, 1H), 7.50 – 7.39 (m, 2H), 3.79 (s, 2H), 3.32 (t, *J* = 6.7 Hz, 2H), 2.80 (t, *J* = 6.7 Hz, 2H), 0.92 (s, 9H) ppm.

^{13}C NMR (101 MHz, Chloroform-*d*): δ = 198.0, 172.9, 136.5, 133.1, 128.5, 128.0, 73.9, 33.3, 31.3, 28.2, 26.4 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{15}H_{20}O_3Na^+$: 271.1304; Found: 271.1303.

Cyclohexyl 4-oxo-4-phenylbutanoate (12b)



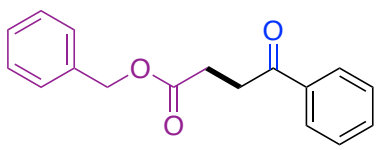
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (71%, 36.8 mg).

^{1}H NMR (400 MHz, Chloroform-*d*): δ = 8.04 – 7.93 (m, 2H), 7.60 – 7.53 (m, 1H), 7.50 – 7.39 (m, 2H), 4.77 (tt, *J* = 9.0, 4.0 Hz, 1H), 3.30 (t, *J* = 6.6 Hz, 2H), 2.74 (t, *J* = 6.7 Hz, 2H), 1.89 – 1.79 (m, 2H), 1.75 – 1.65 (m, 2H), 1.56 – 1.30 (m, 6H) ppm.

^{13}C NMR (101 MHz, Chloroform-*d*): δ = 198.2, 172.3, 136.6, 133.1, 128.5, 128.0, 72.9, 33.4, 31.5, 28.6, 25.3, 23.7 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{16}H_{20}O_3Na^+$: 283.1304; Found: 283.1302.

Benzyl 4-oxo-4-phenylbutanoate (12c)



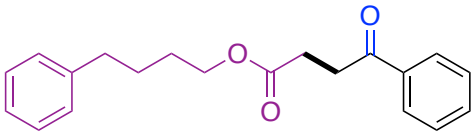
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (88%, 47.5 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.93 – 7.88 (m, 2H), 7.52 – 7.45 (m, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.29 – 7.26 (m, 4H), 7.25 – 7.21 (m, 1H), 5.07 (s, 2H), 3.25 (t, *J* = 6.6 Hz, 2H), 2.75 (t, *J* = 6.6 Hz, 2H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 198.0, 172.7, 136.5, 135.9, 133.2, 128.6, 128.5, 128.21, 128.20, 128.0, 66.5, 33.3, 28.3 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{17}H_{16}O_3Na^+$: 291.0991; Found: 291.0981.

4-Phenylbutyl 4-oxo-4-phenylbutanoate (12d)



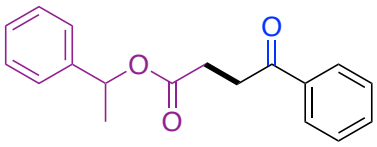
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (73%, 45.5 mg).

^{1}H NMR (400 MHz, Chloroform-*d*): δ = 8.03 – 7.91 (m, 2H), 7.60 – 7.53 (m, 1H), 7.49 – 7.43 (m, 2H), 7.33 – 7.23 (m, 2H), 7.21 – 7.11 (m, 3H), 4.16 – 4.06 (m, 2H), 3.31 (t, *J* = 6.6 Hz, 2H), 2.76 (t, *J* = 6.6 Hz, 2H), 2.66 – 2.60 (m, 2H), 1.68 (p, *J* = 3.5 Hz, 4H) ppm.

^{13}C NMR (101 MHz, Chloroform-*d*): δ = 198.1, 172.9, 142.0, 136.5, 133.2, 128.6, 128.39, 128.32, 128.0, 125.7, 64.5, 35.4, 33.3, 28.2, 28.1, 27.6 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{20}H_{22}O_3Na^+$: 333.1461; Found: 333.1459.

1-Phenylethyl 4-oxo-4-phenylbutanoate (12e)



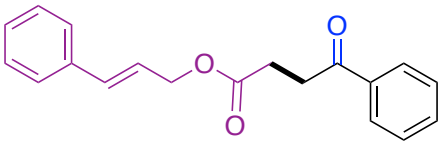
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (85%, 42.5 mg).

^{1}H NMR (400 MHz, Chloroform-*d*): δ = 8.02 – 7.94 (m, 2H), 7.61 – 7.53 (m, 1H), 7.46 (dd, *J* = 8.5, 7.0 Hz, 2H), 7.35 – 7.31 (m, 4H), 7.30 – 7.27 (m, 1H), 5.91 (q, *J* = 6.6 Hz, 1H), 3.45 – 3.18 (m, 2H), 2.94 – 2.63 (m, 2H), 1.55 (d, *J* = 6.6 Hz, 3H) ppm.

^{13}C NMR (101 MHz, Chloroform-*d*): δ = 198.0, 172.1, 141.6, 136.5, 133.1, 128.5, 128.4, 128.0, 127.8, 126.0, 72.6, 33.3, 28.5, 22.2 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{18}H_{18}O_3Na^+$: 305.1148; Found: 305.1143.

Cinnamyl 4-oxo-4-phenylbutanoate (12f)



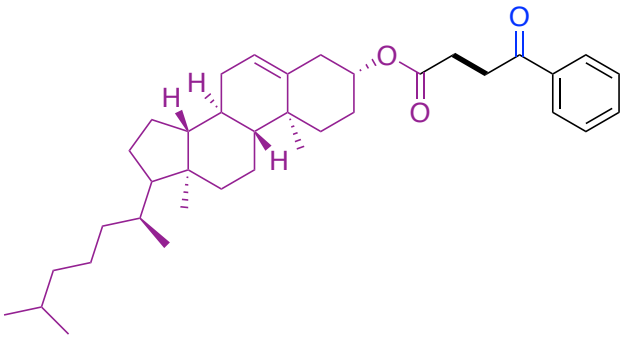
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (61%, 35.7 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 8.05 – 7.96 (m, 2H), 7.63 – 7.57 (m, 1H), 7.49 (t, *J* = 7.8 Hz, 2H), 7.41 (d, *J* = 7.3 Hz, 2H), 7.38 – 7.33 (m, 2H), 7.30 – 7.25 (m, 1H), 6.70 – 6.67 (d, *J* = 15.9 Hz, 1H), 6.34 – 6.29 (m, 1H), 4.81 – 4.79 (dd, *J* = 6.4, 1.4 Hz, 2H), 3.37 (t, *J* = 6.6 Hz, 2H), 2.85 (t, *J* = 6.6 Hz, 2H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 198.0, 172.7, 136.5, 136.2, 134.1, 133.2, 128.64, 128.60, 128.07, 128.05, 126.6, 123.1, 65.3, 33.4, 28.3 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{19}H_{18}O_3Na^+$: 317.1148; Found: 317.1146.

(3*R*,8*R*,9*R*,10*S*,13*S*,14*R*)-10,13-Dimethyl-17-((*S*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl 4-oxo-4-phenylbutanoate (12g)



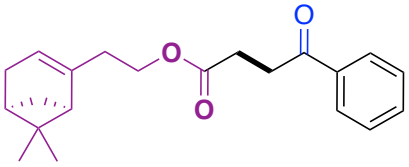
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 20:1 → 2:1) as a colorless oil (70%, 76.9 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.95 – 7.87 (m, 2H), 7.52 – 7.47 (m, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 5.30 (d, *J* = 4.8 Hz, 1H), 4.62 – 4.51 (m, 1H), 3.23 (t, *J* = 6.7 Hz, 2H), 2.67 (t, *J* = 6.6 Hz, 2H), 2.32 – 2.16 (m, 2H), 1.98 – 1.86 (m, 2H), 1.83 – 1.70 (m, 3H), 1.60 – 1.14 (m, 13H), 1.13 – 0.97 (m, 8H), 0.94 (s, 3H), 0.84 (d, *J* = 6.6 Hz, 3H), 0.80 (d, *J* = 2.7 Hz, 3H), 0.79 (d, *J* = 2.7 Hz, 3H), 0.60 (s, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 198.2, 172.3, 139.6, 136.6, 133.1, 128.6, 128.0, 122.6, 74.3, 56.7, 56.1, 50.0, 42.3, 39.7, 39.5, 38.0, 36.9, 36.6, 36.2, 35.8, 33.4, 31.9, 31.8, 28.6, 28.2, 28.0, 27.7, 24.2, 23.8, 22.8, 22.5, 21.0, 19.3, 18.7, 11.8 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{37}H_{54}O_3Na^+$: 569.3965; Found: 569.3990.

2-((1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethyl 4-oxo-4-phenylbutanoate (12h)



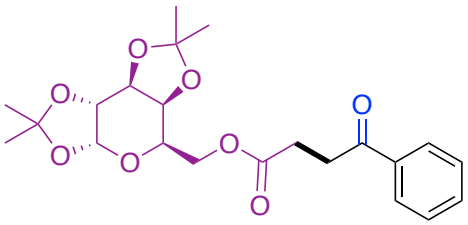
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 40:1 → 10:1) as a colorless oil (81%, 38.1 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.94 – 7.88 (m, 2H), 7.53 – 7.47 (m, 1H), 7.40 (t, *J* = 7.7 Hz, 2H), 5.22 – 5.20 (m, 1H), 4.21 – 3.91 (m, 2H), 3.24 (t, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 6.7 Hz, 2H), 2.28 (dt, *J* = 8.6, 5.6 Hz, 1H), 2.24 – 2.20 (m, 2H), 2.19 – 2.07 (m, 2H), 2.03 – 1.95 (m, 2H), 1.19 (s, 3H), 1.06 (d, *J* = 8.6 Hz, 1H), 0.75 (s, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 198.0, 172.8, 144.0, 136.6, 133.2, 128.6, 128.0, 118.8, 62.9, 45.6, 40.7, 38.0, 35.9, 33.4, 31.6, 31.3, 28.3, 26.2, 21.1 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{21}H_{26}O_3Na^+$: 349.1774; Found: 349.1777.

((3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-Tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-5-yl)methyl 4-oxo-4-phenylbutanoate (12i)



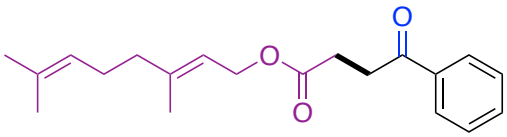
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 20:1 → 4:1) as a colorless oil (56%, 47.2 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.93 – 7.86 (m, 2H), 7.53 – 7.47 (m, 1H), 7.39 (t, *J* = 7.8 Hz, 2H), 5.47 (d, *J* = 5.0 Hz, 1H), 4.54 (dd, *J* = 7.9, 2.5 Hz, 1H), 4.27 – 4.22 (m, 2H), 4.20 – 4.13 (m, 2H), 4.01 – 3.88 (m, 1H), 3.36 – 3.14 (m, 2H), 2.79 – 2.69 (m, 2H), 1.43 (s, 3H), 1.38 (s, 3H), 1.26 (s, 3H), 1.26 (s, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 197.9, 172.7, 136.5, 133.1, 128.6, 128.0, 109.6, 108.7, 96.3, 71.0, 70.7, 70.4, 65.9, 63.5, 33.4, 28.2, 26.0, 25.9, 24.9, 24.4 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{22}H_{28}O_8Na^+$: 443.1676; Found: 443.1665.

(*E*)-3,7-Dimethylocta-2,6-dien-1-yl 4-oxo-4-phenylbutanoate (12j)



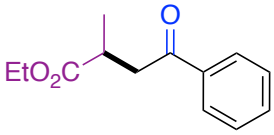
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (94%, 59.1 mg).

^{1}H NMR (400 MHz, Chloroform-*d*): δ = 8.02 – 7.95 (m, 2H), 7.61 – 7.53 (m, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 5.39 – 5.28 (m, 1H), 5.13 – 5.02 (m, 1H), 4.62 (d, *J* = 7.1 Hz, 2H), 3.31 (t, *J* = 6.7 Hz, 2H), 2.77 (t, *J* = 6.7 Hz, 2H), 2.15 – 1.98 (m, 4H), 1.69 (s, 3H), 1.68 (s, 3H), 1.59 (s, 3H) ppm.

^{13}C NMR (101 MHz, Chloroform-*d*): δ = 198.0, 172.9, 142.2, 136.5, 133.1, 131.8, 128.5, 128.0, 123.7, 118.2, 61.6, 39.5, 33.4, 28.3, 26.2, 25.6, 17.6, 16.4 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{20}H_{26}O_3Na^+$: 337.1774; Found: 337.1765.

Ethyl -2-methyl-4-oxo-4-phenylbutanoate (12k)



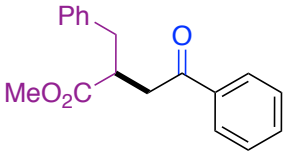
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 40:1 → 10:1) as a colorless oil (42%, 18.5 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.92 – 7.87 (m, 2H), 7.53 – 7.47 (m, 1H), 7.39 (t, *J* = 7.7 Hz, 2H), 4.08 (q, *J* = 7.2 Hz, 2H), 3.41 (dd, *J* = 17.6, 7.9 Hz, 1H), 3.10 – 3.01 (m, 1H), 2.94 (dd, *J* = 17.6, 5.6 Hz, 1H), 1.21 (d, *J* = 7.2 Hz, 3H), 1.18 (t, *J* = 7.1 Hz, 3H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 198.1, 175.9, 136.7, 133.1, 128.6, 128.0, 60.6, 41.9, 35.0, 17.3, 14.1 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{13}H_{16}O_3Na^+$: 243.0991; Found: 243.0983.

Methyl -2-benzyl-4-oxo-4-phenylbutanoate (12l)



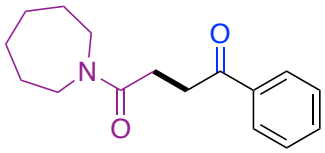
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 40:1 → 4:1) as a colorless oil (45%, 25.5 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.85 – 7.81 (m, 2H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.18 – 7.10 (m, 3H), 3.60 (s, 3H), 3.39 – 3.32 (m, 1H), 3.31 – 3.25 (m, 1H), 3.05 (dd, *J* = 13.6, 6.2 Hz, 1H), 2.94 (dd, *J* = 17.4, 4.1 Hz, 1H), 2.78 (dd, *J* = 13.7, 8.3 Hz, 1H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 198.0, 175.3, 138.5, 136.6, 133.2, 129.0, 128.58, 128.57, 128.0, 126.6, 51.8, 42.2, 39.4, 37.8 ppm.

HRMS (ESI): *m/z*: $[M + H]^+$ Calcd. for $C_{18}H_{19}O_3^+$: 283.1328; Found: 283.1320.

1-(Azepan-1-yl)-4-phenylbutane-1,4-dione (12m)



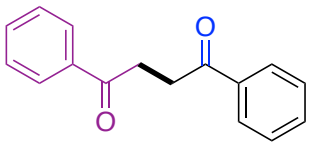
The titled compound was synthesized according to the general procedure GP-2, and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 40:1 → 10:1) as a colorless oil (51%, 26.6 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.95 (d, *J* = 7.7 Hz, 2H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 2H), 3.52 – 3.39 (m, 4H), 3.30 (t, *J* = 6.7 Hz, 2H), 2.73 (t, *J* = 6.7 Hz, 2H), 1.72 (p, *J* = 6.0 Hz, 2H), 1.64 (p, *J* = 6.1 Hz, 2H), 1.53 (d, *J* = 19.6 Hz, 4H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 199.5, 171.2, 136.9, 132.9, 128.5, 128.1, 47.8, 46.1, 33.8, 29.0, 27.6, 27.2, 27.0, 26.9 ppm.

HRMS (ESI): *m/z*: $[M + H]^+$ Calcd. for $C_{16}H_{22}O_2N^+$: 260.1645; Found: 260.1638.

1,4-Diphenylbutane-1,4-dione (12n)



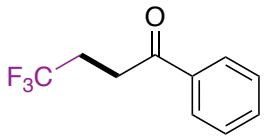
The titled compound was synthesized according to the general procedure GP-2 and was obtained after silica gel column chromatography (*n*-hexane : ethyl acetate 60:1 → 20:1) as a colorless oil (53%, 25.0 mg).

^{1}H NMR (400 MHz, Chloroform-*d*): δ = 8.11 – 8.00 (m, 4H), 7.61 – 7.54 (m, 2H), 7.48 (t, *J* = 7.6 Hz, 4H), 3.47 (s, 4H) ppm.

^{13}C NMR (101 MHz, Chloroform-*d*): δ = 198.6, 136.7, 133.1, 128.6, 128.1, 32.5 ppm.

HRMS (ESI): *m/z*: $[M + Na]^+$ Calcd. for $C_{16}H_{14}O_2Na^+$: 261.0883; Found: 261.0883.

4,4,4-Trifluoro-1-phenyl-1-butanone (12o)



The titled compound was synthesized according to the general procedure GP-3 and was obtained after silica gel column chromatography (n-hexane : ethyl acetate 80:1 → 40:1) as a colorless oil (33%, 13 mg).

^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.93 – 7.83 (m, 2H), 7.56 – 7.51 (m, 1H), 7.46 – 7.39 (m, 2H), 3.22 – 3.17 (m, 2H), 2.60 – 2.47 (m, 2H) ppm.

^{13}C NMR (151 MHz, Chloroform-*d*): δ = 196.3, 136.1, 133.6, 128.7, 128.0, 127.2 (q, *J* = 273.3 Hz), 31.2 (q, *J* = 2.7 Hz), 28.3 (q, *J* = 30.2 Hz) ppm.

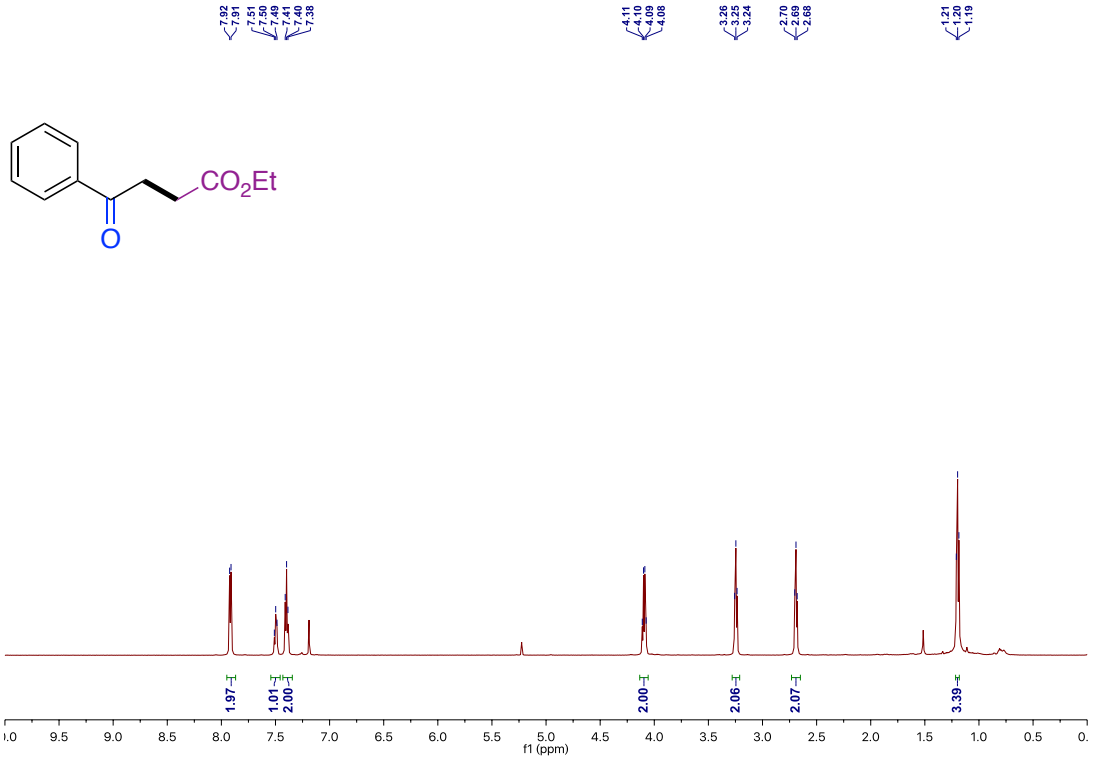
^{19}F NMR (565 MHz, Chloroform-*d*): δ = -66.44 (t, *J* = 11.0 Hz).

The spectroscopic data is in accordance to: Y. Zhou, C. Zhang, Y. Zhao, D. Li, J. Zhao, Z. Wang, J. Qu, *Eur. J. Org. Chem.* 2018, 6217–6222.

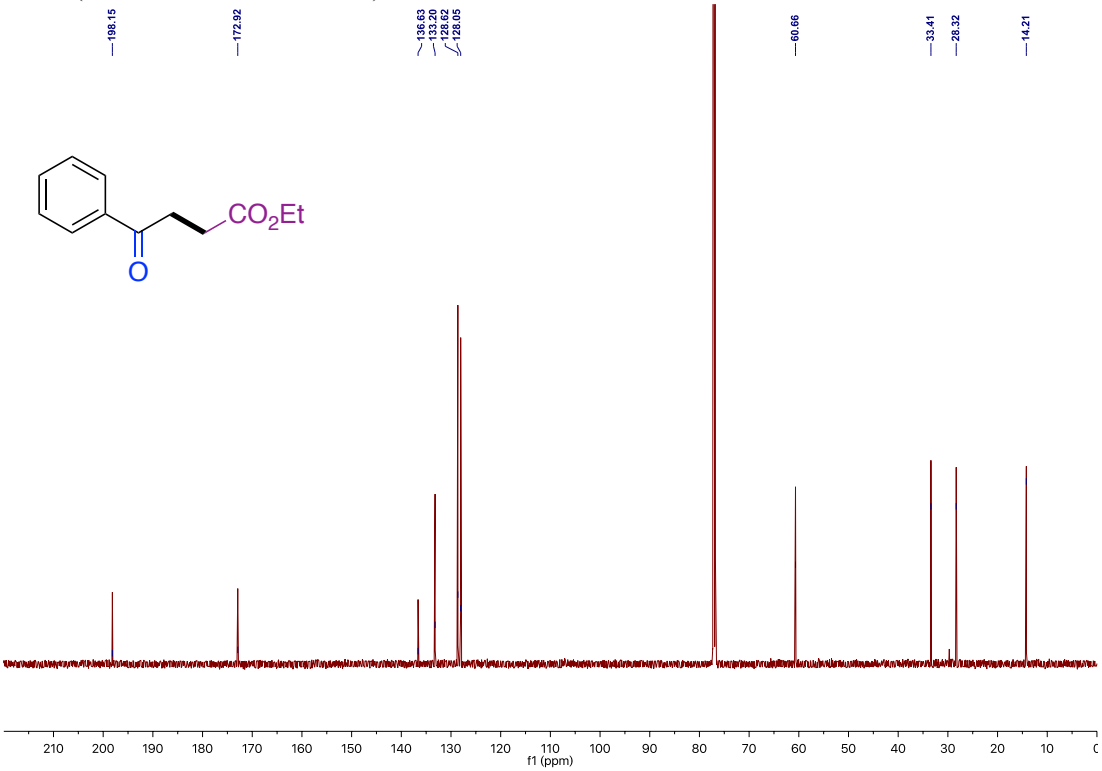
Spectra

Ethyl 4-oxo-4-phenylbutanoate (8a)

^{1}H NMR (600 MHz, Chloroform-*d*)

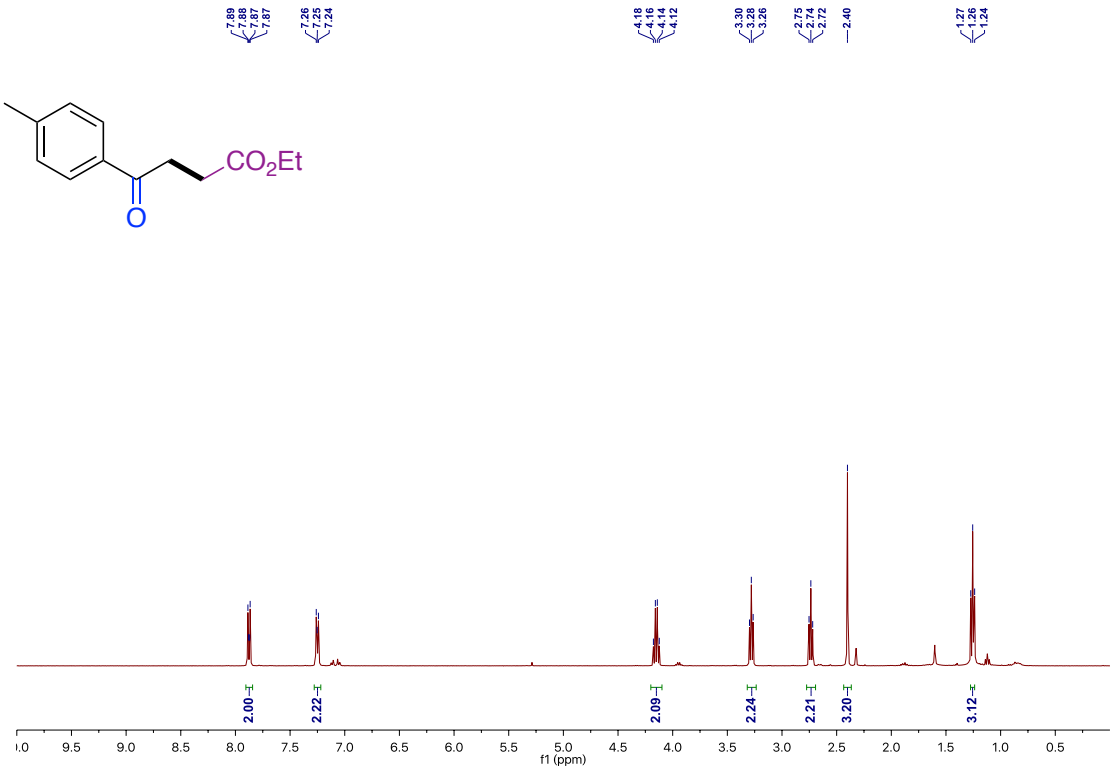


^{13}C NMR (151 MHz, Chloroform-*d*)

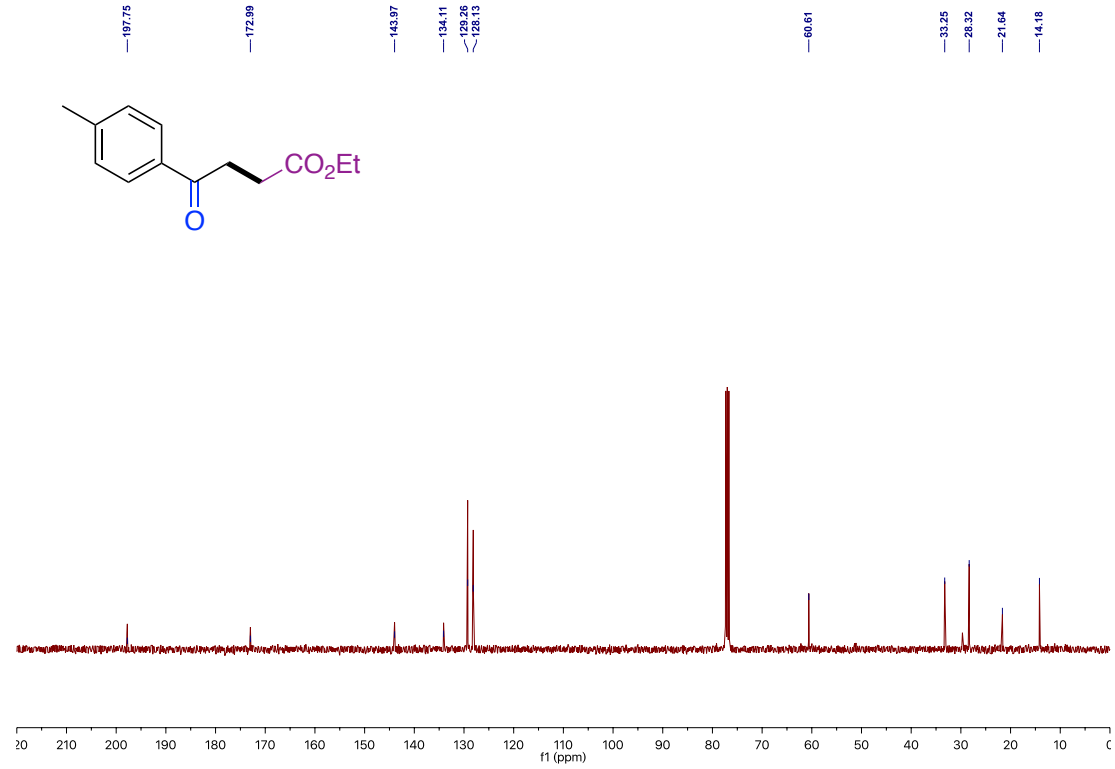


Ethyl 4-oxo-4-(*p*-tolyl)butanoate (8b)

^{1}H NMR (400 MHz, Chloroform-*d*)

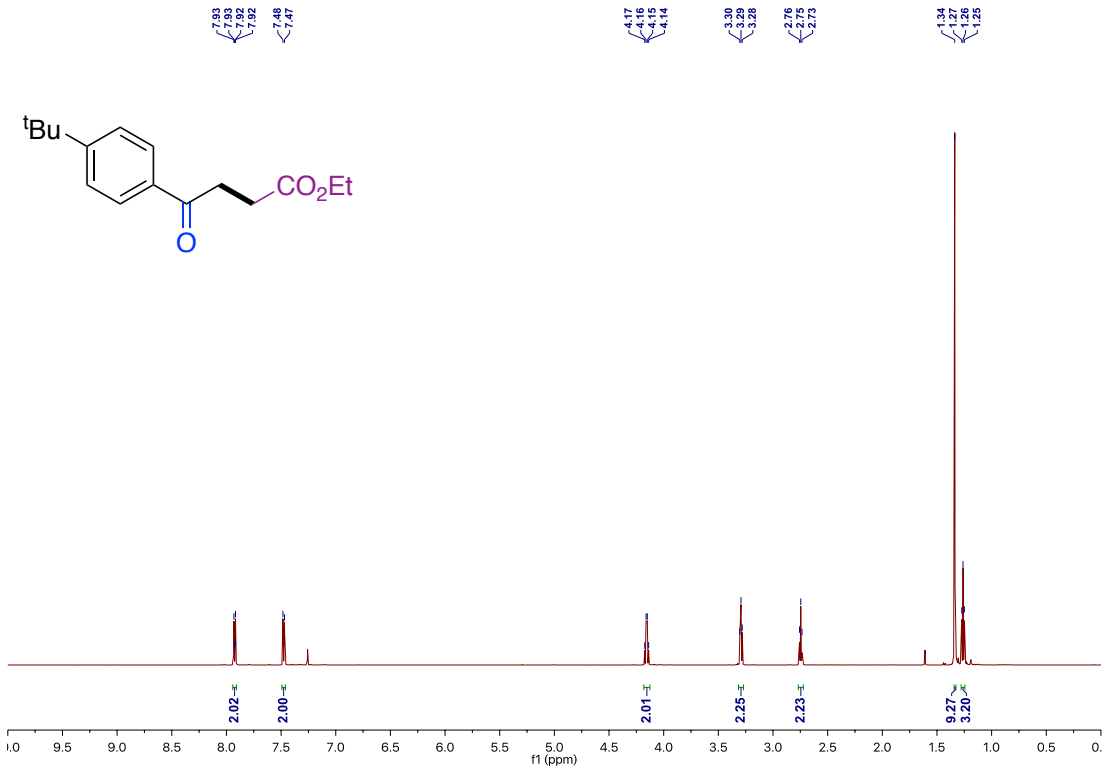


^{13}C NMR (101 MHz, Chloroform-*d*)

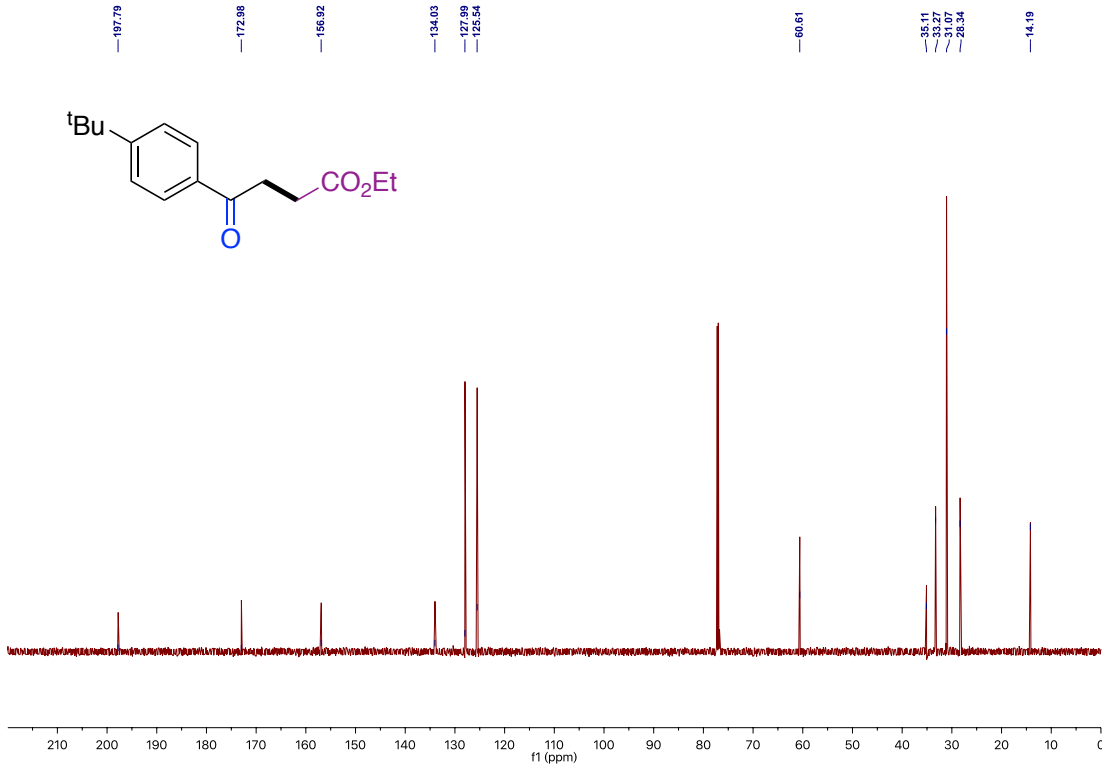


Ethyl 4-(4-(*tert*-butyl)phenyl)-4-oxobutanoate (8c)

^{1}H NMR (600 MHz, Chloroform-*d*)

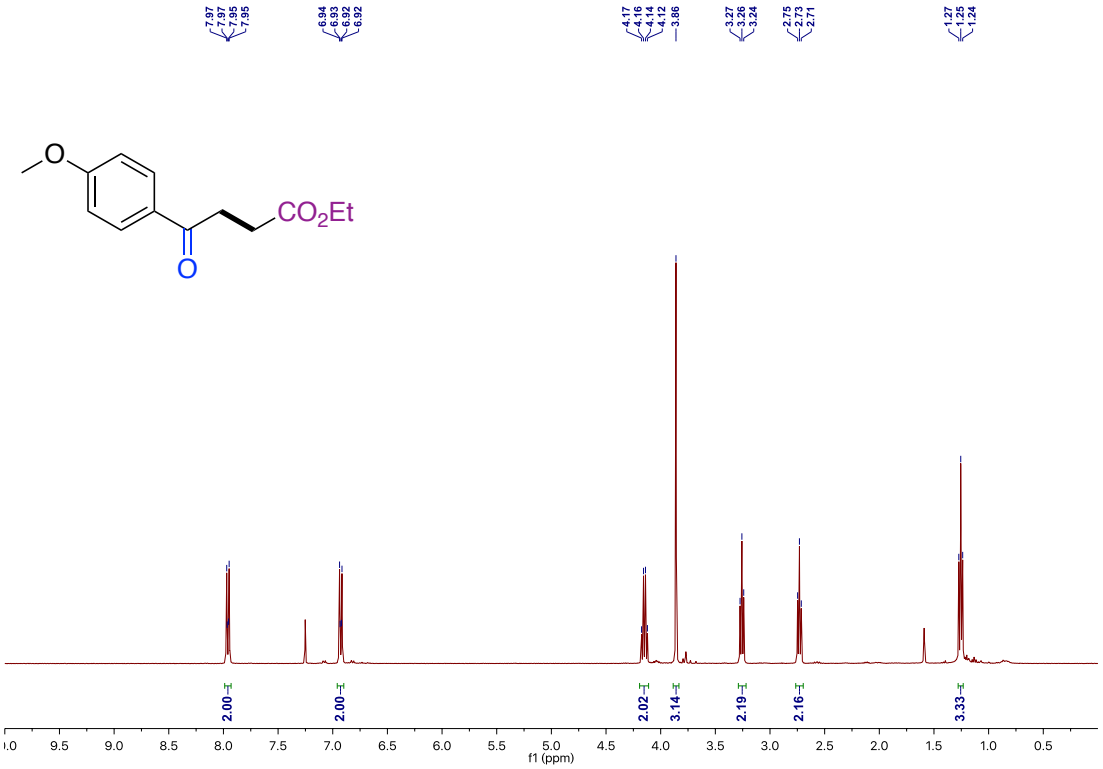


^{13}C NMR (151 MHz, Chloroform-*d*)

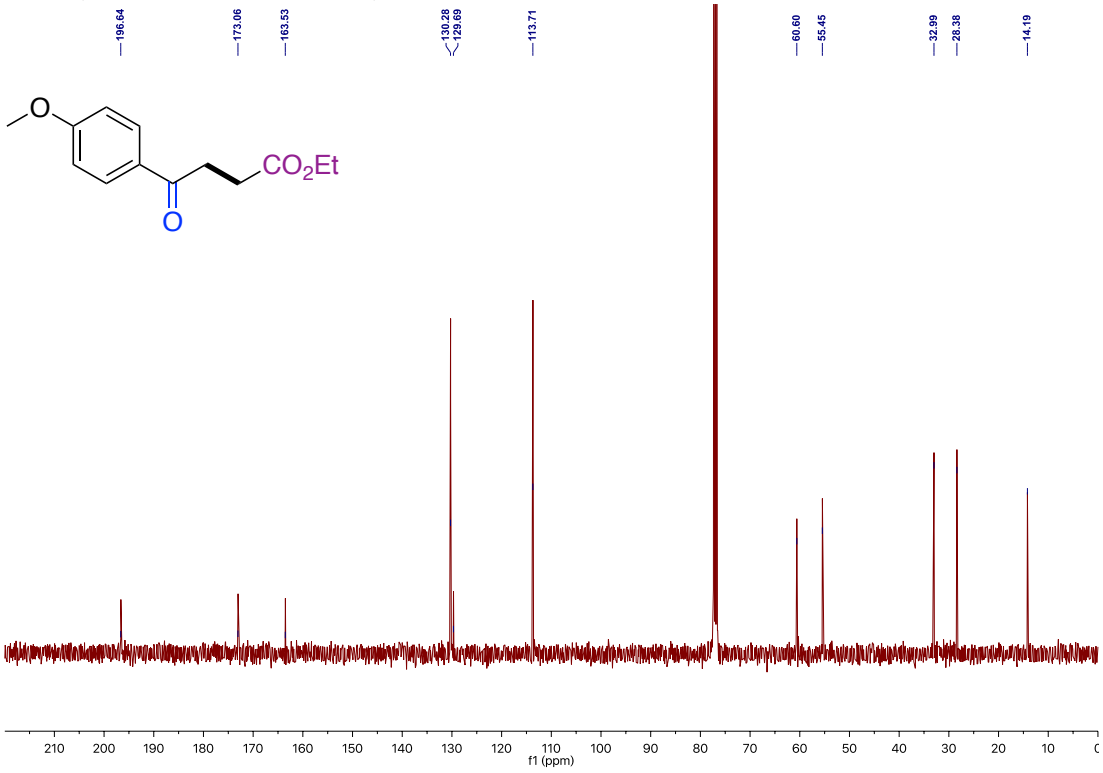


Ethyl 4-(4-methoxyphenyl)-4-oxobutanoate (8d)

^{1}H NMR (400 MHz, Chloroform-*d*)

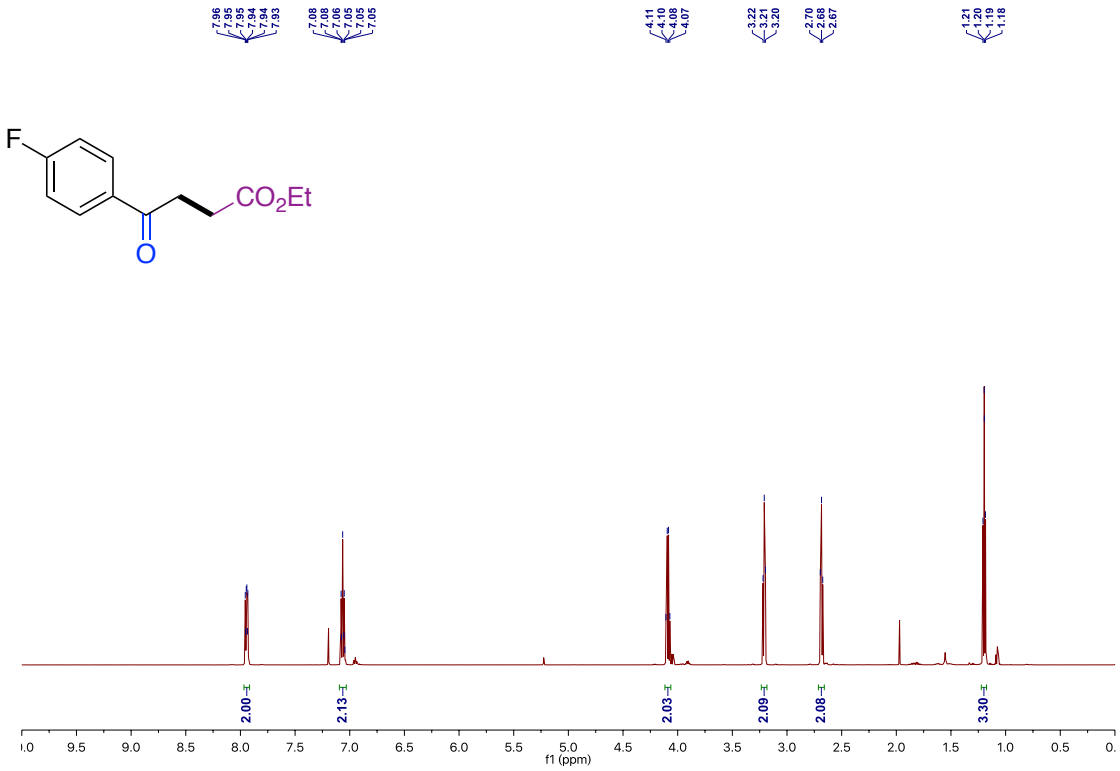


^{13}C NMR (101 MHz, Chloroform-*d*)

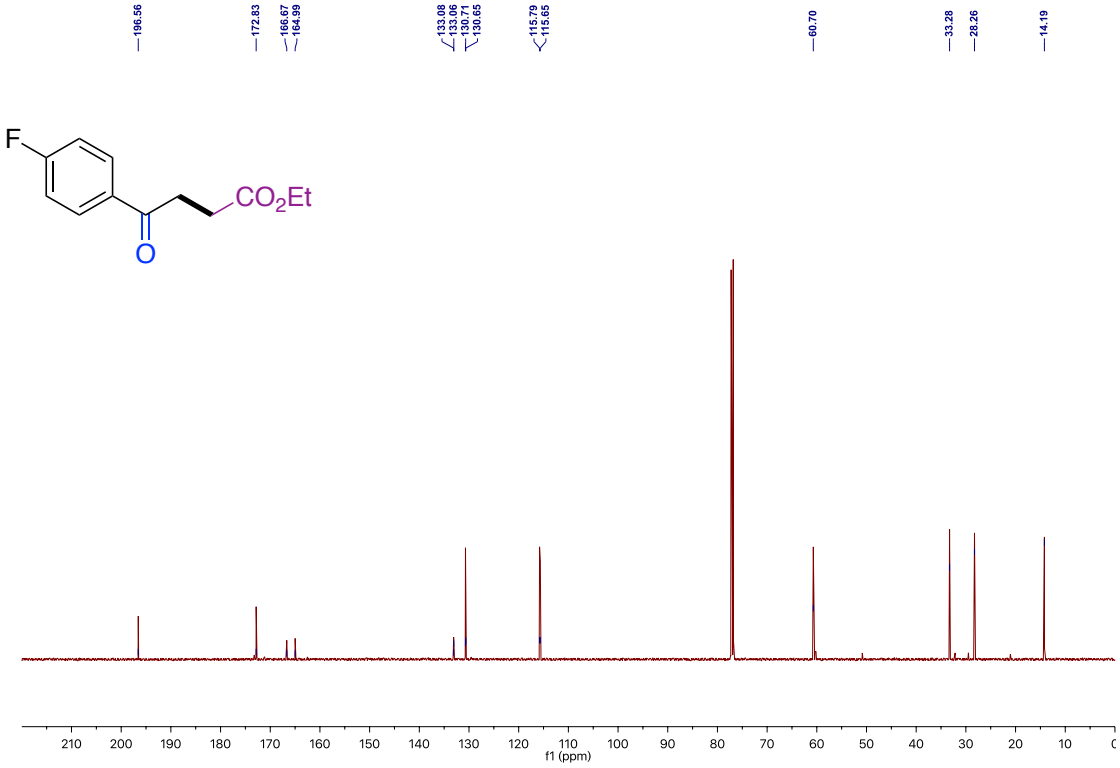


Ethyl 4-(4-fluorophenyl)-4-oxobutanoate (8e)

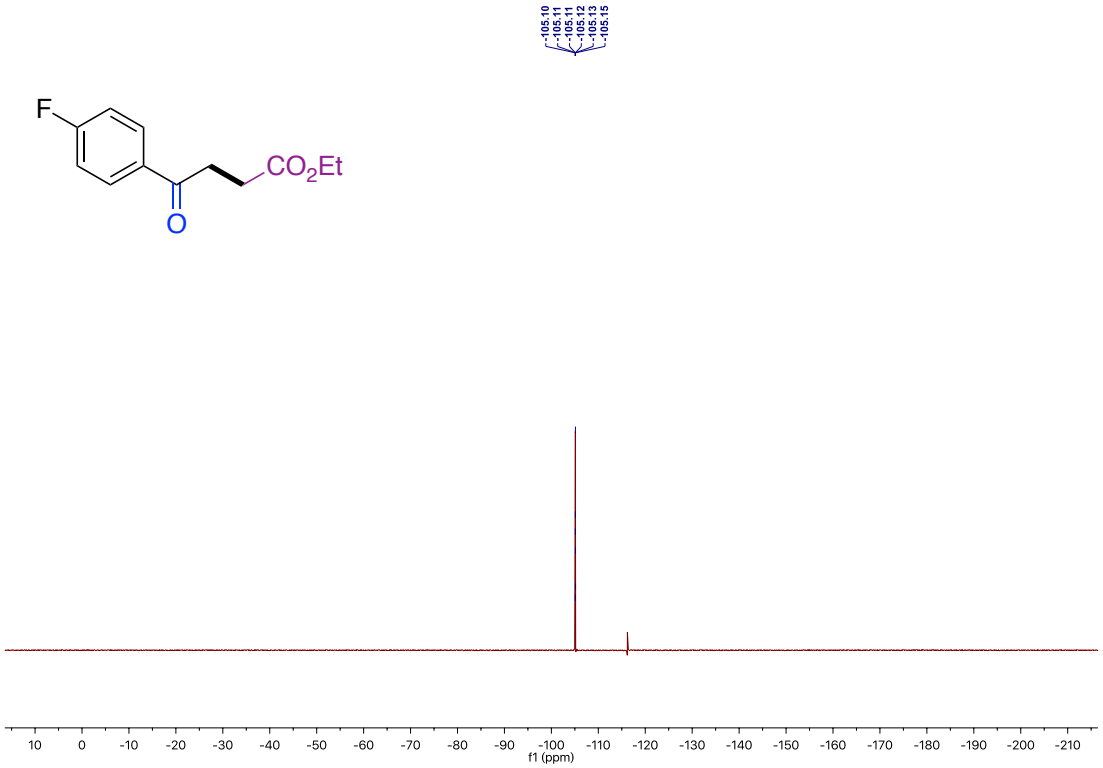
^{1}H NMR (600 MHz, Chloroform-*d*)



^{13}C NMR (151 MHz, Chloroform-*d*)

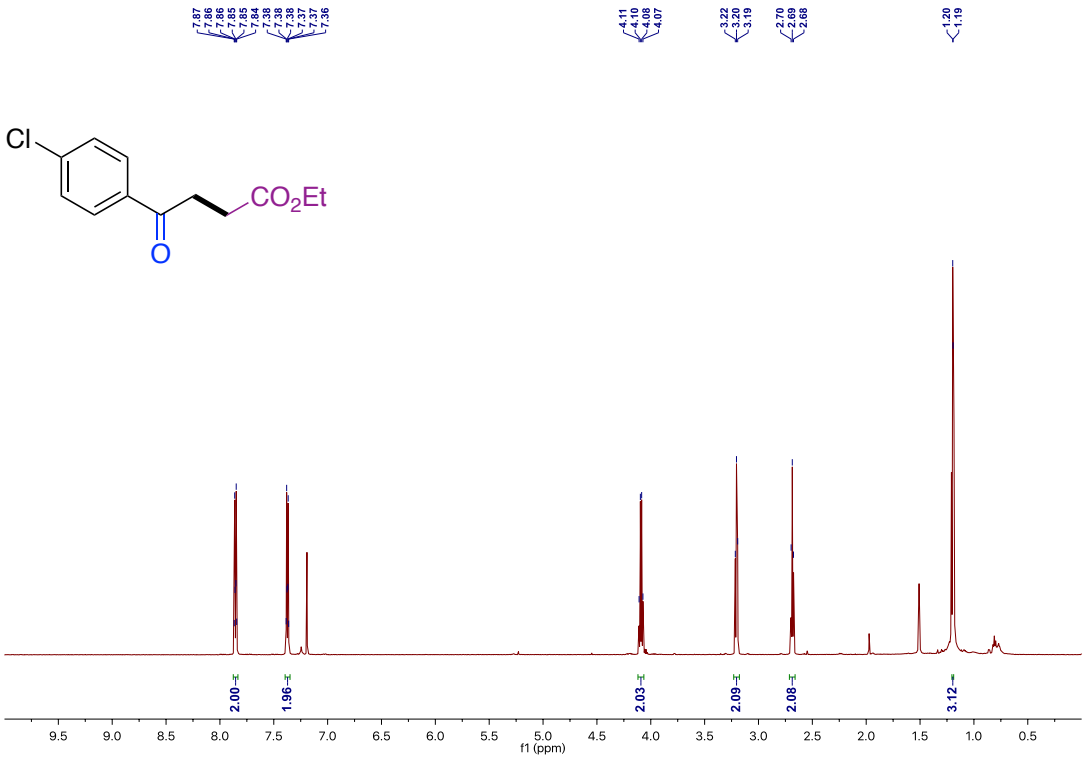


^{19}F NMR (565 MHz, Chloroform-*d*)

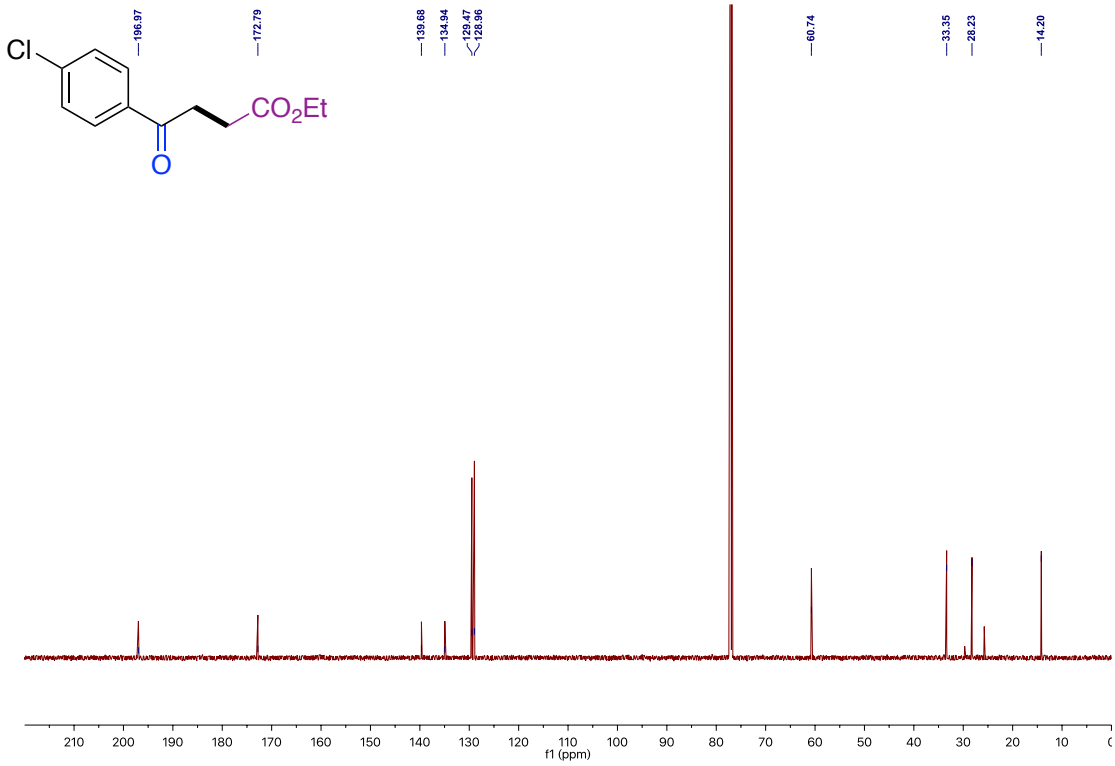


Ethyl 4-(4-chlorophenyl)-4-oxobutanoate (8f)

^{1}H NMR (600 MHz, Chloroform-*d*)

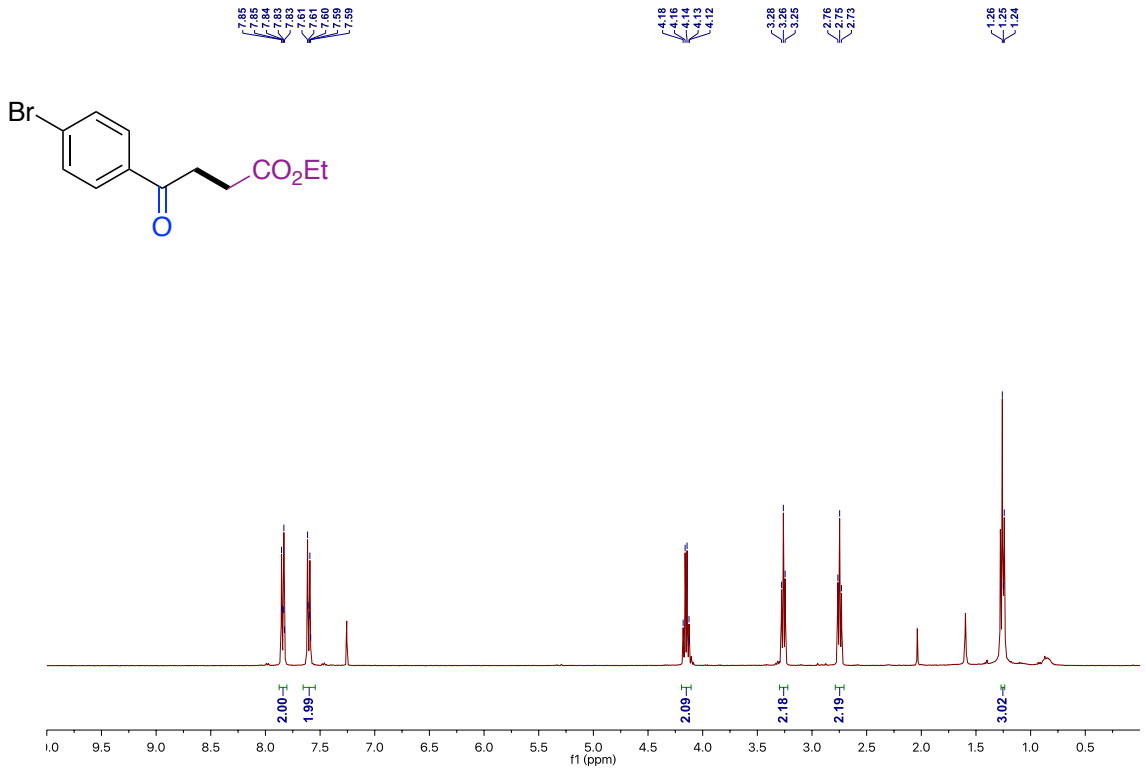


^{13}C NMR (151 MHz, Chloroform-*d*)

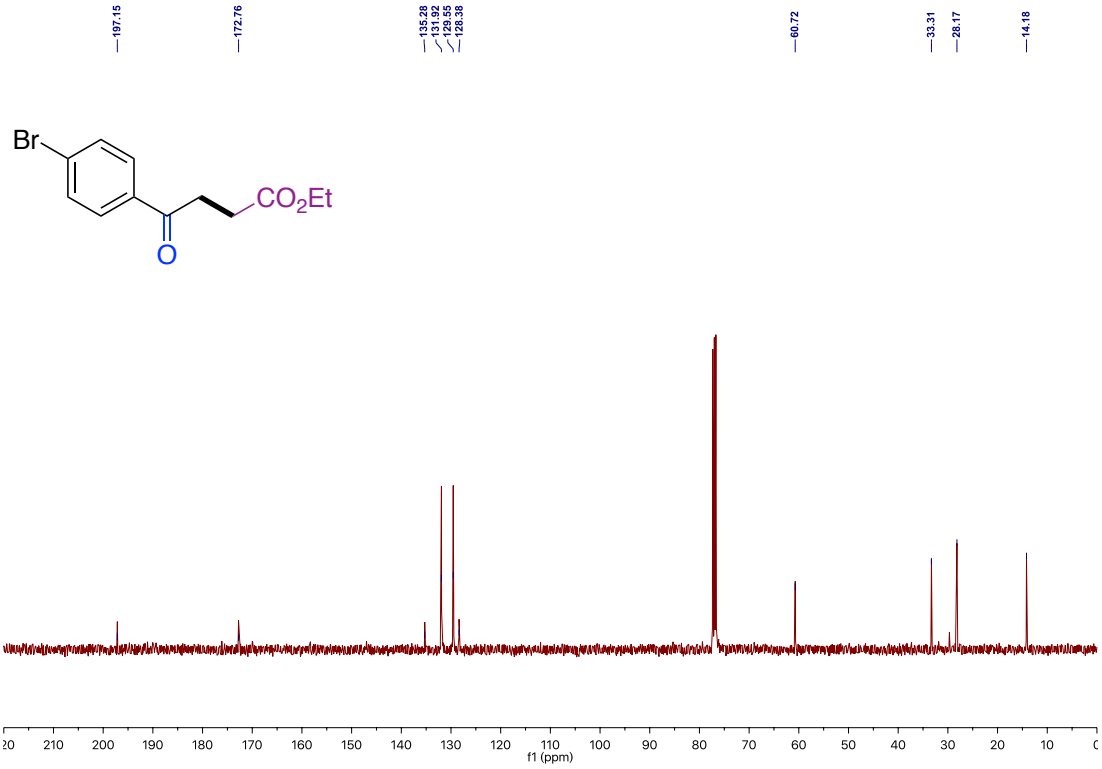


Ethyl 4-(4-bromophenyl)-4-oxobutanoate (8g)

^{1}H NMR (400 MHz, Chloroform-*d*)

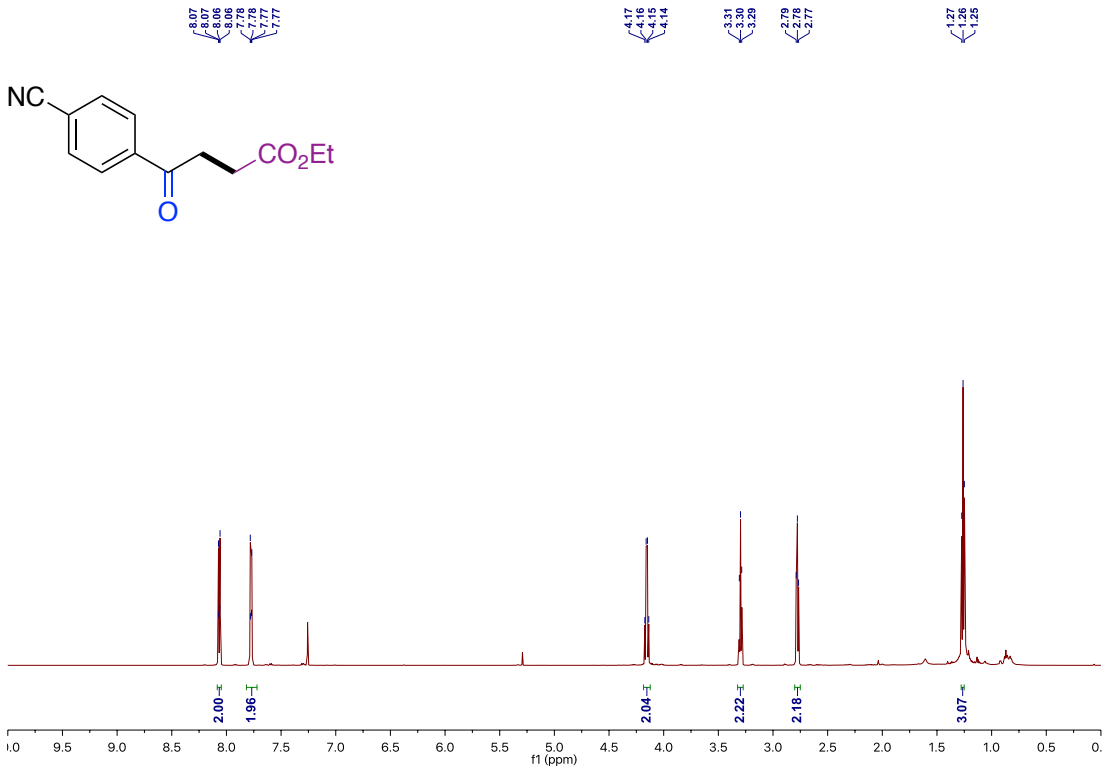


^{13}C NMR (101 MHz, Chloroform-*d*)

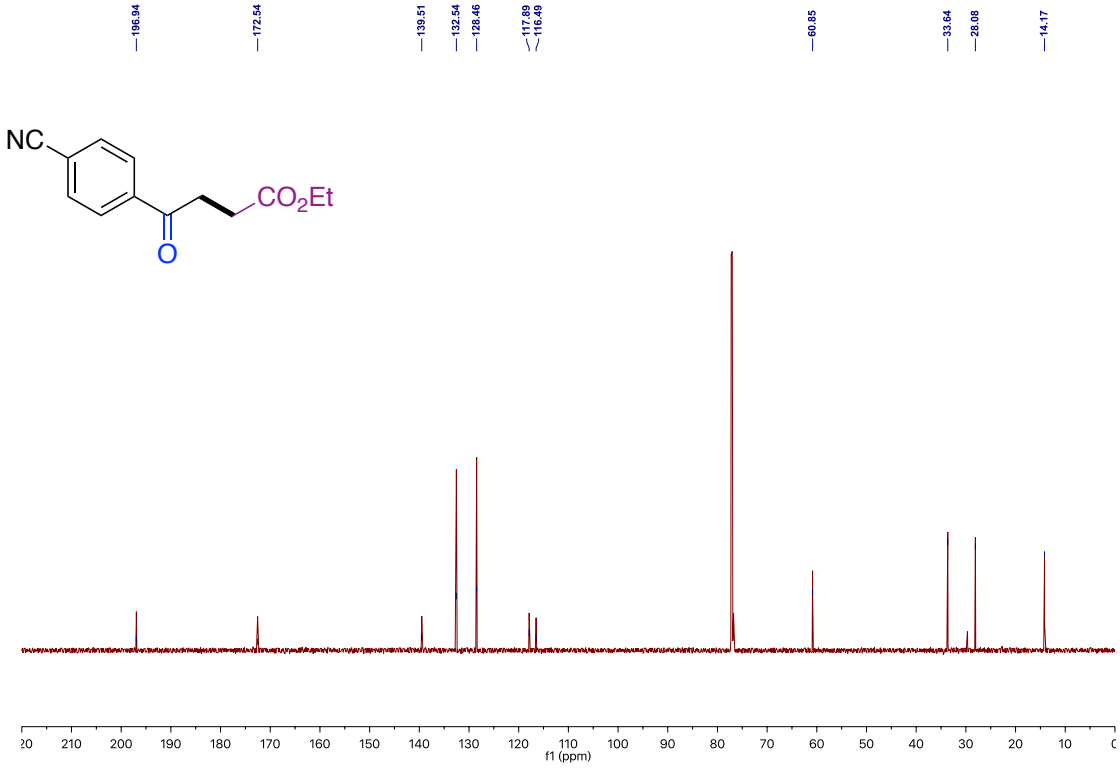


Ethyl 4-(4-cyanophenyl)-4-oxobutanoate (8h)

^{1}H NMR (600 MHz, Chloroform-*d*)

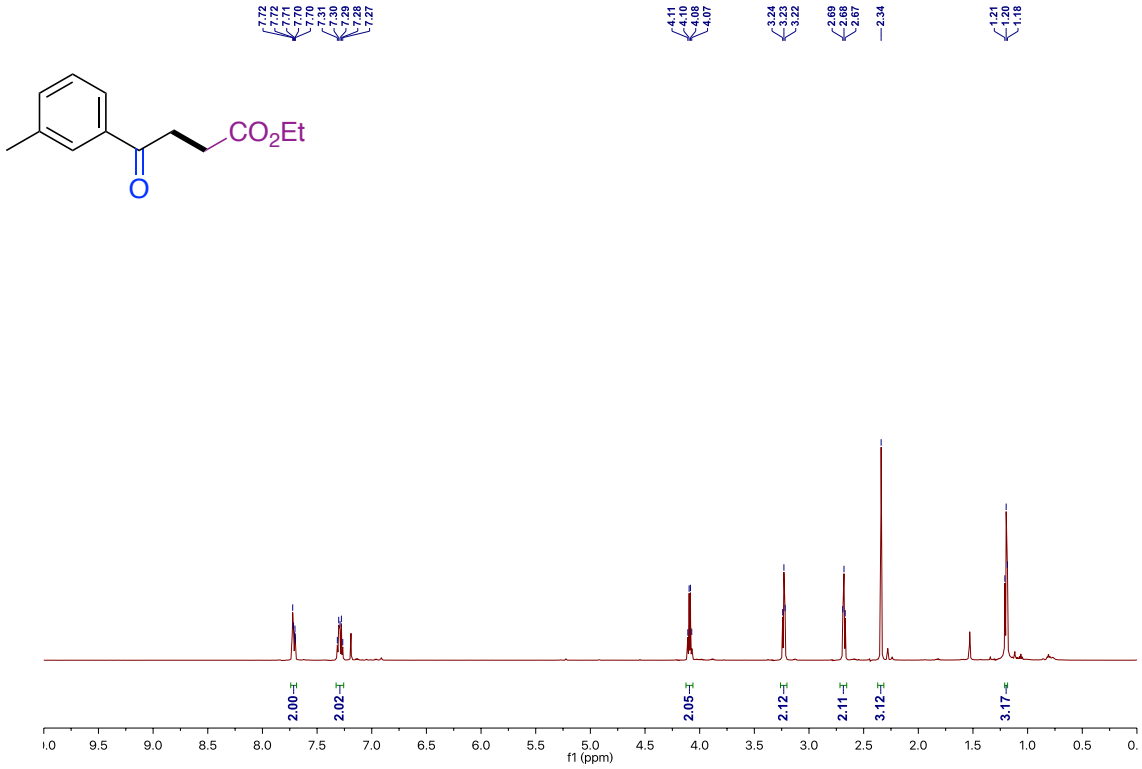


^{13}C NMR (151 MHz, Chloroform-*d*)

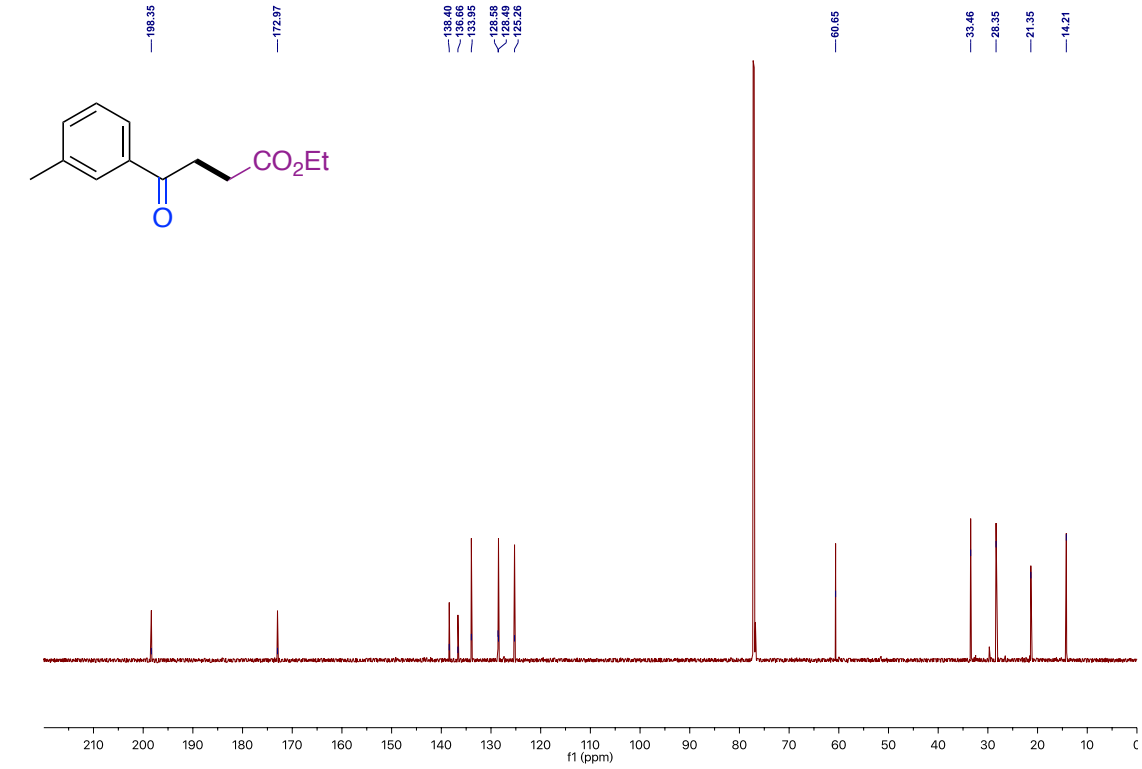


Ethyl 4-oxo-4-(*m*-tolyl)butanoate (8i)

^{1}H NMR (600 MHz, Chloroform-*d*)

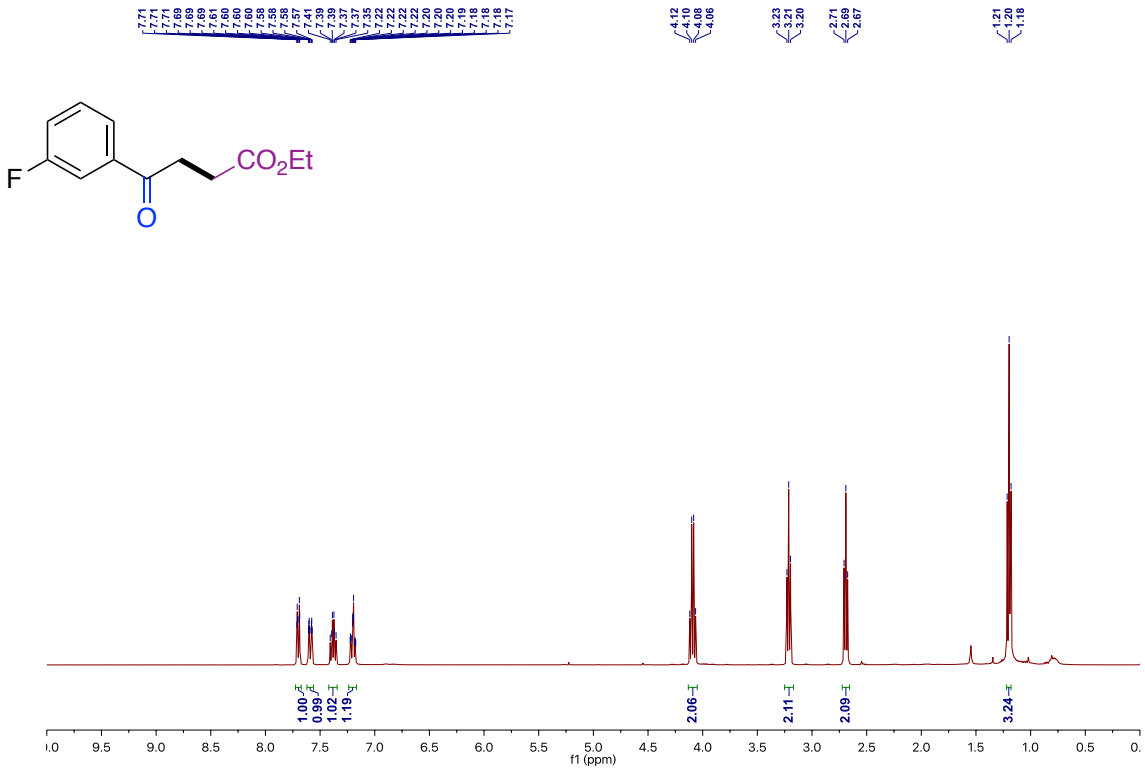


^{13}C NMR (151 MHz, Chloroform-*d*)

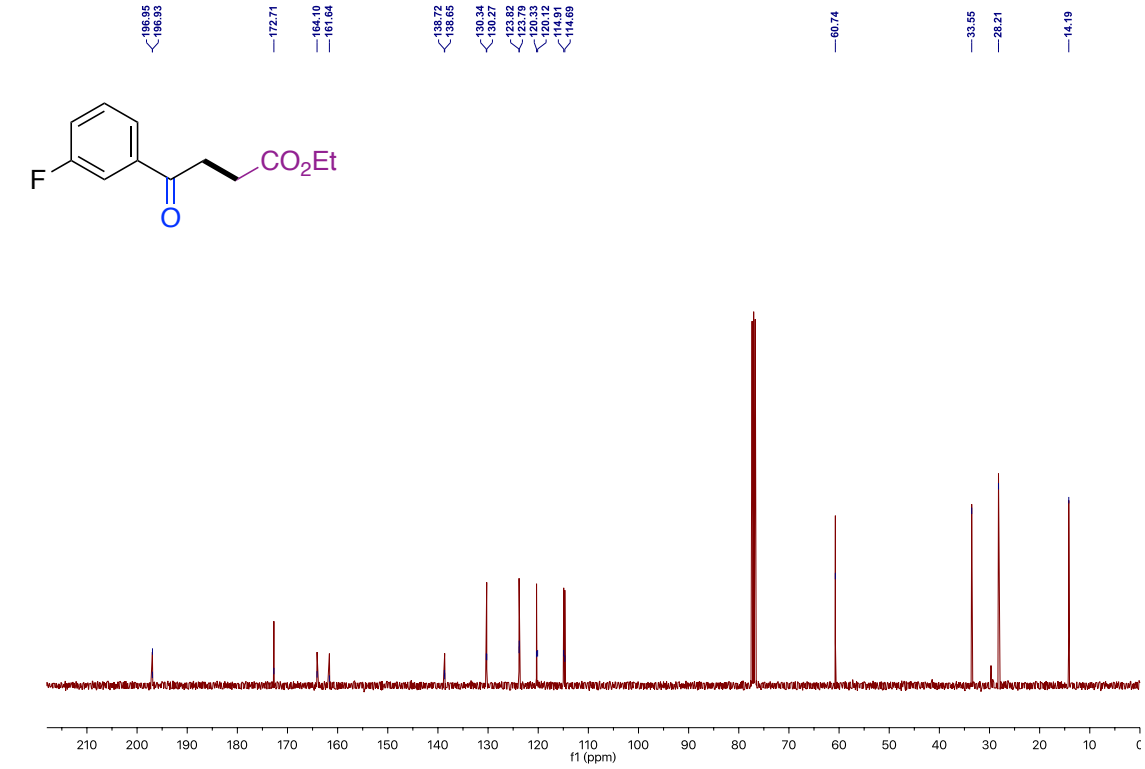


Ethyl 4-(3-fluorophenyl)-4-oxobutanoate (8j)

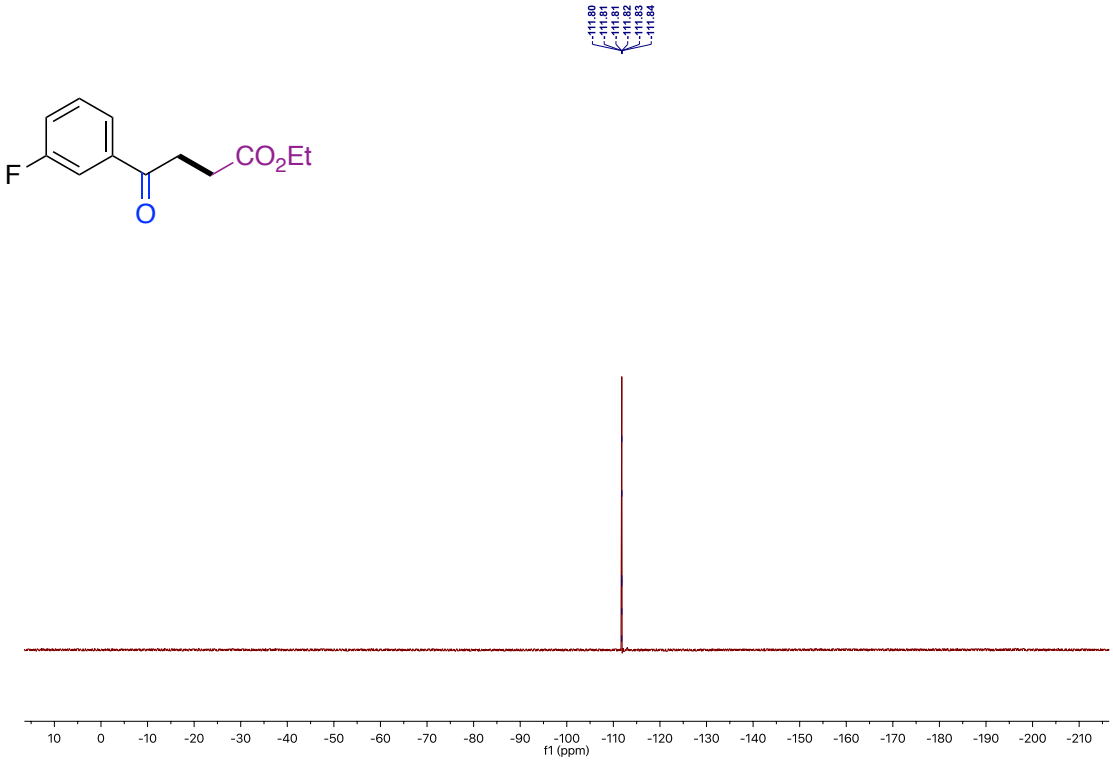
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)

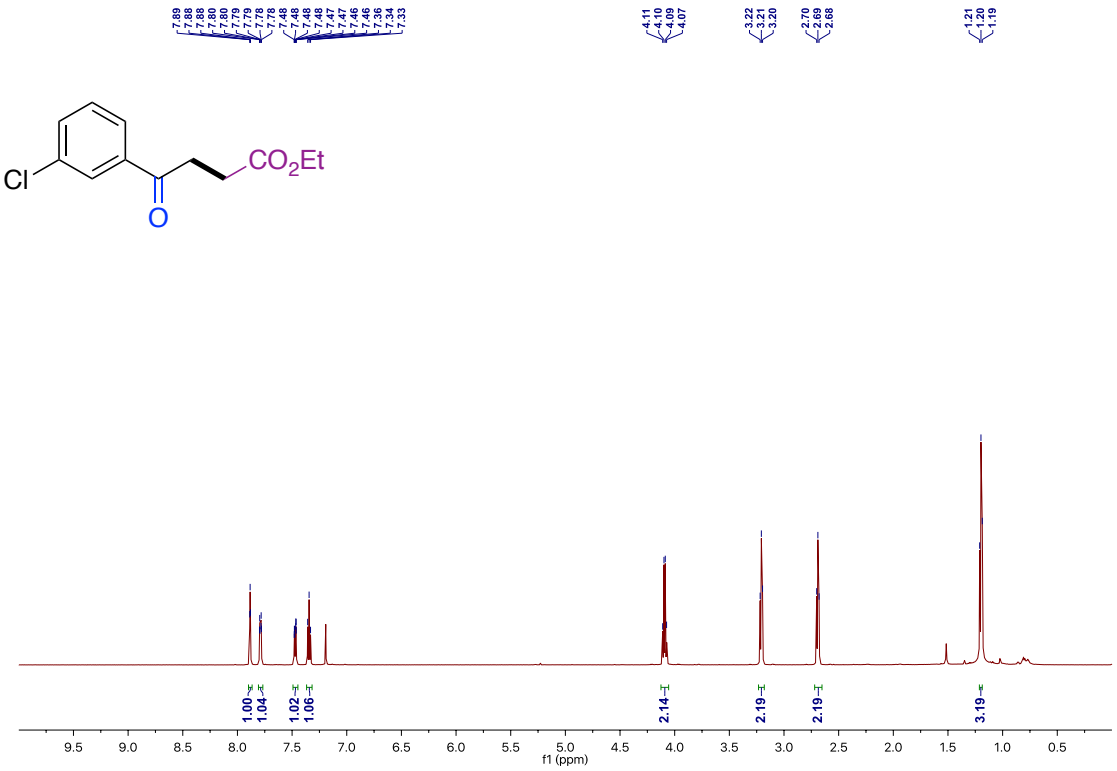


^{19}F NMR (565 MHz, Chloroform-*d*)

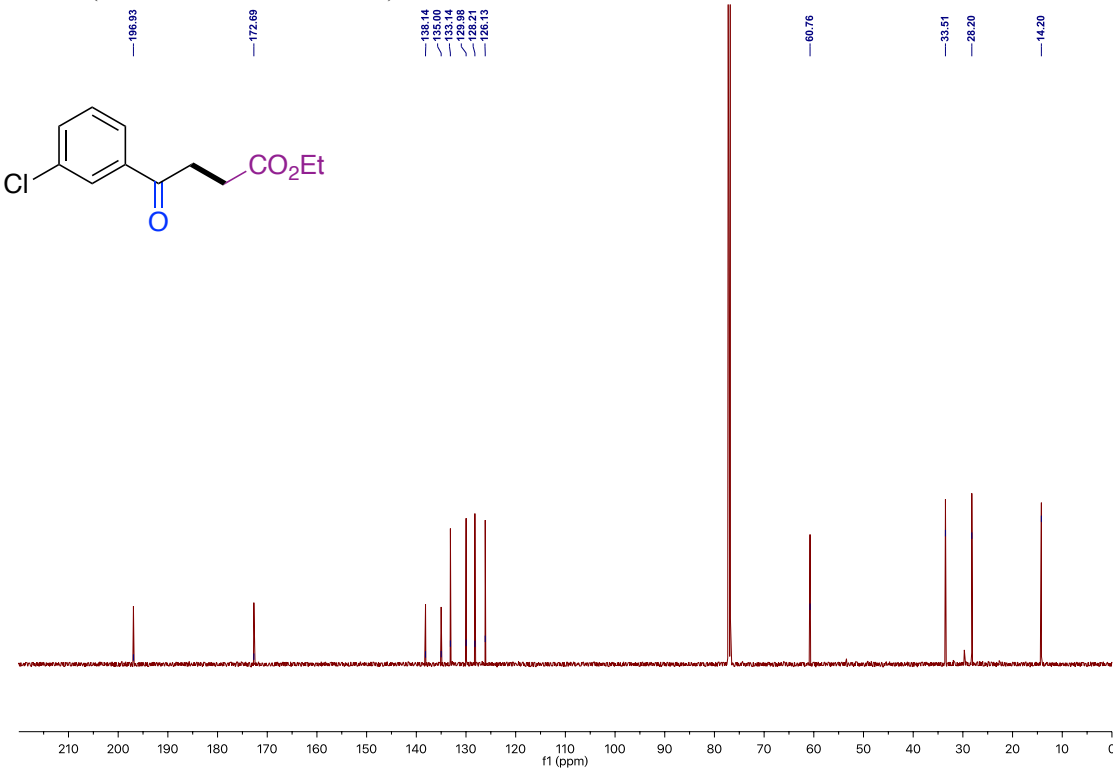


Ethyl 4-(3-chlorophenyl)-4-oxobutanoate (8k)

^{1}H NMR (600 MHz, Chloroform-*d*)

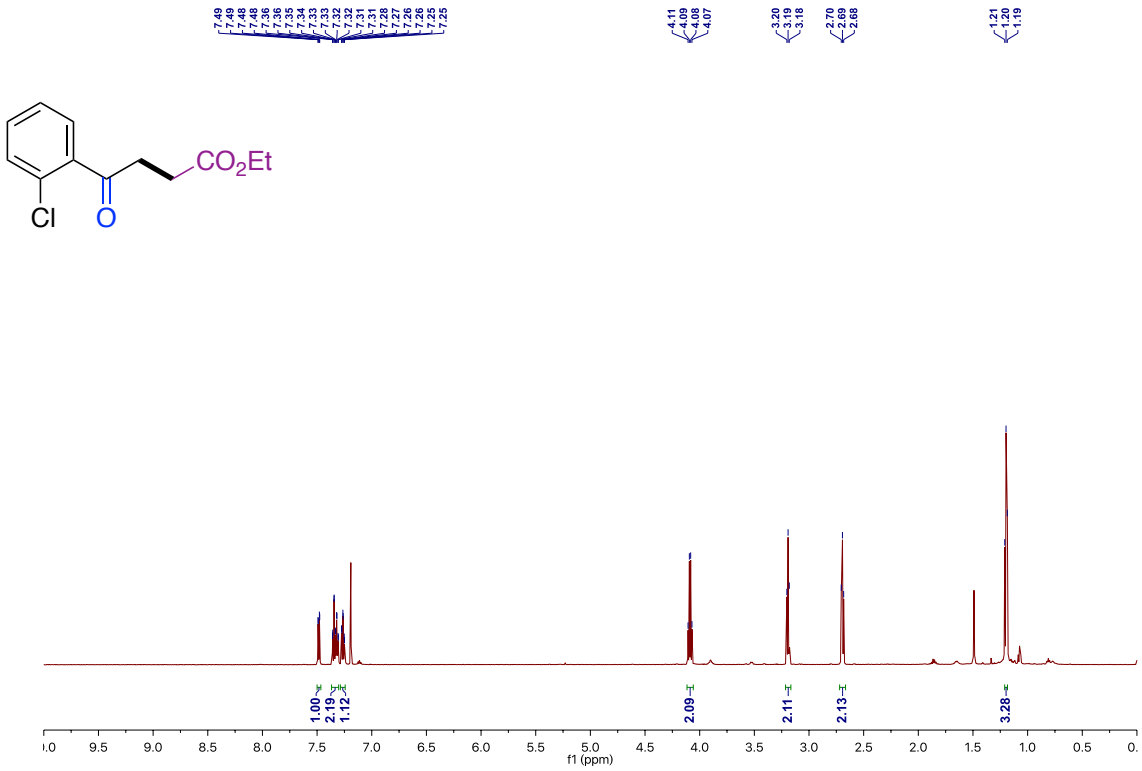


^{13}C NMR (151 MHz, Chloroform-*d*)

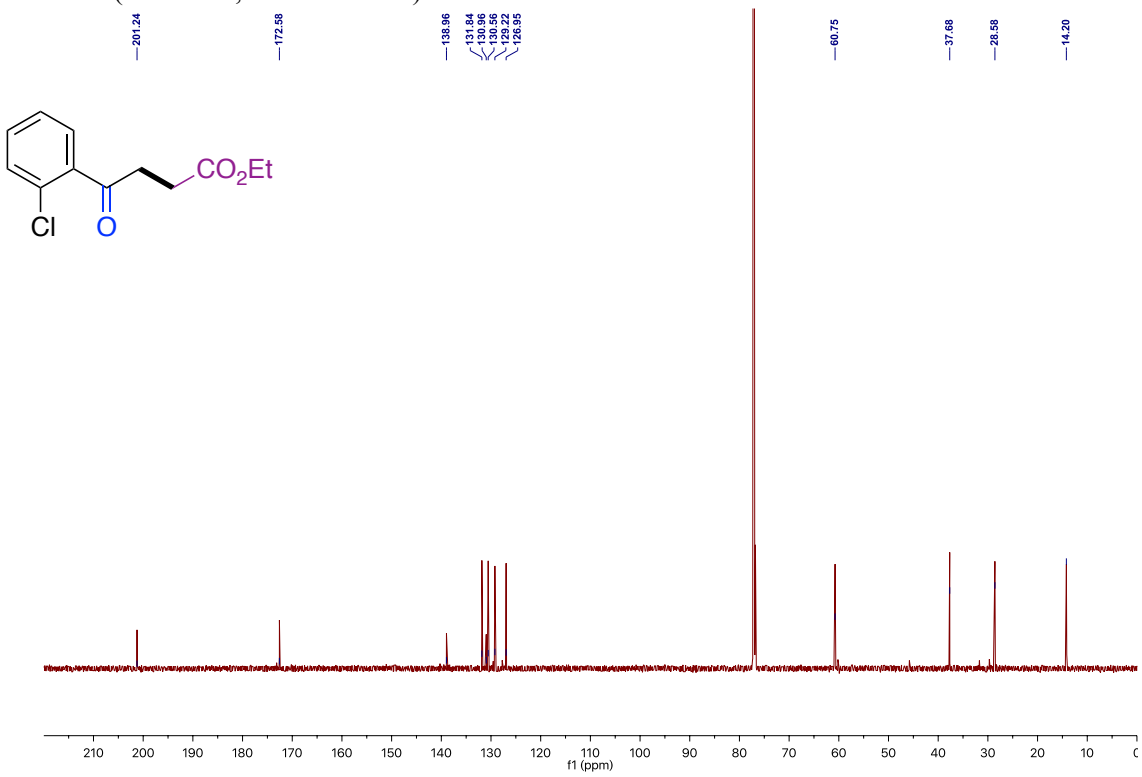


Ethyl 4-(2-chlorophenyl)-4-oxobutanoate (8l)

^{1}H NMR (600 MHz, Chloroform-*d*)

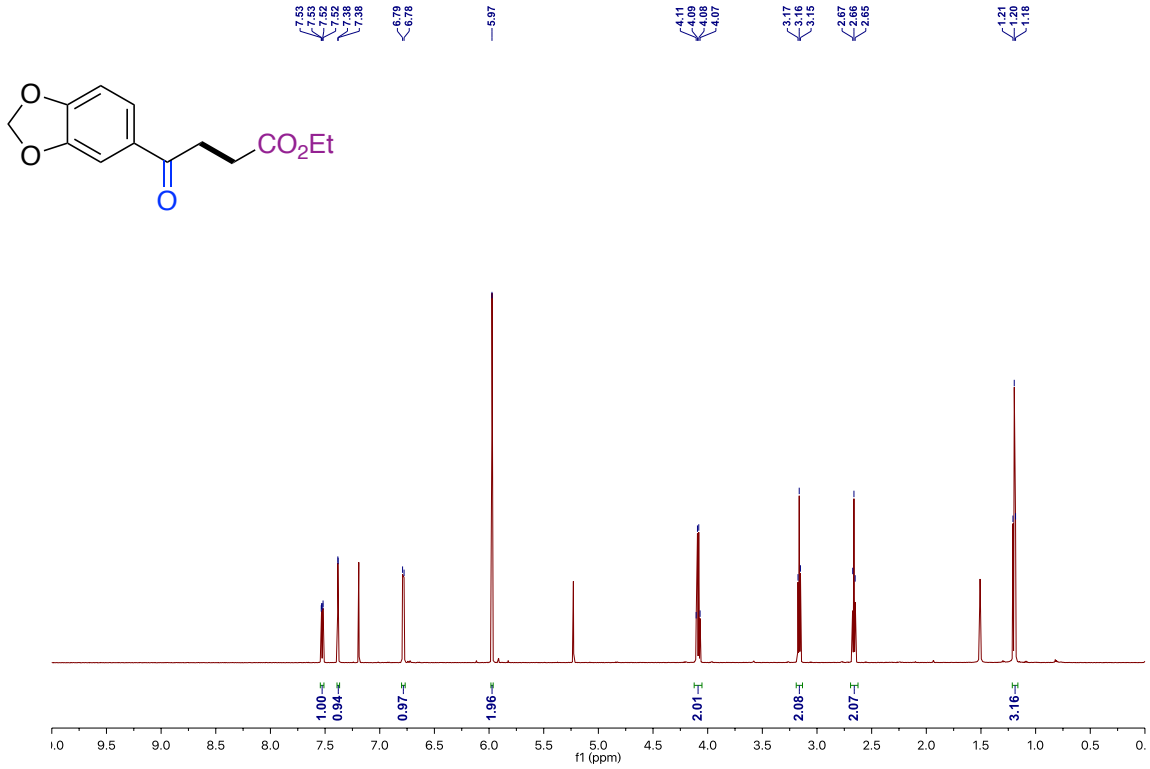


^{13}C NMR (151 MHz, Chloroform-*d*)

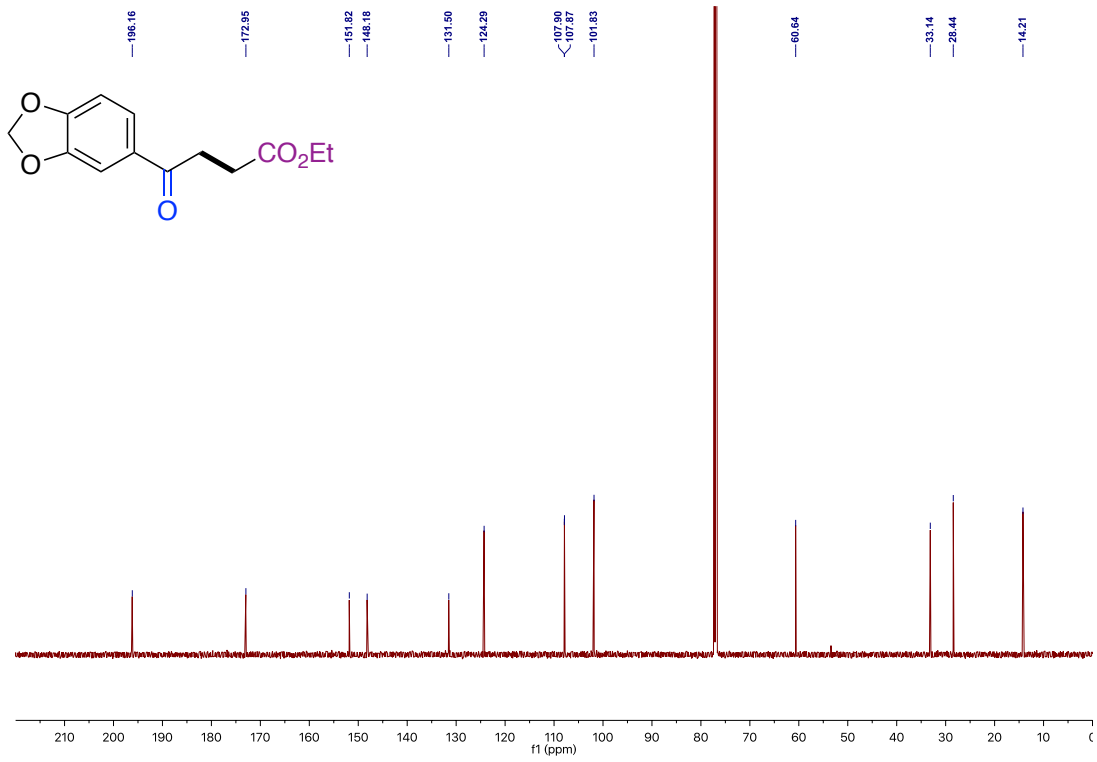


Ethyl 4-(benzo[*d*][1,3]dioxol-5-yl)-4-oxobutanoate (8m)

^{1}H NMR (600 MHz, Chloroform-*d*)

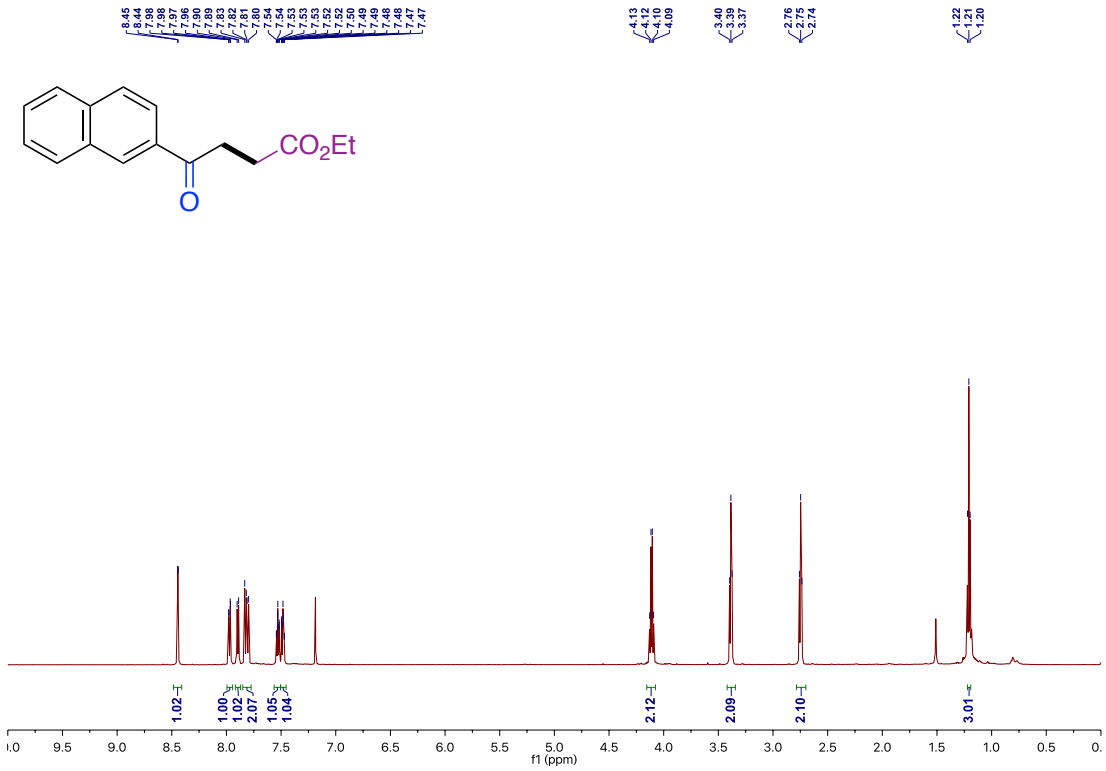


^{13}C NMR (151 MHz, Chloroform-*d*)

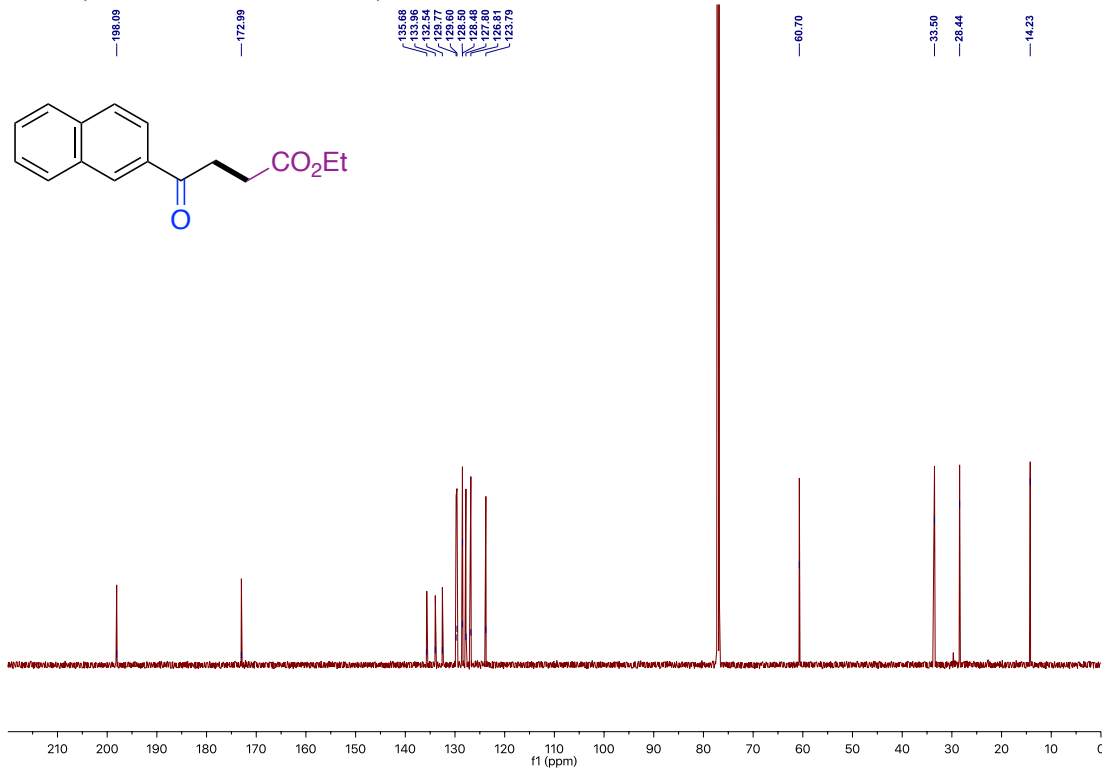


Ethyl 4-(naphthalen-2-yl)-4-oxobutanoate (8n)

^{1}H NMR (600 MHz, Chloroform-*d*)

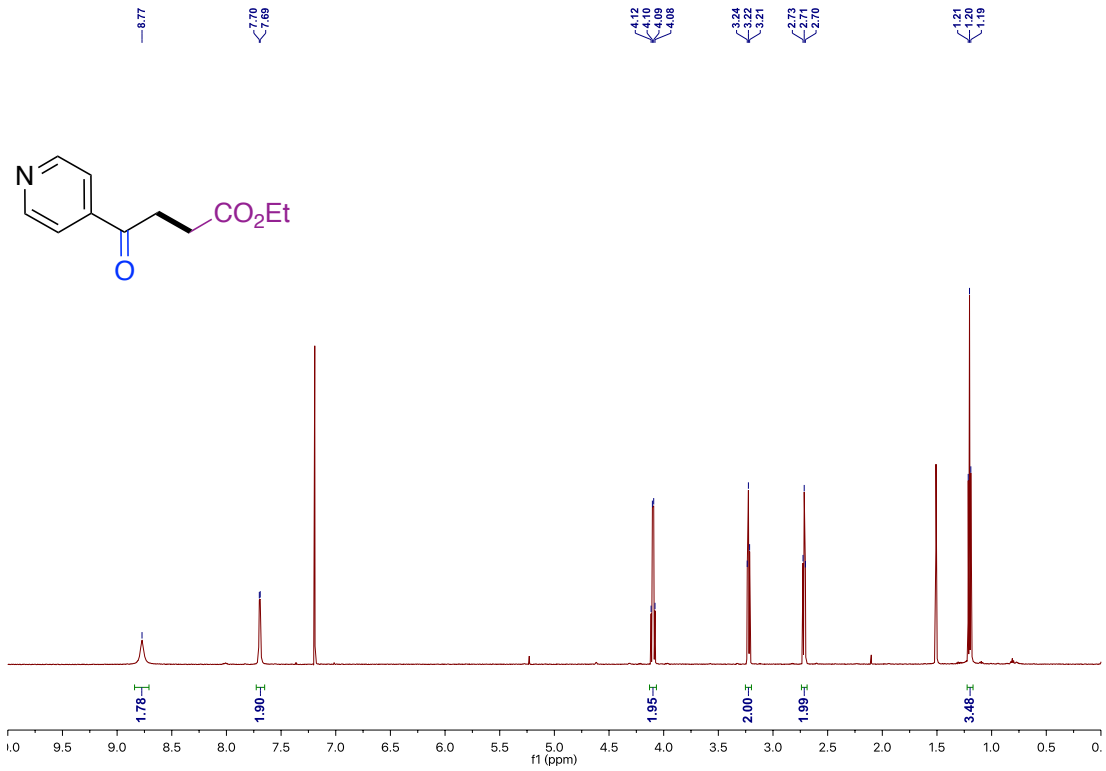


^{13}C NMR (151 MHz, Chloroform-*d*)

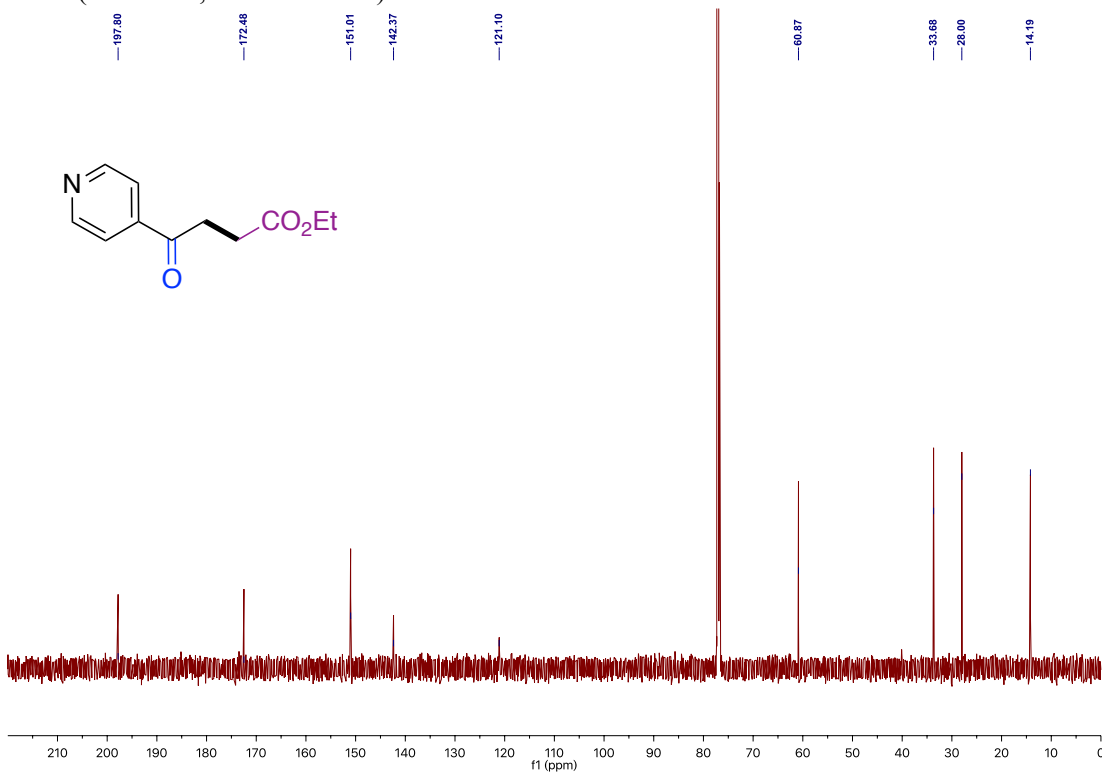


Ethyl 4-oxo-4-(pyridin-4-yl)butanoate (8o)

^{1}H NMR (600 MHz, Chloroform-*d*)

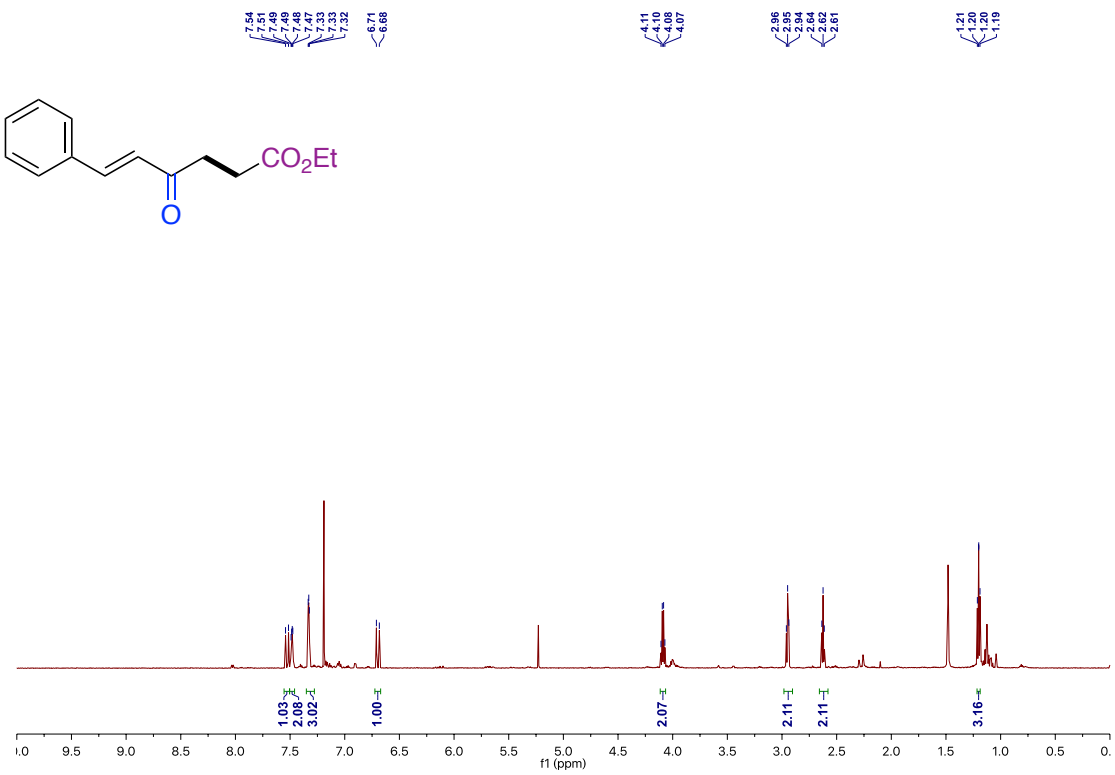


^{13}C NMR (151 MHz, Chloroform-*d*)

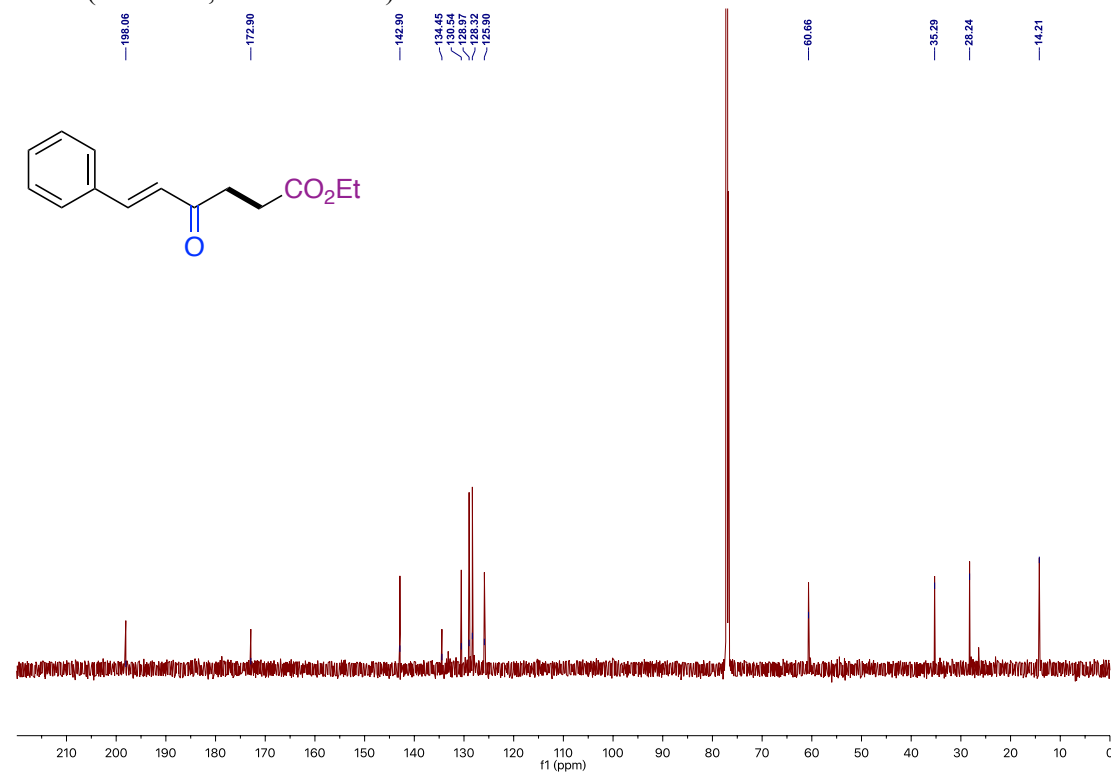


Ethyl (*E*)-4-oxo-6-phenylhex-5-enoate (8p)

^{1}H NMR (600 MHz, Chloroform-*d*)

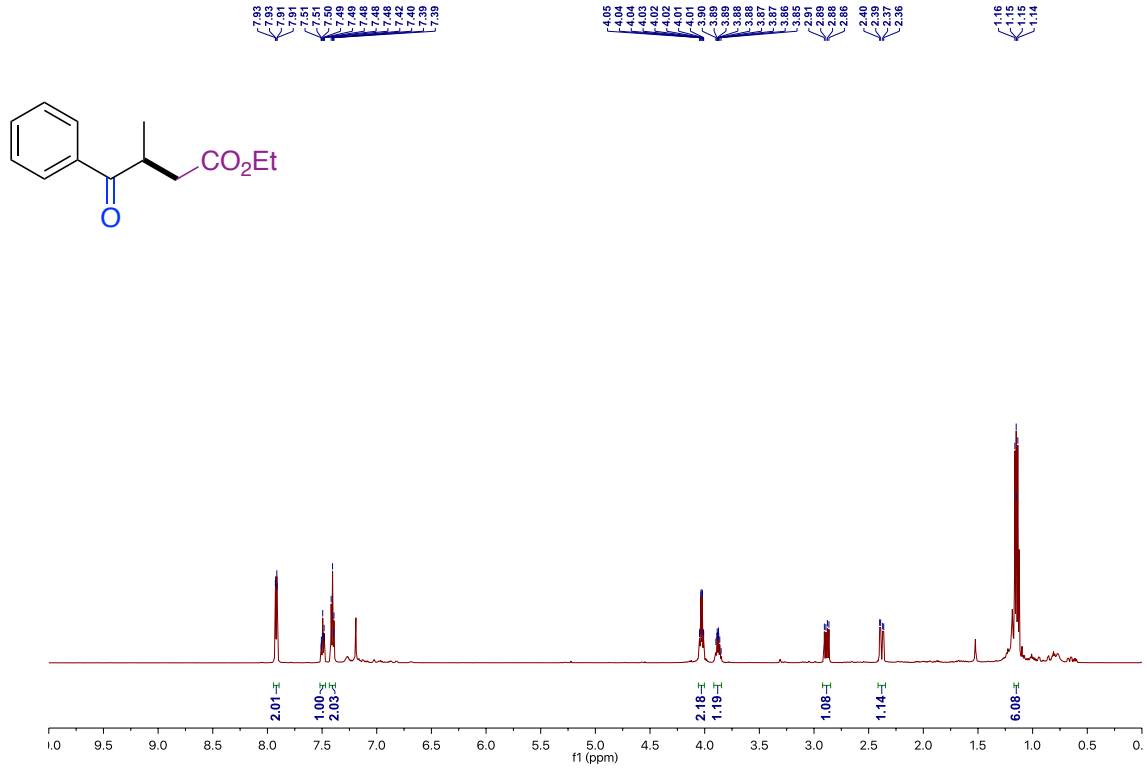


^{13}C NMR (151 MHz, Chloroform-*d*)

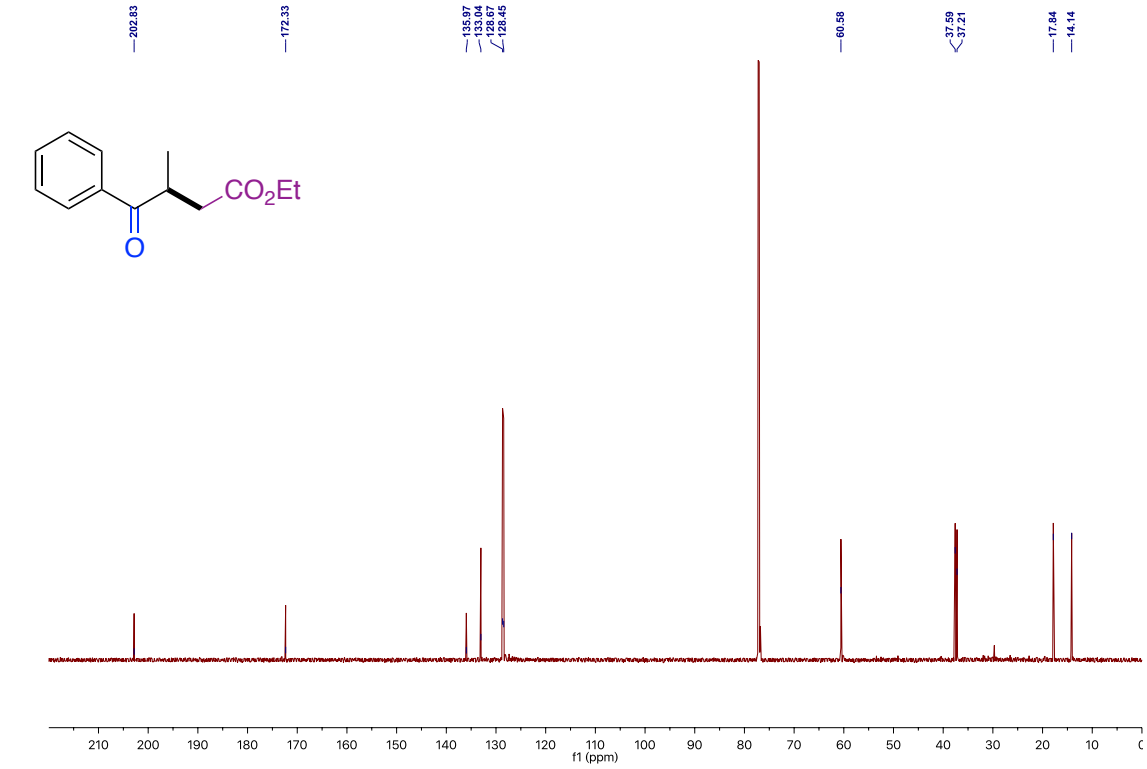


Ethyl 3-methyl-4-oxo-4-phenylbutanoate (8q)

^{1}H NMR (600 MHz, Chloroform-*d*)

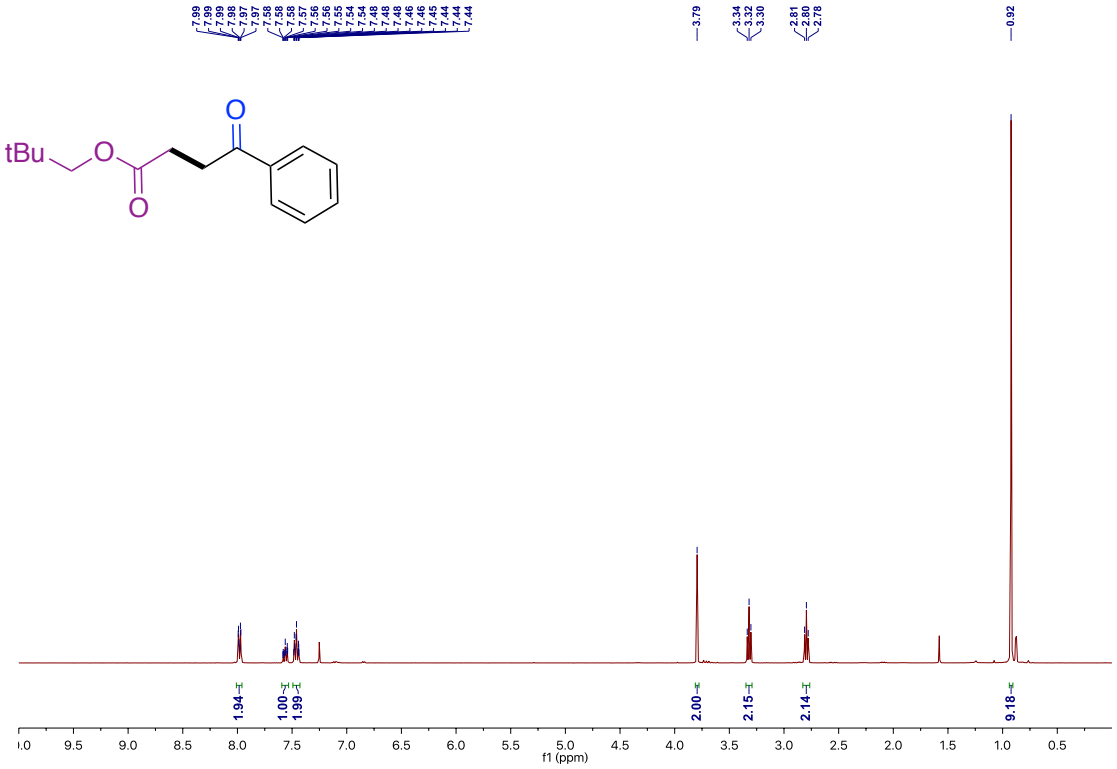


^{13}C NMR (151 MHz, Chloroform-*d*)

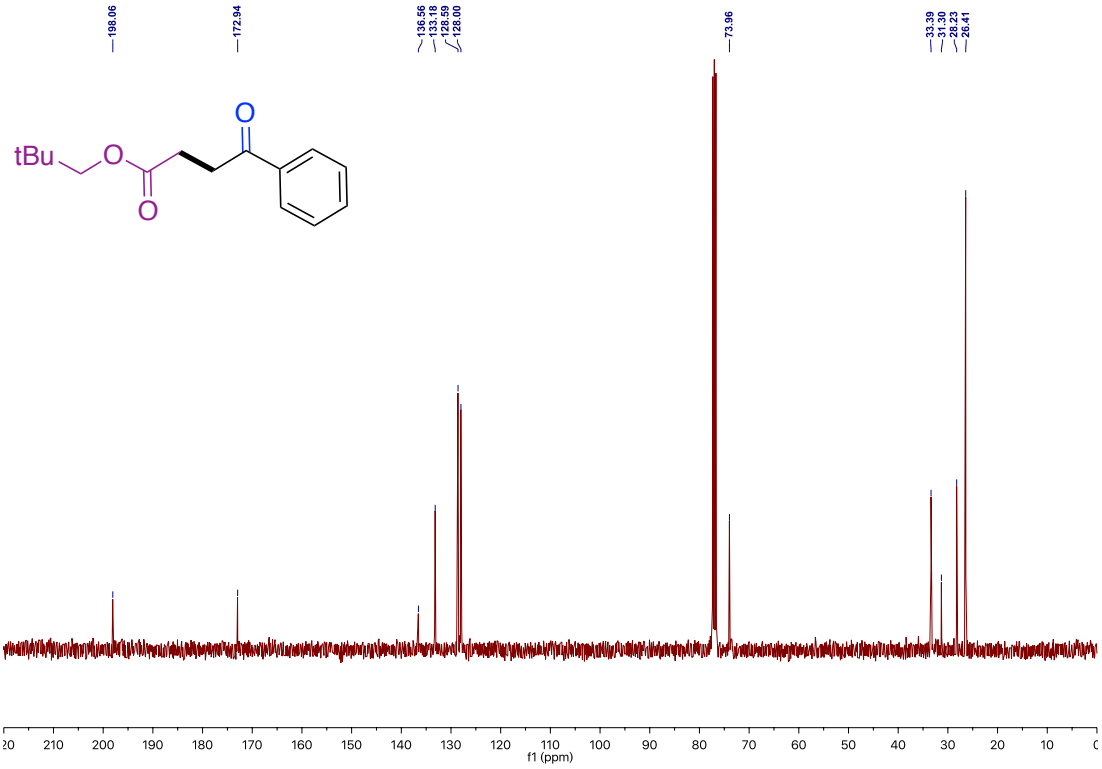


Neopentyl 4-oxo-4-phenylbutanoate (12a)

^{1}H NMR (400 MHz, Chloroform-*d*)

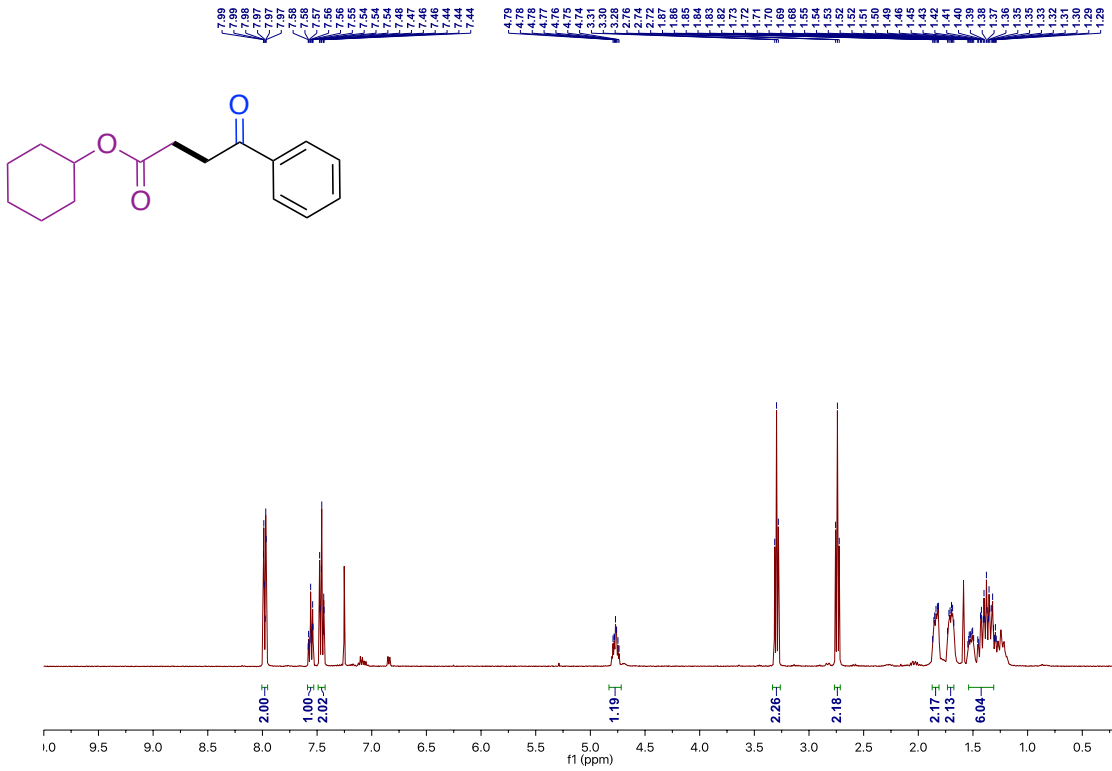


^{13}C NMR (101 MHz, Chloroform-*d*)

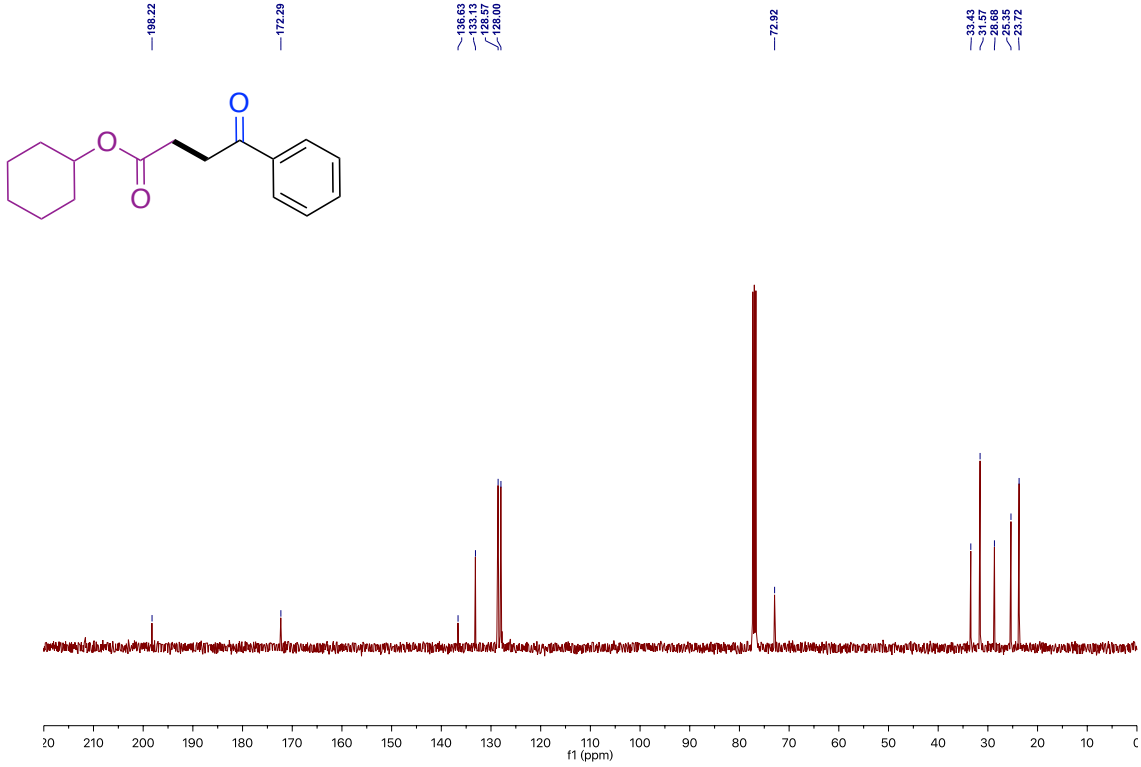


Cyclohexyl 4-oxo-4-phenylbutanoate (12b)

^{1}H NMR (400 MHz, Chloroform-*d*)

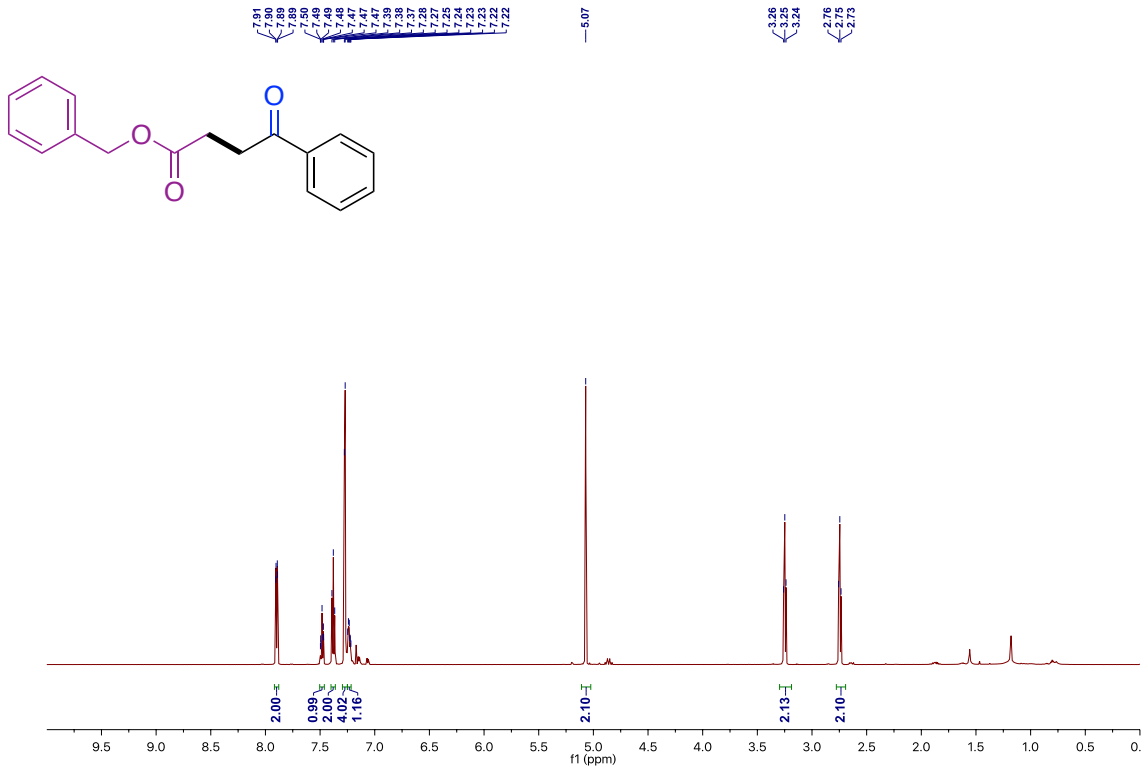


^{13}C NMR (101 MHz, Chloroform-*d*)

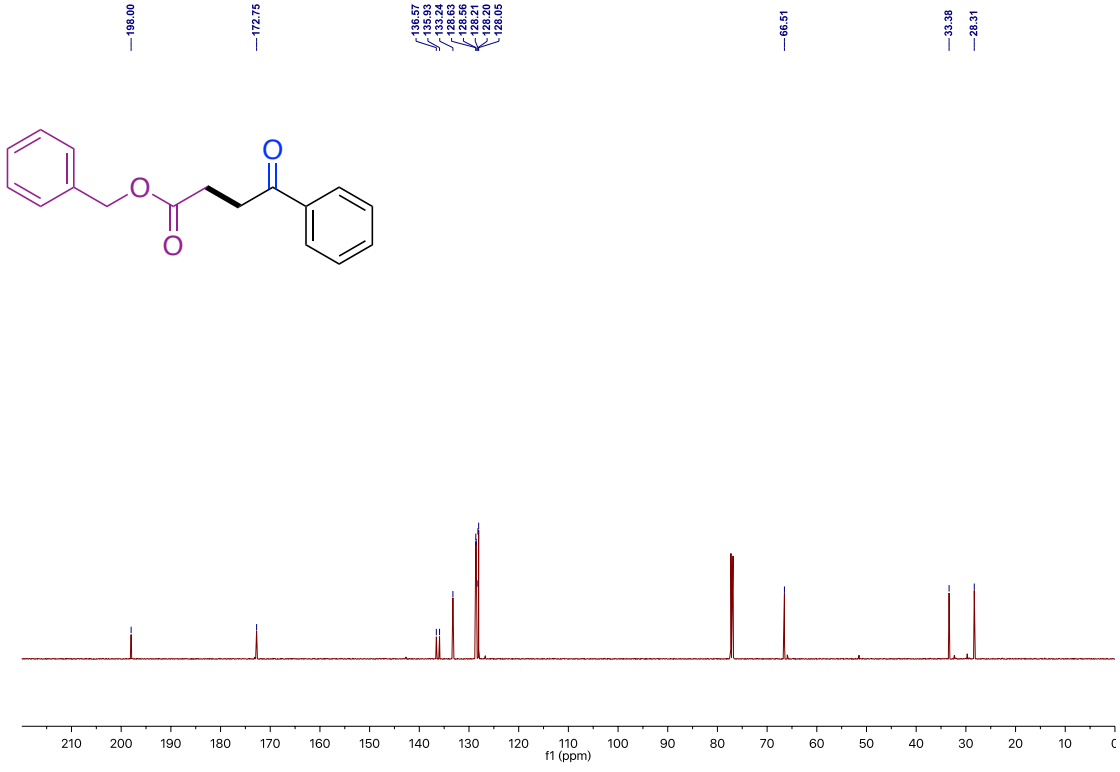


Benzyl 4-oxo-4-phenylbutanoate (12c)

^{1}H NMR (600 MHz, Chloroform-*d*)

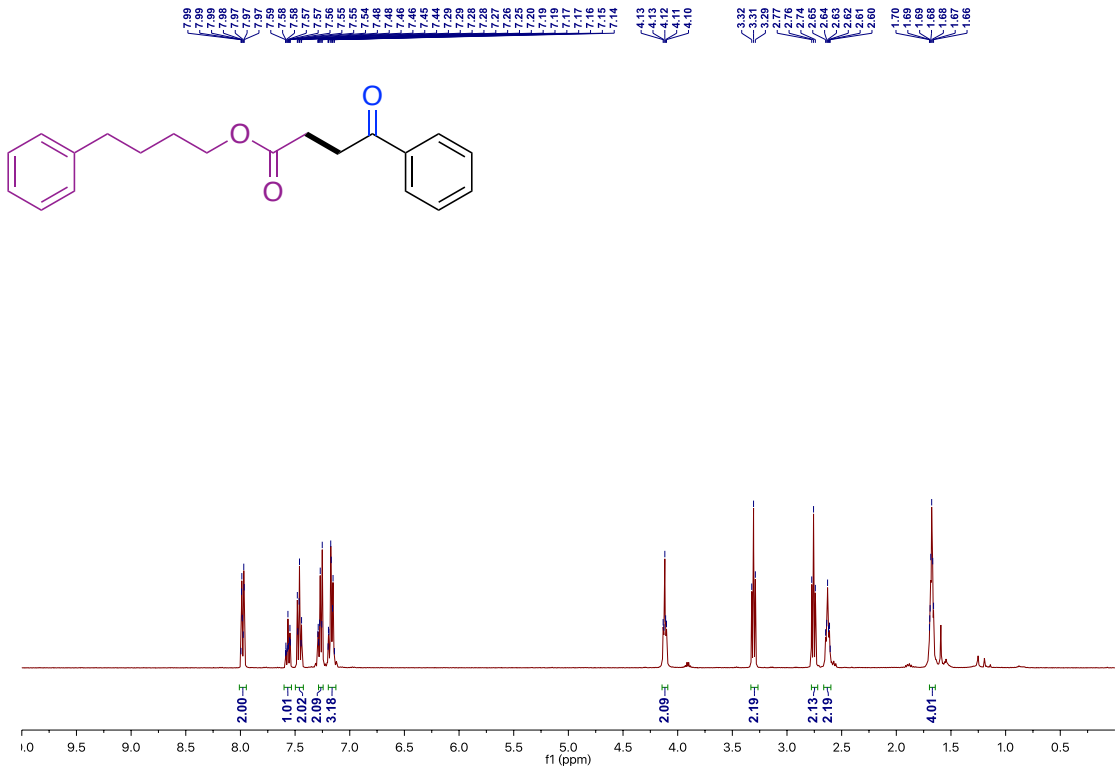


^{13}C NMR (151 MHz, Chloroform-*d*)

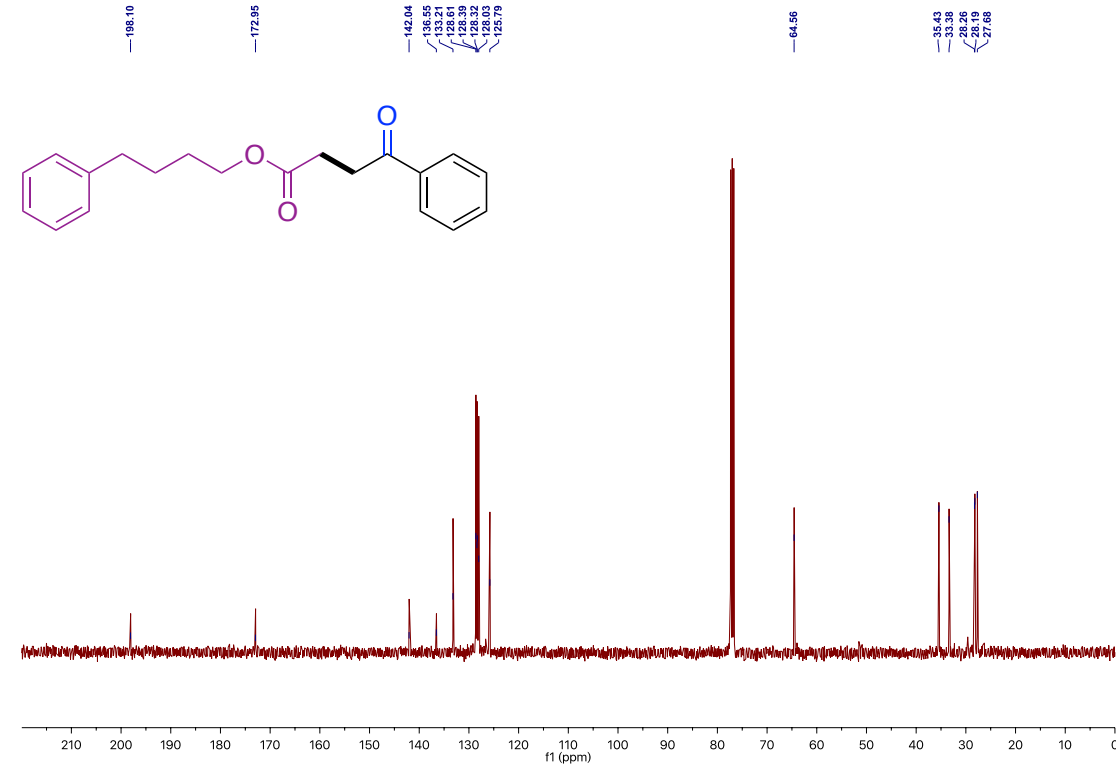


4-Phenylbutyl 4-oxo-4-phenylbutanoate (12d)

^{1}H NMR (400 MHz, Chloroform-*d*)

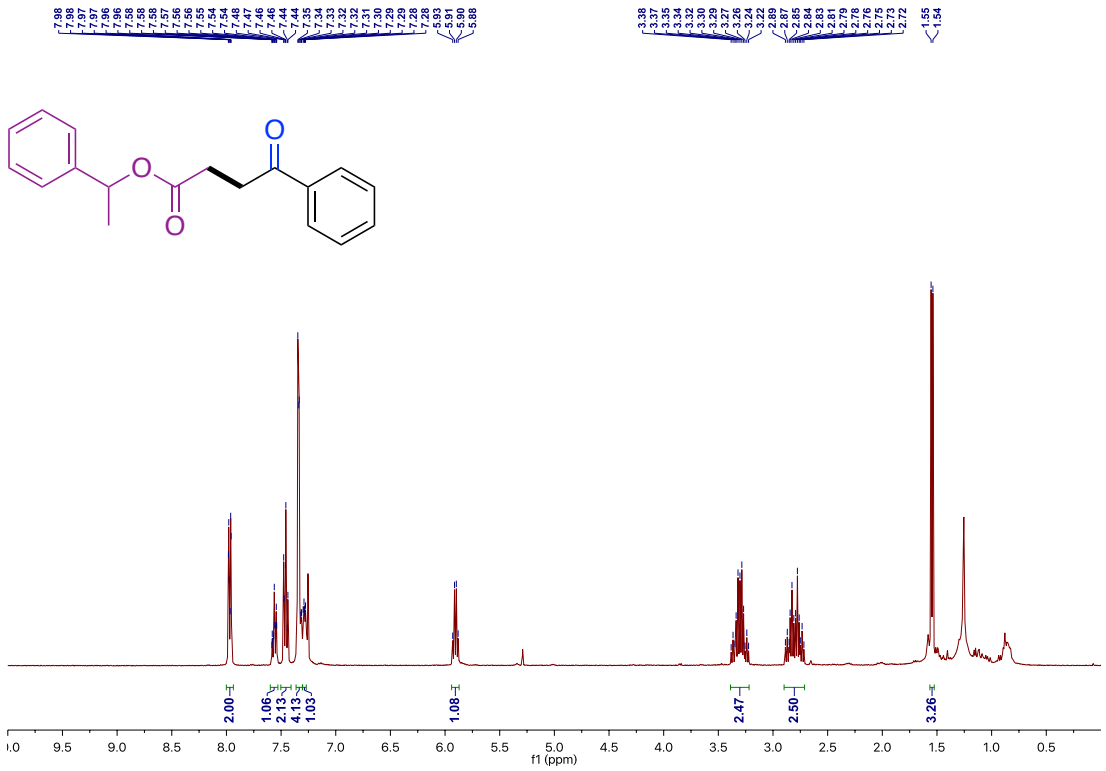


^{13}C NMR (101 MHz, Chloroform-*d*)

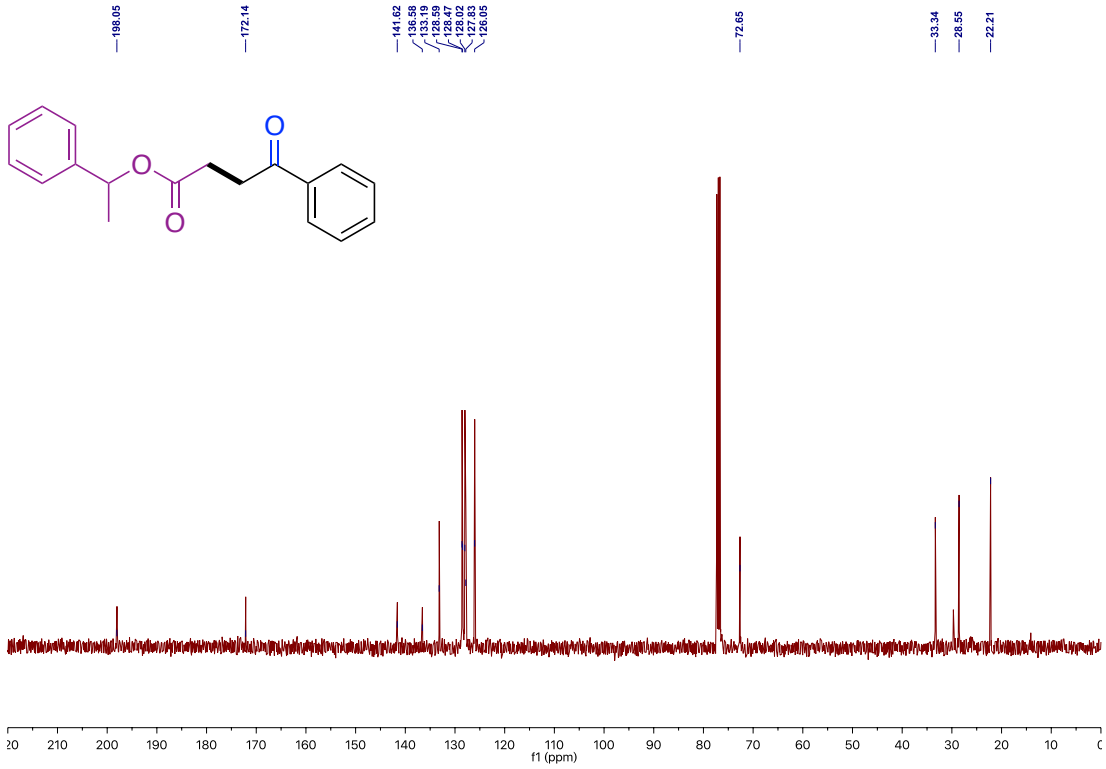


1-Phenylethyl 4-oxo-4-phenylbutanoate (12e)

^{1}H NMR (400 MHz, Chloroform-*d*)

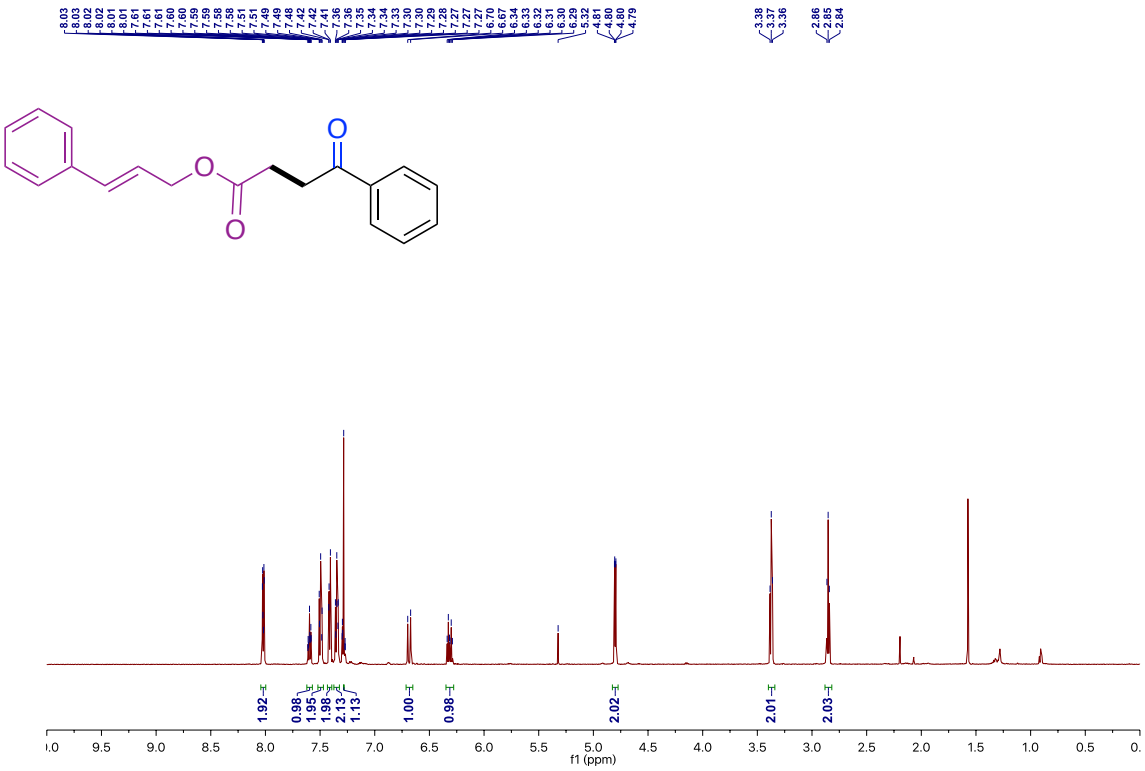


^{13}C NMR (101 MHz, Chloroform-*d*)

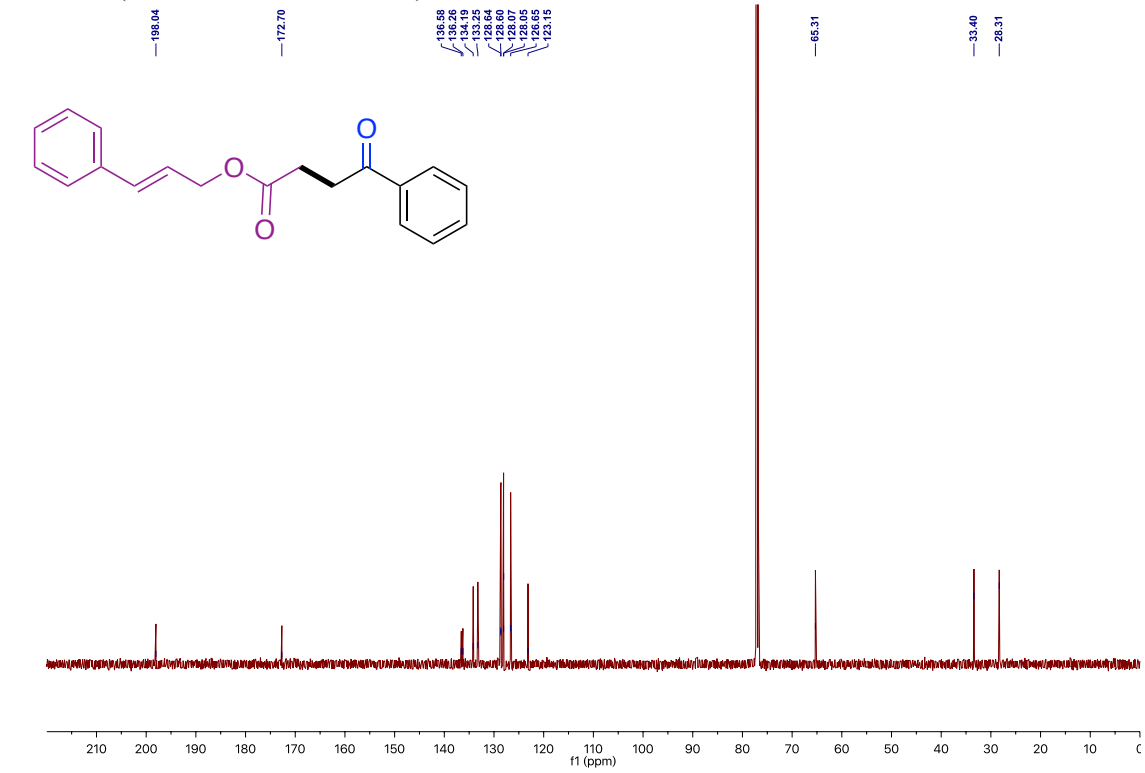


Cinnamyl 4-oxo-4-phenylbutanoate (12f)

^{1}H NMR (600 MHz, Chloroform-*d*)

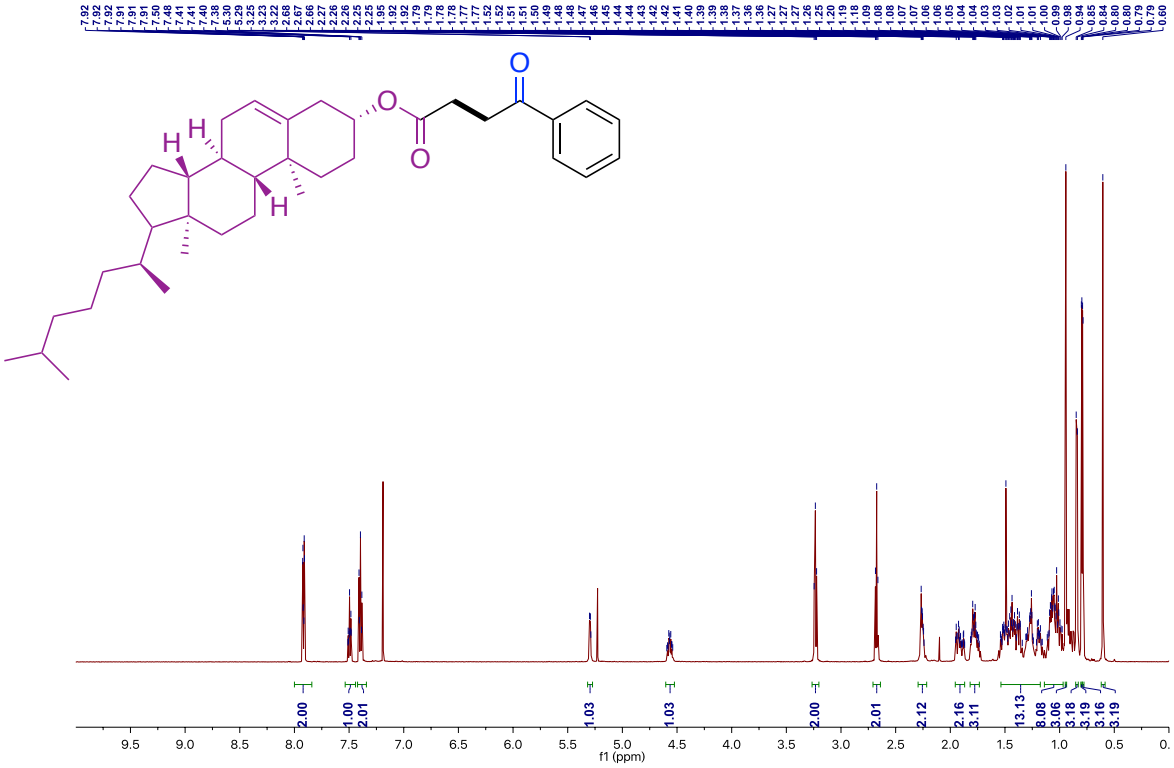


^{13}C NMR (151 MHz, Chloroform-*d*)

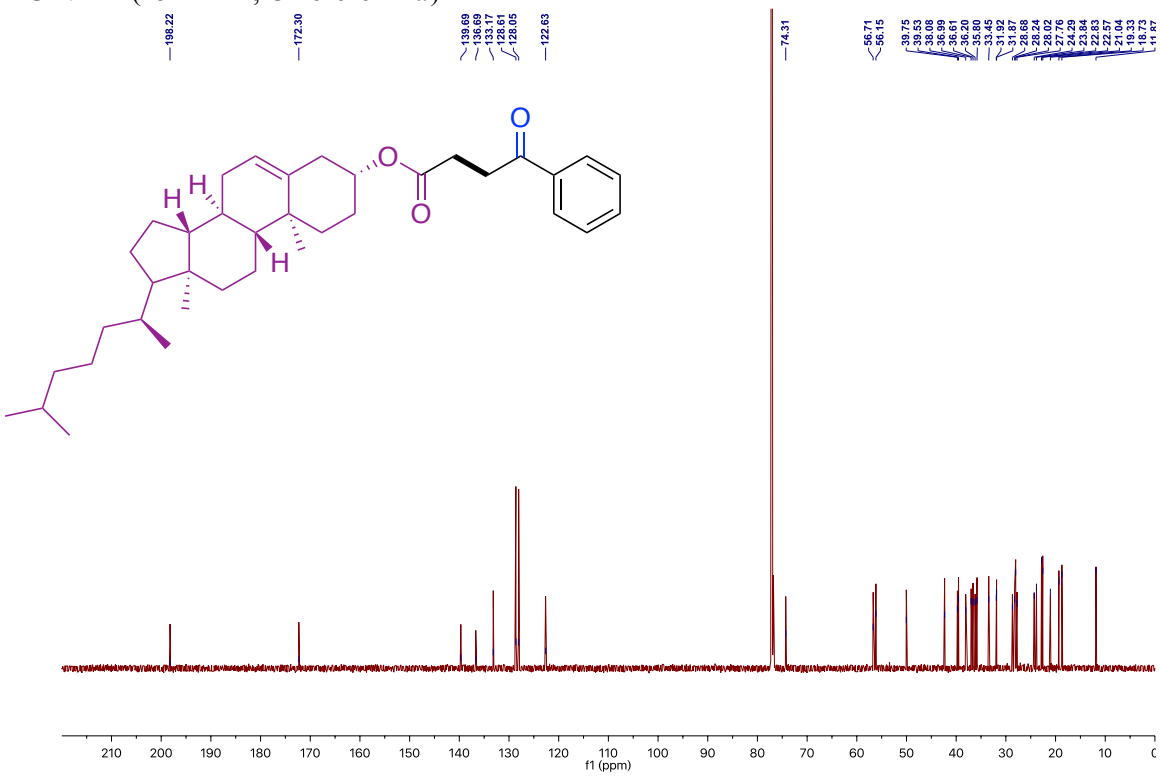


(3*R*,8*R*,9*R*,10*S*,13*S*,14*R*)-10,13-Dimethyl-17-((*S*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl 4-oxo-4-phenylbutanoate (12g)

^{1}H NMR (600 MHz, Chloroform-*d*)

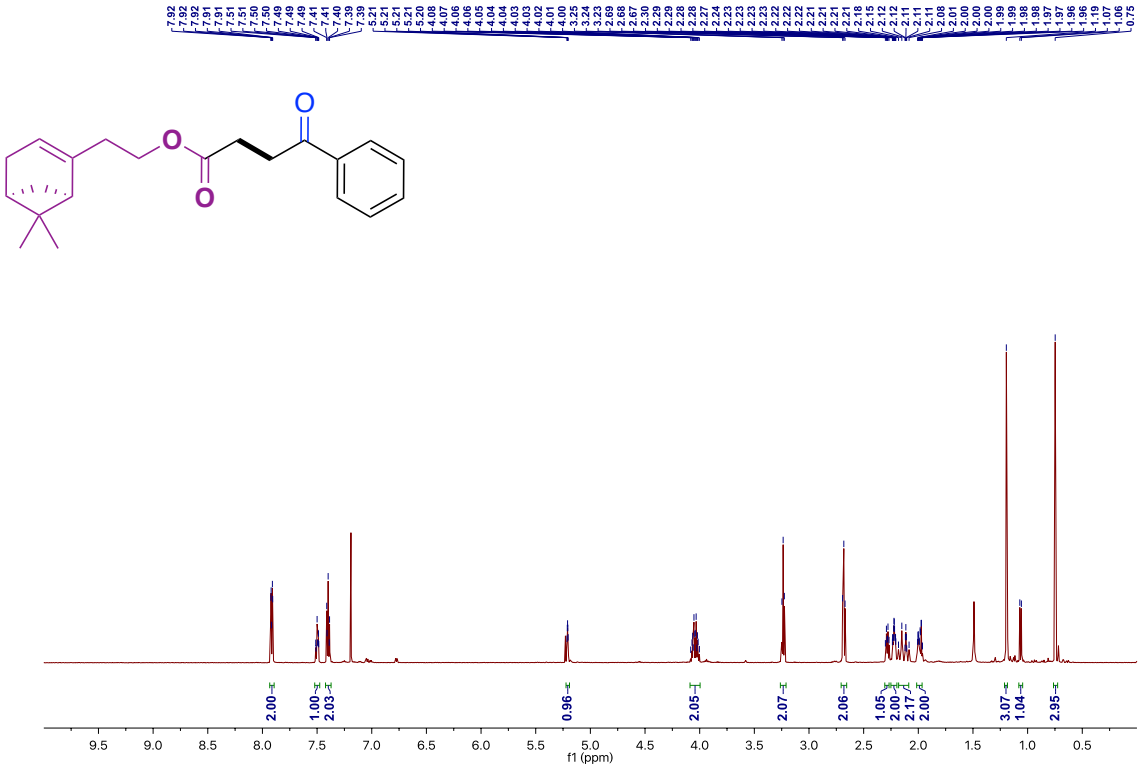


^{13}C NMR (151 MHz, Chloroform-*d*)

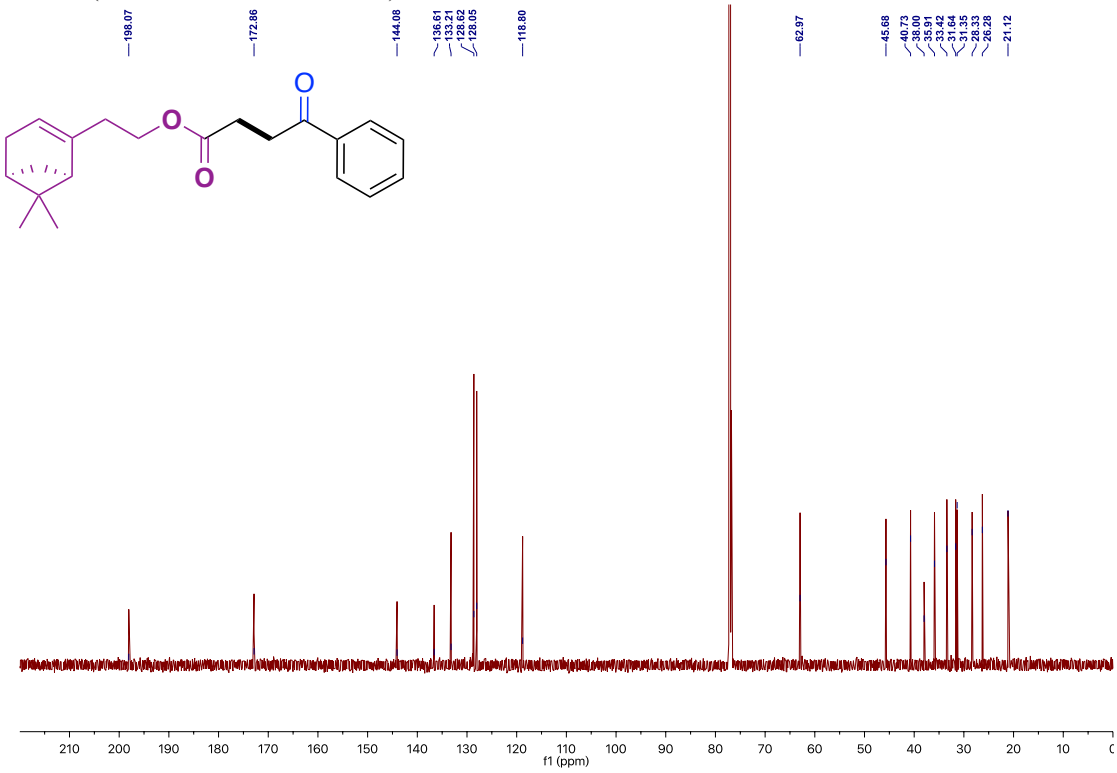


2-((1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethyl 4-oxo-4-phenylbutanoate (12h)

^{1}H NMR (600 MHz, Chloroform-*d*)

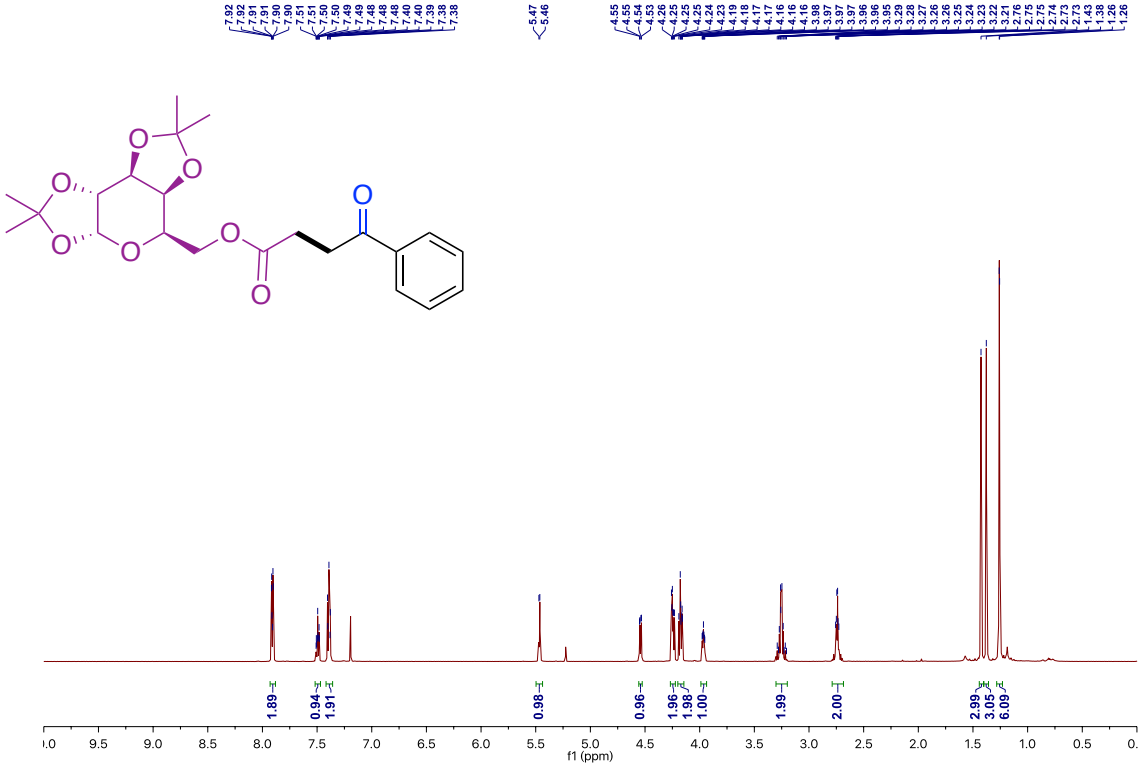


^{13}C NMR (151 MHz, Chloroform-*d*)

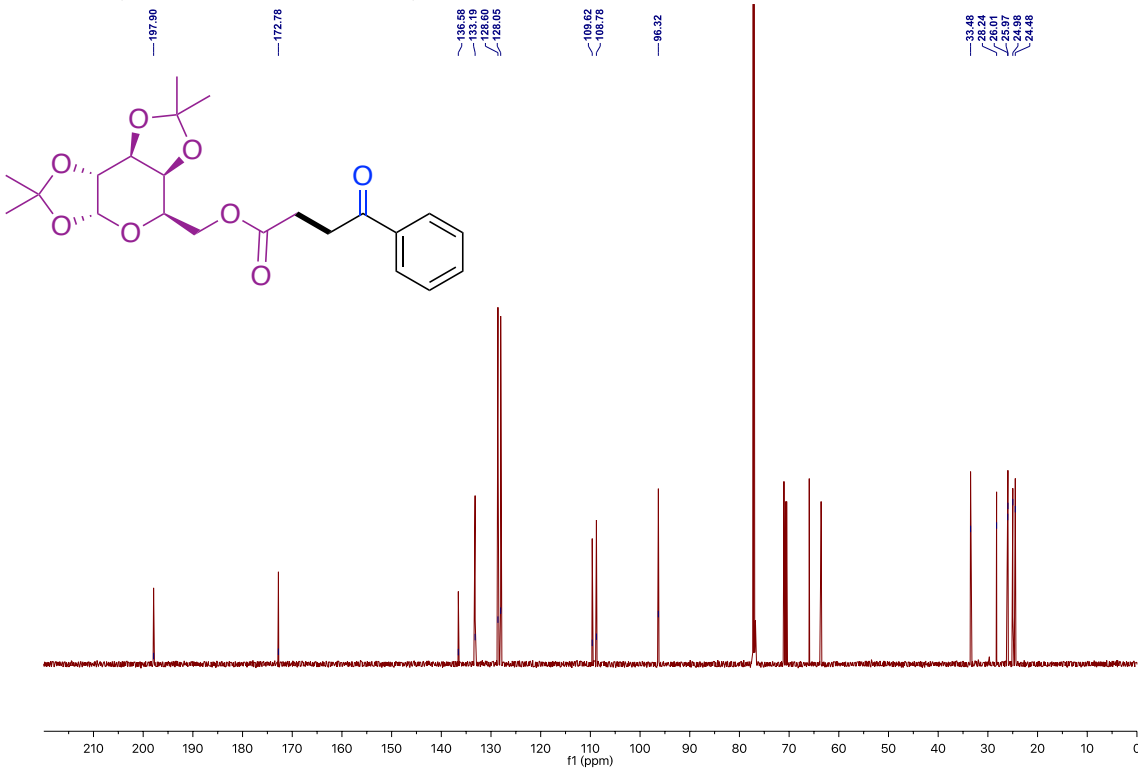


((3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-Tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-5-yl)methyl 4-oxo-4-phenylbutanoate (12i)

^{1}H NMR (600 MHz, Chloroform-*d*)

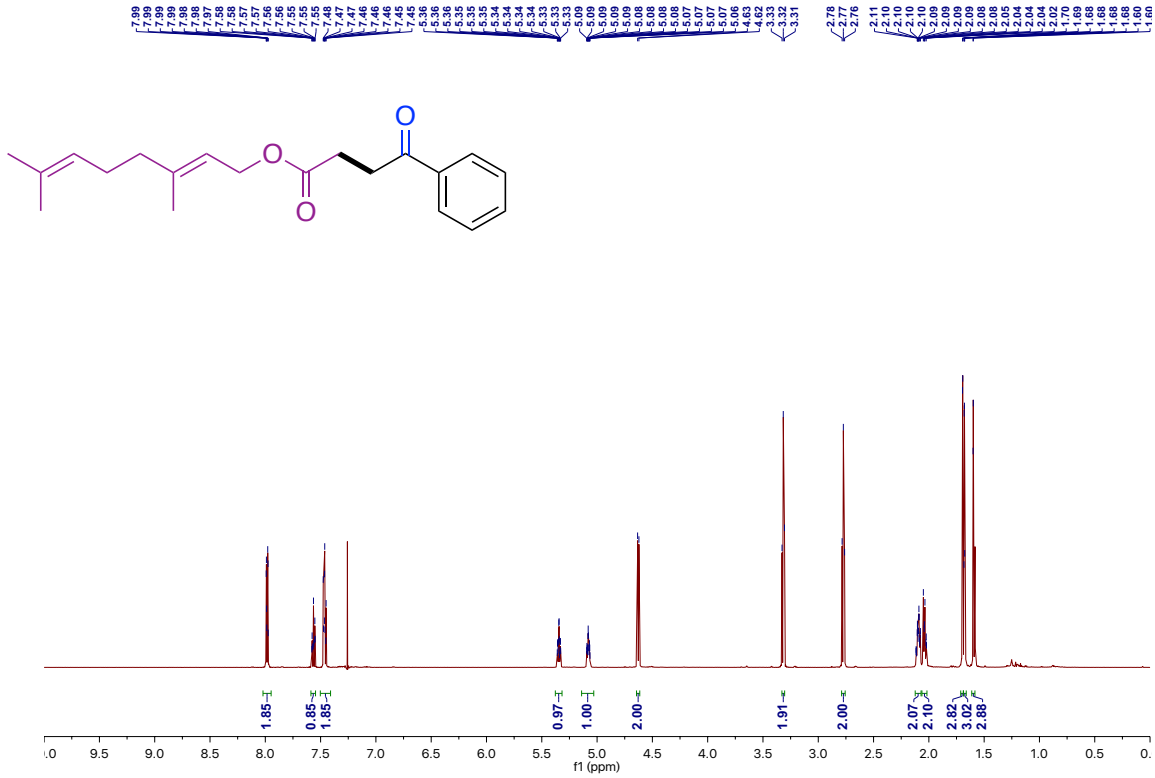


^{13}C NMR (151 MHz, Chloroform-*d*)

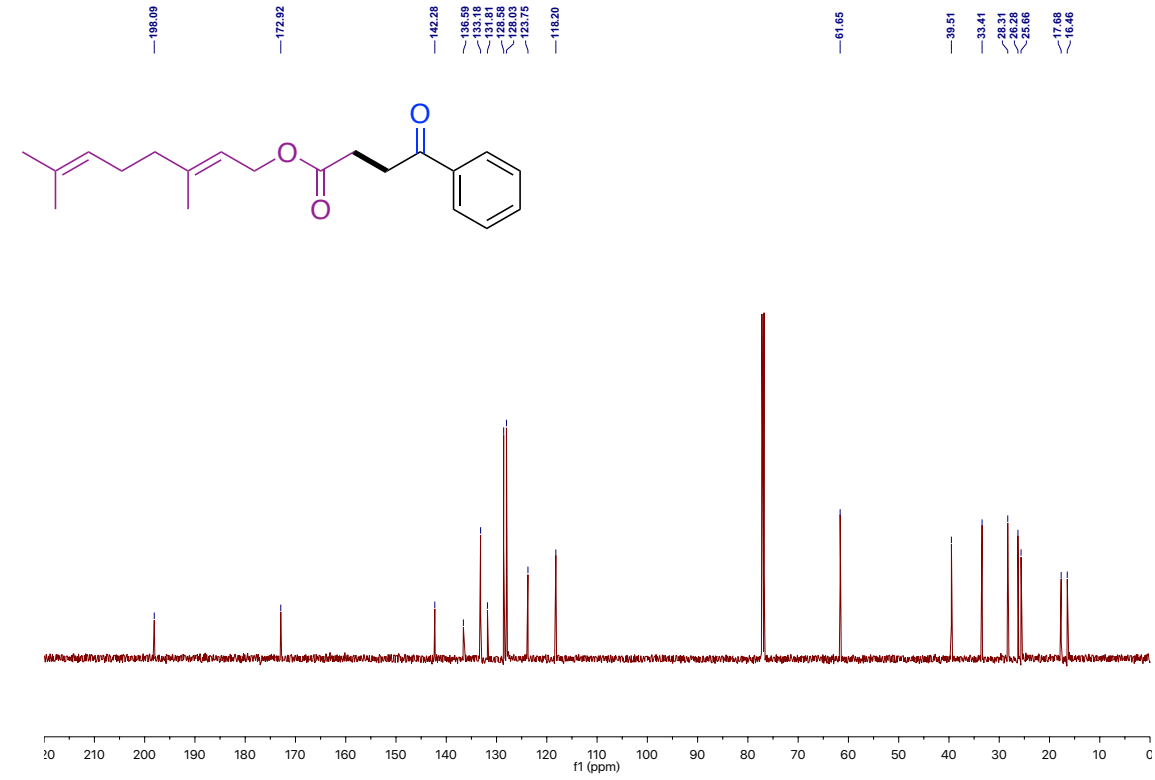


(*E*)-3,7-Dimethylocta-2,6-dien-1-yl 4-oxo-4-phenylbutanoate (12j)

^{1}H NMR (400 MHz, Chloroform-*d*)

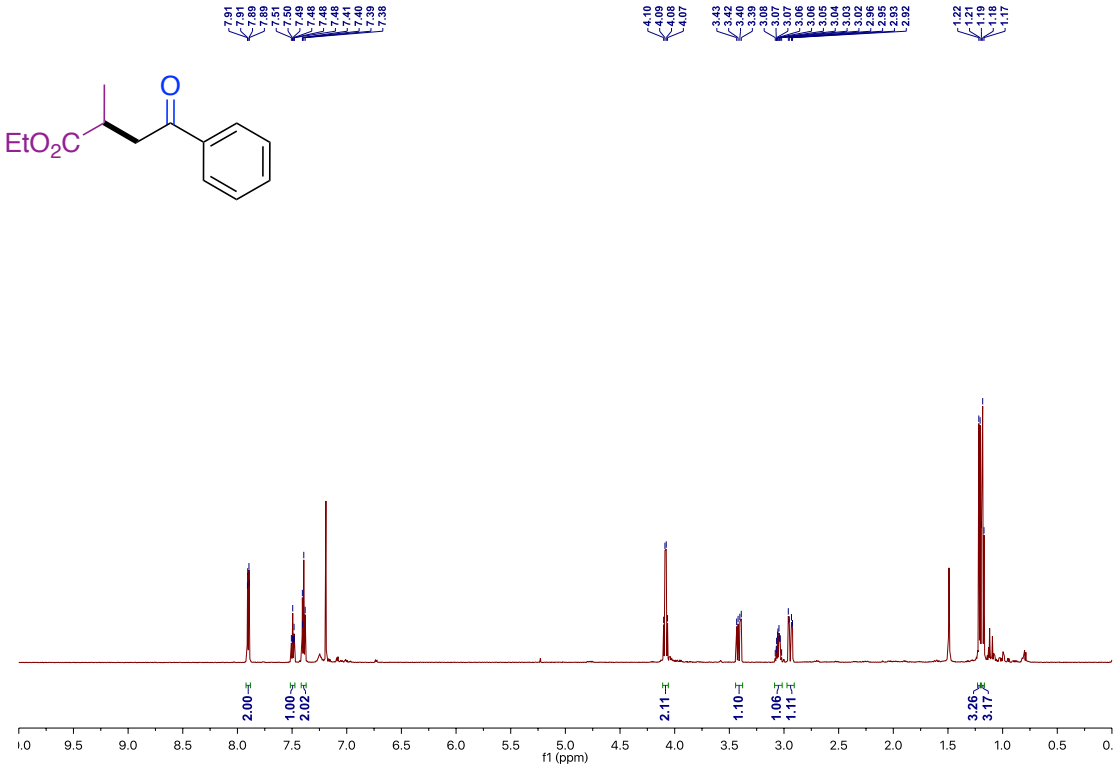


^{13}C NMR (101 MHz, Chloroform-*d*)

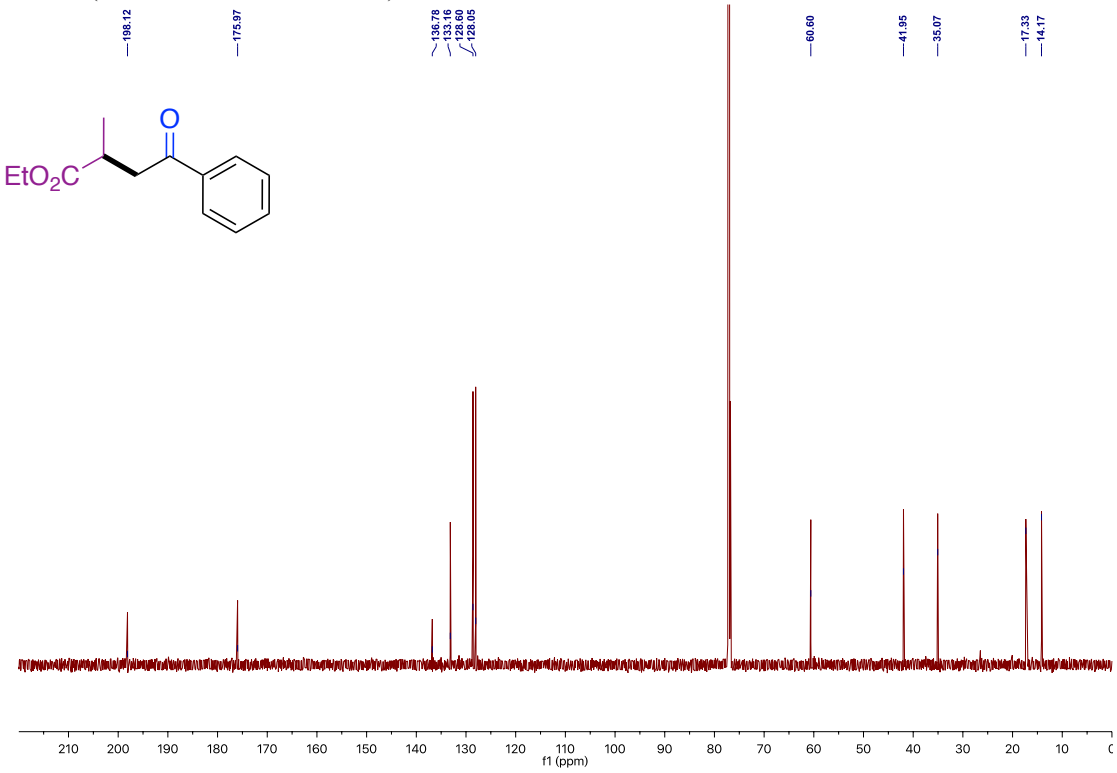


Ethyl -2-methyl-4-oxo-4-phenylbutanoate (12k)

^{1}H NMR (600 MHz, Chloroform-*d*)

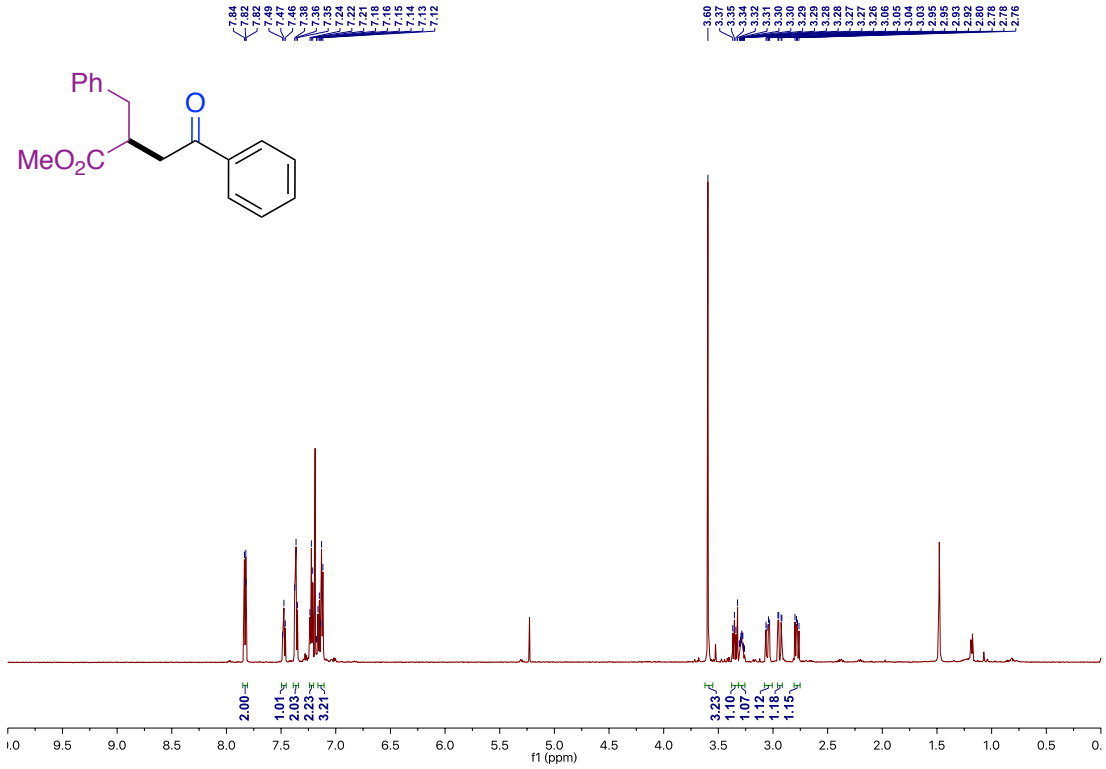


^{13}C NMR (151 MHz, Chloroform-*d*)

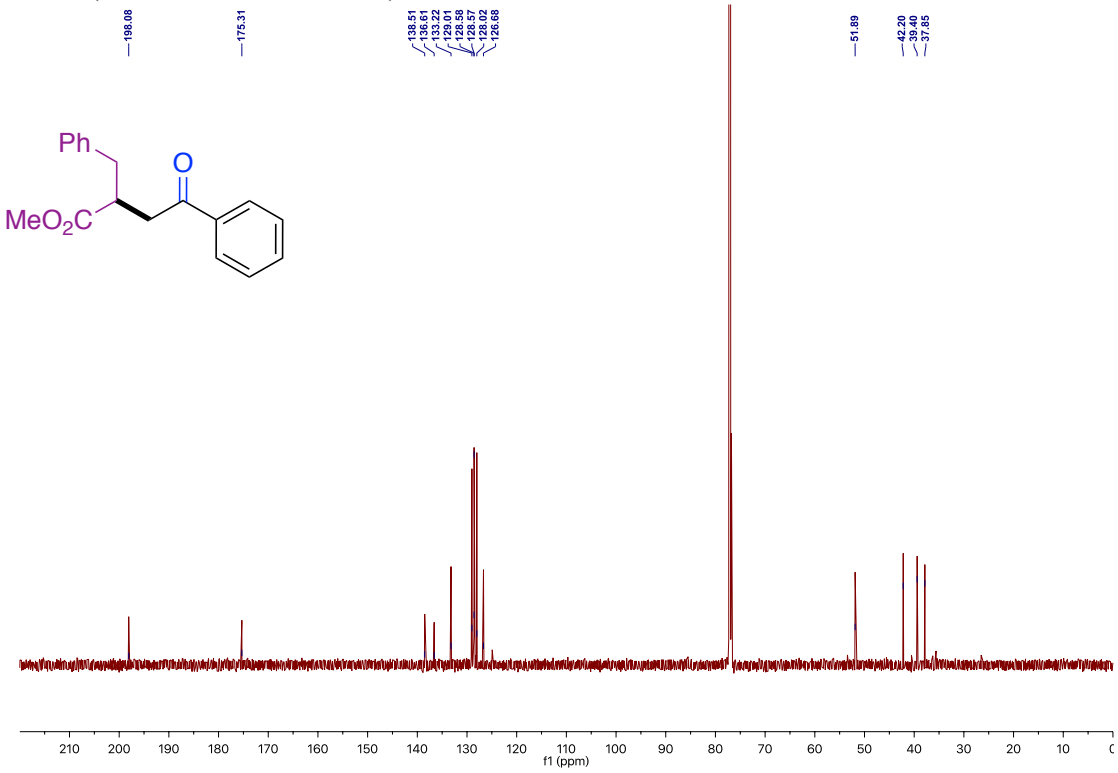


Methyl -2-benzyl-4-oxo-4-phenylbutanoate (12l)

^{1}H NMR (600 MHz, Chloroform-*d*)

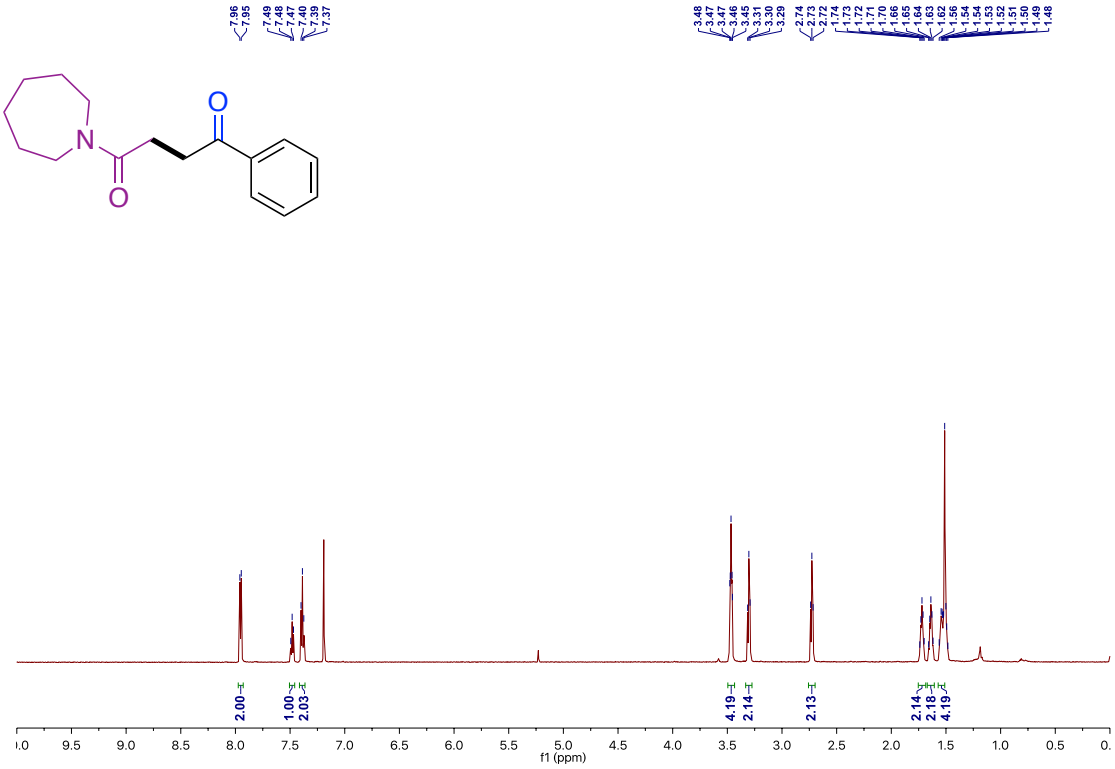


^{13}C NMR (151 MHz, Chloroform-*d*)

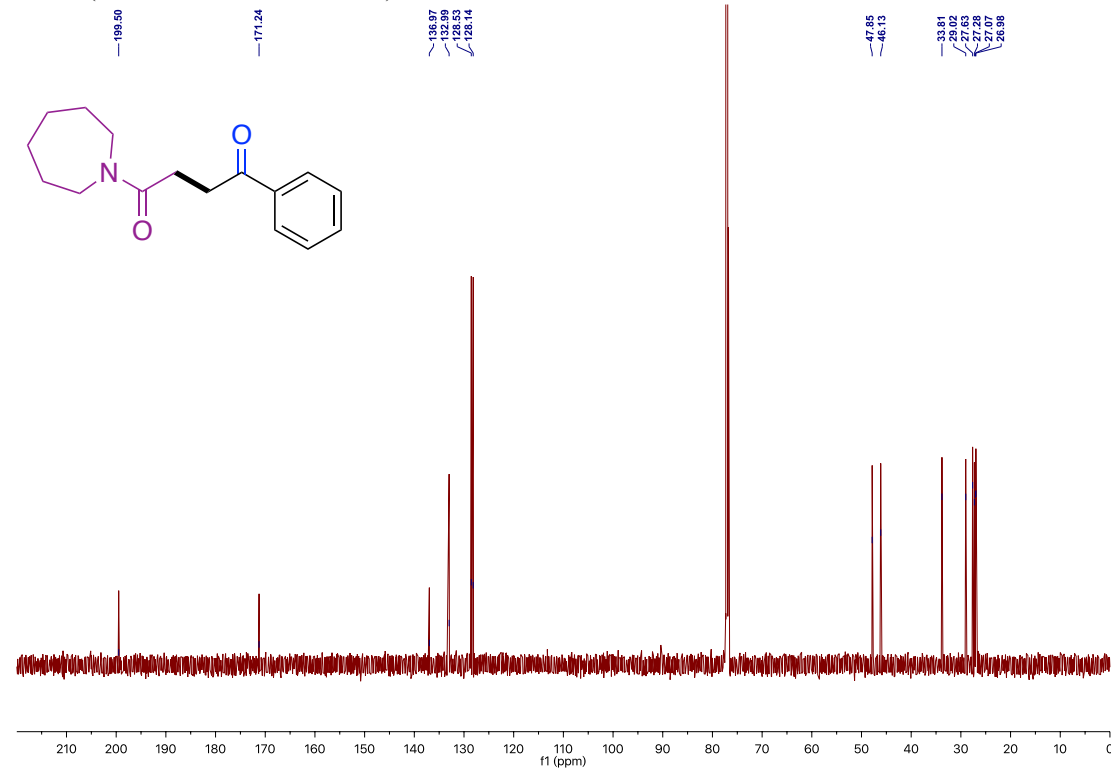


1-(Azepan-1-yl)-4-phenylbutane-1,4-dione (12m)

^{1}H NMR (600 MHz, Chloroform-*d*)

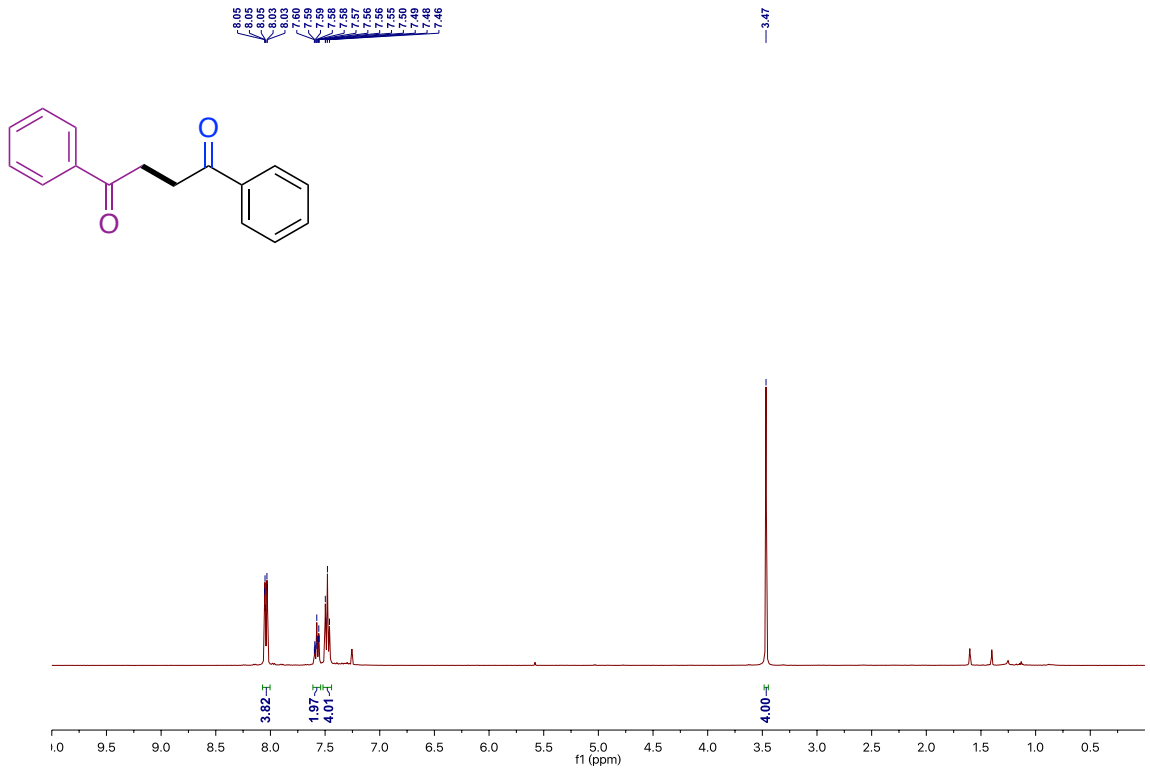


^{13}C NMR (151 MHz, Chloroform-*d*)

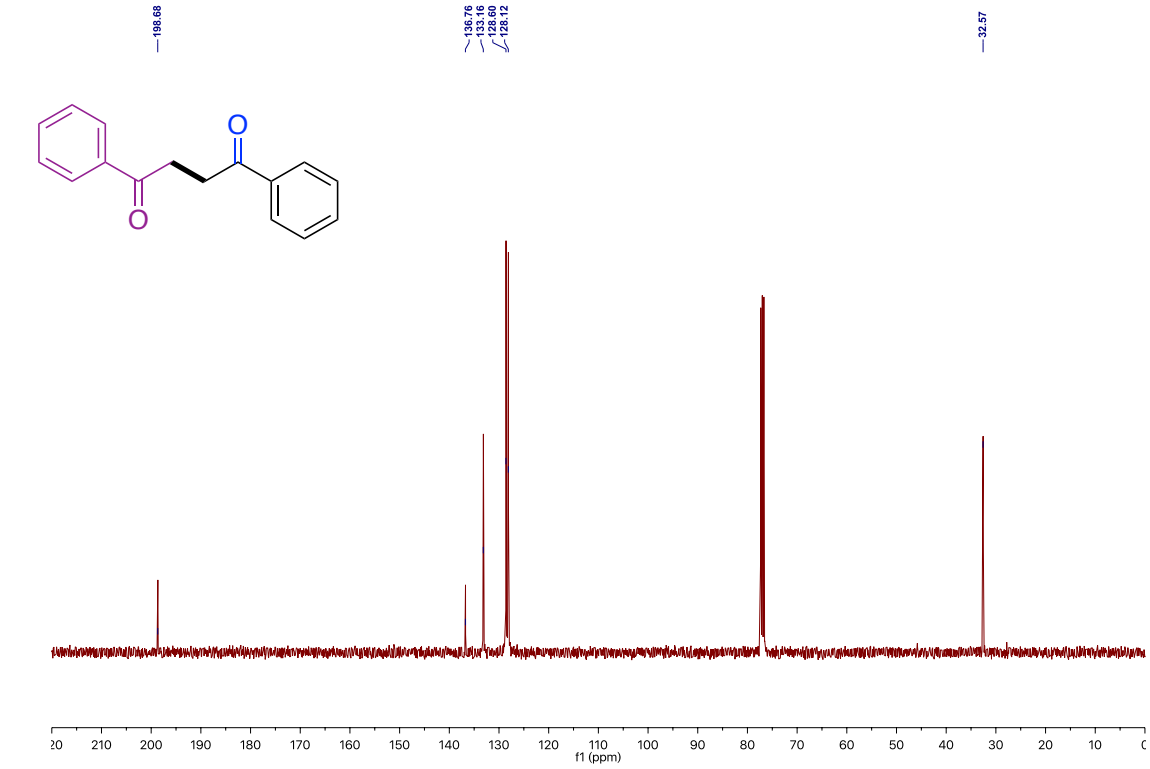


1,4-Diphenylbutane-1,4-dione (12n)

^{1}H NMR (400 MHz, Chloroform-*d*)

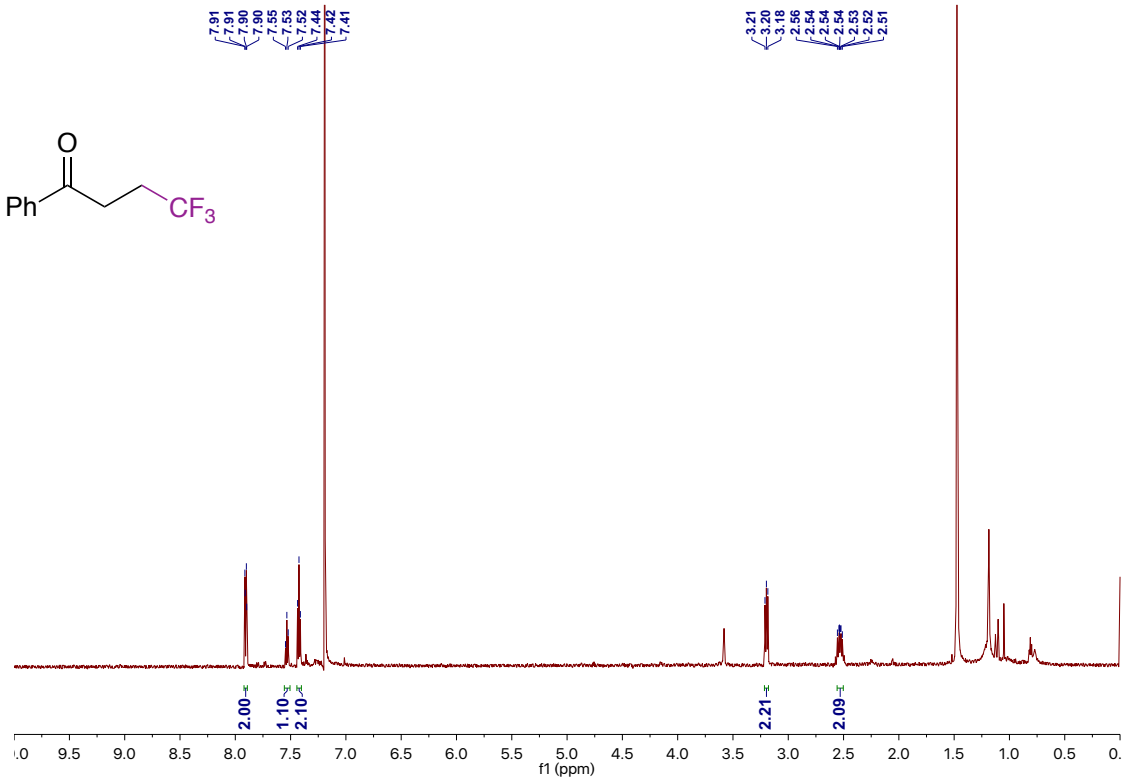


^{13}C NMR (101 MHz, Chloroform-*d*)

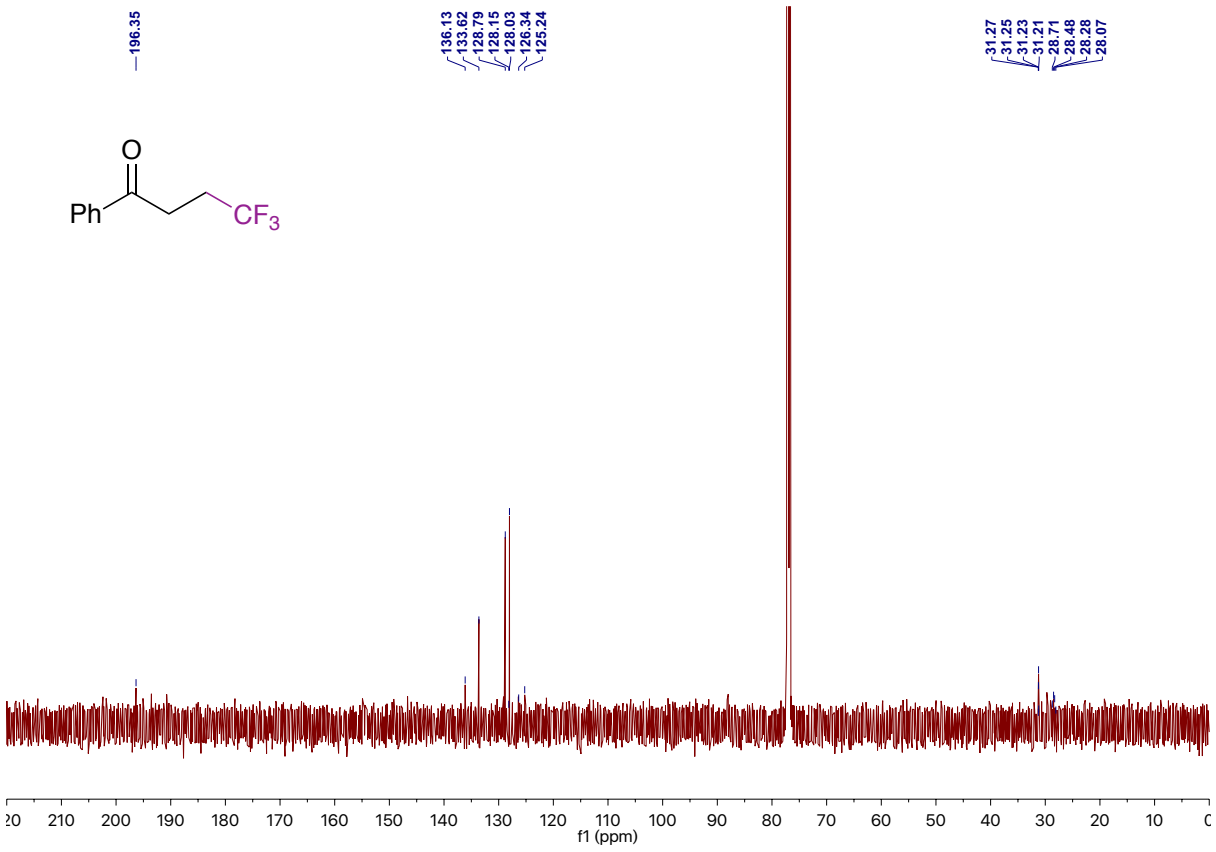


4,4,4-Trifluoro-1-phenyl-1-butanone (12o)

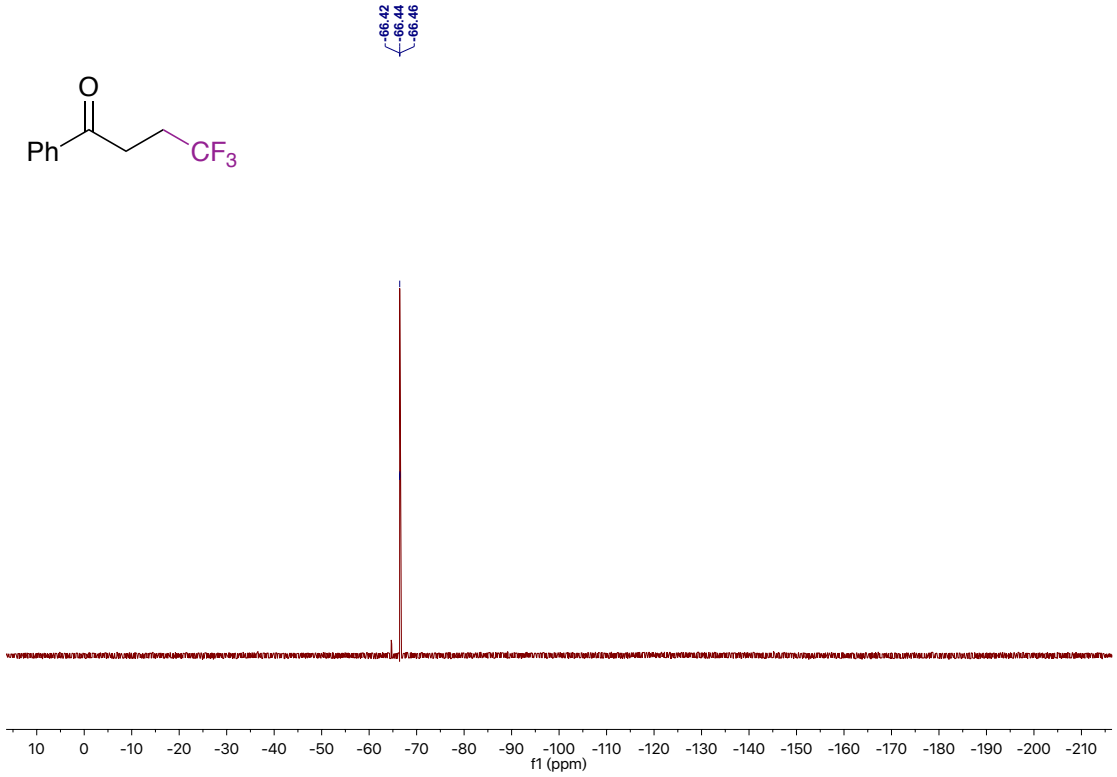
^{1}H NMR (600 MHz, Chloroform-*d*)



^{13}C NMR (151 MHz, Chloroform-*d*)



^{19}F NMR (565 MHz, Chloroform-*d*)



References

(1) T. Toma, J. Shimokawa and T. Fukuyama, *Org. Lett.*, 2007, **9**, 3195–3197.

(2) S. Hyde, J. Veliks, B. Lie´gault, D. Grassi, M. Taillefer and V. Gouverneur, *Angew. Chem., Int. Ed.*, 2016, **55**, 3785–3789.

(3) Y.-L. Su, G.-X. Liu, J.-W. Liu, L. Tram, H. Qiu and M. P. Doyle, *J. Am. Chem. Soc.*, 2020, **142**, 13846–13855.

(4) M. A. Bryden and E. ZysmanColman, *Chem. Soc. Rev.*, 2021, **50**, 7587–7680.

(5) Y. Chen, L. Li, Y. Ma and Z. Li, *J. Org. Chem.*, 2019, **84**, 5328–5338.