HFIP Promoted Carbo-lactonisation as a New Route to Functionalised Lactones

Supporting information

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1.0 General experimental

Reaction Setup: Microwave vials and vial caps (containing a resealing Silicone/PTFE septum) were purchased from Kinesis (Cole-Palmer) and were used without flame-drying. Unless otherwise stated, all other reactions were performed in flame-dried glassware equipped with a stir bar using standard Schlenk techniques under an atmosphere of N_2. Room temperature (rt) refers to 20-25 °C. Temperatures of 0 °C were obtained using an ice/water bath. Temperatures of –17 °C were obtained using a salt/ice bath. Temperatures of –78 °C were obtained using a dry ice/acetone bath. Reflux conditions were obtained using an oil bath equipped with a contact thermometer. Other temperatures were obtained using a Julabo FT902 immersion cooler.

Reagents and solvents: Unless detailed below or otherwise stated, all reagents and solvents were purchased and used as supplied from Sigma-Aldrich (now Merck KGaA), Thermo Fisher Scientific (including Alfa Aesar and Acros Organics), Fluorochem, Honeywell, Tokyo Chemical Industry, Apollo Scientific, Manchester Organics (part of Navin Fluorine Int. Ltd.) and Strem Chemicals. Anhydrous DMSO and Et_3N were purchased from Sigma-Aldrich in Sure/SealTM bottles. Anhydrous Et_2O, CH_2Cl_2, MeOH, THF and toluene were obtained from MBRAUN SPS-5 solvent purification system by passage through double filtration columns under N_2. 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP) was purchased from Fluorochem. Ti(O*i*-Pr)4 (≥97%) and TFA (synthesis grade) were purchased from Sigma-Aldrich. Alcohols were purchased from commercial suppliers or prepared using standard literature procedures unless otherwise stated.

Chromatography: Thin layer chromatography (TLC) was performed on pre-coated aluminium (200 μm) Merck Kieselgel 60 F254 plates, visualised using UV irradiation (λ = 254 nm) and/or staining with potassium permanganate ($KMnO_4$), vanillin, or phosphomolybdic acid (PMA) solutions. Purification by flash column chromatography was performed with Merck Kieselgel 60 (40– 63 μm) or (15–40 μm) silica gel using head pressure by means of a nitrogen line. All solvents used for chromatography were HPLC grade or equivalent and supplied by Honeywell, Sigma-Aldrich or Thermo Fisher Scientific.

Nomenclature: Systematic names were generated by the software ChemDraw according to the guidelines specified by the International Union of Pure and Applied Chemistry (IUPAC). Conventional names are also provided for reference where applicable. All compounds reported are racemates, and stereodescriptors drawn in the structures are relative. For meso and other symmetric achiral cyclic compounds, the prefixes cis and trans are used for clarity where appropriate.

Compound Numbering: Where applicable, atom numbering shown does not follow IUPAC numbering and is therefore different to the compound name.

Melting points: Melting points (M.p.) were obtained using a Eisco Melting Point Apparatus 230V, 50-60Hz and are uncorrected. Melting points were measured on a mixture when compounds could not be separated by column chromatography.

Infrared spectroscopy: Fourier-transform infrared (FT-IR) spectra were recorded from evaporated films on a Bruker Tensor 27 spectrometer equipped with a Pike Miracle Attenuated Total Reflectance (ATR) sampling accessory. Absorption maxima are quoted in wavenumbers (vmax) with units of cm–1 and for the range of 3600–600 cm–1 . IR spectra were measured on a mixture when compounds could not be separated by column chromatography.

NMR spectroscopy: ^{1}H and ^{13}C NMR experiments were carried out using Bruker NMR spectrometers (400, 500 or 600 MHz) in the deuterated solvent stated, using the residual nondeuterated solvent signal as an internal reference. Chemical shifts (δ) are given in ppm and coupling constants (J) are quoted to the nearest 0.1 hertz (Hz) and are presented as observed. Resonances are described as s (singlet), d (doublet), t (triplet), q (quartet), br (broad singlet), dd (double of doublets), dt (doublet of triplets), dq (doublet of quartets), td (triplet of doublets), tt (triplet of triplets), tq (triplet of quartets), ddd (doublet of doublets of doublets), ddt (doublet of doublets of triplets), dddd (doublet of doublet of doublet of doublets), qd (quartet of doublets) and m (multiplet). ^{1}H and ^{13}C NMR peaks for diastereomers were assigned major or minor. Assignments were made with the assistance of gCOSY, gHSQC, gHMBC or NOESY NMR spectra. For unseparable mixtures of diastereomers (>80:20 dr) both isomers are reported separately. When ^{1}H and ^{13}C NMR data for the major diastereoisomer is reported, any signals that overlap with the minor isomer have been integrated without the contribution from the minor isomer being included. In such a case, signals of the minor isomer are not reported. For equimolar mixtures of diastereomers (dr ≤ 70:30) ^{1}H NMR data for isomers is reported together. In some cases the relatively non-polar compounds produced were inseparable from grease contaminants (showing peaks between 0-1.5 ppm in the 1H NMR spectrum) despite multiple attempts at purification by chromatography.

Mass spectrometry (MS): High resolution mass spectrometry (HRMS) under ESI conditions were recorded on a Thermo Exactive Orbitrap mass spectrometer equipped with a Waters Equity LC system, a Bruker MicroToF mass spectrometer equipped with an Agilent 1100 HPLC pump and autosampler, or on a Waters Xevo Quadrupole Time of Flight (Q-ToF) mass spectrometer. The Thermo Exactive system employs a flow rate of 0.2 mL min^{-1} using H2O:MeOH:HCOOH (10:89.9:0.1) as eluent, with a heated electrospray ionisation (HESI-II) probe and has a resolution of 50,000 FWHM. The Bruker system uses the built-in electrospray

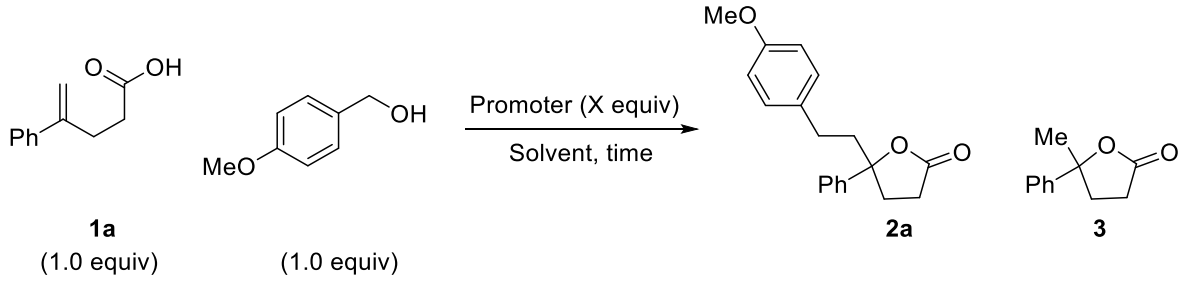
source, while the Waters system runs on a lock-mass mode with ESI performed by a secondary electrospray source, both using conditions identical to the Thermo Exactive S4 system. Instrument control and data processing were performed using the softwares Thermo Xcalibur for the Thermo Exactive system, Compass DataAnalysis 4.0 for the Bruker system, and MassLynx for the Waters system. Atmospheric pressure chemical ionisation (APCI) HRMS were recorded on the abovementioned Thermo Exactive spectrometer under identical conditions using N_2 as the reagent gas. Electron impact ionisation (EI) HRMS were performed on an Agilent 7200 Quadrupole Q-ToF mass spectrometer equipped with a direct insertion probe supplied by Scientific Instrument Manufacturer (SIM) GmbH. Instrument control and data processing were performed using the software Agilent MassHunter. All HRMS conditions were adjusted for maximum sensitivity, with an accuracy of better than 5 ppm for 24 h following external calibration on the day of analysis. Unless otherwise specified, the mass reported for HRMS is the mass-to-charge ratio containing the most abundant isotopes, with each value to 4 or 5 decimal places and within 5 ppm of the calculated mass. HRMS data was collected on a mixture when compounds could not be separated by column chromatography.

X-Ray Crystallography: Single crystal X-ray data collection and structure determination were performed by Timothy C. Jenkins in the Chemistry Research Laboratory, University of Oxford. Crystals were mounted on MiTeGen loops using perfluoropolyether oil and rapidly transferred to a goniometer head on a diffractometer fitted with an Oxford CryoSystems CryoStream open-flow nitrogen cooling device[1]. Data collections were carried out at 150 K using an (Rigaku) Oxford Diffraction Supernova A diffractometer using mirror-monochromated Cu K*α* radiation (λ = 1.54184 Å) and data were processed using CryAlisPro. The structure was solved using charge-flipping algorithm SUPERFLIP[2] and refined by full-matrix least squares using CRYSTALS[3][4]. Structures are visualised and represented using Mercury.

[1] Cosier, J. Glazer, A. M. *J. Appl. Cryst.* 1986, **19**, 105-107.
[2] Palatinus, L. Chapuis, G. *J. Appl. Cryst*. **2007**, *40,* 786-790.
[3] Parois, P. Cooper, R. I. Thompson, A. L. *Chem. Cent. J.* **2015**, *9,* 30.
[4] Cooper, R. I. Thompson, A. L. Watkin, D. J. *J. Appl. Cryst.* **2010**, *43,* 1100-1107.

2.0 Optimisation of the reaction conditions

We began our studies by determining whether terminal alkenes embedded within a carboxylic acid scaffold **1a** could be engaged in the alkylative cyclisation. Using the conditions based on heterocyclisation of 1,2-disubstitited alkenes, we obtained an initial hit of **2a** over 2 h (Table **1**, entries 1-2). Leaving the reaction overnight improved the conversion (Table **1**, entry 3); together with the desired product, a side-reaction to form lactone **3** was observed. At this point, a Lewis and Brønsted acid screen was conducted to improve the yield of the desired lactone **2a** and to minimise the extent of the side-reaction. With $AlCl_3$ Lewis acid nearly equimolar amounts of lactones **2a** and **3** were formed (Table **1**, entry 4), while the use of $Sc(OTf)_3$ resulted in predominate formation of the undesired lactone **3** (Table **1**, entry 5). The use of 30 mol% of $Zn(OAc)_2$ furnished the desired lactone **2a** in 82% yield with no side-product being observed (Table **1**, entry 7). Next, Brønsted acids were screened (Table **1**, entries 8-9). TFA was found to be an effective promoter furnishing the desired lactone **2a** in 90% yield. Interestingly, the carbo-lactonisation also proceeded in HFIP without any promoter added (Table **1**, entry 10). This is consistent with previous reports on the ionising properties of HFIP solvent.



1a (1.0 equiv) (1.0 equiv) **2a** **3**

Promoter scope

Entry	Concentration (M)	Time (h)	Promoter (30 mol%)	**2a** yield[a]	**3** yield[a]
1	0.1	2	$Ti(O\textit{i}\text{-}Pr)_4$	6%	4%
2	0.037	2	$Ti(O\textit{i}\text{-}Pr)_4$	10%	8%
3	0.037	overnight	$Ti(O\textit{i}\text{-}Pr)_4$	40%	37%
4	0.037	overnight	$AlCl_3$	50%	45%
5	0.037	overnight	$Sc(OTf)_3$	27%	66%
6	0.037	overnight	$ZnCl_2$	98%	none
7	0.037	overnight	$Zn(OAc)_2$	82%	Trace
8	0.037	overnight	AcOH	58%	14%

9	0.037	overnight	TFA	90%	11%
10	0.037	overnight	none	53%	18%

*Table **1***. Optimisation of the reaction with respect to concentration, time and promoter used**.** All reactions were conducted in HFIP solvent. [a] Yield was determined by quantitative crude NMR using 1,1,2,2-tetrachloroethane as an internal standard.

We decided to optimise the metal free conditions utilising TFA; an extensive solvent screen was conducted to explore the role of HFIP solvent in this transformation (Table **2**). Only HFIP and TFE were found to be effective, with HFIP affording similar conversion over 2 h when compared to an overnight reaction (entry 7-10). These results highlight the unique properties of fluorinated solvents, and HFIP in particular, in C-C bond forming reactions involving carbocationic species.

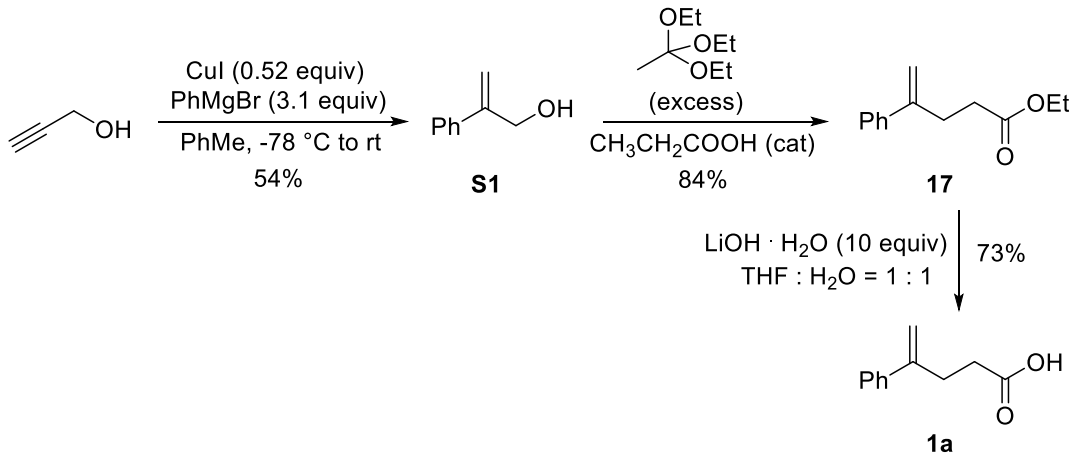
Solvent scope

Entry	Concentration (M)	Time (h)	Solvent	**2a** yield[a]	**3** yield[a]
1	0.037	overnight	IPA	0%	0%
2	0.037	overnight	MeCN	0%	0%
3	0.037	overnight	CH_2Cl_2	0%	0%
4	0.037	overnight	EtOH	0%	0%
5	0.037	overnight	DMF	0%	0%
6	0.037	overnight	Et_2O	0%	0%
7	0.037	overnight	TFE	91%	Trace
8	0.037	2 h	TFE	60%	Trace
9	0.037	overnight	HFIP	90%	11%
10	**0.037**	**2 h**	**HFIP**	**94%**	**6%**

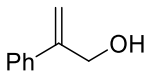
*Table **2***. Optimisation of the reaction with respect to solvent and time**.** All reactions were conducted with 30 mol% of TFA. [a] Yield was determined by quantitative crude NMR using 1,1,2,2-tetrachloroethane as an internal standard.

3.0 Experimental procedures

3.1 Synthesis of unsaturated carboxylic acid 1a



2-Phenylprop-2-en-1-ol S1



S1
$C_9H_{10}O$
134.18 g mol^{-1}

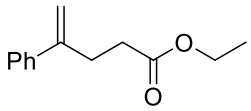
Copper (I) iodide (1.28 g, 6.72 mmol, 0.517 equiv) was suspended in PhMe (16 mL) and cooled to -78 °C. To the solution, propargyl alcohol (0.78 mL, 13 mmol, 1.0 equiv) was added. PhMgBr (40.0 mL, 40.0 mmol, 3.08 equiv, 1.00 M solution in THF) was then added dropwise, and the obtained suspension was allowed to stir at rt for 24 h. The reaction was quenched with sat. aq. NH_4Cl (5 mL), diluted with water (20 mL) and extracted with Et_2O (3 × 20 mL). The organic layers were combined, washed with brine (60 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 3:2) to get 2-phenylprop-2-en-1-ol **S1** as a colourless oil (0.966 g, 54%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.40 (m, 2H), 7.40 – 7.28 (m, 3H), 5.51 – 5.42 (m, 1H), 5.36 (q, *J* = 1.4 Hz, 1H), 4.56 (t, *J* = 1.1 Hz, 2H). The OH was not found.

^{13}C NMR (101 MHz, $CDCl_3$) δ 147.4, 138.6, 128.7 (2C), 128.1, 126.2 (2C), 112.8, 65.2.

The data are consistent with the literature[5]

Ethyl 4-phenylpent-4-enoate 17



17
$C_{13}H_{16}O_2$
204.27 g mol^{-1}

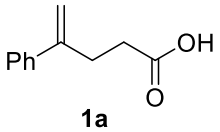
Allylic alcohol **S1** (0.857 g, 6.39 mmol, 1.00 equiv) was dissolved in triethyl orthoacetate (6 mL) and to the obtained solution propionic acid (50 µL, 0.67 mmol, 0.10 equiv) was added in one portion. The reaction mixture was stirred at 140 °C overnight, cooled to rt and diluted with Et_2O (10 mL). The mixture was washed with water (20 mL), 2 M aq. HCl (20 mL), sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL). The organic phase was dried over Na_2SO_4 and volatiles were removed *in vacuo* to obtain the crude product which was purified by flash column chromatography (SiO_2; pentane:Et_2O; 19:1) to furnish ester **17** as a colourless oil (1.09 g, 84%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.19 (m, 5H), 5.31 – 5.28 (m, 1H), 5.09 (q, *J* = 1.4 Hz, 1H), 4.12 (q, *J* = 7.2 Hz, 2H), 2.89 – 2.80 (m, 2H), 2.52 – 2.41 (m, 2H), 1.24 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 147.1, 140.8, 128.5 (2C), 127.7, 126.3 (2C), 112.9, 60.5, 33.4, 30.6, 14.4.

The data are consistent with the literature[6]

4-Phenylpent-4-enoic acid 1a



1a
$C_{11}H_{12}O_2$
176.22 g mol^{-1}

LiOH × H_2O (2.24 g, 53.3 mmol, 9.98 equiv) was added in one portion to the solution of ester **17** (1.09 g, 5.34 mmol, 1.00 equiv) in THF/water (42 mL, 1:1). The obtained suspension was

[5] L. Koser, V. M. Lechner, T. Bach, *Angew. Chem. Int. Ed*., 2021, **60**, 20269 –20273.
[6] C. Jing, B. T. Jones, R. J. Adams, J. F. Bower, *J. Am. Chem. Soc.,* 2022, **144**, 16749–16754.

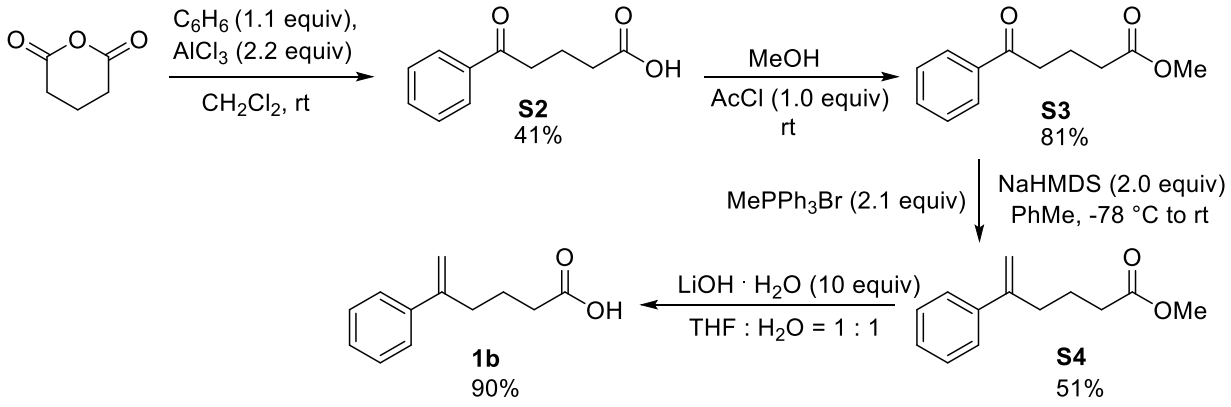
stirred at rt overnight and then diluted with Et_2O (20 mL). The aqueous phase was separated, washed with Et_2O (15 mL) and acidified with 3 M aq. HCl (20 mL) to pH=1. The obtained suspension was extracted with EtOAc (3 × 30 mL). The organic layers were combined, washed with brine (100 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* to obtain carboxylic acid **1a** as a white solid (0.689 g, 73%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.61 (br, 1H), 7.57 – 7.12 (m, 5H), 5.33 (s, 1H), 5.11 (s, 1H), 2.85 (t, *J* = 7.8 Hz, 2H), 2.54 (dd, *J* = 9.0, 6.6 Hz, 2H).

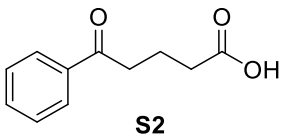
^{13}C NMR (101 MHz, $CDCl_3$) δ 179.9, 146.6, 140.5, 128.6 (2C), 127.8, 126.1 (2C), 113.1, 33.1, 30.2.

The data are consistent with the literature[7]

3.2 Synthesis of 5-phenylhex-5-enoic acid 1b



5-Oxo-5-phenylpentanoic acid S2



S2
$C_{11}H_{12}O_3$
192.21 g mol^{-1}

According to a modified literature procedure,[8] benzene (0.86 mL, 9.6 mmol, 1.1 equiv) was added in one portion to a solution of glutaric anhydride (1.00 g, 8.76 mmol, 1.00 equiv) in

[7] D. von der Heiden, F. B. Németh, M. Andreasson, D. Sethio, I. Pápai, M. Erdelyi, *Org. Biomol. Chem.*, 2021, **19**, 8307–8323.
[8] Y.-Y. Hua, H.-Y Bin, T. Wei, H.-A. Cheng, Z.-P. Lin, X.-F. Fu, Y.-Q. Li, J.-H. Xie, P.-C. Yan, Q.-L. Zhou, *Org. Lett.*, 2020, **22**, 818−822.

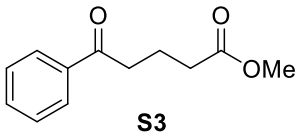
CH_2Cl_2 (30 mL). To the obtained solution, $AlCl_3$ (2.57 g, 19.3 mmol, 2.20 equiv) was added portion-wise at rt. The obtained suspension was stirred at rt overnight, cooled to 0°C and aq. NaOH (3 M, 20 mL) was slowly added. The organic phase was separated, and the aqueous phase was acidified with aq. HCl (3 M) to ph = 1. The aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL), the organic layers were combined, washed with brine (100 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography (SiO_2, pentane:EtOAc; 1:1 to EtOAc) to furnish carboxylic acid **S2** as a pale yellow solid (0.687 g, 41%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 – 7.91 (m, 2H), 7.61 – 7.51 (m, 1H), 7.51 – 7.40 (m, 2H), 3.09 (t, *J* = 7.1 Hz, 2H), 2.51 (t, *J* = 7.1 Hz, 2H), 2.09 (p, *J* = 7.1 Hz, 2H). The carboxylic acid proton was not found.

^{13}C NMR (101 MHz, $CDCl_3$): δ 199.5, 178.9, 136.9, 133.3, 128.8 (2C), 128.2 (2C), 37.4, 33.1, 19.1.

The analytical data are consistent with those previously reported in the literature.[8]

Methyl 5-oxo-5-phenylpentanoate S3



S3
$C_{12}H_{14}O_3$
206.24 g mol^{-1}

According to the literature procedure,[9] AcCl (74 µL, 1.0 mmol, 1.0 equiv) was added dropwise to the solution of acid **S2** (0.20 g, 1.0 mmol, 1.0 equiv) in MeOH (5 mL) at 0 °C. The reaction mixture was allowed to warm to rt overnight and then diluted with CH_2Cl_2 (10 mL). The solution was washed with sat. aq. $NaHCO_3$ (2 × 10 mL), brine (10 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 4:1 to 7:3) to furnish ester **S3** as a colourless oil (0.174 g, 81%).

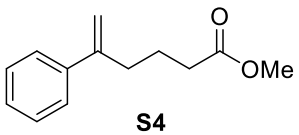
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 – 7.90 (m, 2H), 7.61 – 7.51 (m, 1H), 7.51 – 7.40 (m, 2H), 3.68 (s, 3H), 3.06 (t, *J* = 7.2 Hz, 2H), 2.45 (t, *J* = 7.2 Hz, 2H), 2.08 (p, *J* = 7.1 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 199.5, 173.9, 136.9, 133.2, 128.7 (2C), 128.2 (2C), 51.7, 37.6, 33.3, 19.5.

[9] A. B. Pulipaka, S. C. Bergmeier, *J. Org. Chem*., 2008, **73**, 1462–1467.

The analytical data are consistent with those previously reported in the literature.[9]

Methyl 5-phenylhex-5-enoate S4



S4
$C_{13}H_{16}O_2$
204.27 g mol^{-1}

According to the literature procedure,[10] to the suspension of $MePPh_3Br$ (0.632 g, 1.77 mmol, 2.10 equiv) in PhMe (7 mL) was added NaHMDS (1.0 M in THF, 1.7 mL, 1.7 mmol, 2.0 equiv) at -78 °C. The resulting mixture was stirred at the same temperature for 30 min. Ester **S3** (0.174 g, 0.844 mmol, 1.00 equiv) in toluene (2 mL) was then added dropwise at -78 °C and the obtained suspension was allowed to warm to rt overnight. The reaction was quenched with sat. aq. NH_4Cl (2 mL) and diluted with Et_2O (10 mL). The mixture was washed with water (20 mL), brine (20 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 19:1 to 9:1) to furnish ester **S4** as a pale yellow oil (88.5 mg, 51%).

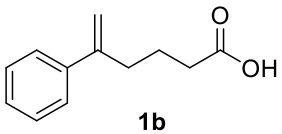
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.23 (m, 5H), 5.30 (d, *J* = 1.4 Hz, 1H), 5.07 (q, *J* = 1.3 Hz, 1H), 3.66 (s, 3H), 2.55 (td, *J* = 7.5, 1.2 Hz, 2H), 2.34 (t, *J* = 7.5 Hz, 2H), 1.79 (p, *J* = 7.5 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 174.1, 147.6, 141.0, 128.5 (2C), 127.6, 126.3 (2C), 113.1, 51.6, 34.7, 33.5, 23.5.

The analytical data are consistent with those previously reported in the literature.[11]

[10] K. Murai, T. Matsushita, A. Nakamura, S. Fukushima, M. Shimura, H. Fujioka, *Angew. Chem. Int. Ed*., 2010, **49**, 9174 –9177.
[11] X.-G. Liu, C.-J. Zhou, E. Lin, X.-L. Han, S.-S. Zhang, Q. Li, H. Wang, *Angew. Chem. Int. Ed*., 2018, **57**, 13096–13100.

5-Phenylhex-5-enoic acid 1b



1b
$C_{12}H_{14}O_2$
190.24 g mol^{-1}

According to a modified literature procedure,[12] LiOH · H_2O (0.33 g, 7.9 mmol, 10 equiv) was added in one portion to a solution of ester **S4** (0.161 g, 0.788 mmol, 1.00 equiv) in THF:H_2O (6 mL, 1:1) at rt. The suspension was stirred overnight and Et_2O (10 mL) was added. The mixture was washed with water (3 × 10 mL), the aqueous phases were combined, washed with Et_2O (30 mL) and acidified with aq. HCl (3 M) to ph = 1. The aqueous phase was extracted with EtOAc (3 × 40 mL), the organic layers were combined, washed with brine (100 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* to give carboxylic acid **1b** as a white solid which did not require any further purification (0.135 g, 90%).

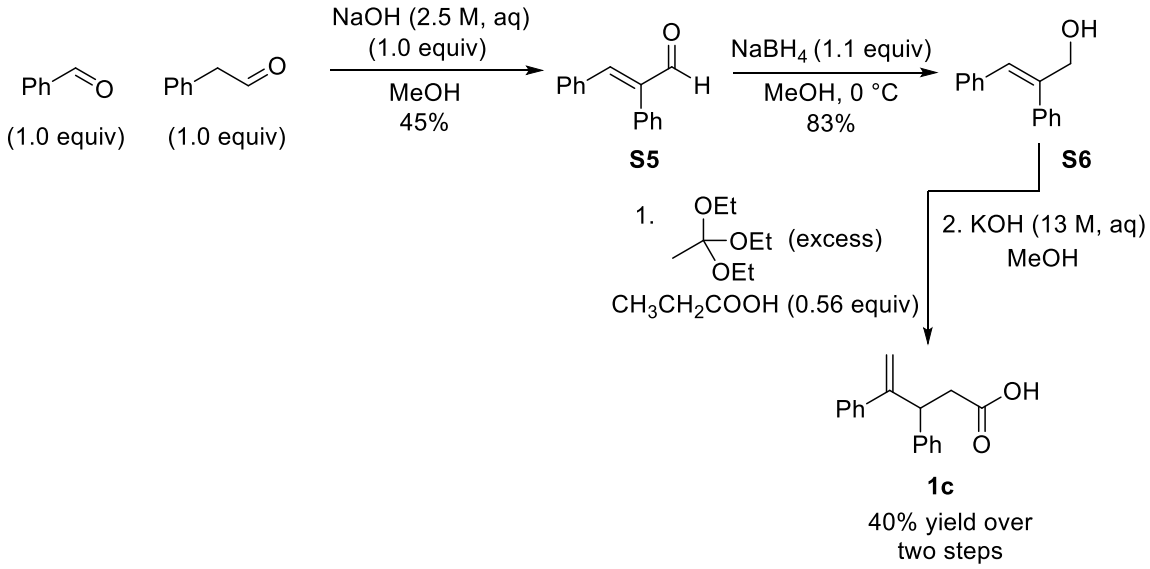
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.20 (m, 5H), 5.31 (d, *J* = 1.4 Hz, 1H), 5.08 (q, *J* = 1.3 Hz, 1H), 2.58 (td, *J* = 7.5, 1.3 Hz, 2H), 2.38 (t, *J* = 7.4 Hz, 2H), 1.80 (p, *J* = 7.5 Hz, 2H). The carboxylic acid proton was not found.

^{13}C NMR (101 MHz, $CDCl_3$): δ 179.3, 147.5, 140.9, 128.5 (2C), 127.6, 126.2 (2C), 113.2, 34.6, 33.3, 23.2.

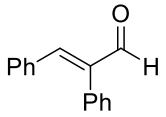
The analytical data are consistent with those previously reported in the literature.[13]

[12] K. Murai, T. Matsushita, A. Nakamura, S. Fukushima, M. Shimura, H. Fujioka, *Angew. Chem. Int. Ed.*, **2010**, **49**, 9174 –9177.
[13] L. Song, Y. Zhou, H. Liang, H. Li, Y. Lai, H. Yao, R. Lin, R. Tong, *J. Org. Chem.*, 2023, **88**, 504−512.

3.3 Synthesis of carboxylic acid 1c



(*E*)-2,3-Diphenylacrylaldehyde S5



S5
$C_{15}H_{12}O$
208.26 g mol^{-1}

According to the literature procedure,[14] benzaldehyde (1.92 mL, 18.8 mmol, 1.00 equiv) was dissolved in MeOH (14.5 mL) and aq NaOH (7.5 mL, 19 mmol, 1.0 equiv, 2.5 M) was added dropwise. The solution was cooled to 0 °C and phenylacetaldehyde (2.20 mL, 18.8 mmol, 1.00 equiv) was added dropwise using a syringe pump (1 mL/hour) over 2.2 h. After the addition was complete, TLC analysis indicated the complete conversion of the starting material. MeOH was removed *in vacuo* and the residue was dissolved in EtOAc (30 mL). Water (30 mL) was added and the organic layer was separated. The aqueous phase was extracted with further EtOAc (2 × 30 mL). The organic layers were combined, washed with brine (90 mL) and dried over Na_2SO_4. Volatiles were removed in vacuo, and the crude product was purified by flash column chromatography (SiO_2, pentane:EtOAc; 47:3 to 9:1) to obtain aldehyde **S5** as a pale yellow solid (1.78 g, 45%).

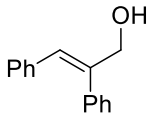
[14] B. T. Jones, J. García-Cárceles, L. Caiger, I. R. Hazelden, R. J. Lewis, T. Langer, J. F. Bower, *J. Am. Chem. Soc.,* 2021, **143**, 15593–15598.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.51 – 7.11 (m, 11H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 194.0, 150.3, 142.0, 134.2, 133.5, 130.9 (2C), 130.4, 129.5 (2C), 129.0 (2C), 128.6 (2C), 128.5.

The analytical data are consistent with those previously reported in the literature.[14]

(*E*)-2,3-Diphenylprop-2-en-1-ol S6



S6
$C_{15}H_{14}O$
210.28 g mol^{-1}

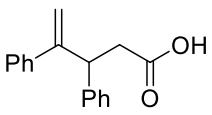
According to the literature procedure,[14] $NaBH_4$ (0.095 g, 2.50 mmol, 1.05 equiv) was added in small portions to a suspension of (*E*)-2,3-diphenylacrylaldehyde **S5** (0.50 g, 2.4 mmol, 1.0 equiv) in MeOH (1.3 mL) at 0 °C and the reaction mixture was stirred at the same temperature for 30 minutes. After complete consumption of the starting material judged by TLC analysis, the reaction was quenched with NH_4Cl (aq) (5 mL), diluted with water (10 mL) and extracted with Et_2O (3 × 10 mL). The organic layers were combined, washed with brine (10 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* to furnish (*E*)-2,3-diphenylprop-2-en-1-ol **S6** as a colourless oil which was used in the next step without purification (0.42 g, 83%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.20 (m, 5H), 7.17 – 7.06 (m, 3H), 7.06 – 6.96 (m, 2H), 6.70 (s, 1H), 4.51 – 4.44 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 141.6, 138.7, 136.6, 129.4 (2C), 129.0 (2C), 128.9 (2C), 128.1 (2C), 127.7, 127.0, 126.7, 68.7.

The analytical data are consistent with those previously reported in the literature.[14]

3,4-Diphenylpent-4-enoic acid 1c



1c
$C_{17}H_{16}O_2$
252.31 g mol^{-1}

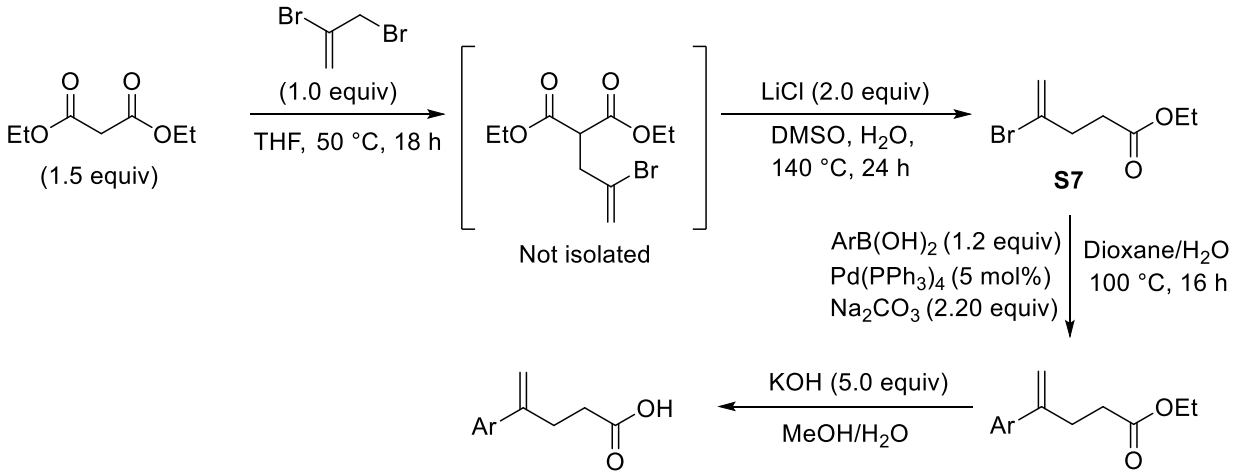
A solution of (*E*)-2,3-diphenylprop-2-en-1-ol **S6** (0.42 g, 2.0 mmol, 1.0 equiv) and propionic acid (84 µL, 1.1 mmol, 0.56 equiv) in triethyl orthoacetate (4.2 mL) was stirred at 120 °C for 18 h. The solution was left to cool to rt, diluted with water (4 mL) and extracted with Et_2O (3 × 4 mL). The organic layers were combined, washed successively with 3M HCl (aq) (2 × 10 mL), sat. aq. $NaHCO_3$ (10 mL), and brine (10 mL), and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 97:3) to obtain ethyl 3,4-diphenylpent-4-enoate together with inseparable impurities as a colourless oil (0.315 g). The obtained material was used in the next step without further purification. Ethyl 3,4-diphenylpent-4-enoate obtained in the previous step (0.315 g) was dissolved in MeOH (2.2 mL) and cooled to 0 °C. To the solution, aq. KOH (13 M, 0.43 mL) was added in one portion and stirred at rt for 2 h. The mixture was diluted with water (3 mL) and washed with Et_2O (3 × 5 mL). The aqueous layer was acidified to pH =1 with 3 M HCl and extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were combined, washed with brine (30 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo*, and the crude product was purified with flash column chromatography (SiO_2, pentane:Et_2O; 85:15) to obtain 3,4-diphenylpent-4-enoic acid **1c** as a white solid (0.20 g, 40% over two steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.06 (m, 10H), 5.38 (s, 1H), 5.14 (d, *J* = 1.3 Hz, 1H), 4.40 (t, *J* = 7.8 Hz, 1H), 2.95 (dd, *J* = 16.1, 7.9 Hz, 1H), 2.80 (dd, *J* = 16.1, 7.7 Hz, 1H)

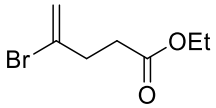
^{13}C NMR (101 MHz, $CDCl_3$) δ 178.3, 150.5, 141.7, 141.5, 128.7 (2C), 128.3 (2C), 128.0 (2C), 127.6, 127.0 (2C), 126.9, 113.6, 46.2, 40.3.

The analytical data are consistent with those previously reported in the literature.[14]

3.4 Synthesis of carboxylic acids 1d – 1m



Ethyl 4-bromopent-4-enoate S7



S7

$C_7H_{11}BrO_2$

207.07 g mol^{-1}

Diethyl malonate (4.2 mL, 28 mmol, 1.5 equiv) was added dropwise to a solution of NaH (0.595 g, 24.8 mmol, 1.35 equiv) in THF (120 mL) at rt. The mixture was left to stir at rt for 1 h and then cooled to 0 °C. 2,3-Dibromopropene (1.8 mL, 18 mmol, 1.0 equiv) was added dropwise and stirred at the same temperature for 5 min. The mixture was then stirred at 50 °C for 18 h. The reaction was quenched with NH_4Cl (50 mL), diluted with water (50 mL) and extracted with Et_2O (3 x 100 mL). The organic layers were combined, washed with brine (100 mL), dried over Na_2SO_4 and concentrated *in vacuo* to obtain the crude product which was used in the next step without further purification. The crude product was dissolved in DMSO (37 mL) and to the obtained solution LiCl (1.56 g, 36.8 mmol, 2.00 equiv) and water (0.33 mL) were then added. The obtained reaction mixture was left to stir at 140 °C for 18 h. After complete consumption of the starting material judged by TLC analysis, the mixture was diluted with water (30 mL) and extracted with Et_2O (3 × 30 mL). The organic layers were combined, washed with brine and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified with flash column chromatography (SiO_2, pentane:Et_2O; 24:1) to obtain ethyl 4-bromopent-4-enoate **S7** as a colourless oil (1.2 g, 32% over two steps).

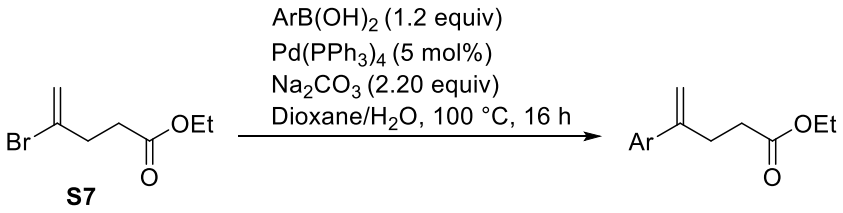
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.64 (dd, *J* = 2.0, 1.0 Hz, 1H), 5.43 (d, *J* = 1.9 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 2.80 – 2.71 (m, 2H), 2.61 – 2.46 (m, 2H), 1.26 (t, J = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 132.4, 117.8, 60.8, 36.8, 33.2, 14.4.

The analytical data are consistent with those previously reported in the literature.[15]

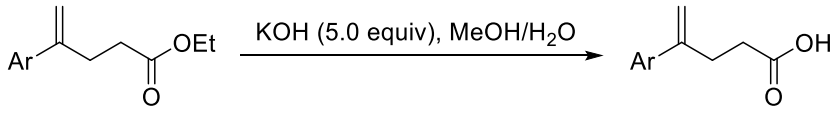
[15] (a) S. Alazet, F. Le Vaillant, S. Nicolai, T. Courant, J. Waser, *Chem. - Eur. J.*, 2017, **23**, 9501–9504; (b) T. Mukaiyama, I. Shiina, H. Iwadare, M. Saitoh, T. Nishimura, N. Ohkawa, H. Sakoh, K. Nishimura, Y.-i. Tani, M. Hasegawa, K. Yamada, K. Saitoh, *Chem. Eur. J.*, 1999, **5**, 121–161.

General procedure 1 for the synthesis of esters from vinyl bromide S7



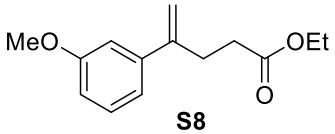
According to the modified literature procedure,[15] a solution of ethyl 4-bromopent-4 enoate **S7** (1.0 equiv), $Pd(PPh_3)_4$ (0.050 equiv), Na_2CO_3 (2.2 equiv), and a corresponding boronic acid (1.2 equiv) in 1,4-dioxane:water (7:1; 0.13 M) was refluxed for 16 h at 100 °C. The reaction mixture was then diluted with water and extracted with Et_2O (3 × 10 mL). The organic layers were combined, washed with brine, and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography using the appropriate mixture of eluents.

General procedure 2 for the ester hydrolysis



The ester from the previous step was redissolved in MeOH to obtain 0.5 M solution which was cooled to 0 °C. 13 M aq KOH (5.0 equiv) was then added at the same temperature and the mixture was warmed to rt and stirred until judged by completion using TLC analysis (approximately 2 h). The reaction mixture was diluted with water and washed with Et_2O. The aqueous layer was acidified to pH = 1 with 3 M HCl and then extracted with CH_2Cl_2. The organic layers were combined, washed with brine and dried over Na_2SO_4. Volatiles were removed *in vacuo* to furnish the corresponding carboxylic acid substrates.

Ethyl 4-(3-methoxyphenyl)pent-4-enoate S8



S8

$C_{14}H_{18}O_3$

234.30 g mol^{-1}

Ethyl 4-bromopent-4 enoate **S7** (0.300 g, 1.45 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (83 mg, 72 µmol, 0.050 equiv), Na_2CO_3 (0.34 g, 3.2 mmol, 2.2 equiv), and (3-methoxyphenyl)boronic acid (0.263 g, 1.73 mmol, 1.19 equiv) in 1,4-dioxane:water (7:1; 11.2 mL) were subjected to the general

procedure **1**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 47:3) to obtain ester **S8** as a colourless oil (0.153 g, 46%).

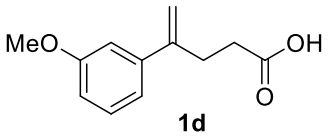
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 1H), 6.99 (ddd, *J* = 7.7, 1.7, 0.9 Hz, 1H), 6.93 (dd, *J* = 2.6, 1.6 Hz, 1H), 6.83 (ddd, *J* = 8.2, 2.6, 1.0 Hz, 1H), 5.32 – 5.27 (m, 1H), 5.09 (q, *J* = 1.3 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 2.86 – 2.78 (m, 2H), 2.51 – 2.43 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 159.6, 146.9, 142.2, 129.3, 118.7, 113.0, 112.8, 112.1, 60.4, 55.2, 33.3, 30.6, 14.2.

IR (film) ν_{max}: 2987, 2359, 1736, 1578, 1289. 1226, 1050, 904, 788 cm^{-1}.

HRMS (ESI): calculated for $C_{14}H_{18}O_3Na$ [M+Na]+ requires m/z 257.1148, found m/z 257.1150 (Δ = 0.70 ppm).

4-(3-Methoxyphenyl)pent-4-enoic acid 1d



1d

$C_{12}H_{14}O_3$

206.24 g mol^{-1}

Ester **S8** (0.153 g, 0.653 mmol, 1.00 equiv) and aq KOH (13 M, 0.25 mL, 3.3 mmol, 5.0 equiv) in MeOH (1.3 mL) were subjected to the general procedure **2** to furnish carboxylic acid **1d** as a yellow solid (0.103 g, 76%).

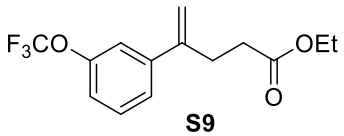
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 1H), 6.99 (ddd, J = 7.7, 1.7, 0.9 Hz, 1H), 6.94 (dd, *J* = 2.6, 1.7 Hz, 1H), 6.87 – 6.79 (m, 1H), 5.34 (m, 1H), 5.15 – 5.10 (m, 1H), 3.82 (s, 3H), 2.88 – 2.79 (m, 2H), 2.58 – 2.45 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.2, 159.7, 146.6, 142.1, 129.5, 118.7, 113.2, 113.0, 112.2, 55.3, 33.1, 30.3

The analytical data are consistent with those previously reported in the literature.[16]

[16] L. Zhou, C. K. Tan, X. Jiang, F. Chen, Y.-Y. Yeung, *J. Am. Chem. Soc.,* 2010, **132**, 15474–15476.

Ethyl 4-(3-(trifluoromethoxy)phenyl)pent-4-enoate S9



S9

$C_{14}H_{15}F_3O_3$

288.27 g mol^{-1}

Ethyl 4-bromopent-4 enoate **S7** (0.300 g, 1.45 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (83 mg, 72 µmol, 0.050 equiv), Na_2CO_3 (0.34 g, 3.2 mmol, 2.2 equiv), and (3-(trifluoromethoxy)phenyl)boronic acid (0.356 g, 1.73 mmol, 1.19 equiv) in 1,4-dioxane:water (7:1; 11.2 mL) were subjected to the general procedure **1**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 9:1) to obtain ester **S9** as a colourless oil (0.200 g, 48%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.30 (m, 2H), 7.25 – 7.22 (m, 1H), 7.17 – 7.11 (m, 1H), 5.34 (s, 1H), 5.17 – 5.14 (m, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.85 – 2.78 (m, 2H), 2.52 – 2.41 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H).

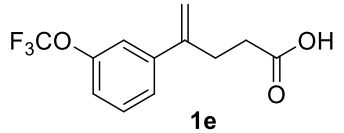
^{13}C NMR {^{19}F} (126 MHz, $CDCl_3$) δ 173.0, 149.5, 145.8, 143.0, 129.8, 124.6, 120.6, 120.0, 119.0, 114.3, 60.6, 33.2, 30.4, 14.3.

^{19}F NMR (377 MHz, $CDCl_3$) δ -57.74.

IR (film) ν_{max}: 2982, 2360, 1737, 1258, 1222, 1164, 797 cm^{-1}.

HRMS (ESI): calculated for $C_{14}H_{15}F_3O_3Na$ [M+Na]+ requires m/z 311.0866, found m/z 311.0868 (Δ = 0.79 ppm).

4-(3-(Trifluoromethoxy)phenyl)pent-4-enoic acid 1e



1e

$C_{12}H_{11}F_3O_3$

260.21 g mol^{-1}

Ester **S9** (0.200 g, 0.694 mmol, 1.00 equiv) and aq KOH (13 M, 0.26 mL, 3.4 mmol, 4.9 equiv) in MeOH (1.4 mL) were subjected to the general procedure **2** to furnish carboxylic acid **1e** as a white solid (0.11 g, 61%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.83 (br, 1H), 7.40 – 7.30 (m, 2H), 7.25 (s, 1H), 7.18 – 7.11 (m, 1H), 5.37 (s, 1H), 5.18 (s, 1H), 2.84 (t, *J* = 7.6 Hz, 2H), 2.55 (t, *J* = 7.7 Hz, 2H).

^{13}C NMR {^{19}F} (126 MHz, $CDCl_3$) δ 179.5, 149.6, 145.4, 142.8, 129.9, 124.6, 120.6, 120.1, 118.9, 114.5, 32.9, 30.0.

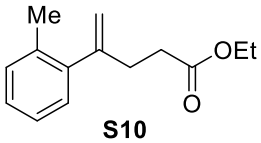
^{19}F NMR (471 MHz, $CDCl_3$) δ -57.75.

M.p.: 29-31 °C

IR (film) ν_{max}: 2981, 2360, 1714, 1259, 1221, 1166, 910, 736 cm^{-1}.

HRMS (ESI): calculated for $C_{12}H_{10}O_3F_3$ $[M-H]^-$ requires m/z 259.0588, found m/z 259.0587 (Δ = -0.26 ppm).

Ethyl 4-(o-tolyl)pent-4-enoate S10



S10

$C_{14}H_{18}O_2$

218.30 g mol^{-1}

Ethyl 4-bromopent-4 enoate **S7** (0.300 g, 1.45 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (83 mg, 72 µmol, 0.050 equiv), Na_2CO_3 (0.34 g, 3.2 mmol, 2.2 equiv), and *m*-tolylboronic acid (0.235 g, 1.73 mmol, 1.19 equiv) in 1,4-dioxane:water (7:1; 11.2 mL) were subjected to the general procedure **1**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 47:3) to obtain ester **S10** as a colourless oil (0.178 g, 57%).

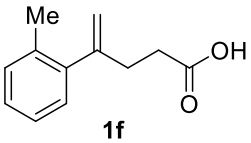
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 – 6.92 (m, 4H), 5.14 (q, J = 1.5 Hz, 1H), 4.83 (dt, *J* = 1.7, 0.9 Hz, 1H), 4.03 (q, *J* = 7.1 Hz, 2H), 2.65 – 2.54 (m, 2H), 2.34 (dd, *J* = 8.8, 6.7 Hz, 2H), 2.22 (s, 3H), 1.16 (t, *J* = 7.1 Hz, 3H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 148.3, 142.1, 134.9, 130.2, 128.4, 127.1, 125.5, 114.4, 60.4, 32.80, 32.75, 19.8, 14.2.

The analytical data are consistent with those previously reported in the literature.[17]

[17] A. L. Hansen, J.-P. Ebran, T. M. Gøgsig and T. Skrydstrup, *J. Org. Chem*. 2007, **72**, 6464–6472.

4-(*o*-Tolyl)pent-4-enoic acid 1f



1f
$C_{12}H_{14}O_2$
190.24 g mol^{-1}

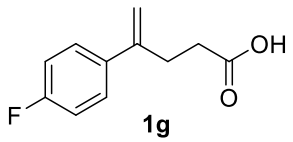
Ester **S10** (0.178 g, 0.815 mmol, 1.00 equiv) and aq KOH (13 M, 0.31 mL, 4.0 mmol, 4.9 equiv) in MeOH (1.6 mL) were subjected to general procedure **2** to furnish carboxylic acid **1f** as a yellow oil (0.121 g, 78%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.02 (m, 4H), 5.26 – 5.22 (m, 1H), 4.96 – 4.91 (m, 1H), 2.72 – 2.64 (m, 2H), 2.52 – 2.44 (m, 2H), 2.30 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.6, 148.0, 142.0, 135.0, 130.3, 128.5, 127.3, 125.7, 114.8, 32.6 (2C), 19.8.

The analytical data are consistent with those previously reported in the literature.[16]

4-(4-Fluorophenyl)pent-4-enoic acid 1g



1g
$C_{11}H_{11}FO_2$
194.21 g mol^{-1}

A solution of ethyl 4-bromopent-4 enoate **S7** (0.300 g, 1.45 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (83 mg, 72 µmol, 0.050 equiv), Na_2CO_3 (0.34 g, 3.2 mmol, 2.2 equiv), and (4-fluorophenyl)boronic acid (0.242 g, 1.73 mmol, 1.19 equiv) in 1,4-dioxane:water (7:1; 11.2 mL) was refluxed for 16 h at 100 °C. The reaction mixture was diluted with water (10 mL) and extracted with Et_2O (3 × 10 mL). The organic layers were combined, washed with brine (30 mL), and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 24:1) to obtain corresponding ester as a colourless oil (0.166 g). Product from the previous step was dissolved in MeOH (1.40 mL) and cooled to 0 °C. To the obtained solution, aq KOH (13 M, 0.27 mL, 3.5 mmol) was added in one portion at the same temperature. The mixture was warmed to rt, stirred for 2 h and then diluted with water (5 mL). The aqueous layer was washed with Et_2O (3 × 5 mL) and then acidified to pH = 1 with 2 M HCl. The obtained suspension was extracted with EtOAc (3 × 10 mL), the organic layers were combined, washed with brine (30 mL) and dried over Na_2SO_4. Volatiles were

removed *in vacuo* and the crude product was recrystallised (hexane:chloroform; 10:1) to afford carboxylic acid **1g** as a white solid (39.7 mg, 14% yield over two steps).

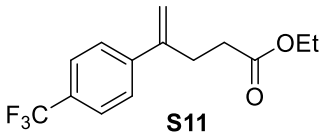
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.31 (m, 2H), 7.07 – 6.97 (m, 2H), 5.27 (s, 1H), 5.12 – 5.06 (m, 1H), 2.87 – 2.77 (m, 2H), 2.59 – 2.48 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.2, 162.6 (d, *J* = 246.6 Hz), 145.7, 136.6 (d, *J* = 3.2 Hz), 127.9 (d, *J* = 8.0 Hz, 2C), 115.4 (d, *J* = 21.3 Hz, 2C), 113.1, 33.0, 30.4.

^{19}F NMR {^{1}H} (377 MHz, $CDCl_3$) δ -114.8

The analytical data are consistent with those previously reported in the literature.[15]

Ethyl 4-(4-(trifluoromethyl)phenyl)pent-4-enoate S11



S11

$C_{14}H_{15}F_3O_2$

272.27 g mol^{-1}

Ethyl 4-bromopent-4 enoate **S7** (0.300 g, 1.44 mmol, 1.00 equiv), $Pd(PPh_3)_4$ (83 mg, 72 µmol, 0.050 equiv), Na_2CO_3 (0.34 g, 3.2 mmol, 2.2 equiv), and (4-(trifluoromethyl)phenyl)boronic acid (0.329 g, 1.73 mmol, 1.20 equiv) in 1,4-dioxane:water (7:1; 11.2 mL) were subjected to the general procedure **1**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 22:3) to obtain ester **S11** as a colourless oil (0.195 g, 50%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.55 (m, 2H), 7.54 – 7.46 (m, 2H), 5.36 (s, 1H), 5.22 – 5.17 (m, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.90 – 2.80 (m, 2H), 2.52 – 2.36 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H).

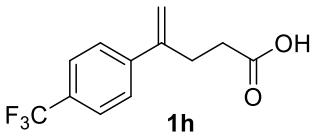
^{13}C NMR {^{19}F} (126 MHz, $CDCl_3$) δ 173.0, 146.1, 144.4, 129.8, 126.6 (2C), 125.5 (2C), 124.3, 114.9, 60.6, 33.2, 30.4, 14.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.73.

The analytical data are consistent with those previously reported in the literature.[18]

[18] G. C. Geary, E. G. Hope, A. M. Stuart, *Angew. Chem. Int. Ed.,* 2015, **54**, 14911–14914.

4-(4-(Trifluoromethyl)phenyl)pent-4-enoic acid 1h



1h
$C_{12}H_{11}F_3O_2$
244.21 g mol^{-1}

Ester **S11** (0.195 g, 0.718 mmol, 1.00 equiv) and aq KOH (13 M, 0.27 mL, 3.4 mmol, 4.9 equiv) in MeOH (1.4 mL) were subjected to the general procedure **2** to furnish carboxylic acid **1h** as a pale pink solid (0.143 g, 82%).

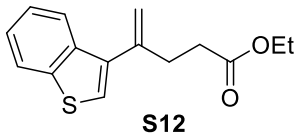
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.55 (m, 2H), 7.55 – 7.46 (m, 2H), 5.39 (s, 1H), 5.25 – 5.20 (m, 1H), 2.91 – 2.80 (m, 2H), 2.60 – 2.46 (m, 2H).

^{13}C NMR {^{19}F} (126 MHz, $CDCl_3$) δ 179.4, 145.6, 144.2, 129.9, 126.6 (2C), 125.6 (2C), 124.3, 115.1, 32.9, 30.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.6 (s).

The analytical data are consistent with those previously reported in the literature.[19]

Ethyl 4-(benzo[b]thiophen-3-yl)pent-4-enoate S12



S12
$C_{15}H_{16}O_2S$
260.35 g mol^{-1}

Ethyl 4-bromopent-4 enoate **S7** (0.300 g, 1.45 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (83 mg, 72 µmol, 0.050 equiv), Na_2CO_3 (0.34 g, 3.2 mmol, 2.2 equiv), and benzo[b]thiophen-3-ylboronic acid (0.308 g, 1.73 mmol, 1.19 equiv) in 1,4-dioxane:water (7:1; 11.2 mL) were subjected to the general procedure **1**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 47:3) to obtain ester **S12** as a colourless oil (0.207 g, 55%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.81 (m, 2H), 7.44 – 7.31 (m, 2H), 7.28 (s, 1H), 5.36 (q, *J* = 1.4 Hz, 1H), 5.32 – 5.30 (m, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 2.91 – 2.81 (m, 2H), 2.52 – 2.42 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H).

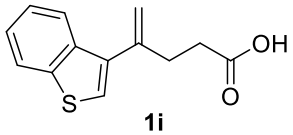
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 142.2, 140.6, 138.1, 137.8, 124.5, 124.3, 123.3, 122.9, 122.9, 115.3, 60.6, 33.3, 32.7, 14.3.

[19] D. C. Whitehead, R. Yousefi, A. Jaganathan, B. Borhan, *J. Am. Chem. Soc.,* 2010, **132**, 3298–3300.

IR (film) ν_{max}: 3093, 2982, 2360, 1734, 1428, 1180, 765, 741 cm^{-1}.

HRMS (ESI): calculated for $C_{15}H_{16}O_2SNa$ [M+Na]+ requires m/z 283.0763, found m/z 283.0762 (Δ = -0.45 ppm).

4-(Benzo[b]thiophen-3-yl)pent-4-enoic acid 1i



1i
$C_{13}H_{12}O_2S$
232.30 g mol^{-1}

Ester **S12** (0.207 g, 0.795 mmol, 1.00 equiv) and aq KOH (13 M, 0.30 mL, 3.9 mmol, 4.9 equiv) in MeOH (1.6 mL) were subjected to general procedure **2** to furnish carboxylic acid **1i** as a yellow gel (0.138 g, 75%).

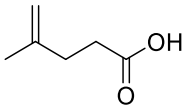
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.84 (m, 2H), 7.44 – 7.32 (m, 2H), 7.29 (s, 1H), 5.38 (s, 1H), 5.34 (s, 1H), 2.87 (t, *J* = 7.7 Hz, 2H), 2.54 (t, *J* = 7.7 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.0, 141.8, 140.6, 138.0, 137.6, 124.5, 124.4, 123.2, 123.00, 122.97, 115.5, 32.9, 32.3.

IR (film) ν_{max}: 3094, 2358, 1707, 1427, 1297, 909, 764, 740 cm^{-1}.

HRMS (ESI): calculated for $C_{13}H_{11}O_2S$ $[M-H]^-$ requires m/z 231.0485, found m/z 231.0483 (Δ = -1.05 ppm).

4-Methylpent-4-enoic acid 1j



1j
$C_6H_{10}O_2$
114.14 g mol^{-1}

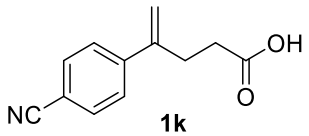
Ethyl 4-methylpent-4-enoate (0.217 g, 1.53 mmol, 1.00 equiv) and aq KOH (13 M, 0.58 mL, 7.5 mmol, 4.9 equiv) in MeOH (3.1 mL) were subjected to general procedure **2** to furnish 4-methylpent-4-enoic acid **1j** as yellow oil (0.124 g, 71%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.78 – 4.75 (m, 1H), 4.73 – 4.69 (m, 1H), 2.56 – 2.47 (m, 2H), 2.34 (dd, *J* = 8.3, 6.6 Hz, 2H), 1.75 (s, 3H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.9, 143.9, 110.7, 32.6, 32.4, 22.7.

The analytical data are consistent with those previously reported in the literature.[20]

4-(4-Cyanophenyl)pent-4-enoic acid 1k



1k

$C_{12}H_{11}NO_2$

201.23 g mol^{-1}

A solution of ethyl 4-bromopent-4 enoate **S7** (0.300 g, 1.45 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (83 mg, 72 µmol, 0.050 equiv), Na_2CO_3 (0.34 g, 3.2 mmol, 2.2 equiv), and (4-cyanophenyl)boronic acid (0.254 g, 1.73 mmol, 1.19 equiv) in 1,4-dioxane:water (7:1; 11.2 mL) was refluxed for 16 h at 100 °C. The reaction mixture was diluted with water (10 mL) and extracted with Et_2O (3 × 10 mL). The organic layers were combined, washed with brine (30 mL), and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 17:3) to obtain the corresponding ester as a colourless oil (0.172 g). Product from the previous step (0.151 g, 0.659 mmol) was dissolved in MeOH (1.3 mL) and cooled to 0 °C. To the obtained solution, aq KOH (13 M, 0.25 mL, 3.3 mmol) was added in one portion at the same temperature. The mixture was warmed to rt, stirred for 2 h and then diluted with water (5 mL). The aqueous layer was washed with Et_2O (3 × 5 mL) and then acidified to pH = 1 with 2 M HCl. The obtained suspension was extracted with EtOAc (3 × 10 mL), the organic layers were combined, washed with brine (30 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* to afford carboxylic acid **1k** as a yellow solid (88.2 mg, 30% yield over two steps).

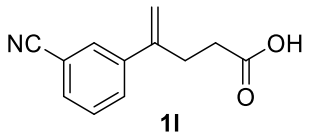
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.58 (m, 2H), 7.55 – 7.46 (m, 2H), 5.43 (s, 1H), 5.28 – 5.24 (m, 1H), 2.89 – 2.81 (m, 2H), 2.57 – 2.49 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 177.9, 145.14, 145.09, 132.3 (2C), 126.8 (2C), 118.8, 115.9, 111.3, 32.5, 29.7.

The analytical data are consistent with those previously reported in the literature.[21]

[20] S. Poplata, A. Bauer, G. Storch, T. Bach, *Chem. - Eur. J.,* 2019, **25**, 8135–8148.
[21] C. Meng, Z. Liu, Y. Liu, Q. Wang, *Org. Biomol. Chem*., 2015, **13**, 6766–6772.

4-(3-Cyanophenyl)pent-4-enoic acid 1l



1l

$C_{12}H_{11}NO_2$

201.23 g mol^{-1}

A solution of ethyl 4-bromopent-4 enoate **S7** (0.300 g, 1.45 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (83 mg, 72 µmol, 0.050 equiv), Na_2CO_3 (0.34 g, 3.2 mmol, 2.2 equiv), and (3-cyanophenyl)boronic acid (0.254 g, 1.73 mmol, 1.19 equiv) in 1,4-dioxane:water (7:1; 11.2 mL) was refluxed for 16 h at 100 °C. The reaction mixture was diluted with water (10 mL) and extracted with Et_2O (3 × 10 mL). The organic layers were combined, washed with brine (30 mL), and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 17:3) to obtain the corresponding ester as a colourless oil (0.162 g). Product from the previous step (0.162 g, 0.707 mmol) was dissolved in MeOH (1.4 mL) and cooled to 0 °C. To the obtained solution, aq KOH (13 M, 0.27 mL, 3.5 mmol) was added in one portion at the same temperature. The mixture was warmed to rt, stirred for 2 h and then diluted with water (5 mL). The aqueous layer was washed with Et_2O (3 × 5 mL) and then acidified to pH = 1 with 2 M HCl. The obtained suspension was extracted with EtOAc (3 × 10 mL), the organic layers were combined, washed with brine (30 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* to afford carboxylic acid **1l** as a pale yellow solid (0.107 g, 37% yield over two steps).

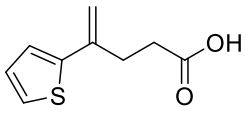
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.66 (m, 1H), 7.63 (ddd, *J* = 7.9, 1.9, 1.2 Hz, 1H), 7.58 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.45 (td, *J* = 7.8, 0.6 Hz, 1H), 5.39 – 5.36 (m, 1H), 5.24 – 5.21 (m, 1H), 2.99 – 2.72 (m, 2H), 2.68 – 2.37 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.6, 144.8, 142.0, 131.3, 130.6, 129.9, 129.5, 118.9, 115.3, 112.8, 32.7, 29.9.

The analytical data are consistent with those previously reported in the literature.[22]

[22] D. H. Paull, C. Fang, J. R. Donald, A. D. Pansick, S. F. Martin, *J. Am. Chem. Soc.*, 2012, **134**, 11128–11131.

4-(Thiophen-2-yl)pent-4-enoic acid 1m



1m
$C_9H_{10}O_2S$
182.24 g mol^{-1}

A solution of ethyl 4-bromopent-4 enoate **S7** (0.290 g, 1.40 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (81 mg, 70 µmol, 0.050 equiv), Na_2CO_3 (0.33 g, 3.1 mmol, 2.2 equiv), and thiophen-2-ylboronic acid (0.215 g, 1.68 mmol, 1.20 equiv) in 1,4-dioxane:water (7:1; 11.2 mL) was refluxed for 16 h at 100 °C. The reaction mixture was diluted with water (10 mL) and extracted with Et_2O (3 × 10 mL). The organic layers were combined, washed with brine (30 mL), and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 24:1) to obtain the corresponding ester as a colourless oil (0.230 g). Product from the previous step (0.215 g, 1.02 mmol) was dissolved in MeOH (2.0 mL) and cooled to 0 °C. To the obtained solution, aq KOH (13 M, 0.40 mL, 5.2 mmol) was added in one portion at the same temperature. The mixture was warmed to rt, stirred for 2 h and then diluted with water (5 mL). The aqueous layer was washed with Et_2O (3 × 5 mL) and then acidified to pH = 1 with 2 M HCl. The obtained suspension was extracted with EtOAc (3 × 10 mL), the organic layers were combined, washed with brine (30 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* to afford carboxylic acid **1m** as a pale yellow oil (0.163 g, 64% yield over two steps).

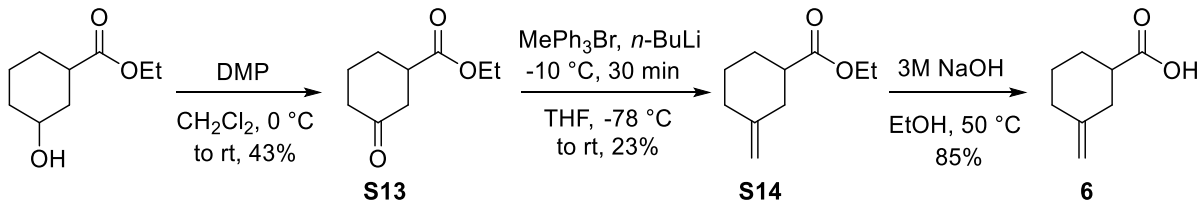
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.06 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.02 – 6.96 (dd, J = 5.1, 3.6 Hz, 1H), 5.44 (s, 1H), 5.03 – 4.98 (m, 1H), 2.87 – 2.79 (m, 2H), 2.70 – 2.62 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.2, 144.5, 139.9, 127.6, 124.7, 123.6, 111.6, 33.1, 30.3.

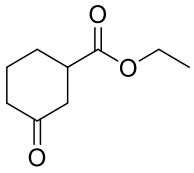
The analytical data are consistent with those previously reported in the literature.[23]

[23] (a) W. Guo, H.-G. Cheng, L.-Y. Chen, J. Xuan, Z.-J. Feng, J.-R. Chen, L.-Q. Lu, W.-J. Xiao, *Adv. Synth. Catal.,* 2014*,* **356***,* 2787–2793.

3.5 Synthesis of 3-methylenecyclohexane-1-carboxylic acid 6



Ethyl 3-oxocyclohexane-1-carboxylate S13



S13
$C_9H_{14}O_3$
170.21 g mol^{-1}

Ethyl 3-hydroxycyclohexane-1-carboxylate (0.50 g, 0.47 mL, 2.9 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (11 mL) and cooled to 0 °C. To the solution, DMP (2.4 g, 5.7 mmol, 2.0 equiv) was added portionwise and the obtained suspension was allowed to warm to rt overnight. Then sat. aq. $NaHCO_3$ (10 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The organic layers were combined, washed with brine (30 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo*, and the crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 7:3 to 3:2) to afford ketone **S13** as a colourless oil (0.213 g, 43%).

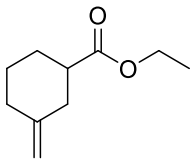
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.15 (q, *J* = 7.1 Hz, 2H), 2.84 – 2.72 (m, 1H), 2.60 – 2.50 (m, 2H), 2.42 – 2.25 (m, 2H), 2.16 – 2.01 (m, 2H), 1.90 – 1.65 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 209.4, 173.8, 61.0, 43.4, 43.3, 41.1, 27.9, 24.6, 14.3.

The analytical data are consistent with those previously reported in the literature.[24]

[24] R. Membrat, A. Vasseur, A. Martinez, L. Giordano, D. Nuel, *Eur. J. Org. Chem.,* 2018, **2018**, 5427–5434.

Ethyl 3-methylenecyclohexane-1-carboxylate S14



S14
$C_{10}H_{16}O_2$
168.24 g mol^{-1}

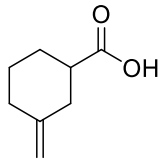
n-BuLi (0.80 mL, 2.0 mmol, 1.6 equiv, 2.5 M in hexanes) was added dropwise to a suspension of $MePPh_3Br$ (0.71 g, 2.0 mmol, 1.6 equiv) in THF (5 mL) at -10 °C. The suspension was stirred at the same temperature for 30 min and then cooled to -78 °C. Ketone **S13** (0.213 g, 1.25 mmol, 1.00 equiv) in THF (2 mL) was then added dropwise at -78 °C and the suspension was stirred at the same temperature for 10 minutes. The cooling bath was removed, and the mixture was warmed to rt overnight. The reaction was quenched with sat. aq. NH_4Cl (0.5 mL) and then diluted with Et_2O (10 mL) and water (10 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (2 × 10 mL). The organic layers were combined, washed with brine (30 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo*, and the crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 49:1 to 7:3) to afford alkene **S14** as a colourless oil (48.9 mg, 23%).[25]

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.68 (t, *J* = 1.6 Hz, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.49 (ddt, *J* = 12.9, 3.6, 1.7 Hz, 1H), 2.37 (tt, *J* = 11.3, 3.8 Hz, 1H), 2.30 – 2.16 (m, 2H), 2.05 – 1.92 (m, 2H), 1.91 – 1.80 (m, 1H), 1.63 – 1.49 (m, 1H), 1.44 – 1.29 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 175.5, 147.2, 108.8, 60.4, 44.5, 37.4, 34.5, 28.8, 26.7, 14.4.

The analytical data are consistent with those previously reported in the literature.[26]

3-Methylenecyclohexane-1-carboxylic acid 6.



6
$C_8H_{12}O_2$
140.18 g mol^{-1}

[25] Alkene **S14** is volatile.
[26] E. W. Della, A. M. Knill, *J. Org. Chem.,* 1995, **60**, 3518–3522.

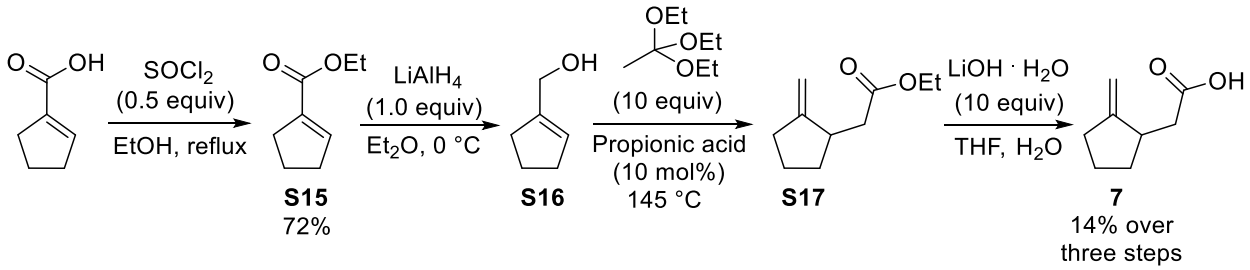
According to a modified literature procedure,[27] ester **S14** (43.1 mg, 0.256 mmol, 1.00 equiv) was dissolved in the mixture of EtOH (1mL) and 3 M aq. NaOH (1 mL). The solution was heated at 50 °C for 3 h, cooled to rt and diluted with H_2O (5 mL). The mixture was washed with Et_2O (3 × 5 mL), and the aqueous layer was acidified to pH = 1 with 3 M aq. HCl. The obtained suspension was extracted with EtOAc (3 × 10 mL), the organic layers were combined, washed with brine (20 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* to afford carboxylic acid **6** as a yellow oil which did not require any further purification (30.4 mg, 85%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.77 – 4.65 (m, 2H), 2.57 – 2.49 (m, 1H), 2.43 (tt, *J* = 11.2, 3.8 Hz, 1H), 2.32 – 2.17 (m, 2H), 2.07 – 1.95 (m, 2H), 1.93 – 1.82 (m, 1H), 1.67 – 1.51 (m, 1H), 1.47 – 1.31 (m, 1H). The carboxylic acid proton was not found.

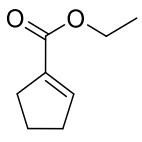
^{13}C NMR (101 MHz, $CDCl_3$): δ 182.3, 146.6, 109.2, 44.1, 37.1, 34.4, 28.6, 26.6.

The analytical data are consistent with those previously reported in the literature.[28]

3.6 Synthesis of 2-(2-Methylenecyclopentyl)acetic acid 7



Ethyl cyclopent-1-ene-1-carboxylate S15



S15
$C_8H_{12}O_2$
140.18 g mol^{-1}

[27] Y. Tsuda, A. Ishiura, S. Takamura, S. Hosoi, K. Isobe, K. Mohri, *Chem. Pharm. Bull.*, 1991, **39**, 2797–2802.
[28] N. Pérez-Hernández, M. Febles, C. Pérez, R. Pérez, M. L. Rodríguez, C. Foces-Foces, J. D. Martín, *J. Org. Chem.,* 2006*,* **71***,* 1139–1151.

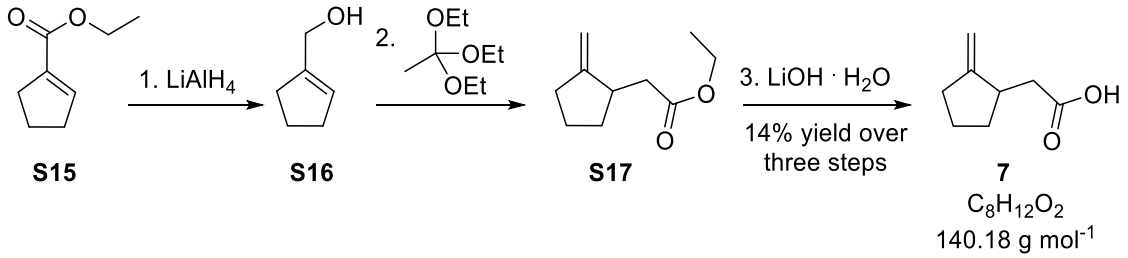
According to the literature procedure,[29] $SOCl_2$ (0.27 mL, 3.7 mmol, 1.0 equiv) was added dropwise to a solution of cyclopent-1-ene-1-carboxylic acid (0.83 g, 7.4 mmol, 1.0 equiv) in EtOH (15 mL) at rt. The reaction mixture was heated under reflux for 4 h and solvent was removed *in vacuo*. The crude product was purified by short path vacuum distillation (b.p. 95 °C/47 mbar) to afford ester **S15** as a colourless oil (0.75 g, 72%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.80 – 6.74 (m, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 2.60 – 2.45 (m, 4H), 2.01 – 1.89 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.6, 143.6, 136.9, 60.2, 33.5, 31.5, 23.3, 14.5.

The analytical data are consistent with those previously reported in the literature.[29]

2-(2-Methylenecyclopentyl)acetic acid 7



S15 **S16** **S17** **7**

$C_8H_{12}O_2$

140.18 g mol^{-1}

$LiAlH_4$ (0.20 g, 5.3 mmol, 0.98 equiv) was added portion-wise to the solution of ester **S15** (0.75 g, 5.4 mmol, 1.0 equiv) in Et_2O (40 mL) at 0 °C. The reaction mixture was stirred at the same temperature for 2 h and then quenched by dropwise addition of water (0.2 mL), 15% aq. NaOH (0.2 mL) and water (0.6 mL). The obtained suspension was allowed to warm to rt over 1 h, washed with water (40 mL), brine (40 mL) and the organic phase was dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude alcohol **S16** was subjected to the next step without purification (0.525 g).[30,31]

The crude alcohol **S16** (0.525 g) was dissolved in triethyl orthoacetate (10 mL) and propionic acid (40 µL, 0.53 mmol) was added. The solution was stirred at 145 °C for 24 h, cooled to rt and then diluted with Et_2O (20 mL). The mixture was washed with water (20 mL), 2 M aq. HCl (2 × 20 mL), brine (20 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* to furnish

[29] X.-H. Hu, J. Zhang, X.-F. Yang, Y.-H. Xu, T.-P. Loh, *J. Am. Chem. Soc.*, 2015, **137**, 3169–3172.
[30] Y. Xu, Y. J. Hong, D. J. Tantillo, M. Kevin Brown, *Org. Lett.*, 2017, **19**, 3703–3706.
[31] The presence of the product in the crude was confirmed by ^{1}H and ^{13}C NMR data. Due to volatility concern, the crude material was taken to the next step without purification.

the crude product which was purified by flash column chromatography (SiO_2, pentane:Et_2O; 47:3) to furnish ester **S17** as a colourless oil (0.311 g).[32,33]

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.93 – 4.85 (m, 1H), 4.80 – 4.74 (m, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 2.85 – 2.70 (m, 1H), 2.56 (dd, *J* = 15.2, 5.4 Hz, 1H), 2.43 – 2.19 (m, 3H), 2.06 – 1.91 (m, 1H), 1.79 – 1.65 (m, 1H), 1.65 – 1.50 (m, 1H), 1.39 – 1.23 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 173.2, 155.3, 105.0, 60.4, 40.6, 39.4, 33.2, 33.0, 24.1, 14.4.

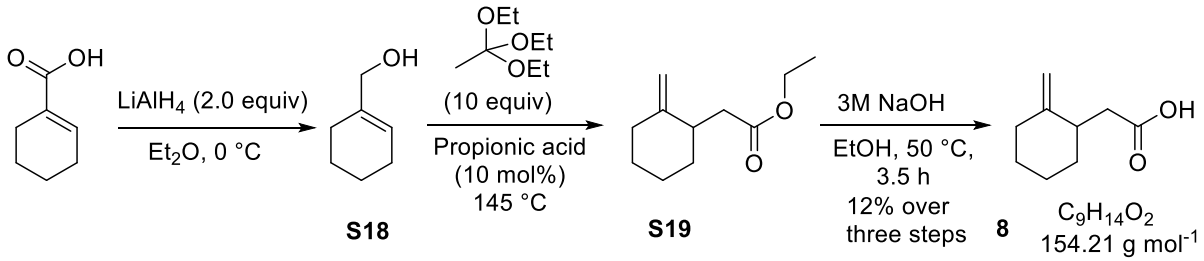
According to a modified literature procedure,[34] LiOH · H_2O (0.770 g, 18.4 mmol, 9.90 equiv) was added in one portion to a solution of ester **S17** (0.311 g, 1.85 mmol, 1.00 equiv) in THF:H_2O (14 mL, 1:1) at rt. The suspension was stirred overnight and Et_2O (20 mL) was added. The mixture was extracted with water (3 × 20 mL), the aqueous phases were combined, washed with Et_2O (50 mL) and acidified with 3 M aq. HCl until pH = 1. The obtained suspension was extracted with EtOAc (3 × 70 mL), the organic layers were combined, washed with brine (200 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* to afford carboxylic acid **7** as a colourless solid which did not require any further purification (0.100 g, 14% over three steps).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.92 (q, *J* = 2.3 Hz, 1H), 4.81 (q, *J* = 2.3 Hz, 1H), 2.86 – 2.74 (m, 1H), 2.63 (dd, *J* = 15.7, 5.3 Hz, 1H), 2.44 – 2.26 (m, 3H), 2.11 – 1.95 (m, 1H), 1.80 – 1.67 (m, 1H), 1.66 – 1.52 (m, 1H), 1.43 – 1.30 (m, 1H). The carboxylic acid proton was not found.

^{13}C NMR (101 MHz, $CDCl_3$): δ 178.9, 155.0, 105.3, 40.3, 39.0, 33.2, 33.0, 24.1.

The analytical data are consistent with those previously reported in the literature.[35]

3.7 Synthesis of 2-(2-methylenecyclohexyl)acetic acid 8



[32] R. G. Salomon, S. Ghosh, M.I G. Zagorski, M. Reitz, *J. Org. Chem.,* 1982*,* **47***, 829–836.*
[33] The identity of the product was confirmed by ^{1}H and ^{13}C NMR data. Due to volatility concerns, the product was not fully dried and contained residual solvent peaks.
[34] K. Murai, T. Matsushita, A. Nakamura, S. Fukushima, M. Shimura, H. Fujioka, *Angew. Chem. Int. Ed.*, 2010, **49**, 9174 –9177.
[35] K.-T. Yip, D. Yang, *Org. Lett.,* 2011*,* **13***,* 2134–2137.

$LiAlH_4$ (0.38 g, 10 mmol, 1.3 equiv) was suspended in Et_2O (25 mL) and cooled to 0 °C. To the suspension, cyclohex-1-ene-1-carboxylic acid (1.0 g, 7.9 mmol, 1.0 equiv) in Et_2O (20 mL) was added dropwise, and the obtained mixture was stirred at the same temperature for 1 h. The reaction was quenched by sequential dropwise addition of water (0.38 mL), 15% aq. NaOH (0.38 mL) and water (1.1 mL) at 0 °C. The suspension was allowed to warm to rt and diluted with water (40 mL). The organic layer was separated, and the aqueous layer washed with Et_2O (2 × 40 mL). The organic layers wee combined, washed with brine (100 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude alcohol **S18** was subjected to the next step without purification (0.402 g).[30, 36]

The crude alcohol **S18** (0.402 g) was dissolved in triethyl orthoacetate (6.5 mL) and propionic acid (26 µL, 0.35 mmol) was added. The solution was stirred at 145 °C for 24 h, cooled to rt and then diluted with Et_2O (15 mL). The mixture was washed with water (15 mL), 2 M aq. HCl (15 mL), brine (15 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 97:3) to furnish ester **S19** as a colourless oil (0.233 g).[37,38]

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.70 – 4.61 (m, 1H), 4.55 – 4.50 (m, 1H), 4.17 – 4.08 (m, 2H), 2.64 – 2.50 (m, 2H), 2.35 – 2.23 (m, 2H), 2.10 – 1.98 (m, 1H), 1.83 – 1.63 (m, 3H), 1.54 – 1.35 (m, 2H), 1.28 – 1.17 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 173.2, 151.7, 105.4, 60.4, 40.0, 38.2, 35.7, 34.2, 28.6, 25.2, 14.4.

According to a modified literature procedure,[39] ester **S19** (0.233 g) was dissolved in a mixture of EtOH (5 mL) and 3 M aq. NaOH (5 mL). The solution was heated at 50 °C for 3.5 h, cooled to rt and diluted with H_2O (10 mL). The mixture was washed with Et_2O (3 × 10 mL), and the aqueous layer was acidified to pH = 1 with 3 M aq. HCl. The obtained suspension was extracted with EtOAc (3 × 25 mL), the organic layers were combined, washed with brine (70 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* to afford carboxylic acid **8** as a colourless oil which did not require any further purification (0.1474 g, 12% over three steps).

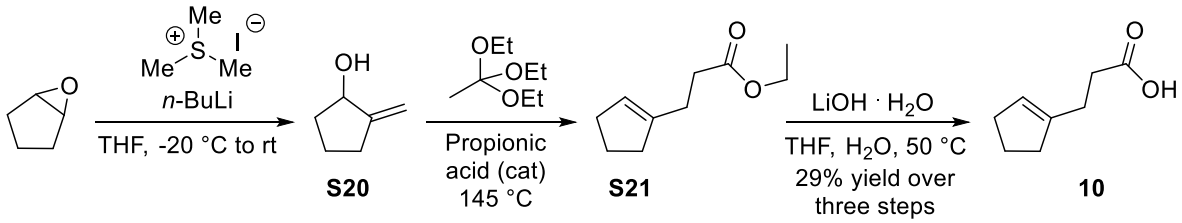
[36] The presence of the product in the crude was confirmed by ^{1}H and ^{13}C NMR data. Due to volatility concerns, the crude material was taken to the next step without purification.
[37] W.-H. Chiou, Y.-W. Wang, C.-L. Kao, P.-C. Chen, C.-C. Wu, *Organometallics,* 2014*,* **33***,* 4240–4244.
[38] The identity of the product was confirmed by ^{1}H and ^{13}C NMR data. Due to volatility concerns, the product was not fully dried and contained residual solvent peaks.
[39] Y. Tsuda, A. Ishiura, S. Takamura, S. Hosoi, K. Isobe, K. Mohri, *Chem. Pharm. Bull*., 1991, **39**, 2797–2802.

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.69 (s, 1H), 4.55 (s, 1H), 2.71 – 2.61 (m, 1H), 2.60 – 2.50 (m, 1H), 2.42 – 2.23 (m, 2H), 2.13 – 1.98 (m, 1H), 1.91 – 1.78 (m, 1H), 1.78 – 1.65 (m, 2H), 1.57 – 1.32 (m, 2H), 1.29 – 1.13 (m, 1H). The carboxylic acid proton was not found.

^{13}C NMR (101 MHz, $CDCl_3$): δ 151.4, 105.6, 39.7, 37.9, 35.8, 34.2, 28.6, 25.2.[40]

The analytical data are consistent with those previously reported in the literature.[35]

3.8 Synthesis of 3-(cyclopent-1-en-1-yl)propanoic acid 10



According to a literature procedure,[41] trimethylsulfonium iodide (6.0 g, 0.029 mol, 3.9 equiv) was dissolved in THF (37 mL) and cooled to -20 °C. *n*-BuLi (9.7 mL, 0.024 mol, 3.2 equiv) was added dropwise at the same temperature, and the solution was stirred for 30 min. 6-Oxabicyclo[3.1.0]hexane (0.62 g, 7.4 mmol, 1.0 equiv) in THF (6 mL) was then added, and the reaction mixture was warmed to rt over 1 h and then stirred for additional 2 h. The reaction was quenched with sat. aq. NH_4Cl (5 mL) and then diluted with Et_2O (40 mL). The mixture was washed with H_2O (40 mL), 1 M aq. NaOH (40 mL), brine (40 mL), and the organic phase was dried over Na_2SO_4. Volatiles were removed *in vacuo* to obtain crude allylic alcohol **S20** which was used in the next step without purification (0.7325 g).[42,43]

The crude alcohol **S20** (0.70 g) was dissolved in triethyl orthoacetate (9 mL) and propionic acid (54 µL, 0.72 mmol) was added. The solution was stirred at 145 °C for 24 h, cooled to rt and then diluted with Et_2O (25 mL). The mixture was washed with water (25 mL), 2 M aq. HCl (25 mL), brine (25 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude

[40] Note: ^{13}C NMR signal for a carboxylic acid functional group is missing.
[41] R. Kato, H. Saito, S. Uda, D. Domon, K. Ikeuchi, T. Suzuki, K. Tanino, *Org. Lett.*, 2021, **23**, 8878–8882.
[42] The presence of the product in the crude was confirmed by ^{1}H and ^{13}C NMR data. Due to volatility concern, the crude material was taken to the next step without purification.
[43] L. Alcaraz, A. Cridland, E. Kinchin, *Org. Lett.,* 2001, **3**, 4051–4053.

product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 49:1) to furnish ester **S21** as a colourless oil (0.527 g).[44,45]

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.39 – 5.29 (m, 1H), 4.13 (q, *J* = 7.2 Hz, 2H), 2.50 – 2.43 (m, 2H), 2.42 – 2.34 (m, 2H), 2.33 – 2.19 (m, 4H), 1.93 – 1.79 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 173.6, 143.1, 124.0, 60.4, 35.3, 33.0, 32.6, 26.6, 23.5, 14.4.

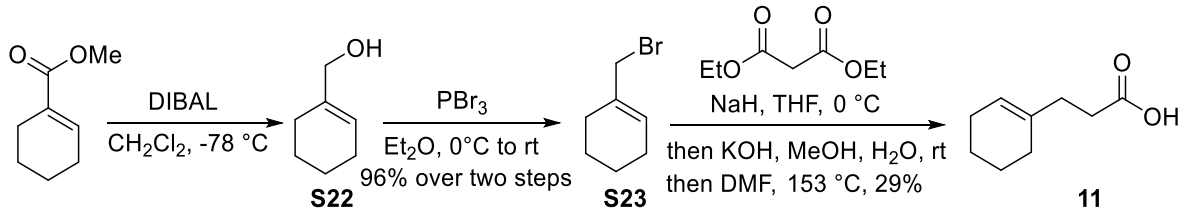
According to a modified literature procedure,[45] LiOH (0.375 g, 15.7 mmol, 5.02 equiv) was added in one portion to the solution of ester **S21** (0.527 g, 3.13 mmol, 1.00 equiv) in THF:H_2O (10.6 mL, 1:1) at rt. The suspension was stirred at 50 °C overnight and then cooled to rt. Et_2O (20 mL) was added. The mixture was extracted with water (3 × 20 mL), the aqueous phases were combined, washed with Et_2O (50 mL) and acidified with 3 M aq. HCl until pH = 1. The obtained suspension was extracted with EtOAc (3 × 50 mL), the organic layers were combined, washed with brine (100 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* to afford carboxylic acid **10** as a colourless oil which did not require any further purification (0.301 g, 29% over three steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.41 – 5.33 (m, 1H), 2.59 – 2.47 (m, 2H), 2.44 – 2.35 (m, 2H), 2.34 – 2.20 (m, 4H), 1.86 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 179.4, 142.8, 124.3, 35.3, 32.7, 32.6, 26.2, 23.5.

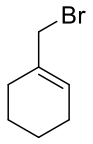
The analytical data are consistent with those previously reported in the literature.[46]

3.9 Synthesis of 3-(cyclohex-1-en-1-yl)propanoic acid 11



[44] The identity of the product was confirmed by ^{1}H and ^{13}C NMR data. Due to volatility concerns, the product was not fully dried and contained residual solvent peaks.
[45] S. -H. Huang, X. Tian, X. Mi, Y. Wang, R. Hong, *Tetrahedron Lett.*, 2015, **56**, 6656–6658.
[46] Q. Liu, E. M. Ferreira, B. M. Stoltz, *J. Org. Chem.*, 2007, **72**, 7352–7358.

1-(Bromomethyl)cyclohex-1-ene S23



S23
$C_7H_{11}Br$
175.07 g mol^{-1}

Methyl cyclohex-1-ene-1-carboxylate (2.0 g, 14 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (40 mL) and cooled to -78 °C. DIBAL-H (31 mL, 31 mmol, 2.2 equiv, 1.0 M in CH_2Cl_2) was then added dropwise, and the obtained solution was stirred at the same temperature for 3.5 h. The mixture was quenched by dropwise addition of MeOH (25 mL) at -78 °C, warmed to 0 °C and sat. aq. Rochelle salt (25 mL) was added. The obtained mixture was allowed to warm to rt overnight and was then diluted with water (40 mL). The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (2 × 40 mL). The organic layers were combined, washed with brine (100 mL) and then dried over Na_2SO_4. The solvent was carefully removed *in vacuo* and crude allylic alcohol **S22** was subjected to the next step without purification (1.59 g).[47]

Crude allylic alcohol **S22** (1.59 g) was dissolved in Et_2O (70 mL) and cooled to 0 °C. PBr_3 (0.67 mL, 7.1 mmol, 0.51 equiv) was added dropwise at the same temperature, and the reaction mixture was allowed to warm to rt over 3 h. The solution was poured onto sat. aq. Na_2CO_3 (30 mL), and the organic layer was separated. The aqueous layer was extracted with Et_2O (2 × 30 mL), the organic layers were combined, washed with brine (100 mL) and dried over Na_2SO_4. The solvent was carefully removed *in vacuo* to obtain bromide **S23** as a colourless oil which did not require purification (2.35 g, 96% over two steps).

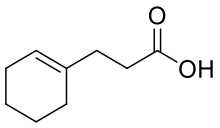
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 – 5.82 (m, 1H), 3.94 (s, 2H), 2.17 – 2.08 (m, 2H), 2.08 – 1.99 (m, 2H), 1.72 – 1.50 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 134.8, 128.3, 40.0, 26.5, 25.6, 22.5, 22.0.

The analytical data are consistent with those previously reported in the literature.[48]

[47] Due to volatility concerns, the product from this step was not purified by chromatography.
[48] I. R. Hazelden, R. C. Carmona, T. Langer, P. G. Pringle, J. F. Bower, *Angew. Chem. Int. Ed.,* 2018, **57**, 5124–5128.

3-(Cyclohex-1-en-1-yl)propanoic acid 11



11
$C_9H_{14}O_2$
154.21 g mol^{-1}

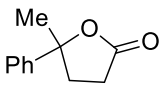
According to a modified literature procedure,[48] to a suspension of NaH (0.536 g, 13.4 mmol, 2.00 equiv, 60% weight in mineral oil) in THF (40 mL) at 0 °C was added diethyl malonate (2.0 mL, 13 mmol, 2.0 equiv) dropwise. The reaction mixture was stirred at 0 °C for 1 hour before dropwise addition of bromide **S23** (0.91 mL, 1.2 g, 6.7 mmol, 1.0 equiv). The reaction mixture was warmed to room temperature and monitored by TLC. Upon completion, the reaction mixture was poured into a solution of KOH (4.5 g, 80 mmol, 12 equiv) in water:MeOH (20 mL, 1:1) and stirred for 40 minutes at rt. The reaction mixture was acidified with 10 M aq. HCl to pH = 1, concentrated to an aqueous solution and extracted with EtOAc (3 × 20 mL). The combined organic layers were dried with Na_2SO_4 and volatiles were removed *in vacuo*. The obtained crude mixture of malonic acids was dissolved in DMF (14 mL) and heated at reflux for 3 h. Solvent was removed *in vacuo* and the crude product was redissolved in THF (10 mL). 3M aq. NaOH (10 mL) was added, and the solution was stirred for 10 min at rt. The mixture was washed with Et_2O (3 × 10 ml), and the aqueous phase was then acidified with 3M aq. HCl to pH = 1. The mixture was extracted with EtOAc (3 × 15 mL), the organic layers were combined, washed with brine (40 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo*, and the crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 3:2) to afford carboxylic acid **11** as a colourless oil (0.2971 g, 29%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 – 5.40 (m, 1H), 2.46 (dd, *J* = 8.8, 6.7 Hz, 2H), 2.32 – 2.20 (m, 2H), 2.03 – 1.87 (m, 4H), 1.69 – 1.48 (m, 4H). The carboxylic acid proton was not found.

^{13}C NMR (101 MHz, $CDCl_3$): δ 179.7, 135.9, 121.9, 32.8, 32.7, 28.4, 25.3, 23.0, 22.5.

The analytical data are consistent with those previously reported in the literature.[48]

5-Methyl-5-phenyldihydrofuran-2(3H)-one 3



3
$C_{11}H_{12}O_2$
176.22 g mol^{-1}

Carboxylic acid **1a** (35.2 mg, 0.200 mmol, 1.00 equiv) and *N*, *N*-dimethylmethaniminium iodide (0.148 g, 0.800 mmol, 4.00 equiv) were transferred to a microwave vial which was capped and purged with argon for 15 min. The balloon of argon was removed and HFIP (0.33 mL) was added. The reaction mixture was stirred at rt overnight and then diluted with Et_2O (5 mL). The obtained solution was washed with water (5 mL) and brine (5 mL). The organic layer was dried over Na_2SO_4 and volatiles were removed *in vacuo* to obtain lactone **3** as a colourless oil which did not require any purification (35.5 mg, quantitative).[49]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.26 (m, 5H), 2.71 – 2.32 (m, 4H), 1.72 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6, 144.4, 128.7 (2C), 127.8, 124.2 (2C), 87.1, 36.3, 29.6, 29.1.

The data are consistent with the literature[50]

3.10 Alkylative lactonization and derivatisations

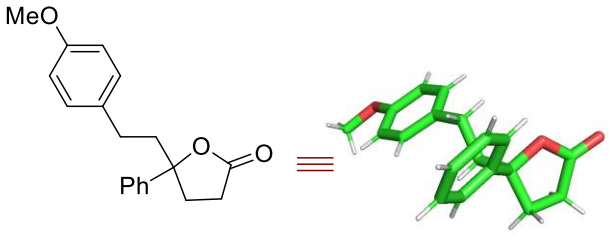
General procedure 3: Alkylative lactonisation in HFIP

(1.0 equiv) (1.0 equiv)

The corresponding carboxylic acid (1.0 equiv) and alcohol (1.0 equiv) were transferred to a microwave vial, which was caped and purged with N_2 for 15 min. HFIP (0.037 M) followed by TFA (0.30 equiv) were added and the reaction mixture was stirred at rt for 2 h. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography using the appropriate mixture of eluents.

[49] The desired amine containing product was not observed or isolated.
[50] R. Maji, S. Ghosh, O. Grossmann, P. Zhang, M. Leutzsch, N. Tsuji, B. List, *J. Am. Chem. Soc.,* 2023, **145**, 8788–8793.

5-(4-Methoxyphenethyl)-5-phenyldihydrofuran-2(3H)-one 2a



2a
$C_{19}H_{20}O_3$
296.37 g mol^{-1}

[X-ray]

4-Phenylpent-4-enoic acid **1a** (34 mg, 0.19 mmol, 1.0 equiv), 4-methoxybenzyl alcohol (26 mg, 0.19 mmol, 1.0 equiv) and TFA (4.4 µL, 57 µmol, 0.30 equiv) in HFIP (5.1 mL) were subjected to general procedure **3**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 7:3) to obtain lactone **2a** as a pale yellow oil which crystallised on standing (53 mg, 94%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.27 (m, 5H), 7.03 – 6.95 (m, 2H), 6.82 – 6.75 (m, 2H), 3.76 (s, 3H), 2.69 – 2.40 (m, 5H), 2.35 – 2.15 (m, 3H).

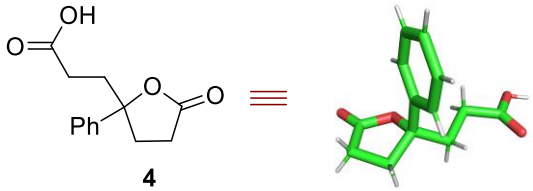
^{13}C NMR (101 MHz, $CDCl_3$): δ 176.7, 158.0, 142.7, 133.4, 129.2 (2C), 128.8 (2C), 127.8, 124.7 (2C), 114.0 (2C), 89.2, 55.4, 44.8, 35.5, 29.5, 28.7.

M.p: 70-71 °C.

IR (film) ν_{max}: 2953, 2360, 1780, 1513, 1247, 1179, 1039, 939, 704 cm^{-1}.

HRMS (ESI): calculated for $C_{19}H_{20}O_3Na$ $[M+Na]^+$ requires m/z 319.1305, found m/z 319.1305 (Δ = 0.09 ppm).

3-(5-Oxo-2-phenyltetrahydrofuran-2-yl)propanoic acid 4



4
$C_{13}H_{14}O_4$
234.25 g mol^{-1}

[X-ray]

Lactone **2a** (19.0 mg, 64.1 µmol, 1.00 equiv) was dissolved in CCl_4:CH_3CN:pH 7 buffer (2:2:3; 0.7 mL) and cooled to 0 °C. $NaIO_4$ (271 mg, 1.27 mmol, 19.8 equiv) was added in one portion and the obtained suspension was cooled to 0 °C and stirred at the same temperature for 15 min. $RuCl_3$ (0.6 mg, 3 µmol, 0.05 equiv) was added at 0 °C in one portion and the reaction

mixture was allowed to slowly warm to rt overnight. Then water (3 mL) and Et_2O (3 mL) were added. The organic layer was separated and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the residue was purified by flash column chromatography (SiO_2; EtOAc to EtOAc:MeOH; 9:1) to furnish carboxylic acid **4** as a pale yellow oil (4.0 mg, 27%).

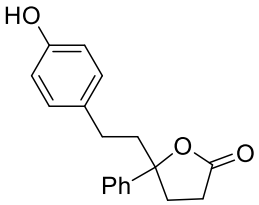
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 2H), 7.35 – 7.28 (dt, *J* = 8.2, 2.1 Hz, 3H), 2.67 – 2.57 (m, 1H), 2.52 – 2.40 (m, 4H), 2.32 (t, *J* = 7.8 Hz, 2H), 2.09 (dt, *J* = 16.1, 7.7 Hz, 1H).The carboxylic acid proton was not found.

^{13}C NMR (151 MHz, $CDCl_3$) δ 177.9, 176.3, 141.8, 129.0 (2C), 128.1, 124.7 (2C), 88.3, 36.9, 35.8, 29.0, 28.6.[51]

IR (film) ν_{max}: 2918, 2362, 1780, 1714, 1198, 1056, 943, 913, 769, 737, 705, 640, 630 cm^{-1}.

HRMS (ESI): calculated for $C_{13}H_{13}O_4$ $[M-H]^-$ requires m/z 233.0819, found m/z 233.0828 (Δ = 3.73 ppm).

5-(4-Hydroxyphenethyl)-5-phenyldihydrofuran-2(3H)-one 2b



2b
$C_{18}H_{18}O_3$
282.34 g mol^{-1}

4-Phenylpent-4-enoic acid **1a** (22 mg, 0.12 mmol, 1.0 equiv), 4-hydroxybenzyl alcohol (15 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.3 mL) were subjected to general procedure **3**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 1:1) to obtain lactone **2b** as a colourless oil (27 mg, 74%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.29 (m, 4H), 7.03 – 6.86 (m, 2H), 6.81 – 6.65 (m, 2H), 5.81 – 5.33 (m, 1H), 2.72 – 2.39 (m, 5H), 2.33 – 2.12 (m, 3H).

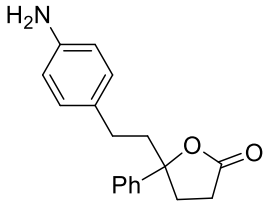
^{13}C NMR (101 MHz, $CDCl_3$): δ 177.4, 154.2, 142.5, 133.1, 129.4 (2C), 128.8 (2C), 127.8, 124.7 (2C), 115.5 (2C), 89.6, 44.7, 35.5, 29.4, 28.8.

IR (film) ν_{max}: 3377, 2925, 2361, 1757, 1515, 1448, 1198, 912, 832, 762, 734, 703 cm^{-1}.

[51] Note: Two ^{13}C NMR signals have low intensity due to peak broadness.

HRMS (ESI): calculated for $C_{18}H_{19}O_3$ $[M+H]^+$ requires m/z 283.1329, found m/z 283.1329 (Δ = 0.09 ppm).

5-(4-Aminophenethyl)-5-phenyldihydrofuran-2(3H)-one 2c



2c
$C_{18}H_{19}NO_2$
281.36 g mol^{-1}

4-Phenylpent-4-enoic acid **1a** (20 mg, 0.11 mmol, 1.0 equiv), 4-aminobenzyl alcohol (14 mg, 0.11 mmol, 1.0 equiv) and TFA (2.6 µL, 34 µmol, 0.31 equiv) in HFIP (3.1 mL) were subjected to general procedure **3**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 7:3) to obtain lactone **2c** as a pale brown oil (15 mg, 47%).

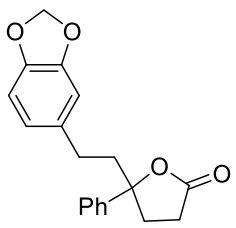
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.28 (m, 5H), 6.91 – 6.82 (m, 2H), 6.61 – 6.55 (m, 2H), 3.83 – 3.26 (m, 2H), 2.67 – 2.39 (m, 5H), 2.32 – 2.12 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.8, 144.5, 142.8, 131.3, 129.1 (2C), 128.8 (2C), 127.8, 124.7 (2C), 115.4 (2C), 89.3, 44.9, 35.5, 29.5, 28.7.

IR (film) ν_{max}: 3367, 2938, 1771, 1625, 1518, 1196, 938, 829, 735, 703, 652 cm^{-1}.

HRMS (ESI): calculated for $C_{18}H_{19}NO_2Na$ $[M+Na]^+$ requires m/z 304.1308, found m/z 304.1310 (Δ = 0.64 ppm).

5-(2-(Benzo[d][1,3]dioxol-5-yl)ethyl)-5-phenyldihydrofuran-2(3H)-one 2d



2d
$C_{19}H_{18}O_4$
310.35 g mol^{-1}

4-Phenylpent-4-enoic acid **1a** (22 mg, 0.12 mmol, 1.0 equiv), piperonyl alcohol (19 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.3 mL) were subjected to general procedure **3**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 3:2) to obtain lactone **2d** as a colourless oil (29 mg, 75%).

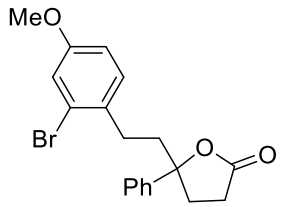
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.29 (m, 5H), 6.68 (d, *J* = 7.8 Hz, 1H), 6.59 – 6.47 (m, 2H), 5.89 (s, 2H), 2.68 – 2.39 (m, 5H), 2.31 – 2.15 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.7, 147.7, 145.8, 142.6, 135.2, 128.8 (2C), 127.8, 124.7 (2C), 121.0, 108.8, 108.3, 100.9, 89.1, 44.8, 35.6, 30.2, 28.7.

IR (film) ν_{max}: 2921, 2361, 1777, 1490, 1243, 1038, 936, 811, 703 cm^{-1}.

HRMS (ESI): calculated for $C_{19}H_{19}O_4$ $[M+H]^+$ requires m/z 311.1278, found m/z 311.1277 (Δ = -0.29 ppm).

5-(2-Bromo-4-methoxyphenethyl)-5-phenyldihydrofuran-2(3H)-one 2e



2e
$C_{19}H_{19}BrO_3$
375.26 g mol^{-1}

4-Phenylpent-4-enoic acid **1a** (22 mg, 0.12 mmol, 1.0 equiv), (2-bromo-4-methoxyphenyl)methanol (27 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.3 mL) were subjected to general procedure **3**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 3:2) to obtain lactone **2e** as a pale colourless oil (35.5 mg, 79%).

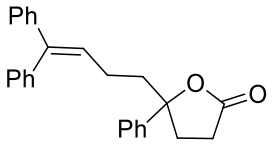
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.28 (m, 5H), 7.07 – 6.96 (m, 2H), 6.74 (dd, *J* = 8.5, 2.7 Hz, 1H), 3.74 (s, 3H), 2.77 – 2.35 (m, 6H), 2.33 – 2.22 (m, 1H), 2.20 – 2.09 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.7, 158.6, 142.5, 132.6, 130.8, 128.7 (2C), 127.9, 124.8 (2C), 124.3, 118.1, 113.8, 89.1, 55.6, 42.8, 35.4, 30.2, 28.7.

IR (film) ν_{max}: 2922, 1778, 1605, 1494, 1238, 1194, 1029, 936, 761, 702 cm^{-1}.

HRMS (ESI): calculated for $C_{19}H_{20}BrO_3$ $[M+H]^+$ requires m/z 375.0590, found m/z 375.0586 (Δ = -1.16 ppm).

5-(4,4-Diphenylbut-3-en-1-yl)-5-phenyldihydrofuran-2(3H)-one 2f



2f

$C_{26}H_{24}O_2$

368.48 g mol^{-1}

Carboxylic acid **1a** (22 mg, 0.12 mmol, 1.0 equiv), 1,1-diphenylprop-2-en-1-ol **14b** (26 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.3 mL) were subjected to the general procedure **3.** The crude product was purified by flash column chromatography (SiO_2; pentane:Et_2O; 3:2) to furnish lactone **2f** as a colourless oil (34.5 mg, 75%).

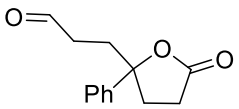
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.12 (m, 13H), 7.11 – 6.98 (m, 2H), 5.97 (t, *J* = 7.3 Hz, 1H), 2.61 – 2.27 (m, 4H), 2.24 – 1.92 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.5, 142.59, 142.57, 142.55, 139.8, 129.7 (2C), 128.6 (2C), 128.3 (2C), 128.17 (2C), 128.15, 127.7, 127.3 (2C), 127.1, 127.1, 124.7 (2C), 89.2, 42.3, 35.1, 28.7, 24.5.

IR (film) ν_{max}: 2980, 2360, 1777, 1193, 916, 763, 701 cm^{-1}.

HRMS (ESI): calculated for $C_{26}H_{25}O_2$ $[M+H]^+$ requires m/z 369.1849, found m/z 369.1858 (Δ = 2.41 ppm).

3-(5-Oxo-2-phenyltetrahydrofuran-2-yl)propanal 5



5

$C_{13}H_{14}O_3$

218.25 g mol^{-1}

Lactone **2f** (28 mg, 75 µmol, 1.0 equiv) was dissolved in CH_2Cl_2 (25 mL) and cooled to -78 °C. O_3/O_2 was bubbled through the solution until blue colour was observed and then left for an additional 2 min. O_2 was then bubbled through the solution until the blue colour was no longer seen, followed by N_2 for an additional 15 min. The reaction was then quenched by dropwise addition of DMS (2.2 mL) at -78 °C. The mixture was stirred at the same temperature for 30 min and then slowly warmed to rt over 3 h. Volatiles were removed *in vacuo* and the crude

product was purified by flash column chromatography (SiO_2; pentane:Et_2O; 1:1) to obtain aldehyde **5** as a colourless oil (11 mg, 67%).

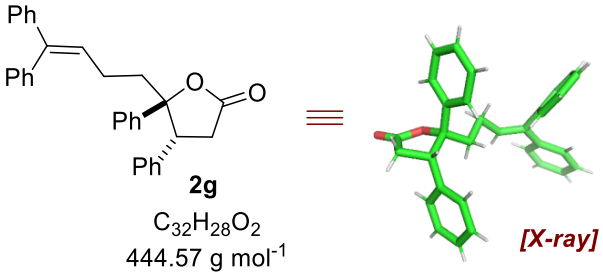
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.65 (t, *J* = 0.9 Hz, 1H), 7.43 – 7.23 (m, 5H), 2.68 – 2.54 (m, 2H), 2.54 – 2.40 (m, 3H), 2.39 – 2.16 (m, 3H)

^{13}C NMR (101 MHz, $CDCl_3$): δ 200.8, 176.2, 141.9, 129.0 (2C), 128.1, 124.7 (2C), 88.3, 39.0, 36.0, 34.3, 28.6.

IR (film) ν_{max}: 2364, 1780, 1723, 1195, 1092, 1009, 912, 737 cm^{-1}.

HRMS (ESI): calculated for $C_{13}H_{15}O_3$ $[M+H]^+$ requires m/z 219.1016, found m/z 219.1016 (Δ = 0.11 ppm).

(±)-(4*R*,5*S*)-5-(4,4-Diphenylbut-3-en-1-yl)-4,5-diphenyldihydrofuran-2(3H)-one 2g



Carboxylic acid **1c** (30 mg, 0.12 mmol, 1.0 equiv), 1,1-diphenylprop-2-en-1-ol **14b** (25 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.2 mL) were subjected to the general procedure **3.** The crude product was purified by flash column chromatography (SiO_2; pentane:Et_2O; 21:4) to furnish lactone **2g** as a colourless oil (45 mg, 84%, >95:5 dr).

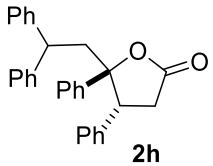
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 – 7.09 (m, 18H), 7.00 – 6.90 (m, 2H), 5.90 – 5.82 (m, 1H), 3.72 (t, *J* = 7.3 Hz, 1H), 2.96 – 2.80 (m, 2H), 2.15 – 2.00 (m, 1H), 1.82 – 1.57 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.2, 142.5, 142.3, 142.2, 139.7, 137.4, 129.6 (2C), 128.9 (2C), 128.7 (2C), 128.6 (2C), 128.4, 128.2 (2C), 128.13 (2C), 128.11, 127.7, 127.2 (2C), 127.00, 126.98, 124.8 (2C), 91.8, 53.5, 37.1, 35.5, 24.3.

IR (film) ν_{max}: 3028, 2360, 1779, 1215, 911, 768, 735, 700 cm^{-1}.

HRMS (ESI): $C_{32}H_{28}O_2Na$ $[M+Na]^+$ requires m/z 467.1982, found m/z 467.1988 (Δ = 1.38 ppm).

(±)-(4*R*,5*S*)-5-(2,2-Diphenylethyl)-4,5-diphenyldihydrofuran-2(3H)-one 2h



2h

$C_{30}H_{26}O_2$

418.54 g mol^{-1}

Carboxylic acid **1c** (30 mg, 0.12 mmol, 1.0 equiv), benzhydrol (22 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.2 mL) were subjected to the general procedure **3**. The crude product was purified by flash column chromatography (SiO_2; pentane:Et_2O; 22:3) to furnish lactone **2h** as a single diastereomer as a white solid (37 mg, 74%, >95:5 dr).[52]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.33 (m, 3H), 7.29 – 7.07 (m, 10H), 7.06 – 6.88 (m, 5H), 6.80 – 6.69 (m, 2H), 3.83 (t, *J* = 6.3 Hz, 1H), 3.71 (t, *J* = 6.8 Hz, 1H), 2.86 – 2.71 (m, 2H), 2.52 (dd, *J* = 14.9, 6.7 Hz, 1H), 2.39 (dd, *J* = 14.9, 5.9 Hz, 1H).

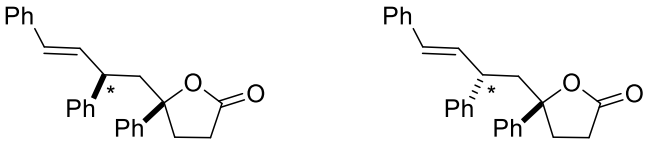
^{13}C NMR (101 MHz, $CDCl_3$): δ 176.0, 145.1, 144.8, 142.0, 137.6, 129.0 (2C), 128.7 (2C), 128.5 (4C), 128.25 (2C), 128.22, 127.8 (2C), 127.73, 127.69 (2C), 126.2, 125.7, 125.3 (2C), 91.7, 54.1, 46.9, 43.4, 35.6.

M.p.: 148-150 °C

IR (film) ν_{max}: 3028, 2361, 1784, 1497, 1213, 913, 742, 701 cm^{-1}.

HRMS (ESI): $C_{32}H_{28}O_2Na$ $[M+Na]^+$ requires m/z 441.1825, found m/z 441.1831 (Δ = 1.35 ppm).

(±)-(*R*)-5-((*R*,*E*)-2,4-Diphenylbut-3-en-1-yl)-5-phenyldihydrofuran-2(3H)-one and **(±)-(*R*)-5-((*S*,*E*)-2,4-diphenylbut-3-en-1-yl)-5-phenyldihydrofuran-2(3H)-one 2i**



2i

$C_{26}H_{24}O_2$

368.48 g mol^{-1}

*64:36 dr

[52] Relative stereochemistry is assigned based on X-ray crystal structure of lactone **2g**.

Carboxylic acid **1a** (22 mg, 0.12 mmol, 1.0 equiv), (*E*)-1,3-diphenylprop-2-en-1-ol (26 mg, 0.12 mmol, 1.0 equiv) and TFA (2.6 µL, 34 µmol, 0.29 equiv) in HFIP (3.3 mL) were subjected to the general procedure **3**. The crude product was purified by flash column chromatography (SiO_2; pentane:Et_2O; 3:2) to furnish lactone **2i** as an inseparable mixture of diastereomers as a colourless oil colourless (38 mg, 83%, 64:36 dr).[53,54]

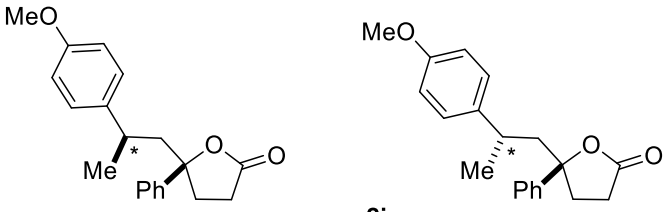
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.06 (m, 15H_{maj}, 15H_{min}), 6.34 (dd, *J* = 15.8, 7.9 Hz, 1H_{maj}), 6.18 – 6.06 (m, 1H_{maj}, 1H_{min}), 6.01 (dd, *J* = 15.8, 7.8 Hz, 1H_{min}), 3.62 (td, *J* = 7.9, 5.4 Hz, 1H_{min}), 3.45 – 3.38 (m, 1H_{maj}), 2.66 – 2.32 (m, 6H_{maj}, 6H_{min}).

^{13}C NMR (101 MHz, $CDCl_3$) **for the major diastereomer** (from the mixture): δ 176.5, 144.0, 142.3, 137.4, 133.6, 129.8, 128.7 (2C), 128.6 (4C), 127.8, 127.7 (2C), 127.3, 126.5, 126.3 (2C), 125.2 (2C), 89.3, 48.3, 45.2, 35.5, 28.6. **Selected peaks for the minor diastereomer** (from the mixture): δ 176.4, 144.4, 142.8, 137.3, 133.4, 128.8, 128.7, 128.4, 127.9, 127.2, 126.6, 126.2, 125.1, 89.0, 48.3, 45.1, 35.5, 28.7.

IR (film) ν_{max}: 3027, 1776, 1175, 912, 746, 700 cm^{-1}.

HRMS (ESI): $C_{26}H_{24}O_2Na$ $[M+Na]^+$ requires m/z 391.1669, found m/z 391.1675 (Δ = 1.65 ppm).

(±)-(*R*)-5-((*R*)-2-(4-Methoxyphenyl)propyl)-5-phenyldihydrofuran-2(3H)-one and **(±)-(*R*)-5-((*S*)-2-(4-Methoxyphenyl)propyl)-5-phenyldihydrofuran-2(3H)-one 2j**



2j
$C_{20}H_{22}O_3$
310.39 g mol^{-1}
*65:35 dr

Carboxylic acid **1a** (20 mg, 0.11 mmol, 1.0 equiv), (1-(4-methoxyphenyl)ethan-1-ol (17 mg, 0.11 mmol, 1.0 equiv) and TFA (2.6 µL, 34 µmol, 0.31 equiv) in HFIP (3.1 mL) were subjected to the general procedure **3**. The crude product was purified by flash column chromatography

[53] dr determined based on the crude reaction mixture.
[54] Relative stereochemistry of the major and minor diastereomers could not be determined.

(SiO_2; pentane:Et_2O; 3:2) to furnish lactone **2j** as an inseparable mixture of diastereomers as a colourless oil colourless (32 mg, 92%, 65:35 dr).[55,56]

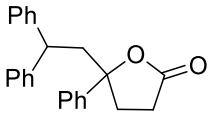
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.27 (m, $5H_{maj}$, $5H_{min}$), 7.08 – 7.02 (m, $2H_{min}$), 6.94 – 6.88 (m, $2H_{maj}$), 6.85 – 6.79 (m, $2H_{min}$), 6.78 – 6.71 (m, $2H_{maj}$), 3.78 (s, $3H_{min}$), 3.76 (s, $3H_{maj}$), 2.86 (q, J = 6.7 Hz, $1H_{min}$), 2.56 – 2.15 (m, $7H_{maj}$, $6H_{min}$), 1.20 (d, J = 6.8 Hz, $3H_{maj}$), 1.00 (d, J = 7.0 Hz, $3H_{min}$).

^{13}C NMR (101 MHz, $CDCl_3$) **for the major diastereomer** (from the mixture): δ 176.8, 157.9, 142.1, 139.6, 128.6 (2C), 127.8, 127.7 (2C), 125.2 (2C), 113.9 (2C), 89.8, 55.4, 50.8, 36.2, 35.4, 28.5, 23.3. **Selected peaks for the minor diastereomer** (from the mixture): δ 128.7, 127.9, 124.7, 114.1, 50.4, 35.04, 34.98, 28.6, 24.2.

IR (film) ν_{max}: 2958, 1778, 1513, 1246, 1178, 1034, 832, 704 cm^{-1}.

HRMS (ESI): $C_{20}H_{22}O_3Na$ $[M+Na]^+$ requires m/z 333.1461, found m/z 333.1463 (Δ = 0.54 ppm).

5-(2,2-Diphenylethyl)-5-phenyldihydrofuran-2(3H)-one 2k



2k
$C_{24}H_{22}O_2$
342.44 g mol^{-1}

Experimental procedure of the reaction conducted on 0.12 mmol scale:

Carboxylic acid **1a** (22 mg, 0.12 mmol, 1.0 equiv), benzhydrol (23 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.3 mL) were subjected to the general procedure **3**. The crude product was purified by flash column chromatography (SiO_2; pentane:Et_2O; 3:2) to furnish lactone **2k** as a white solid (42.5 mg, quant).

Experimental procedure for the reaction conducted on 1.2 mmol scale:

Carboxylic acid **1a** (0.210 g, 1.19 mmol, 1.00 equiv) and benzhydrol (0.220 g, 1.19 mmol, 1.00 equiv) were transferred to a round bottom flask and flushed with nitrogen for 10 min. HFIP (32 mL) followed by TFA (27.5 µL, 0.37 mmol, 0.31 equiv) were then added in one portion. The reaction mixture was stirred at RT for 2 h, and the volatiles were removed *in vacuo*. The crude

[55] dr determined based on the crude reaction mixture.
[56] Relative stereochemistry of the major and minor diastereomers could not be determined.

product was purified by flash column chromatography (SiO_2; pentane:Et_2O; 3:2) to furnish lactone **2k** as a white solid (0.400 g, 98%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 6.93 (m, 15H), 3.93 (t, *J* = 6.7 Hz, 1H), 2.82 (d, *J* = 6.6 Hz, 2H), 2.51 – 2.08 (m, 4H).

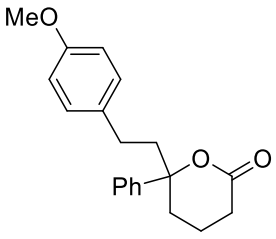
^{13}C NMR (101 MHz, $CDCl_3$): δ 176.4, 144.7, 144.5, 142.4, 128.7 (2C), 128.6 (2C), 128.5 (2C), 127.8 (3C), 127.7 (2C), 126.4, 126.3, 125.1 (2C), 89.4, 47.8, 47.1, 34.5, 28.8.

M.p.: 98-99 °C

IR (film) ν_{max}: 3028, 2360, 1776, 1494, 1451, 1174, 1029, 932, 744, 701 cm^{-1}.

HRMS (ESI): calculated for $C_{24}H_{22}O_2Na$ $[M+Na]^+$ requires m/z 365.1512, found m/z 365.1519 (Δ = 1.90 ppm).

6-(4-Methoxyphenethyl)-6-phenyltetrahydro-2H-pyran-2-one 2l



2l
$C_{20}H_{22}O_3$
310.39 g mol^{-1}

Carboxylic acid **1b** (24.2 mg, 0.127 mmol, 1.00 equiv), 4-methoxybenzyl alcohol (17.5 mg, 0.127 mmol, 1.00 equiv) and TFA (2.9 µL, 38 µmol, 0.30 equiv) in HFIP (3.4 mL) were subjected to the general procedure **3**. The crude product was purified by flash column chromatography (SiO_2; pentane:Et_2O; 1:1) to furnish lactone **2l** as a colourless oil (16.5 mg, 42%).

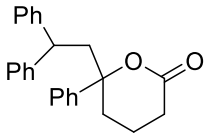
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.27 (m, 5H), 7.08 – 6.95 (m, 2H), 6.84 – 6.71 (m, 2H), 3.76 (s, 3H), 2.79 – 2.67 (m, 1H), 2.55 – 2.41 (m, 2H), 2.37 – 1.99 (m, 5H), 1.82 – 1.71 (m, 1H), 1.63 – 1.50 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 171.8, 157.9, 142.9, 133.8, 129.3 (2C), 128.9 (2C), 127.5, 125.1 (2C), 113.9 (2C), 87.5, 55.4, 46.2, 33.4, 29.4, 28.6, 16.4.

IR (film) ν_{max}: 2981, 2888, 1732, 1513, 1382, 1245, 1178, 1050, 952, 824, 735, 703 cm^{-1}.

HRMS (ESI): calculated for $C_{20}H_{22}O_3Na$ $[M+Na]^+$ requires m/z 333.1461, found m/z 333.1464 (*Δ* = 0.84 ppm).

6-(2,2-Diphenylethyl)-6-phenyltetrahydro-2H-pyran-2-one 2m



2m
$C_{25}H_{24}O_2$
356.47 g mol^{-1}

Carboxylic acid **1b** (19.1 mg, 0.100 mmol, 1.00 equiv), benzhydrol (18.4 mg, 0.100 mmol, 1.00 equiv) and TFA (2.3 µL, 0.030 mmol, 0.30 equiv) in HFIP (2.7 mL) were subjected to the general procedure **3**. The crude product was purified by flash column chromatography (SiO_2; pentane:Et_2O; 3:2) to furnish lactone **2m** as a colourless oil (27.1 mg, 76%).

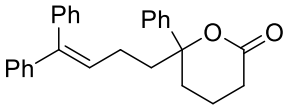
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.00 (m, 15H), 4.14 (t, *J* = 6.5 Hz, 1H), 2.79 (d, *J* = 6.6 Hz, 2H), 2.44 – 2.26 (m, 2H), 2.07 (dt, *J* = 14.3, 4.2 Hz, 1H), 1.82 (ddd, *J* = 14.3, 12.2, 4.5 Hz, 1H), 1.69 – 1.56 (m, 1H), 1.54 – 1.38 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 171.6, 145.3, 144.9, 142.9, 128.7 (2C), 128.6 (2C), 128.4 (2C), 127.9 (2C), 127.8 (2C), 127.5, 126.3, 126.0, 125.3 (2C), 87.7, 49.7, 46.6, 32.4, 29.2, 16.4.

IR (film) ν_{max}: 2980, 2361, 1733, 1599, 1494, 1449, 1256, 1236, 1047, 912, 735, 701 cm^{-1}.

HRMS (ESI): calculated for $C_{25}H_{25}O_2$ $[M+H]^+$ requires m/z 357.1849, found m/z 357.1849 (*Δ* = -0.03 ppm).

6-(4,4-Diphenylbut-3-en-1-yl)-6-phenyltetrahydro-2H-pyran-2-one 2n



2n
$C_{27}H_{26}O_2$
382.50 g mol^{-1}

Carboxylic acid **1b** (19.1 mg, 0.100 mmol, 1.00 equiv), 1,1-diphenylprop-2-en-1-ol **14b** (21.0 mg, 0.100 mmol, 1.00 equiv) and TFA (2.3 µL, 0.030 mmol, 0.30 equiv) in HFIP (2.7 mL) were subjected to the general procedure **3**. The crude product was purified by flash column chromatography (SiO_2; 60 Å, 15–40 µm; pentane:Et_2O; 3:2 to 1:1) to furnish lactone **2n** as a colourless oil (17.7 mg, 46%).

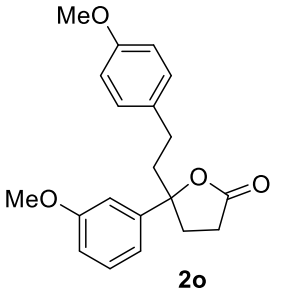
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 6.96 (m, 15H), 5.96 (t, *J* = 7.3 Hz, 1H), 2.50 – 2.33 (m, 2H), 2.28 – 2.17 (m, 2H), 2.14 – 1.89 (m, 4H), 1.78 – 1.67 (m, 1H), 1.59 – 1.45 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 142.8, 142.7, 142.4, 139.9, 129.8 (2C), 128.7 (2C), 128.7, 128.3 (2C), 128.2 (2C), 127.4, 127.3 (2C), 127.1, 127.0, 125.1 (2C), 87.5, 43.7, 32.7, 29.3, 23.9, 16.4.

IR (film) ν_{max}: 3025, 2359, 1735, 1495, 1446, 1241, 1047, 912, 764, 735, 701 cm^{-1}.

HRMS (ESI): calculated for $C_{27}H_{27}O_2$ $[M+H]^+$ requires m/z 383.2006, found m/z 383.2002 (Δ = -0.94 ppm).

5-(4-Methoxyphenethyl)-5-(3-methoxyphenyl)dihydrofuran-2(3H)-one 2o



2o
$C_{20}H_{22}O_4$
326.39 g mol^{-1}

4-(3-Methoxyphenyl)pent-4-enoic acid **1d** (25 mg, 0.12 mmol, 1.0 equiv), 4-methoxybenzyl alcohol (17 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.2 mL) were subjected to general procedure **3**. The crude product was purified by flash column chromatography (SiO_2, 60 Å, 15–40 µm; pentane:EtOAc; 7:3) to obtain lactone **2o** as a colourless oil (11 mg, 28%).

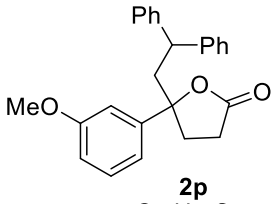
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.28 (m, 1H), 7.02 – 6.97 (m, 2H), 6.97 – 6.92 (m, 2H), 6.85 (ddd, *J* = 8.2, 2.4, 1.1 Hz, 1H), 6.81 – 6.75 (m, 2H), 3.83 (s, 3H), 3.76 (s, 3H), 2.69 – 2.38 (m, 5H), 2.34 – 2.14 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.7, 160.0, 158.0, 144.5, 133.4, 129.9, 129.3 (2C), 117.0, 114.0 (2C), 112.9, 110.9, 89.1, 55.5, 55.4, 44.8, 35.6, 29.5, 28.7.

IR (film) ν_{max}: 2995, 2360, 1778, 1611, 1513, 1247, 1181, 1040 cm^{-1}.

HRMS (ESI): calculated for $C_{20}H_{22}O_4Na$ $[M+Na]^+$ requires m/z 349.1410, found m/z 349.1417 (Δ = 1.90 ppm).

5-(2,2-Diphenylethyl)-5-(3-methoxyphenyl)dihydrofuran-2(3H)-one 2p



2p
$C_{25}H_{24}O_3$
372.46 g mol^{-1}

4-(3-Methoxyphenyl)pent-4-enoic acid **1d** (25 mg, 0.12 mmol, 1.0 equiv), benzhydrol (22 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.2 mL) were subjected to general procedure **3**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 3:2) to obtain lactone **2p** as a colourless oil (29 mg, 65%).

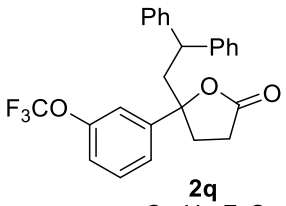
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 – 7.02 (m, 11H), 6.91 – 6.70 (m, 3H), 3.98 (t, *J* = 6.7 Hz, 1H), 3.76 (s, 3H), 2.91 – 2.76 (m, 2H), 2.51 – 2.13 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.4, 159.7, 144.7, 144.5, 144.1, 129.6, 128.7 (2C), 128.5 (2C), 127.9 (2C), 127.7 (2C), 126.5, 126.3, 117.4, 113.2, 111.2, 89.3, 55.4, 47.8, 47.1, 34.7, 28.8.

IR (film) ν_{max}: 3027, 2940, 1776, 1494, 1184, 1042, 743, 704 cm^{-1}.

HRMS (ESI): calculated for $C_{25}H_{24}O_3Na$ $[M+Na]^+$ requires m/z 395.1618, found m/z 395.1633 (Δ = 3.87 ppm).

5-(2,2-Diphenylethyl)-5-(3-(trifluoromethoxy)phenyl)dihydrofuran-2(3H)-one 2q



2q
$C_{25}H_{21}F_3O_3$
426.44 g mol^{-1}

4-(3-(Trifluoromethoxy)phenyl)pent-4-enoic acid **1e** (31 mg, 0.12 mmol, 1.0 equiv), benzhydrol (22 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.2 mL) were subjected to general procedure **3**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 3:2) to obtain lactone **2q** as a colourless oil (34 mg, 66%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 6.94 (m, 14H), 4.00 (dd, *J* = 7.9, 5.7 Hz, 1H), 2.94 – 2.71 (m, 2H), 2.56 – 2.42 (m, 1H), 2.42 – 2.20 (m, 3H).

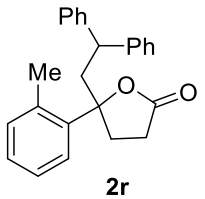
^{13}C NMR {^{19}F} (126 MHz, $CDCl_3$) δ 175.8, 149.3, 144.9, 144.6, 143.8, 130.0, 128.8 (2C), 128.6 (2C), 127.8 (2C), 127.6 (2C), 126.6, 126.4, 123.6, 120.5, 120.1, 118.0, 88.4, 47.8, 47.1, 35.2, 28.5.

^{19}F NMR (471 MHz, $CDCl_3$) δ -57.68.

IR (film) ν_{max}: 3028, 2359, 1783, 1494, 1258, 1220, 1170, 704 cm^{-1}.

HRMS (ESI): calculated for $C_{25}H_{21}F_3O_3Na$ $[M+Na]^+$ requires m/z 449.1335, found m/z 449.1335 (Δ = -0.01 ppm).

5-(2,2-Diphenylethyl)-5-(o-tolyl)dihydrofuran-2(3H)-one 2r



2r
$C_{25}H_{24}O_2$
356.47 g mol^{-1}

4-(*o*-Tolyl)pent-4-enoic acid **1f** (23 mg, 0.12 mmol, 1.0 equiv), benzhydrol (22 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.2 mL) were subjected to general procedure **3**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 7:3) to obtain lactone **2r** as a colourless oil (28 mg, 65%).

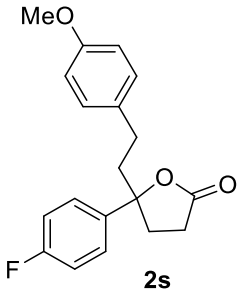
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 6.85 (m, 14H), 3.99 (t, *J* = 6.6 Hz, 1H), 3.01 – 2.82 (m, 2H), 2.54 – 2.23 (m, 7H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.2, 144.8, 144.3, 140.3, 133.9, 132.5, 128.7 (2C), 128.5 (2C), 128.0, 127.8 (2C), 127.7 (2C), 126.5, 126.2, 125.9 (2C), 90.1, 47.4, 45.9, 34.0, 28.6, 21.7.

IR (film) ν_{max}: 3062, 2359, 1776, 1493, 1453, 1194, 934, 740, 704 cm^{-1}.

HRMS (ESI): calculated for $C_{25}H_{24}O_2Na$ $[M+Na]^+$ requires m/z 379.1669, found m/z 379.1686 (Δ = 4.60 ppm).

5-(4-Fluorophenyl)-5-(4-methoxyphenethyl)dihydrofuran-2(3H)-one 2s



2s
$C_{19}H_{19}FO_3$
314.36 g mol^{-1}

4-(4-Fluorophenyl)pent-4-enoic acid **1g** (23 mg, 0.12 mmol, 1.0 equiv), 4-methoxybenzyl alcohol (17 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.2 mL) were subjected to general procedure **3**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 11:9) to obtain lactone **2s** as a colourless oil (29 mg, 77%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.32 (m, 2H), 7.09 (t, *J* = 8.7 Hz, 2H), 7.02 – 6.94 (m, 2H), 6.82 – 6.74 (m, 2H), 3.76 (s, 3H), 2.69 – 2.39 (m, 5H), 2.32 – 2.16 (m, 3H).

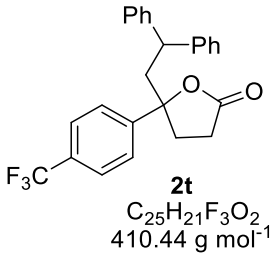
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.4, 162.3 (d, *J* = 246.8 Hz), 158.1, 138.5 (d, *J* = 3.2 Hz), 133.1, 129.2 (2C), 126.6 (d, *J* = 8.0 Hz, 2C), 115.7 (d, *J* = 21.5 Hz, 2C), 114.0 (2C), 88.8, 55.4, 44.9, 35.5, 29.4, 28.7.

^{19}F NMR (377 MHz, $CDCl_3$) δ -114.69.

IR (film) ν_{max}: 2936, 1781, 1513, 1246, 1182, 1037, 938, 839 cm^{-1}.

HRMS (ESI): calculated for $C_{19}H_{19}FO_3Na$ $[M+Na]^+$ requires m/z 337.1210, found m/z 337.1226 (Δ = 4.60 ppm).

5-(2,2-Diphenylethyl)-5-(4-(trifluoromethyl)phenyl)dihydrofuran-2(3H)-one 2t



2t
$C_{25}H_{21}F_3O_2$
410.44 g mol^{-1}

4-(4-(Trifluoromethyl)phenyl)pent-4-enoic acid **1h** (29.3 mg, 0.120 mmol, 1.00 equiv), benzhydrol (22.1 mg, 0.120 mmol, 1.00 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP

(3.2 mL) were subjected to general procedure **3**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 7:3) to obtain lactone **2t** as a white solid (33.1 mg, 67%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 6.87 (m, 14H), 4.02 (dd, *J* = 8.0, 5.5 Hz, 1H), 2.99 – 2.88 (m, 1H), 2.86 – 2.78 (m, 1H), 2.59 – 2.45 (m, 1H), 2.43 – 2.26 (m, 3H).

^{13}C NMR {^{19}F} (126 MHz, $CDCl_3$) δ 175.9, 146.4, 144.6, 143.8, 130.0, 128.8 (2C), 128.6 (2C), 127.8 (2C), 127.6 (2C), 126.6, 126.3, 125.5 (2C), 125.4 (2C), 124.0, 88.6, 47.8, 47.1, 35.4, 28.5.

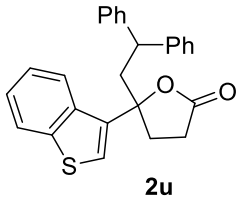
^{19}F NMR (471 MHz, $CDCl_3$) δ -62.75.

M.p.: 120-123 °C

IR (film) ν_{max}: 3029, 1781, 1328, 1169, 1124, 1071, 705 cm^{-1}.

HRMS (ESI): calculated for $C_{25}H_{21}F_3O_2Na$ [M+Na]+ requires m/z 433.1386, found m/z 433.1385 (Δ = -0.21 ppm).

5-(Benzo[b]thiophen-3-yl)-5-(2,2-diphenylethyl)dihydrofuran-2(3H)-one 2u



2u
$C_{26}H_{22}O_2S$
398.52 g mol^{-1}

4-(Benzo[b]thiophen-3-yl)pent-4-enoic acid **1i** (28 mg, 0.12 mmol, 1.0 equiv), benzhydrol (22 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.2 mL) were subjected to general procedure **3**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 7:3) to obtain lactone **2u** as a white solid (30 mg, 63%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.71 (m, 2H), 7.39 – 7.09 (m, 8H), 7.02 – 6.85 (m, 5H), 4.04 (dd, *J* = 8.1, 5.4 Hz, 1H), 3.19 – 3.07 (m, 1H), 3.05 – 2.94 (m, 1H), 2.62 – 2.30 (m, 4H).

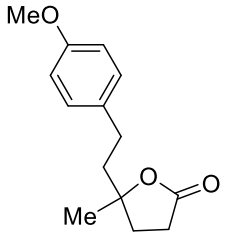
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.3, 144.7, 143.3, 141.6, 136.5, 135.8, 128.6 (2C), 128.1 (2C), 127.6 (4C), 126.4, 126.0, 124.4, 124.2, 123.4, 123.2, 122.9, 88.6, 47.4, 45.8, 33.6, 28.6.

M.p.: 74-77 °C

IR (film) ν_{max}: 3027, 2360, 1776, 1181, 911, 737, 704 cm^{-1}.

HRMS (ESI): calculated for $C_{26}H_{22}SO_2Na$ $[M+Na]^+$ requires m/z 421.1233, found m/z 421.1243 (Δ = 2.43 ppm).

5-(4-Methoxyphenethyl)-5-methyldihydrofuran-2(3H)-one 2v



2v
$C_{14}H_{18}O_3$
234.30 g mol^{-1}

4-Methylpent-4-enoic acid **1j** (14 mg, 0.12 mmol, 1.0 equiv), 4-methoxybenzyl alcohol (17 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.2 mL) were subjected to general procedure **3**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 3:2) to obtain lactone **2v** as a colourless oil (15 mg, 53%).

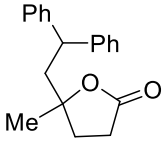
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 – 7.05 (m, 2H), 6.88 – 6.78 (m, 2H), 3.79 (s, 3H), 2.72 – 2.52 (m, 4H), 2.18 – 1.87 (m, 4H), 1.45 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.8, 158.1, 133.4, 129.3 (2C), 114.1 (2C), 86.5, 55.4, 43.3, 33.3, 29.4, 29.2, 25.8.

IR (film) ν_{max}: 2980, 1769, 1514, 1247, 1178, 937, 824, 745, 648 cm^{-1}.

HRMS (ESI): calculated for $C_{14}H_{19}O_3$ $[M+H]^+$ requires m/z 235.1329, found m/z 235.1330 (Δ = 0.53 ppm).

5-(2,2-Diphenylethyl)-5-methyldihydrofuran-2(3H)-one 2w



2w
$C_{19}H_{20}O_2$
280.37 g mol^{-1}

4-Methylpent-4-enoic acid **1j** (14 mg, 0.12 mmol, 1.0 equiv), benzhydrol (22 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.2 mL) were subjected to general

procedure **3**. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 13:7) to obtain lactone **2w** as a colourless oil (32 mg, 95%).

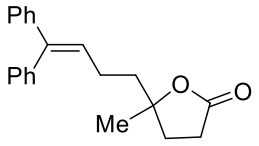
^{1}H NMR (700 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 8H), 7.21 – 7.14 (m, 2H), 4.17 (dd, *J* = 7.7, 6.2 Hz, 1H), 2.60 – 2.49 (m, 3H), 2.47 – 2.38 (m, 1H), 1.88 (ddd, *J* = 13.0, 9.8, 8.0 Hz, 1H), 1.77 (ddd, *J* = 13.0, 9.8, 5.6 Hz, 1H), 1.27 (s, 3H).

^{13}C NMR (176 MHz, $CDCl_3$) δ 176.6, 145.0, 144.8, 128.9 (2C), 128.8 (2C), 127.8 (2C), 127.6 (2C), 126.6, 126.6, 86.9, 47.2, 46.2, 33.4, 29.1, 26.6.

IR (film) ν_{max}: 3027, 2361, 1768, 1452, 1179, 1071, 912, 737, 705 cm^{-1}.

HRMS (ESI): calculated for $C_{19}H_{20}O_2Na$ $[M+Na]^+$ requires m/z 303.1356, found m/z 303.1354 (*Δ* = -0.51 ppm).

5-(4,4-Diphenylbut-3-en-1-yl)-5-methyldihydrofuran-2(3H)-one 2x



2x
$C_{21}H_{22}O_2$
306.41 g mol^{-1}

4-Methylpent-4-enoic acid **1j** (11.4 mg, 0.100 mmol, 1.00 equiv), 1,1-diphenylprop-2-en-1-ol **14b** (21.0 mg, 0.100 mmol, 1.00 equiv) and TFA (2.3 µL, 30 µmol, 0.3 equiv) in HFIP (2.7 mL) were subjected to general procedure **3**, except that the reaction was left for 3 h. The crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 1:1) to obtain lactone **2x** as a colourless oil (21.4 mg, 70%).

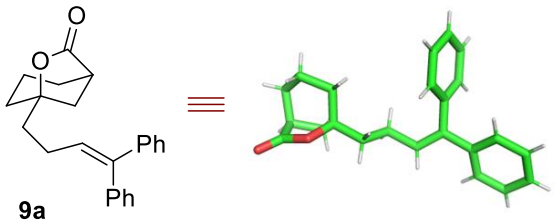
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.11 (m, 10H), 6.06 (t, *J* = 7.4 Hz, 1H), 2.65 – 2.43 (m, 2H), 2.29 – 2.11 (m, 2H), 2.03 – 1.75 (m, 4H), 1.32 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.7, 142.7, 142.4, 139.9, 129.8 (2C), 128.4 (2C), 128.25 (2C), 128.18, 127.3 (3C), 127.2, 86.5, 41.0, 32.9, 29.2, 25.6, 24.6.

IR (film) ν_{max}: 2972, 2360, 2342, 1769, 1383, 1252, 1177, 1149, 954, 938, 765, 702 cm^{-1}.

HRMS (ESI): calculated for $C_{21}H_{22}O_2Na$ $[M+Na]^+$ requires m/z 329.1512, found m/z 329.1510 (*Δ* = -0.62 ppm).

(±)-(1*R*,5*R*)-5-(4,4-Diphenylbut-3-en-1-yl)-6-oxabicyclo[3.2.1]octan-7-one 9a



9a
$C_{23}H_{24}O_2$
332.44 g mol^{-1}

[X-ray]

Carboxylic acid **6** (29.0 mg, 0.207 mmol, 1.00 equiv), 1,1-diphenylprop-2-en-1-ol **14b** (43.5 mg, 0.207 mmol, 1.00 equiv) and TFA (4.8 µL, 0.062 mmol, 0.30 equiv) in HFIP (5.6 mL) were subjected to the general procedure **3**, except the reaction was performed in a round bottomed flask, instead of a microwave vial. The crude product was purified by flash column chromatography (SiO_2; 60 Å, 15–40 µm; pentane:Et_2O; 7:3) to furnish lactone **9a** as a colourless oil (31.7 mg, 46%, >95:5 dr).

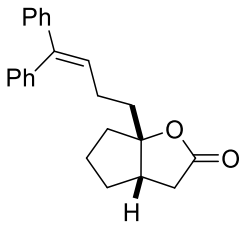
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.11 (m, 10H), 6.06 (t, *J* = 7.4 Hz, 1H), 2.74 – 2.65 (m, 1H), 2.28 – 2.15 (m, 2H), 2.11 – 2.02 (m, 1H), 1.94 – 1.56 (m, 7H), 1.55 – 1.40 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 178.5, 142.5 (2C), 140.0, 129.8 (2C), 128.5, 128.4 (2C), 128.2 (2C), 127.3 (2C), 127.3, 127.1, 86.9, 41.3, 41.2, 38.9, 32.5, 26.3, 24.0, 19.4.

IR (film) ν_{max}: 2944, 2874, 1773, 1494, 1444, 1286, 1134, 917, 765, 733, 701 cm^{-1}.

HRMS (ESI): calculated for $C_{23}H_{25}O_2$ $[M+H]^+$ requires m/z 333.1849, found m/z 333.1857 (*Δ* = 2.37 ppm).

(±)-(3*aS*,6*aR*)-6*a*-(4,4-Diphenylbut-3-en-1-yl)hexahydro-2H-cyclopenta[b]furan-2-one 9b



9b
$C_{23}H_{24}O_2$
332.44 g mol^{-1}

2-(2-Methylenecyclopentyl)acetic acid **7** (17 mg, 0.12 mmol, 1.0 equiv), 1,1-diphenylprop-2-en-1-ol **14b** (25 mg, 0.12 mmol, 1.0 equiv) and TFA (2.8 µL, 37 µmol, 0.31 equiv) in HFIP (3.2 mL) were subjected to the general procedure **3**. The crude product was purified by flash

column chromatography (SiO_2; pentane:EtOAc; 8:2) to furnish lactone **9b** as a single diastereomer as a colourless oil (26 mg, 65%).

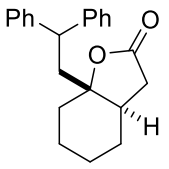
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.05 (m, 10H), 6.06 (t, *J* = 7.4 Hz, 1H), 2.81 – 2.69 (m, 1H), 2.45 – 2.36 (m, 1H), 2.31 – 2.17 (m, 3H), 1.99 (dddd, *J* = 13.6, 5.5, 3.7, 1.5 Hz, 1H), 1.94 – 1.79 (m, 3H), 1.73 – 1.60 (m, 2H), 1.56 – 1.45 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 177.3, 142.60, 142.57, 139.9, 129.8 (2C), 128.4 (3C), 128.3 (2C), 127.34 (2C), 127.31, 127.2, 97.8, 42.3, 39.5, 38.1, 37.0, 34.5, 25.1, 24.0.

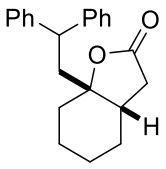
IR (film) ν_{max}: 2980, 2251, 1768, 1197, 913, 736, 703, 649 cm^{-1}.

HRMS (ESI): calculated for $C_{23}H_{24}O_2Na$ $[M+Na]^+$ requires m/z 355.1669, found m/z 355.1670 (*Δ* = 0.41 ppm).

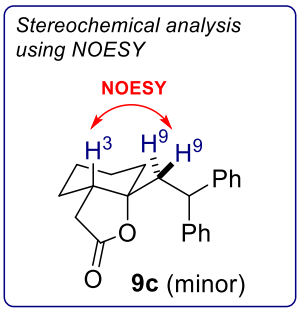
(±)-(3*aR*,7*aR*)-7*a*-(2,2-Diphenylethyl)hexahydrobenzofuran-2(3H)-one 9c-major and (±)-(3*aS*,7*aR*)-7*a*-(2,2-diphenylethyl)hexahydrobenzofuran-2(3H)-one 9c-minor



Major-9c
$C_{22}H_{24}O_2$
320.43 g mol^{-1}



Minor-9c
$C_{22}H_{24}O_2$
320.43 g mol^{-1}



Carboxylic acid **8** (30.8 mg, 0.200 mmol, 1.00 equiv), benzhydrol (36.8 mg, 0.200 mmol, 1.00 equiv) and TFA (4.6 µL, 0.060 mmol, 0.30 equiv) in HFIP (5.4 mL) were subjected to the general procedure **3**, except that the rection was performed at 0 °C. The crude product was purified by flash column chromatography (SiO_2; pentane:Et_2O; 7:3) to furnish lactone **9c** as an inseparable mixture of diastereomers as a colourless oil (45.6 mg, 71%, 70:30 dr).[57,58]

^{1}H NMR (700 MHz, $CDCl_3$) δ 7.43 – 6.98 (m, $10H_{maj}$, $10H_{min}$), 4.34 – 4.22 (m, $1H_{maj}$, $1H_{min}$), 2.72 (dd, *J* = 14.6, 8.9 Hz, $1H_{maj}$), 2.61 – 2.51 (m, $2H_{min}$), 2.47 – 2.32 (m, $2H_{maj}$, $2H_{min}$), 2.26 – 2.19 (m, $1H_{min}$), 2.13 – 2.05 (m, $2H_{maj}$), 1.82 – 1.72 (m, $3H_{maj}$), 1.71 –1.64 (m, $1H_{min}$) 1.55 – 1.18 (m, $5H_{maj}$, $7H_{min}$).

[57] dr was calculated after column chromatography.
[58] Relative stereochemistry of the major and minor diastereomer is assigned based on the NOESY analysis of the mixture.

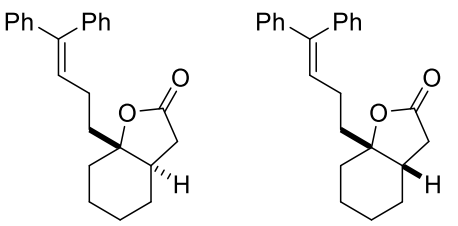
^{13}C NMR (176 MHz, $CDCl_3$) **for the major diastereomer** (from the mixture): δ 176.3, 145.9, 144.8, 128.8 (2C), 128.8 (2C), 128.2 (2C), 127.6 (2C), 126.6, 126.3, 87.6, 48.8, 46.5, 35.3, 33.6, 33.2, 25.4, 24.3, 22.5. **Selected peaks for the minor diastereomer** (from the mixture): δ 176.7, 145.4, 145.2, 128.8 (2C), 128.8 (2C), 127.9 (2C), 127.7 (2C), 126.50, 126.48, 87.4, 46.8, 43.2, 38.7, 34.5, 25.8, 21.8, 20.6.

NOESY-2D (700 MHz, $CDCl_3$): between H-3_{min} and H-9_{min}.

IR (film) ν_{max}: 2981, 2884, 1776, 1494, 1452, 1382, 1202, 1146, 966, 910, 734, 704 cm^{-1}.

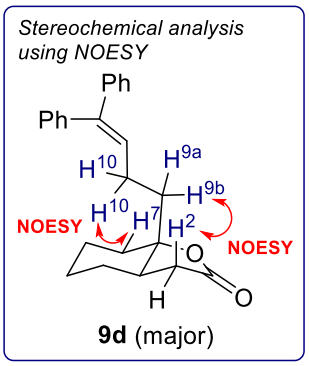
HRMS (ESI): calculated for $C_{22}H_{24}O_2Na$ $[M+Na]^+$ requires m/z 343.1669, found m/z 343.1683 (*Δ* = 4.21 ppm).

(±)-(3*aR*,7*aR*)-7*a*-(4,4-Diphenylbut-3-en-1-yl)hexahydrobenzofuran-2(3H)-one 9d-major and (±)-(3*aS*,7*aR*)-7a-(4,4-diphenylbut-3-en-1-yl)hexahydrobenzofuran-2(3H)-one 9d-minor



Major-9d
$C_{24}H_{26}O_2$
346.47 g mol^{-1}

Minor-9d
$C_{24}H_{26}O_2$
346.47 g mol^{-1}



Carboxylic acid **8** (15.4 mg, 0.100 mmol, 1.00 equiv), 1,1-diphenylprop-2-en-1-ol **14b** (21.0 mg, 0.100 mmol, 1.00 equiv) and TFA (2.3 µL, 0.030 mmol, 0.30 equiv) in HFIP (2.7 mL) were subjected to the general procedure **3**, except that the rection was performed at 0 °C. The crude product was purified by flash column chromatography (SiO_2; 60 Å, 15–40 µm; pentane:Et_2O; 7:3) to furnish lactone **9d** as an inseparable mixture of diastereomers as a colourless oil (22.3 mg, 64%, 70:30 dr).[59] An analytical amount of the major diastereomer was separated to assist the data analysis.

Data for major diastereomer 9d

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.05 (m, 10H), 6.08 (dd, *J* = 8.1, 7.0 Hz, 1H), 2.42 – 2.32 (m, 2H), 2.29 – 1.97 (m, 4H), 1.92 – 1.64 (m, 4H), 1.56 – 1.20 (m, 5H).

[59] dr was determined of the crude reaction mixture (700 MHz, THF-d8).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.5, 142.8, 142.5, 139.9, 129.8 (2C), 128.6, 128.4 (2C), 128.3 (2C), 127.3 (3C), 127.1, 87.3, 47.8, 33.3, 33.2, 29.5, 25.4, 24.6, 23.3, 22.6.

NOESY-2D (600 MHz, $CDCl_3$) δ between H-2 and H-9_b, between H-7_a and H-10.

IR (film) ν_{max}: 2981, 1778, 1657, 1383, 1072, 966, 909, 732, 703 cm^{-1}.

HRMS (ESI): calculated for $C_{24}H_{26}O_2Na$ $[M+Na]^+$ requires m/z 369.1825, found m/z 369.1826 (Δ = 0.26 ppm).

Selected peaks for the minor diastereomer (from the mixture):

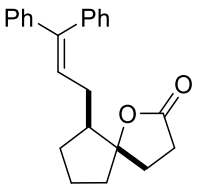
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.06 (t, *J* = 7.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.7, 142.6, 140.0, 129.8, 128.5, 86.8, 38.6, 37.6, 34.8, 32.2, 26.2, 24.1, 21.8, 20.9.

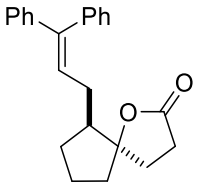
IR (film) ν_{max}: 2980, 2884, 1778, 1444, 1382, 1146, 1073, 966, 905, 764, 733, 701 cm^{-1}.

HRMS (ESI): calculated for $C_{24}H_{26}O_2Na$ $[M+Na]^+$ requires m/z 369.1825, found m/z 369.1841 (Δ = 4.32 ppm).

(±)-(5*S*,6*S*)-6-(3,3-Diphenylallyl)-1-oxaspiro[4.4]nonan-2-one 12a-major and (±)-(5*R*,6*S*)-6-(3,3-diphenylallyl)-1-oxaspiro[4.4]nonan-2-one 12a-minor



Major-12a
$C_{23}H_{24}O_2$
332.44 g mol^{-1}



Minor-12a
$C_{23}H_{24}O_2$
332.44 g mol^{-1}

Carboxylic acid **10** (14.0 mg, 0.100 mmol, 1.00 equiv), 1,1-diphenylprop-2-en-1-ol **14b** (21.0 mg, 0.100 mmol, 1.00 equiv) and TFA (2.3 µL, 0.030 mmol, 0.30 equiv) in HFIP (2.7 mL) were subjected to the general procedure **3**. The crude product was purified by flash column chromatography (SiO_2; 60 Å, 15–40 µm; PhMe:Et_2O; 47:3) to furnish lactone **12a** as an inseparable mixture of diastereomers as a colourless oil (12.6 mg, 38%, 75:25 dr).[60,61]

[60] Relative stereochemistry of the major diastereomer **12a** is assigned in analogy to lactone **12b** and based on aldehyde **13**.
[61] dr was calculated based on the crude reaction mixture.

Major diastereomer 12a (from the mixture):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.10 (m, 10H), 6.04 (dd, *J* = 8.1, 6.2 Hz, 1H), 2.61 – 2.36 (m, 2H), 2.33 – 2.17 (m, 2H), 2.14 – 1.89 (m, 4H), 1.88 – 1.69 (m, 2H), 1.69 – 1.51 (m, 2H), 1.50 – 1.37 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.7, 143.1, 142.5, 140.0, 129.9 (2C), 128.4 (2C), 128.3 (2C), 127.32 (3C), 127.28, 127.2, 96.2, 47.6, 37.2, 30.5, 29.6, 28.9, 28.0, 20.5.

Characteristic peaks for minor diastereomer 12a (from the mixture):

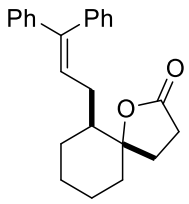
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.10 (dd, *J* = 8.0, 7.1 Hz, 1H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.9, 142.9, 139.9, 129.9, 128.3, 127.8, 127.1, 95.2, 49.7, 39.3, 30.14, 30.09, 29.5, 28.7, 21.4.

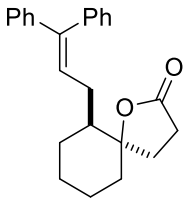
IR (film) ν_{max}: 2980, 2362, 1771, 1444, 1382, 1243, 1152, 1074, 949, 914, 771, 702 cm^{-1}.

HRMS (ESI): calculated for $C_{23}H_{24}O_2Na$ $[M+Na]^+$ requires m/z 355.1669, found m/z 355.1676 (*Δ* = 2.10 ppm).

(±)-(5*S*,6*S*)-6-(3,3-Diphenylallyl)-1-oxaspiro[4.5]decan-2-one 12b-major and (±)-(5*R*,6*S*)-6-(3,3-diphenylallyl)-1-oxaspiro[4.5]decan-2-one 12b-minor



Major-12b
$C_{24}H_{26}O_2$
346.47 g mol^{-1}



Minor-12b
$C_{24}H_{26}O_2$
346.47 g mol^{-1}

Carboxylic acid **11** (30.0 mg, 0.195 mmol, 1.00 equiv), 1,1-diphenylprop-2-en-1-ol **14b** (40.9 mg, 0.195 mmol, 1.00 equiv) and TFA (4.5 µL, 0.059 mmol, 0.30 equiv) in HFIP (5.3 mL) were subjected to the general procedure **3**. The crude product was purified by flash column chromatography (SiO_2; pentane:Et_2O; 7:3 to 3:2) to furnish lactone **12b** as an inseparable mixture of diastereomers as a colourless oil (50.8 mg, 75%, 71:29 dr).[62, 63]

Major diastereomer 12b (from the mixture):

[62] dr was calculated after column chromatography.
[63] Relative stereochemistry of the major diastereomer is assigned based on aldehyde **13**.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 – 7.08 (m, 10H), 6.05 (dd, *J* = 8.0, 6.0 Hz, 1H), 2.64 – 2.47 (m, 1H), 2.45 – 2.26 (m, 2H), 2.09 – 1.43 (m, 9H), 1.39 – 1.23 (m, 2H), 1.07 (dtd, *J* = 14.6, 10.8, 4.0 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.7, 143.0, 142.5, 140.0, 129.9 (2C), 128.3 (2C), 128.2 (2C), 127.7, 127.3 (2C), 127.13, 127.09, 89.3, 45.6, 37.1, 29.3, 29.0, 28.2, 26.5, 24.1, 23.1.

Characteristic peaks for minor diastereomer 12b (from the mixture):

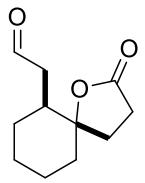
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.13 (dd, *J* = 8.1, 6.9 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 177.0, 143.1, 142.5, 139.9, 129.8, 128.4, 127.7, 127.2, 88.0, 45.9, 38.1, 31.4, 29.1, 28.8, 27.8, 22.4.

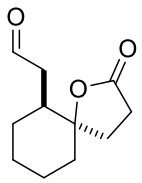
IR (film) ν_{max}: 2981, 1769, 1494, 1446, 1382, 1148, 1131, 966, 952, 912, 762, 733, 702 cm^{-1}.

HRMS (ESI): calculated for $C_{24}H_{27}O_2$ $[M+H]^+$ requires m/z 347.2006, found m/z 347.2003 (*Δ* = -0.75 ppm).

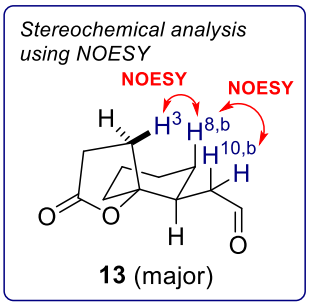
(±)-2-((5*S*,6*S*)-2-Oxo-1-oxaspiro[4.5]decan-6-yl)acetaldehyde 13-major and (±)-2-((5*R*,6*S*)-2-oxo-1-oxaspiro[4.5]decan-6-yl)acetaldehyde 13-minor



Major-13
$C_{11}H_{16}O_3$
196.25 g mol^{-1}



Minor-13
$C_{11}H_{16}O_3$
196.25 g mol^{-1}



Lactone **12b** (45.3 mg, 0.131 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (25 mL) and cooled to -78 °C. O_3/O_2 was bubbled through the solution until blue colour was observed and then left for an additional 2 min. O_2 was then bubbled through the solution until the blue colour was no longer seen, followed by N_2 for an additional 15 min. The reaction was then quenched by dropwise addition of DMS (4.5 mL) at -78 °C. The mixture was stirred at the same temperature for 30 min and then slowly warmed to rt overnight. The solution was washed with water (20 mL) and brine (20 mL). The organic layer was dried over Na_2SO_4 and volatiles were removed *in vacuo*. The crude product was purified by flash column chromatography (SiO_2; pentane:Et_2O;

1:1) to obtain aldehyde **13** as an inseparable mixture of diastereomers as a colourless oil (16.1 mg, 63%, 74:26 dr).[64]

Major diastereomer 13 (from the mixture):

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 – 9.66 (m, 1H), 2.69 – 2.47 (m, 3H), 2.46 – 2.33 (m, 1H), 2.28 – 2.16 (m, 1H), 2.03 – 1.94 (m, 2H), 1.85 – 1.47 (m, 5H), 1.45 – 1.29 (m, 2H), 1.11 (dtd, *J* = 15.0, 11.2, 3.8 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 200.8, 176.2, 88.1, 44.2, 39.4, 37.1, 29.1, 28.7, 26.0, 24.3, 23.2.

NOESY-2D (600 MHz, $CDCl_3$): between H-8_b and H-3, between H-8_b and H-10_b.

Characteristic peaks for minor diastereomer 13 (from the mixture):

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 – 9.76 (m, 1H), 2.16 – 2.06 (m, 1H), 1.94 – 1.86 (m, 1H).

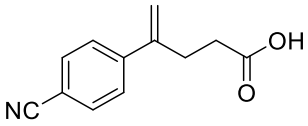
^{13}C NMR (151 MHz, $CDCl_3$) δ 201.1, 176.5, 87.3, 38.3, 31.4, 28.9, 28.7, 22.2.

IR (film) ν_{max}: 2981, 1771, 1722, 1453, 1383, 1205, 1150, 956, 913 cm^{-1}.

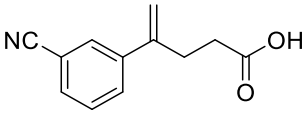
HRMS (ESI): calculated for $C_{11}H_{16}O_3Na$ $[M+Na]^+$ requires m/z 219.0992, found m/z 219.1000 (Δ = 3.79 ppm).

3.11 Unsuccessful attempts

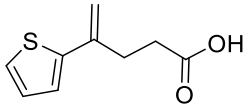
Unsuccessful substrates



No reaction

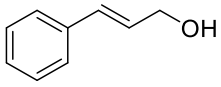


No reaction

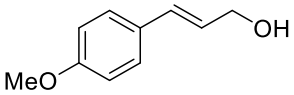


Complex reaction

Unsuccessful alcohols



Low reactivity/conversion

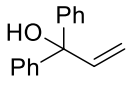


Complex reaction mixture

[64] dr was calculated after column chromatography. Relative stereochemistry was assigned based on the NOESY analysis of the mixture.

3.12 Mechanistic experiments

1,1-Diphenylprop-2-en-1-ol 14b



14b

$C_{15}H_{14}O$

210.28 g mol^{-1}

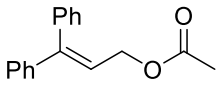
Benzophenone (0.300 g, 1.65 mmol, 1.00 equiv) was dissolved in THF (10 mL) and cooled to 0 °C. Vinyl magnesium bromide (1.0 M in THF, 1.8 mL, 1.8 mmol, 1.1 equiv) was added dropwise at the same temperature and the obtained solution was allowed to slowly warm to rt overnight. Additional vinyl magnesium bromide (1.0 M in THF, 1.0 mL, 1.0 mmol, 0.61 equiv) was then added and the solution was stirred at rt for 3 h. The reaction mixture was quenched with sat. aq. NH_4Cl (2 mL) and diluted with Et_2O (10 mL) and water (10 mL). The organic phase was separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The organic layers were combined, washed with brine (40 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography (SiO_2; pentane:Et_2O; 19:1 to 9:1) to obtain alcohol **14b** as a colourless oil (0.202 g, 58%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.19 (m, 10H), 6.58 – 6.45 (m, 1H), 5.41 – 5.27 (m, 2H). The OH proton was not found.

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.9 (2C), 143.6, 128.3 (4C), 127.4 (2C), 127.0 (4C), 114.2, 79.5.

The data are consistent with the literature[65]

3,3-Diphenylallyl acetate S24



S24

$C_{17}H_{16}O_2$

252.31 g mol^{-1}

1,1-Diphenylprop-2-en-1-ol **14b** (0.165 g, 0.787 mmol, 1.00 equiv) was dissolved in HFIP (8 mL) and KOAc (0.386 g, 3.94 mmol, 5.01 equiv) followed by AcOH (1.6 mL) were added in one portion at rt. The reaction mixture was heated at 50 °C for 4 h, cooled to rt and quenched

[65] A. Boelke, B. J. Nachtsheim, *Adv. Synth. Catal.,* 2020, **362**, 184–191.

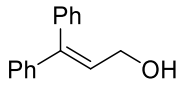
with H_2O (8 mL). The solution was extracted with CH_2Cl_2 (3 × 10 mL), the organic layers were combined, washed with brine and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography (SiO_2; pentane:Et_2O; 47:3 to 9:1) to obtain acetate **S24** as a colourless oil (0.146 g, 74%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.08 (m, 10H), 6.18 (t, *J* = 7.1 Hz, 1H), 4.64 (d, *J* = 7.1 Hz, 2H), 2.08 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 146.5, 141.6, 138.8, 129.8 (2C), 128.5 (2C), 128.3 (2C), 128.0, 127.9, 127.8 (2C, 122.5, 62.8, 21.2.

The data are consistent with the literature.[66]

3,3-Diphenylprop-2-en-1-ol 14a



14a
$C_{15}H_{14}O$
210.28 g mol^{-1}

According to the modified literature procedure,[67] acetate **S24** (0.116 g, 0.460 mmol, 1.00 equiv) was dissolved in MeOH (4.7 mL) and to the obtained solution K_2CO_3 (0.32 g, 2.3 mmol, 5.0 equiv) was added in one portion. The solution was stirred at rt overnight and then diluted with Et_2O (5 mL) and H_2O (5 mL). The organic phase was separated, and the aqueous phase was extracted with Et_2O (3 × 5 mL). The organic layers were combined, washed with brine (20 mL) and dried over Na_2SO_4. Volatiles were removed *in vacuo* and the crude product was purified by flash column chromatography (SiO_2, pentane:Et_2O; 7:3) to furnish alcohol **14a** as a colourless solid (89.4 mg, 92%)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 – 7.04 (m, 10H), 6.24 (t, *J* = 6.8 Hz, 1H), 4.21 (dd, *J* = 6.8, 5.5 Hz, 2H), 1.46 – 1.34 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 144.4, 141.9, 139.2, 129.9 (2C), 128.4 (2C), 128.3 (2C), 127.8 (3C), 127.7, 127.6, 60.9.

The analytical data are consistent with those previously reported in the literature.[68]

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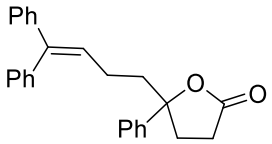
[66] Z. Zhang, C. Li, S. H. Wang, F. M. Zhang, X. Han, Y. Q. Tu, X. M. Zhang, *Org. Biomol. Chem*., 2017, **15**, 3239–3247.
[67] Y. Ishizuka, H. Fujimori, T. Noguchi, M. Kawasaki, M. Kishida, T. Nagai, N. Imai, M. Kirihara, *Chem. Lett*., 2013, **42**, 1311–1313.
[68] J. Li, C. Tan, J. Gong, Z. Yang, *Org. Lett*., 2014, **16**, 5370–5373.

5-(4,4-Diphenylbut-3-en-1-yl)-5-phenyldihydrofuran-2(3H)-one 2f using alcohol 14a



2f

$C_{26}H_{24}O_2$

368.48 g mol^{-1}

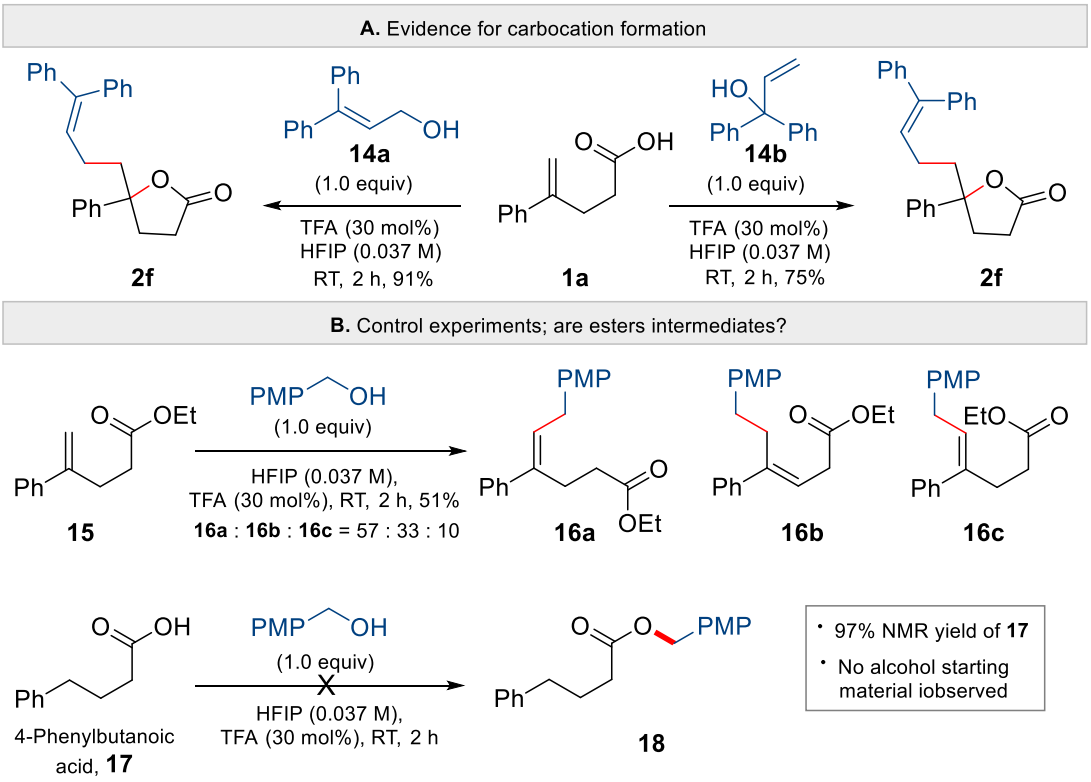
Carboxylic acid **1a** (15.4 mg, 0.100 mmol, 1.00 equiv), primary alcohol **14a** (21.0 mg, 0.100 mmol, 1.00 equiv) and TFA (2.3 µL, 0.030 mmol, 0.30 equiv) were subjected to the general procedure **3**. The crude product was purified by flash column chromatography (SiO_2; pentane:Et_2O; 3:2) to furnish lactone **2f** as a colourless oil (33.4 mg, 91% with **14a** and 75% with **14b**).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.12 (m, 13H), 7.11 – 6.98 (m, 2H), 5.97 (t, *J* = 7.3 Hz, 1H), 2.60 – 2.27 (m, 4H), 2.24 – 2.03 (m, 3H), 2.03 – 1.92 (m, 1H).

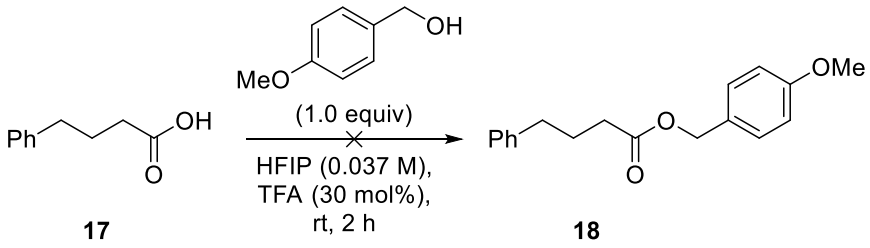
^{13}C NMR (101 MHz, $CDCl_3$): δ 176.5, 142.51, 142.49, 142.47, 139.7, 129.7 (2C), 128.6 (2C), 128.3 (2C), 128.16 (2C) 128.15, 127.7, 127.3 (2C), 127.1, 127.1, 124.7 (2C), 89.2, 42.3, 35.0, 28.7, 24.5.

The analytical data is consistent with the data obtained for this compound using alcohol **14b** (see page S43)

Control experiments



Control experiment using carboxylic acid 17



4-Phenylbutanoic acid (16.4 mg, 0.100 mmol, 1.00 equiv), 4-methoxybenzyl alcohol (13.8 mg, 1.00 mmol, 1.00 equiv) and TFA (2.3 µL, 0.30 mmol, 0.30 equiv) in HFIP (2.7 mL) were subjected to the general procedure **3**. Volatiles were removed *in vacuo* and the reaction outcome was analysed by NMR analysis of the crude reaction mixture. Quantitative ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard indicated no conversion to ester **18** (97% NMR yield of acid **17**).

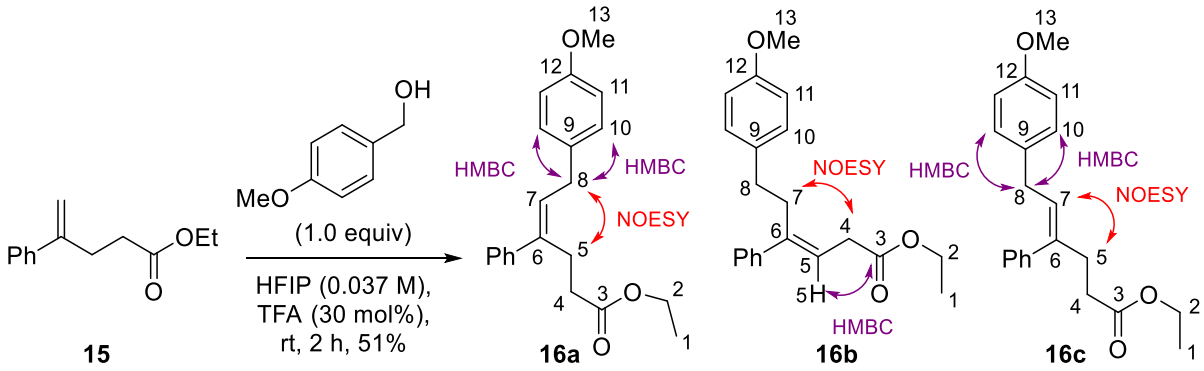
Data for 4-phenylbutanoic acid **from the crude mixture**:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.15 (m, 5H), 2.69 (t, *J* = 7.6 Hz, 2H), 2.40 (t, *J* = 7.4 Hz, 2H), 1.99 (p, *J* = 7.5 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.8, 141.3, 128.61 (2C), 128.56 (2C), 126.2, 35.1, 33.4, 26.3.

The data are consistent with the literature[69]

Control experiment using ester 15



16a : **16b** : **16c** = 57 : 33 : 10

Ester **15** (20.4 mg, 0.100 mmol, 1.00 equiv), 4-methoxybenzyl alcohol (13.8 mg, 0.100 mmol, 1.00 equiv) and TFA (2.3 µL, 0.030 mmol, 0.30 equiv) in HFIP (2.7 mL) were subjected to the general procedure **3**. The crude product was purified by flash column chromatography (SiO_2; 60 Å, 15–40 µm; pentane:Et_2O; 9:1 to 17:3) to furnish inseparable mixture of esters **16a**, **16b** and **16c** as a colourless oil (16.7 mg, 51%, **16a**:**16b**:**16c** = 57:33:10).[70]

Characteristic peaks for major ester 16a (from the mixture):

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17 – 7.14 (m, 2H, H-10), 6.88 – 6.84 (m, 2H, H-11), 5.89 – 5.84 (m, 1H, H-7), 4.011 – 4.05 (m, 2H, H-2), 3.80 (s, 3H, H-13), 3.54 (d, *J* = 7.4 Hz, 2H, H-8), 2.98 – 2.92 (m, 2H, H-5), 2.40 – 2.33 (m, 2H, H-4), 1.24 – 1.18 (m, 3H, H-1).

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.2 (C-3), 158.1 (C-12), 139.0 (C-6), 129.4 (2C, C-10), 128.9 (C-7), 114.1 (2C, C-11), 60.5 (C-2), 55.4 (C-13), 33.9 (C-8), 33.5 (C-4), 25.3 (C-5), 14.3 (C-1).

NOESY-2D (600 MHz, $CDCl_3$): between H-8 and H-5.

HMBC-2D (600 MHz -151 MHz, $CDCl_3$): between C-10 and H-8.

Characteristic peaks for ester 16b (from the mixture):

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.08 – 7.05 (m, 2H, H-10), 6.83 – 6.79 (m, 2H, H-11), 5.89 – 5.84 (m, 1H, H-5), 4.14 (q, *J* = 7.2 Hz, 2H, H-2), 3.79 (s, 3H, H-13), 3.05 (d, *J* = 7.2 Hz, 2H, H-4),

[69] P. Shao, S. Wang, C. Chen, C. Xi, *Org. Lett.*, 2016, **18**, 2050–2053.
[70] Ratio of **16a**, **16b** and **16c** measured after column chromatography.

2.78 (dd, *J* = 9.0, 6.7 Hz, 2H, H-7), 2.59 (dd, *J* = 8.9, 6.7 Hz, 2H, H-8), 1.27 (t, *J* = 7.2 Hz, 3H, H-1).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.9 (C-3), 158.02 (C-12), 129.5 (2C, C-10), 120.7 (C-5), 113.9 (2C, C-11), 60.8 (C-2), 55.4 (C-13), 34.3 (C-4), 33.7 (C-8), 32.6 (C-7).

NOESY-2D (600 MHz, $CDCl_3$): between H-7 and H-4.

HMBC-2D (600 MHz -151 MHz, $CDCl_3$): between C-3 and H-5.

Characteristic peaks for ester 16c (from the mixture):

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.05 – 7.02 (m, 2H, H-10), 5.70 – 5.64 (m, 1H, H-7), 3.78 (s, 3H, H-13), 3.21 (d, *J* = 7.5 Hz, 2H, H-8), 2.74 – 2.69 (m, 2H, H-5).

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.3 (C-3), 157.97 (C-12), 129.3 (2C, C-10), 126.9 (C-7), 114.0 (2C, C-11), 34.7 (C-5), 34.3 (C-8).

NOESY-2D (600 MHz, $CDCl_3$): between H-7 and H-5.

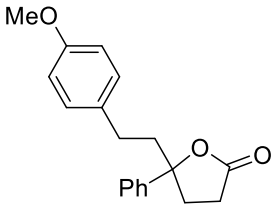
HMBC-2D (600 MHz -151 MHz, $CDCl_3$): between C-10 and H-8.

IR (film) ν_{max}: 2981, 2890, 1733, 1512, 1374, 1246, 1176, 1155, 1036, 826, 766, 700 cm^{-1}.

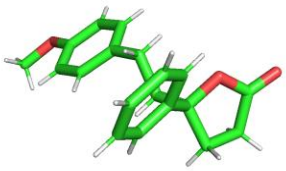
HRMS (ESI): calculated for $C_{21}H_{25}O_3$ $[M+H]^+$ requires m/z 325.1798, found m/z 325.1808 (Δ = 3.00 ppm).

4.0 X-ray crystallography data

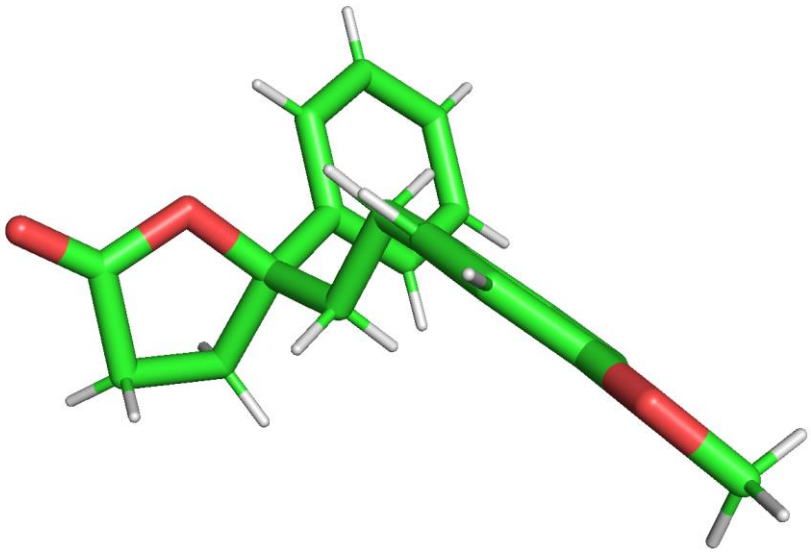
Date for lactone **2a**



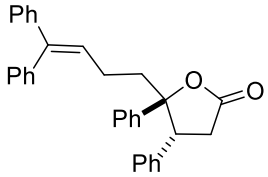
2a



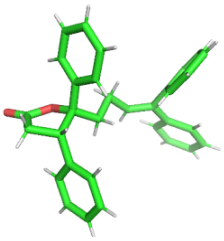
Formula	$C_{19}H_{20}O_3$		
M_r	296.37		
T	150 K		
Crystal Class	Orthorhombic		
Space Group	P 21 21 21		
a	5.6987(2) Å	alpha	90°
b	7.5431(3) Å	beta	90°
c	35.7122(11) Å	gamma	90°
Volume	1535.12(9) Å^3		



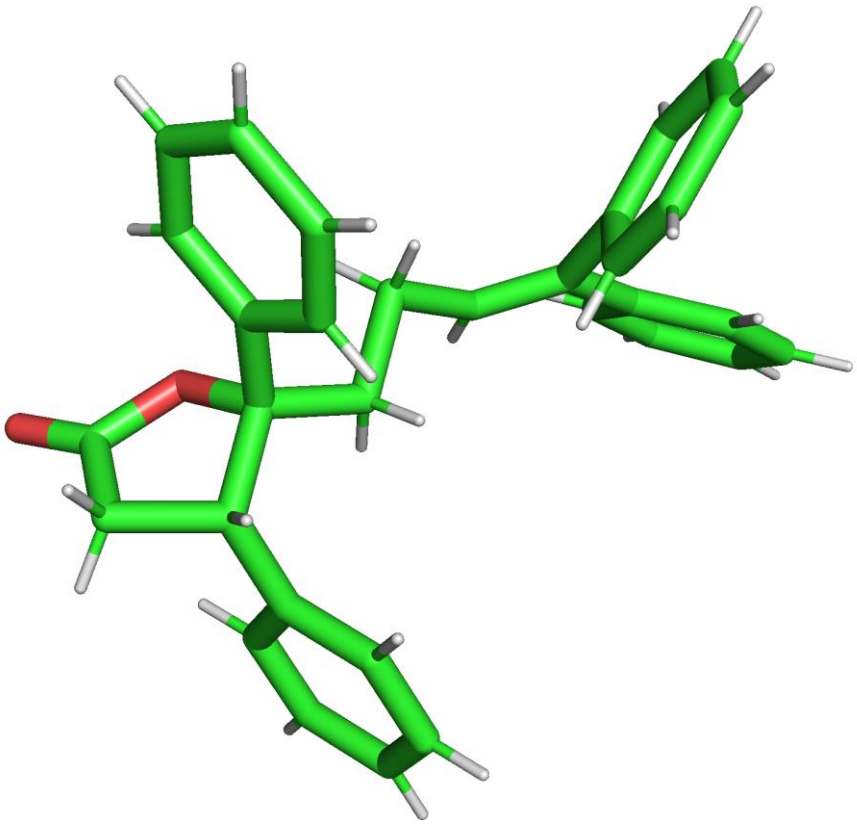
Date for lactone **2g**



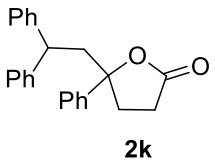
2g



Formula	$C_{32}H_{28}O_2$		
M_r	444.57		
T	150 K		
Crystal Class	Triclinic		
Space Group	P -1		
a	5.9846(3) Å	alpha	94.785(4)°
b	8.7340(4) Å	beta	93.664(4)°
c	23.1074(10) Å	gamma	93.898(4)°
Volume	1197.87(10) Å^3		

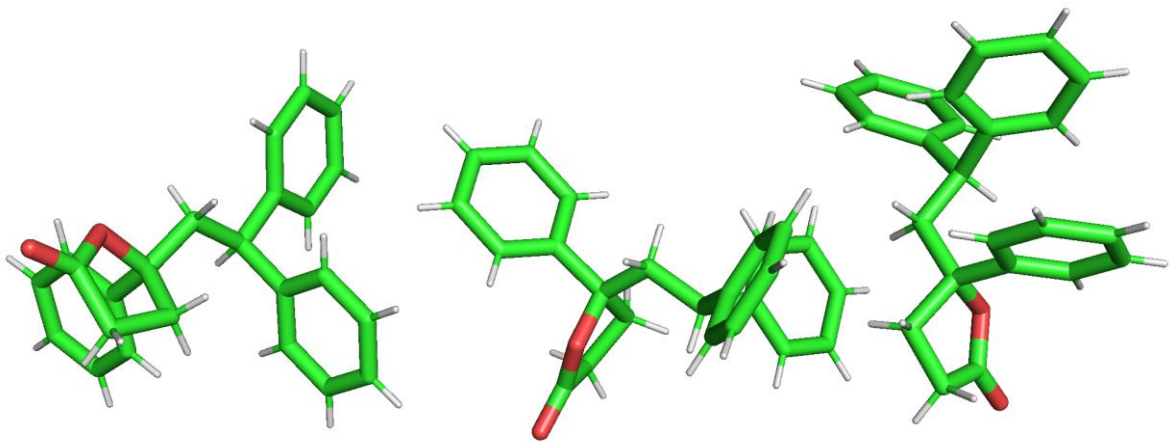


Date for lactone **2k**

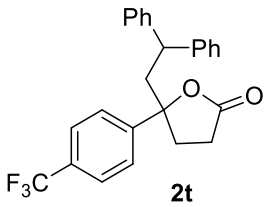


2k

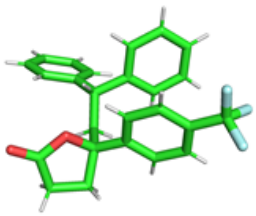
Formula	$C_{24}H_{22}O_2$		
M_r	342.42		
T	150 K		
Crystal Class	Monoclinic		
Space Group	P 2_1/c		
a	9.3701(2) Å	alpha	90°
b	40.8864(8) Å	beta	94.7820(19)°
c	14.5271(3) Å	gamma	90°
Volume	5546.1(2) Å^3		



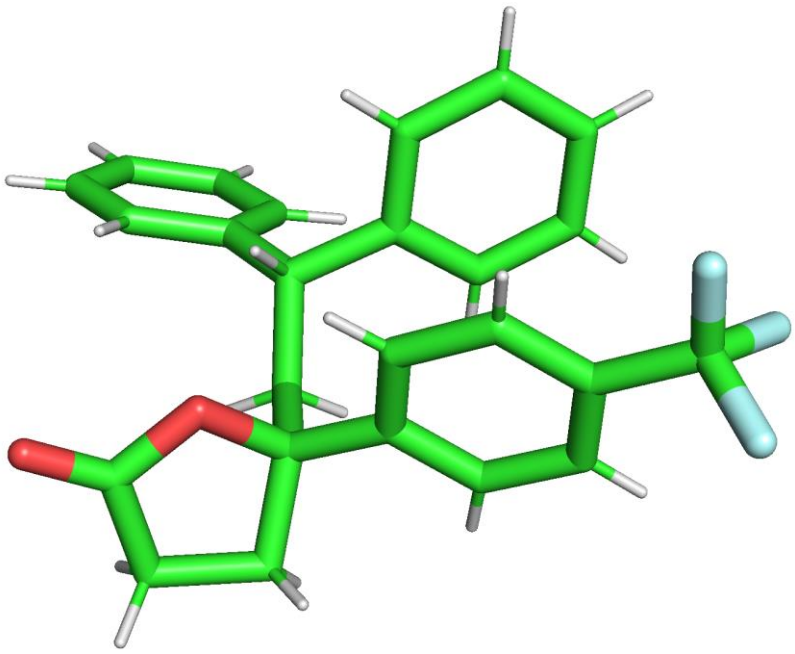
Date for lactone **2t**



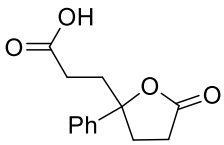
2t



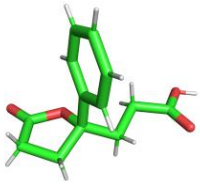
Formula	$C_{25}H_{21}F_3O_2$		
M_r	410.42		
T	150 K		
Crystal Class	Monoclinic		
Space Group	P 2_1		
a	12.0864(2) Å	alpha	90°
b	6.0321(1) Å	beta	92.8739(17)°
c	13.7269(2) Å	gamma	90°
Volume	999.52(3) Å^3		



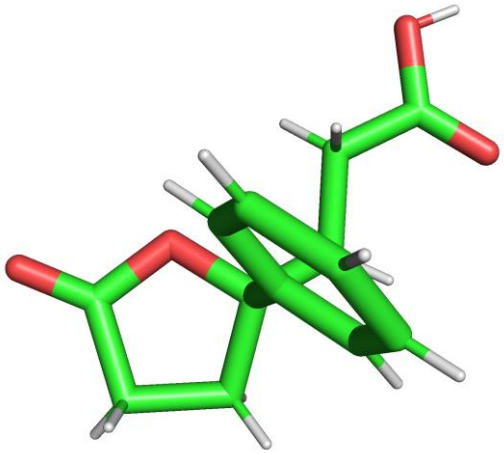
Data for lactone **4**



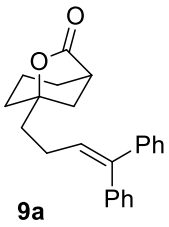
4



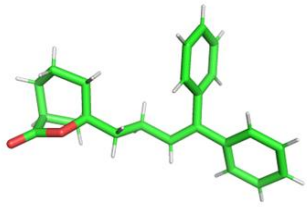
Formula	$C_{13}\ H_{14}O_4$		
M_r	234.25		
T	150 K		
Crystal class	Monoclinic		
Space group	P $2_1/c$		
a	5.7618(1) Å,	alpha	90°
b	7.2943(2) Å,	beta	93.910(2)°
c	27.0456(7) Å	gamma	90°
Volume	1134.03(5) $Å^3$		



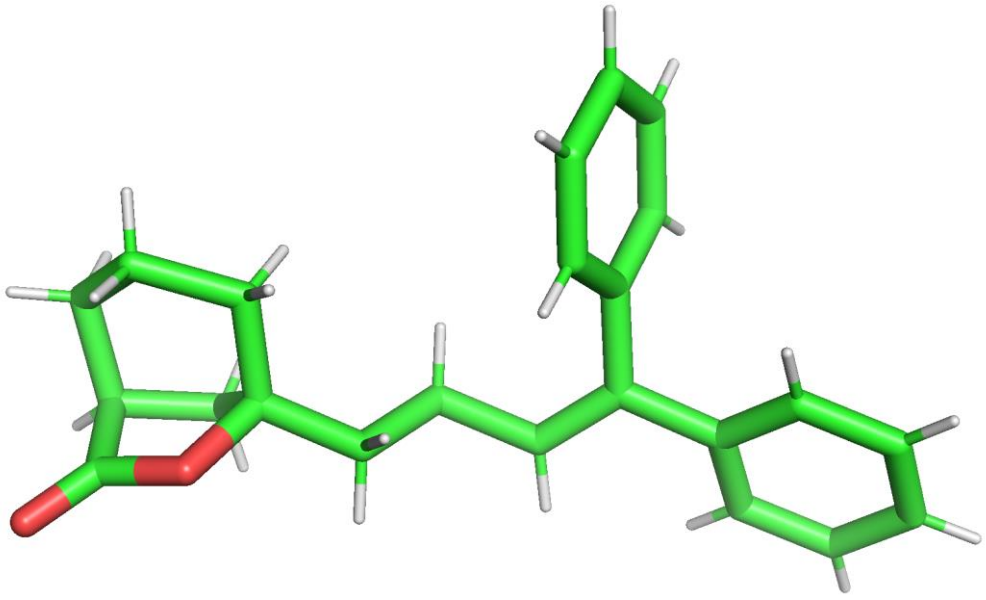
Data for lactone **9a**



9a



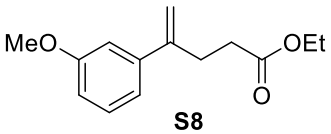
Formula	$C_{23}H_{24}O_2$		
M_r	332.44		
T	150 K		
Crystal class	Monoclinic		
Space group	P 2_1/n		
a	6.1184(1) Å	alpha	90°
b	33.9883(5) Å	beta	90.5312(15)°
c	8.7255(1) Å	gamma	90°
Volume	1814.43(4) Å^3		



5.0 NMR spectra (1H & 13C) of starting materials and products

Ethyl 4-(3-methoxyphenyl)pent-4-enoate S8 (^{1}H and ^{13}C NMR in $CDCl_3$).

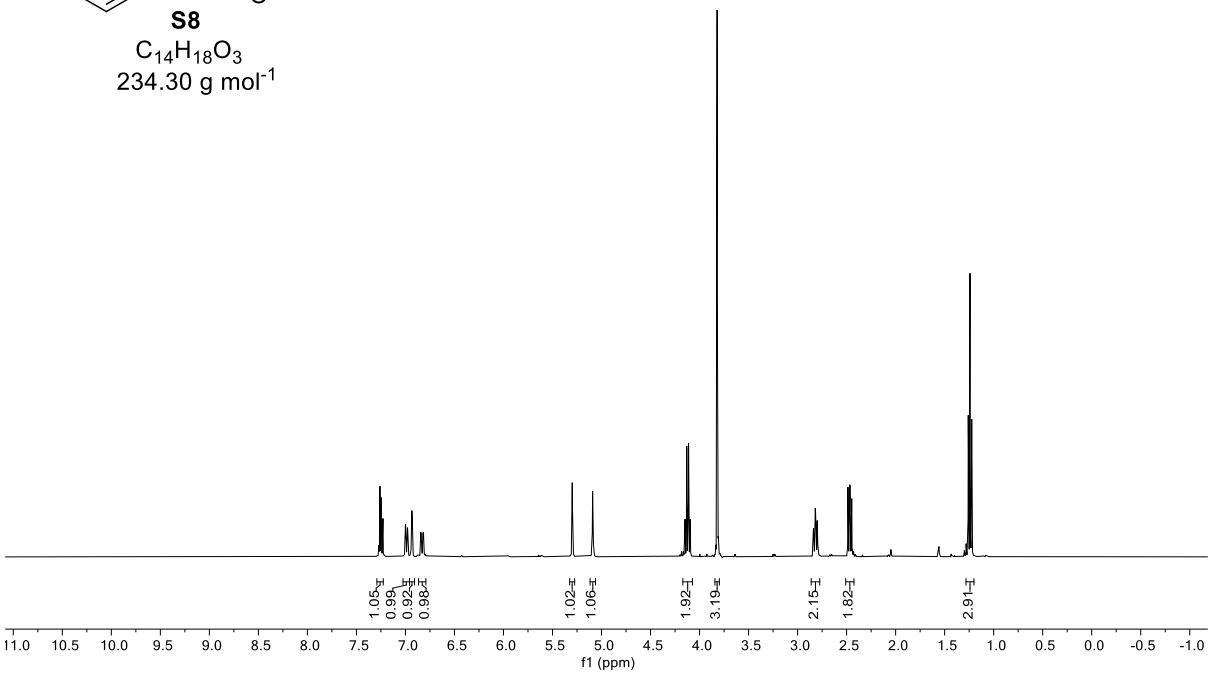
^{1}H NMR ($CDCl_3$, 400 MHz)



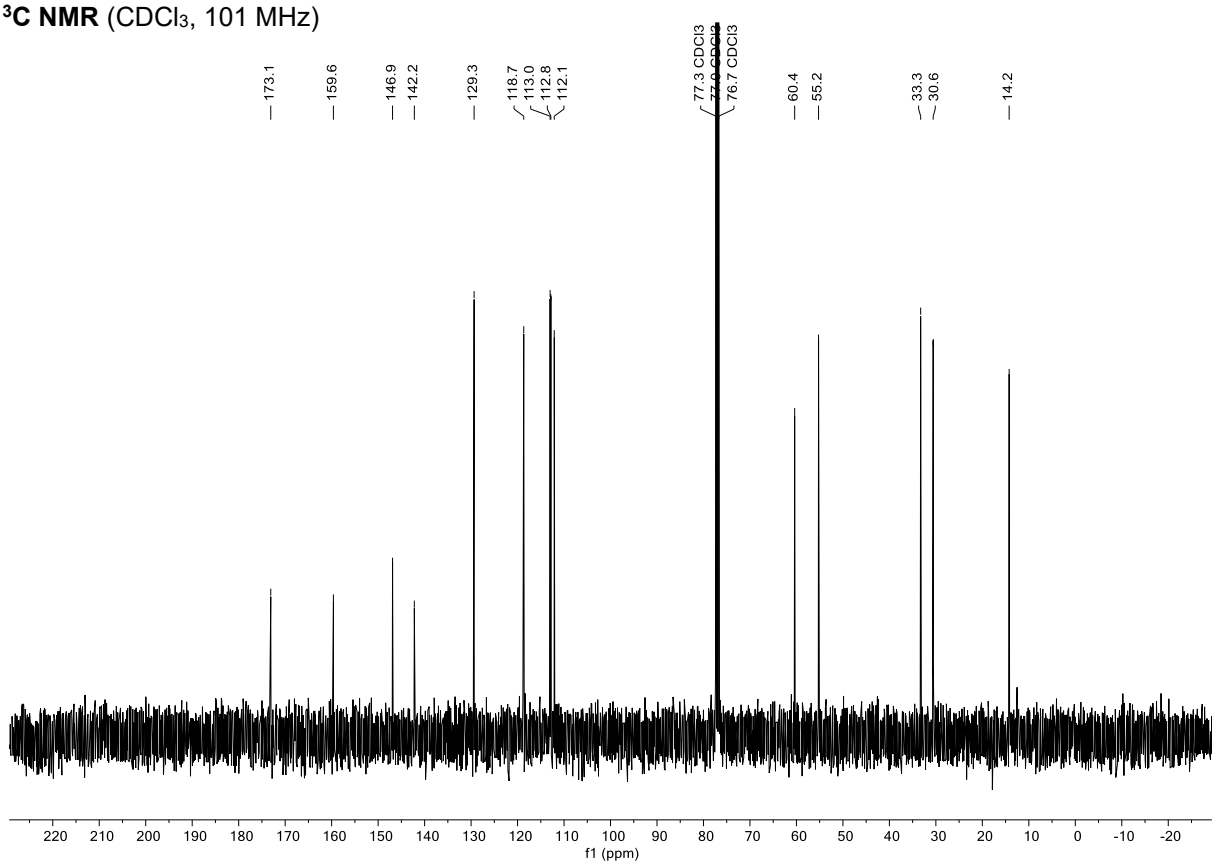
S8

$C_{14}H_{18}O_3$

234.30 g mol^{-1}

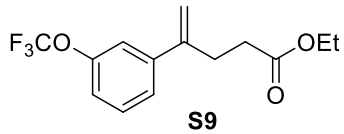


^{13}C NMR ($CDCl_3$, 101 MHz)



Ethyl 4-(3-(trifluoromethoxy)phenyl)pent-4-enoate S9

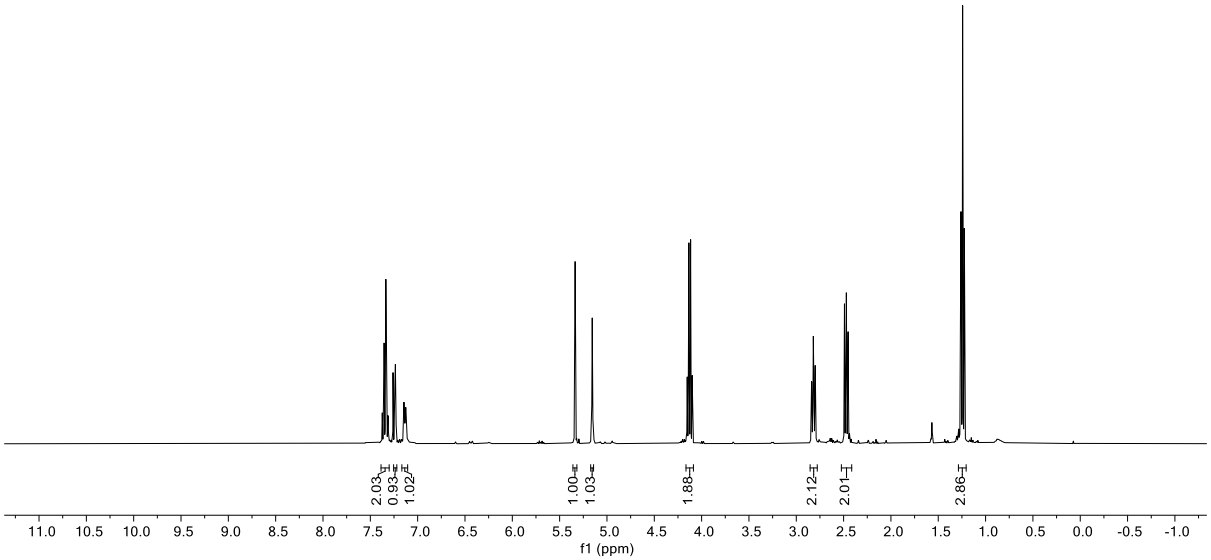
^{1}H NMR (400 MHz, $CDCl_3$)



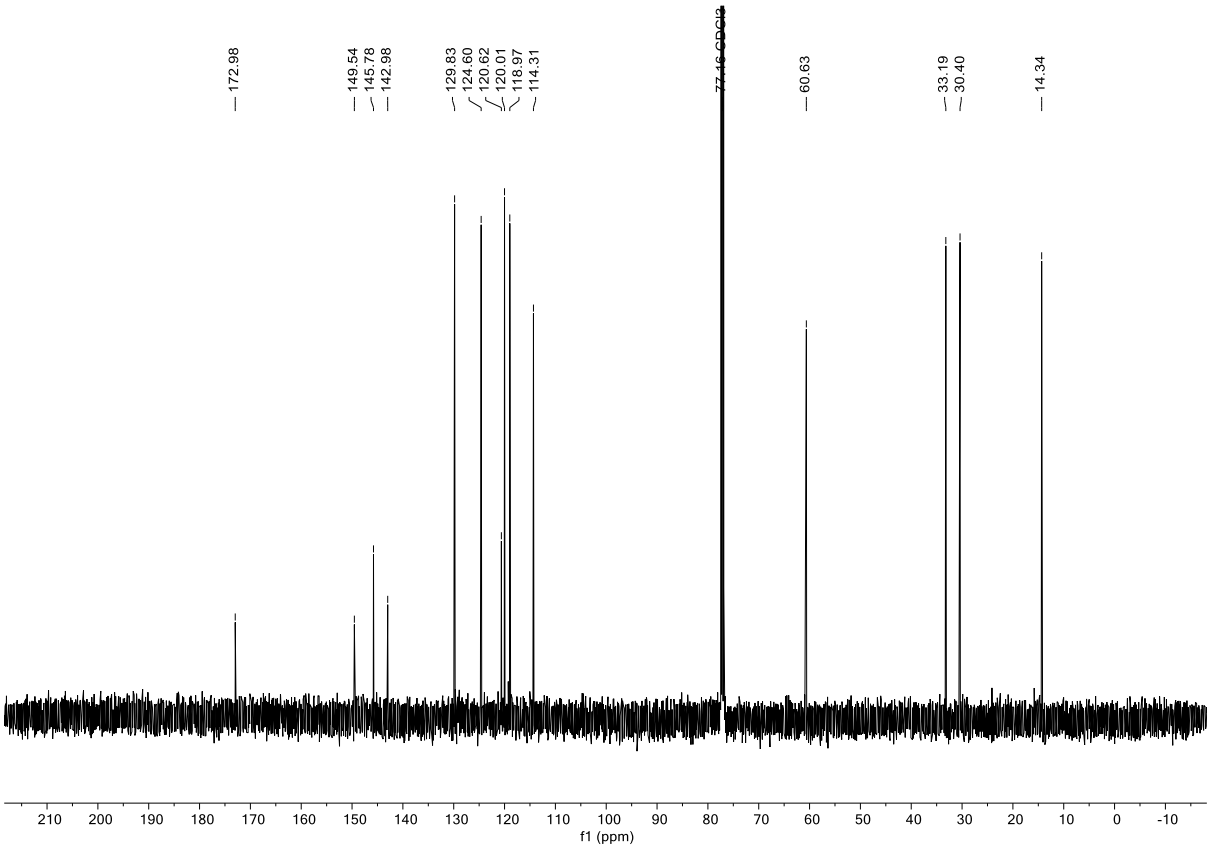
S9

$C_{14}H_{15}F_3O_3$

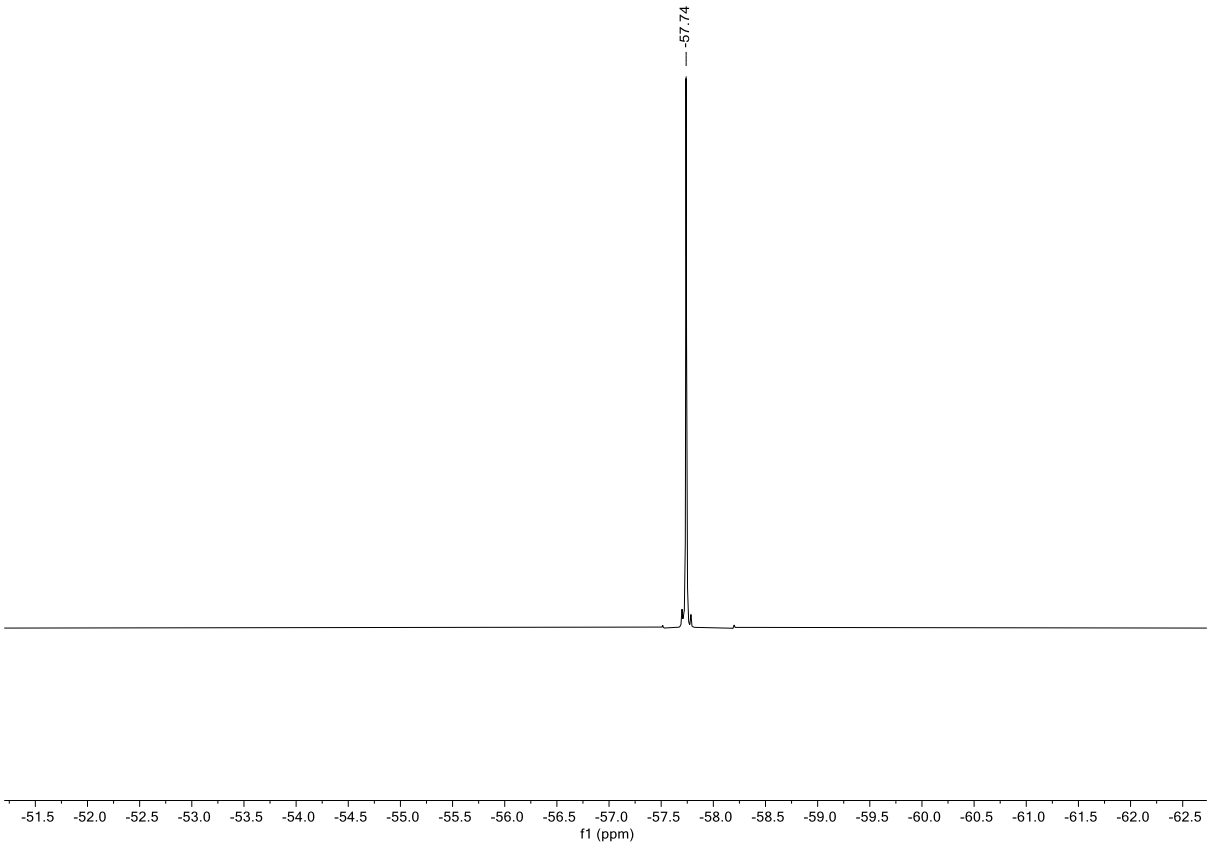
288.27 g mol^{-1}



^{13}C {^{19}F} NMR (126 MHz, $CDCl_3$)

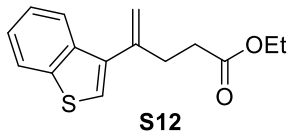


^{19}F NMR (377 MHz, $CDCl_3$)

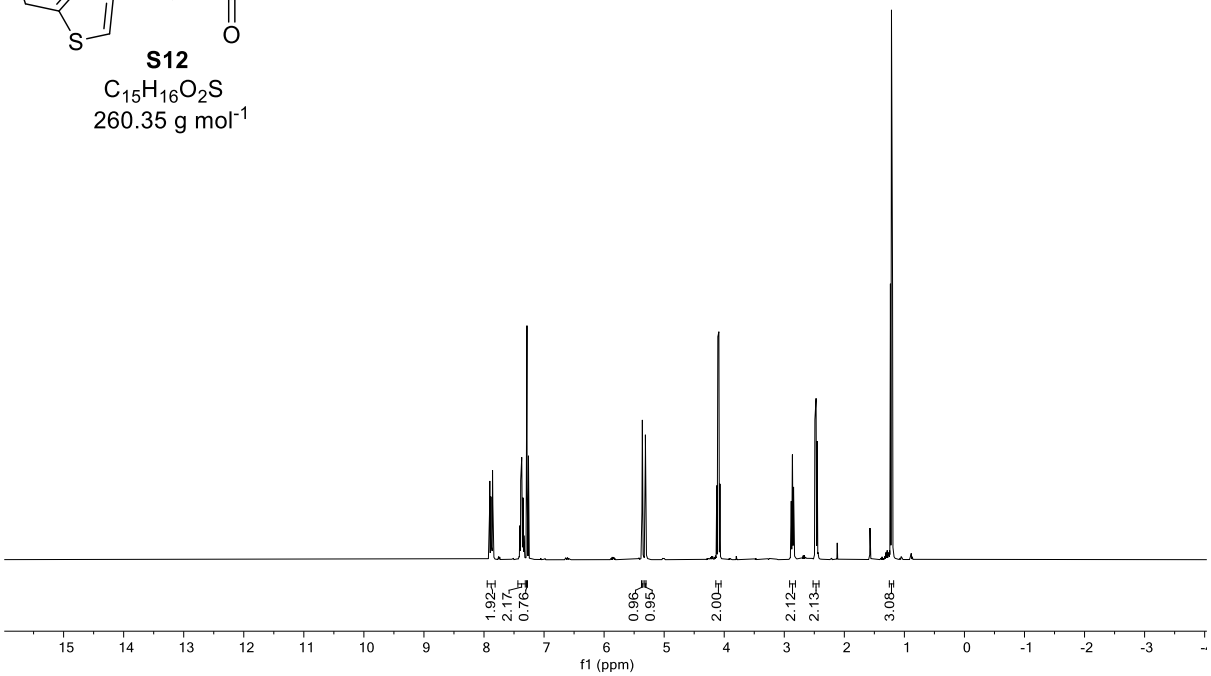


Ethyl 4-(benzo[b]thiophen-3-yl)pent-4-enoate S12

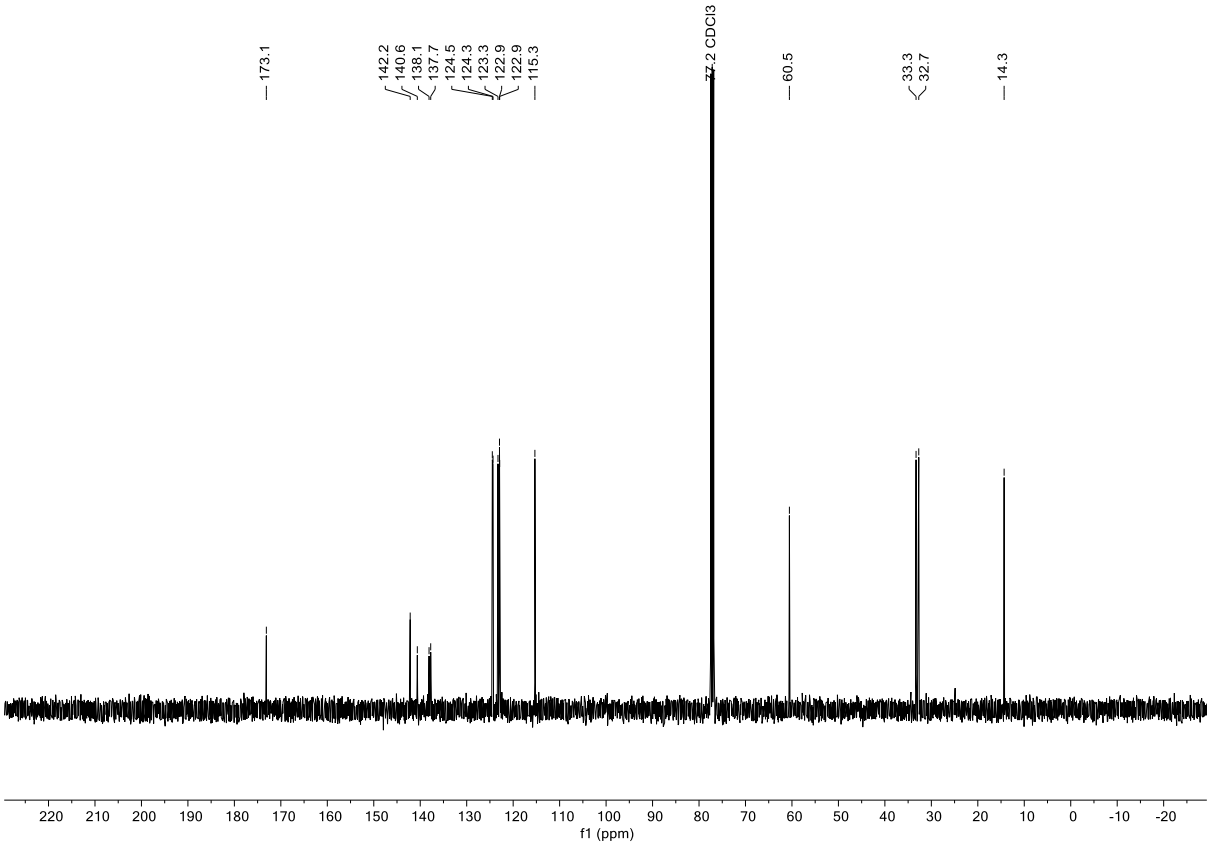
^{1}H NMR ($CDCl_3$, 400 MHz)



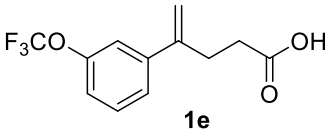
S12
$C_{15}H_{16}O_2S$
260.35 g mol^{-1}



^{13}C NMR ($CDCl_3$, 101 MHz)



4-(3-(Trifluoromethoxy)phenyl)pent-4-enoic acid 1e

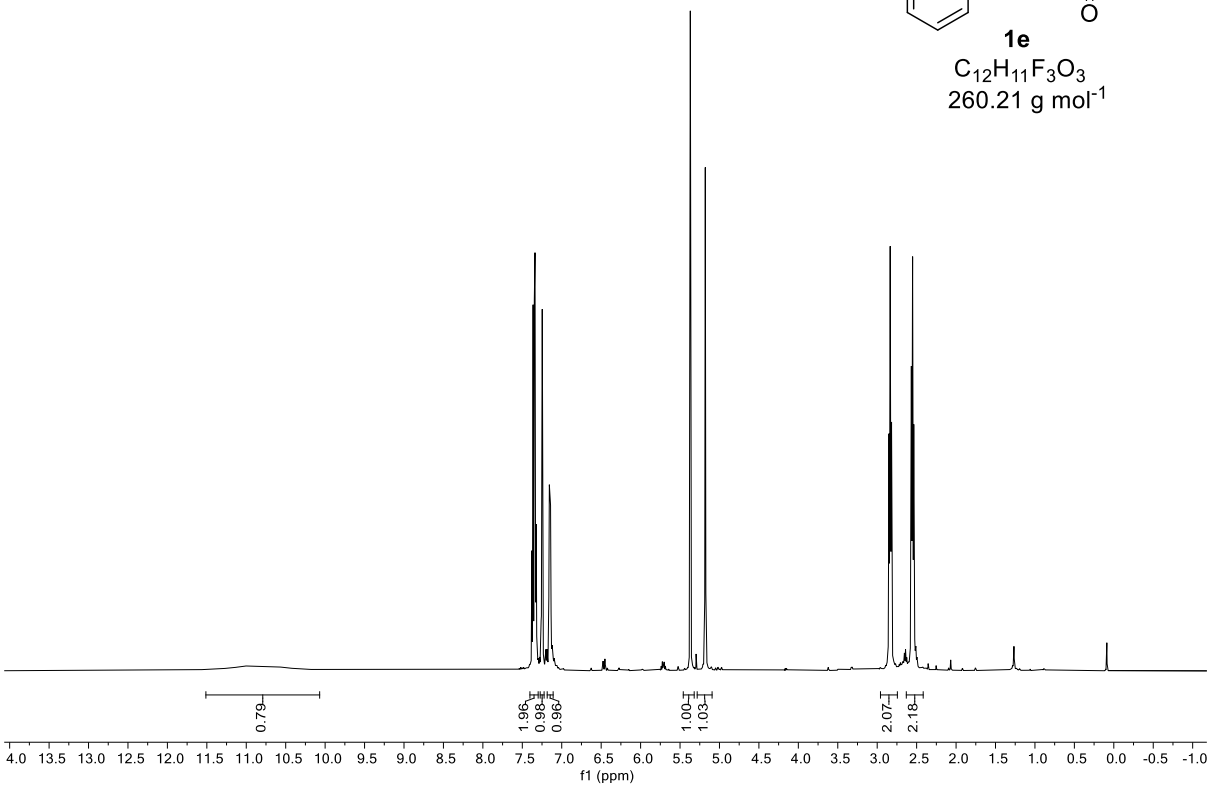


1e

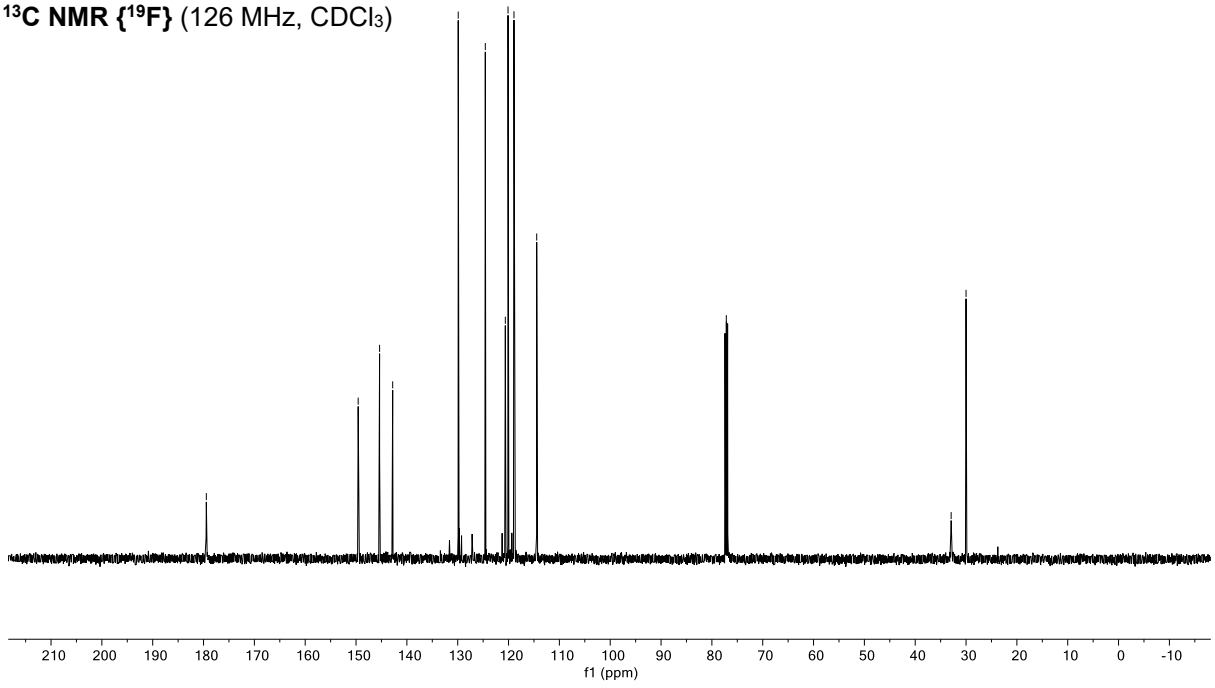
$C_{12}H_{11}F_3O_3$

260.21 g mol^{-1}

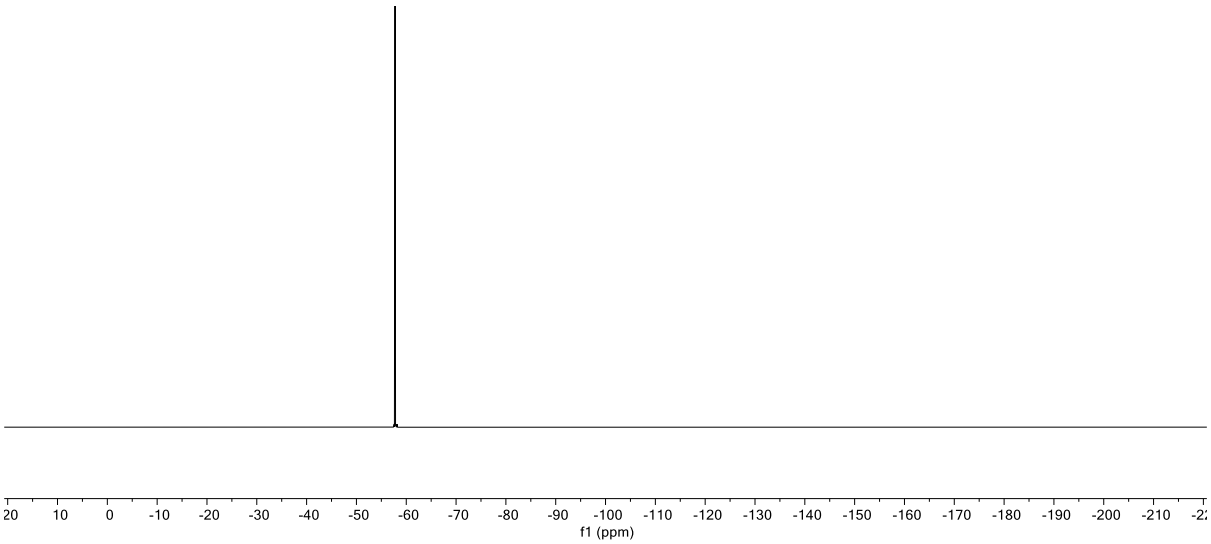
^{1}H NMR (500 MHz, $CDCl_3$)



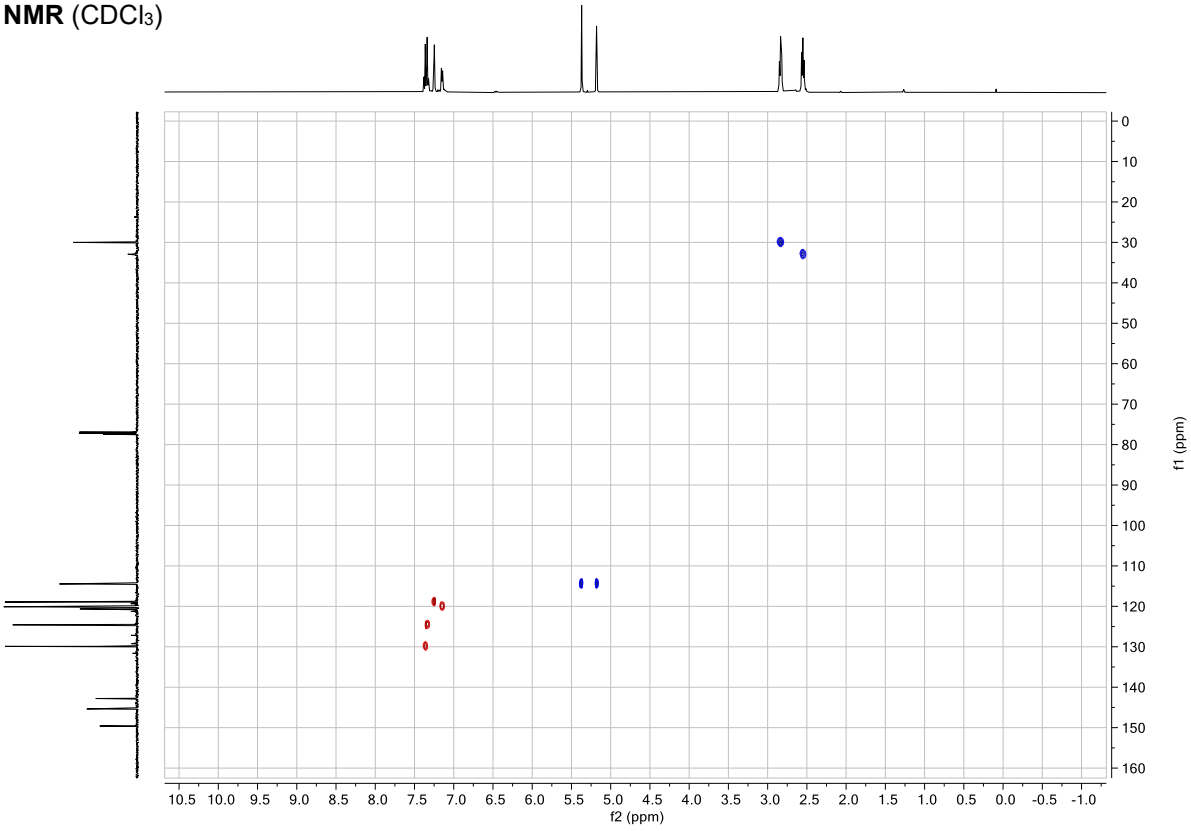
^{13}C NMR {^{19}F} (126 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

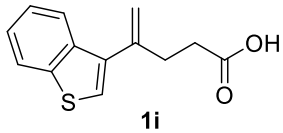


HSQC NMR ($CDCl_3$)



4-(Benzo[b]thiophen-3-yl)pent-4-enoic acid 1i

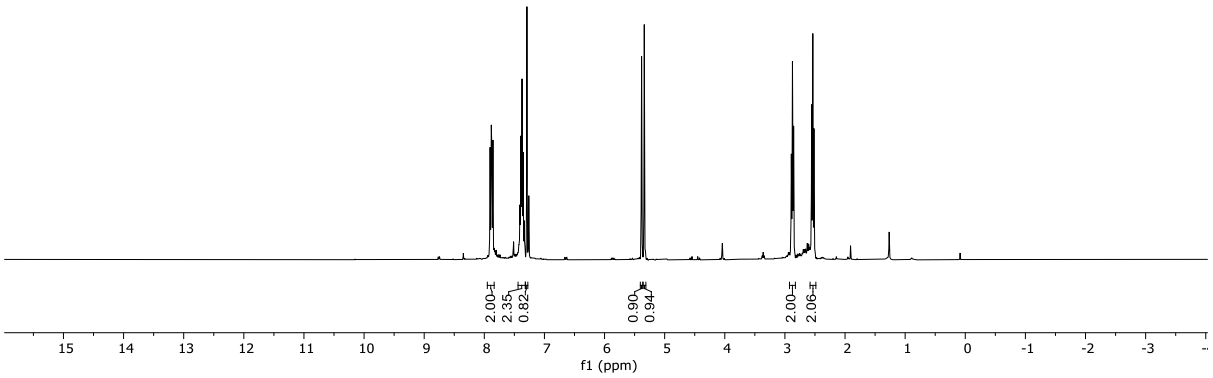
^{1}H NMR ($CDCl_3$, 400 MHz)



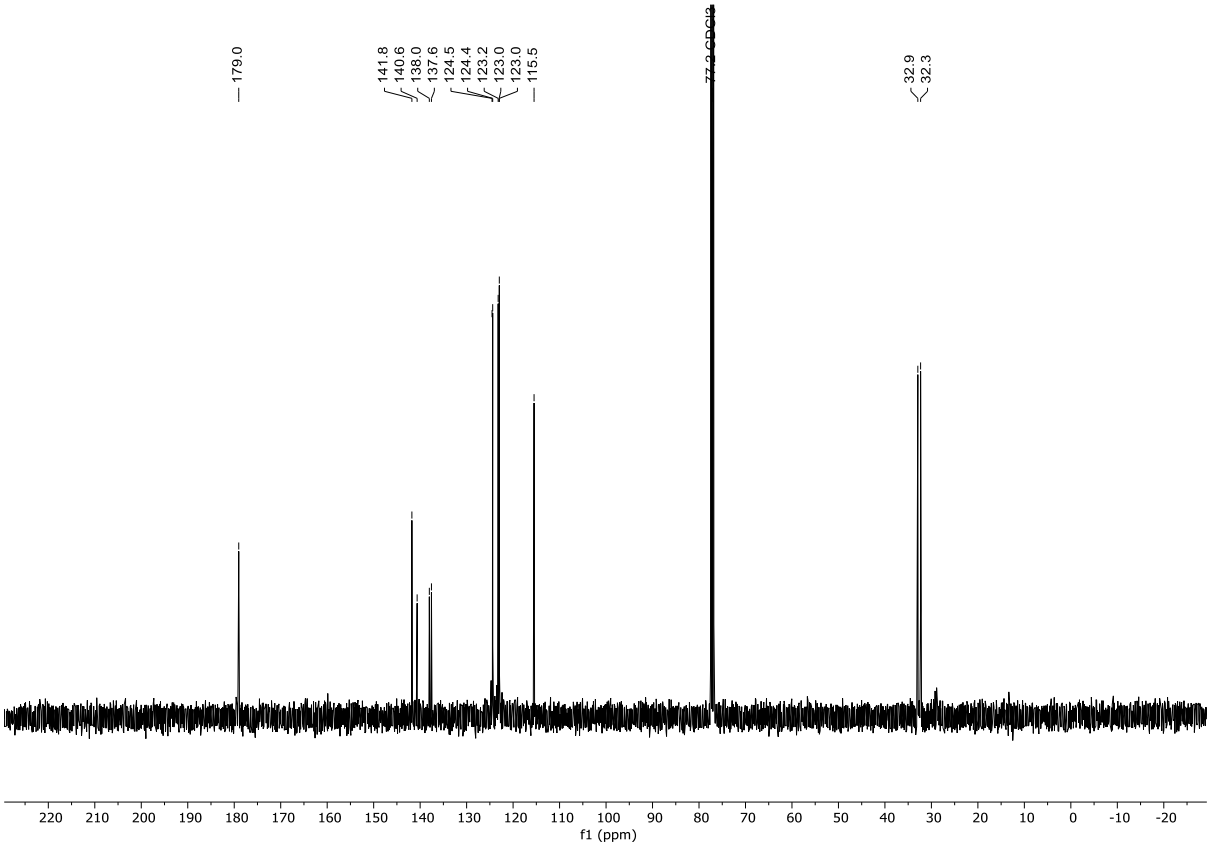
1i

$C_{13}H_{12}O_2S$

232.30 g mol^{-1}

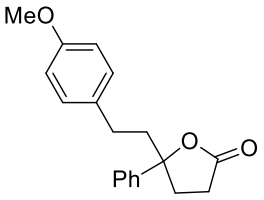


^{13}C NMR ($CDCl_3$, 101 MHz)



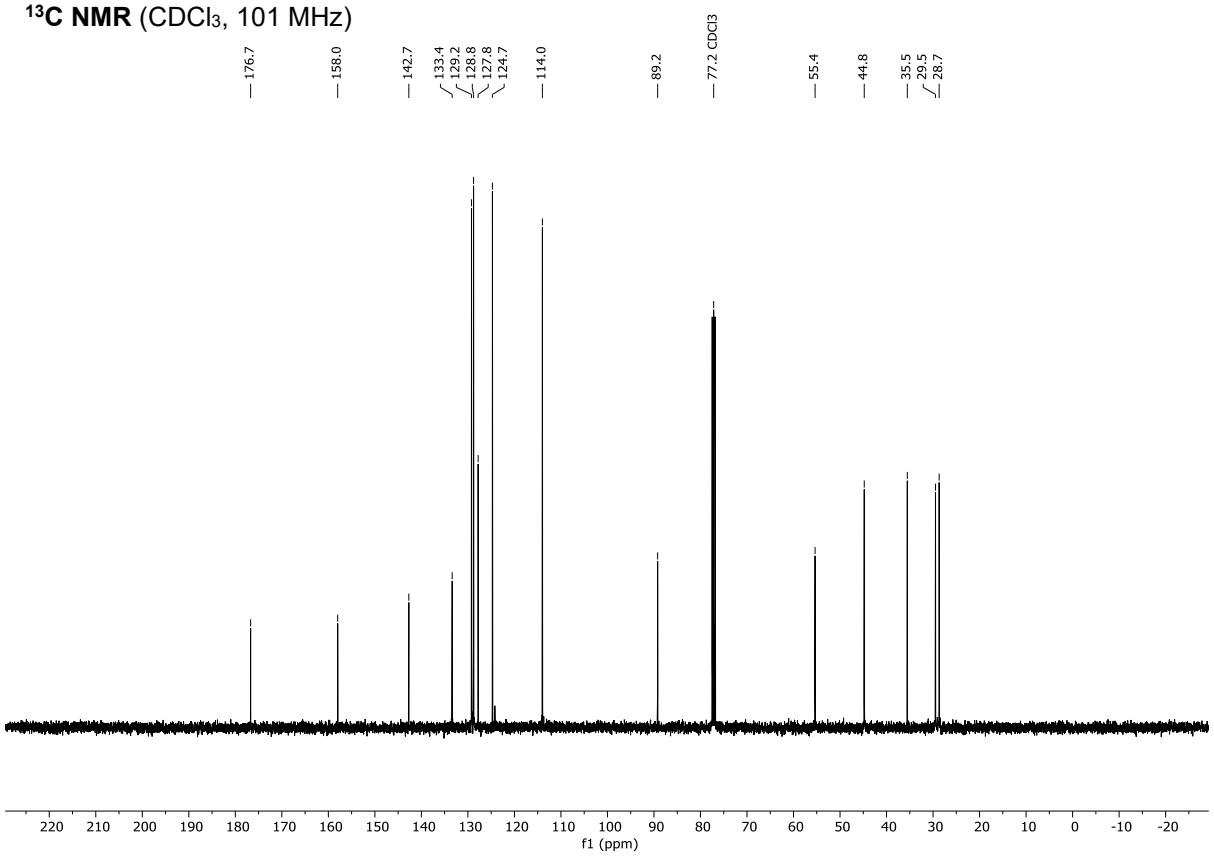
5-(4-Methoxyphenethyl)-5-phenyldihydrofuran-2(3H)-one 2a (^{1}H and ^{13}C NMR in $CDCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz)



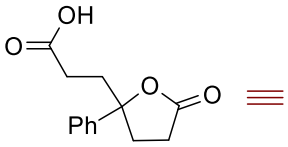
2a
$C_{19}H_{20}O_3$
296.37 g mol^{-1}

^{13}C NMR ($CDCl_3$, 101 MHz)



3-(5-Oxo-2-phenyltetrahydrofuran-2-yl)propanoic acid 4

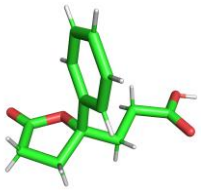
^{1}H NMR (600 MHz, $CDCl_3$)



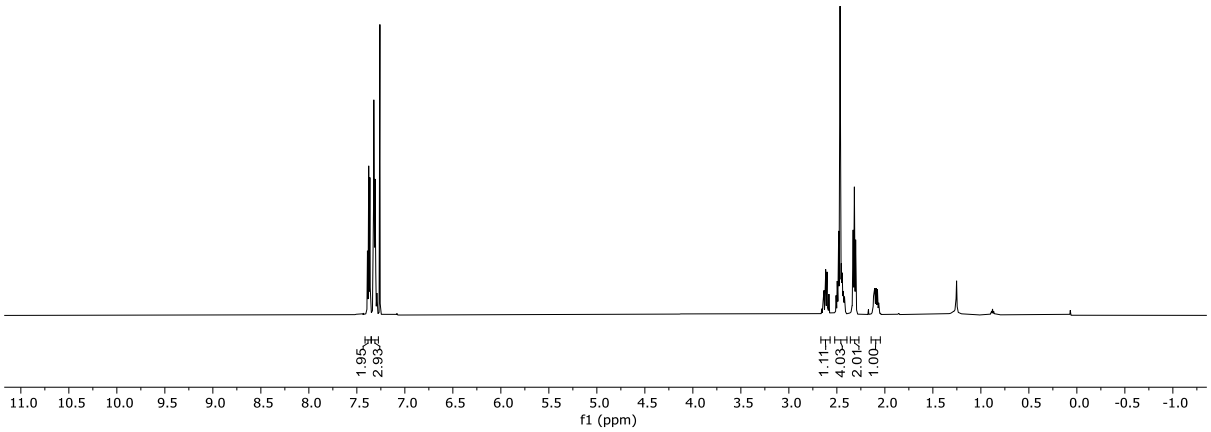
4

$C_{13}H_{14}O_4$

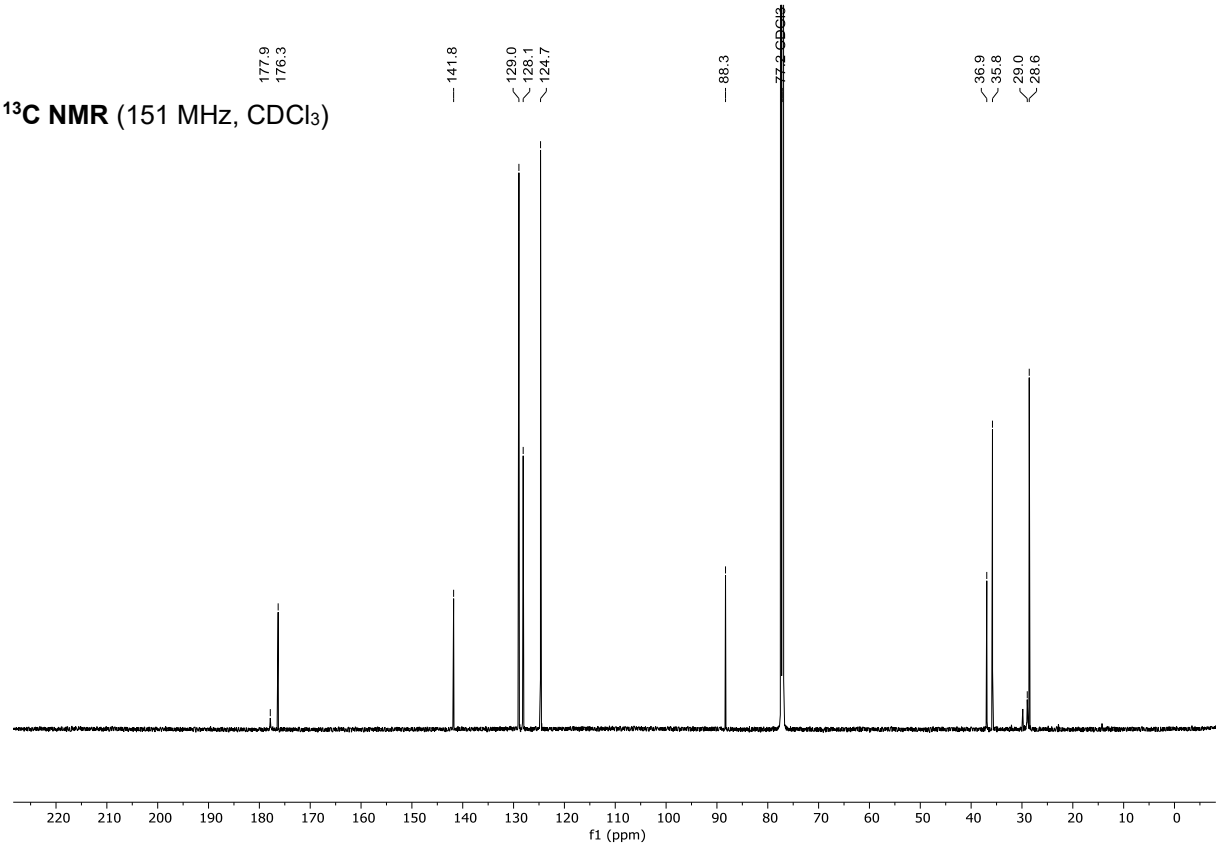
234.25 g mol^{-1}



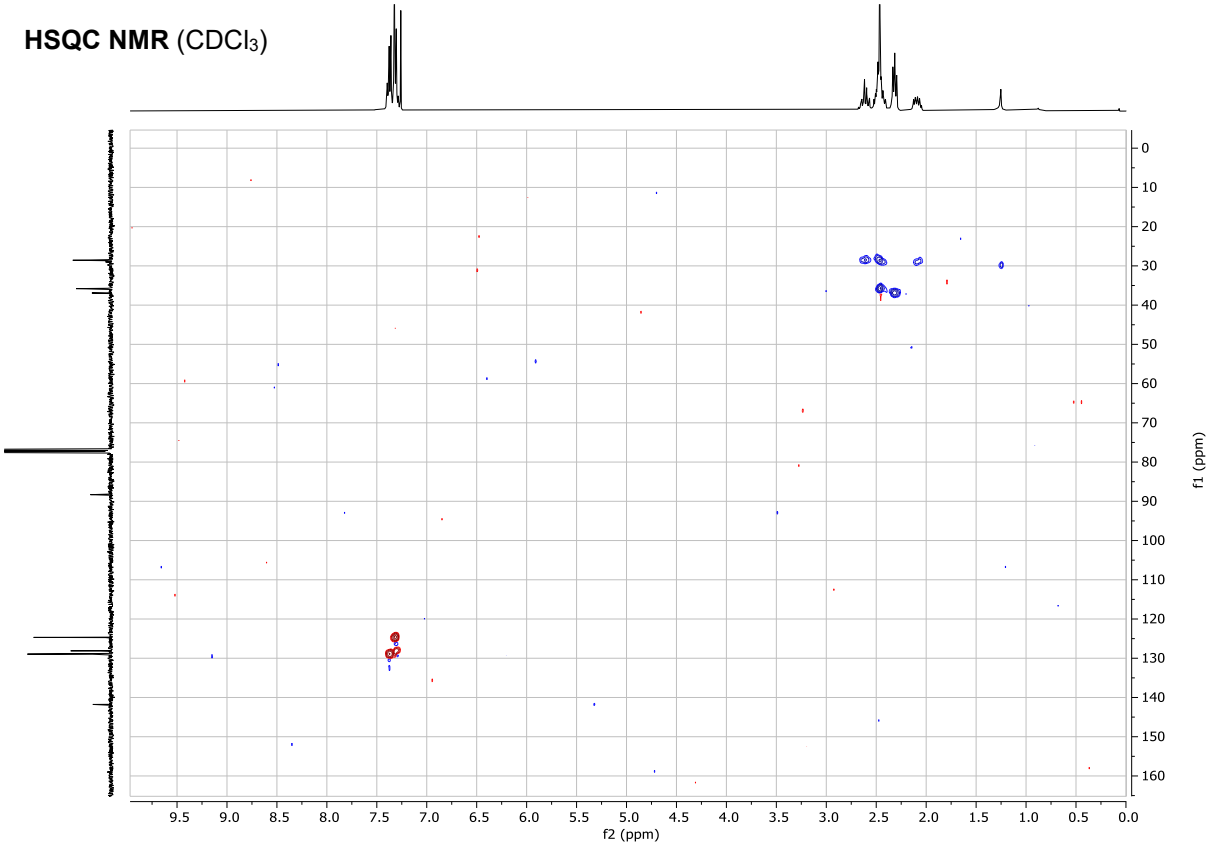
[X-ray]



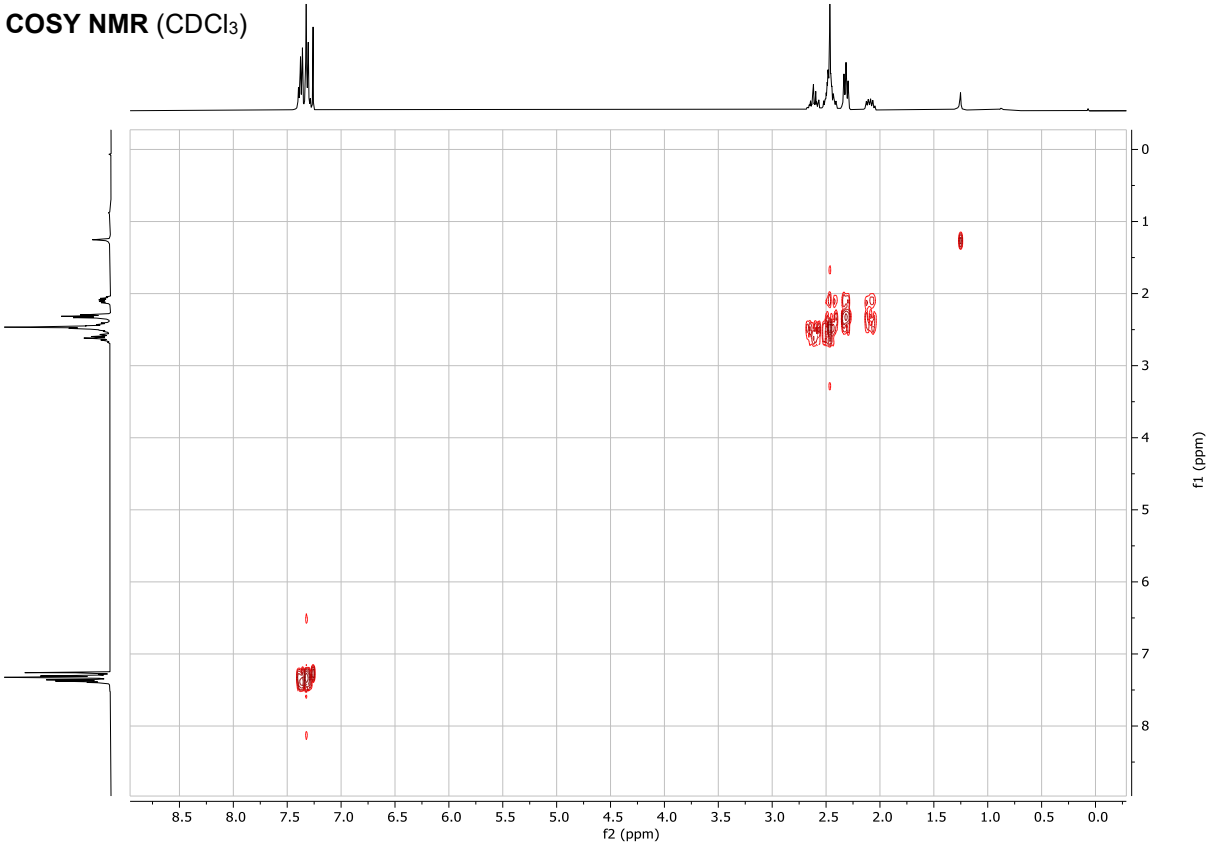
^{13}C NMR (151 MHz, $CDCl_3$)



HSQC NMR ($CDCl_3$)

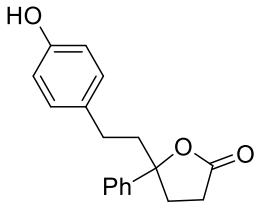


COSY NMR ($CDCl_3$)

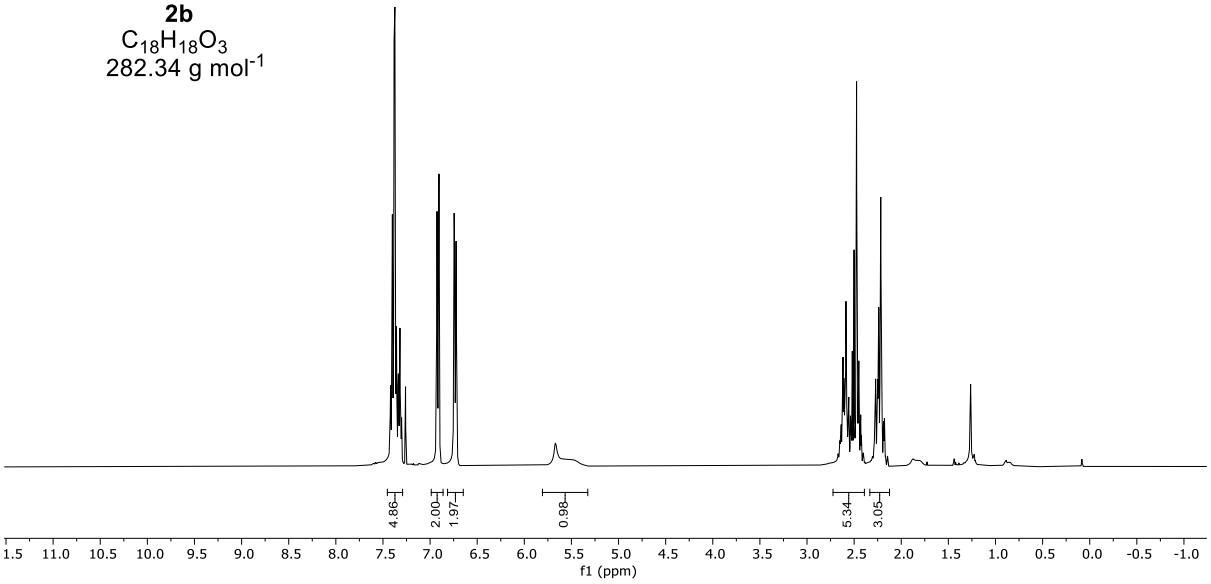


5-(4-Hydroxyphenethyl)-5-phenyldihydrofuran-2(3H)-one 2b.

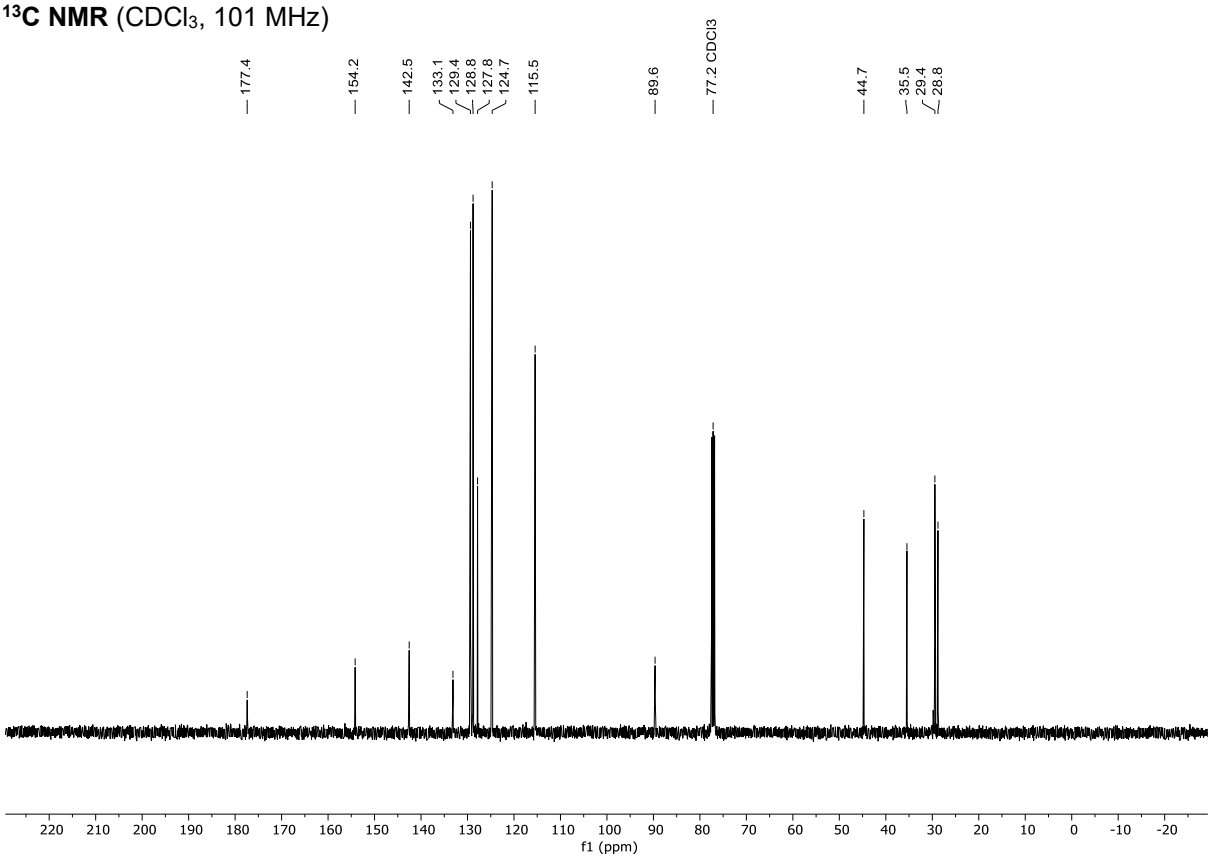
^{1}H NMR ($CDCl_3$, 400 MHz)



2b
$C_{18}H_{18}O_3$
282.34 g mol^{-1}

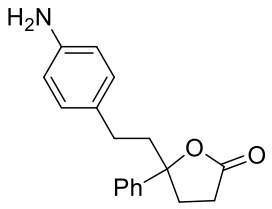


^{13}C NMR ($CDCl_3$, 101 MHz)



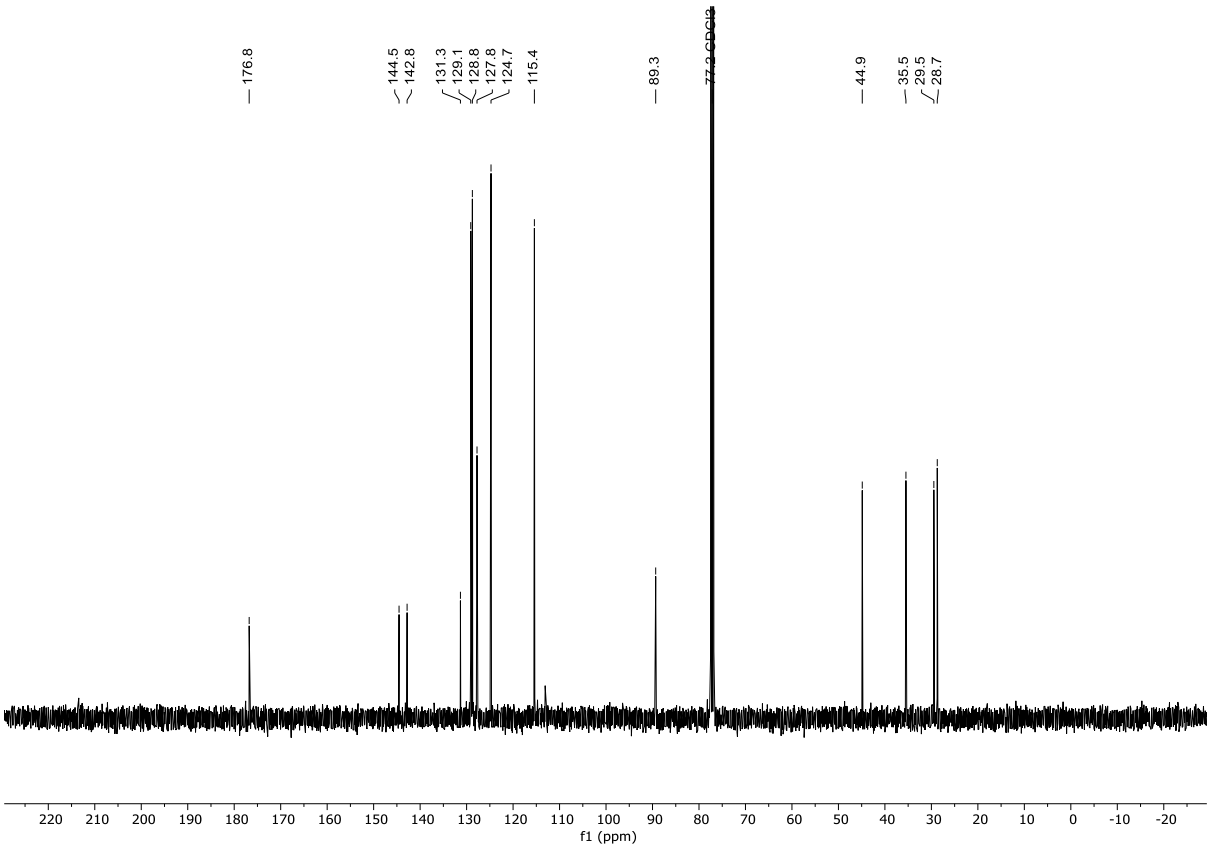
5-(4-Aminophenethyl)-5-phenyldihydrofuran-2(3H)-one 2c.

^{1}H NMR ($CDCl_3$, 400 MHz)



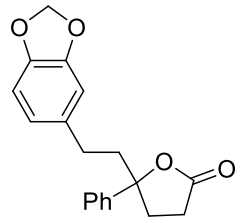
2c
$C_{18}H_{19}NO_2$
281.36 g mol^{-1}

^{13}C NMR ($CDCl_3$, 101 MHz)



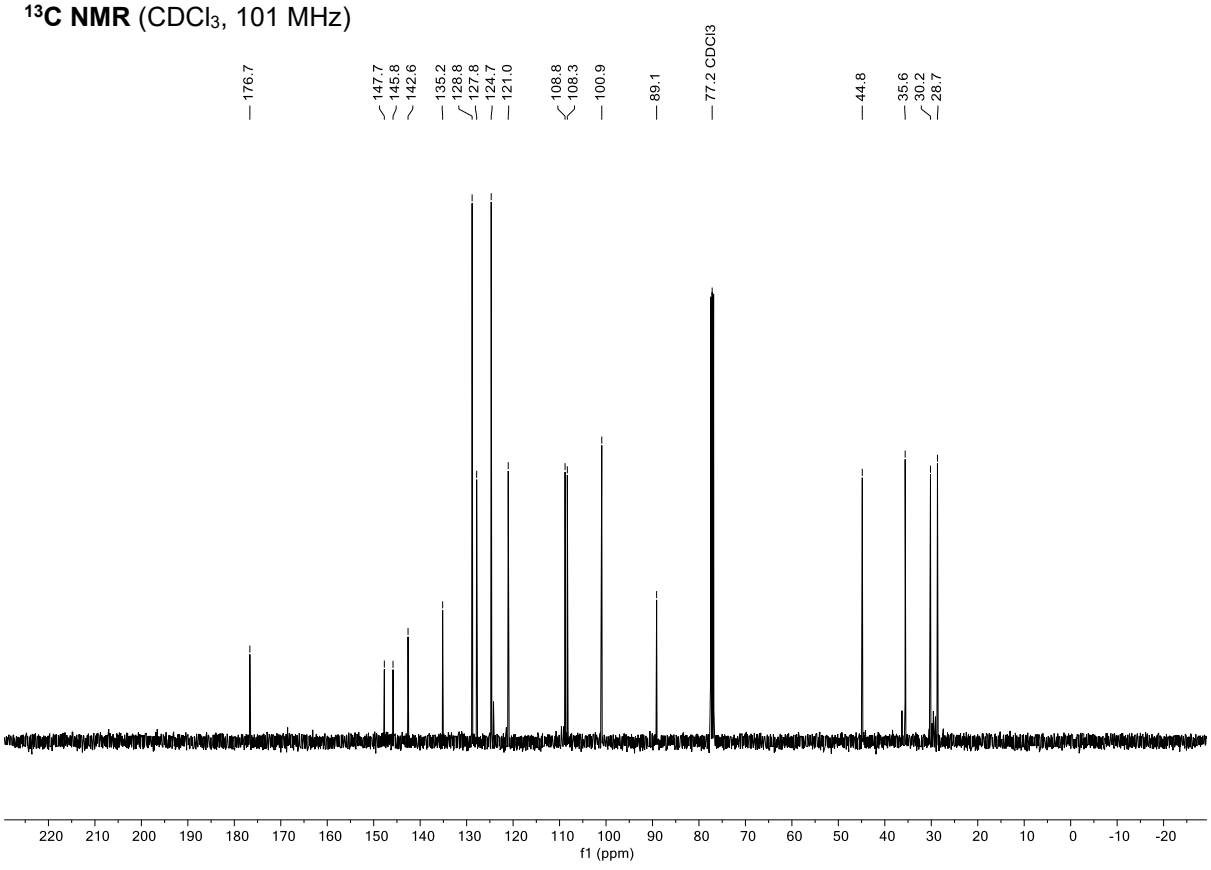
5-(2-(Benzo[d][1,3]dioxol-5-yl)ethyl)-5-phenyldihydrofuran-2(3H)-one 2d

^{1}H NMR ($CDCl_3$, 400 MHz)



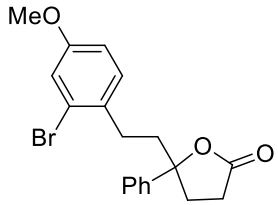
2d
$C_{19}H_{18}O_4$
310.35 g mol^{-1}

^{13}C NMR ($CDCl_3$, 101 MHz)

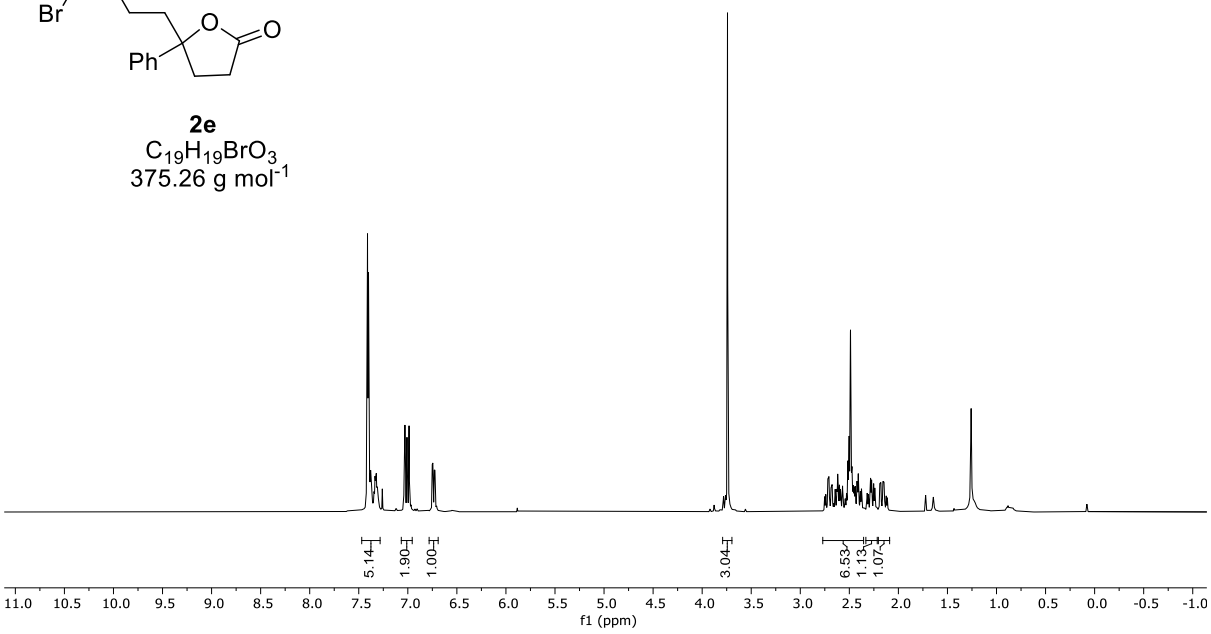


5-(2-Bromo-4-methoxyphenethyl)-5-phenyldihydrofuran-2(3H)-one 2e

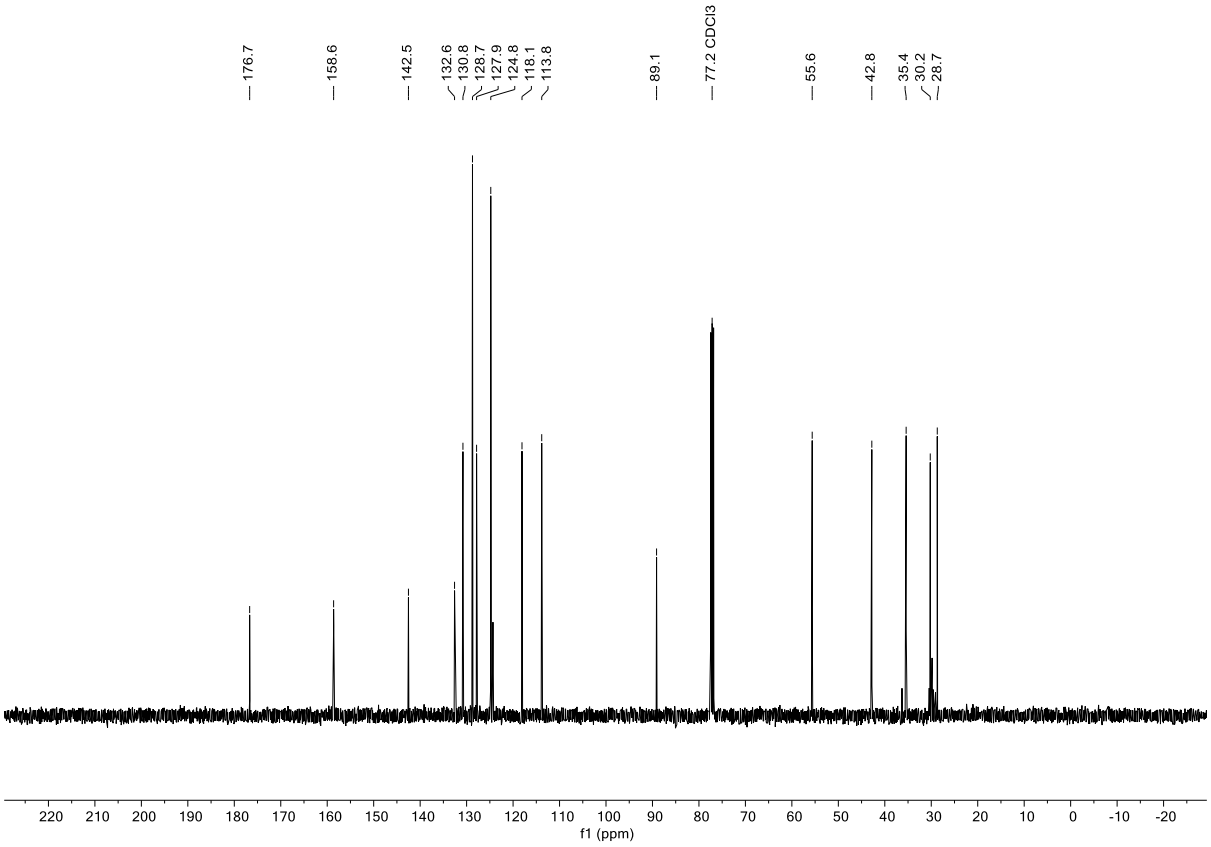
^{1}H NMR ($CDCl_3$, 400 MHz)



2e
$C_{19}H_{19}BrO_3$
375.26 g mol^{-1}

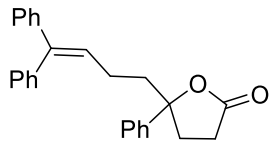


^{13}C NMR ($CDCl_3$, 101 MHz)



5-(4,4-Diphenylbut-3-en-1-yl)-5-phenyldihydrofuran-2(3H)-one 2f (^{1}H and ^{13}C NMR in $CDCl_3$).

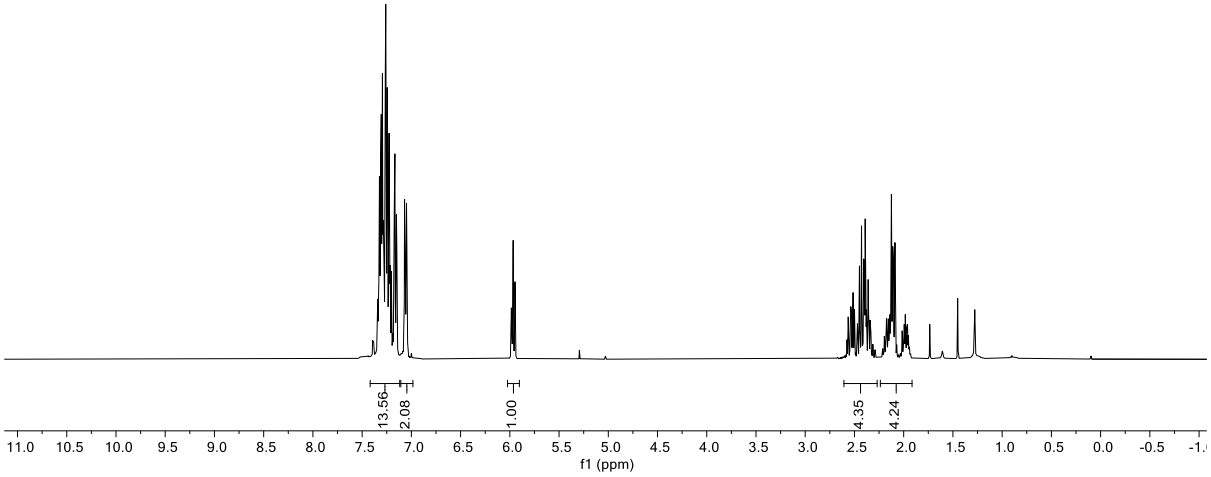
^{1}H NMR ($CDCl_3$, 400 MHz)



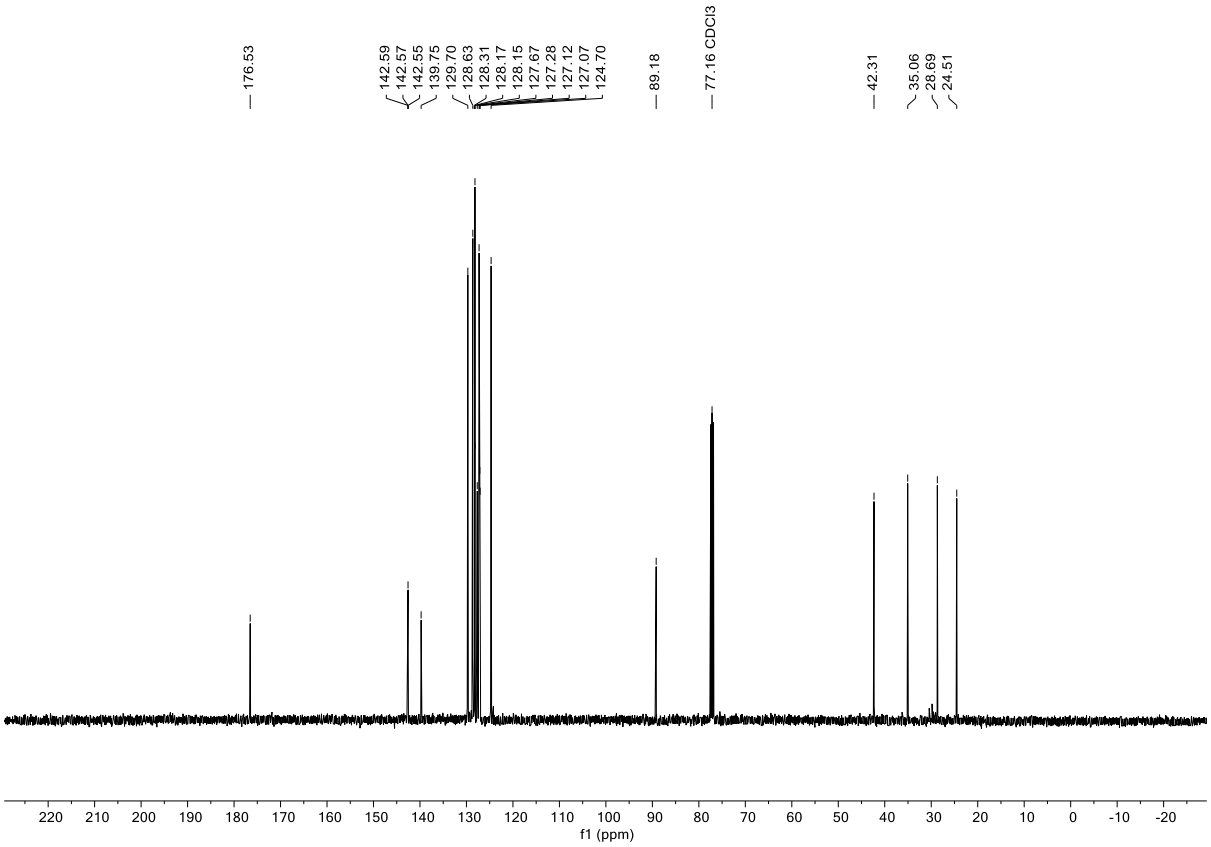
2f

$C_{26}H_{24}O_2$

368.48 g mol^{-1}

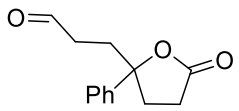


^{13}C NMR ($CDCl_3$, 101 MHz)



3-(5-Oxo-2-phenyltetrahydrofuran-2-yl)propanal 5.

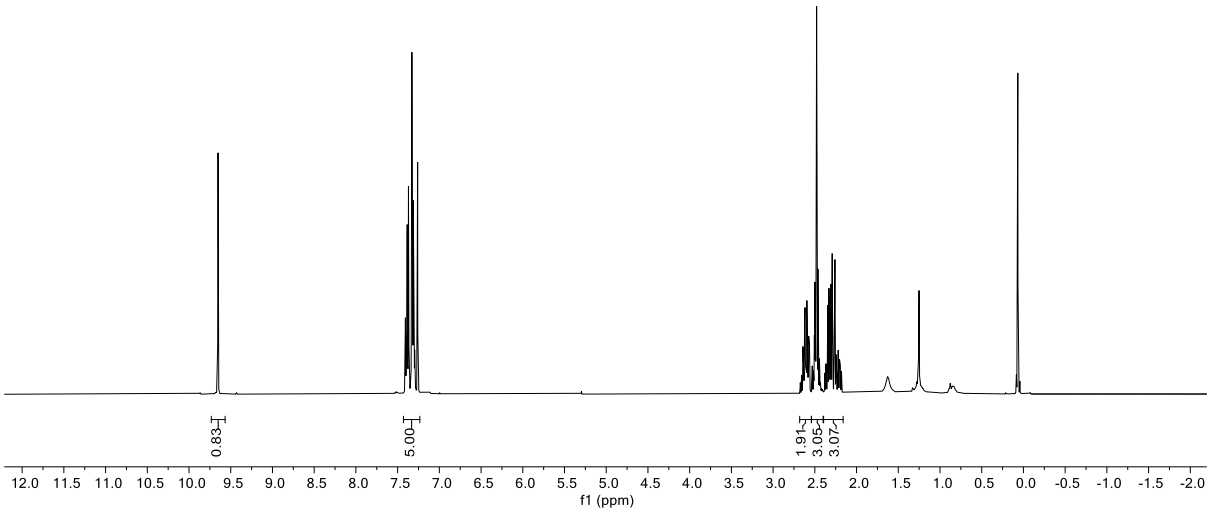
^{1}H NMR ($CDCl_3$, 400 MHz)



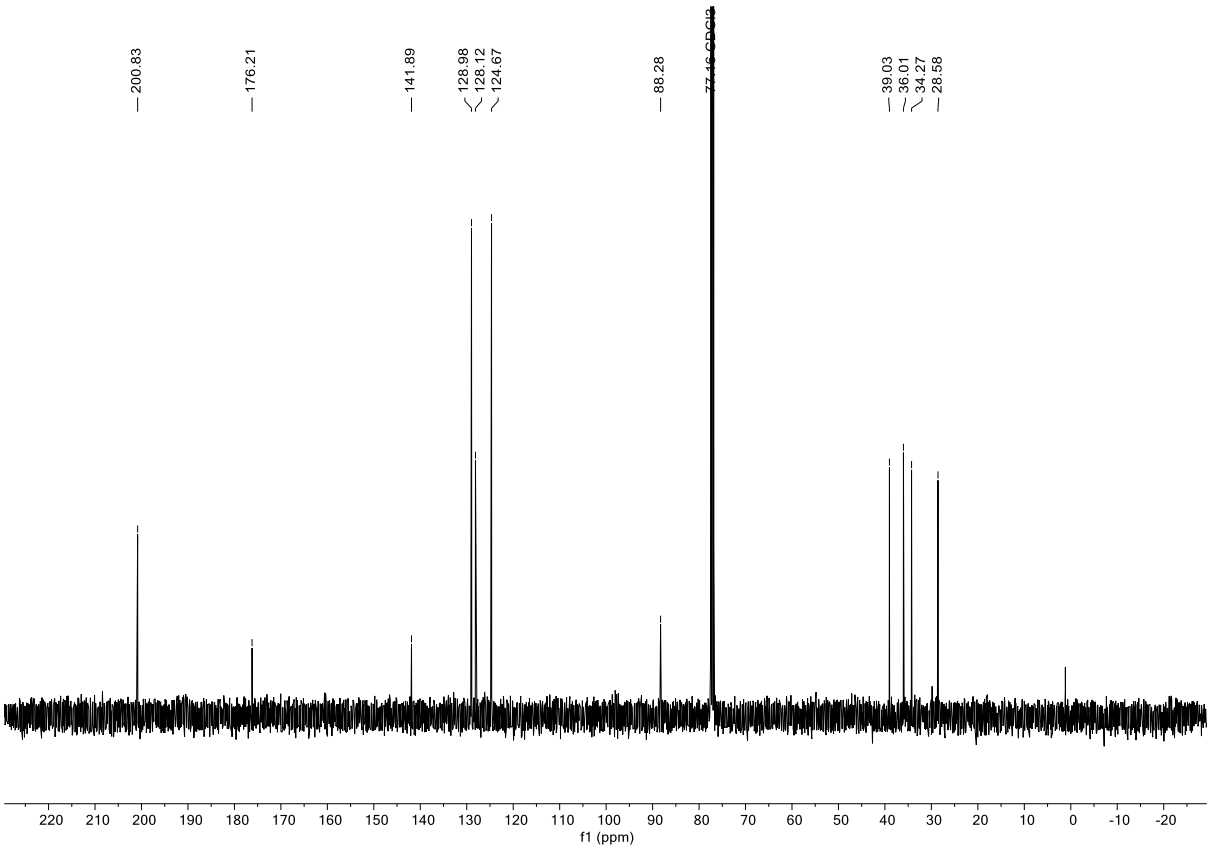
5

$C_{13}H_{14}O_3$

218.25 g mol^{-1}

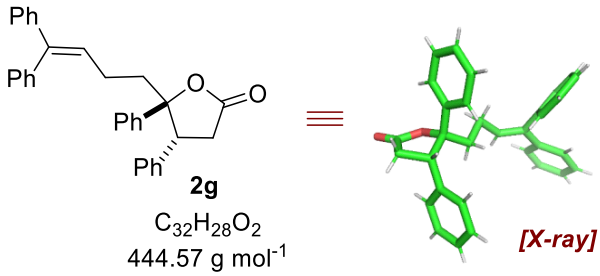


^{13}C NMR ($CDCl_3$, 101 MHz)



(±)-(4*R*,5*S*)-5-(4,4-diphenylbut-3-en-1-yl)-4,5-diphenyldihydrofuran-2(3H)-one 2g

^{1}H NMR ($CDCl_3$, 400 MHz)

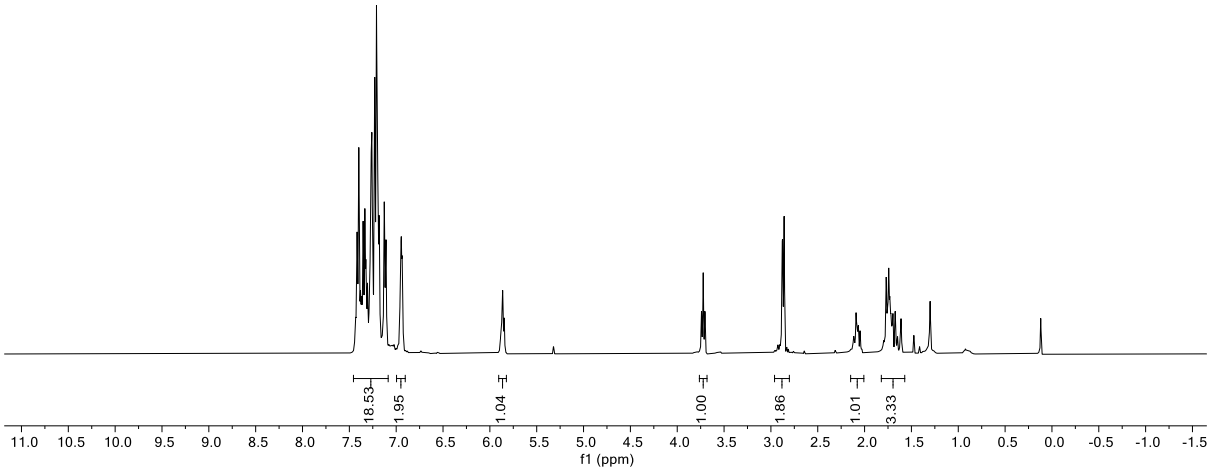


2g

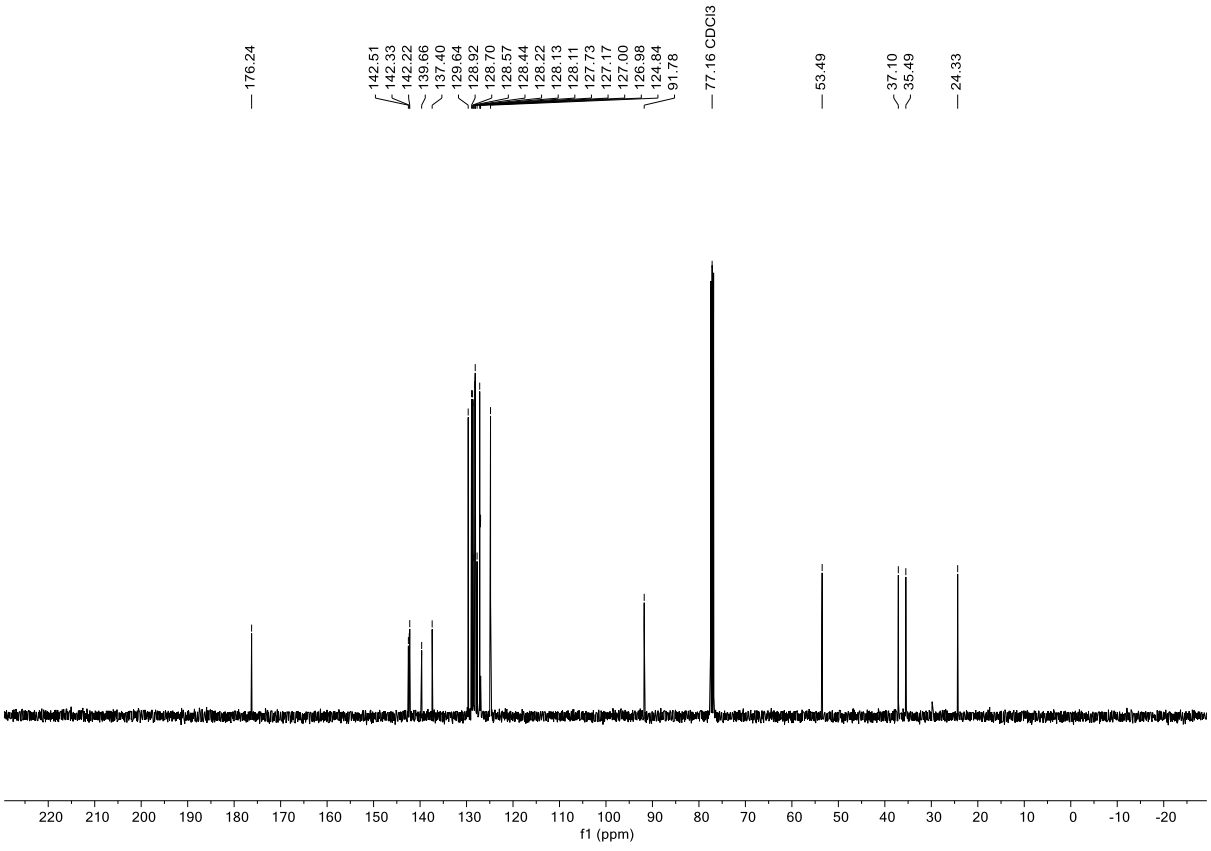
$C_{32}H_{28}O_2$

444.57 g mol^{-1}

[X-ray]

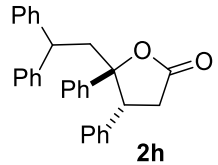


^{13}C NMR ($CDCl_3$, 101 MHz)



(±)-(4*R*,5*S*)-5-(2,2-Diphenylethyl)-4,5-diphenyldihydrofuran-2(3H)-one 2h.

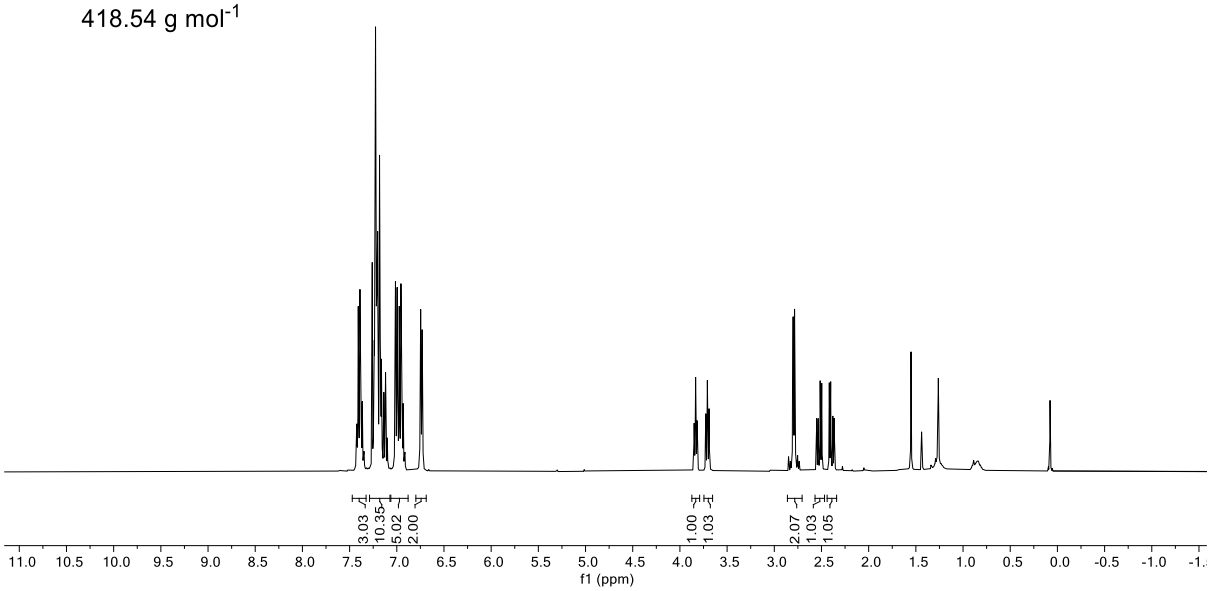
^{1}H NMR ($CDCl_3$, 400 MHz)



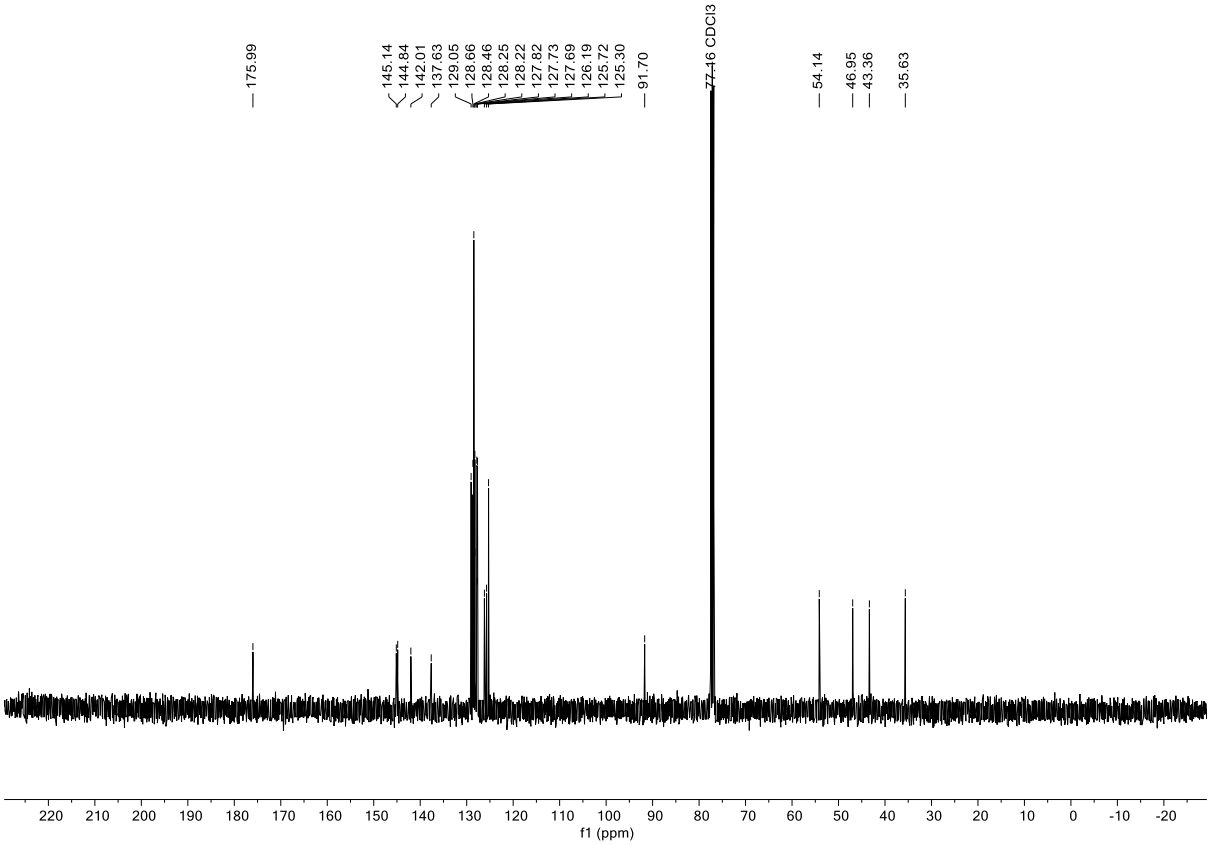
2h

$C_{30}H_{26}O_2$

418.54 g mol^{-1}

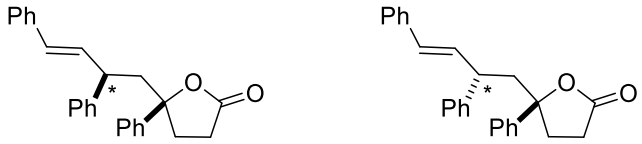


^{13}C NMR ($CDCl_3$, 101 MHz)



(±)-(*R*)-5-((*R*,*E*)-2,4-Diphenylbut-3-en-1-yl)-5-phenyldihydrofuran-2(3H)-one and **(±)-(*R*)-5-((*S*,*E*)-2,4-diphenylbut-3-en-1-yl)-5-phenyldihydrofuran-2(3H)-one 2i.**

^{1}H NMR ($CDCl_3$, 400 MHz)

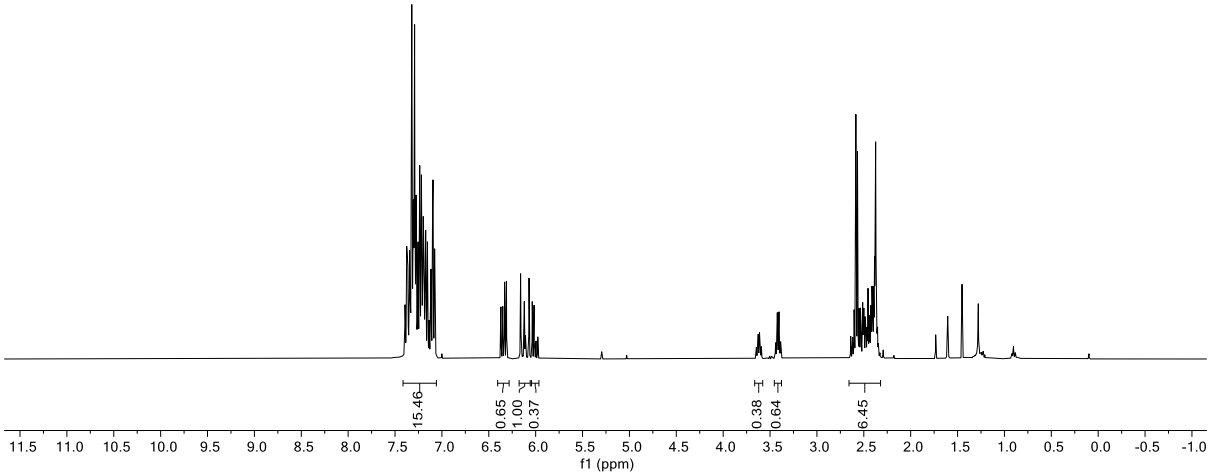


2i

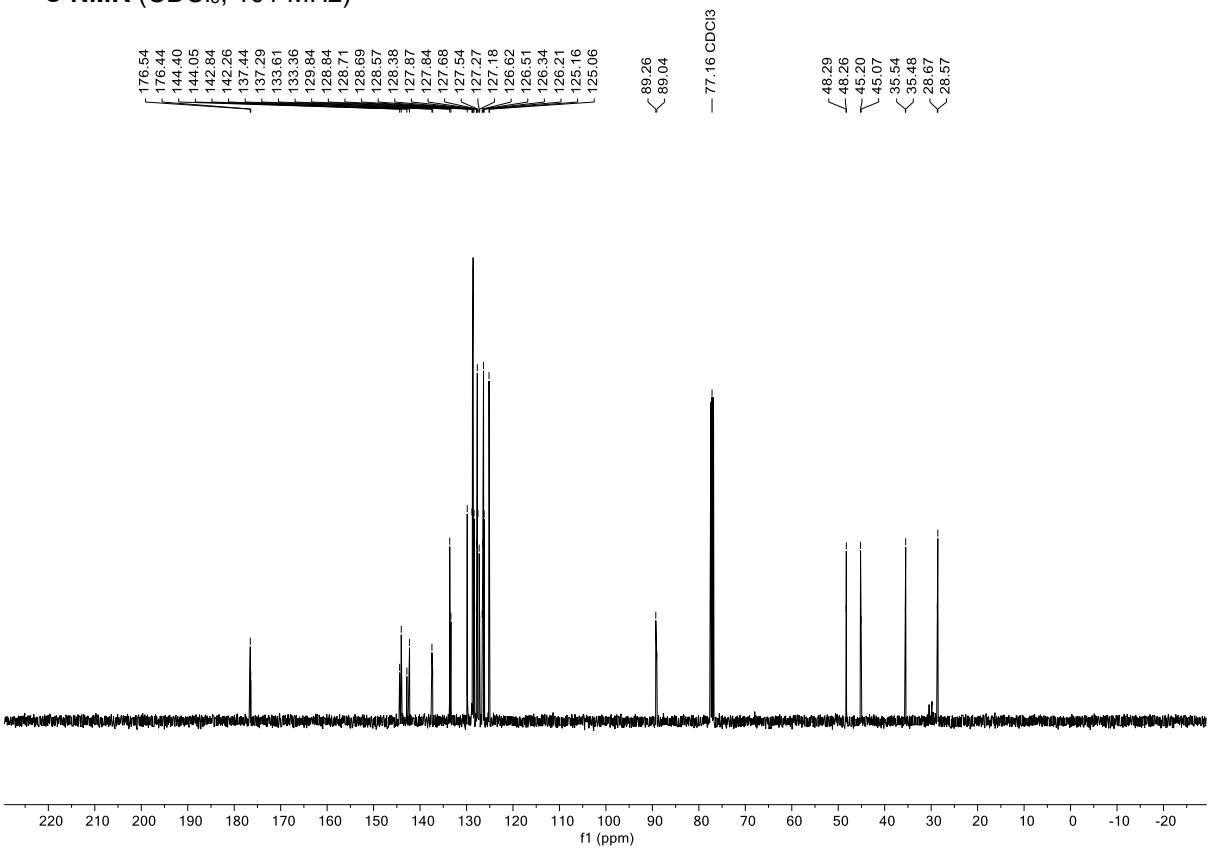
$C_{26}H_{24}O_2$

368.48 g mol^{-1}

64:36 dr

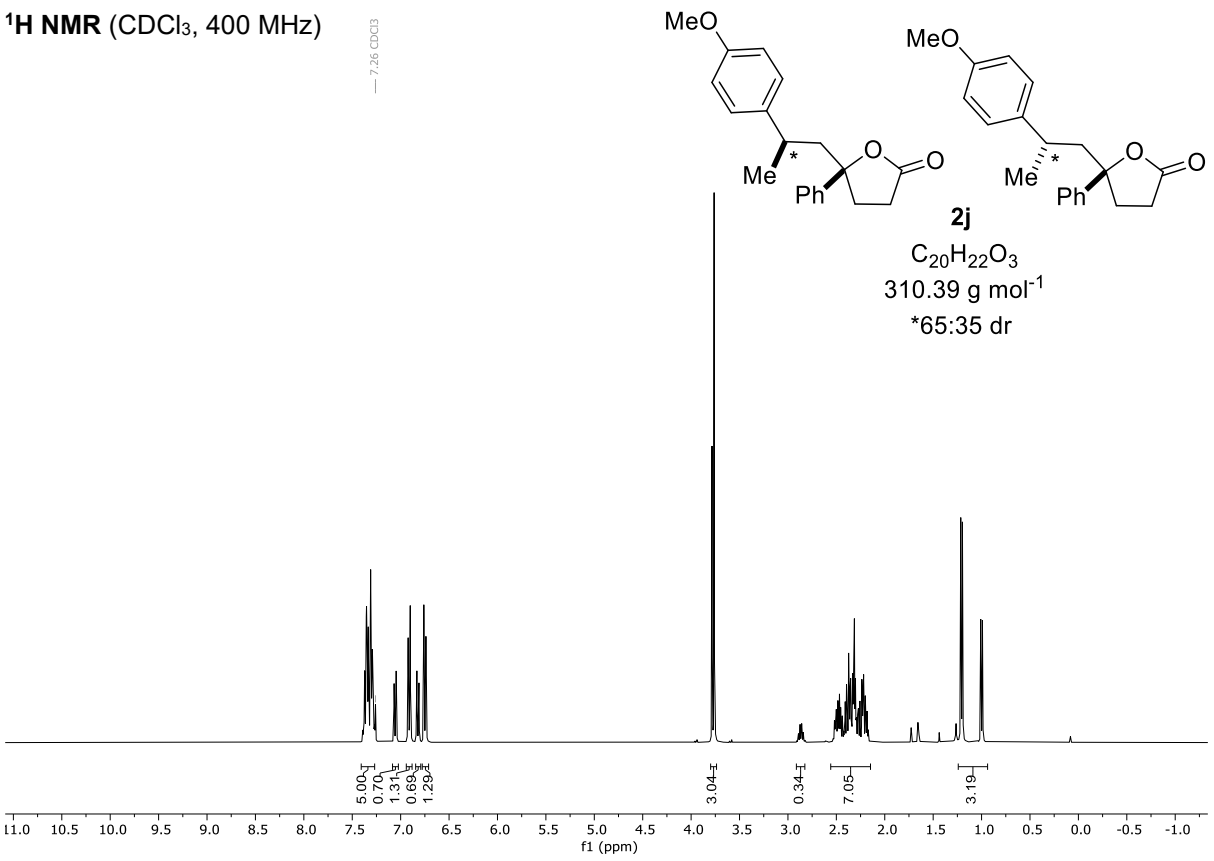


^{13}C NMR ($CDCl_3$, 101 MHz)

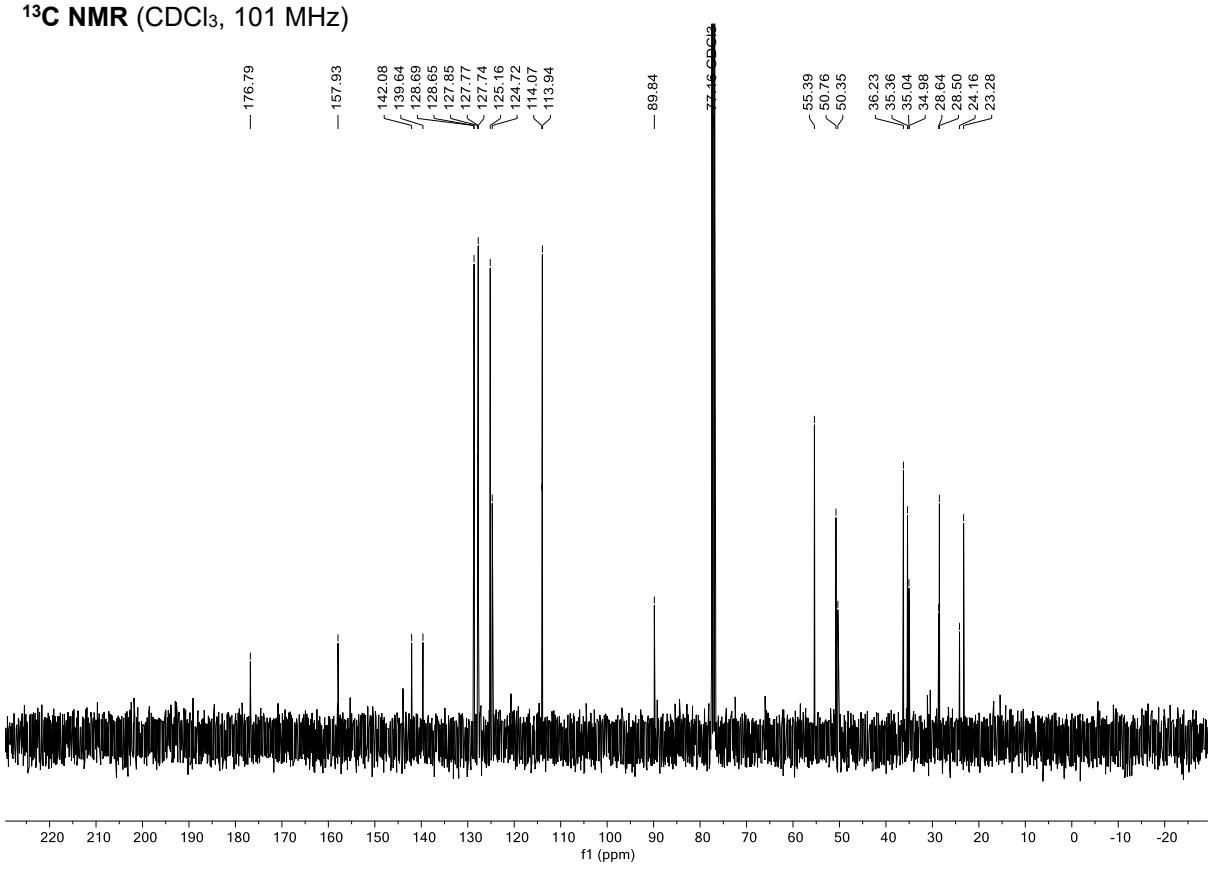


(±)-(*R*)-5-((*R*)-2-(4-Methoxyphenyl)propyl)-5-phenyldihydrofuran-2(3H)-one and (±)-(*R*)-5-((*S*)-2-(4-Methoxyphenyl)propyl)-5-phenyldihydrofuran-2(3H)-one 2j

^{1}H NMR ($CDCl_3$, 400 MHz)

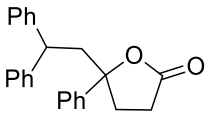


^{13}C NMR ($CDCl_3$, 101 MHz)



5-(2,2-Diphenylethyl)-5-phenyldihydrofuran-2(3H)-one 2k.

^{1}H NMR ($CDCl_3$, 400 MHz)

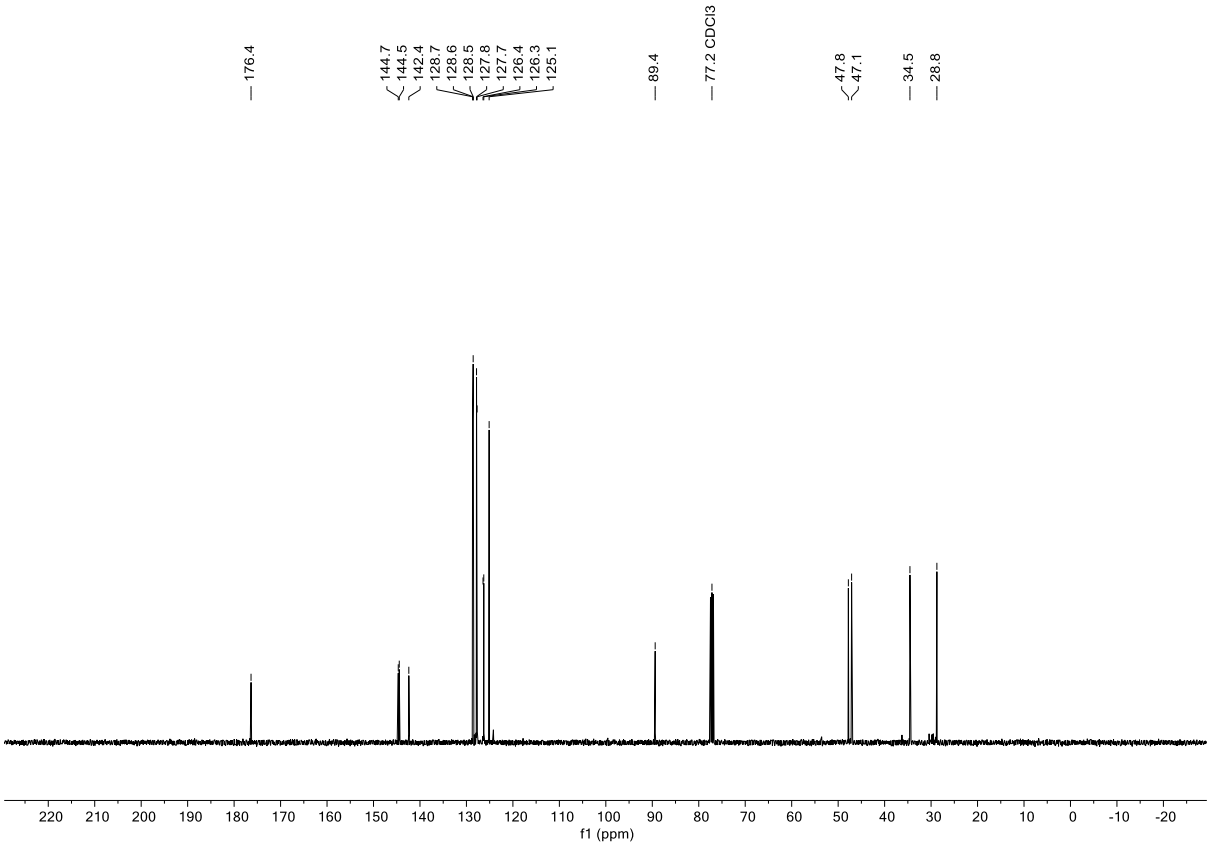


2k

$C_{24}H_{22}O_2$

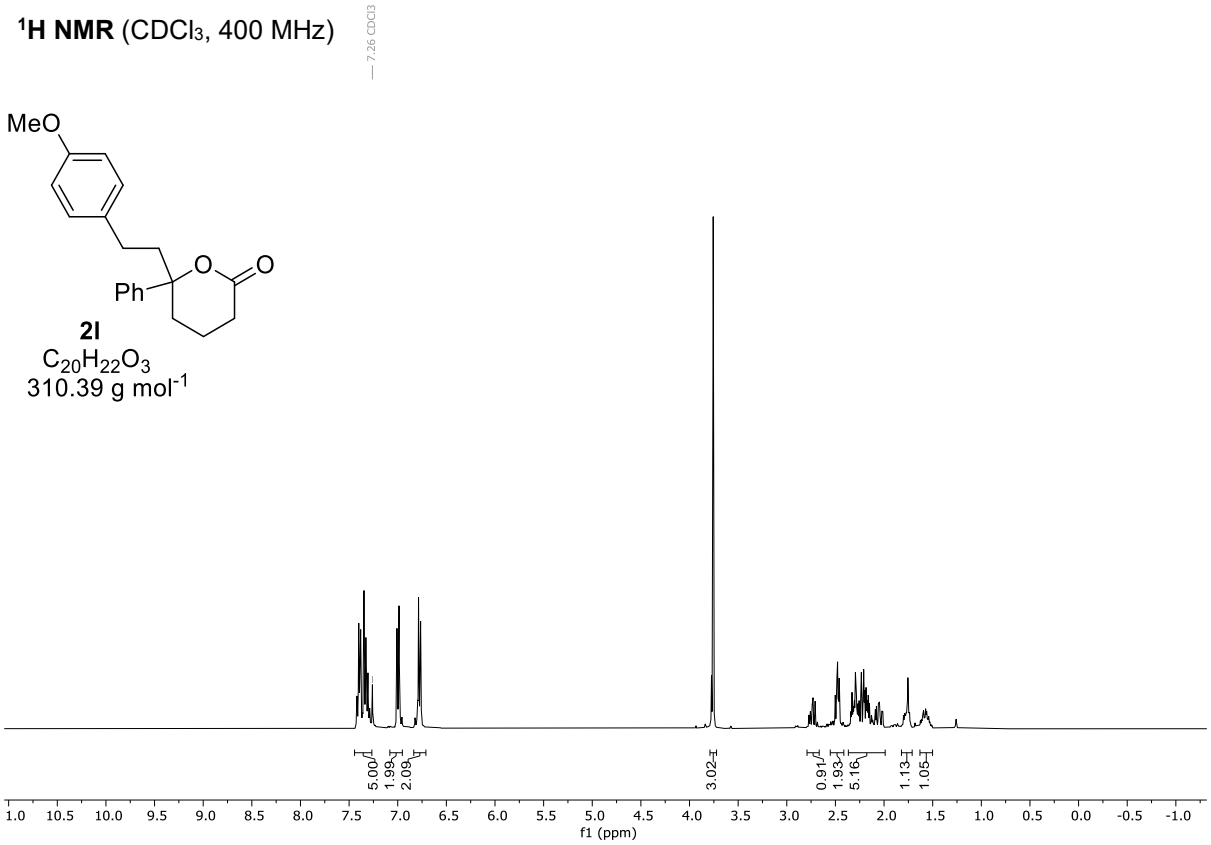
342.44 g mol^{-1}

^{13}C NMR ($CDCl_3$, 101 MHz)

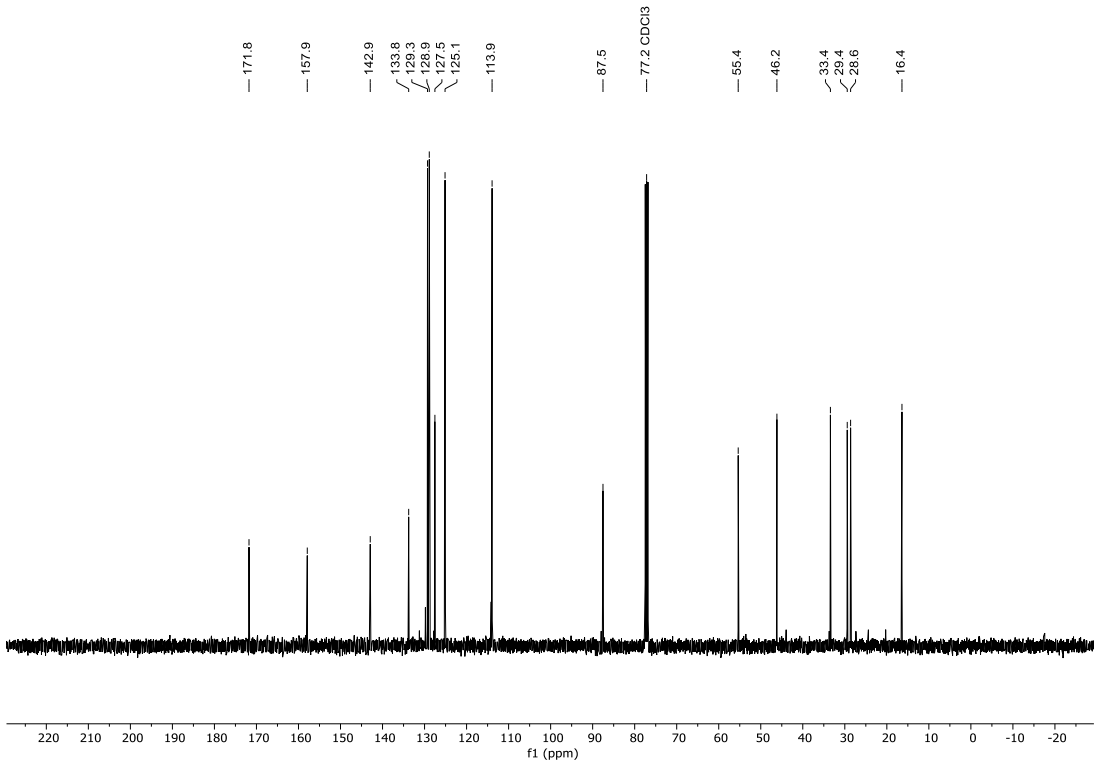


6-(4-Methoxyphenethyl)-6-phenyltetrahydro-2H-pyran-2-one 2l.

^{1}H NMR ($CDCl_3$, 400 MHz)

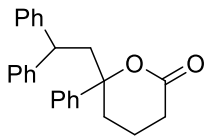


^{13}C NMR ($CDCl_3$, 101 MHz)



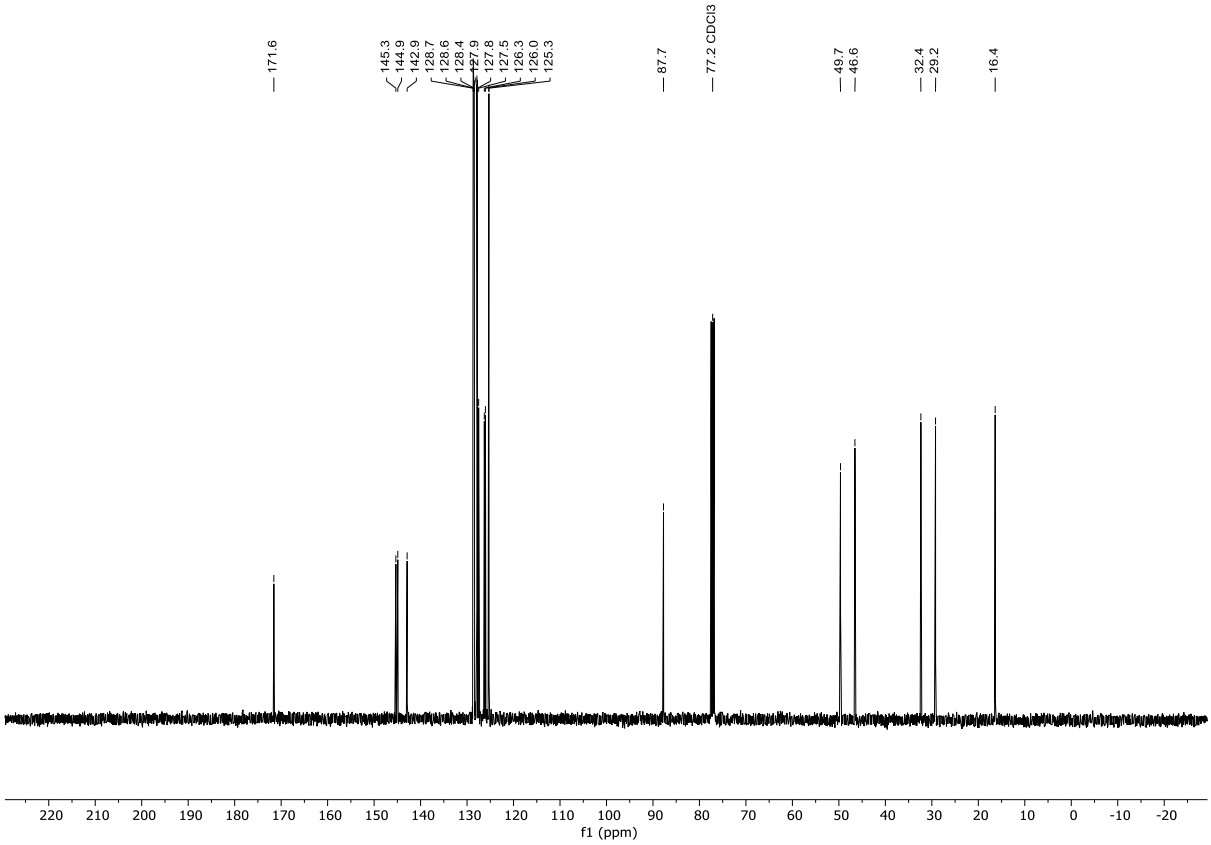
6-(2,2-Diphenylethyl)-6-phenyltetrahydro-2H-pyran-2-one 2m

^{1}H NMR ($CDCl_3$, 400 MHz)



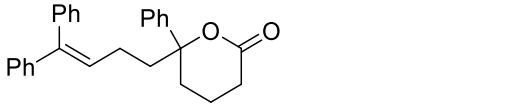
2m
$C_{25}H_{24}O_2$
356.47 g mol^{-1}

^{13}C NMR ($CDCl_3$, 101 MHz)



6-(4,4-Diphenylbut-3-en-1-yl)-6-phenyltetrahydro-2H-pyran-2-one 2n.

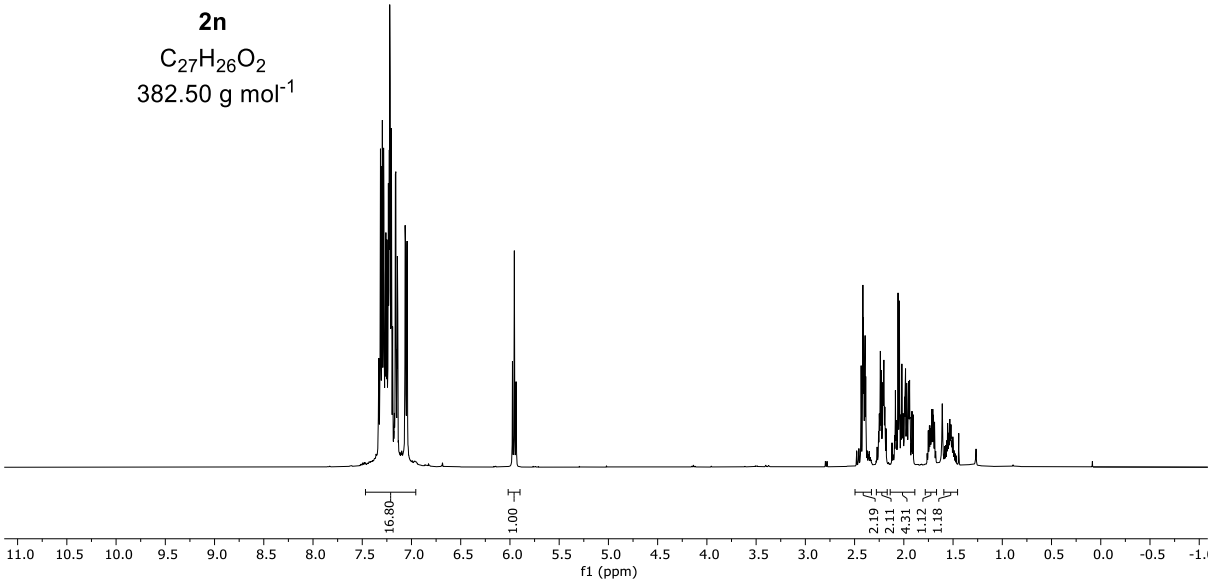
^{1}H NMR ($CDCl_3$, 400 MHz)



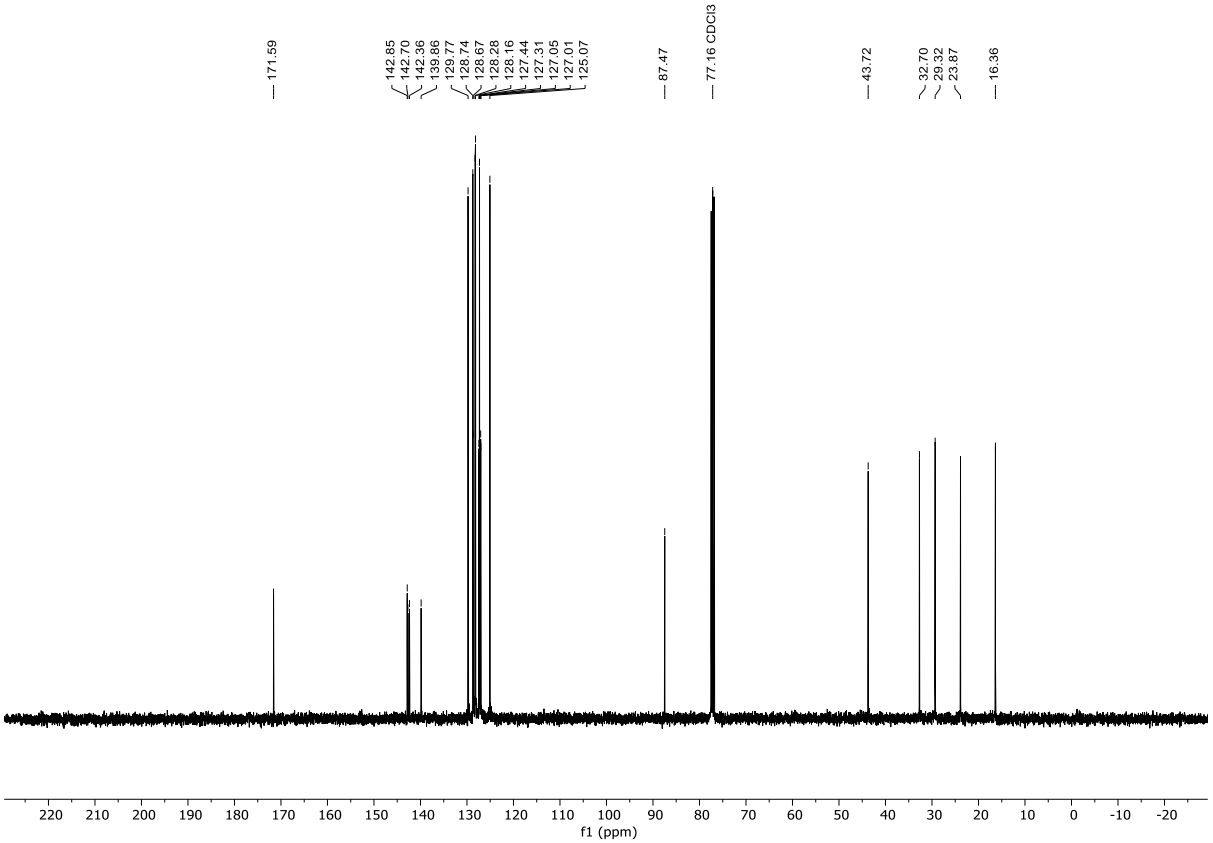
2n

$C_{27}H_{26}O_2$

382.50 g mol^{-1}

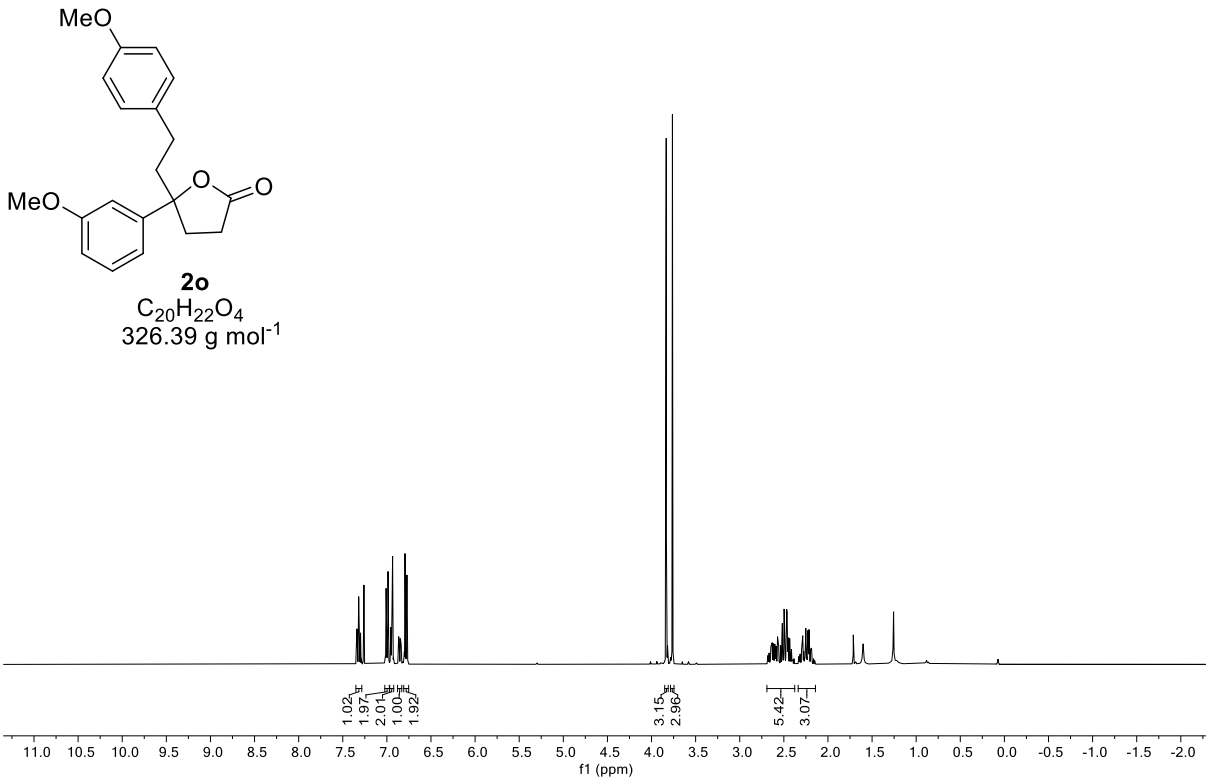


^{13}C NMR ($CDCl_3$, 101 MHz)

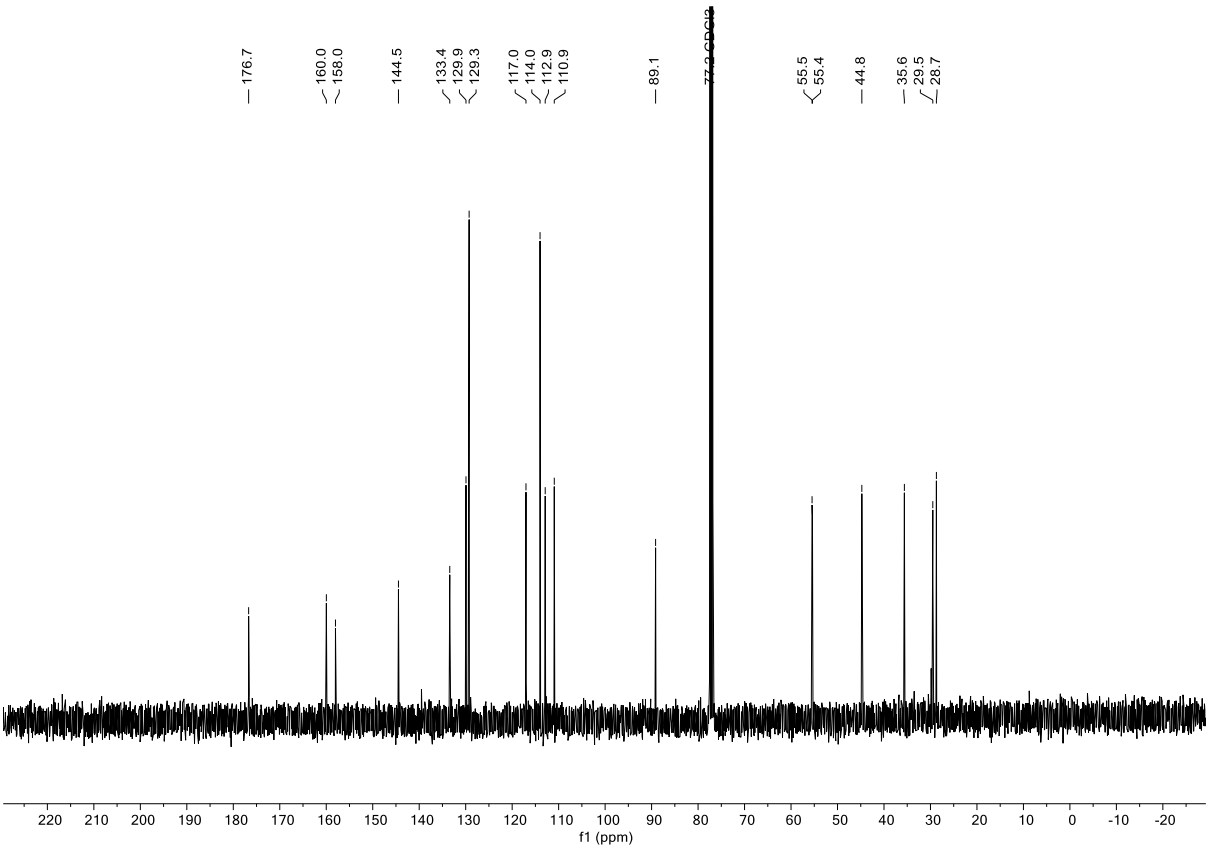


5-(4-Methoxyphenethyl)-5-(3-methoxyphenyl)dihydrofuran-2(3H)-one 2o.

^{1}H NMR ($CDCl_3$, 400 MHz)

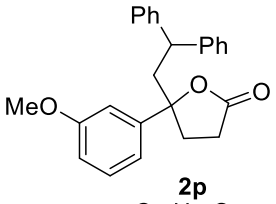


^{13}C NMR ($CDCl_3$, 101 MHz)

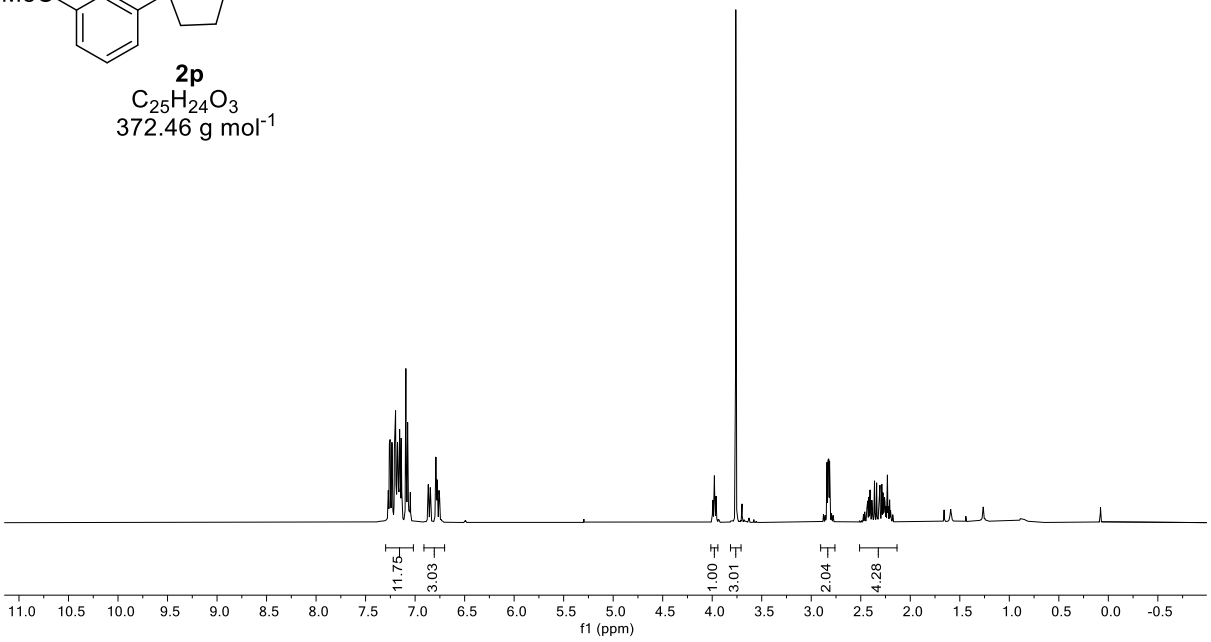


5-(2,2-Diphenylethyl)-5-(3-methoxyphenyl)dihydrofuran-2(3H)-one 2p.

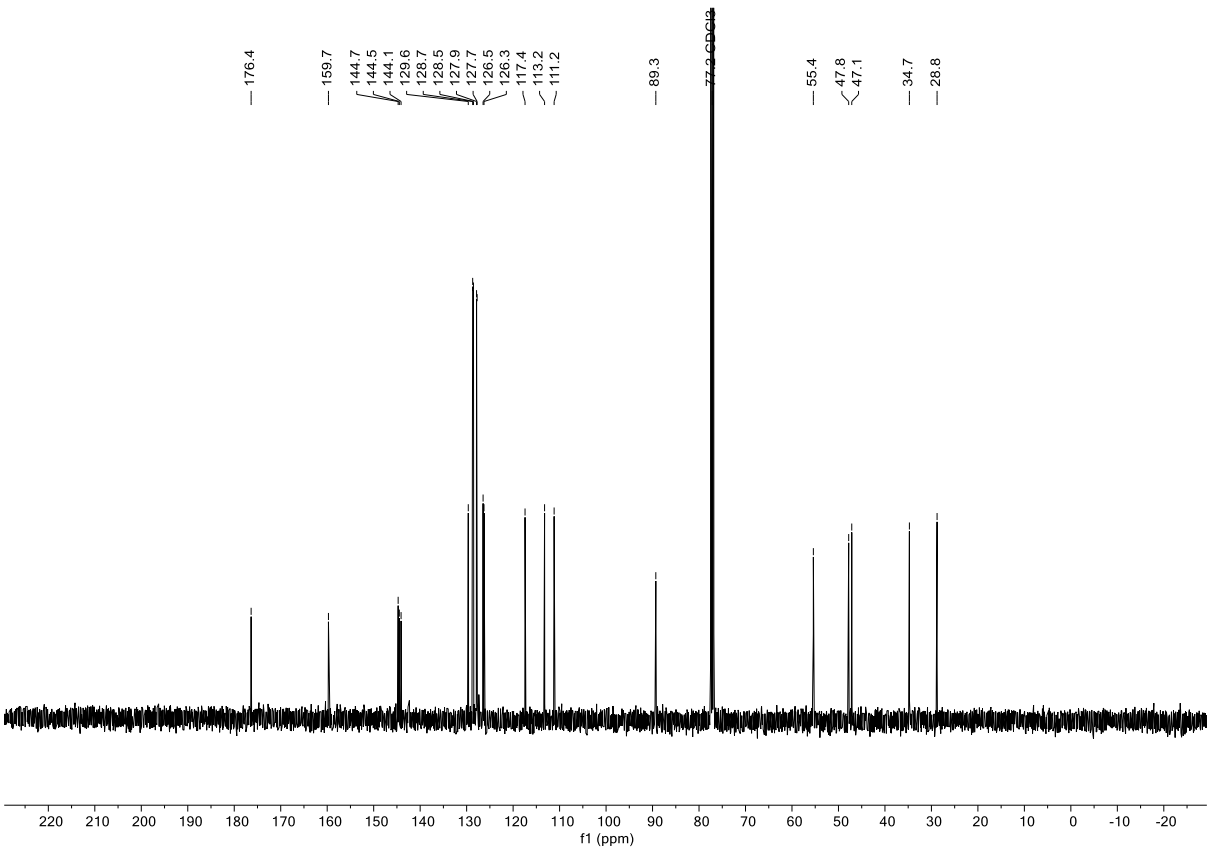
^{1}H NMR ($CDCl_3$, 400 MHz)



2p
$C_{25}H_{24}O_3$
372.46 g mol^{-1}

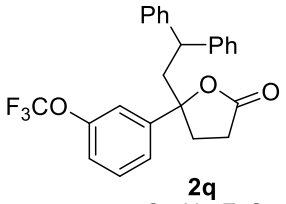


^{13}C NMR ($CDCl_3$, 101 MHz)

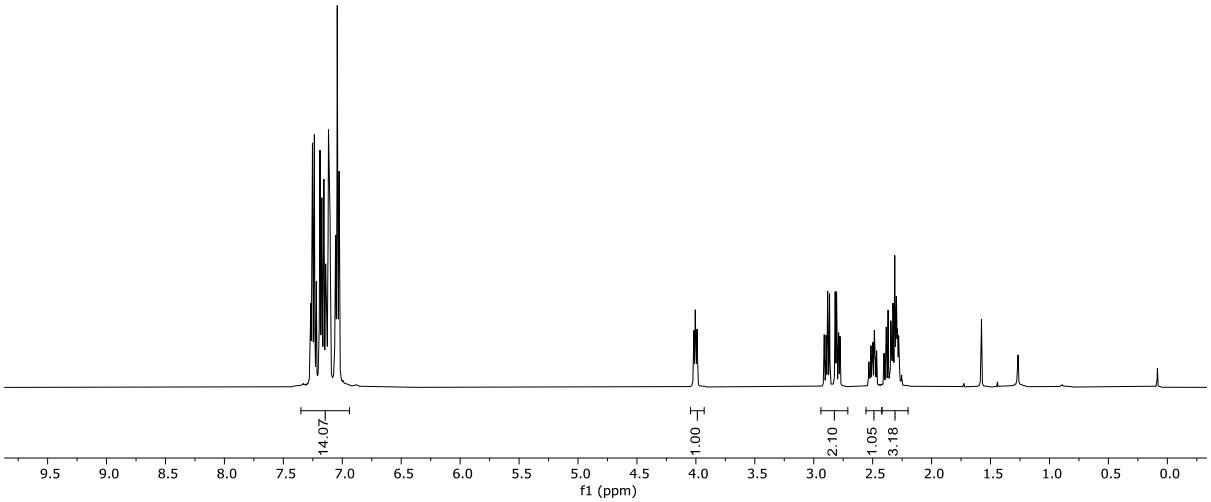


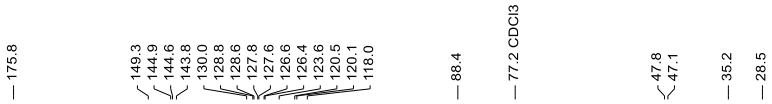
5-(2,2-Diphenylethyl)-5-(3-(trifluoromethoxy)phenyl)dihydrofuran-2(3H)-one 2q.

^{1}H NMR (500 MHz, $CDCl_3$)

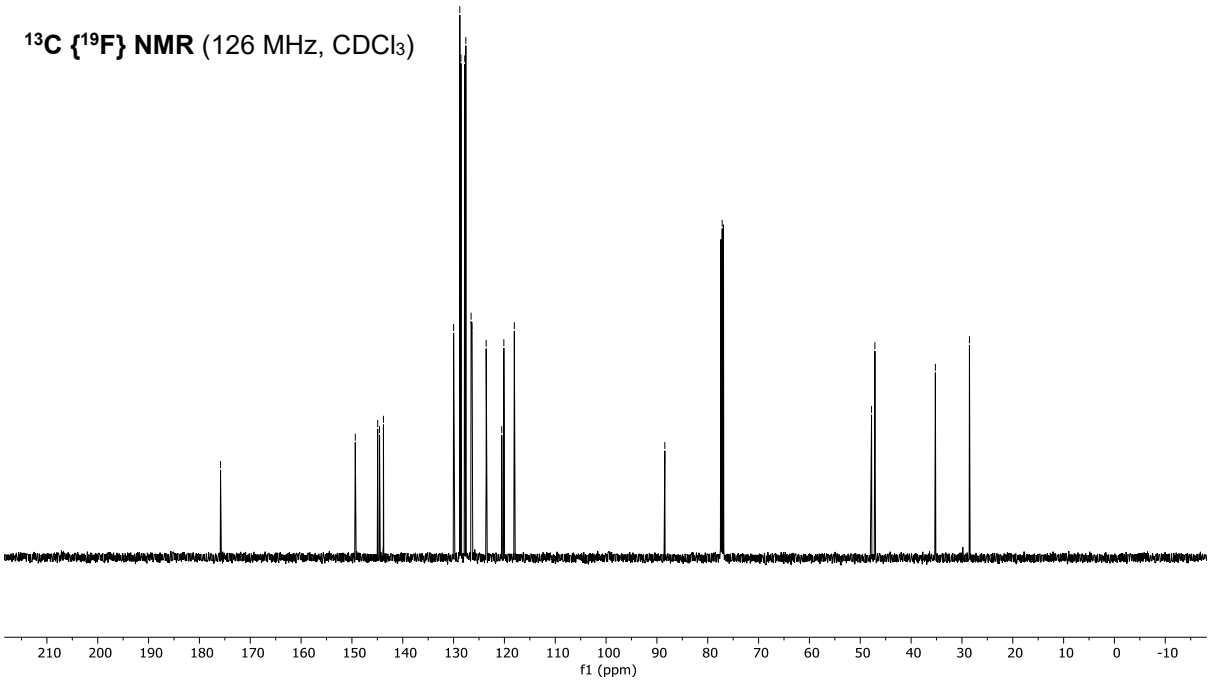


2q
$C_{25}H_{21}F_3O_3$
426.44 g mol^{-1}

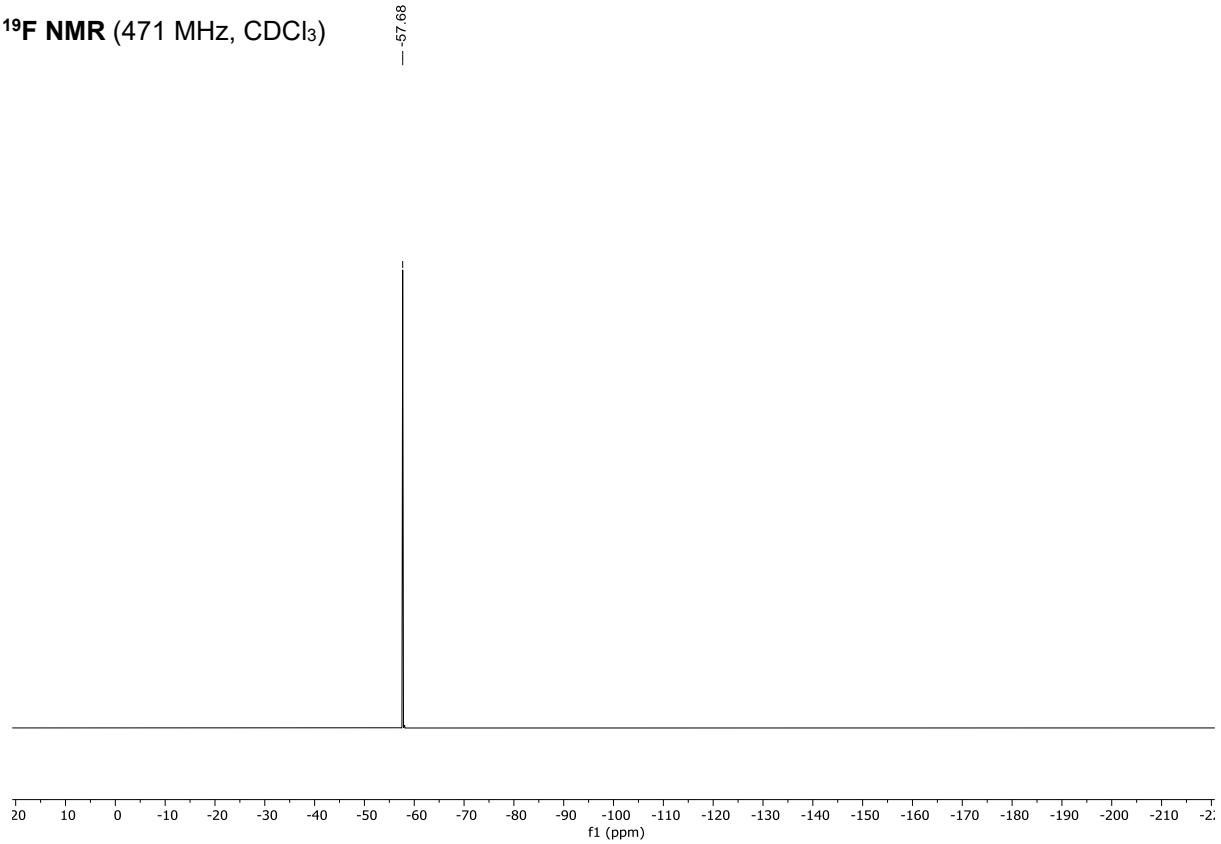




^{13}C {^{19}F} NMR (126 MHz, $CDCl_3$)

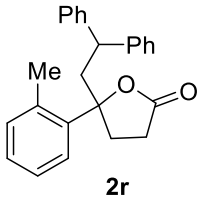


^{19}F NMR (471 MHz, $CDCl_3$)



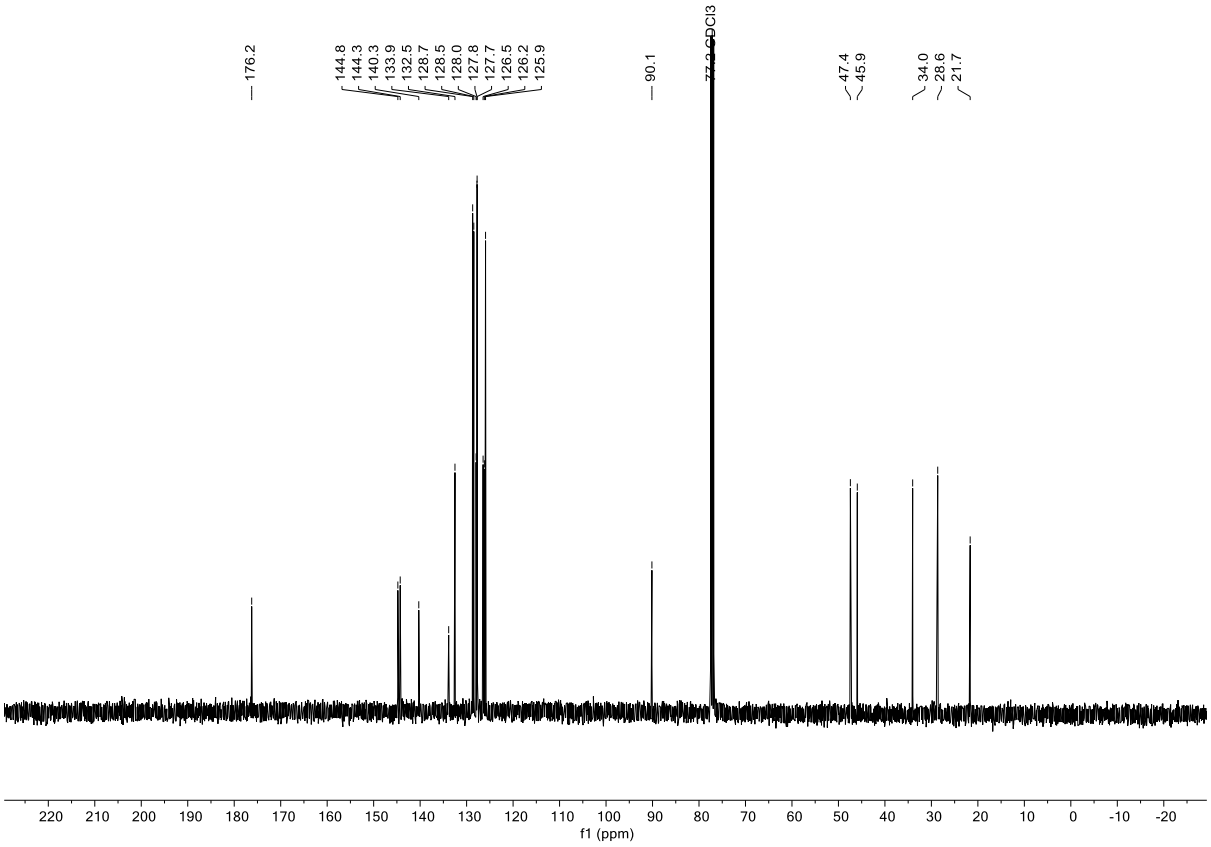
5-(2,2-Diphenylethyl)-5-(o-tolyl)dihydrofuran-2(3H)-one 2r.

^{1}H NMR ($CDCl_3$, 400 MHz)



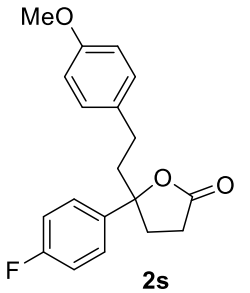
2r
$C_{25}H_{24}O_2$
356.47 g mol^{-1}

^{13}C NMR ($CDCl_3$, 101 MHz)

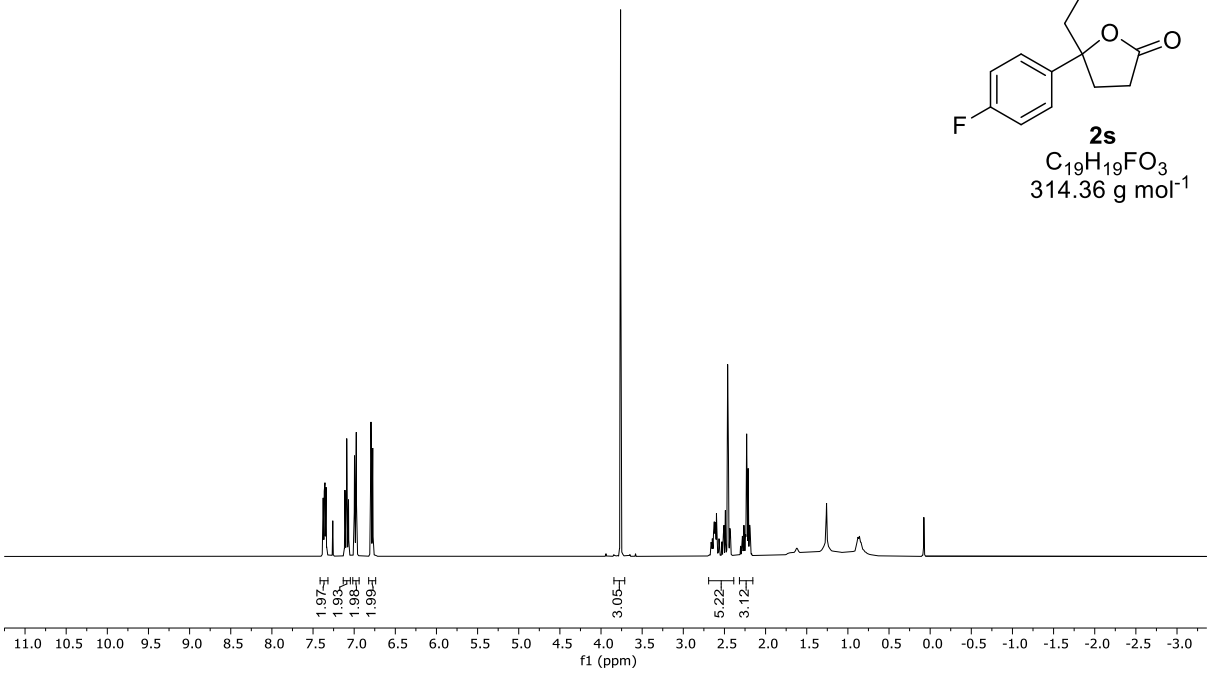


5-(4-Fluorophenyl)-5-(4-methoxyphenethyl)dihydrofuran-2(3H)-one 2s.

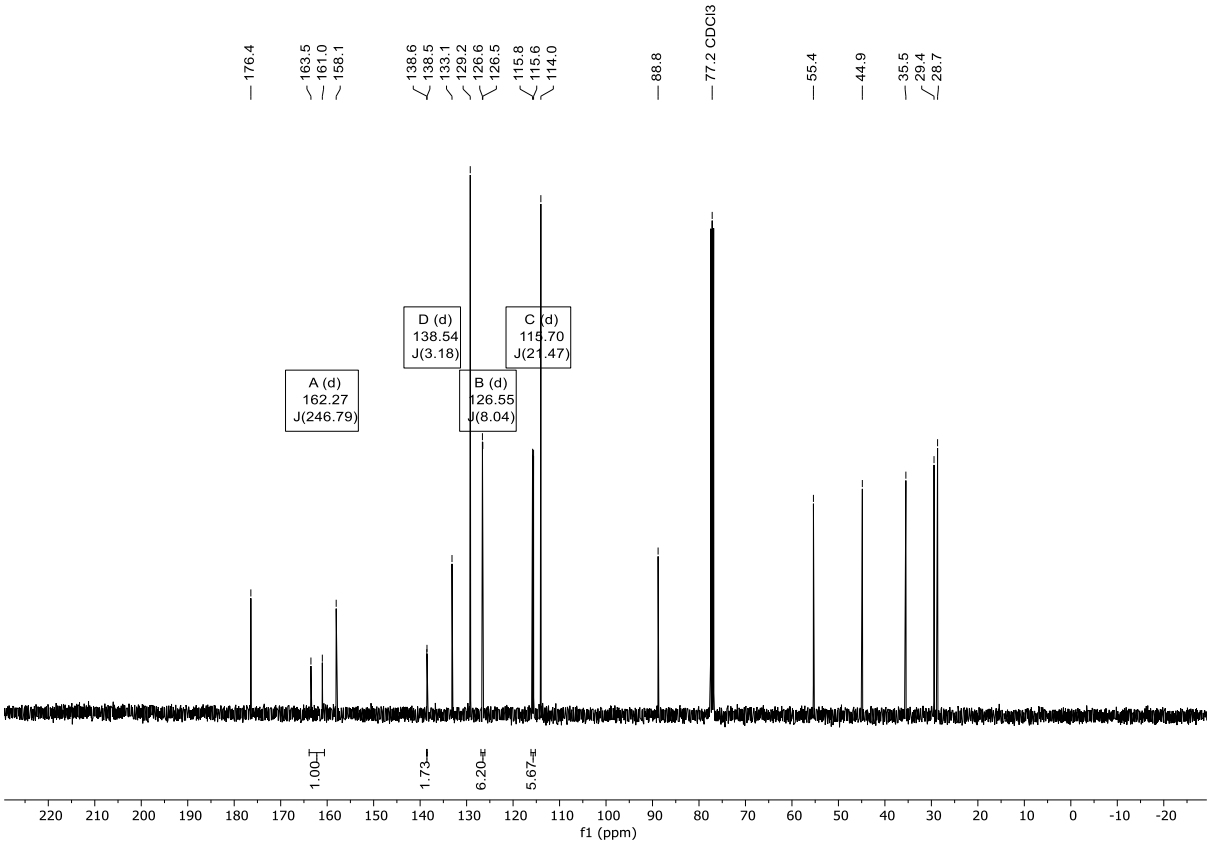
^{1}H NMR (400 MHz, $CDCl_3$)



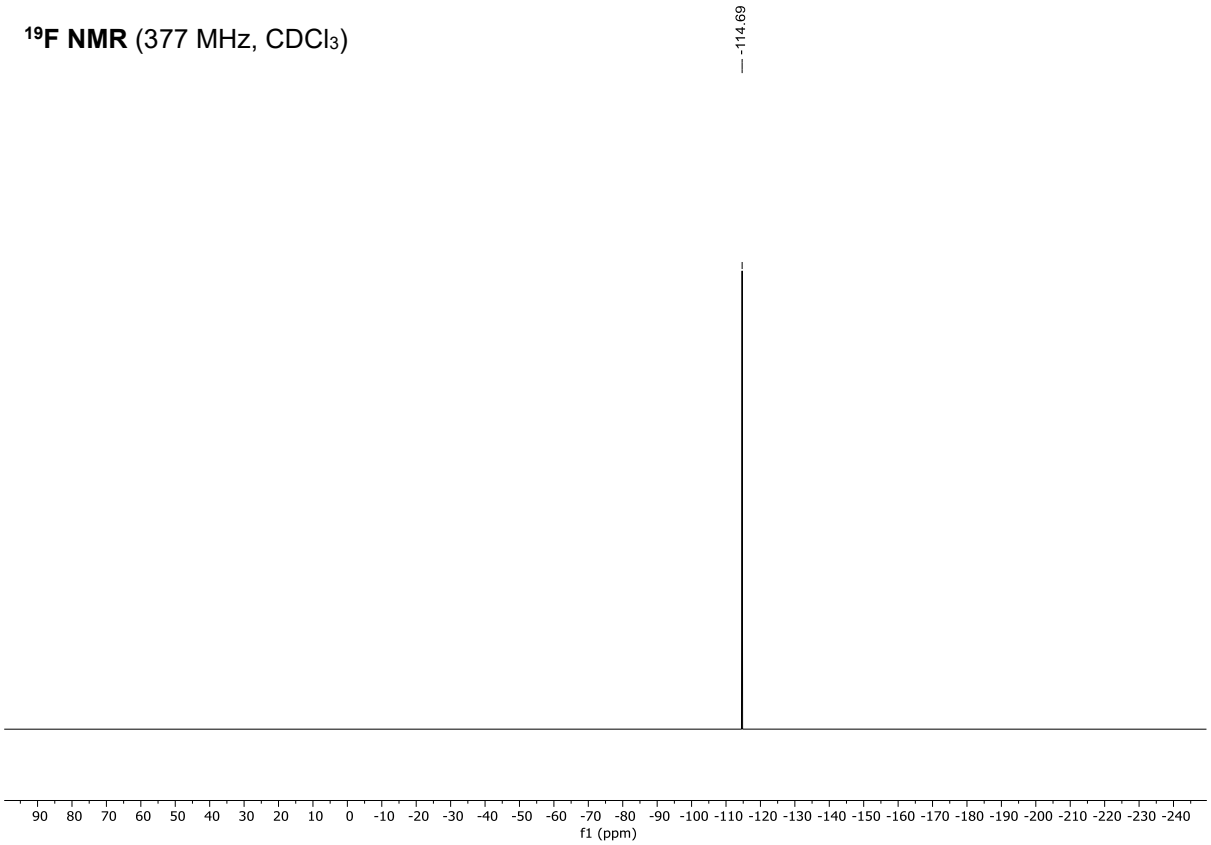
2s
$C_{19}H_{19}FO_3$
314.36 g mol^{-1}



^{13}C NMR (101 MHz, $CDCl_3$)

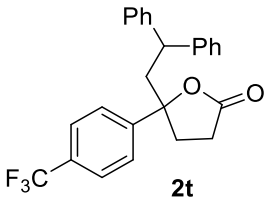


^{19}F NMR (377 MHz, $CDCl_3$)

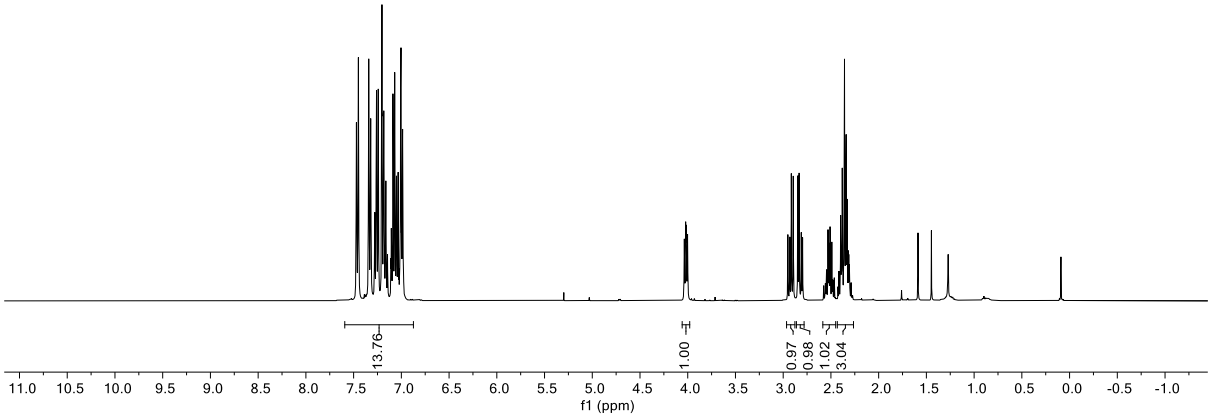


5-(2,2-Diphenylethyl)-5-(4-(trifluoromethyl)phenyl)dihydrofuran-2(3H)-one 2t

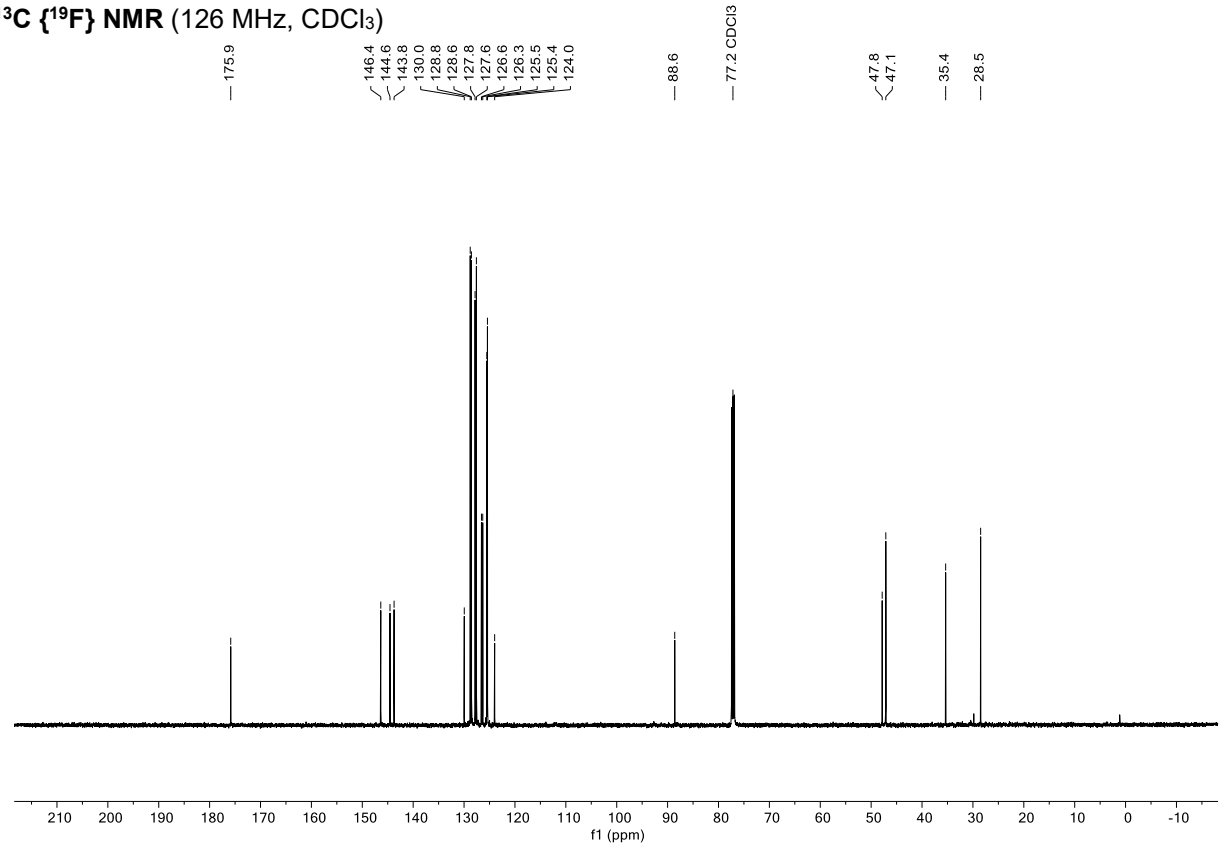
^{1}H NMR (400 MHz, $CDCl_3$)



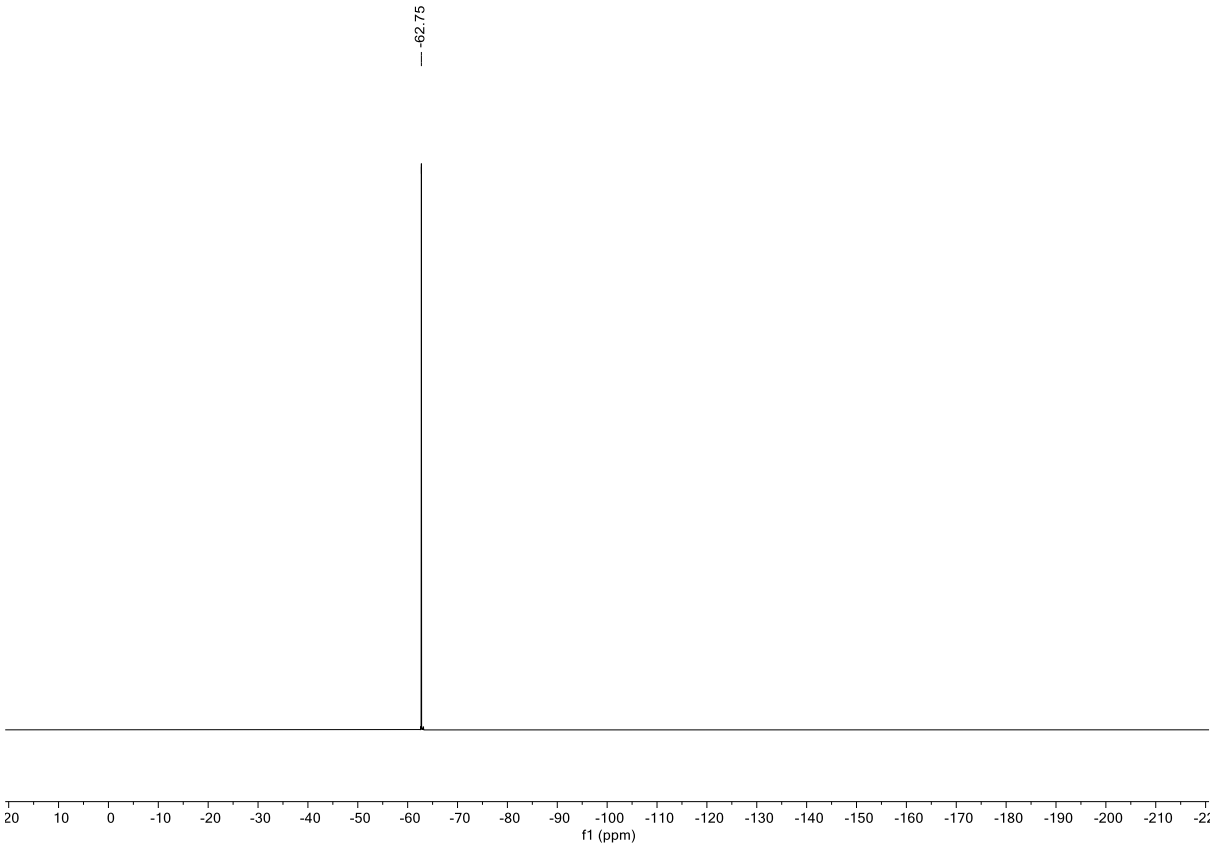
2t
$C_{25}H_{21}F_3O_2$
410.44 g mol^{-1}



^{13}C {^{19}F} NMR (126 MHz, $CDCl_3$)

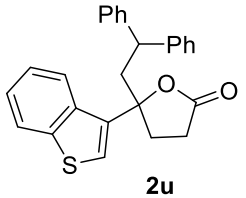


^{19}F NMR (471 MHz, $CDCl_3$)

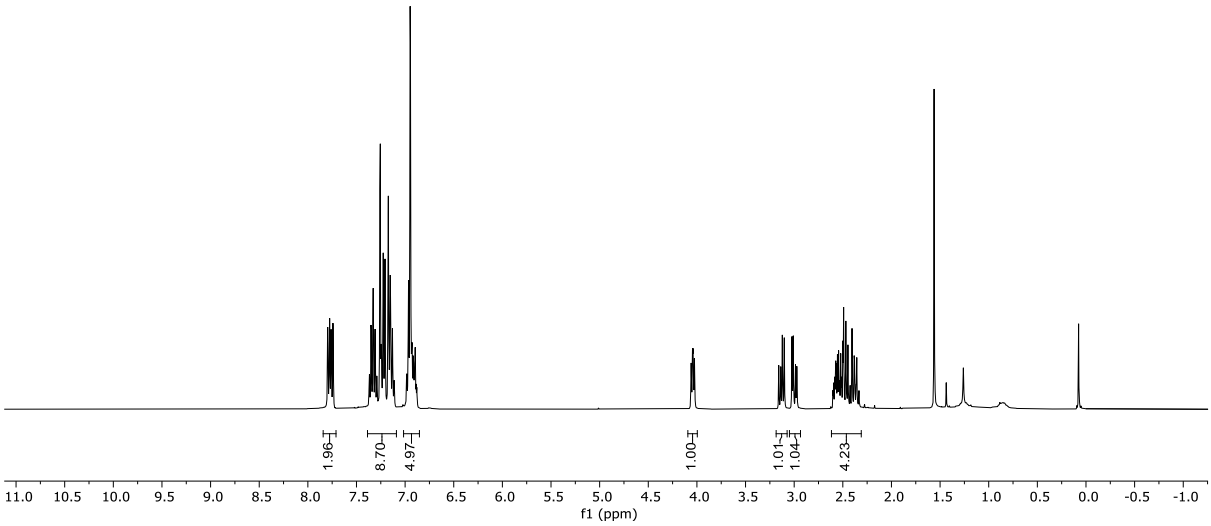


5-(Benzo[b]thiophen-3-yl)-5-(2,2-diphenylethyl)dihydrofuran-2(3H)-one 2u

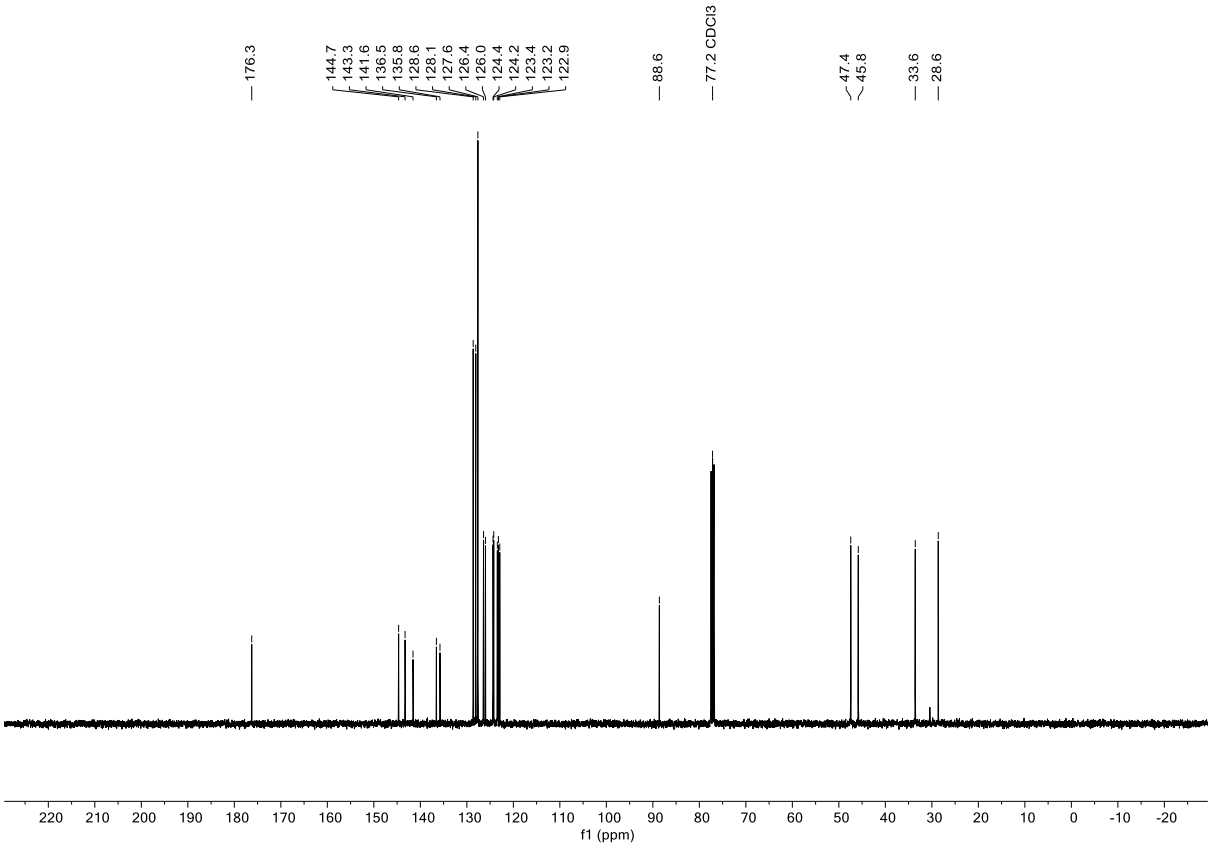
^{1}H NMR ($CDCl_3$, 400 MHz)



2u
$C_{26}H_{22}O_2S$
398.52 g mol^{-1}

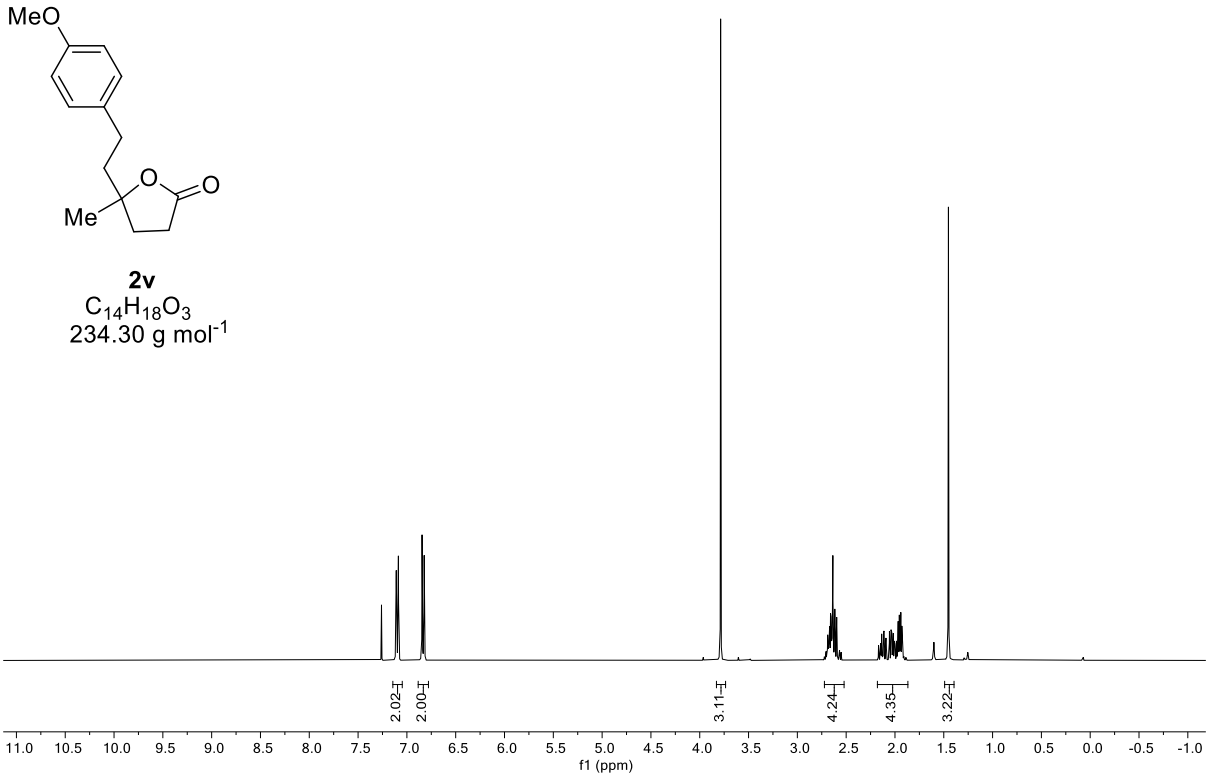


^{13}C NMR ($CDCl_3$, 101 MHz)



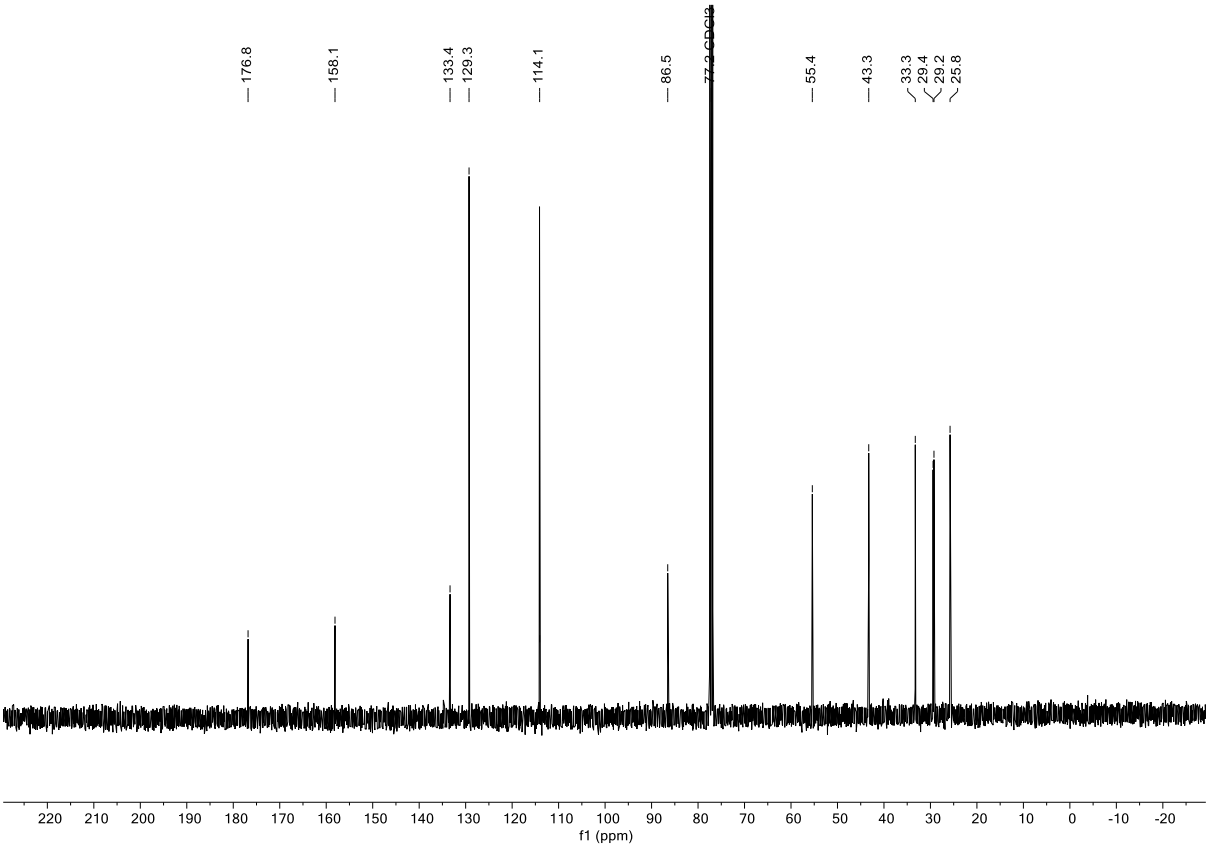
5-(4-Methoxyphenethyl)-5-methyldihydrofuran-2(3H)-one 2v.

^{1}H NMR ($CDCl_3$, 400 MHz)



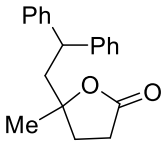
2v
$C_{14}H_{18}O_3$
234.30 g mol^{-1}

^{13}C NMR ($CDCl_3$, 101 MHz)

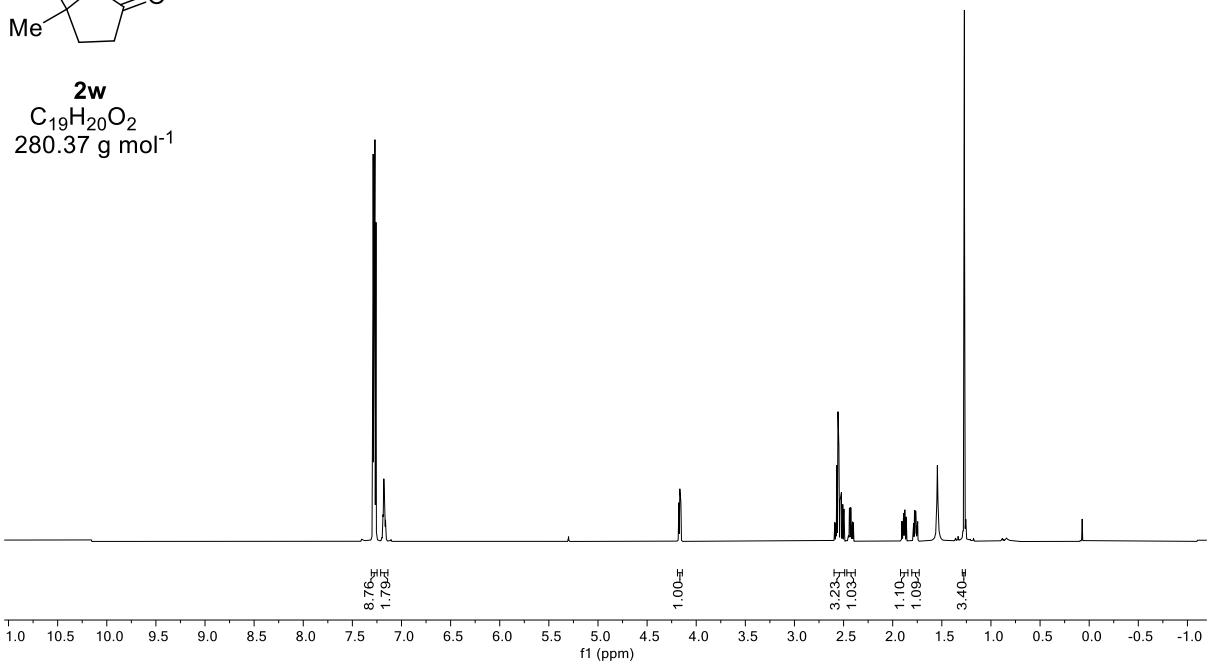


5-(2,2-Diphenylethyl)-5-methyldihydrofuran-2(3H)-one 2w.

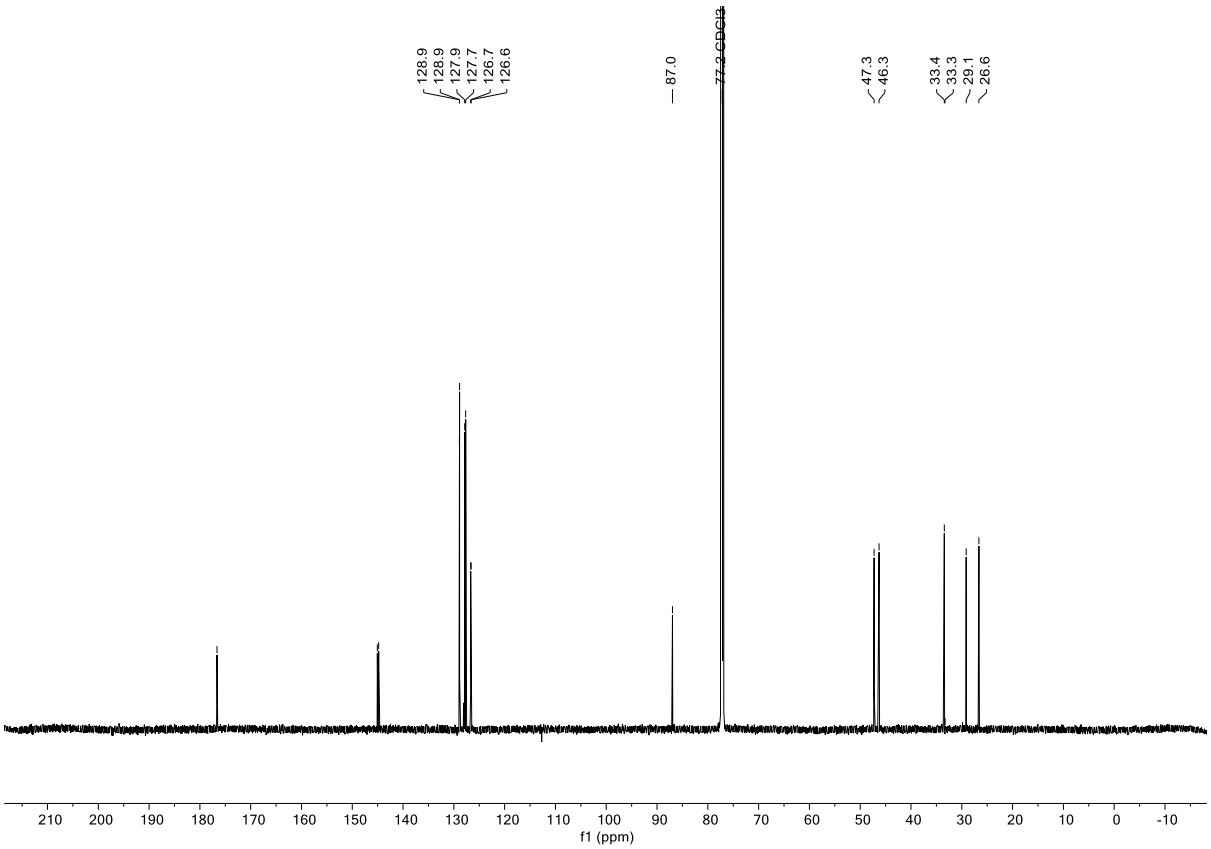
^{1}H NMR (700 MHz, $CDCl_3$)



2w
$C_{19}H_{20}O_2$
280.37 g mol^{-1}

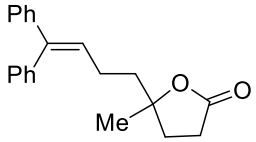


^{13}C NMR (176 MHz, $CDCl_3$)

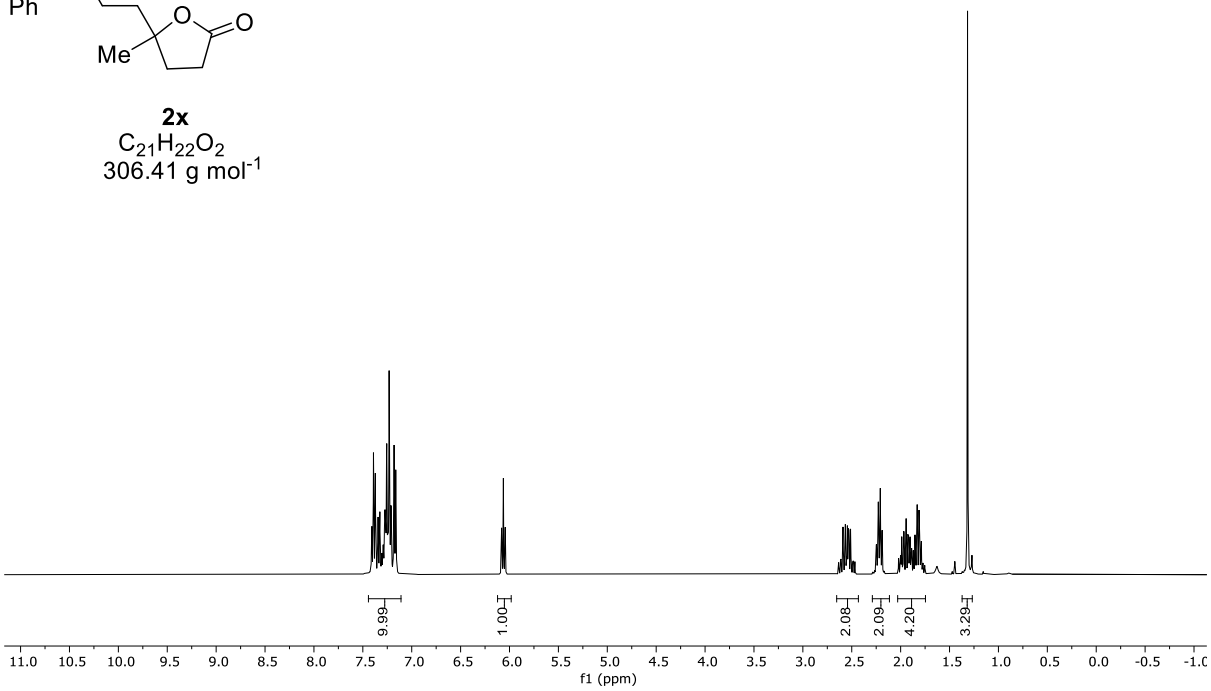


5-(4,4-Diphenylbut-3-en-1-yl)-5-methyldihydrofuran-2(3H)-one 2x.

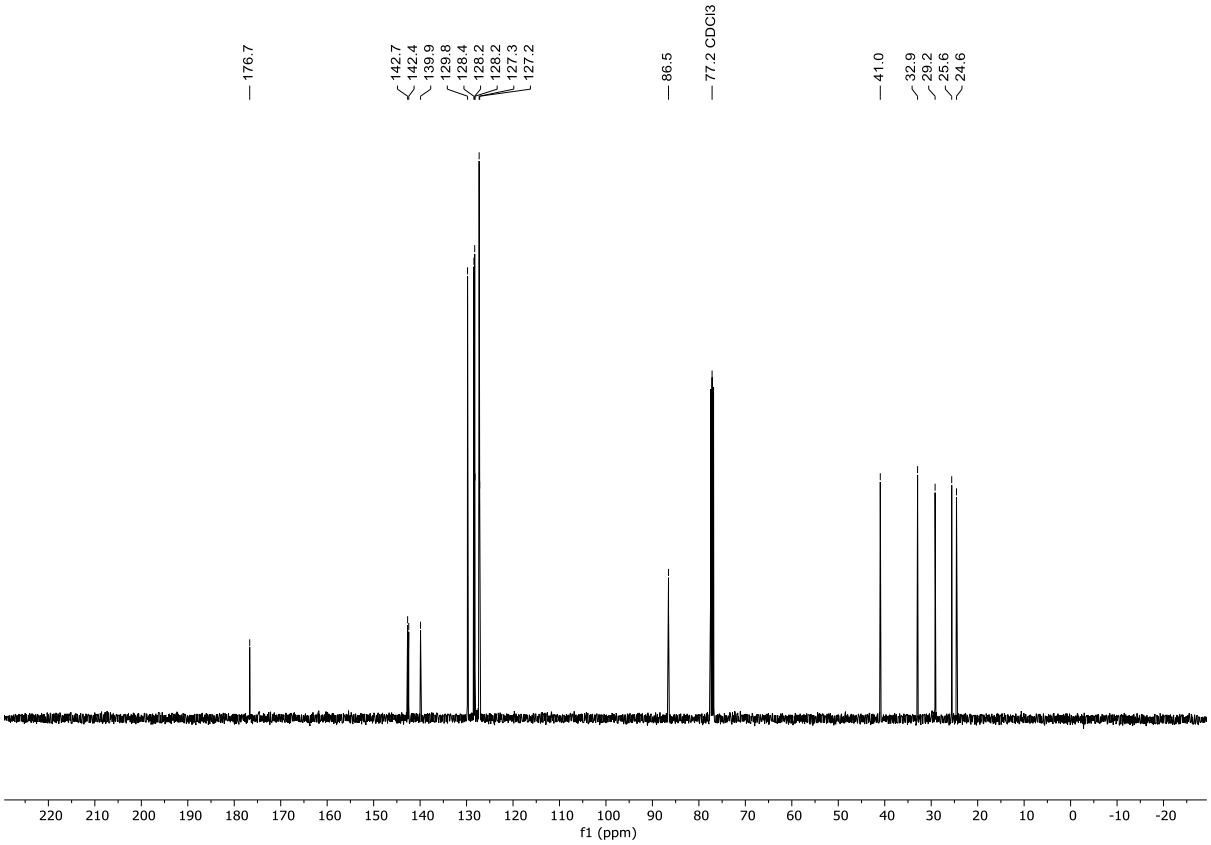
^{1}H NMR ($CDCl_3$, 400 MHz)



2x
$C_{21}H_{22}O_2$
306.41 g mol^{-1}

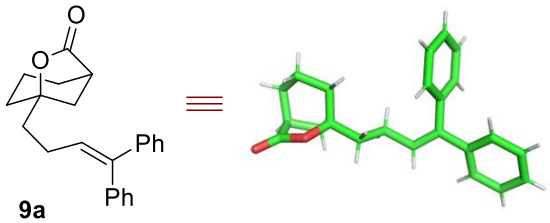


^{13}C NMR ($CDCl_3$, 101 MHz)



(±)-(1*R*,5*R*)-5-(4,4-Diphenylbut-3-en-1-yl)-6-oxabicyclo[3.2.1]octan-7-one 9a.

^{1}H NMR (400 MHz, $CDCl_3$)

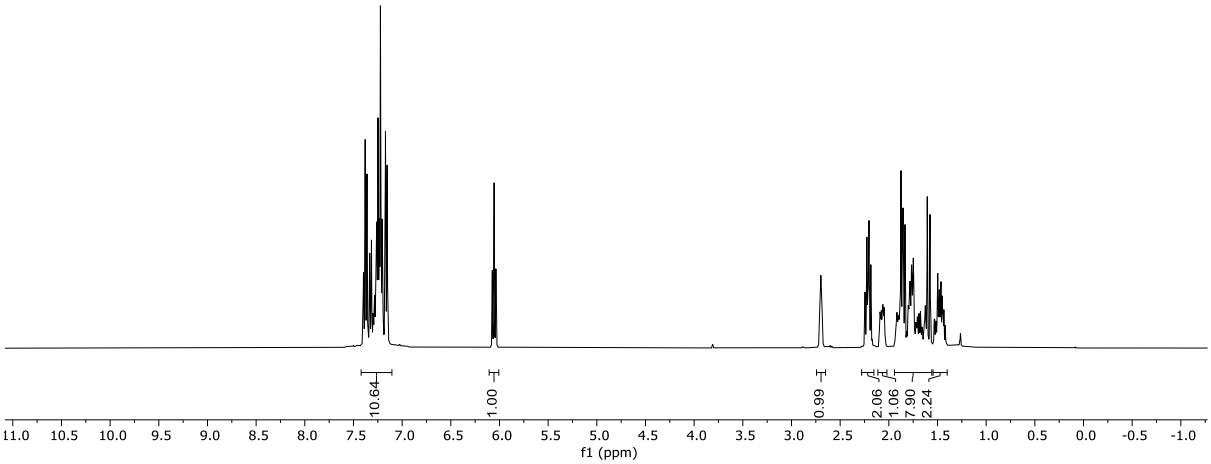


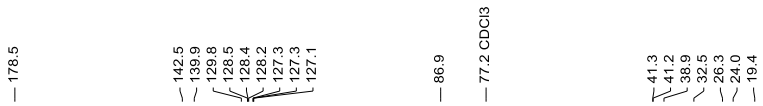
9a

$C_{23}H_{24}O_2$

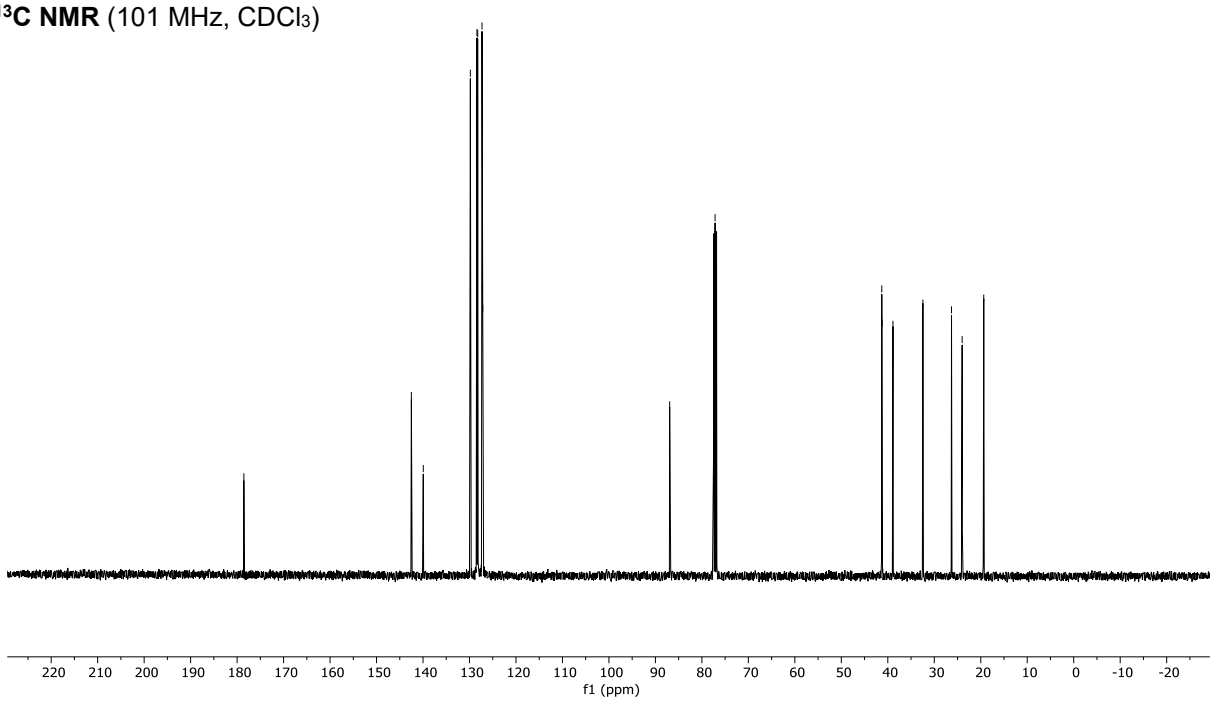
332.44 g mol^{-1}

[X-ray]

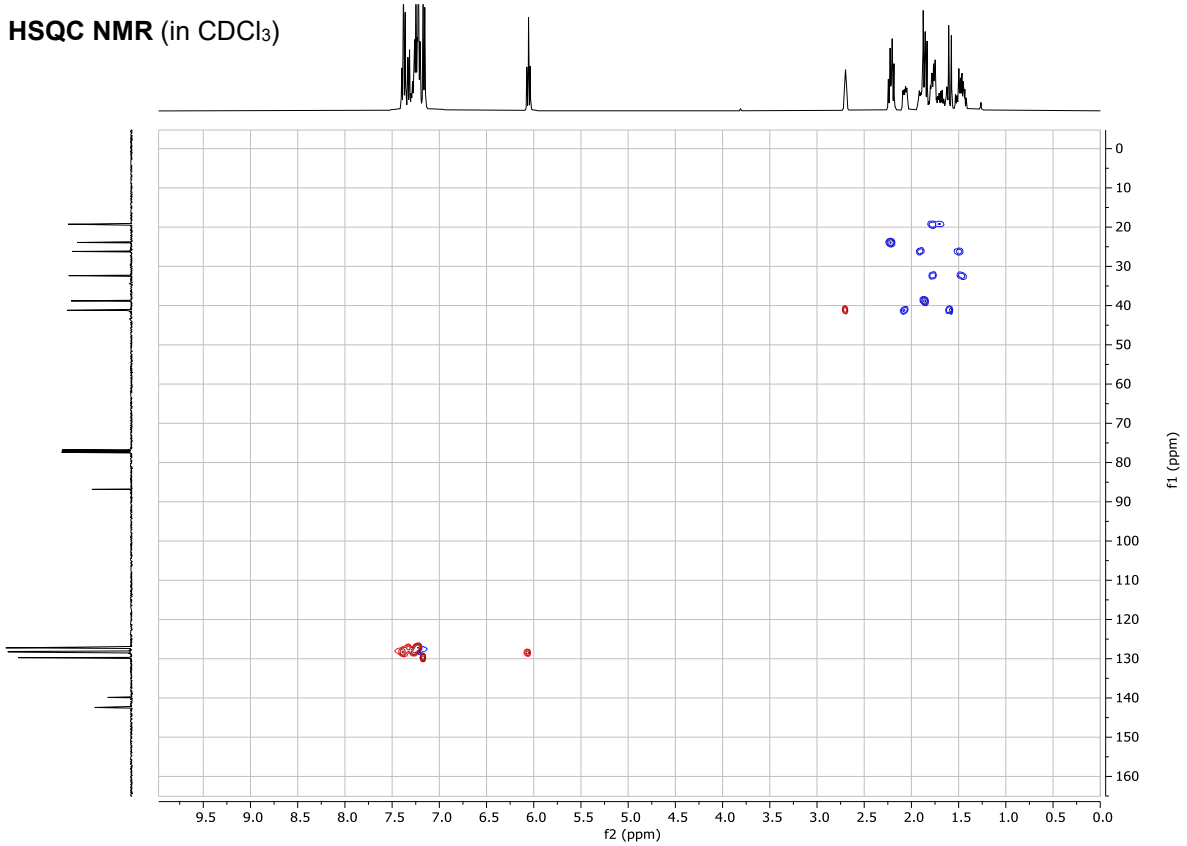




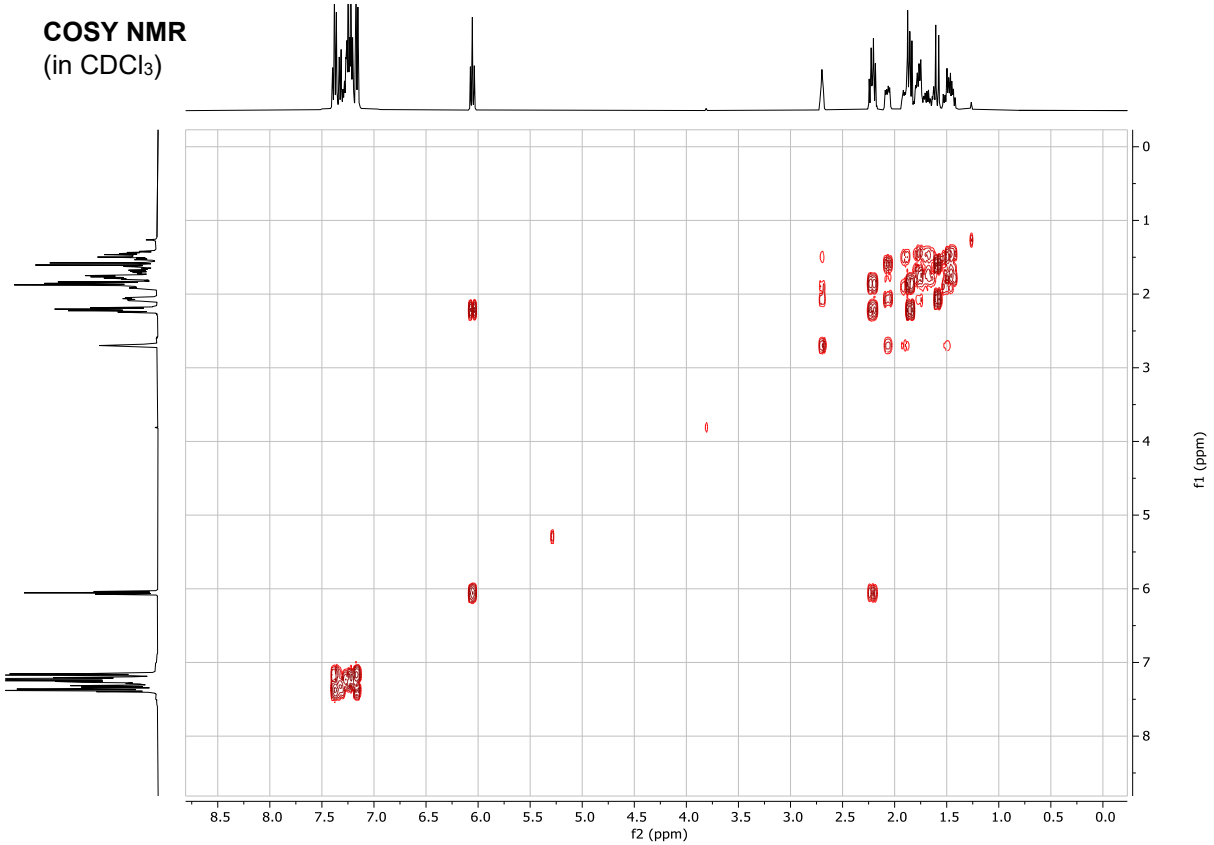
^{13}C NMR (101 MHz, $CDCl_3$)



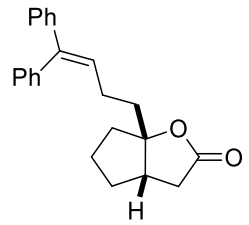
HSQC NMR (in $CDCl_3$)



COSY NMR
(in $CDCl_3$)

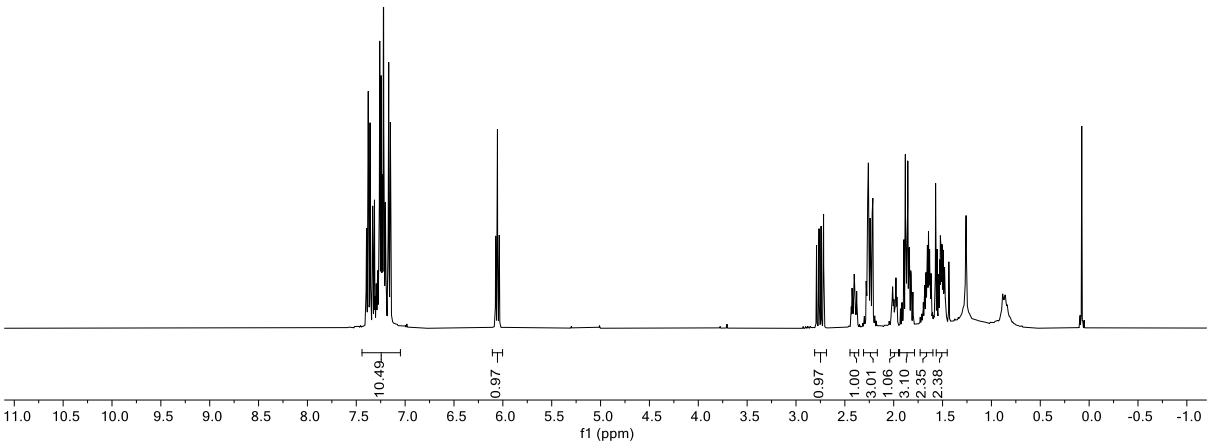


(±)-(3*aS*,6*aR*)-6*a*-(4,4-Diphenylbut-3-en-1-yl)hexahydro-2H-cyclopenta[b]furan-2-one 9b.

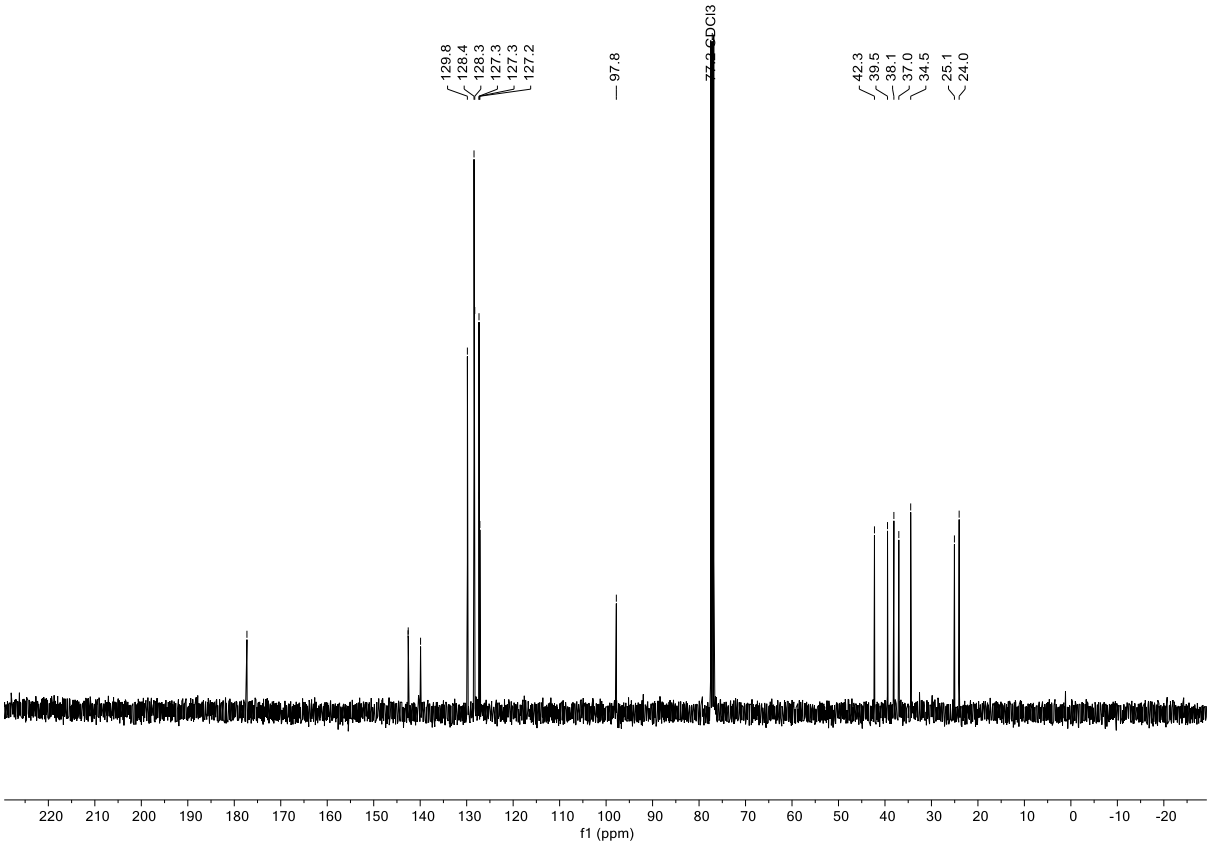


9b
$C_{23}H_{24}O_2$
332.44 g mol^{-1}

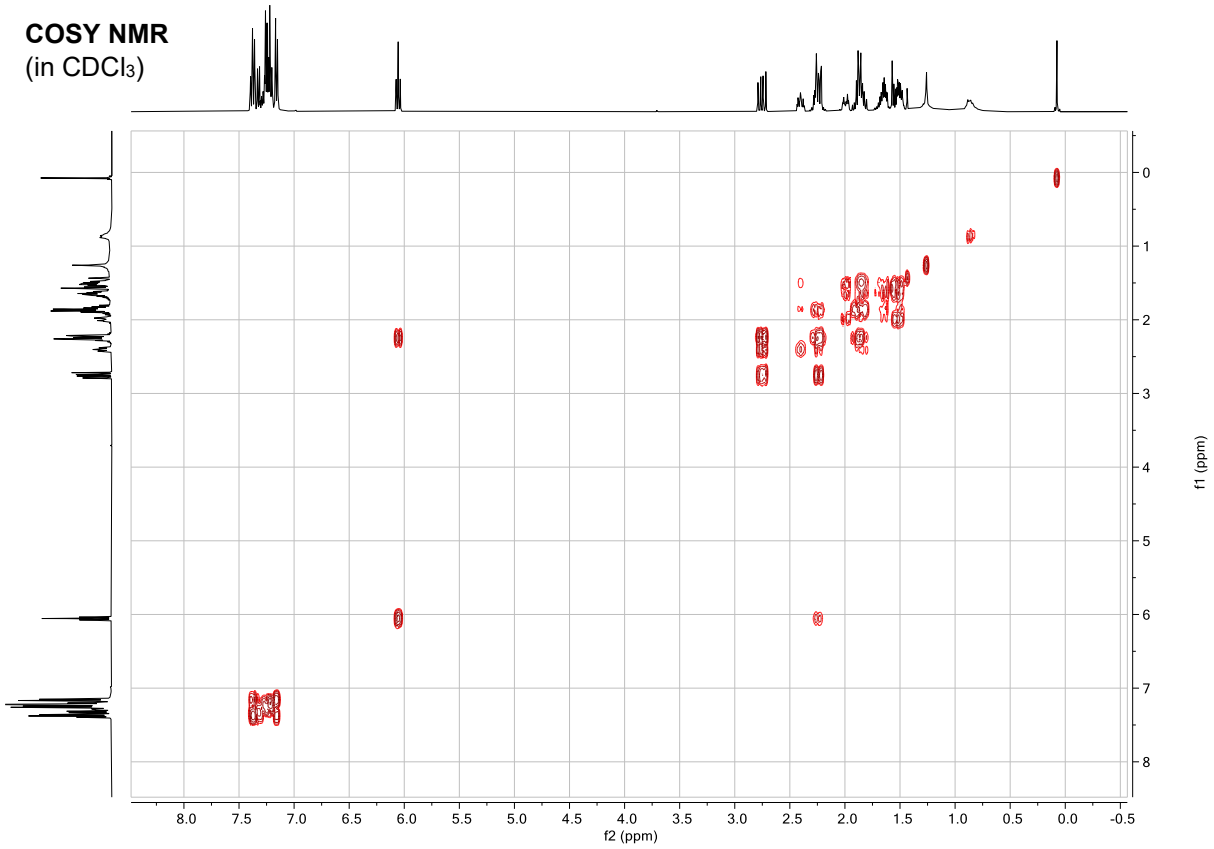
^{1}H NMR (400 MHz, $CDCl_3$)



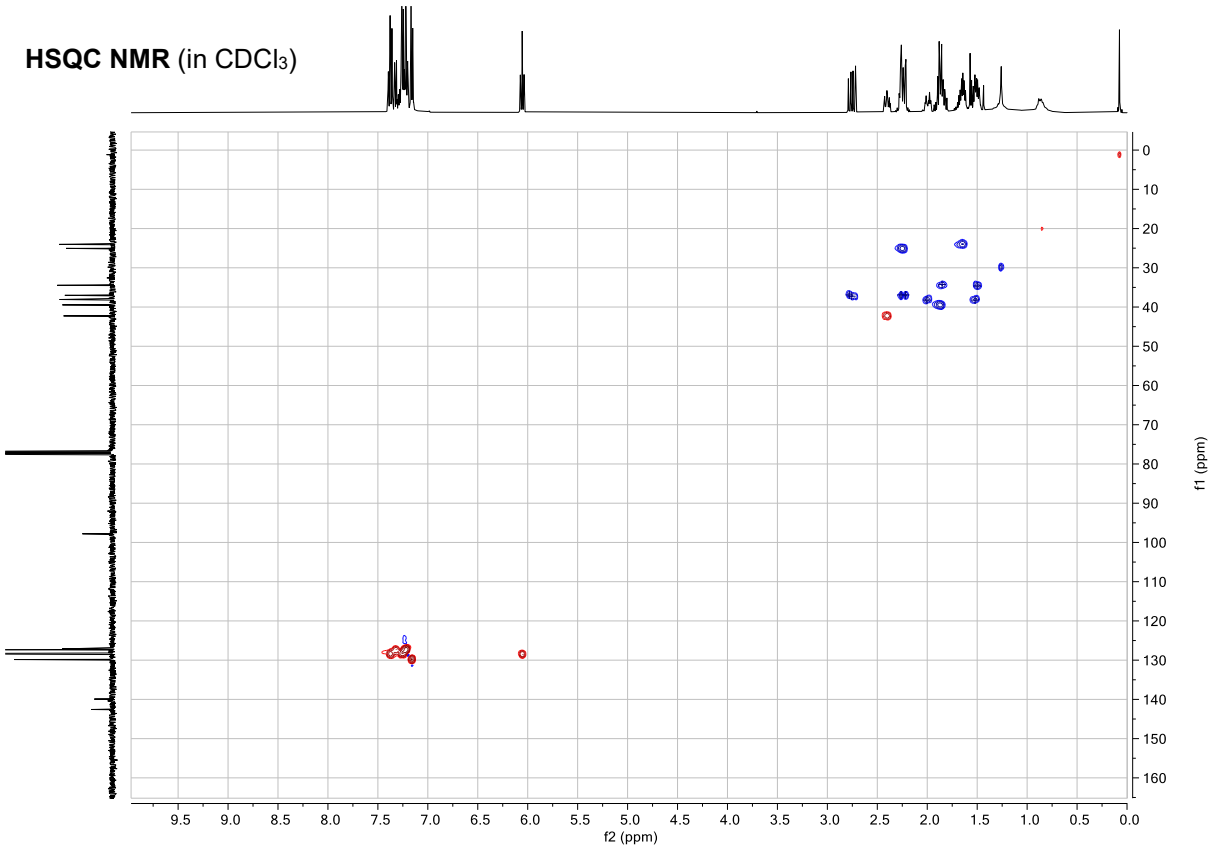
^{13}C NMR (101 MHz, $CDCl_3$)



COSY NMR
(in $CDCl_3$)

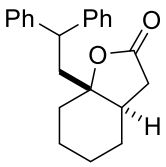


HSQC NMR (in $CDCl_3$)

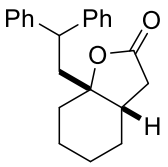


(±)-(3aR,7aR)-7a-(2,2-Diphenylethyl)hexahydrobenzofuran-2(3H)-one 9c-major and (±)-(3aS,7aR)-7a-(2,2-diphenylethyl)hexahydrobenzofuran-2(3H)-one 9c-minor.

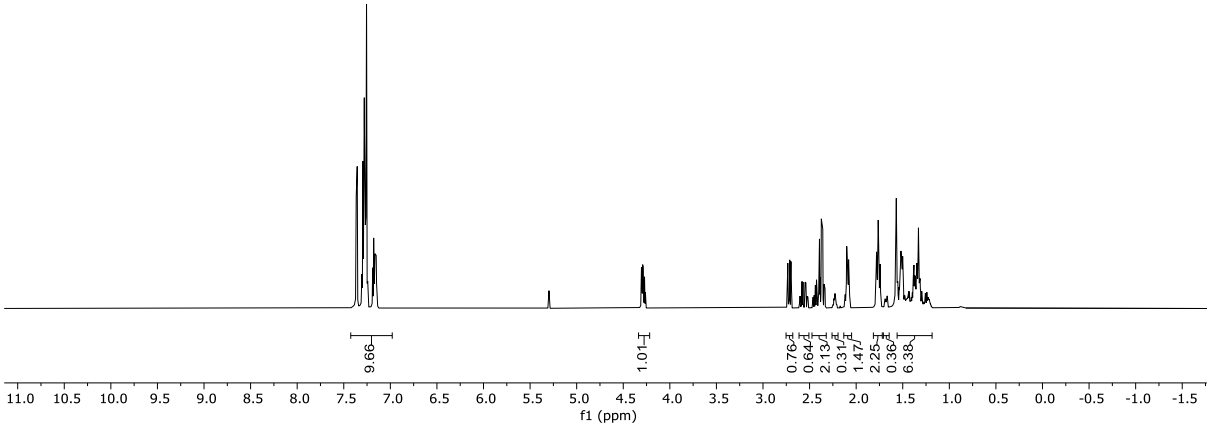
^{1}H NMR (700 MHz, $CDCl_3$)



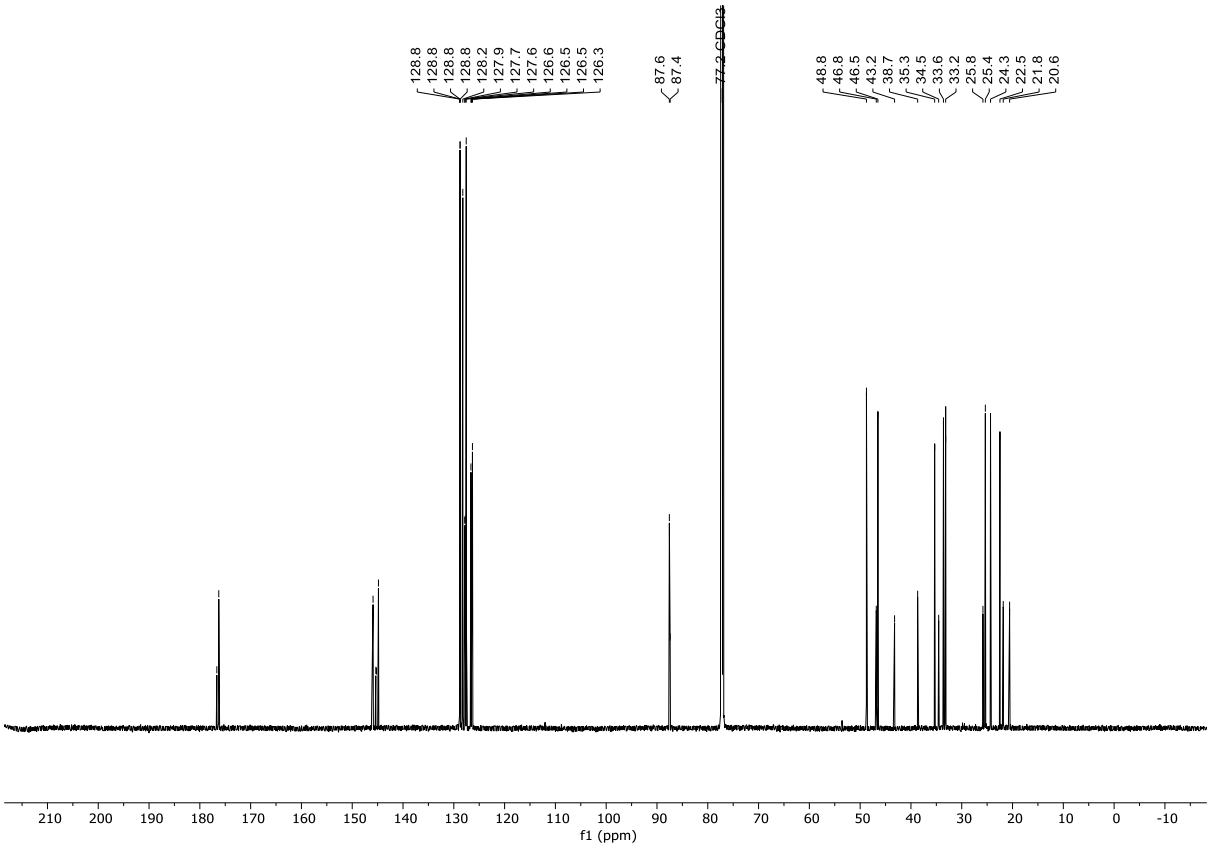
Major-9c
$C_{22}H_{24}O_2$
320.43 g mol^{-1}



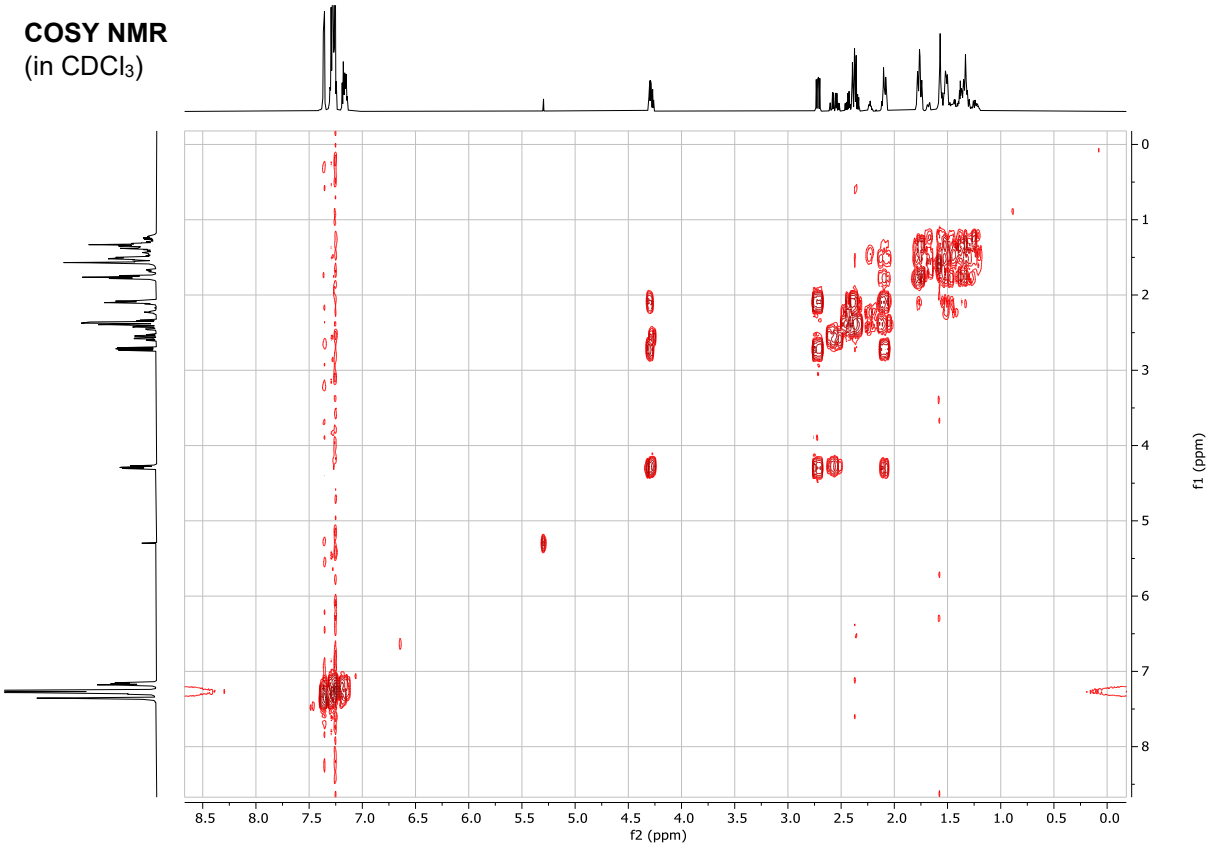
Minor-9c
$C_{22}H_{24}O_2$
320.43 g mol^{-1}



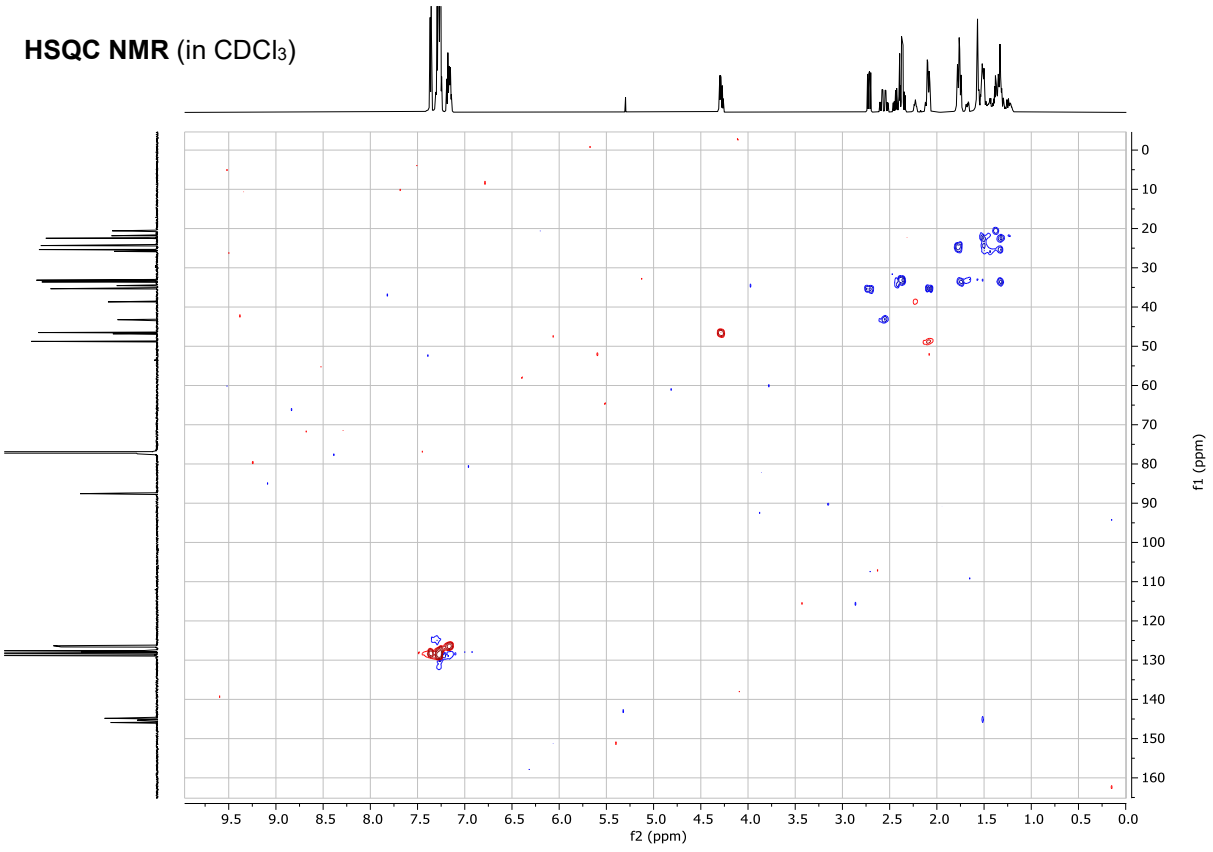
^{13}C NMR (176 MHz, $CDCl_3$)



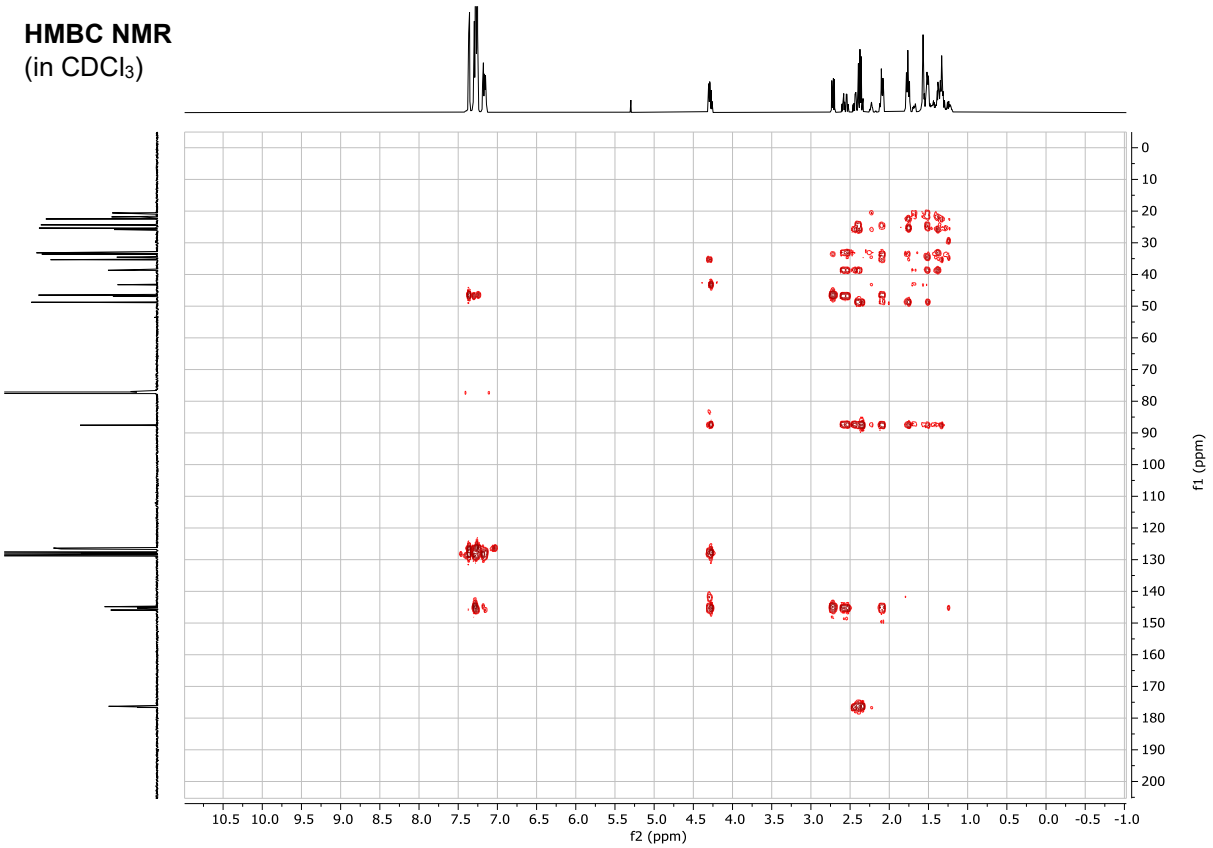
COSY NMR
(in $CDCl_3$)



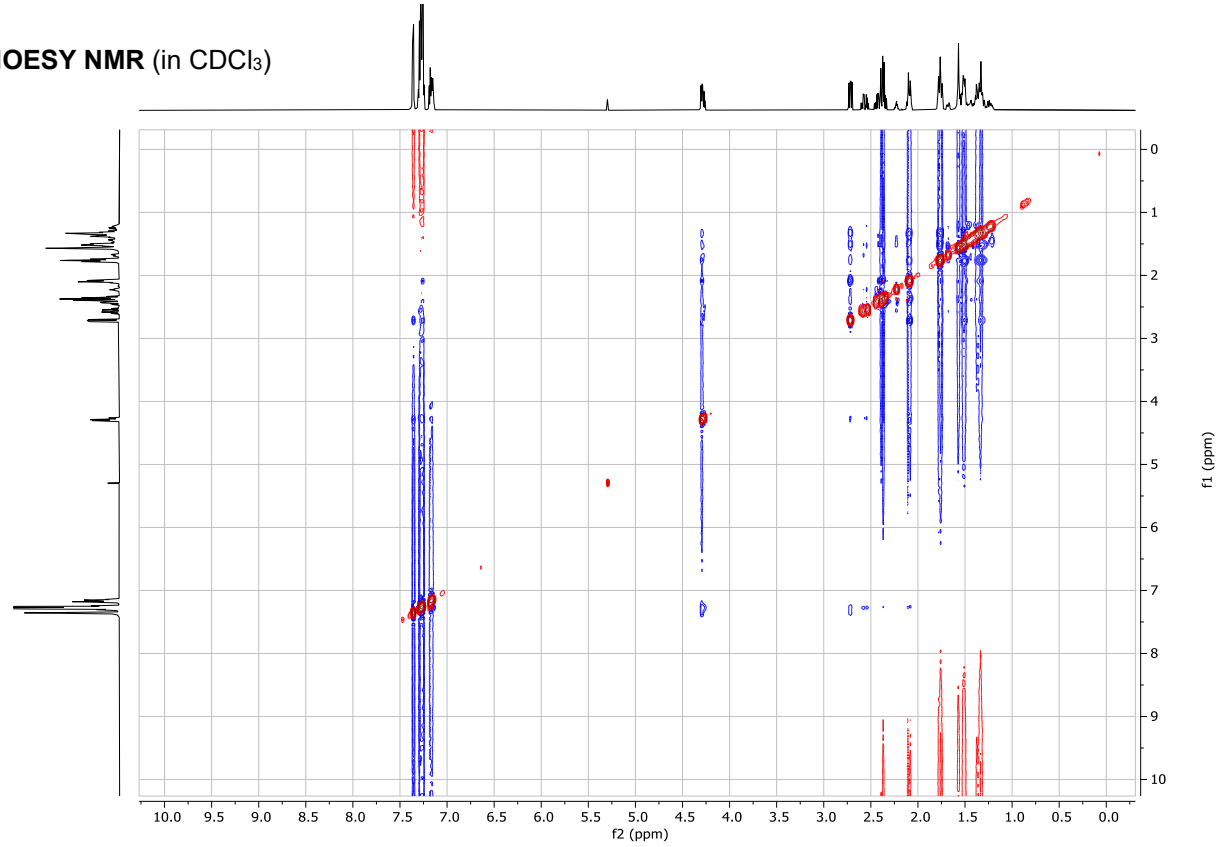
HSQC NMR (in $CDCl_3$)

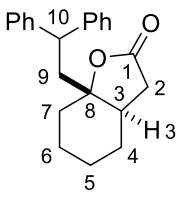


HMBC NMR
(in $CDCl_3$)



NOESY NMR (in $CDCl_3$)

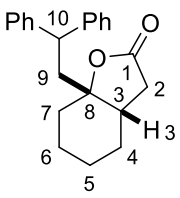




Major-9c

$C_{22}H_{24}O_2$

320.43 g mol^{-1}

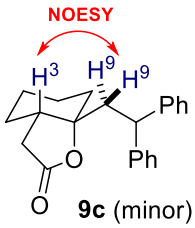


Minor-9c

$C_{22}H_{24}O_2$

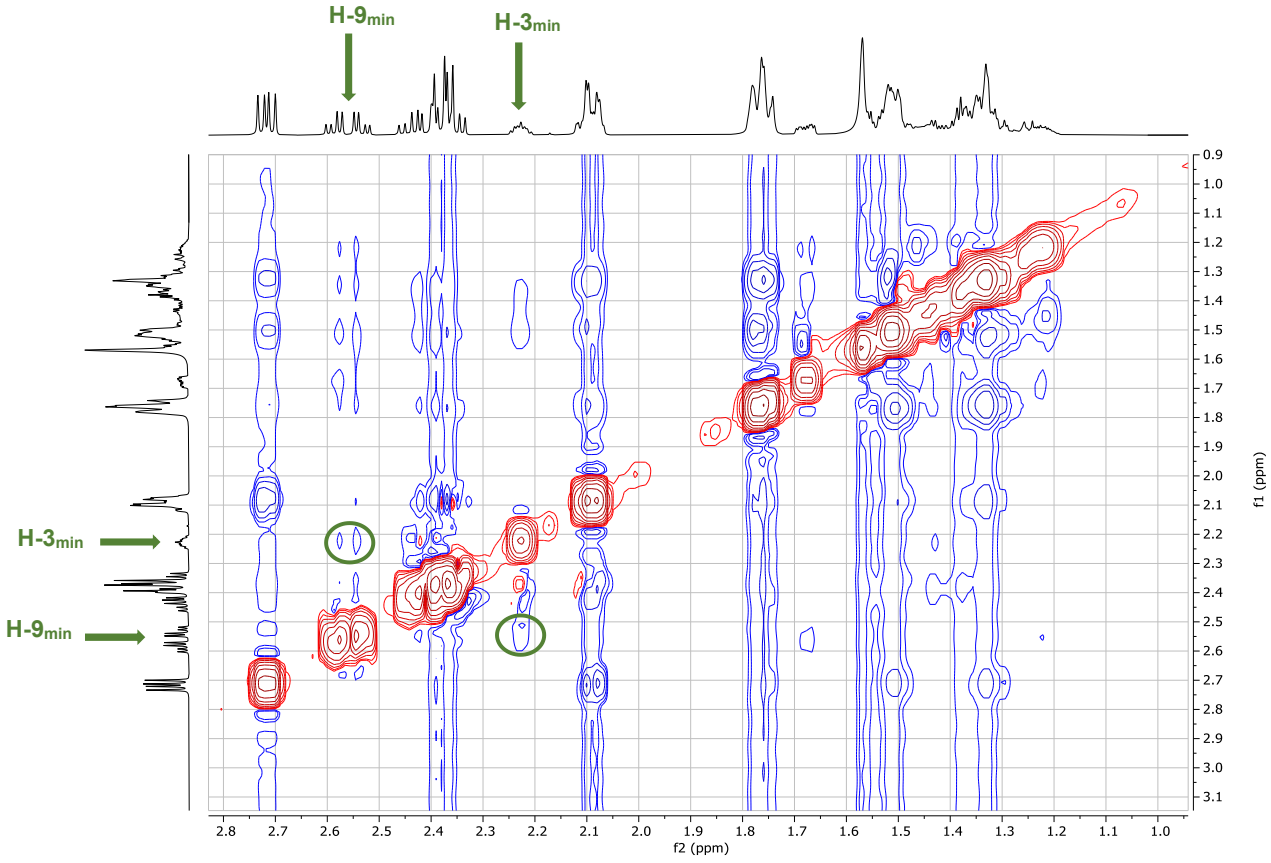
320.43 g mol^{-1}

Stereochemical analysis using NOESY



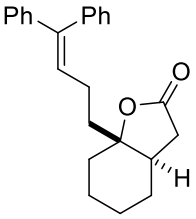
9c (minor)

NOESY-2D (600 MHz, $CDCl_3$)

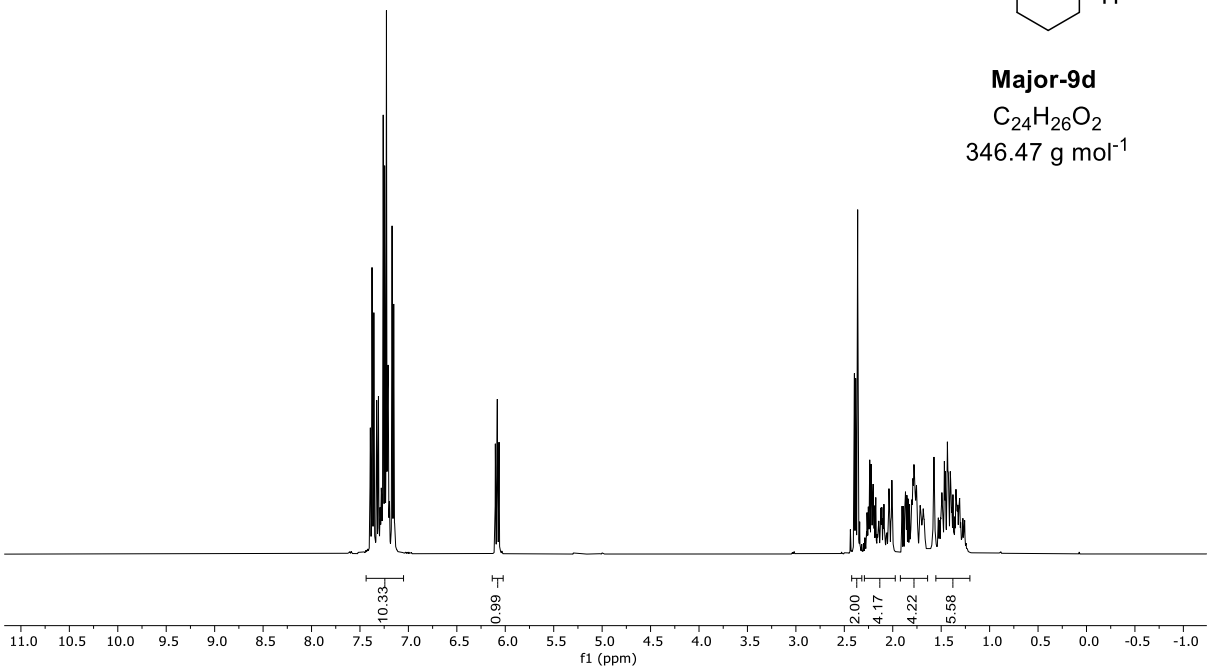


(3*aR*,7*aR*)-7*a*-(4,4-Diphenylbut-3-en-1-yl)hexahydrobenzofuran-2(3H)-one Major-9d

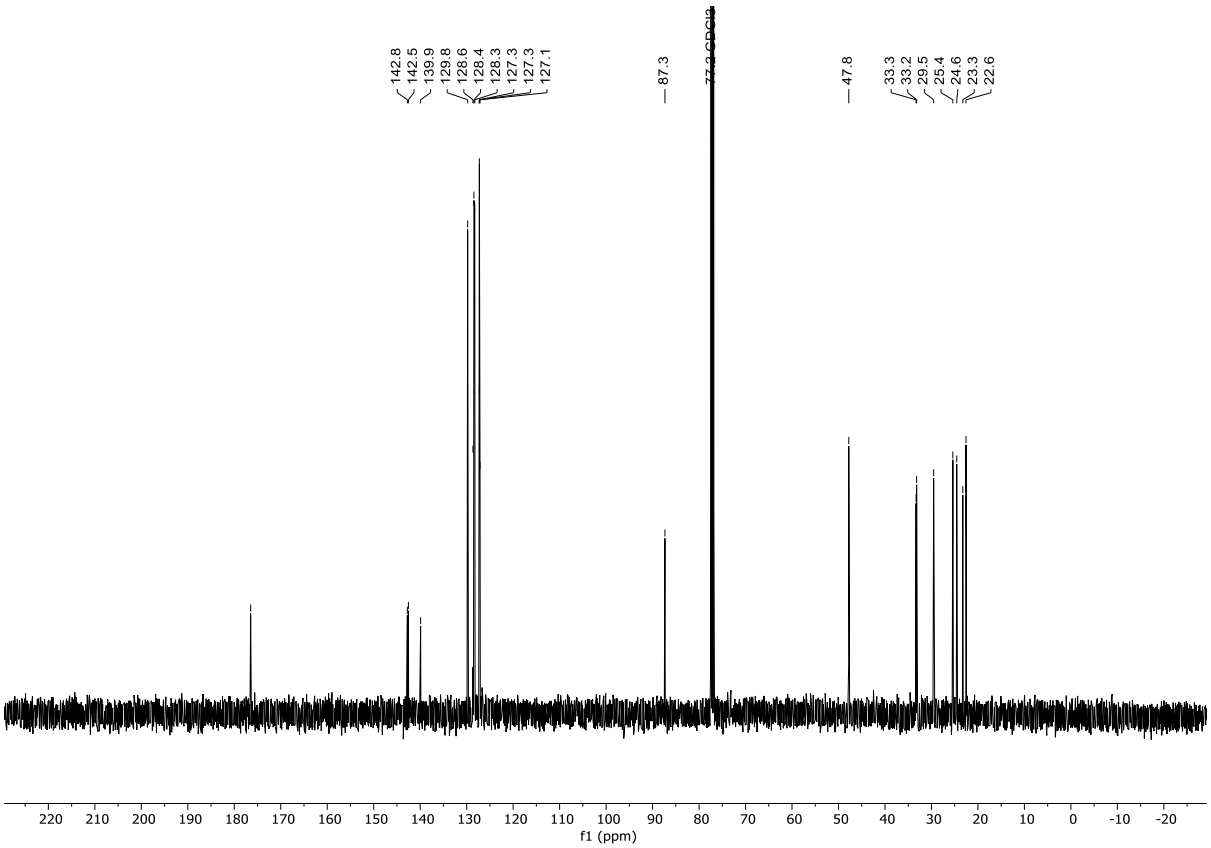
^{1}H NMR (400 MHz, $CDCl_3$)



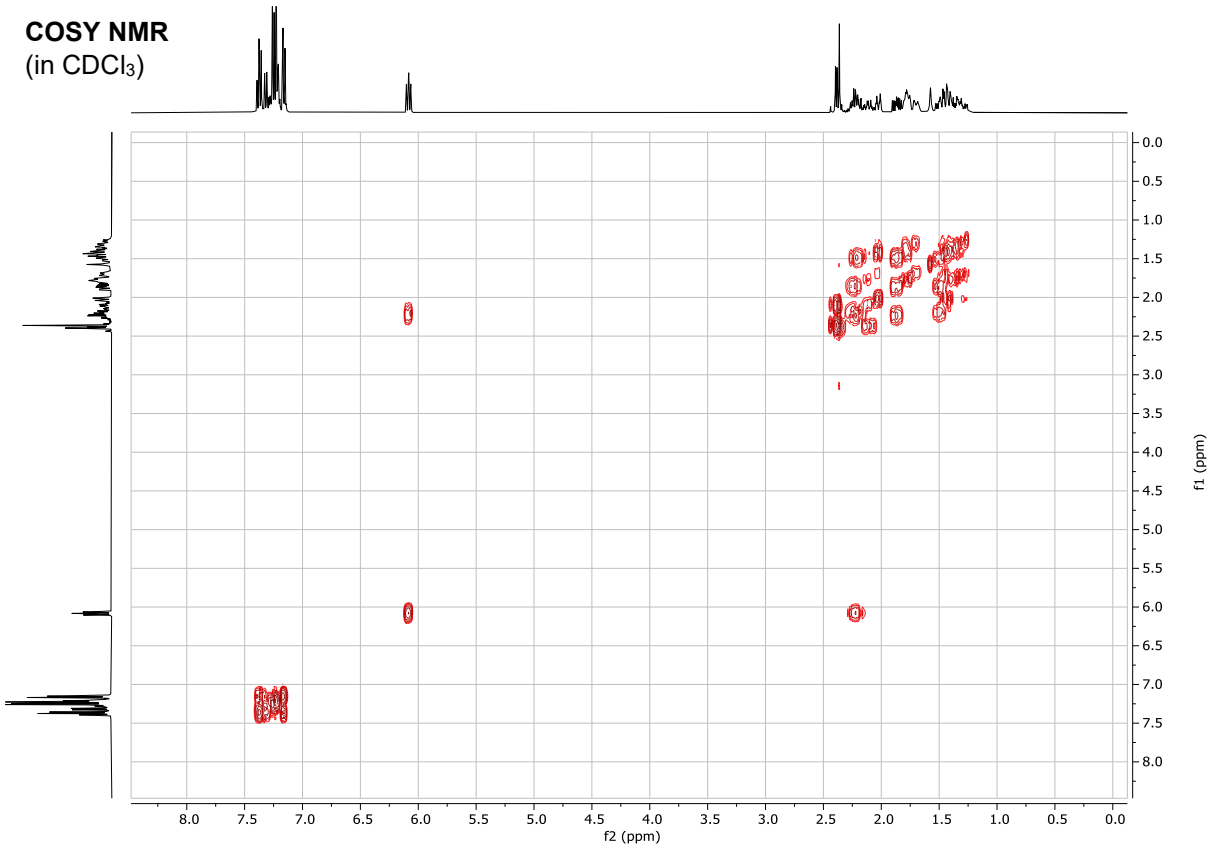
Major-9d
$C_{24}H_{26}O_2$
346.47 g mol^{-1}



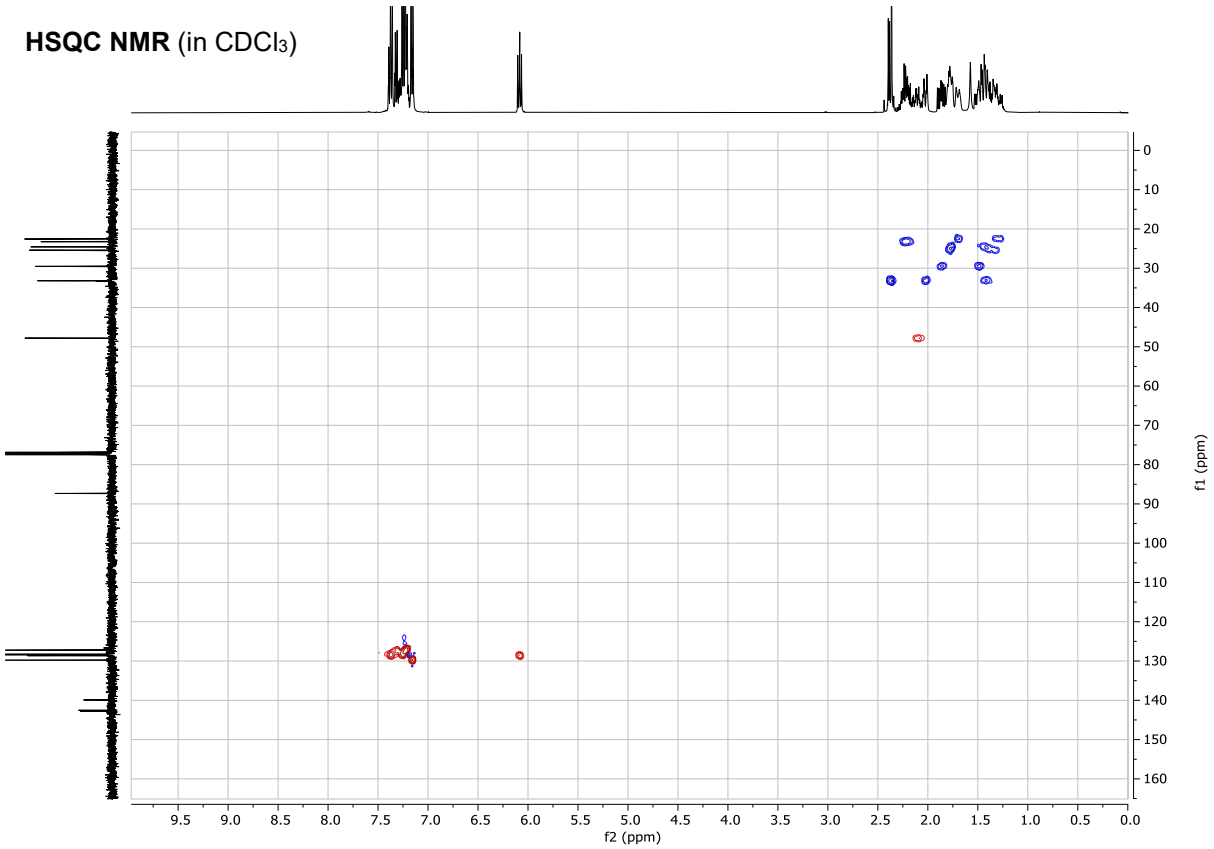
^{13}C NMR (101 MHz, $CDCl_3$)



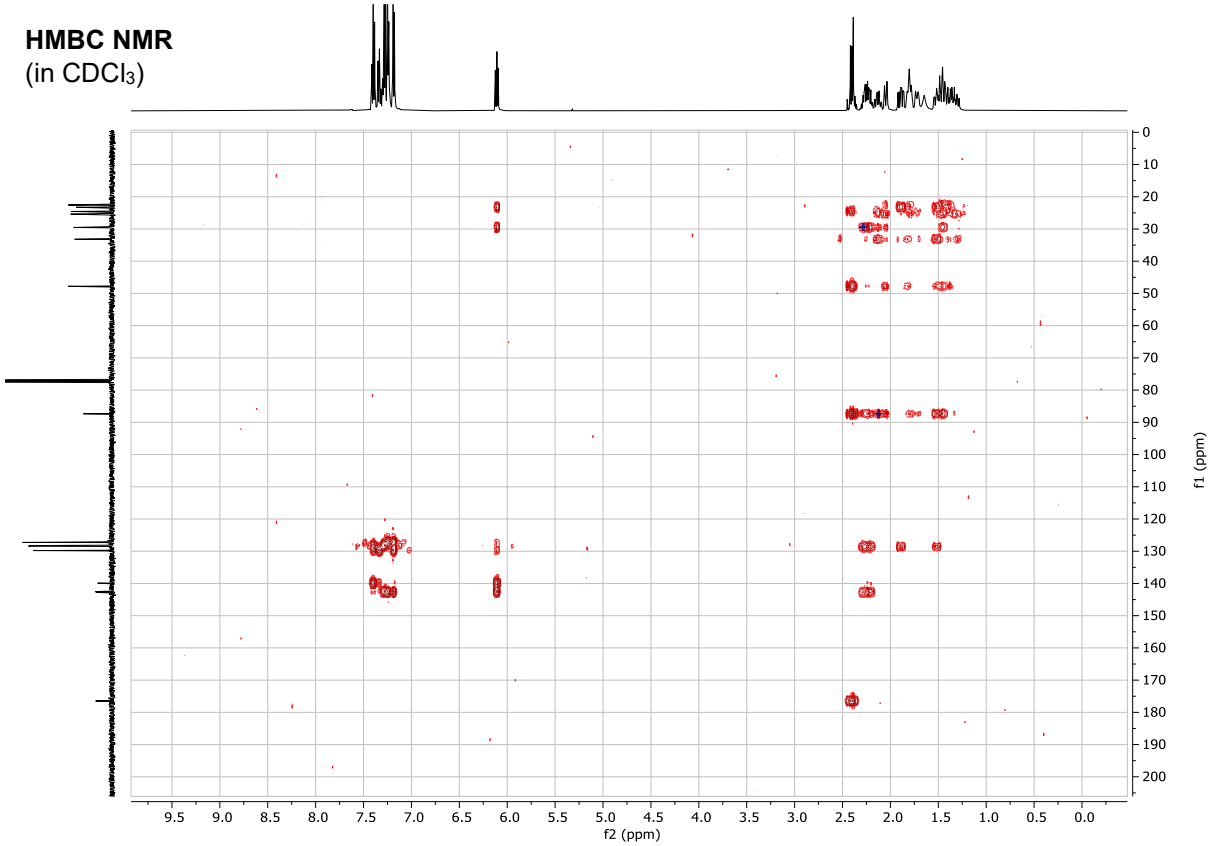
COSY NMR
(in $CDCl_3$)



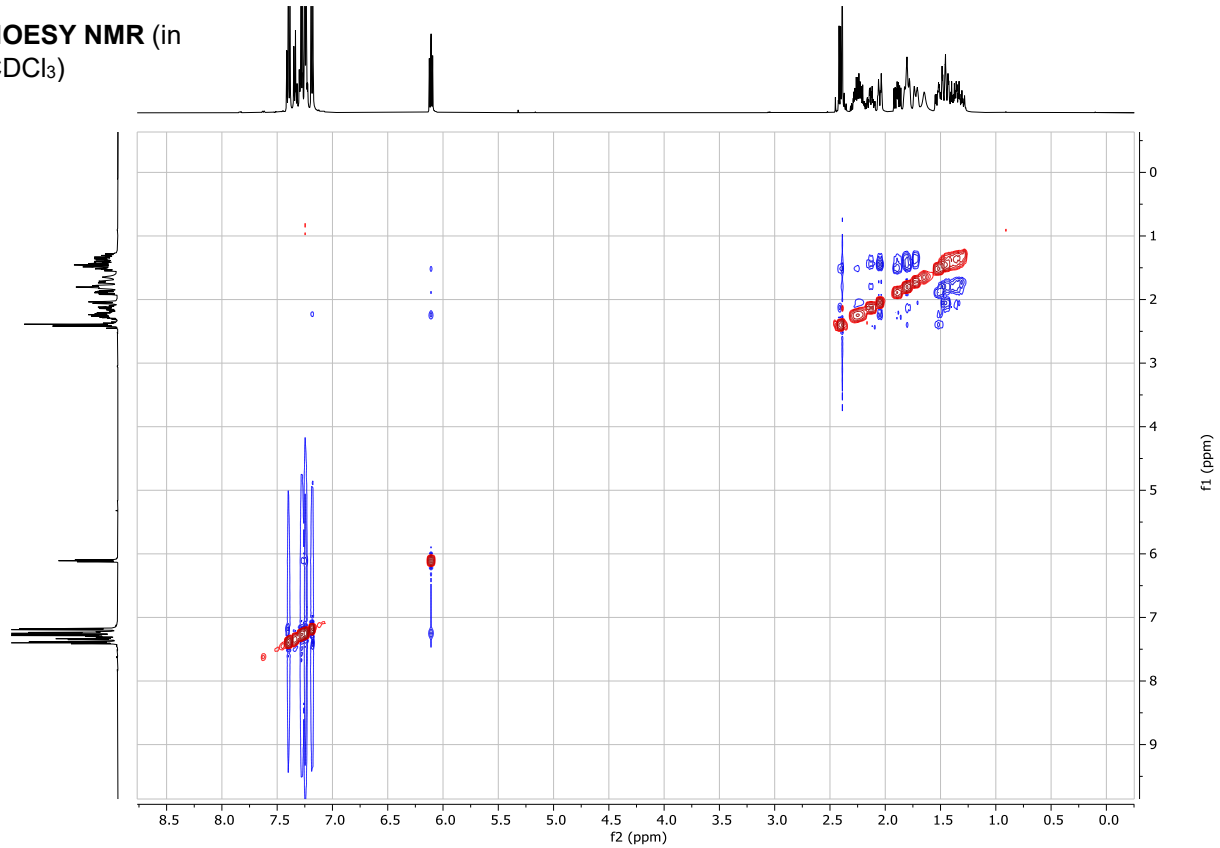
HSQC NMR (in $CDCl_3$)

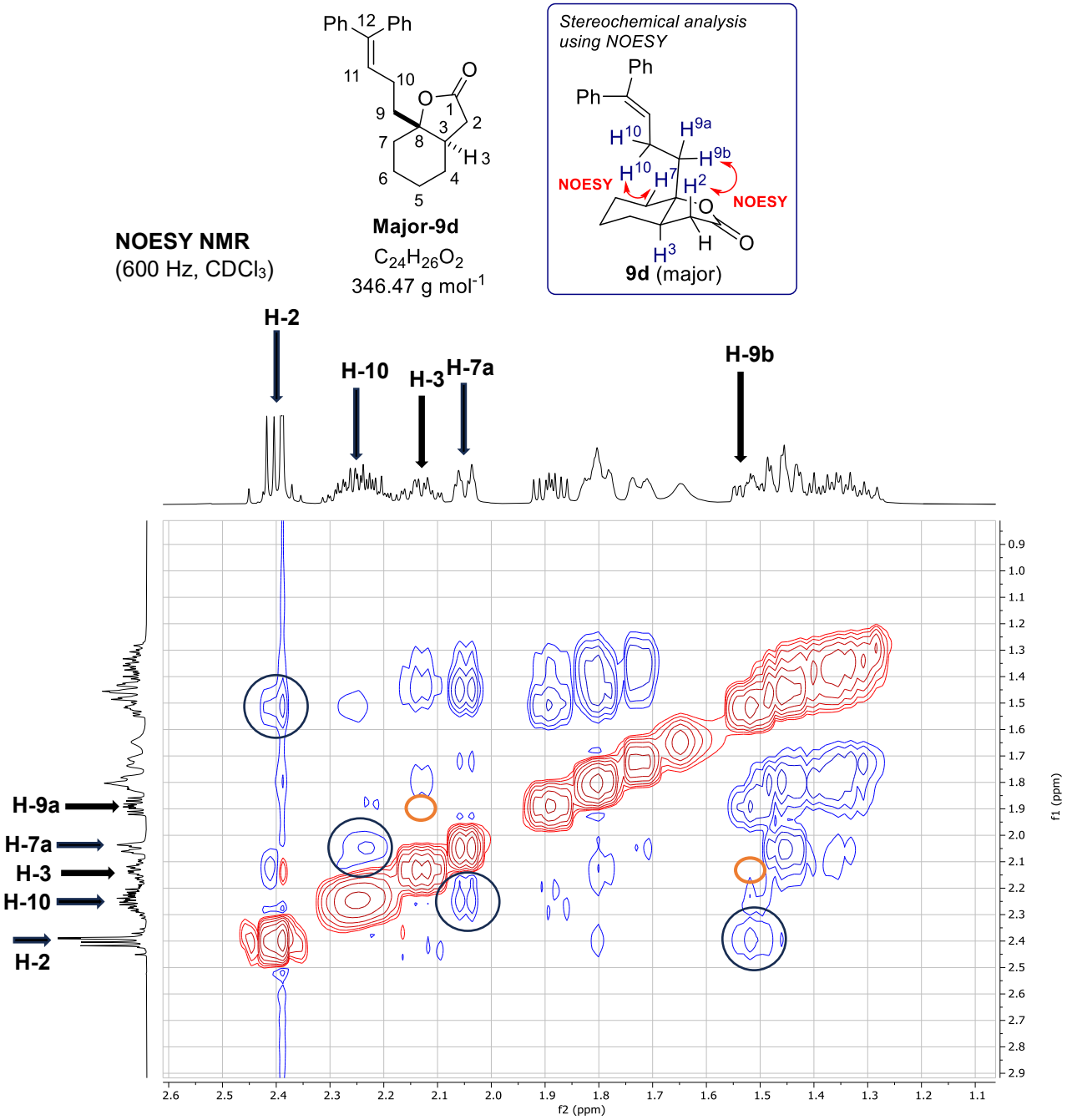


HMBC NMR
(in $CDCl_3$)



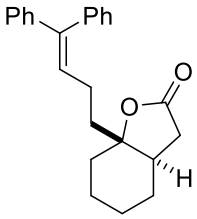
NOESY NMR (in $CDCl_3$)



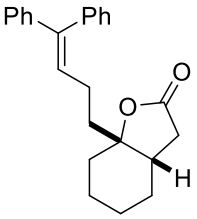

Ph 12 Ph
11
10
O
O
1
9
2
3
7
8
H 3
6
4
5
Major-9d
C24H26O2
346.47 g mol-1
Stereochemical analysis
using NOESY
Ph
Ph
H10
H9a
H9b
NOESY
H10
H7
H2
NOESY
O
H3
H
O
9d (major)
NOESY NMR
(600 Hz, CDCl3)
H-2
H-10
H-3
H-7a
H-9b
H-9a
H-7a
H-3
H-10
H-2
f2 (ppm)
f1 (ppm)

(±)-(3*aR*,7*aR*)-7*a*-(4,4-Diphenylbut-3-en-1-yl)hexahydrobenzofuran-2(3H)-one 9d-major and (±)-(3*aS*,7*aR*)-7a-(4,4-diphenylbut-3-en-1-yl)hexahydrobenzofuran-2(3H)-one 9d-minor

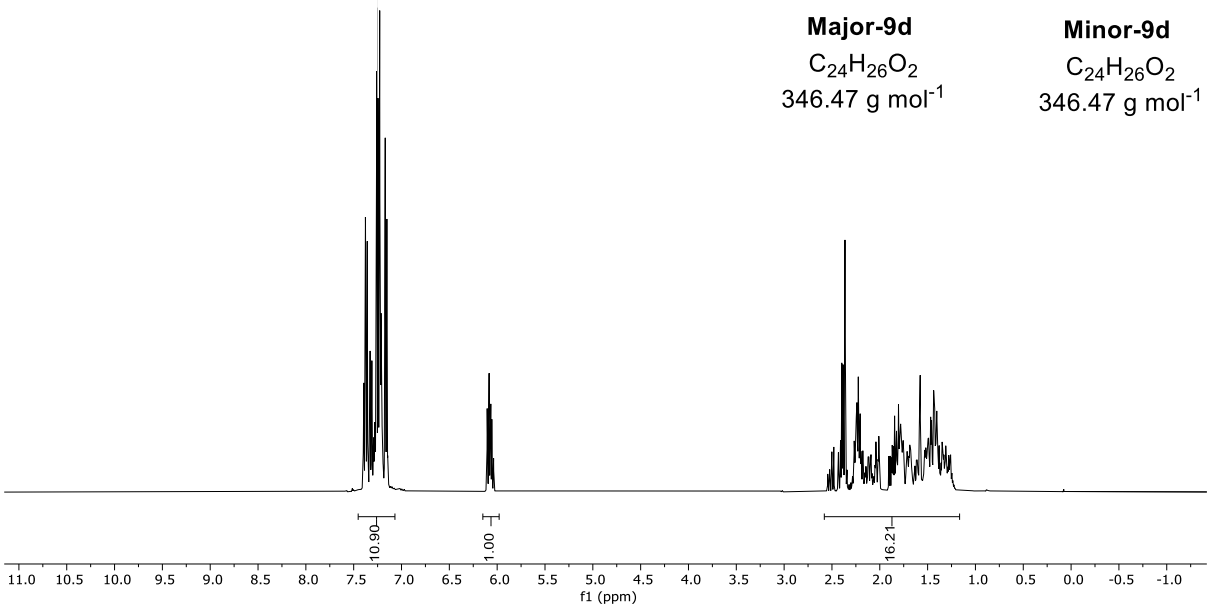
^{1}H NMR (400 MHz, $CDCl_3$)



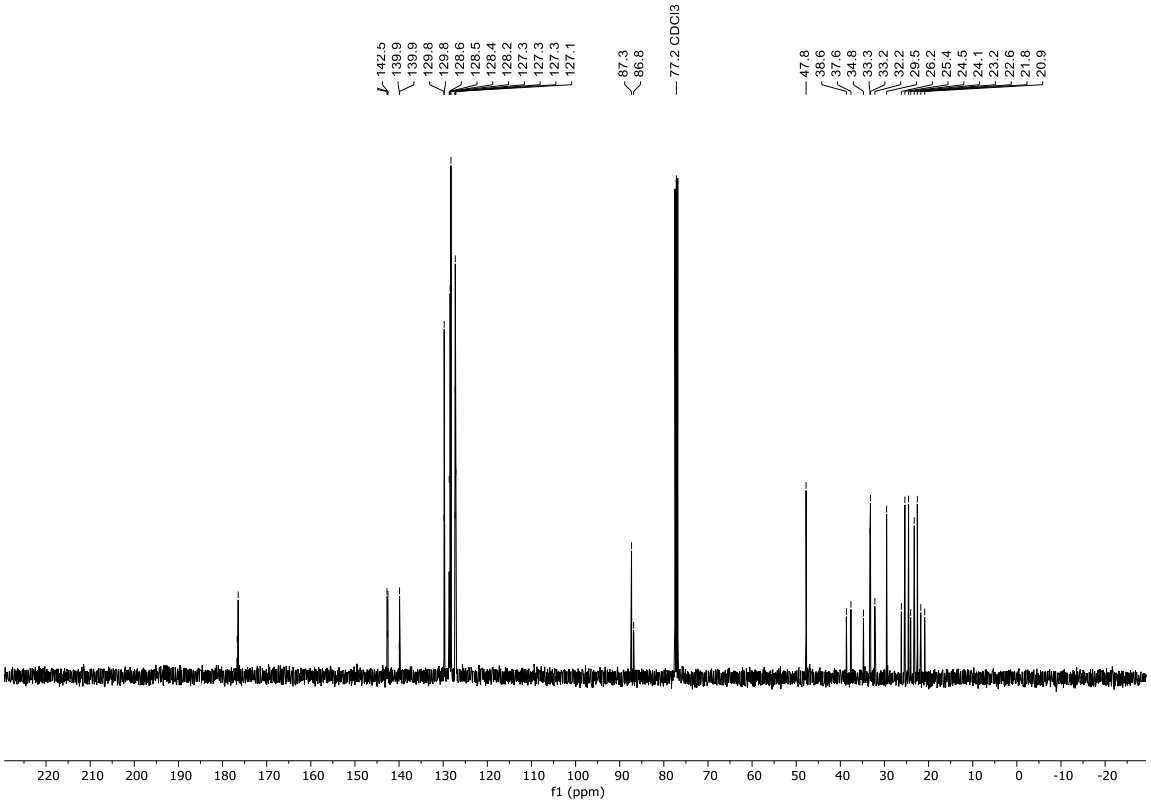
Major-9d
$C_{24}H_{26}O_2$
346.47 g mol^{-1}



Minor-9d
$C_{24}H_{26}O_2$
346.47 g mol^{-1}

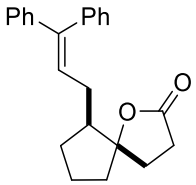


^{13}C NMR (101 MHz, $CDCl_3$)

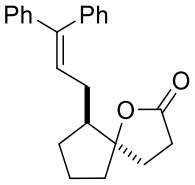


(±)-(5*S*,6*S*)-6-(3,3-Diphenylallyl)-1-oxaspiro[4.4]nonan-2-one 12a-major and (±)-(5*R*,6*S*)-6-(3,3-diphenylallyl)-1-oxaspiro[4.4]nonan-2-one 12a-minor.

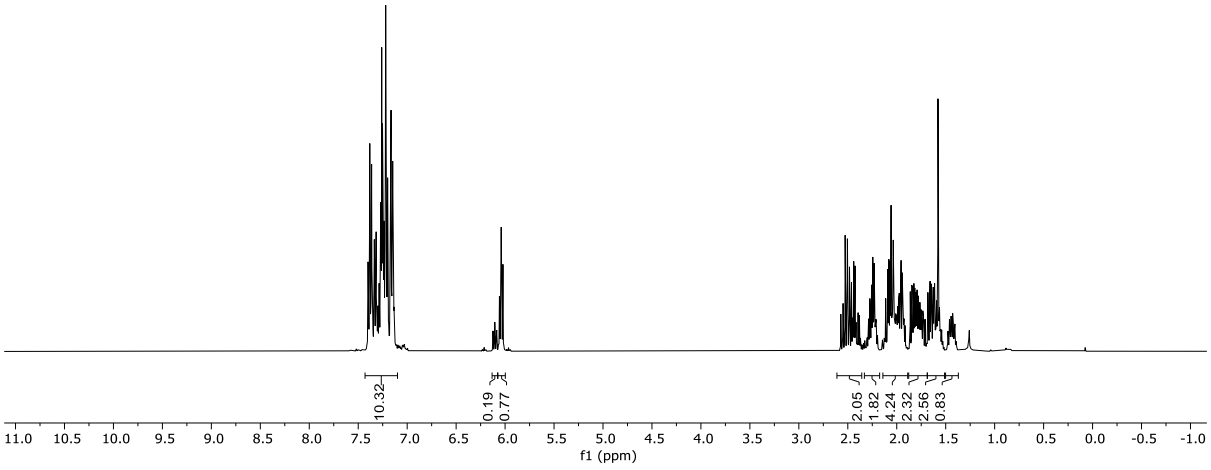
^{1}H NMR (400 MHz, $CDCl_3$)



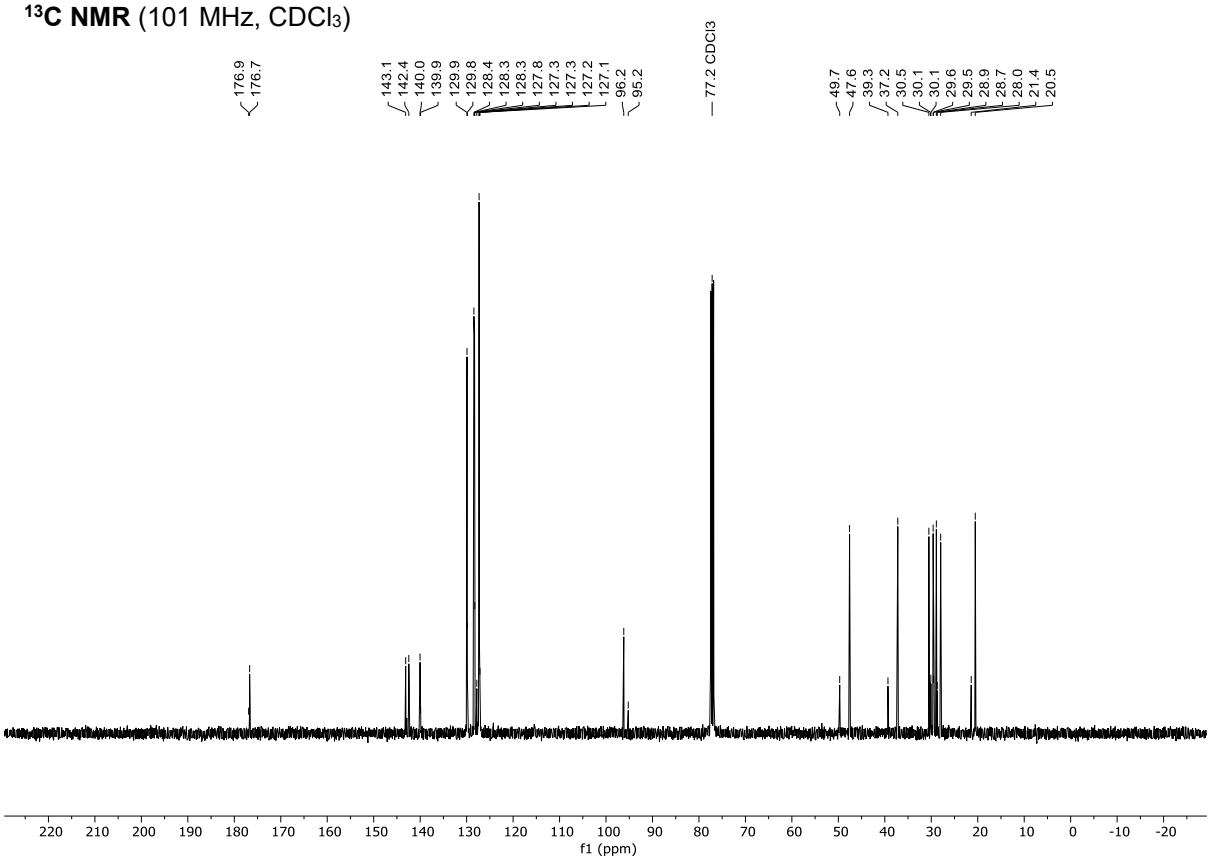
Major-12a
$C_{23}H_{24}O_2$
332.44 g mol^{-1}



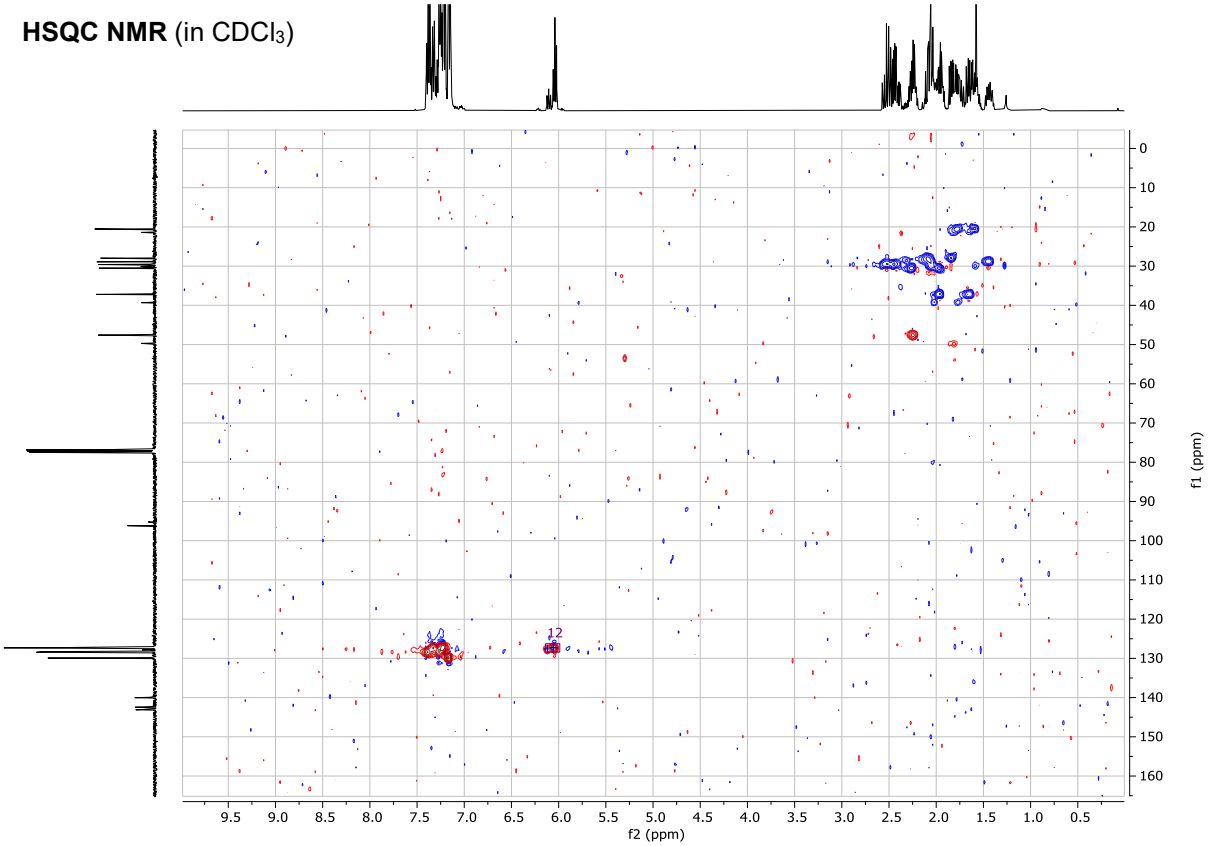
Minor-12a
$C_{23}H_{24}O_2$
332.44 g mol^{-1}



^{13}C NMR (101 MHz, $CDCl_3$)

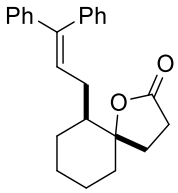


HSQC NMR (in $CDCl_3$)

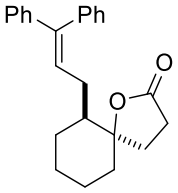


(±)-(5*S*,6*S*)-6-(3,3-Diphenylallyl)-1-oxaspiro[4.5]decan-2-one 12b-major and (±)-(5*R*,6*S*)-6-(3,3-diphenylallyl)-1-oxaspiro[4.5]decan-2-one 12b-minor.

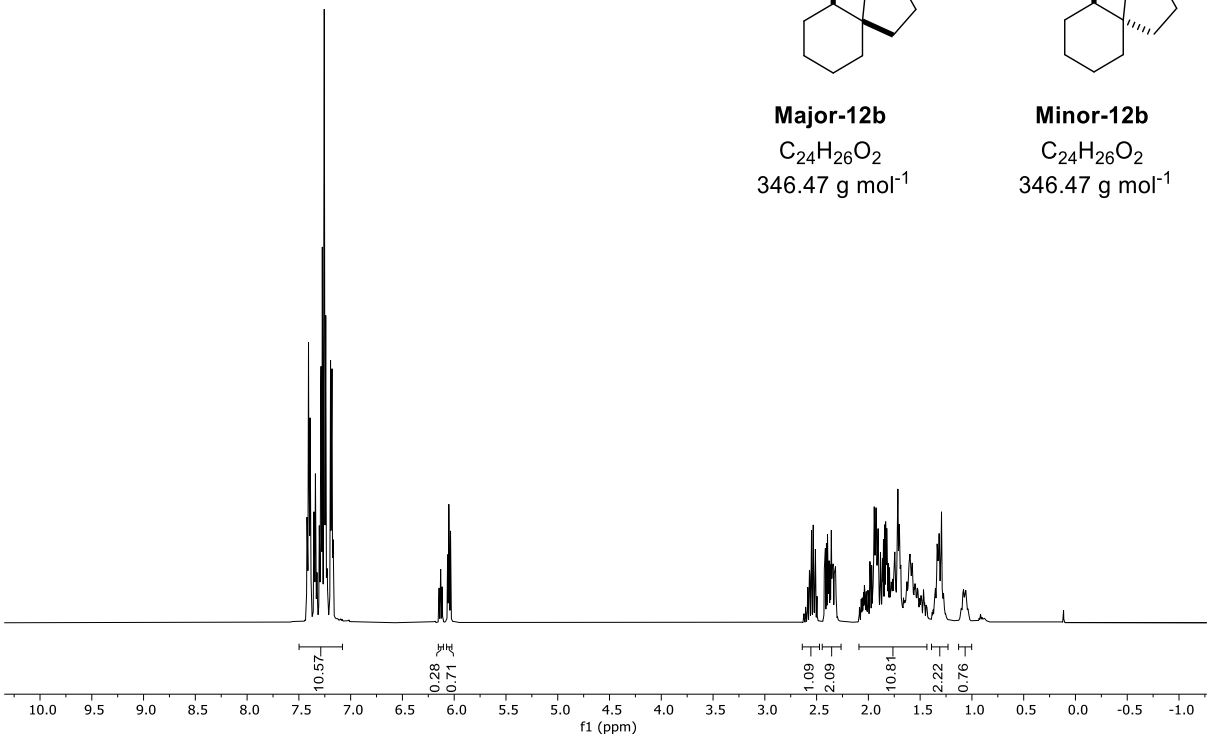
^{1}H NMR (500 MHz, $CDCl_3$)



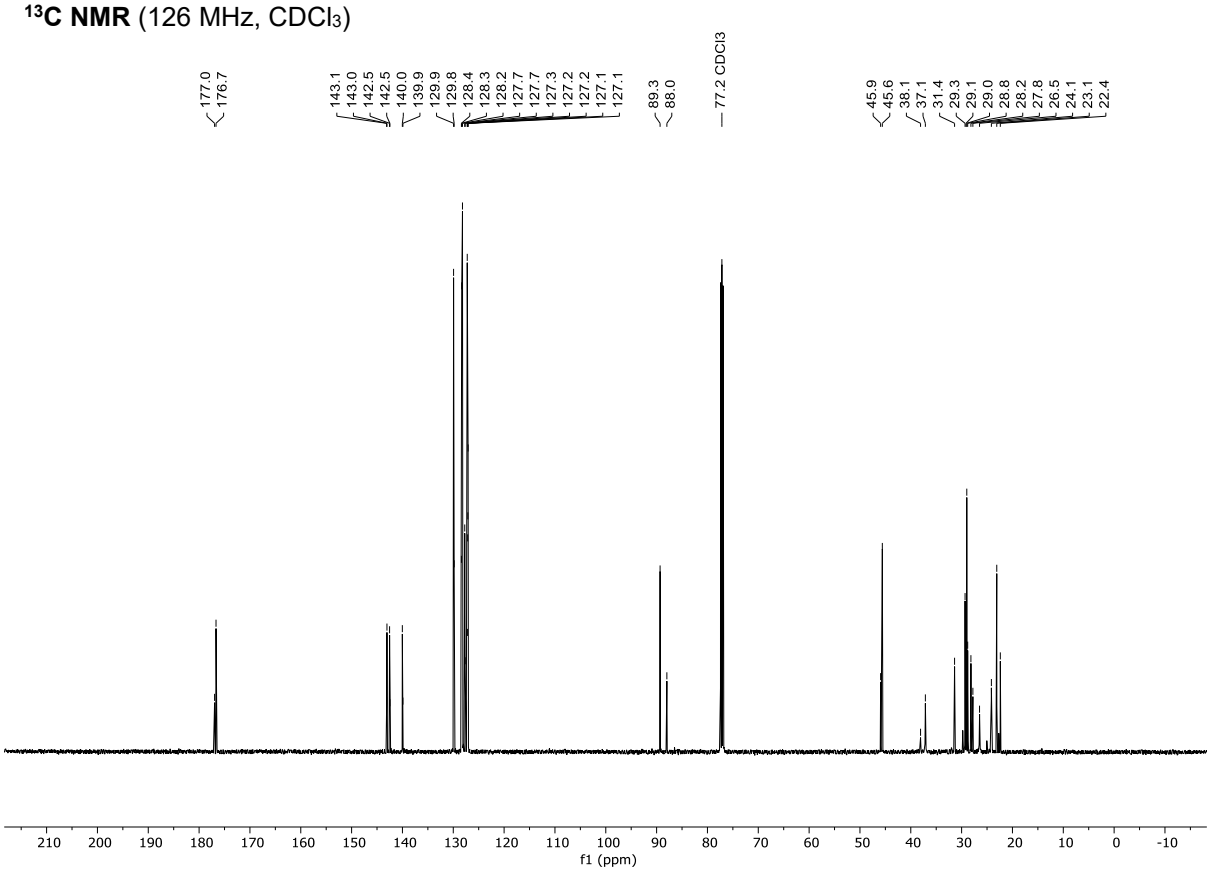
Major-12b
$C_{24}H_{26}O_2$
346.47 g mol^{-1}



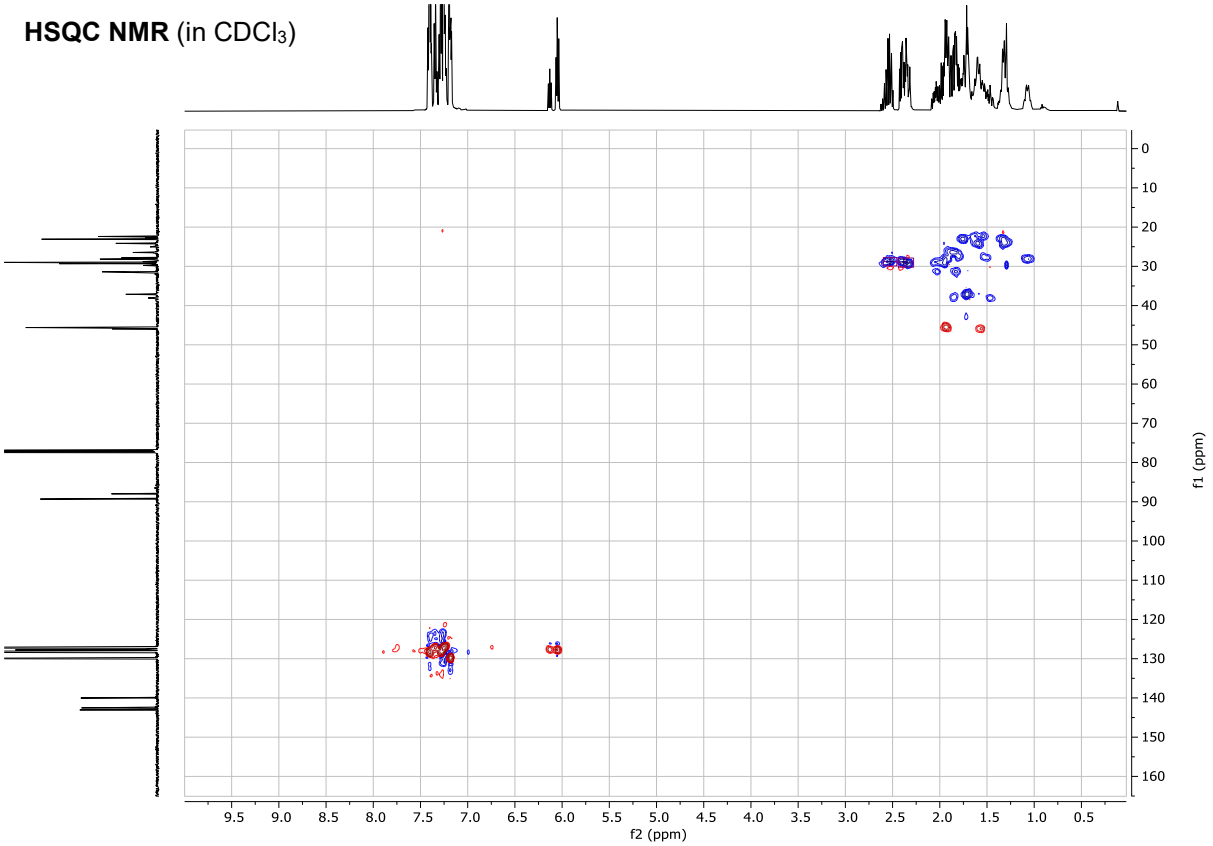
Minor-12b
$C_{24}H_{26}O_2$
346.47 g mol^{-1}



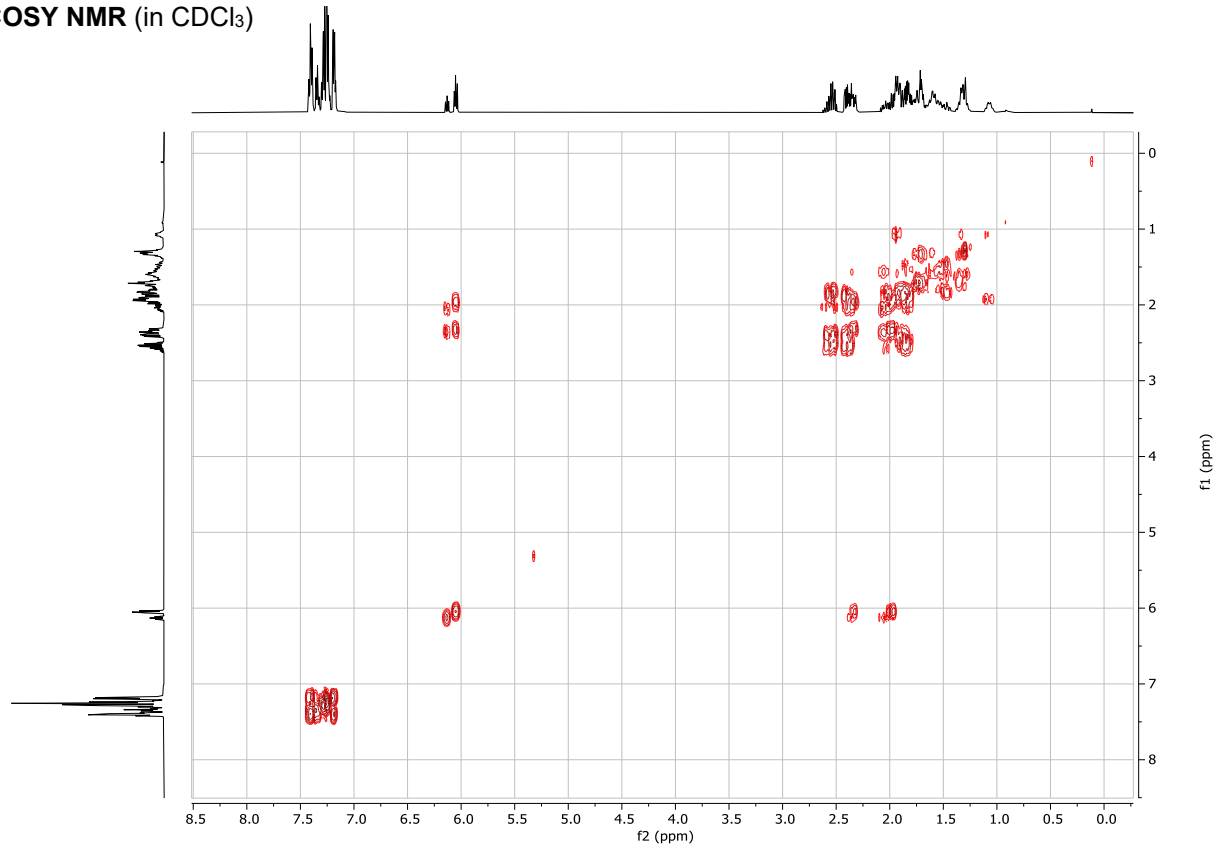
^{13}C NMR (126 MHz, $CDCl_3$)



HSQC NMR (in $CDCl_3$)

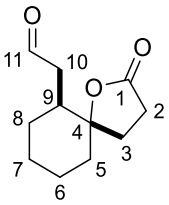


COSY NMR (in $CDCl_3$)

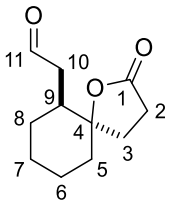


(±)-2-((5*S*,6*S*)-2-Oxo-1-oxaspiro[4.5]decan-6-yl)acetaldehyde 13-major and (±)-2-((5*R*,6*S*)-2-oxo-1-oxaspiro[4.5]decan-6-yl)acetaldehyde 13-minor.

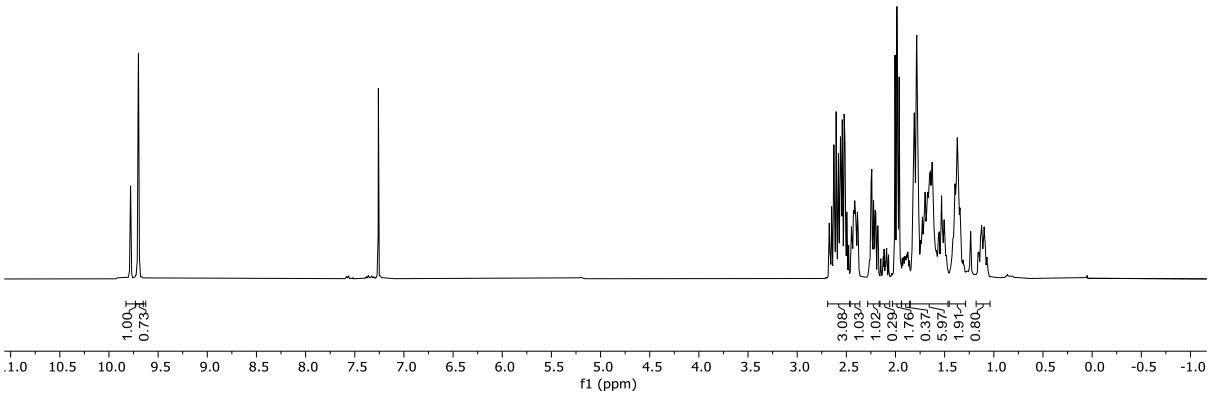
^{1}H NMR (400 MHz, $CDCl_3$)



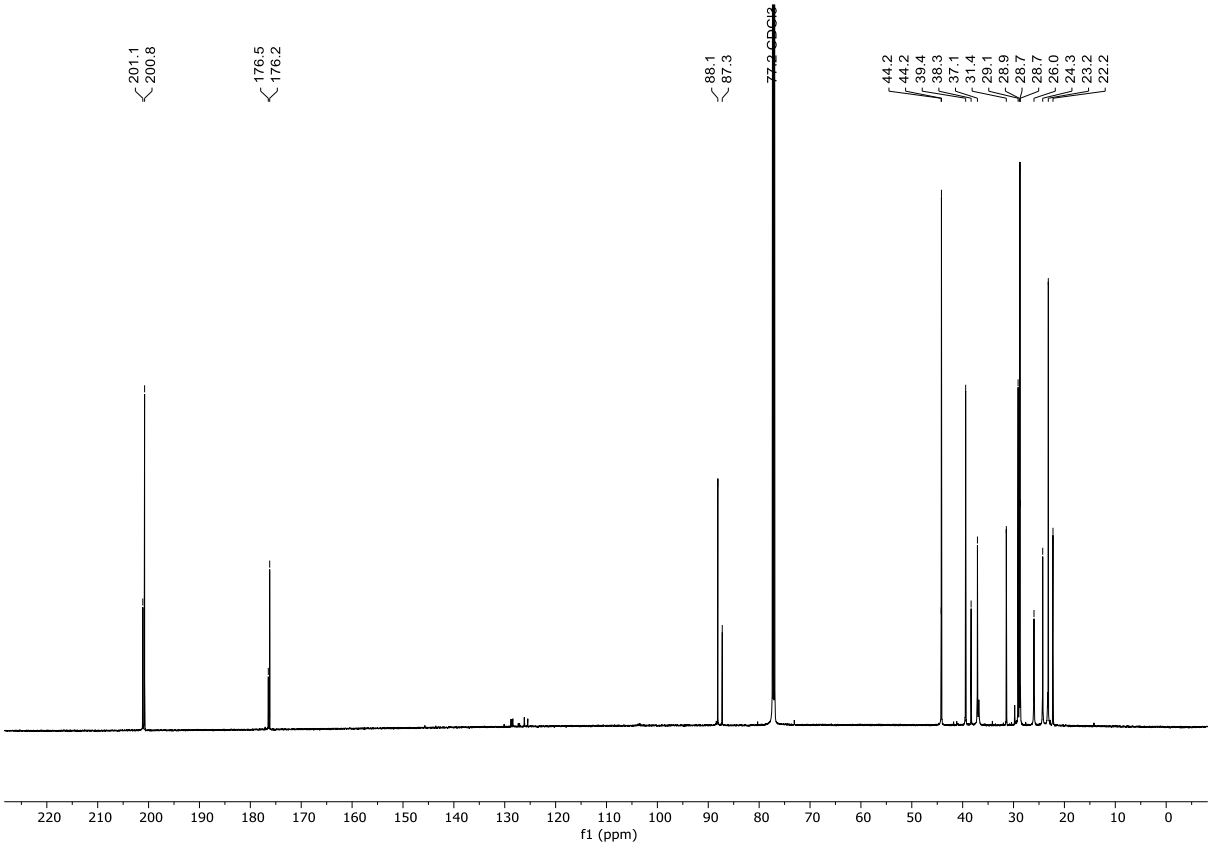
Major-13
$C_{11}H_{16}O_3$
196.25 g mol^{-1}



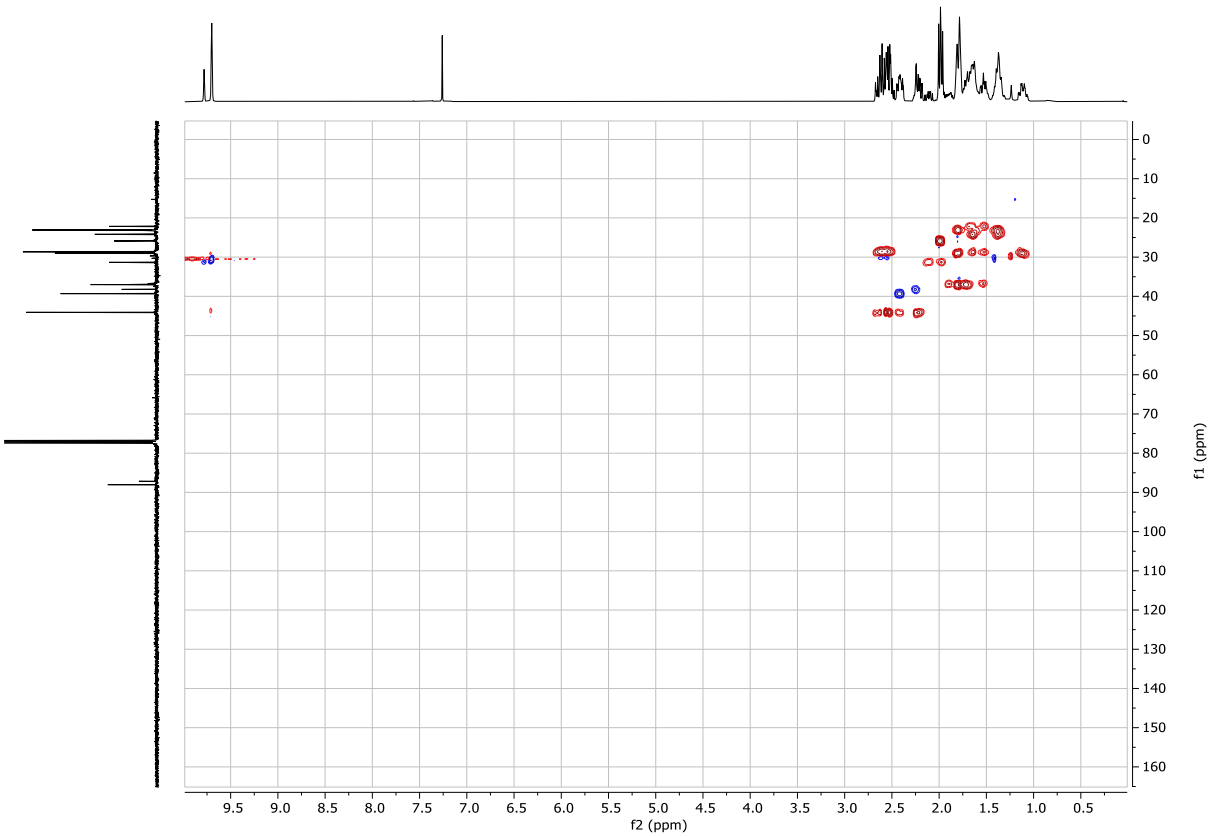
Minor-13
$C_{11}H_{16}O_3$
196.25 g mol^{-1}



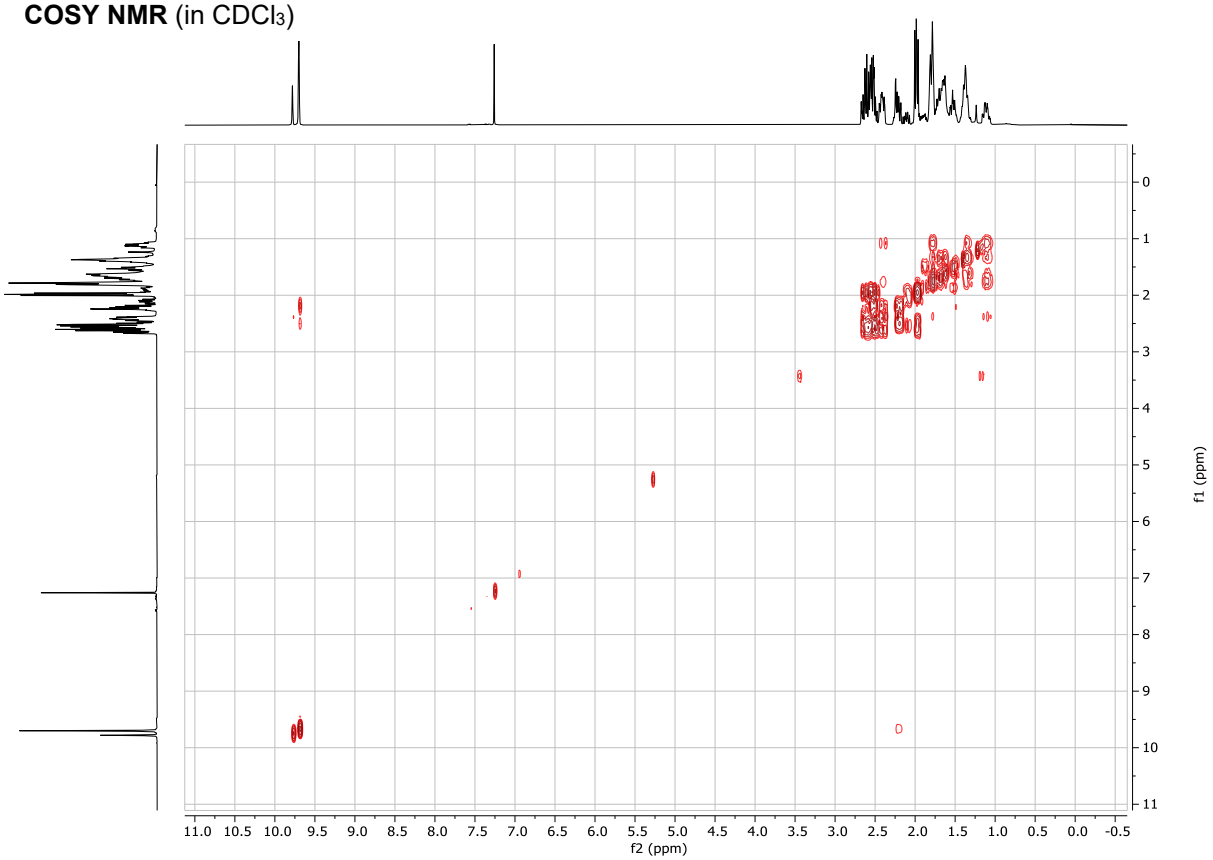
^{13}C NMR (151 MHz, $CDCl_3$)



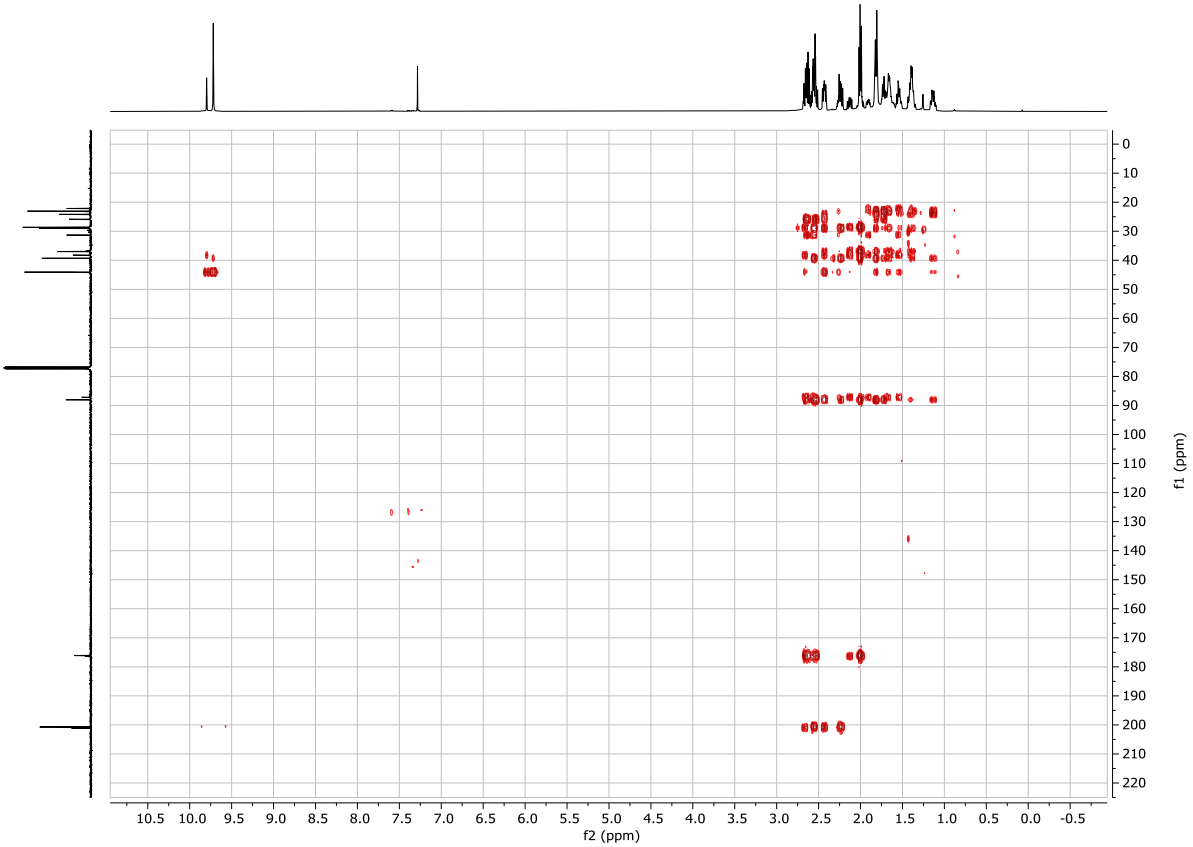
HSQC NMR (in $CDCl_3$)

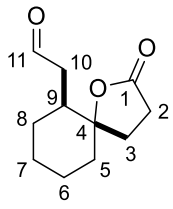


COSY NMR (in $CDCl_3$)



HMBC NMR (in $CDCl_3$)

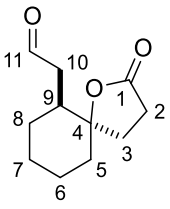




Major-13

$C_{11}H_{16}O_3$

196.25 g mol^{-1}

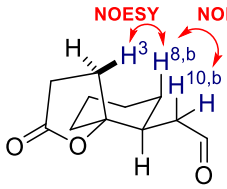


Minor-13

$C_{11}H_{16}O_3$

196.25 g mol^{-1}

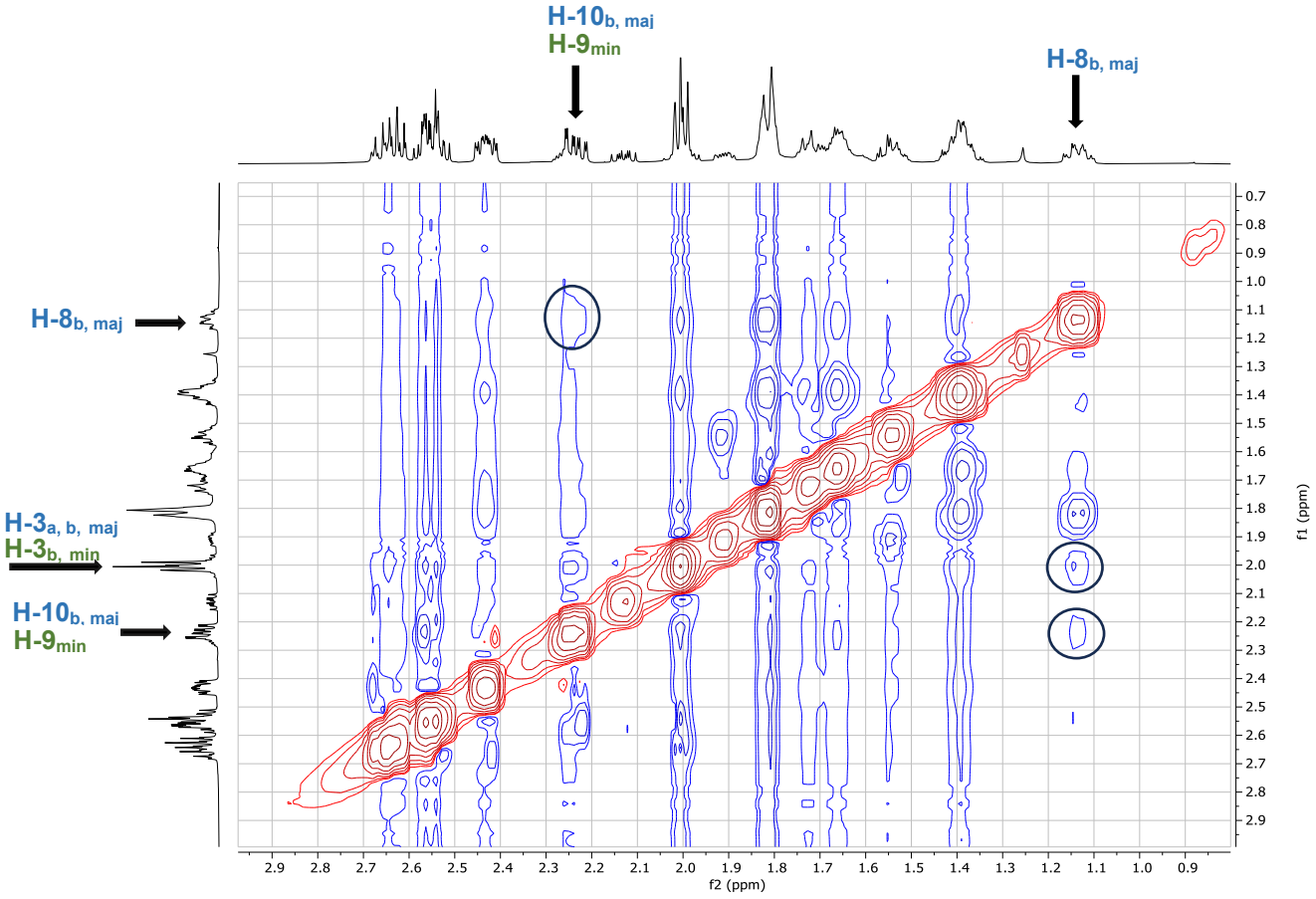
Stereochemical analysis using NOESY



13 (major)

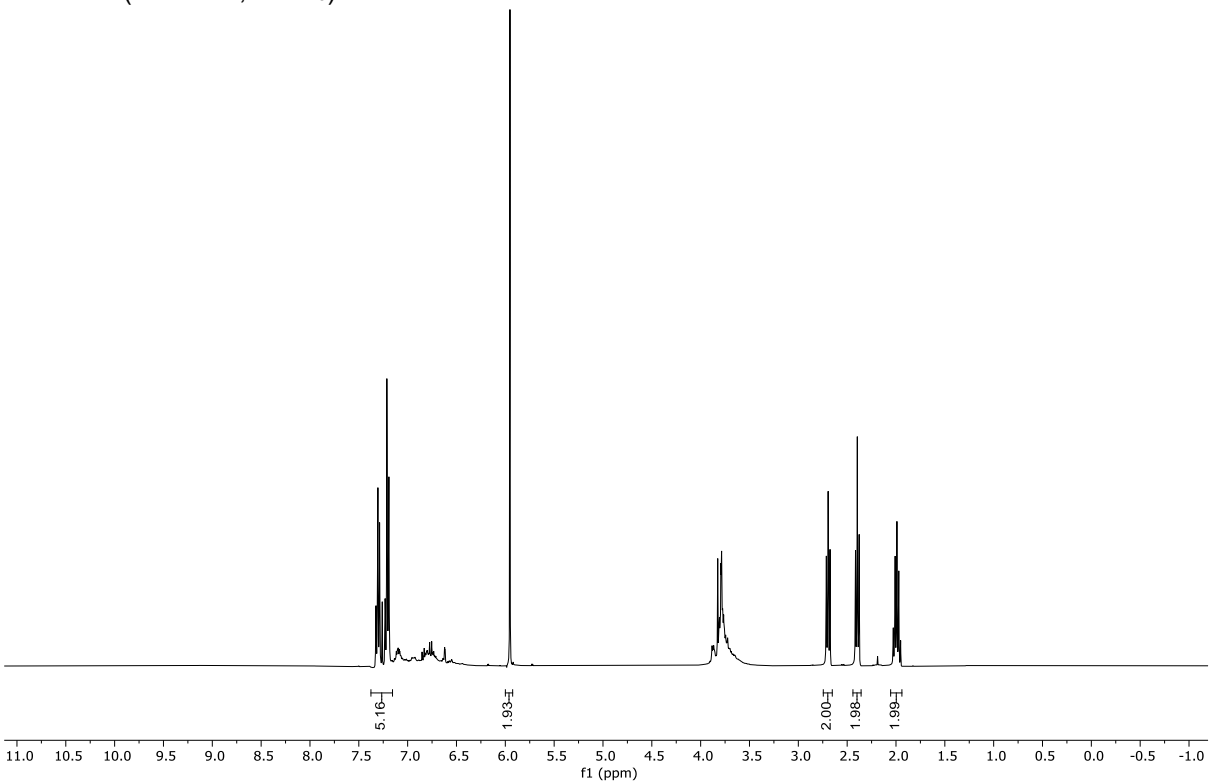
H-8$_{b, maj}$

1.11 (dtd, *J* = 15.0, 11.2, 3.8 Hz, 1H)

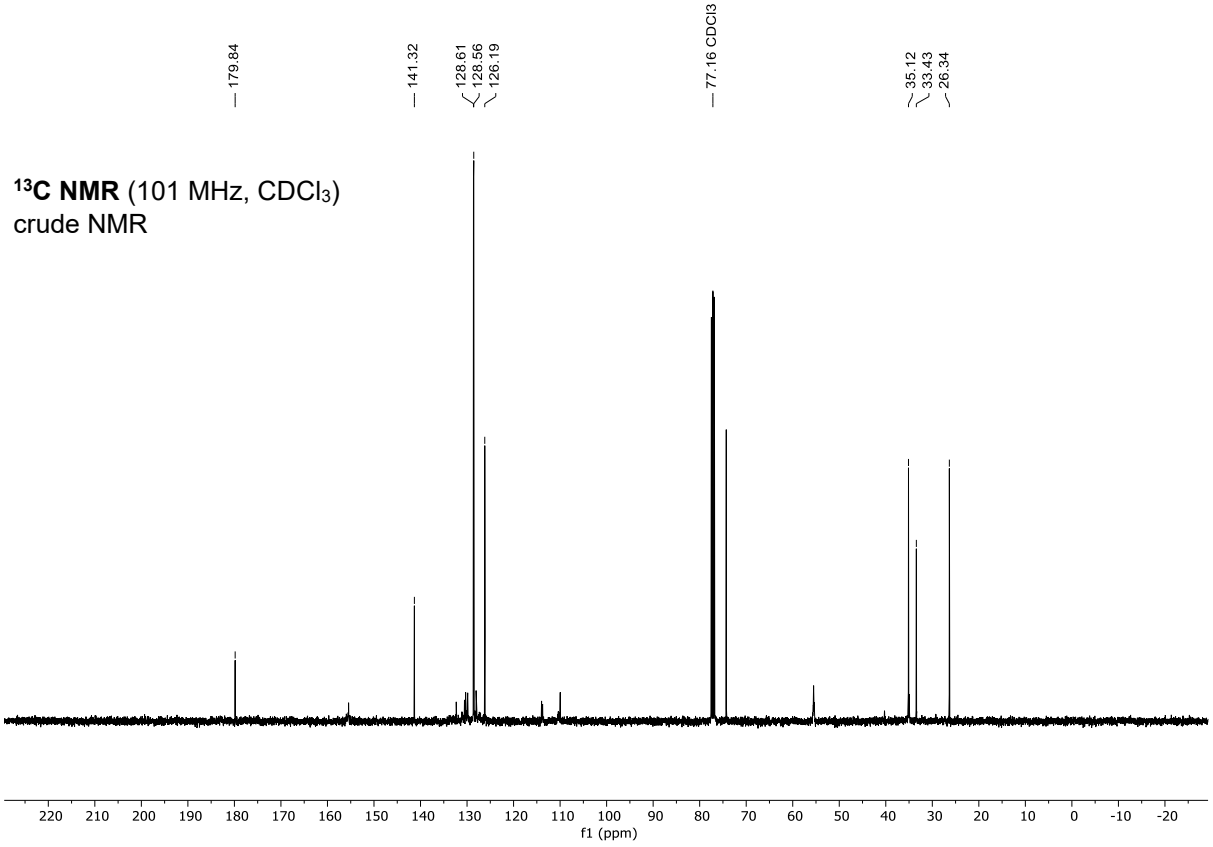


Control experiment using 4-phenylbutanoic acid 17.

^{1}H NMR (400 MHz, $CDCl_3$) crude NMR

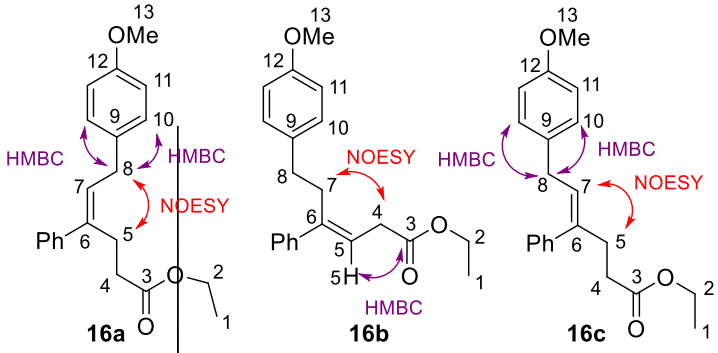


^{13}C NMR (101 MHz, $CDCl_3$) crude NMR



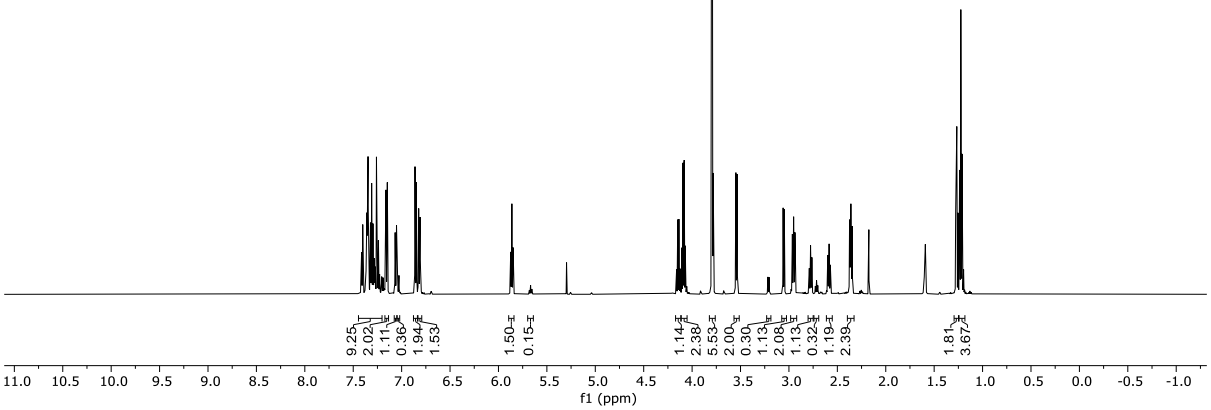
Control experiment using ester 15

^{1}H NMR (600 MHz, $CDCl_3$)

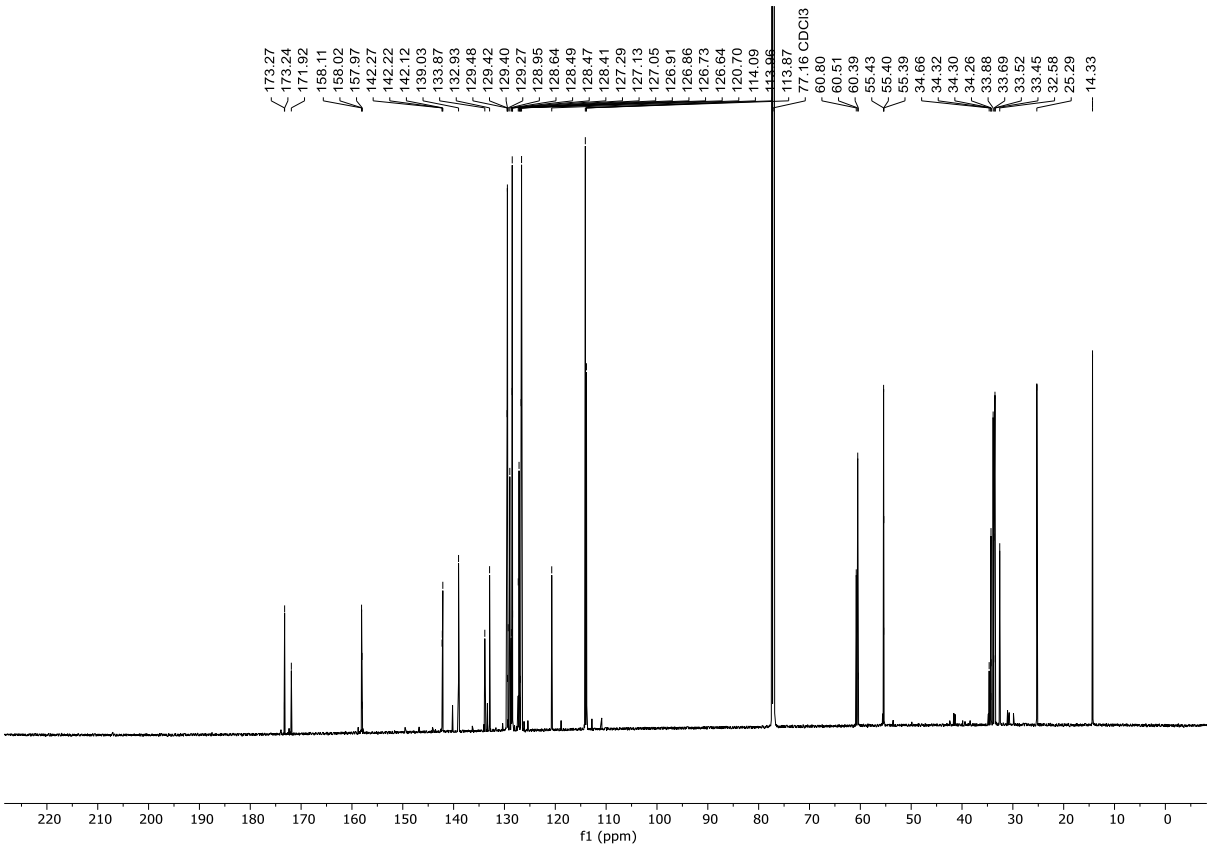


Chemical Formula: $C_{21}H_{24}O_3$
Molecular Weight: 324.42

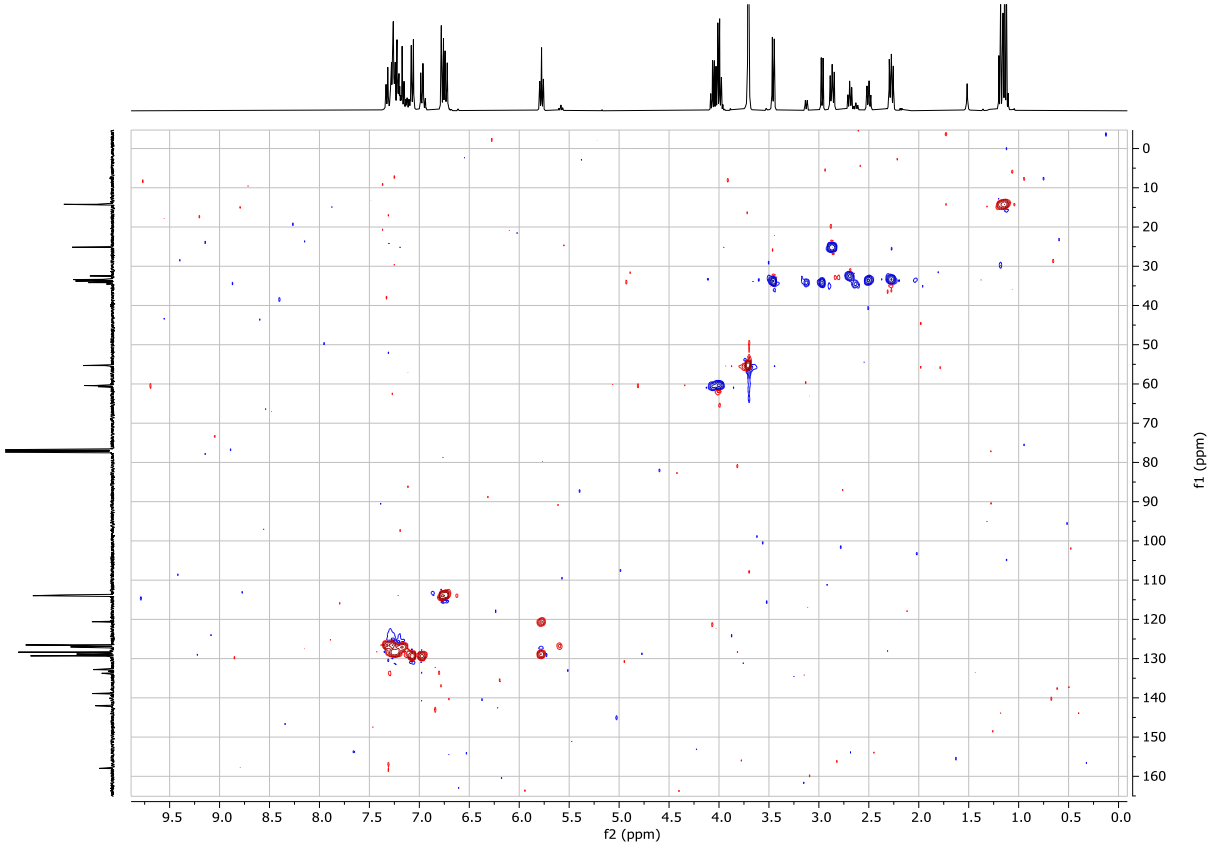
16a : **16b** : **16c** = 57 : 33 : 10



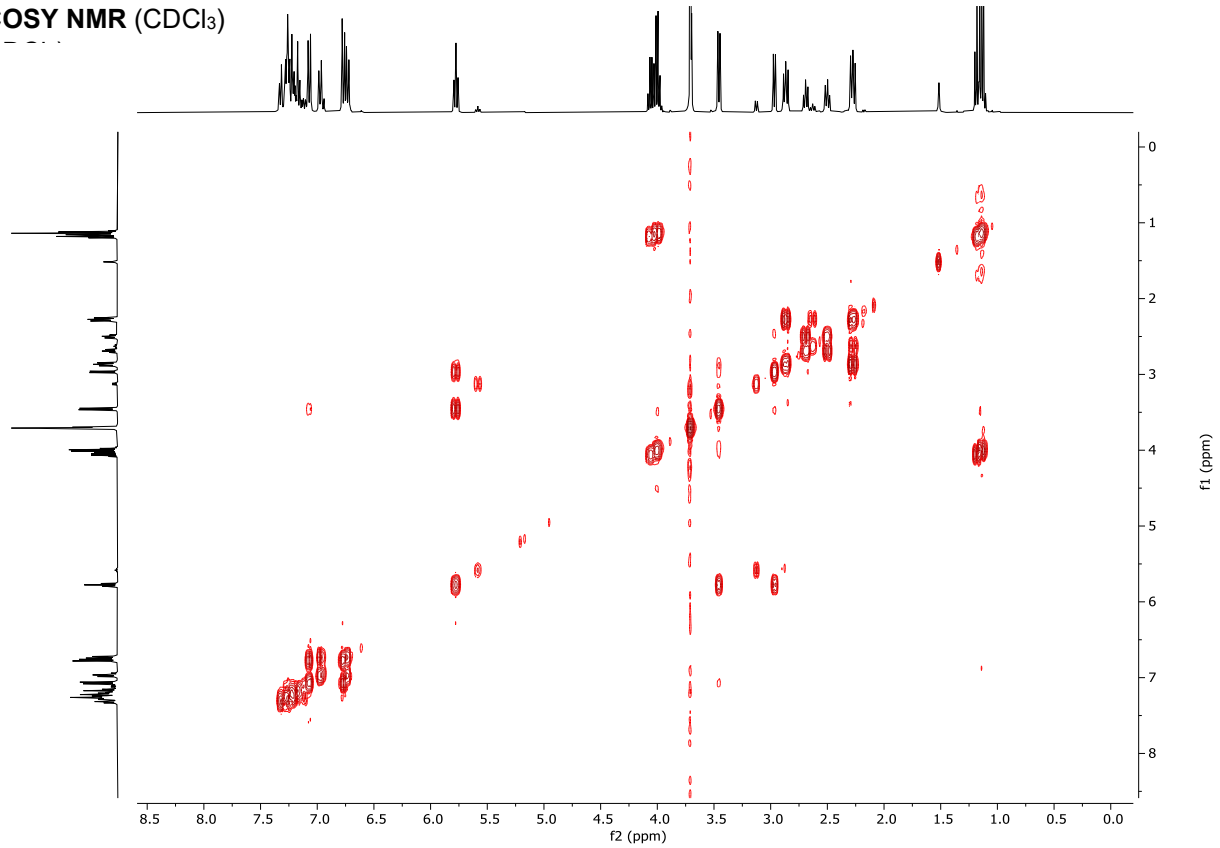
^{13}C NMR (151 MHz, $CDCl_3$)



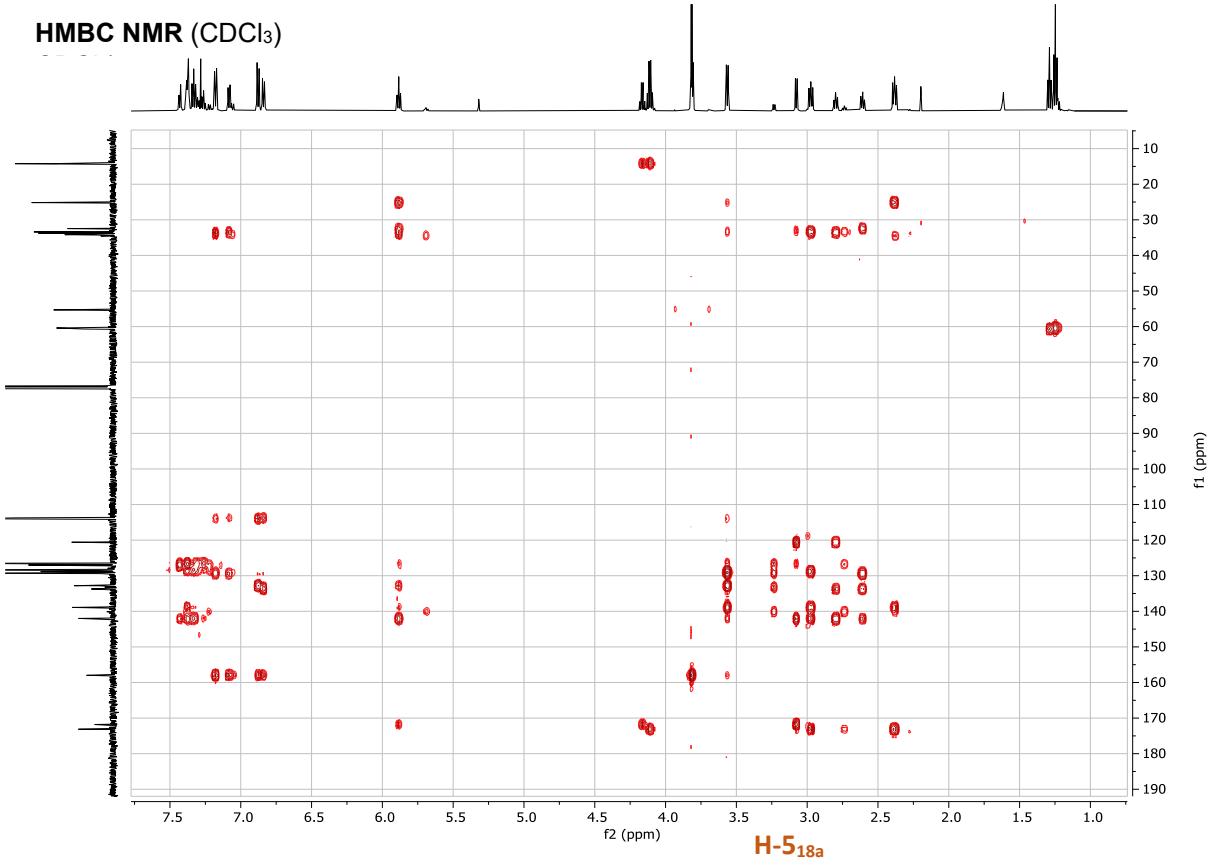
HSQC NMR ($CDCl_3$)



COSY NMR ($CDCl_3$)



HMBC NMR ($CDCl_3$)



NOESY NMR ($CDCl_3$)