Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Umpolung Synthesis of Branched α-Functionalized Amines from Imines via Photocatalytic Three-Component Reductive Coupling Reactions

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1. General information

Solvents and Reagents. Concentration under reduced pressure was performed by rotary evaporation at the appropriate pressure and temperature. Reagents used were obtained from commercial suppliers or purified according to standard procedures. Petroleum ether refers to distilled light petroleum of fraction 30 - 40 °C. Anhydrous toluene, tetrahydrofuran, dichloromethane and diethyl ether were dried by filtration through activated alumina (powder ~150 mesh, pore size 58 Å, basic, Sigma-Aldrich) columns. Dimethyl sulfoxide and dimethylformamide were used as supplied. Deuterated solvents were used as supplied.

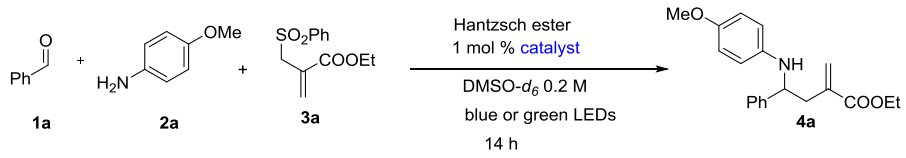
Chromatography. Reactions were monitored by thin layer chromatography (TLC) using Merck silica gel 60 F254 plates and visualized by fluorescence quenching under UV light. In addition, TLC plates were stained with potassium permanganate solution. Flash column chromatography (FCC) was performed on VWR 60 silica gel 40 - 63 µm using technical grade solvents that were used as supplied.

Instrumentation. Melting points were obtained on a Leica Galen III Hot-stage melting point apparatus and microscope and on a Kofler hot block and are reported uncorrected. NMR spectra were recorded on a Bruker Spectrospin spectrometer operating at 200, 400 or 500 MHz (^{1}H acquisitions), 100 or 125 MHz (^{13}C acquisitions). Chemical shifts (δ) are reported in ppm with the solvent resonance as the internal standard (e.g. Chloroform δ 7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C). Coupling constants (J) are reported in hertz (Hz), and rounded to the nearest 0.5 Hz. Data are reported as follows: multiplicity [s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, ddd = doublet of doublets of doublets, td = triplet of doublets, m = multiplet, br = broad], coupling constants in Hz, integration. Two-dimensional spectroscopy (COSY, HSQC and HMBC) was used to assist in the assignment and the data is not reported. High-resolution mass spectra (ESI) were recorded on Bruker µTOF mass spectrometer. Infrared spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer as a thin film. Only selected maximum absorbances are reported. Fluorescence measurements were recorded on a Fluorescence Spectrophotometer Varian Cary Eclipse. Photoredox reactions were run using Tingkam waterproof strip 150 LEDs 30W output, and a photoreactor composed of 5 green LEDs (Green LED Emitters LZ4-00G108 from LED engine).

2. Optimisation experiments

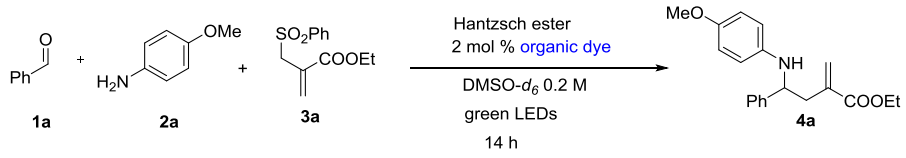
General procedure for optimisation experiments: sulfone **3** (0.1 mmol, 2.5 eq), Hantzsch ester (0.15 mmol, 1.5 eq), anisidne **2** (0.1 mmol, 1.0 eq) and catalyst were added to a vial, followed by 0.5 mL of solvent and benzaldehyde **1** (0.1 mmol, 1.0 eq). The mixture was bubbled with N_2 for 1 min, then closed and irradiated under 1 W Blue or Green LEDs for 14 h. An NMR sample was taken for analysis after 90 min and after 14 h.

Optimisation of the catalyst



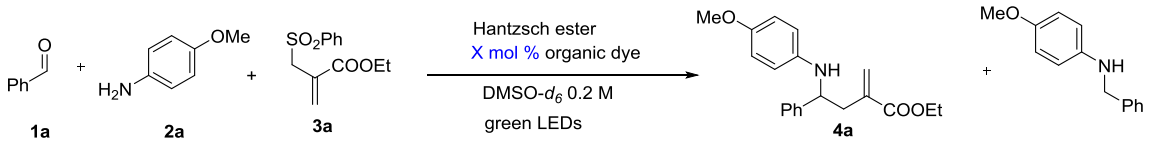
Entry	Catalyst	LEDs	NMR yield (%) 1 h 30 min	NMR yield (%) 14 h
1	$[Ru(bpy)_3]Cl_2$	Blue	67	71
2	$[Ru(bpz)_3][PF_6]_2$	Blue	5	24
3	$[Ir(dtbbpy)(ppy)_2][PF_6]$	Blue	81	94
4	$[Ir\{dF(CF_3)ppy\}_2(dtbpy)][PF_6]$	Blue	76	83
5	Eosin Y	Blue	34	93
6	Eosin Y	Green	49	90

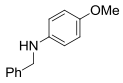
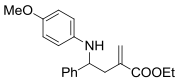
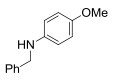
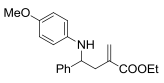
Screening or organic dyes



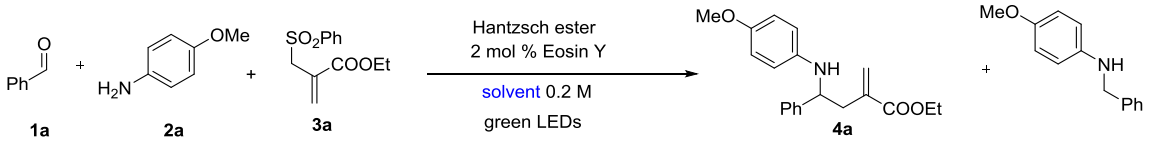
Entry	Catalyst	NMR yield (%) 1 h 30 min	NMR yield (%) 14 h
1	Fluorescein (FL)	10	38
2	FL (+ $Bu_4N^+OH^-$)	-	34
3	Eosin Y (EO)	58	91
4	Rose Bengal (RB)	65	87
5	RB (0.5 mol %)	27	76

Optimisation of the catalyst loading



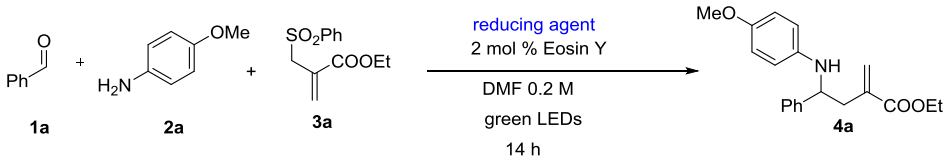
Entry	Eosin mol %	conversion after 90 min (%)		Conversion after 14 h (%)	
					
1	0.5	11	26	17	59
2	1	7	41	11	85
3	2	4	60	5	93
4	5	-	37	traces	95
5	10	-	21	-	94

Solvent screening



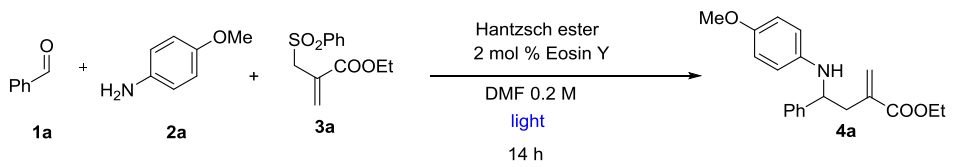
Entry	Solvent	NMR yield (%) **4**	NMR yield (%) overreduction
1	DMSO-d_6	93	7
2	DMF	94	Traces
3	IPA	50	33
4	CH_3CN	41	11
5	DCM	5	62
6	MeOH	2	98
7	toluene	1	29

Reducing agent screening



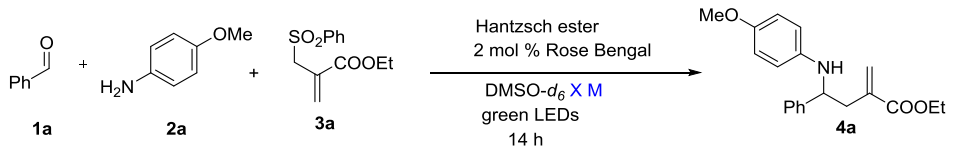
Entry	Reducing agent	NMR yield (%)
1	Hantzsch ester	84
2	NEt_3	7
3	Hünig base	4
4	*N,N*-diphenylanisole	-
5	1,4-cyclohexadiene	-
6	NEt_3 + HCOOH	-

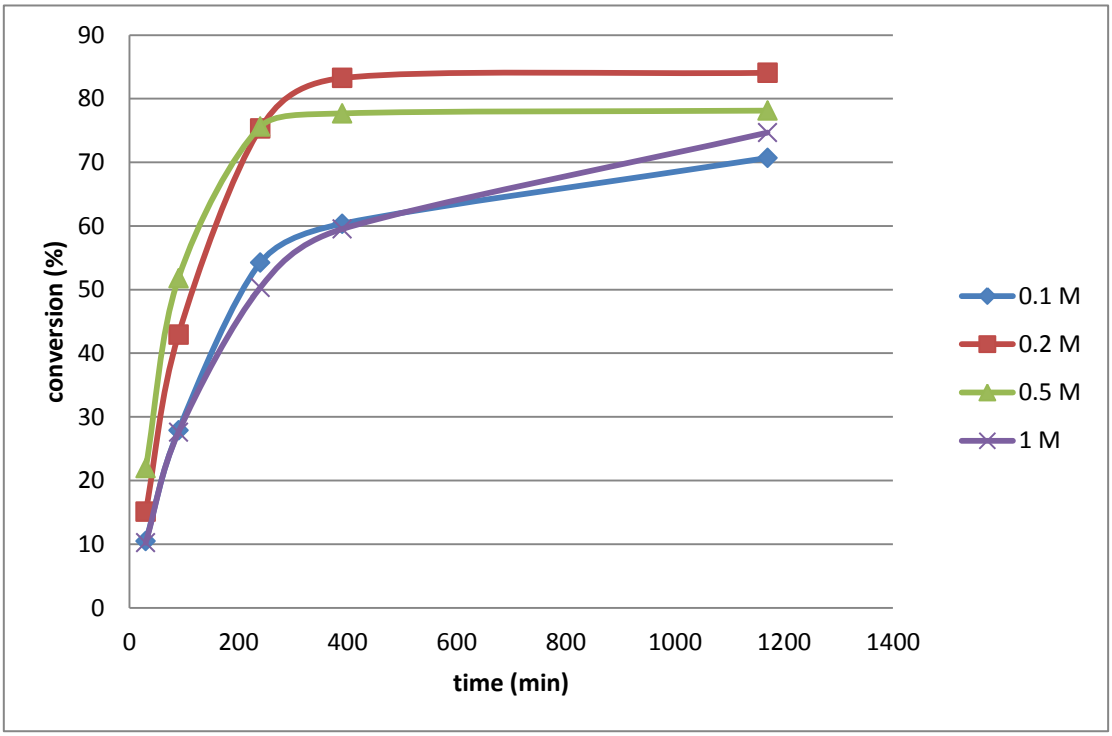
Screening source of light



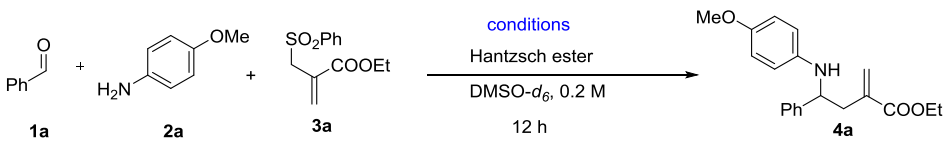
Entry	Light source	conversion (%) 1 h 30 min	Conversion (%) 4 h	Conversion (%) 6 h	Conversion (%) 14 h
1	Blue LEDs strip	34			93
2	Green LEDs strip	49			90
3	20 W CFL	47	74	79	91

Concentration screening





3. Control experiments



Entry	conditions	NMR yield (%)
1	2 mol% EO, no light	0
2	no EO, Green LEDs	overreduction (80%)
3	2 mol% EO, 3 eq TEMPO, Green LEDs	0
4	2 mol% EO, Green LEDs, air	52

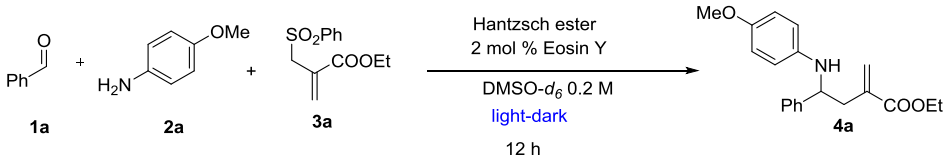
Change of the solution colour observed before and after the reaction, probably because of a change in the pH after the Hantzsch ester oxidation. EO can behave as a pH indicator (2.9-4.5).[1]

Before

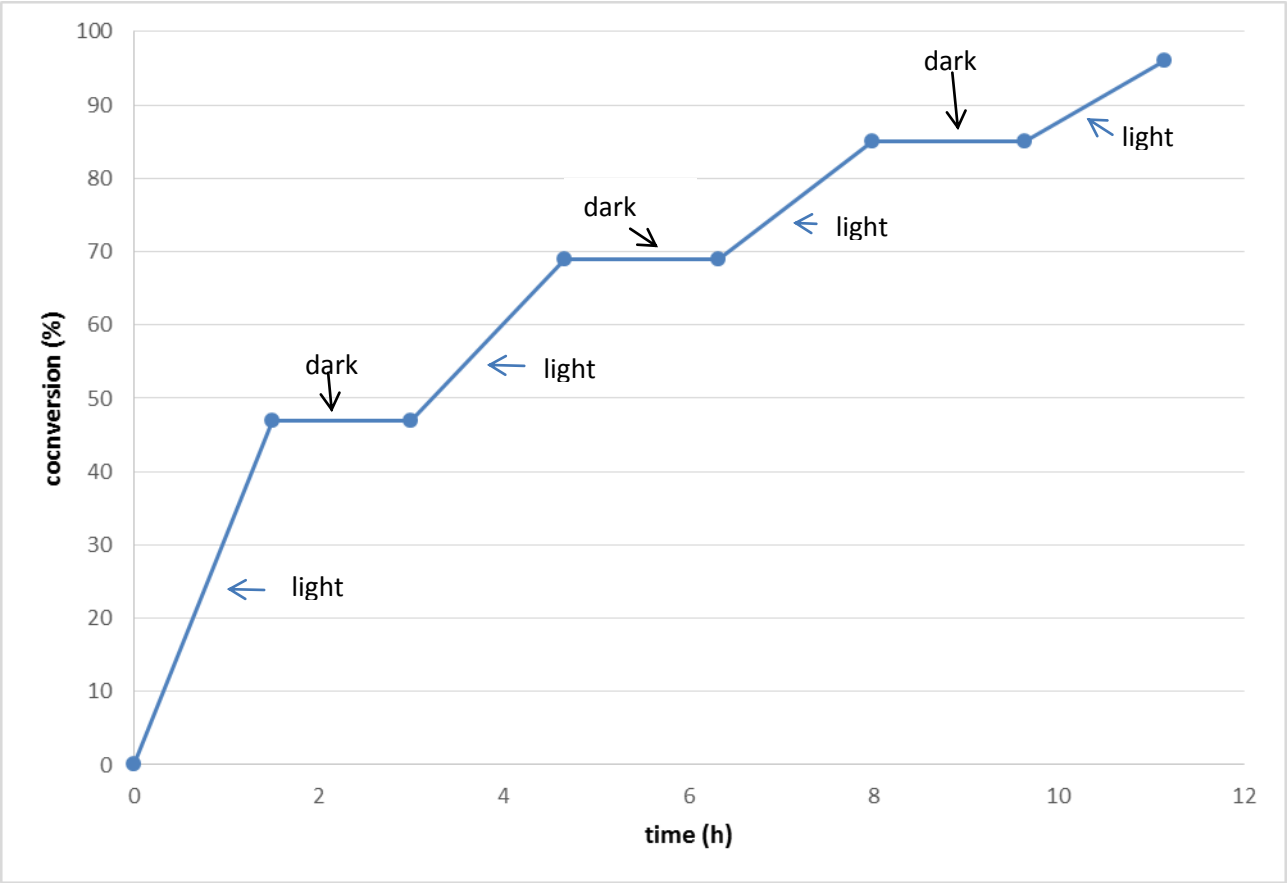
After

4. Mechanistic studies

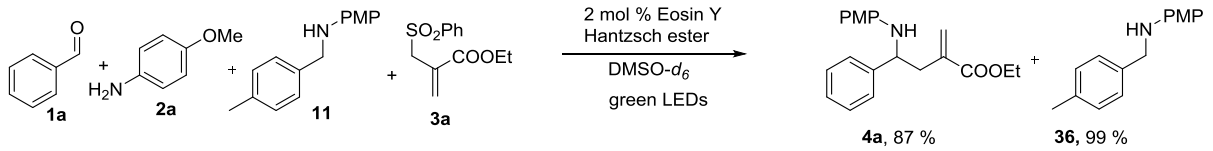
Dependency on light

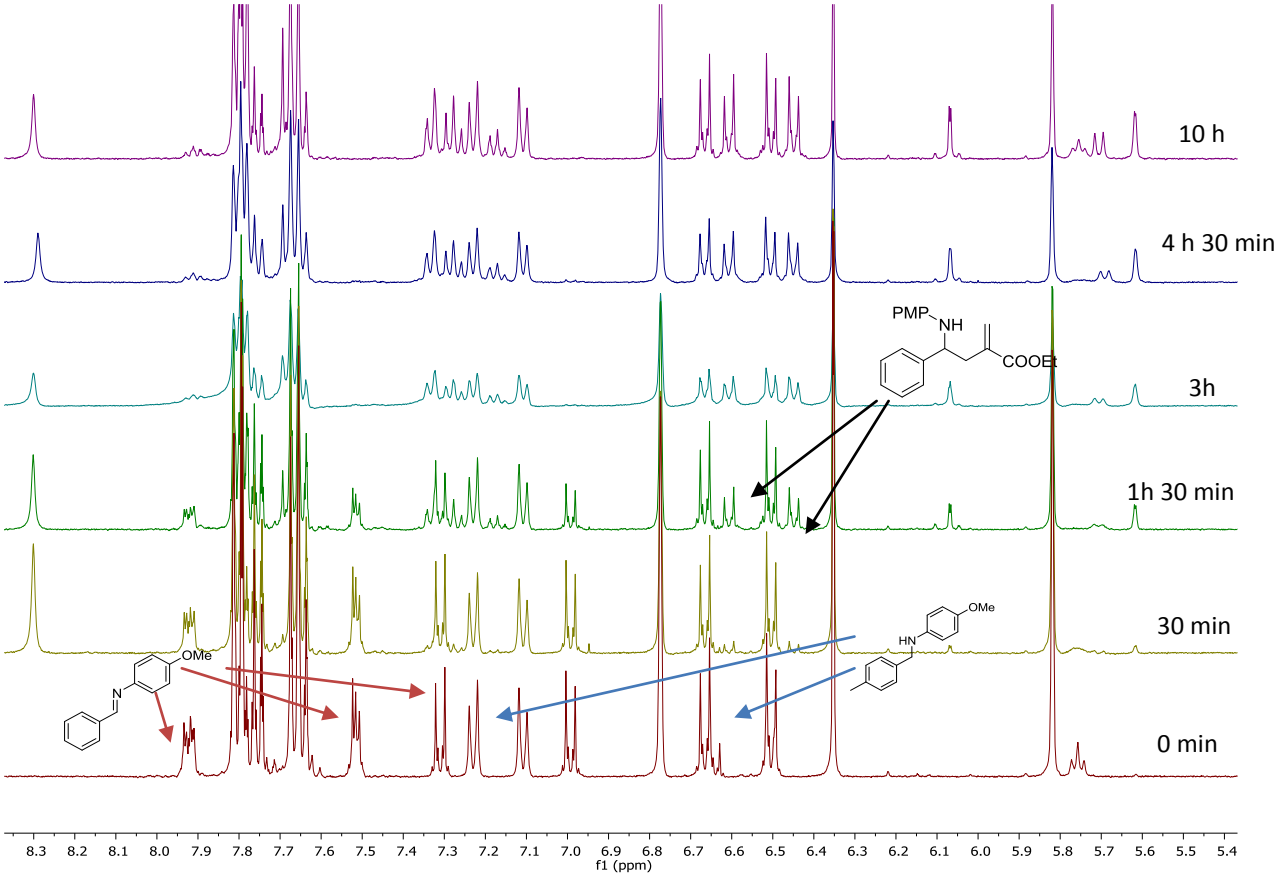


1a 2a 3a 4a

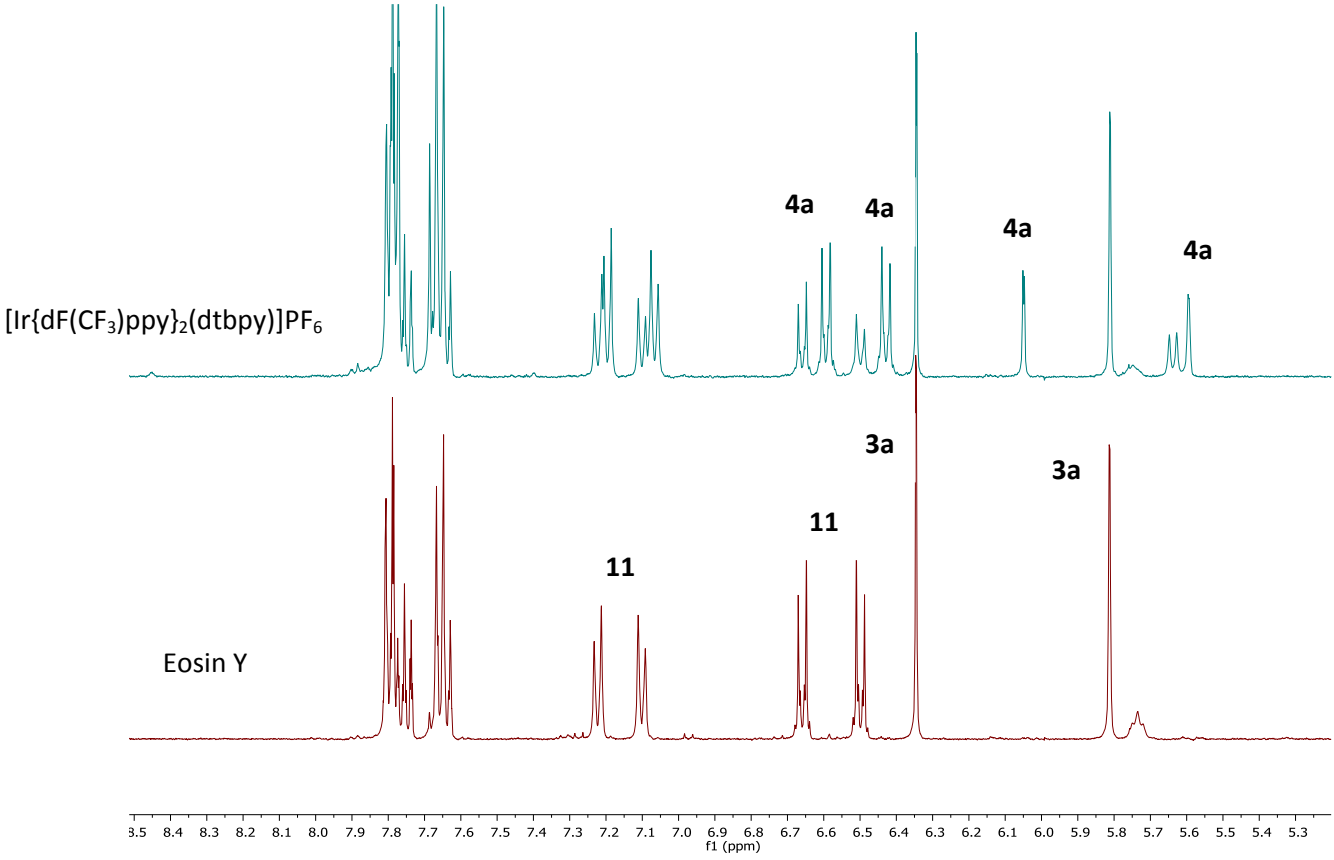


Cross experiment



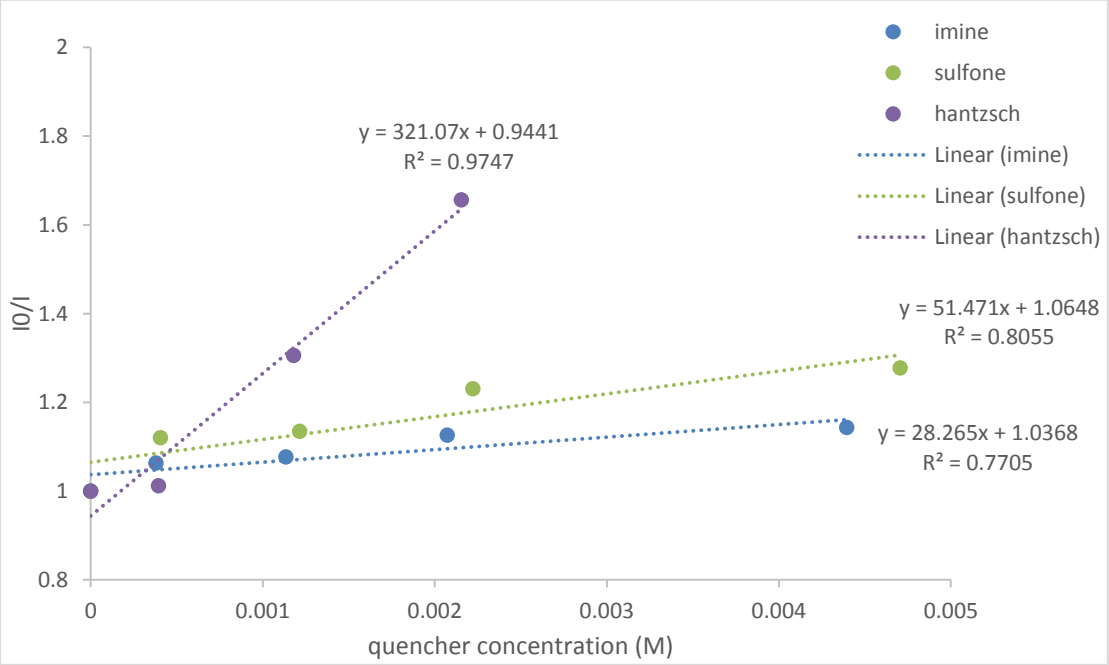


Reaction with amine 36

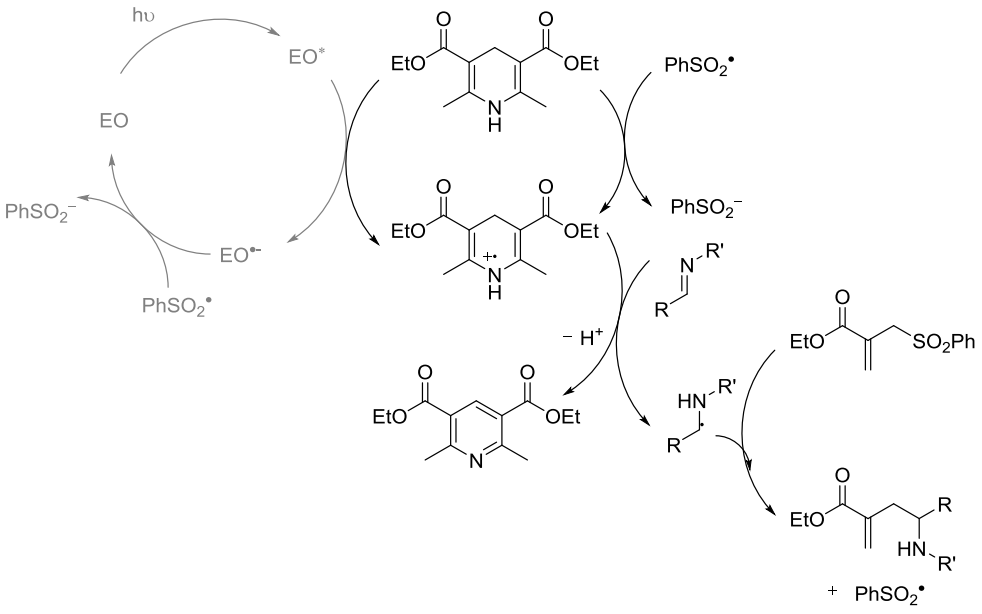


Stern-Volmer quenching experiments

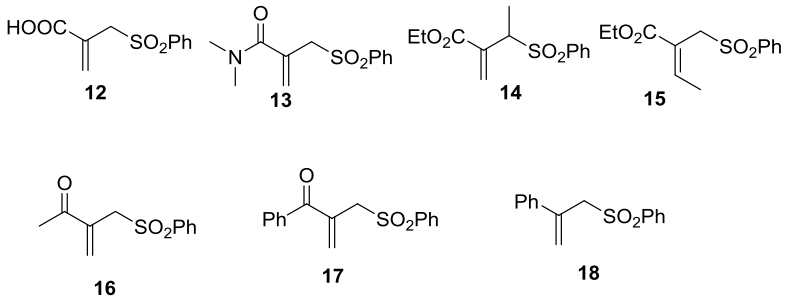
A 2.9x 10^{-5} M solution of eosin Y was irradiated at 545.97 nm and the emission intentisity was measured at 546-600 nm. Aliquots of the appropriate quencher (0.3 M) dissolved in the stock solution of eosin Y were sequentially added, stirred with a test tube shaker for 1 min and degassed bubbling N_2 for 15 min. Then, the emission spectra of the samples were collected. Although some quenching could be observed with the sulfone or the imine, the fluorescence decay observed with the Hantzsch ester was much more pronounced.



Alternative radical propagation mechanism

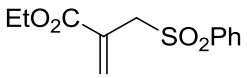


Unreactive sulfones



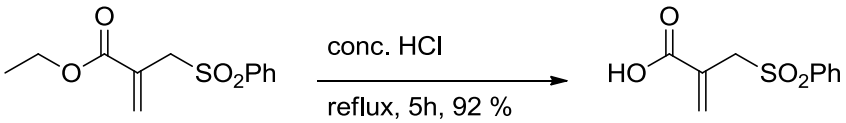
5. Preparation of the Sulfones

Ethyl 2-((phenylsulfonyl)methyl)acrylate (**3a**)



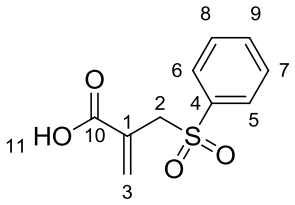
Ethyl 2-((phenylsulfonyl)methyl)acrylate was prepared according to a literature procedure. Analytical data matched the reported data therein.[2]

2-((Phenylsulfonyl)methyl)acrylic acid (**12**)



2-((phenylsulfonyl)methyl)acrylic acid was prepared following a known procedure for its preparation from methyl 2-((phenylsulfonyl)methyl)acrylate.[3]

5.0 g (19.7 mmol) Ethyl 2-((phenylsulfonyl)methyl)acrylate were dissolved in 20 ml of concentrated hydrochloric acid and refluxed for 5 hours. The solution was cooled to room temperature, the white solid was filtered off and washed with 20 ml of ice cold water. After drying under vacuum 2-((phenylsulfonyl)methyl)acrylic acid was obtained as a white solid (4.1 g, 92 %).



m p: 168-170 °C

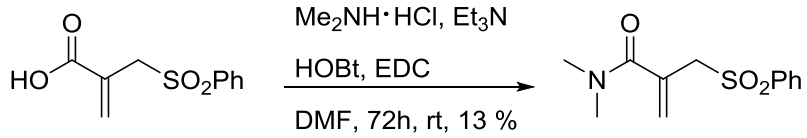
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3062 (br, O-H), 1698 (m, C=O), 1303 (m, S=O), 1147 (s, S=O).

^{1}H NMR (400 MHz, DMSO-d_6) δ 4.31 (d, *J* = 0.8 Hz, 2H, H-2), 5.72 (d, *J* = 1.1 Hz, 1H, H-3cis), 6.31 (d, *J* = 1.2 Hz, 1H, H-3trans), 7.59 – 7.69 (m, 2H, H-7, H-8), 7.71 – 7.77 (m, 1H, H-9), 7.77 – 7.85 (m, 2H, H-5, H-6), 12.84 (s, 1H, H-11).

^{13}C NMR (101 MHz, DMSO) δ 56.5 (C-2), 128.2 (C-5, C-6), 129.3 (C-7, C-8), 129.8 (C-4), 132.6 (C-3), 134.0 (C-9), 138.3 (C-1), 166.2 (C-10).

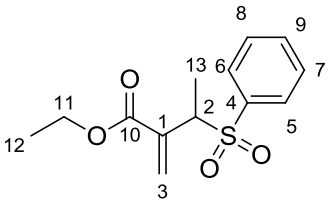
HRMS (ES+) exact mass calculated for $[M+Na]^+$ ($C_{10}H_{10}O_4N^{23}Na^{32}S$) requires **m/z** 249.0192, found **m/z** 249.0192.

N,N-dimethyl-2-((phenylsulfonyl)methyl)acrylamide (**13**)



N,N-dimethyl-2-((phenylsulfonyl)methyl)acrylamide was prepared from 2-((phenylsulfonyl)methyl)acrylic acid according to the following protocol. HOBt (514.8 mg, 3.81 mmol, 1.0 eq), dimethylamine hydrochloride (341.7 mg, 4.20 mmol, 1.1 eq) and EDC (730.4 mg, 3.81 mmol, 1.0 eq) were weighed into a flask. A solution of 2-((phenylsulfonyl)methyl)acrylic acid (863.1 mg, 3.81 mmol, 1.0 eq) in 15 ml DMF and 0.59 ml of Et_3N (4.10 mmol 1.1 eq) was added thereto and the resulting mixture stirred for 2 days. The reaction mixture was diluted with 150 ml of ethyl acetate and washed with 3x40ml of H_2O, 20 ml of 1N HCl and 20 ml of brine. The organic layer was dried over Na_2SO_4. Subsequently the drying agent was filtered off and the organic phase evaporated under reduced pressure to yield a yellowish oil. Purification by column chromatography (Petrol/Et_2O 1:4 to 1:9) afforded 125.5 mg of a colourless oil (13 % yield). Analytical data were in accordance with the literature.[4]

Ethyl 2-methylene-3-(phenylsulfonyl)butanoate (**14**)



Ethyl 2-methylene-3-(phenylsulfonyl)butanoate was prepared according to a literature procedure. However, full analytical data is not available for this compound and we wish to include these in our report.[5]

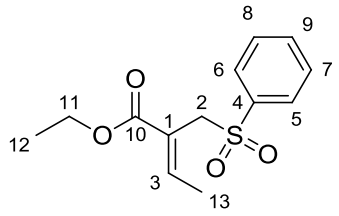
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 1719 (m, C=O), 1307 (m, S=O), 1145 (s, S=O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.19 (t, *J* = 7.1 Hz, 3H, H-12), 1.55 (d, *J* = 7.2 Hz, 3H, H-13), 4.02 (qd, *J* = 7.1, 4.6 Hz, 2H, H-11), 4.63 (q, *J* = 7.2 Hz, 1H, H-2), 6.03 (s, 1H, H-3cis), 6.56 (s, 1H, H-3trans), 7.40 – 7.57 (m, 2H, H-7, H-8), 7.58 – 7.70 (m, 1H, H-9), 7.73 – 7.98 (m, 2H, H-5, H-6).

^{13}C NMR (101 MHz, $CDCl_3$) δ 13.9 (C-13), 14.2 (C-12), 58.6 (C-2), 61.6 (C-11), 129.0 (C-7, C-8), 129.6 (C-5, C-6), 130.5 (C-3), 133.9 (C-9), 137.6 (C-1), 165.4 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{13}H_{17}O_4{}^{32}S$) requires **m/z** 269.0842, found **m/z** 269.0844.

(Z)-Ethyl 2-((phenylsulfonyl)methyl)but-2-enoate (**15**)



(Z)-ethyl 2-((phenylsulfonyl)methyl)but-2-enoate was prepared according to a literature procedure. However, full analytical data is not available for this compound and we wish to include these in our report.[5]

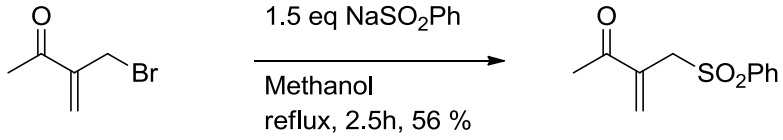
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 1710 (m, C=O), 1317 (m, C=C), 1309 (m, S=O), 1148 (s, S=O), 732 (C=CH).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.02 – 1.20 (m, 3H, H-12), 1.78 – 1.87 (m, 3H, H-13), 3.86 – 3.99 (m, 2H, H-11), 4.25 (d, *J* = 1.5 Hz, 2H, H-2), 7.20 – 7.27 (m, 1H, H-3), 7.47 – 7.56 (m, 2H, H-7, H-8), 7.59 – 7.66 (m, 1H, H-9), 7.85 (ddd, *J* = 8.5, 2.5, 1.3 Hz, 2H, H-5, H-6).

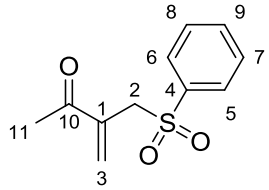
^{13}C NMR (101 MHz, $CDCl_3$) δ 14.2 (C-12), 15.5 (C-13), 53.8 (C-2), 61.2 (C-11), 122.1 (C-1), 128.8 (C-5, C-6), 129.1 (C-7, C-8), 133.9 (C-9), 138.9 (C-4), 146.6 (C-3), 165.6 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{13}H_{17}O_4{}^{32}S$) requires **m/z** 269.0842, found **m/z** 269.0840.

3-((Phenylsulfonyl)methyl)but-3-en-2-one (**16**)



A mixture of 3-(bromomethyl)but-3-en-2-one[5] (260.0 mg, 1.78 mmol, 1.0 eq) and sodium benzenesulfinate (910.5 mg, 5.55 mmol, 3.1 eq) in methanol (8 ml) was refluxed for 2.5 h. The reaction mixture was diluted with 10 ml of water and extracted with 3x 10 ml ethyl acetate, before being washed with brine and dried over sodium sulfate. After evaporation the organic solvent, the crude was purified by flash column chromatography (Petrol/ Et_2O 2:1) to yield 220.3 mg (56 % yield) of an off-white solid.



m p: 78-80 °C

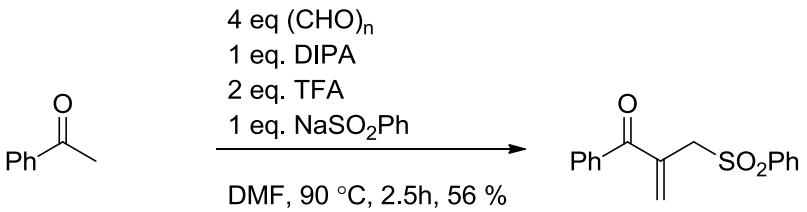
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 1683 (m, C=O), 1317 (m, C=C), 1307 (m, S=O), 1148 (s, S=O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 2.24 (s, 3H, H-11), 4.16 (d, *J* = 0.8 Hz, 2H, H-2), 6.27 (d, *J* = 0.9 Hz, 1H, H-3cis), 6.37 (s, 1H, H-3trans), 7.50 – 7.59 (m, 2H, H-7, H-8), 7.61 – 7.70 (m, 1H, H-9), 7.73 – 7.90 (m, 2H, H-5, H-6).

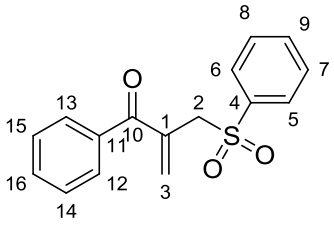
^{13}C NMR (101 MHz, $CDCl_3$) δ 25.1 (C-11), 55.6 (C-2), 128.6 (C-5, C-6), 129.2 (C-7, C-8), 132.8 (C-3), 134.0 (C-9), 137.0 (C-4), 138.7 (C-1), 196.4 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{11}H_{13}O_3{}^{32}S$) requires **m/z** 225.0580, found **m/z** 225.0583.

1-Phenyl-2-((phenylsulfonyl)methyl)prop-2-en-1-one (**17**)



A mixture of acetophenone (0.59 ml, 5.0 mmol, 1eq), DIPA (0.71 ml, 5.0 mmol, 1 eq), TFA (0.77 ml, 10.0 mmol, 2.0 eq), sodium benzenesulfinate (821 mg, 5.0 mmol, 1.0 eq) and para-formaldehyde (602 mg, 20.0 mmol, 4.0 eq) in 10 ml DMF was heated to 90 °C in a sealed vessel for 20 h. The reaction mixture was cooled to room temperature, diluted with 150 ml ethyl acetate, washed with 3x 20ml LiCl (5wt%) and dried over magnesium sulfate. The solid was filtered off and the organic solvent evaporated. The viscous crude oil was purified by flash column chromatography (Petrol/EtOAc 4:1 to 1:1) to yield 766.8 mg of a white solid (54 % yield).



m p: 99-100 °C

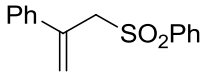
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 1657 (m, C=O), 1317 (m, C=C), 1307 (m, S=O), 1150 (s, S=O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 4.36 (d, *J* = 0.9 Hz, 2H, H-2), 6.03 (s, 1H, H-3cis), 6.17 – 6.34 (m, 1H, H-3trans), 7.39 – 7.45 (m, 2H, H-14, H-15), 7.48 – 7.55 (m, 3H, H-16, H-7, H-8), 7.55 – 7.62 (m, 1H, H-9), 7.63 – 7.68 (m, 2H, H-12, H-13), 7.83 – 7.98 (m, 2H, H-5, H-6).

^{13}C NMR (101 MHz, $CDCl_3$) δ 57.8 (C-2), 128.4 (C-14, C-15), 128.5 (C-5, C-6), 129.3 (C-7, C-8), 129.7 (C-12, C-13), 132.8 (C-9), 134.1 (C-16), 134.3 (C-3), 135.7 (C-4), 136.2 (C-11), 138.9 (C-1), 194.8 (C-10).

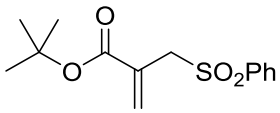
HRMS (ES+) exact mass calculated for $[M+Na]^+$ ($C_{16}H_{14}O_3{}^{23}Na^{32}S$) requires **m/z** 309.0556, found **m/z** 309.0555.

Ethyl 2-((phenylsulfonyl)methyl)acrylate (**18**)



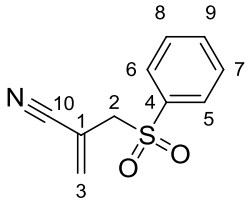
Ethyl 2-((phenylsulfonyl)methyl)acrylate was prepared according to a literature procedure. Analytical data matched the reported data therein.[2]

Tert-butyl 2-((phenylsulfonyl)methyl)acrylate (**3b**)



Compound **37** was refluxed in $SOCl_2$ for one hour, and after evaporation of the excess of $SOCl_2$, it was coupled with tertbutanol following literature .[8] Analytical data matched the reported data.[9]

2-((Phenylsulfonyl)methyl)acrylonitrile (**3c**)



2-((phenylsulfonyl)methyl)acrylonitrile was prepared according to a literature procedure.[10]

m p: 60-62 °C

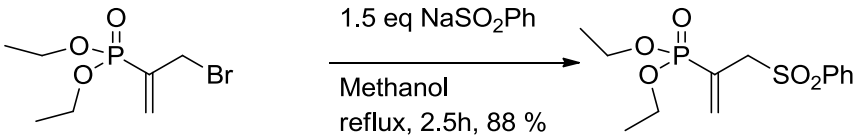
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 2228 (m, C≡N), 1310 (m, S=O), 1152 (s, S=O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 3.93 (d, *J* = 1.0 Hz, 2H, H-2), 6.01 (t, *J* = 1.0 Hz, 1H, H-3cis), 6.22 (s, 1H, H-3trans), 7.59 – 7.69 (m, 2H, H-5, H-6), 7.69 – 7.80 (m, 1H, H-9), 7.84 – 8.05 (m, 2H, H-7, H-8).

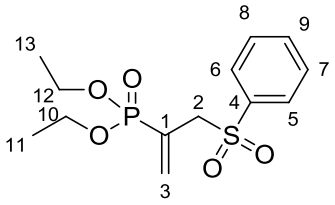
^{13}C NMR (101 MHz, $CDCl_3$) δ 60.0 (C-2), 111.5 (C-1), 116.5 (C-10), 128.9 (C-7, C-8), 129.7 (C-5, C-6), 134.9 (C-9), 137.4 (C-4), 139.7 (C-3).

HRMS (ES+) exact mass calculated for $[M+Na]^+$ ($C_{10}H_9O_2N^{23}Na^{32}S$) requires **m/z** 230.0246, found **m/z** 230.0247.

Diethyl (3-(phenylsulfonyl)prop-1-en-2-yl)phosphonate (**3d**)



A mixture of diethyl (3-bromoprop-1-en-2-yl)phosphonate[7] (1.82 g, 7.0 mmol, 1.0 eq) and sodium benzenesulfinate (1.73 g, 10.5 mmol, 1.5 eq) in methanol (15 ml) was refluxed for 2.5 h. The reaction mixture was diluted with 20 ml of water and extracted with 3x 20 ml ethyl acetate, before being washed with brine and dried over sodium sulfate. After evaporation the organic solvent, the crude was purified by flash column chromatography (Petrol/EtOAc 2:1 to 0:1) to yield 1.98 g (88 % yield) of a yellow oil.



IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 1320 (m, S=O), 1152 (s, S=O/P=O), 1017 (vs, P-O-C).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.23 (t, *J* = 7.1 Hz, 6H, H-13, H-11), 3.69 – 4.22 (m, 6H, H-2, H-12, H-10), 6.31 (d, *J* = 45.6 Hz, 1H, H-3cis), 6.40 (d, *J* = 22.2 Hz, 1H, H-3trans), 7.49 – 7.58 (m, 2H, H-7, H-8), 7.61 – 7.69 (m, 1H, H-9), 7.79 – 7.92 (m, 2H, H-5, H-6).

^{13}C NMR (101 MHz, $CDCl_3$) δ 16.3 (C-13), 16.4 (C-11), 56.65 (d, *J* = 12.6 Hz, C-2), 62.48 (d, *J* = 5.6 Hz, C-12, C-10), 127.38 (d, *J* = 185.4 Hz, C-1), 138.10 (d, *J* = 6.6 Hz, C-3), 128.8 (C-5, C-6), 129.3 (C-7, C-8), 134.0 (C-9), 138.8 (C-4).

HRMS (ES+) exact mass calculated for $[M+Na]^+$ ($C_{13}H_{19}O_5{}^{23}NaP^{32}S$) requires **m/z** 341.0583, found **m/z** 341.0580.

6. General protocol for the photoredox reaction

Method A (imine formation *in situ*)

The following procedure for product (**4**) is exemplary for easily formed imines.

A vial was charged with ethyl 2-((phenylsulfonyl)methyl)acrylate (127.2 mg, 0.5 mmol, 2.5 eq), Hantzsch ester (76.0 mg, 0.3 mmol, 1.5 eq), *p*-anisidine (24.6 mg, 0.2 mmol, 1.0 eq), Eosin Y (2.8 mg, 0.004 mmol, 0.02 eq) and benzaldehyde (20.3 µl, 0.2 mmol, 1.0 eq). Degassed DMF (1.0 ml) was added and the solution sparged with N_2 for 10 seconds to replace the atmosphere. The solution was stirred and irradiated (1W, λ_{max}=525 nm) overnight. Upon completion of the reaction (checked by crude NMR, ca. 10 µl of reaction medium + 0.5 ml of $CDCl_3$), it was worked up by diluting with 50 ml of Et_2O, washing with LiCl-solution (5wt%, 3x 20ml) and drying the organic layer over $MgSO_4$. The crude product was purified by flash column chromatography (DCM/Petrol 2:1 w/ 1% Et_2O). Compound (**4**) was obtained as a yellowish oil, 56.7 mg, 87% yield.

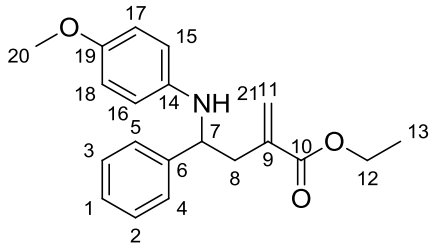
Method B (imine formation *in situ* is slow)

The following procedure for product (**26**) is exemplary for imines which form only slowly under the conditions of Method A.

A vial was charged with ethyl 2-((phenylsulfonyl)methyl)acrylate (127.2 mg, 0.5 mmol, 2.5 eq), Hantzsch ester (76.0 mg, 0.3 mmol, 1.5 eq), (*E*)-N-benzylidene-4-nitroaniline (45.3 mg, 0.2 mmol, 1.0 eq) and Eosin Y (2.8 mg, 0.004 mmol, 0.02 eq). Degassed DMF (1.0 ml) was added and the solution sparged with N_2 for 10 seconds to replace the atmosphere. The solution was stirred and irradiated (1W, λ_{max}=525 nm) overnight. Upon completion of the reaction (checked by crude NMR, ca. 10 µl of reaction medium + 0.5 ml of $CDCl_3$), it was worked up by diluting with 50 ml of Et_2O, washing with LiCl-solution (5wt%, 3x 20ml) and drying the organic layer over $MgSO_4$. The crude product was purified by flash column chromatography (Petrol/Et_2O 4:1 to 0:1). Compound (**33**) was obtained as a yellowish oil, 31.3 mg, 46% yield.

7. Characterization of the products

Ethyl 4-((4-methoxyphenyl)amino)-2-methylene-4-phenylbutanoate (**4a**)



protocol: method A

purification: column chromatography (DCM/Petrol 2:1 w/ 1% Et_2O) afforded 56.7 mg (87% yield) of a pale yellow oil.

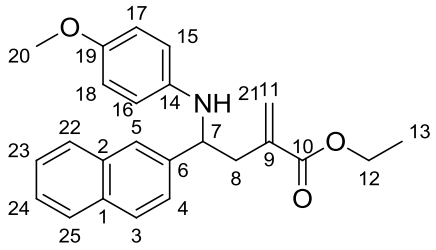
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3397 (br, N-H), 1707 (m, C=O), 1511 (s, C=C), 1238 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.34 (t, *J* = 7.1 Hz, 3H, H-13), 2.69 – 2.85 (m, 2H, H-8), 3.70 (s, 3H, H-20), 4.24 (qd, *J* = 7.2, 1.8 Hz, 2H, H-12), 4.48 (dd, *J* = 8.5, 5.2 Hz, 1H, H-7), 5.57 (q, *J* = 1.2 Hz, 1H, H-11cis), 6.25 (d, *J* = 1.3 Hz, 1H, H-11trans), 6.43 – 6.52 (m, 2H, H-17, H-18), 6.65 – 6.74 (m, 2H, H-15, H-16), 7.18 – 7.28 (m, 1H, H-1), 7.30 – 7.37 (m, 2H, H-2, H-3), 7.37 – 7.44 (m, 2H, H-4, H-5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 41.5 (C-8), 55.8 (C-20), 58.7 (C-7), 61.1 (C-12), 114.5 (C-17, C-18), 114.8 (C-15, C-16), 126.5 (C-4, C-5), 127.1 (C-1), 127.8 (C-11), 128.7 (C-2, C-3), 137.7 (C-9), 141.7 (C-14), 143.8 (C-6), 151.9 (C-19), 167.4 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{20}H_{24}O_3N$) requires **m/z** 326.1751, found **m/z** 326.1750.

Ethyl 4-((4-methoxyphenyl)amino)-2-methylene-4-(naphthalen-2-yl)butanoate (**4b**)



protocol: method A

purification: column chromatography (DCM/Petrol 2:1 w/ 1% Et_2O) afforded 63.8 mg (85% yield) of a pale yellow oil.

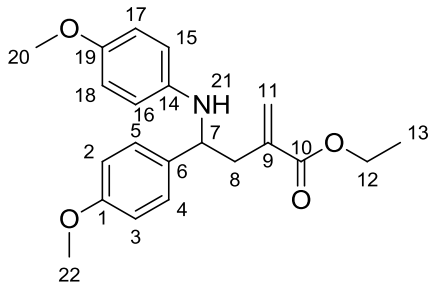
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3393 (br, N-H), 1706 (m, C=O), 1510 (s, C=C), 1236 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.33 (t, *J* = 7.1 Hz, 3H, H-13), 2.82 (ddd, *J* = 14.1, 8.8, 0.8 Hz, 1H, H-8'), 2.90 (ddd, *J* = 14.2, 4.9, 1.1 Hz, 1H, H-8''), 3.68 (s, 3H, H-20), 4.24 (qd, *J* = 7.1, 3.1 Hz, 2H, H-12), 4.64 (dd, *J* = 8.7, 4.9 Hz, 1H, H-7), 5.59 (q, *J* = 1.1 Hz, 1H, H-11cis), 6.25 (d, *J* = 1.3 Hz, 1H, H-11trans), 6.37 – 6.60 (m, 2H, H-17, H-18), 6.63 – 6.82 (m, 2H, H-15, H-16), 7.42 – 7.51 (m, 2H, H-23, 24), 7.55 (dd, *J* = 8.6, 1.7 Hz, 1H, H-4), 7.80 – 7.88 (m, 4H, H-3, H-5, H-22, H-25).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 41.4 (C-8), 55.8 (C-20), 59.0 (C-7), 61.2 (C-12), 114.7 (C-17, C-18), 114.8 (C-15, C-16), 124.8 (C-4), 125.2 (C-5), 125.7 (C-24), 126.1 (C-23), 127.8 (C-3), 127.9 (C-11), 128.0 (C-22), 128.5 (C-25), 133.0 (C-1), 133.6 (C-2), 137.6 (C-9), 141.3 (C-14), 141.7 (C-6), 152.0 (C-19), 167.5 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{24}H_{26}O_3N$) requires **m/z** 376.1907, found **m/z** 376.1904.

Ethyl 4-(4-methoxyphenyl)-4-((4-methoxyphenyl)amino)-2-methylenebutanoate (**4c**)



protocol: method A

purification: column chromatography (Petrol/Et_2O 5:1) afforded 56.1 mg (80% yield) of a pale yellow oil.

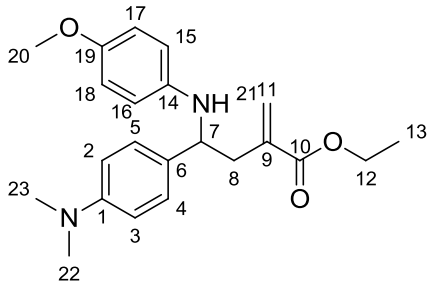
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3393 (br, N-H), 1707 (m, C=O), 1510 (s, C=C), 1238 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.31 (t, *J* = 7.1 Hz, 3H, H-13), 2.68 – 2.76 (m, 2H, H-8), 3.68 (s, 3H, H-20), 3.78 (s, 3H, H-22), 4.15 (s, 1H, H-21), 4.21 (qd, *J* = 7.2, 1.3 Hz, 2H, H-12), 4.40 (dd, *J* = 7.7, 6.0 Hz, 1H, H-7), 5.50 – 5.56 (m, 1H, H-11cis), 6.21 (d, *J* = 1.3 Hz, 1H, H-11trans), 6.41 – 6.49 (m, 2H, H-17, H-18), 6.63 – 6.71 (m, 2H, H-15, H-16), 6.81 – 6.89 (m, 2H, H-2, H-3), 7.24 – 7.31 (m, 2H, H-4, H-5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.4 (C-13), 41.6 (C-8), 55.4 (C-22), 55.9 (C-20), 58.1 (C-7), 61.1 (C-12), 114.1 (C-2, C-3), 114.6 (C-17, C-18), 114.8 (C-15, C-16), 127.6 (C-4, C-5), 127.8 (C-11), 135.8 (C-6), 137.8 (C-9), 141.8 (C-14), 152.0 (C-19), 158.7 (C-1), 167.5 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{21}H_{26}O_4N$) requires **m/z** 356.1856, found **m/z** 356.1855.

Ethyl 4-(4-(dimethylamino)phenyl)-4-((4-methoxyphenyl)amino)-2-methylenebutanoate (**4d**)



protocol: method A

purification: column chromatography (Petrol/Et_2O 4:1 to 1:1) afforded 98.3 mg (97% yield) of an inseparable mixture with Hantzsch ester as a pale yellow oil. An analytically pure sample was obtained by preparative HPLC (Hexane/IPA 97/3).

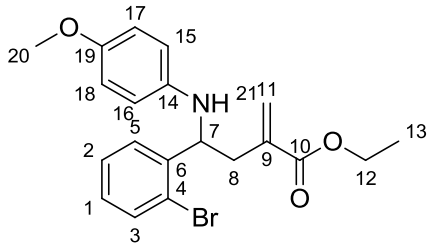
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3391 (br, N-H), 1709 (m, C=O), 1597 (s, C=C), 1512 (s, C=C), 1238 (m, C-O), 1165 (m, N-C).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.31 (t, *J* = 7.1 Hz, 3H, H-13), 2.73 (dd, *J* = 6.9, 1.0 Hz, 2H, H-8), 2.92 (s, 6H, H-22, H-23), 3.69 (s, 3H, H-20), 4.10 (s, 1H, H-21), 4.22 (qd, *J* = 7.1, 1.0 Hz, 2H, H-12), 4.37 (t, *J* = 6.9 Hz, 1H, H-7), 5.54 (q, *J* = 1.1 Hz, 1H, H-11cis), 6.20 (d, *J* = 1.4 Hz, 1H, H-11trans), 6.42 – 6.56 (m, 2H, H-17, H-18), 6.66 – 6.69 (m, 3H, H-15, H-16), 6.69 – 6.73 (m, 2H, H-4, H-5), 7.22 (d, *J* = 8.6 Hz, 2H, H-2, H-3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.4 (C-13), 40.8 (C-22, C-23), 41.4 (C-8), 55.9 (C-20), 58.1 (C-7), 61.1 (C-12), 112.8 (C-4, C-5), 114.6 (C-17, C-18), 114.8 (C-15, C-16), 127.2 (C-2, C-3), 127.6 (C-11), 131.5 (C-6), 138.0 (C-9), 142.0 (C-14), 149.8 (C-1), 151.8 (C-19), 167.6 (C-10).

HRMS (ES+) exact mass calculated for $[M+Na]^+$ ($C_{22}H_{28}O_3N_2{}^{23}Na$) requires **m/z** 391.1992, found **m/z** 391.1992.

Ethyl 4-(2-bromophenyl)-4-((4-methoxyphenyl)amino)-2-methylenebutanoate (**4e**)



protocol: method A

purification: column chromatography (Petrol/DCM 2:1 w/ 1% Et_2O) afforded 59.8 mg (74% yield) of a pale yellow oil.

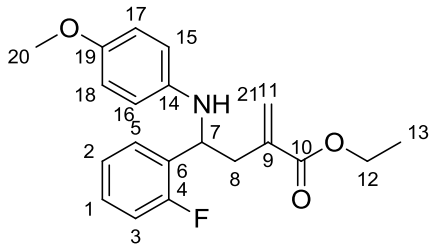
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3392 (br, N-H), 1702 (m, C=O), 1512 (s, C=C), 1238 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.35 (t, *J* = 7.2 Hz, 3H, H-13), 2.70 (dd, *J* = 14.3, 9.2 Hz, 1H, H-8'), 2.81 (ddd, *J* = 14.3, 4.0, 1.1 Hz, 1H, H-8''), 3.69 (s, 3H, H-20), 4.26 (qd, *J* = 7.1, 2.7 Hz, 2H, H-12), 4.68 (s, 1H, H-21), 4.83 (dd, *J* = 9.3, 4.0 Hz, 1H, H-7), 5.73 (d, *J* = 1.2 Hz, 1H, H-11cis), 6.30 (d, *J* = 1.3 Hz, 1H, H-11trans), 6.35 – 6.44 (m, 2H, H-17, H-18), 6.65 – 6.77 (m, 2H, H-15, H-16), 7.11 (td, *J* = 7.6, 1.8 Hz, 1H, H-5), 7.26 (td, *J* = 7.5, 1.4 Hz, 1H, H-2), 7.49 (dd, *J* = 7.8, 1.8 Hz, 1H, H-1), 7.59 (dd, *J* = 7.9, 1.2 Hz, 1H, H-3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 38.4 (C-8), 55.8 (C-20), 58.5 (C-7), 61.3 (C-12), 114.1 (C-17,C-18), 114.8 (C-15,C-16), 123.1 (C-4), 128.0 (C-1, C-2), 128.2 (C-11), 128.7 (C-5), 133.0 (C-3), 137.6 (C-9), 141.1 (C-14), 142.0 (C-6), 151.9 (C-19), 168.0 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{20}H_{23}O_3N^{79}Br$) requires **m/z** 404.0856, found **m/z** 404.0848.

Ethyl 4-(2-fluorophenyl)-4-((4-methoxyphenyl)amino)-2-methylenebutanoate (**4f**)



protocol: method A

purification: column chromatography (Petrol/Et_2O 1:1 to 0:1) afforded 58.4 mg (85% yield) of a pale yellow oil.

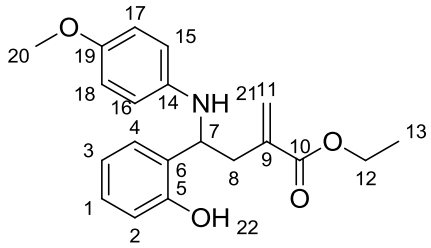
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3393 (br, N-H), 1709 (m, C=O), 1511 (s, C=C), 1237 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.32 (t, *J* = 7.1 Hz, 3H, H-13), 2.64 – 2.97 (m, 2H, H-8), 3.69 (s, 3H, H-20), 4.23 (qd, *J* = 7.1, 1.7 Hz, 2H, H-12), 4.32 (s, 1H, H-21), 4.83 (dd, *J* = 8.2, 5.5 Hz, 1H, H-7), 5.57 (q, *J* = 1.1 Hz, 1H, H-11cis), 6.23 (d, *J* = 1.4 Hz, 1H, H-11trans), 6.40 – 6.54 (m, 2H, H-17, H-18), 6.60 – 6.76 (m, 2H, H-15, H-16), 7.01 – 7.11 (m, 2H, H-2, H-3), 7.16 – 7.24 (m, 1H, H-1), 7.37 (td, *J* = 7.7, 1.9 Hz, 1H, H-5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 39.2 (C-8), 52.9 (C-20), 55.8 (C-7), 61.1 (C-12), 114.4 (C-17, C-18), 114.8 (C-15, C-16), 115.48 (d, *J* = 22.1 Hz, C-3), 124.41 (d, *J* = 3.2 Hz, C-2), δ 128.0 (C-d, *J* = 6.3 Hz, C-5), 128.0 (C-11), 128.6 (C-d, *J* = 8.2 Hz, C-1), 130.10 (d, *J* = 12.8 Hz, C-6), 137.5 (C-9), 141.2 (C-14), 152.1 (C-19), 160.72 (C-d, *J* = 244.8 Hz, C-4), 167.6 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{20}H_{23}O_3NF$) requires **m/z** 344.1657, found **m/z** 344.1658.

Ethyl 4-(2-hydroxyphenyl)-4-((4-methoxyphenyl)amino)-2-methylenebutanoate (**4g**)



protocol: method A

purification: column chromatography (Petrol/Et_2O 3:1 to 2:1) afforded 43.2 mg (64% yield) of a pale yellow oil.

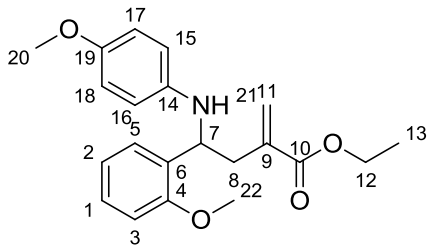
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3331 (br, N-H/O-H), 1708 (m, C=O), 1511 (s, C=C), 1239 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.33 (t, *J* = 7.1 Hz, 3H, H-13), 2.77 – 2.96 (m, 2H, H-8), 3.70 (s, 3H, H-20), 4.25 (qd, *J* = 7.2, 1.2 Hz, 2H, H-12), 4.41 (dd, *J* = 8.5, 5.0 Hz, 1H, H-7), 5.59 (q, *J* = 1.1 Hz, 1H, H-11cis), 6.30 (d, *J* = 1.3 Hz, 1H, H-11trans), 6.71 (m, 4H, H-15, H-16, H-17, H-18), 6.81 (dd, *J* = 8.1, 1.2 Hz, 1H, H-2), 6.86 (td, *J* = 7.4, 1.2 Hz, 1H, H-3), 7.09 (dd, *J* = 7.6, 1.7 Hz, 1H, H-4), 7.16 (ddd, *J* = 8.1, 7.3, 1.7 Hz, 1H, H-1), 10.12 (s, 1H, H-22).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 40.0 (C-8), 55.6 (C-20), 61.4 (C-12), 61.4 (C-7), 114.7 (C-17, C-18), 117.2 (C-2), 118.3 (C-15, C-16), 119.9 (C-3), 125.9 (C-6), 128.1 (C-4), 128.7 (C-1), 129.0 (C-11), 137.0 (C-9), 140.2 (C-14), 154.6 (C-5), 156.9 (C-19), 167.3 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{20}H_{24}O_4N$) requires **m/z** 342.1700, found **m/z** 342.1698.

Ethyl 4-(2-methoxyphenyl)-4-((4-methoxyphenyl)amino)-2-methylenebutanoate (**4h**)



protocol: method A

purification: column chromatography (Petrol/Acetone 19:1) afforded 40.5 mg (57% yield) of a pale yellow oil. Using 10W LEDs a yield of 78% was obtained.

IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3395 (br, N-H), 1713 (m, C=O), 1512 (s, C=C), 1238 (m, C-O).

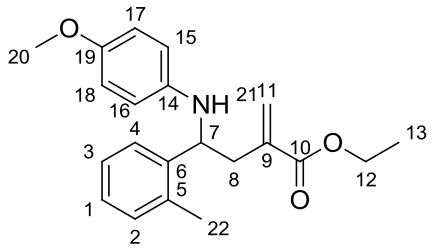
^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.31 (t, *J* = 7.1 Hz, 3H, H-13), 2.69 – 2.76 (m, 1H, H-8'), 2.77 – 2.84 (m, 1H, H-8''), 3.68 (s, 3H, H-20), 3.89 (s, 3H, H-22), 4.21 (q, *J* = 7.1 Hz, 2H, H-12), 4.33 (s, 1H, H-21), 4.83

(dd, *J* = 8.0, 5.6 Hz, 1H, H-7), 5.48 (d, *J* = 1.5 Hz, 1H, H-11cis), 6.15 (d, *J* = 1.5 Hz, 1H, H-11trans), 6.36 – 6.49 (m, 2H, H-17, H-18), 6.66 – 6.70 (m, 2H, H-15, H-16), 6.86 – 6.92 (m, 2H, H-1, H-3), 7.19 (td, *J* = 7.7, 1.7 Hz, 1H, H-2), 7.29 (dd, *J* = 7.7, 1.7 Hz, 1H, H-5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.4 (C-13), 38.6 (C-8), 53.8 (C-7), 55.4 (C-22), 55.9 (C-20), 61.0 (C-12), 110.4 (C-3), 114.4 (C-17, C-18), 114.8 (C-15, C-16), 120.8 (C-1), 127.2 (C-11), 127.4 (C-5), 128.0 (C-2), 130.9 (C-6), 138.2 (C-9), 141.8 (C-14), 151.8 (C-19), 157.0 (C-4), 167.8 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{21}H_{26}O_4N$) requires **m/z** 356.1856, found **m/z** 356.1856.

Ethyl 4-((4-methoxyphenyl)amino)-2-methylene-4-(o-tolyl)butanoate (**4i**)



protocol: method A

purification: column chromatography (Petrol/Et_2O 5:1) afforded 63.6 mg (94% yield) of a pale yellow oil.

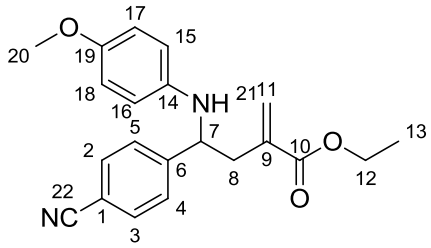
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3399 (br, N-H), 1709 (m, C=O), 1511 (s, C=C), 1237 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.32 (t, *J* = 7.1 Hz, 3H, H-13), 2.50 (s, 3H, H-22), 2.61 (ddd, *J* = 14.3, 9.3, 0.9 Hz, 1H, H-8''), 2.76 (ddd, *J* = 14.4, 4.3, 1.1 Hz, 1H, H-8'), 3.68 (s, 3H, H-20), 4.17 (s, 1H, H-21), 4.23 (qd, *J* = 7.1, 2.7 Hz, 2H, H-12), 4.66 (dd, *J* = 9.3, 4.3 Hz, 1H, H-7), 5.63 (q, *J* = 1.1 Hz, 1H, H-11cis), 6.27 (d, *J* = 1.4 Hz, 1H, H-11trans), 6.35 – 6.42 (m, 2H, H-17, H-18), 6.64 – 6.71 (m, 2H, H-15, H-16), 7.09 – 7.23 (m, 3H, H-1, H-3, H-4), 7.40 – 7.49 (m, 1H, H-2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 19.2 (C-22), 39.8 (C-8), 54.6 (C-7), 55.9 (C-20), 61.2 (C-12), 114.3 (C-15, C-16), 114.9 (C-17, C-18), 125.4 (C-11), 126.6 (C-4), 126.9 (C-3), 127.9 (C-1), 130.7 (C-2), 134.9 (C-5), 137.9 (C-9), 141.5 (C-6), 141.7 (C-14), 151.9 (C-19), 167.4 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{21}H_{26}O_3N$) requires **m/z** 340.1907, found **m/z** 340.1905.

Ethyl 4-(4-cyanophenyl)-4-((4-methoxyphenyl)amino)-2-methylenebutanoate (**4j**)



protocol: method A

purification: column chromatography (Petrol/Et_2O 4:1 to 0:1) afforded 132.1 mg (54% yield by NMR) of an inseperable mixture of product and the reduced imine of the corresponding aldehyde and amine component. An analytically pure sample was obtained by preparative HPLC (Hex/IPA 97/3).

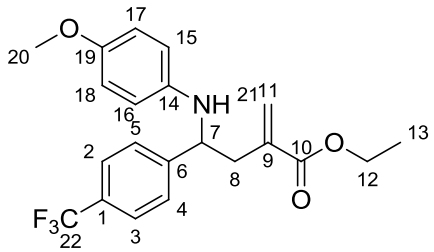
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3392 (br, N-H), 2228 (m, C≡N), 1709 (m, C=O), 1512 (s, C=C), 1238 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.31 (t, *J* = 7.2 Hz, 3H, H-13), 2.65 (ddd, *J* = 14.0, 9.0, 0.8 Hz, 1H, H-8'), 2.78 (ddd, *J* = 14.1, 4.6, 1.1 Hz, 1H, H-8''), 3.68 (s, 3H, H-20), 4.16 – 4.26 (m, 1H, H-12), 4.28 (s, 1H, H-21), 4.49 (dd, *J* = 9.0, 4.6 Hz, 1H, H-7), 5.56 (q, *J* = 1.1 Hz, 1H, H-11cis), 6.25 (d, *J* = 1.1 Hz, 1H, H-11trans), 6.31 – 6.43 (m, 2H, H-17, H-18), 6.59 – 6.82 (m, 2H, H-15, H-16), 7.44 – 7.56 (m, 2H, H-4, H-5), 7.57 – 7.67 (m, 2H, H-2, H-3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 41.3 (C-8), 55.8 (C-20), 58.5 (C-7), 61.4 (C-12), 111.1 (C-1), 114.6 (C-17, C-18), 114.9 (C-15, C-16), 119.0 (C-22), 127.4 (C-4, C-5), 128.4 (C-11), 132.7 (C-2, C-3), 137.0 (C-9), 140.9 (C-14), 149.7 (C-19), 152.4 (C-6), 167.3 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{21}H_{23}O_3N_2$) requires **m/z** 351.1703, found **m/z** 351.1701.

Ethyl 4-((4-methoxyphenyl)amino)-2-methylene-4-(4-(trifluoromethyl)phenyl)butanoate (**4k**)



protocol: method A

purification: column chromatography (DCM/Et_2O 2:1 w/ 1% Et_2O) afforded 64.5 mg (82% yield at 10W) of a pale yellow oil.

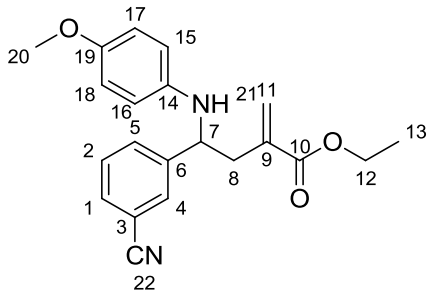
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3393 (br, N-H), 1708 (m, C=O), 1512 (s, C=C), 1239 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.31 (t, *J* = 7.1 Hz, 3H, H-13), 2.69 (ddd, *J* = 14.1, 8.9, 0.8 Hz, 1H, H-8'), 2.80 (ddd, *J* = 14.1, 4.7, 1.1 Hz, 1H, H-8''), 3.69 (s, 3H, H-20), 4.22 (qd, *J* = 7.1, 2.4 Hz, 2H, H-12), 4.27 (s, 1H, H-21), 4.51 (dd, *J* = 8.9, 4.7 Hz, 1H, H-7), 5.57 (q, *J* = 1.1 Hz, 1H, H-11cis), 6.26 (d, *J* = 1.2 Hz, 1H, H-11trans), 6.34 – 6.48 (m, 2H, H-17, H-18), 6.61 – 6.72 (m, 2H, H-15, H-16), 7.50 (d, *J* = 8.1 Hz, 2H, H-4, H-5), 7.58 (d, *J* = 8.7 Hz, 2H, H-2, H-3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 41.4 (C-8), 55.8 (C-20), 58.4 (C-7), 61.3 (C-12), 114.6 (C-17, C-18), 114.9 (C-15, C-16), 125.7 (q, *J* = 272.0 Hz, C-22), 125.7 (q, *J* = 3.7 Hz, C-2, C-3), 126.9 (C-4, C-5), 128.3 (C-11), 129.46 (q, *J* = 32.0 Hz, C-1), 137.2 (C-9), 141.2 (C-14), 148.1 (C-6), 152.2 (C-19), 167.3 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{21}H_{23}O_3NF_3$) requires **m/z** 394.1625, found **m/z** 394.1617.

Ethyl 4-(3-cyanophenyl)-4-((4-methoxyphenyl)amino)-2-methylenebutanoate (**4l**)



protocol: method A

purification: column chromatography (Petrol/Et_2O 3:1 to 1:1) afforded 59.6 mg (85% yield) of a pale yellow oil.

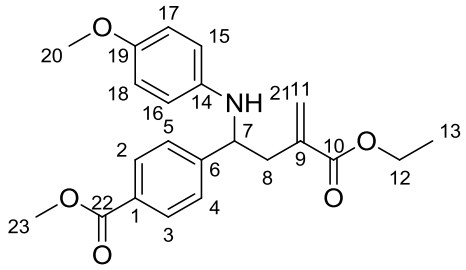
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3391 (br, N-H), 2229 (m, C≡N), 1707 (m, C=O), 1511 (s, C=C), 1238 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.32 (t, *J* = 7.1 Hz, 3H, H-13), 2.67 (ddd, *J* = 14.1, 8.9, 0.8 Hz, 1H, H-8'), 2.78 (ddd, *J* = 14.1, 4.7, 1.1 Hz, 1H, H-8''), 3.68 (s, 3H, H-20), 4.23 (qd, *J* = 7.1, 2.3 Hz, 2H, H-12), 4.30 (s, 1H, H-21), 4.48 (dd, *J* = 8.9, 4.7 Hz, 1H, H-7), 5.57 (q, *J* = 1.1 Hz, 1H, H-11cis), 6.26 (d, *J* = 1.2 Hz, 1H, H-11trans), 6.33 – 6.48 (m, 2H, H-17, H-18), 6.62 – 6.84 (m, 2H, H-15, H-16), 7.43 (td, *J* = 7.7, 0.5 Hz, 1H, H-2), 7.53 (dt, *J* = 7.7, 1.4 Hz, 1H, H-5), 7.63 (dt, *J* = 7.9, 1.6 Hz, 1H, H-1), 7.69 (t, *J* = 1.7 Hz, 1H, H-4).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 41.3 (C-8), 55.8 (C-20), 58.1 (C-7), 61.3 (C-12), 112.7 (C-3), 114.6 (C-17, C-18), 114.9 (C-15, C-16), 119.0 (C-22), 128.4 (C-11), 129.5 (C-2), 130.2 (C-4), 131.0 (C-5), 131.1 (C-1), 136.9 (C-9), 140.9 (C-14), 145.6 (C-6), 152.3 (C-19), 167.2 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{21}H_{23}O_3N_2$) requires **m/z** 351.1703, found **m/z** 351.1702.

Methyl 4-(3-(ethoxycarbonyl)-1-((4-methoxyphenyl)amino)but-3-en-1-yl)benzoate (**4m**)



protocol: method A

purification: column chromatography (Petrol/Et_2O 5:1 to 2:1) afforded 48.3 mg (63% yield) of a white solid. Using 10W LEDs a yield of 78% was obtained.

m p: 95-97 °C

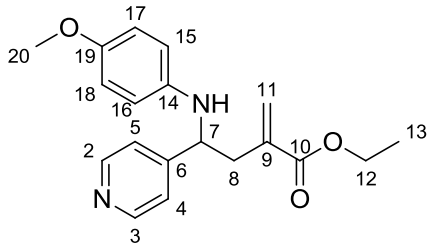
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3392 (br, N-H), 1718 (m, C=O), 1512 (s, C=C), 1279 (m, C_{23}-O), 1238 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.31 (t, *J* = 7.1 Hz, 3H, H-13), 2.70 (ddd, *J* = 14.1, 8.8, 0.9 Hz, 1H, H-8'), 2.79 (ddd, *J* = 14.1, 4.8, 1.0 Hz, 1H, H-8''), 3.67 (s, 3H, H-20), 3.90 (s, 3H, H-23), 4.22 (m, *J* = 7.1, 2.3 Hz, 3H, H-21, H-12), 4.50 (dd, *J* = 8.7, 4.8 Hz, 1H, H-7), 5.54 (q, *J* = 1.1 Hz, 1H, H-11cis), 6.23 (d, *J* = 1.2 Hz, 1H, H-11trans), 6.32 – 6.49 (m, 2H, H-17, H-18), 6.61 – 6.75 (m, 2H, H-15, H-16), 7.37 – 7.57 (m, 2H, H-4, H-5), 7.88 – 8.07 (m, 2H, H-2, H-3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 41.3 (C-8), 52.2 (C-23), 55.8 (C-20), 58.6 (C-7), 61.3 (C-12), 114.6 (C-17, C-18), 114.8 (C-15, C-16), 126.6 (C-4, C-5), 128.2 (C-11), 129.2 (C-1), 130.1 (C-2, C-3), 137.2 (C-9), 141.3 (C-14), 149.3 (C-6), 152.2 (C-19), 167.1 (C-22), 167.4 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{22}H_{26}O_5N$) requires **m/z** 384.1806, found **m/z** 384.1807.

Ethyl 4-((4-methoxyphenyl)amino)-2-methylene-4-(pyridin-4-yl)butanoate (**4n**)



protocol: method A

purification: column chromatography (Petrol/Et_2O 2:1 to 0:1, then ethyl acetate) afforded 44.2 mg (65% yield) of a pale yellow oil.

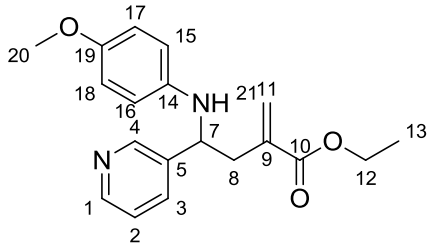
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3392 (br, N-H), 2923 (m, C-$H_{pyridine}$) 1713 (m, C=O), 1512 (s, C=C), 1240 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.31 (t, *J* = 7.1 Hz, 3H, H-13), 2.66 (dd, *J* = 14.1, 8.9 Hz, 1H, H-8), 2.79 (ddd, *J* = 14.1, 4.6, 1.1 Hz, 1H, H-8), 3.67 (s, 3H, H-20), 4.22 (dd, *J* = 7.1, 2.6 Hz, 1H, H-12), 4.44 (dd, *J* = 8.9, 4.6 Hz, 1H, H-7), 5.56 (d, *J* = 1.2 Hz, 1H, H-11cis), 6.25 (d, *J* = 1.1 Hz, 1H, H-11trans), 6.32 – 6.43 (m, 2H, H-17, H-18), 6.58 – 6.74 (m, 2H, H-15, H-16), 7.27 – 7.37 (m, 2H, H-4, H-5), 8.32 – 8.58 (m, 2H, H-2, H-3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 40.8 (C-8), 55.8 (C-20), 57.9 (C-7), 61.3 (C-12), 114.6 (C-17, C-18), 114.9 (C-15, C-16), 121.9 (C-4, C-5), 128.4 (C-11), 136.9 (C-9), 140.9 (C-14), 150.0 (C-2, C-3), 152.3 (C-19), 153.2 (C-6), 167.2 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{19}H_{23}O_3N_2$) requires **m/z** 327.1703, found **m/z** 327.1700.

Ethyl 4-((4-methoxyphenyl)amino)-2-methylene-4-(pyridin-3-yl)butanoate (**4o**)



protocol: method A

purification: column chromatography (Petrol/Et_2O 1:1 to 0:1) afforded 54.1 mg (83% yield) of a pale yellow oil.

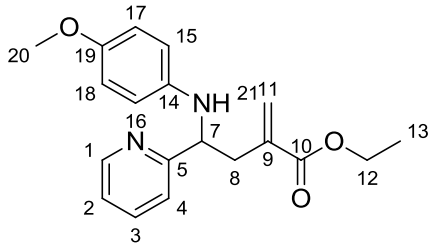
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3389 (br, N-H), 1708 (m, C=O), 1512 (s, C=C), 1238 (m, C-O).

^{1}H NMR (400 MHz, CDCl3-*d*) δ 1.30 (t, *J* = 7.1 Hz, 3H, H-13), 2.59 – 2.89 (m, 2H, H-8), 3.66 (s, 3H, H-20), 4.21 (qd, *J* = 7.1, 1.9 Hz, 2H, H-12), 4.32 (s, 1H, H-21), 4.51 (dd, *J* = 8.3, 5.4 Hz, 1H, H-7), 5.55 (q, *J* = 1.1 Hz, 1H, H-11cis), 6.24 (d, *J* = 1.2 Hz, 1H, H-11trans), 6.37 – 6.49 (m, 2H, H-17, H-18), 6.55 – 6.76 (m, 2H, H-15, H-16), 7.22 (dd, *J* = 7.9, 4.8 Hz, 1H, H-2), 7.68 (dt, *J* = 7.8, 2.0 Hz, 1H, H-3), 8.44 – 8.54 (m, 1H, H-1), 8.63 (s, 1H, H-4).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 41.2 (C-8), 55.8 (C-20), 56.5 (C-7), 61.2 (C-12), 114.7 (C-17, C-18), 114.8 (C-15, C-16), 123.7 (C-2), 128.4 (C-11), 134.1 (C-3), 137.0 (C-9), 139.0 (C-5), 141.0 (C-14), 148.7 (C-1), 148.8 (C-4), 152.2 (C-19), 167.2 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{19}H_{23}O_3N_2$) requires **m/z** 327.1703, found **m/z** 327.1700.

Ethyl 4-((4-methoxyphenyl)amino)-2-methylene-4-(pyridin-2-yl)butanoate (**4p**)



protocol: method A

purification: column chromatography (Petrol/Et_2O 1:1 to 0:1) afforded 34.6 mg (53% yield) of a pale yellow oil.

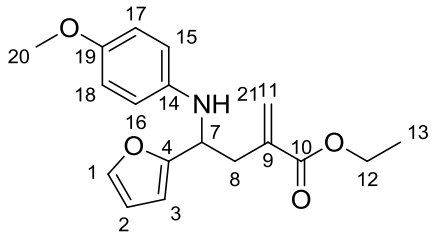
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3392 (br, N-H), 1709 (m, C=O), 1512 (s, C=C), 1238 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.31 (t, *J* = 7.1 Hz, 3H, H-13), 2.81 (ddd, *J* = 13.9, 5.8, 1.0 Hz, 1H, H-8'), 2.89 (ddd, *J* = 13.9, 7.8, 0.9 Hz, 1H, H-8''), 3.69 (s, 3H, H-20), 4.21 (q, *J* = 7.1 Hz, 2H, H-12), 4.62 (dd, *J* = 7.8, 5.8 Hz, 1H, H-7), 5.50 (d, *J* = 1.3 Hz, 1H, H-11cis), 6.17 (d, *J* = 1.3 Hz, 1H, H-11trans), 6.50 – 6.61 (m, 2H, H-17, H-18), 6.56 – 6.80 (m, 2H, H-15, H-16), 7.14 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H, H-2), 7.28 (dt, *J* = 7.9, 1.1 Hz, 1H, H-4), 7.59 (td, *J* = 7.7, 1.8 Hz, 1H, H-3), 8.59 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H, H-1).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.4 (C-13), 39.1 (C-8), 55.9 (C-20), 60.1 (C-7), 61.1 (C-12), 114.7 (C-17, C-18), 114.9 (C-15, C-16), 121.8 (C-4), 122.3 (C-2), 128.2 (C-11), 136.7 (C-3), 137.4 (C-9), 141.4 (C-14), 149.5 (C-1), 152.1 (C-19), 162.2 (C-5), 167.7 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{19}H_{23}O_3N_2$) requires **m/z** 327.1703, found **m/z** 327.1695.

Ethyl 4-(furan-2-yl)-4-((4-methoxyphenyl)amino)-2-methylenebutanoate (**4q**)



protocol: method A

purification: column chromatography (Petrol/EtOAc 3:1 to 1:1) afforded 53.0 mg (84% yield) of a pale yellow oil.

IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3391 (br, N-H), 1709 (m, C=O), 1512 (s, C=C), 1238 (m, C-O).

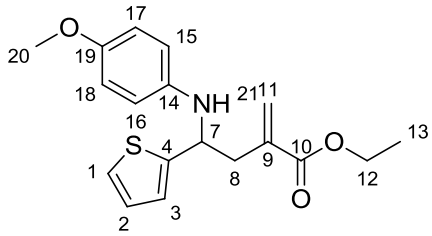
^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.30 (t, *J* = 7.2 Hz, 3H, H-13), 2.82 (ddd, *J* = 13.8, 6.5, 1.0 Hz, 1H, H-8'), 2.92 (ddd, *J* = 13.9, 7.5, 1.0 Hz, 1H, H-8''), 3.72 (s, 3H, H-20), 3.95 (s, 1H, H-21), 4.21 (q, *J* = 7.1 Hz, 2H, H-12), 4.63 (t, *J* = 7.0 Hz, 1H, H-7), 5.52 (q, *J* = 1.2 Hz, 1H, H-11cis), 6.13 (dt, *J* = 3.2, 0.7 Hz, 1H, H-3),

6.19 (d, *J* = 1.4 Hz, 1H, H-11trans), 6.26 (dd, *J* = 3.2, 1.8 Hz, 1H, H-2), 6.53 – 6.64 (m, 2H, H-17, H-18), 6.66 – 6.84 (m, 2H, H-15, H-16), 7.33 (dd, *J* = 1.9, 0.9 Hz, 1H, H-1).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 37.7 (C-8), 52.9 (C-7), 55.9 (C-20), 61.1 (C-12), 106.5 (C-3), 110.2 (C-2), 114.9 (C-17, C-18), 115.0 (C-15, C-16), 127.9 (C-11), 137.1 (C-9), 141.2 (C-1), 141.6 (C-14), 152.4 (C-19), 155.5 (C-4), 167.3 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{18}H_{22}O_4N$) requires **m/z** 316.1543, found **m/z** 316.1540.

Ethyl 4-((4-methoxyphenyl)amino)-2-methylene-4-(thiophen-2-yl)butanoate (**4r**)



protocol: method A

purification: column chromatography (Petrol/DCM 2:1 w/ 1% Et_2O) afforded 57.7 mg (87% yield) of a pale yellow oil.

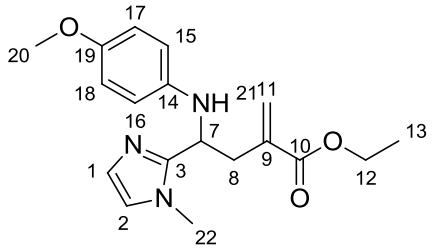
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3385 (br, N-H), 1707 (m, C=O), 1510 (s, C=C), 1237 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.32 (t, *J* = 7.1 Hz, 3H, H-13), 2.71 – 3.04 (m, 2H, H-8), 3.71 (s, 3H, H-20), 4.13 (s, 1H, H-21), 4.23 (q, *J* = 7.1 Hz, 2H, H-12), 4.67 – 4.85 (m, 1H, H-7), 5.58 (q, *J* = 1.2 Hz, 1H, H-11cis), 6.24 (d, *J* = 1.3 Hz, 1H, H-11trans), 6.52 – 6.63 (m, 2H, H-17, H-18), 6.67 – 6.78 (m, 2H, H-15, H-16), 6.91 – 7.00 (m, 2H, H-2, H-3), 7.17 (dd, *J* = 4.9, 1.4 Hz, 1H, H-1).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 41.7 (C-8), 54.9 (C-7), 55.8 (C-20), 61.1 (C-12), 114.8 (C-17, C-18), 114.9 (C-15, C-16), 123.7 (C-2), 123.9 (C-1), 126.8 (C-3), 128.2 (C-11), 137.2 (C-9), 141.3 (C-14), 149.0 (C-4), 152.4 (C-19), 167.3 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{18}H_{22}O_3N^{32}S$) requires **m/z** 332.1315, found **m/z** 332.1306.

Ethyl 4-((4-methoxyphenyl)amino)-4-(1-methyl-1H-imidazol-2-yl)-2-methylenebutanoate (**4s**)



protocol: method A

purification: column chromatography (Et_2O to EtOAc) afforded 52.0 mg (79% yield) of a pale yellow oil.

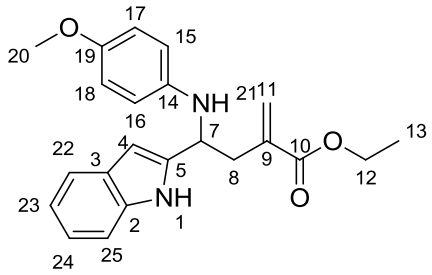
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3353 (br, N-H), 1706 (m, C=O), 1511 (s, C=C), 1236 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.30 (t, *J* = 7.1 Hz, 3H, H-13), 2.79 (ddd, *J* = 13.4, 7.0, 0.9 Hz, 1H, H-8'), 3.01 (ddd, *J* = 13.4, 6.7, 0.8 Hz, 1H, H-8''), 3.57 (s, 3H, H-22), 3.70 (s, 3H, H-20), 4.19 (m, *J* = 7.1 Hz, 3H, H-21, H-12), 4.81 (q, *J* = 7.2 Hz, 1H, H-7), 5.53 (d, *J* = 1.4 Hz, 1H, H-11cis), 6.15 (d, *J* = 1.5 Hz, 1H, H-11trans), 6.58 – 6.67 (m, 2H, H-15, H-16), 6.68 – 6.77 (m, 3H, H-2, H-17, H-18), 6.93 (d, *J* = 1.1 Hz, 1H, H-1).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 32.7 (C-22), 37.8 (C-8), 50.8 (C-7), 55.8 (C-20), 61.0 (C-12), 114.9 (C-15, C-16), 115.3 (C-17, C-18), 120.8 (C-2), 127.4 (C-1), 129.0 (C-11), 136.4 (C-9), 141.0 (C-14), 148.5 (C-3), 152.5 (C-19), 167.3 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{18}H_{24}O_3N_3$) requires **m/z** 330.1812, found **m/z** 330.1809.

Ethyl 4-(1*H*-indol-2-yl)-4-((4-methoxyphenyl)amino)-2-methylenebutanoate (**4t**)



protocol: method B, imine prepared according to literature method[10]

purification: column chromatography (Petrol/Et_2O 2:1 to 0:1) afforded 77.6 mg (52% yield) of a mixture with unreacted starting material as a pale yellow oil. An analytically pure sample was obtained by preparative HPLC (Hex/IPA 95/5).

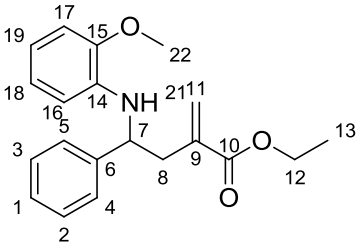
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3405 (br, N-H), 1704 (m, C=O), 1511 (s, C=C), 1238 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.30 (t, *J* = 7.1 Hz, 3H, H-13), 2.86 (ddd, *J* = 14.1, 8.2, 0.9 Hz, 1H, H-8'), 3.07 (ddd, *J* = 14.2, 5.3, 1.1 Hz, 1H, H-8''), 3.69 (s, 3H, H-20), 4.14 (s, 1H, H-21), 4.21 (qd, *J* = 7.2, H-3.3 Hz, 2H, H-12), 4.83 (ddd, *J* = 8.2, 5.3, 0.8 Hz, 1H, H-7), 5.56 (q, *J* = 1.1 Hz, 1H, H-11cis), 6.21 (d, *J* = 1.5 Hz, 1H, H-11trans), 6.48 – 6.63 (m, 2H, H-17, H-18), 6.64 – 6.79 (m, 2H, H-15, H-16), 7.07 (dd, *J* = 2.4, 0.8 Hz, 1H, H-4), 7.16 (ddd, *J* = 8.0, 7.1, 1.1 Hz, 1H, H-24), 7.22 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H, H-23), 7.37 (dt, *J* = 8.1, 1.0 Hz, 1H, H-22), 7.79 (ddt, *J* = 7.8, 1.5, 0.8 Hz, 1H, H-25), 7.98 (s, 1H, H-1).

^{13}C NMR (126 MHz, $CDCl_3$) δ 14.3 (C-13), 39.6 (C-8), 52.0 (C-7), 55.9 (C-20), 61.1 (C-12), 111.5 (C-22), 114.7 (C-17, C-18), 114.8 (C-15, C-16), 118.4 (C-5), 119.3 (C-25), 119.7 (C-24), 122.1 (C-4), 122.3 (C-23), 126.0 (C-3), 127.7 (C-11), 136.9 (C-2), 138.1 (C-9), 142.1 (C-14), 152.0 (C-19), 167.6 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{22}H_{25}O_3N_2$) requires **m/z** 365.1860, found **m/z** 365.1859.

Ethyl 4-((2-methoxyphenyl)amino)-2-methylene-4-phenylbutanoate (**5a**)



protocol: method B, imine prepared according to literature method[11]

purification: column chromatography (DCM/Petrol 2:1 w/ 1% Et_2O) afforded 65.1 mg (quantitative yield) of a yellowish oil.

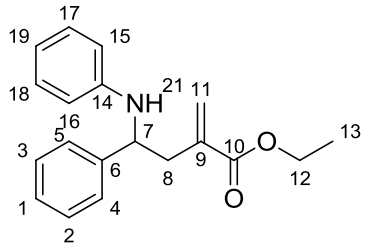
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3417 (br, N-H), 1710 (m, C=O), 1602 (s, C=C), 1512 (s, C=C), 1224 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.33 (t, *J* = 7.1 Hz, 3H, H-13), 2.80 – 2.85 (m, 2H, H-8), 3.88 (s, 3H, H-22), 4.23 (qt, *J* = 7.1, 3.7 Hz, 2H, H-12), 4.46 – 4.62 (m, 1H, H-7), 4.90 (s, 1H, H-21), 5.57 (q, *J* = 1.1 Hz, 1H, H-11cis), 6.24 (d, *J* = 1.3 Hz, 1H, H-11trans), 6.35 (dd, *J* = 7.8, 1.6 Hz, 1H, H-17), 6.60 (td, *J* = 7.6, 1.6 Hz, 1H, H-18), 6.69 (td, *J* = 7.6, 1.5 Hz, 1H, H-19), 6.76 (dd, *J* = 7.8, 1.5 Hz, 1H, H-16), 7.20 – 7.26 (m, 1H, H-1), 7.29 – 7.35 (m, 2H, H-4, H-5), 7.36 – 7.42 (m, 2H, H-2, H-3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 41.4 (C-8), 55.6 (C-22), 57.6 (C-7), 61.1 (C-12), 109.4 (C-16), 111.1 (C-17), 116.4 (C-18), 121.2 (C-19), 126.5 (C-2, C-3), 127.1 (C-1), 127.8 (C-11), 128.7 (C-4, C-5), 137.3 (C-6), 137.6 (C-9), 143.7 (C-14), 146.9 (C-15), 167.2 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{20}H_{24}O_3N$) requires **m/z** 326.1751, found **m/z** 326.1748.

Ethyl 2-methylene-4-phenyl-4-(phenylamino)butanoate (**5b**)



protocol: method A

purification: column chromatography (DCM/Petrol 2:1) afforded 50.2 mg (86% yield) of a pale yellow oil.

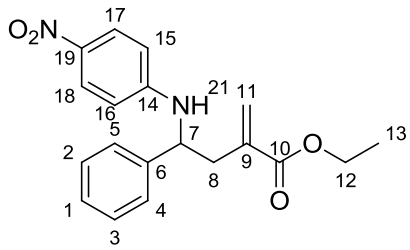
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3401 (br, N-H), 1709 (m, C=O), 1602 (s, C=C), 1504 (s, C=C), 1269 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.32 (t, *J* = 7.1 Hz, 3H, H-13), 2.57 – 2.91 (m, 2H, H-8), 4.22 (qd, *J* = 7.1, 1.8 Hz, 2H, H-12), 4.51 (m, 2H, H-7, H-21), 5.56 (d, *J* = 1.2 Hz, 1H, H-11cis), 6.23 (d, *J* = 1.3 Hz, 1H, H-11trans), 6.44 – 6.51 (m, 2H, H-15, H-16), 6.62 (tt, *J* = 7.3, 1.1 Hz, 1H, H-19), 7.02 – 7.10 (m, 2H, H-17, H-18), 7.19 – 7.25 (m, 1H, H-1), 7.29 – 7.35 (m, 2H, H-4, H-5), 7.35 – 7.40 (m, 2H, H-2, H-3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 41.4 (C-8), 58.2 (C-7), 61.2 (C-12), 113.4 (C-15, C-16), 117.3 (C-19), 126.5 (C-2, C-3), 127.2 (C-1), 128.0 (C-11), 128.8 (C-4, C-5), 129.2 (C-17, C-18), 137.7 (C-9), 143.6 (C-14), 147.4 (C-6), 167.6 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{19}H_{22}O_2N$) requires **m/z** 296.1645, found **m/z** 296.1646.

ethyl 2-methylene-4-((4-nitrophenyl)amino)-4-phenylbutanoate (**5c**)



protocol: method B, imine prepared according to literature method[12]

purification: column chromatography (Petrol/Et_2O 4:1 to 0:1) afforded 31.3 mg (46% yield) of a yellowish oil.

IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3368 (br, N-H), 1708 (m, C=O), 1600 (s, C=C), 1307 (s, N=O), 1283 (m, C-O).

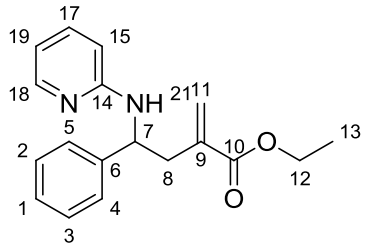
^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.34 (t, *J* = 7.1 Hz, 3H, H-13), 2.72 – 2.88 (m, 2H, H-8), 4.27 (qd, *J* = 7.2, 1.0 Hz, 2H, H-12), 4.60 (td, *J* = 6.7, 5.3 Hz, 1H, H-7), 5.58 (d, *J* = 1.1 Hz, 1H, H-11cis), 5.87 (d, *J* = 5.2

Hz, 1H, H-21), 6.25 (d, *J* = 1.1 Hz, 1H, H-11trans), 6.38 – 6.59 (m, 2H, H-15, H-16), 7.22 – 7.39 (m, 5H, H-2, H-1, H-3, H-4, H-5), 7.82 – 8.10 (m, 2H, H-17, H-18).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 40.9 (C-8), 58.7 (C-7), 61.6 (C-12), 112.0 (C-15, C-16), 126.3 (C-17, C-18), 126.3 (C-4, C-5), 127.9 (C-1), 129.1 (C-2, C-3), 129.1 (C-11), 136.8 (C-19), 138.1 (C-9), 141.5 (C-6), 152.6 (C-14), 168.2 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{19}H_{21}O_4N_2$) requires **m/z** 341.1496, found **m/z** 341.1497.

Ethyl 2-methylene-4-phenyl-4-(pyridin-2-ylamino)butanoate (**5d**)



protocol: method B, imine prepared according to literature method[13]

purification: column chromatography (Petrol/Et_2O 1:1 to 0:1) afforded 81.7 mg (93% yield) of an inseparable mixture of product and Hantzsch ester as a yellowish oil. An analytically pure sample was obtained by preparative HPLC (Hex/IPA 97/3).

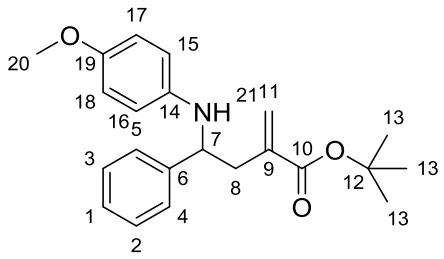
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3390 and 3254 (br, N-H), 1710 (m, C=O), 1600 (s, C=C), 1512 (s, C=C).

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 1.30 (t, *J* = 7.1 Hz, 3H, H-13), 2.75 (ddd, *J* = 14.1, 8.9, 0.9 Hz, 1H, H-8'), 2.84 (ddd, *J* = 14.1, 5.2, 1.2 Hz, 1H, H-8''), 4.21 (qd, *J* = 7.1, 2.3 Hz, 2H, H-12), 4.80 (dt, *J* = 9.0, 5.6 Hz, 1H, H-7), 5.24 (d, *J* = 6.1 Hz, 1H, H-21), 5.58 (q, *J* = 1.1 Hz, 1H, H-11cis), 6.15 – 6.25 (m, 2H, H-15, H-11trans), 6.52 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1H, H-19), 7.18 – 7.30 (m, 2H, H-1, H-17), 7.28 – 7.35 (m, 3H, H-4, H-5), 7.34 – 7.43 (m, 2H, H-2, H-3), 8.04 (ddd, *J* = 5.0, 2.0, 0.9 Hz, 1H, H-18).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 41.2 (C-8), 56.1 (C-7), 61.2 (C-12), 106.8 (C-15), 113.3 (C-19), 126.4 (C-2, C-3), 127.3 (C-1), 128.2 (C-11), 128.7 (C-4, C-5), 137.2 (C-9), 137.5 (C-17), 143.0 (C-6), 148.4 (C-18), 158.1 (C-14), 167.3 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{18}H_{21}O_2N_2$) requires **m/z** 297.1598, found **m/z** 297.1595.

Tert-butyl 4-((4-methoxyphenyl)amino)-2-methylene-4-phenylbutanoate (**5e**)



protocol: method A

purification: column chromatography (DCM/Petrol 2:1 w/ 1% Et_2O) afforded 58.0 mg (82% yield) of a pale yellow oil.

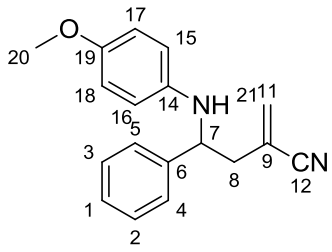
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3398 (br, N-H), 1705 (m, C=O), 1513 (s, C=C), 1239 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.51 (s, 9H, H-13), 2.70 (m, 2H, H-8), 3.68 (s, 3H), 4.28 (br s, NH), 4.42 (dd, *J* = 8.5, 5.4 Hz, 2H, H-7), 5.50 (d, *J* = 1.3 Hz, 1H, H-11cis), 6.14 (d, *J* = 1.4 Hz, 1H, H-11trans), 6.43 (d, *J* = 8.9 Hz, 2H, H-15,H-16), 6.67 (d, *J* = 9.0 Hz, 2H, H-17, H-18), 7,22 (t, *J* = 7.2 Hz, 1H, H-1), 7.31 (t, *J* = 7.5 Hz, 2H, H-2, H-3), 7.37 (d, *J* = 7.1 Hz, 2H, H-4, H-5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 28.2 (C-13), 41.5 (C-8), 55.9 (C-20), 59.1 (C-7), 81.3 (C-12), 114.5 (C-17, C-18), 114.8 (C-15, C-16), 126.5 (C-4, C-5), 127.0 (C-11), 127.1 (C-1), 128.7 (C-2, C-3), 139.2 (C-9), 141.9 (C-14), 144.0 (C-6), 151.9 (C-19), 166.9 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{22}H_{27}O_3N$) requires **m/z** 354.2064, found **m/z** 354.2061.

4-((4-Methoxyphenyl)amino)-2-methylene-4-phenylbutanenitrile (**5f**)



protocol: method A

purification: column chromatography (DCM/Petrol 2:1 w/ 1% Et_2O) afforded 26.1 mg (47% yield) of a yellowish oil.

IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3387 (br, N-H), 2222 (m, C≡N), 1511 (s, C=C), 1238 (m, C-O).

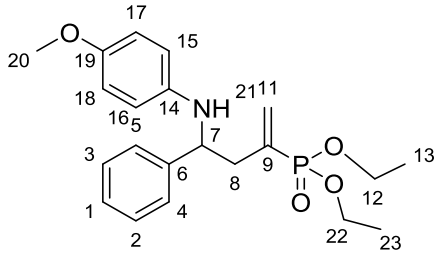
^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 2.66 – 2.74 (m, 2H, H-8), 3.70 (s, 3H, H-20), 3.78 (s, 1H, H-21), 4.57 (dd, *J* = 7.7, 6.6 Hz, 1H, H-7), 5.62 – 5.72 (m, 1H, H-11cis), 5.91 (d, *J* = 0.6 Hz, 1H, H-11trans), 6.48 – 6.55

(m, 2H, H-17, H-18), 6.66 – 6.75 (m, 2H, H-15, H-16), 7.26 (s, 1H, H-1), 7.31 – 7.38 (m, 4H, H-2, H-3, H-4, H-5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 43.5 (C-8), 55.8 (C-20), 57.5 (C-7), 114.9 (C-15, C-16), 115.3 (C-17, C-18), 118.4 (C-12), 120.0 (C-9), 126.5 (C-4, C-5), 127.8 (C-1), 129.0 (C-2, C-3), 133.2 (C-11), 140.7 (C-14), 142.0 (C-6), 152.6 (C-19).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{18}H_{19}ON_2$) requires **m/z** 279.1492, found **m/z** 279.1491.

Diethyl (4-((4-methoxyphenyl)amino)-4-phenylbut-1-en-2-yl)phosphonate (**5g**)



protocol: method A

purification: column chromatography (DCM/Petrol 2:1 w/ 1% Et_2O) afforded 38.2 mg (49% yield) of a pale yellow oil.

IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3331 (br, N-H), 1513 (s, C=C), 1235 (s, P=O), 1025 (s, P-O).

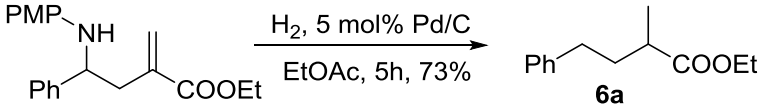
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.26 (t, J = 7.1 Hz, 3H, H-13 or H-23), 1.33 (t, J = 7.1 Hz, 3H, H13 or H-23), 2.59 – 2.79 (m, 2H, H-8), 3.68 (s, 3H, H-20), 3.95 – 4.06 (m, 1H, H-12 or H-22), 4.07 – 4.18 (m, 3H, H-12 or H-22), 4.48 (dd, J = 8.8, 4.6 Hz, 1H, H-7), 5.89 (d, J = 164.9 Hz, 1H, H-11), 5.96 (d, J = 139.8 Hz, 1H, H-11), 6.47 (d, J = 8.4 Hz, 2H, H-15, H-16), 6.66 (d, J = 8.9 Hz, 2H, H-17, H-18), 7.23 (t, J = 7.3 Hz, 1H, H-1), 7.32 (t, J = 7.6 Hz, 2H, H-2, H-3), 7.40 (d, J = 7.3 Hz, 2H, H-4, H-5).

^{13}C NMR (126 MHz, $CDCl_3$) δ 16.5 (dd, J = 13.8, 6.3 Hz, C-13, C-23), 41.8 (d, J = 11.7 Hz, C-8), 55.9 (C-20), 58.8 (C-7), 62.4 (dd, J = 22.4, 5.9 Hz, C-12, C-22), 114.8 (C-15, C-16, C-17, C-18), 126.6 (C-1), 127.3 (C-2, C-3), 128.8 (C-4, C-5), 132.3 (d, J = 8.8 Hz, C-11)), 136.3 (d, J = 173.6 Hz, C-9), 141.5 (C-14), 143.5 (C-6), 152.2 (C-19).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{21}H_{28}O_4NP$) requires **m/z** 390.1829, found **m/z** 390.1823.

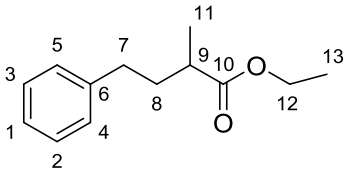
8. Product **4a** derivatization

Ethyl 2-methyl-4-phenylbutanoate (**6a**)



6a

Compound **4a** (64 mg, 0.2 mmol) was dissolved in EtOAc (1 mL) and Pd/C 10 wt% was added (10 mg, 0.01 mmol, 0.05 eq). The reaction mixture was stirred under a balloon of H_2 for 5 h. Then it was filtered through a pad of celite and purified by flash column chromatography affording 30.1 mg (73% yield) of a pale yellow oil.



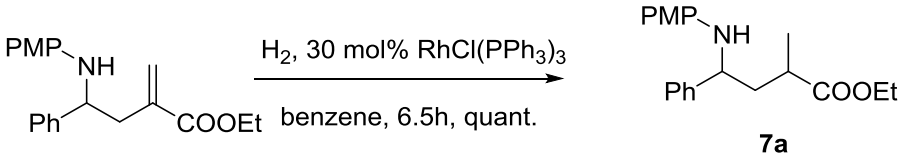
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 2977 (s, C-H), 1732 (m, C=O).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (d, *J* = 7.0 Hz, 3H, H-11), 1.28 (t, *J* = 7.1 Hz, 3H, H-13), 1.65 – 1.79 (m, 1H, H-8), 2.02 (dq, *J* = 13.6, 7.9 Hz, 1H, H-8), 2.47 (h, *J* = 7.0 Hz, 1H, H-9), 2.63 (*t*, J = 8.0 Hz, 2H, H-7), 4.15 (q, *J* = 7.1 Hz, 2H, H-12), 7.15 - 7.32 (m, 5H, H-1 to H-5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.4 (C-13), 17.3 (C-11), 33.6 (C-7), 35.6 (C-8), 39.2 (C-9), 60.3 (C-12), 126.0 (C-1), 128.5 (C-2, C-3), 128.5 (C-4, C5), 141.9 (C-6), 176.7 (C-10).

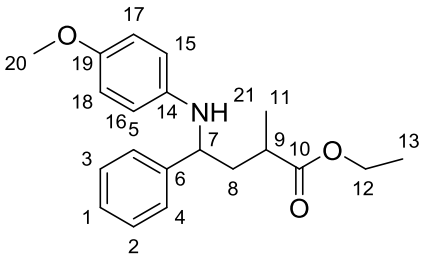
HRMS (ES+) exact mass calculated for $[M+Na]^+$ ($C_{13}H_{18}O_2$) requires **m/z** 229.1199, found **m/z** 229.1202.

Ethyl 4-((4-methoxyphenyl)amino)-2-methyl-4-phenylbutanoate (**7a**)



7a

Compound **4a** (34.8 mg, 0.11 mmol) and $RhCl(PPh_3)_3$ (25.5 mg, 0.028 mmol, 0.27 eq) were dissolved in 1 mL of benzene and stirred under H_2 atmosphere (p=1 bar) for 6.5 h. The crude mixture was filtered through a small pad of silica and the solvent was evaporated to obtain compound **7a** as a 1:1 mixture of diastereomers (pale yellow oil, 35 mg, quantitative).



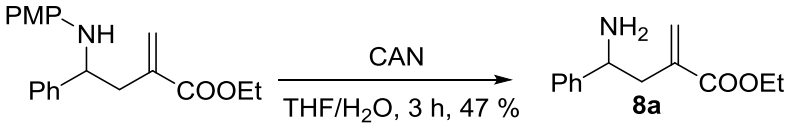
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3396 (br, N-H), 1724 (m, C=O), 1238 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 – 1.28 (m, 6H, H-11, H-13)), 1.76 (dt, *J* = 14.0, 5.7 Hz, 0.5 H, H-8), 1.85 (ddd, *J* = 13.9, 8.3, 5.1 Hz, 0.5H, H-8'), 2.17 – 2.30 (m, 1H, H8), 2.49 – 2.67 (m, 1H, H-9), 3.69 (s, 1H, H-20), 3.91 (br s, NH, H-21), 4.10 (q, *J* = 7.1 Hz, 1H, H12), 4.15 (q, *J* = 7.2 Hz, 1H, H12'),4.31 (dd, *J* = 8.5, 5.9 Hz, 0.5H, H-7), 4.35 (dd, *J* = 8.2, 5.4 Hz, 0.5H, H-7'), 6.47 (dd, *J* = 9.0, 4.8 Hz, 2H, H-15, H-16), 6.68 (dd, *J* = 9.0, 1.3 Hz, 2H, H-17, H-18), 7.17 – 7.38 (m, 5H, H-1 to H-5).

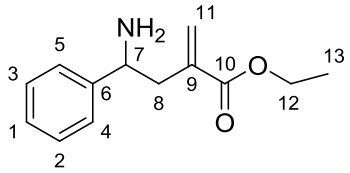
^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 14.4 (C-13'), 17.9 (C-11), 18.1 (C-11'), 36.7 (C-9), 37.7 (C-9'), 42.4 (C-8), 42.7 (C-8'), 55.8 (C-20), 57.2 (C-7), 57.6 (C-7'), 60.6 (C-12), 60.7 (C-12'), 114.5 (C-15 or C-16 or C-17 or C-18) 114. (C-15 or C-16 or C-17 or C-18), 114.8 (C-15 or C-16 or C-17 or C-18), 114.9 (C-15 or C-16 or C-17 or C-18), 126.4 (C-2, C-3 or C-2', C-3'), 126.5 (C-2, C-3 or C-2', C-3'), 127.1 (C-1), 127.2 (C-1'), 128.7 (C-4, C-5), 128.8 (C-4',C-5'), 141.4 (C-14), 141.6 (C-14'), 143.7 (C-6), 144.0 (C-6'), 152.0 (C-19), 152.1 (C-19'), 176.5 (C-10), 176.9 (C-10').

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{20}H_{25}O_3N$) requires **m/z** 328.1907, found **m/z** 328.1902.

<u>Ethyl 4-amino-2-methylene-4-phenylbutanoate (**8a**)</u>



Compound **4a** (80.4 mg, 0.25 mmol) was dissolved in 8 mL of CH_3CN and added dropwise during 10 min to a stirred solution of CAN (360 mg, 0.66 mmol, 2.6 eq) in 8 mL of water at 0 °C. The solution was stirred at room temperature for 3 h and then was basified to pH=12 with 1 M NaOH. Then it was extracted with DCM three times, dried over Na_2SO_4 and evaporated under reduced pressure. The crude compound was purified by flash column chromatography (Et_2O – Et_2O/MeOH 1% - Et_2O – MeOH 10 %), yielding compound **8a** as a pale yellow oil (25.9 mg, 47 % yield).



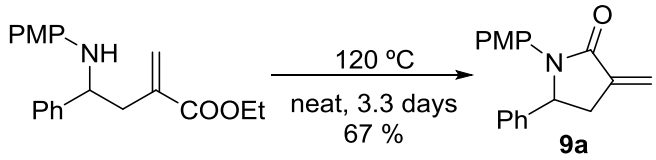
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3373 (br, N-H), 1711 (m, C=O), 1493 (s, C=C), 1182 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (t, *J* = 7.1 Hz, 3H, H-13), 1.49 (s, 2H, NH_2), 2.46 (dd, *J* = 13.3, 8.8 Hz, 1H, H-8), 2.67 (dd, *J* = 13.5, 4.9 Hz, 1H, H-8), 4.09 (dd, *J* = 6.9 Hz, 14.6 Hz, 1H, H-7), 4.13 (q, *J* = 9.2, 8.1 Hz, 2H, H-12), 5.46 (s, 1H, H-11), 6.13 (s, 1H, H-11), 7.10 – 7.32 (m, 5H).

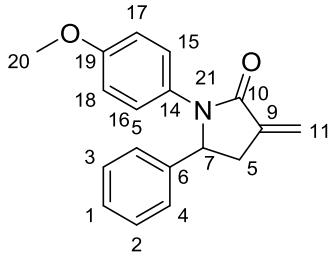
^{13}C NMR (101 MHz, $CDCl_3$) δ 14.4 (C-13), 42.9 (C-8), 54.8 (C-7), 60.9 (C-12), 126.4 (C-2, C-3), 127.2 (C-1), 127.5 (C-11), 128.6 (C-4, C-5), 138.1 (C-9), 145.8 (C-6), 167.2 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{13}H_{17}O_2N$) requires **m/z** 220.1332, found **m/z** 220.1333.

1-(4-Methoxyphenyl)-3-methylene-5-phenylpyrrolidin-2-one (**9a**)



Compound **4a** (neat) was heated at 120 – 130 ° for 3.3 days and purified by flash column chromatography (Petrol/Et_2O 1:1) affording 7.7 mg of product **9a** (67 % yield).



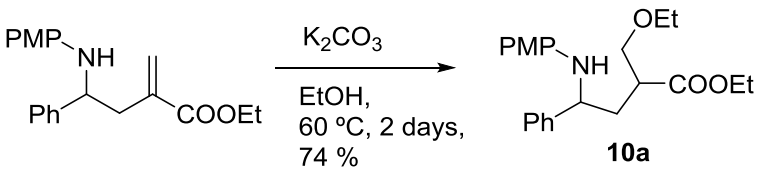
IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 1691 (m, C=O), 1512 (s, C=C), 1178 (m, C-O).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.72 (ddt, *J* = 16.9, 3.5, 2.4 Hz, 1H, H-8), 3.37 (ddt, *J* = 16.9, 8.7, 2.8 Hz, 1H, H-8), 3.73 (s, 3H, H-20), 5.17 (dd, *J* = 8.7, 3.5 Hz, 1H, H-7), 5.44 (t, *J* = 2.3 Hz, 1H, H-11), 6.20 (t, *J* = 2.7 Hz, 1H, H-11), 6.78 (d, *J* = 9.2 Hz, 2H, H-17, H-18), 7.19 (d, *J* = 6.9 Hz, 2H, H-4, H-5), 7.23 (t, *J* = 7.3 Hz, 1H, H-1), 7.29 (t, *J* = 7.2 Hz, 2H, H-2, H-3), 7.36 (d, *J* = 9.2 Hz, 2H, H-15, H-16).

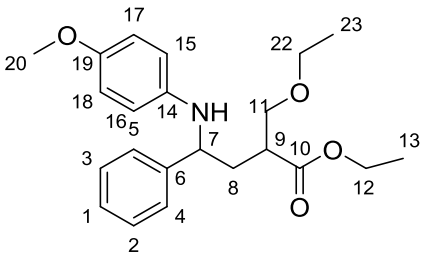
^{13}C NMR (126 MHz, $CDCl_3$) δ 35.5 (C-8), 55.5 (C-20), 61.2 (C-7), 114.1 (C-17, C-18), 117.2 (C-11), 124.1 (C-15, C-16), 126.1 (C-4, C-5), 128.0 (C-1), 129.1 (C-2, C-3), 131.4 (C-14), 139.2 (C-9), 141.8 (C-6), 157.1 (C-19), 167.6 (C-10).

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{18}H_{17}NO_2$) requires **m/z** 280.1332, found **m/z** 280.1332.

Ethyl 2-(ethoxymethyl)-4-((4-methoxyphenyl)amino)-4-phenylbutanoate (**10a**)



Compound **4a** (67.8 mg, 0.21 mmol) was dissolved in 1.4 mL of EtOH and K_2CO_3 (68.2 mg, 0.49 mmol, 2.3 eq) and 10 molecular sieves 3 Å were added. The reaction mixture was heated at 60 ˚C for 2 days under N_2 atmosphere. Then, it was filtered through a short pad of celite and purified by flash column chromatography (Petrol/Et_2O 4:1), affording compound **10a** as a pale yellow oil (45.3 mg, 58% yield, 74 % based on unreacted starting material).



IR (thin film) $\tilde{\nu}_{max}{}^{-1}$ 3383 (br, N-H), 1726 (m, C=O), 1513 (s, C=C), 1237 (m, C-O).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (t, *J* = 7.0 Hz, 3H, H-23), 1.21 (t, *J* = 6.9 Hz, 3H, H-13), 1.25 (t, *J* = 7.0 Hz, 3H, H-13'), 1.91 – 2.03 (m, 1H, H-8), 2.17 – 2.29 (m, 1H, H-8'), 2.70 – 2.79 (m, 1H, H-9), 2.83 – 2.92 (m, 1H, H-9'), 3.39 – 3.55 (m, 1H, H-11), 3.58 – 3.68 (m, 1H, H-11'), 3.69 (s, 3H, H-20), 3.49 (q, *J* = 7Hz, 2H, H-22), 4.02 – 4.24 (m, 2H, H-12, H-12'), 4.07 (br s, NH), 4.30 – 4.38 (m, 1H, H-7, H-7'), 6.47 (dd, *J* = 9.0, 3.3 Hz, 2H, H-15, H-16), 6.69 (d, *J* = 8.9 Hz, 2H, H-17, H-18), 7.17 – 7.39 (m, 5H, H-1 to H-5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (C-13), 14.3 (C-13'), 15.1 (C-23), 15.2 (C-23'), 37.6 (C-8), 37.9 (C-8'), 43.4 (C-7), 44.0 (C-7'), 55.8 (C-20), 57.4 (C-7), 57.8 (C-7'), 60.8 (C-12), 60.8 (C-12), 66.6 (C-11), 66.7 (C-11'), 71.2 (C-22), 71.4 (C-22'), 114.5 (C-15, C-16), 114.6 (C-15', C-16'), 114.8 (C-17, C-18), 126.4 (C-2, C-3), 126.5 (C-2', C-3'), 127.1 (C-1), 127.2 (C-1)', 128.7 (C-4, C-5), 128.7 (C-4', C-5'), 141.4 (C-14), 141.7 (C-14'), 143.8 (C-6), 143.9 (C-6'), 151.9 (C-19), 152.0 (C-19'), 174.1 (C-10), 174.6 (C-10') .

HRMS (ES+) exact mass calculated for $[M+H]^+$ ($C_{22}H_{29}O_4N$) requires **m/z** 372.2169, found **m/z** 372.2166.

9. References

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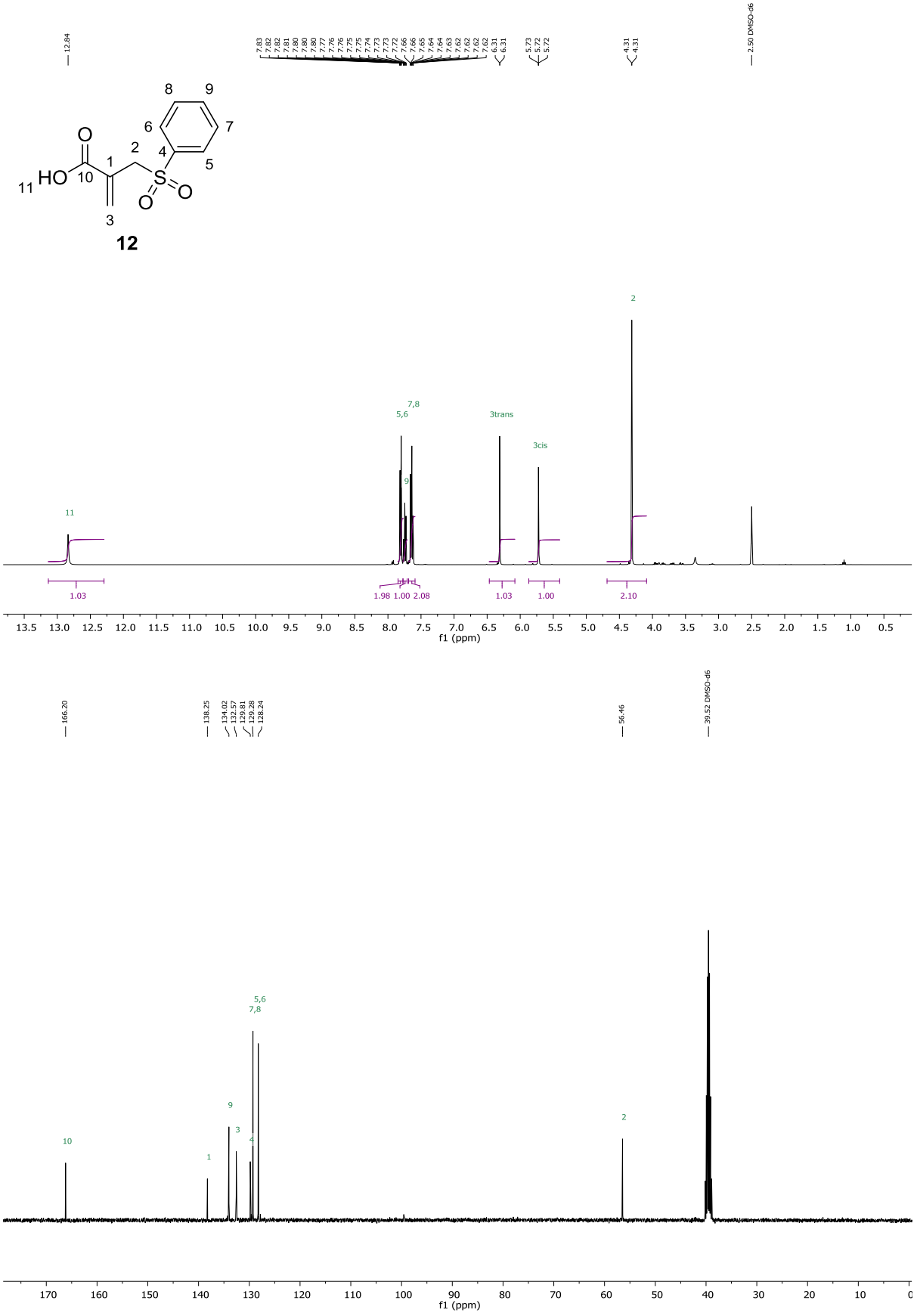
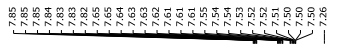
10. NMR spectra

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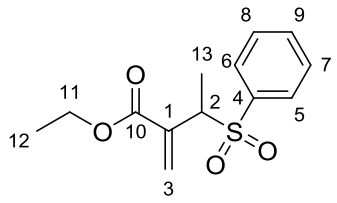
1.17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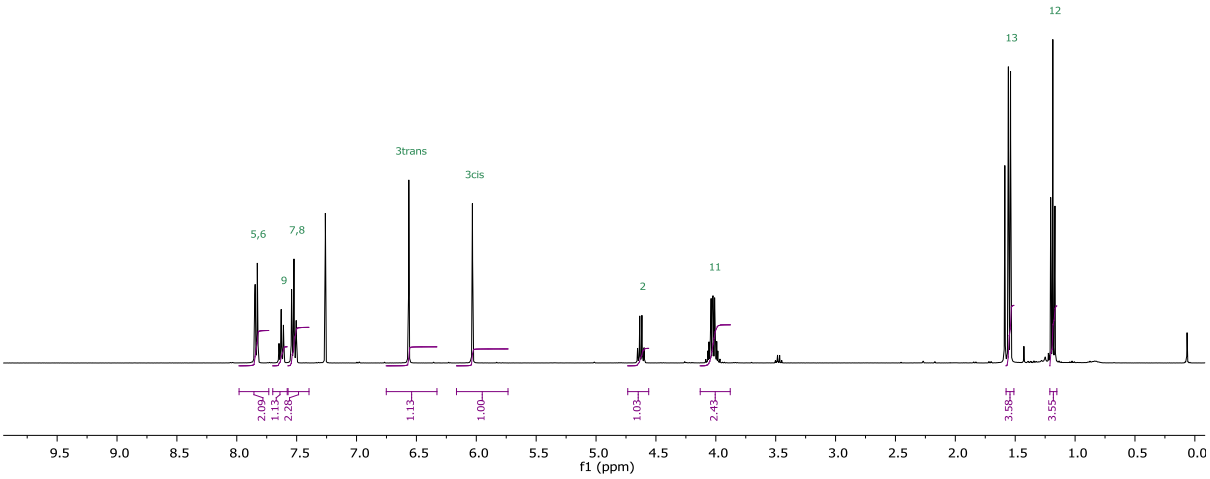
14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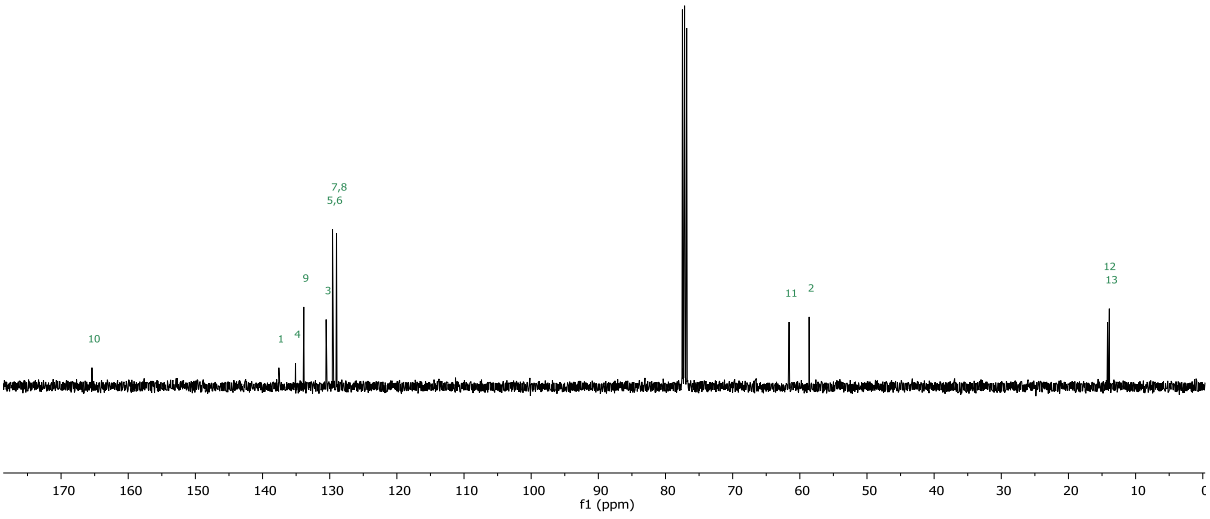
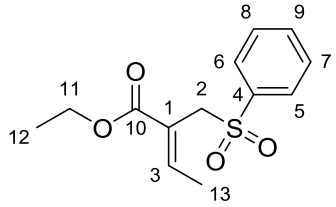
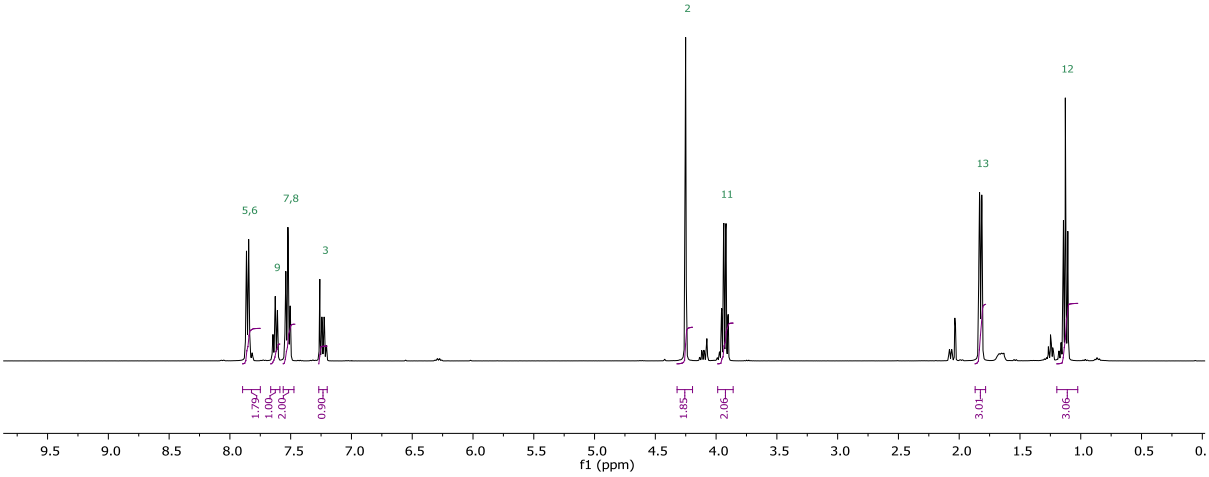
0.0
f1 (ppm)

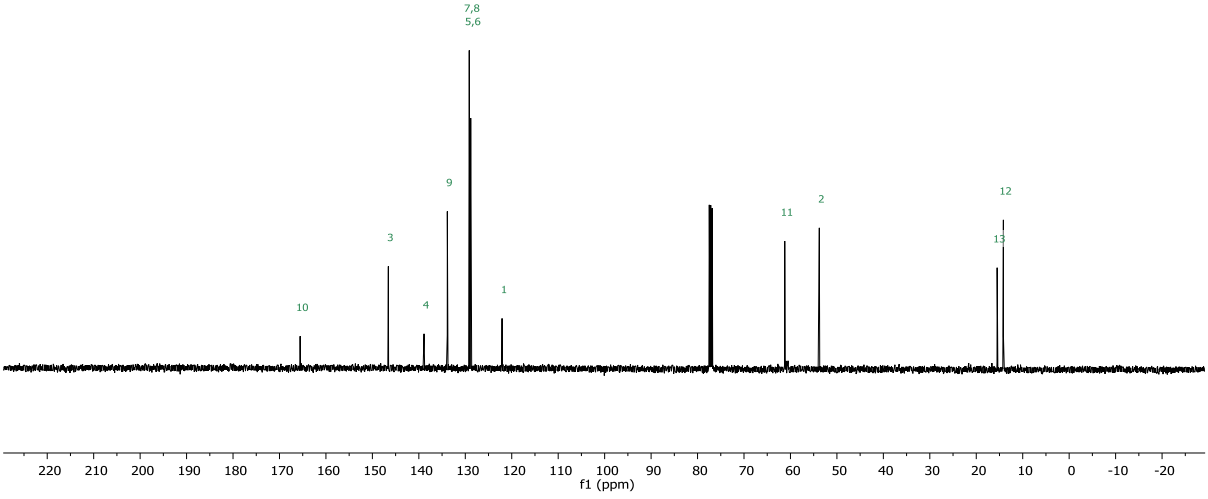

165.40
137.57
133.86
130.53
129.58
128.99
61.60
58.61
14.18
13.91

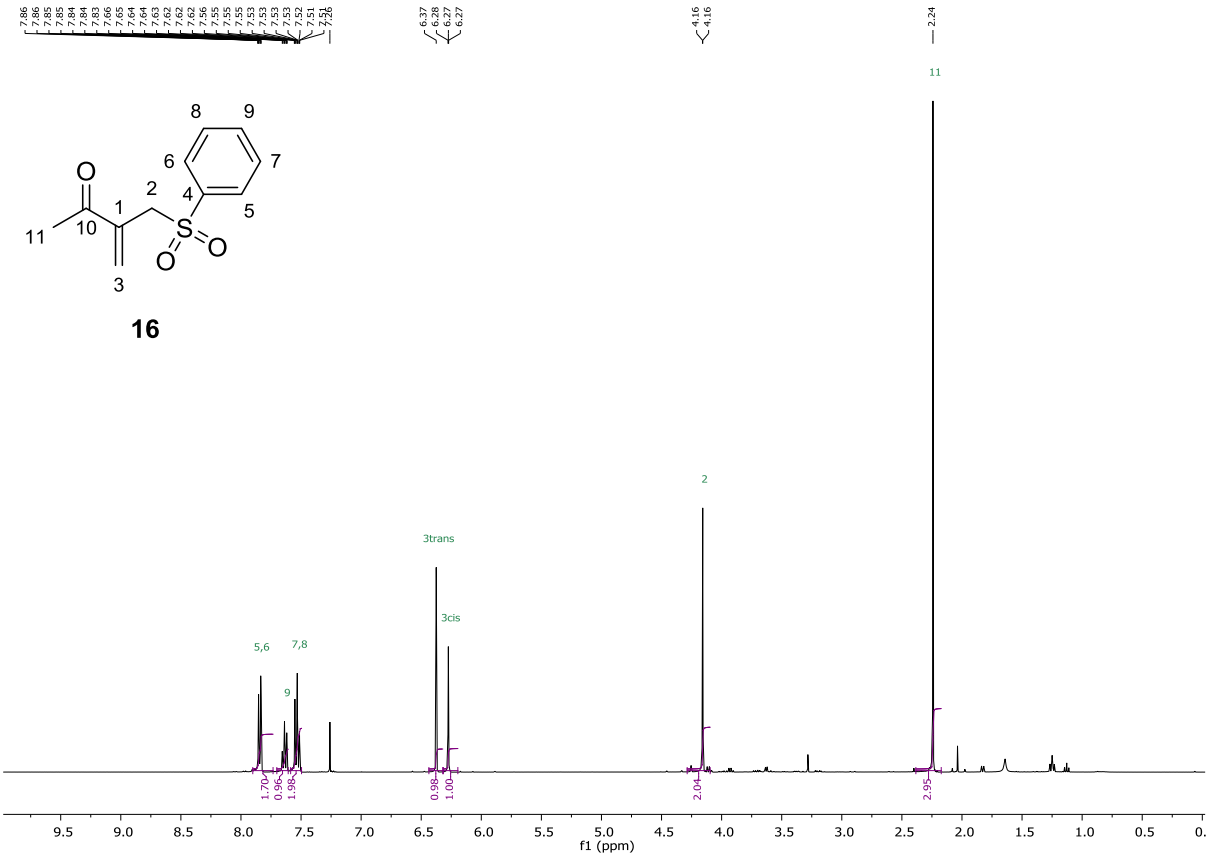

7,8
5,6
9
3
10
1
4
11
2
12
13
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



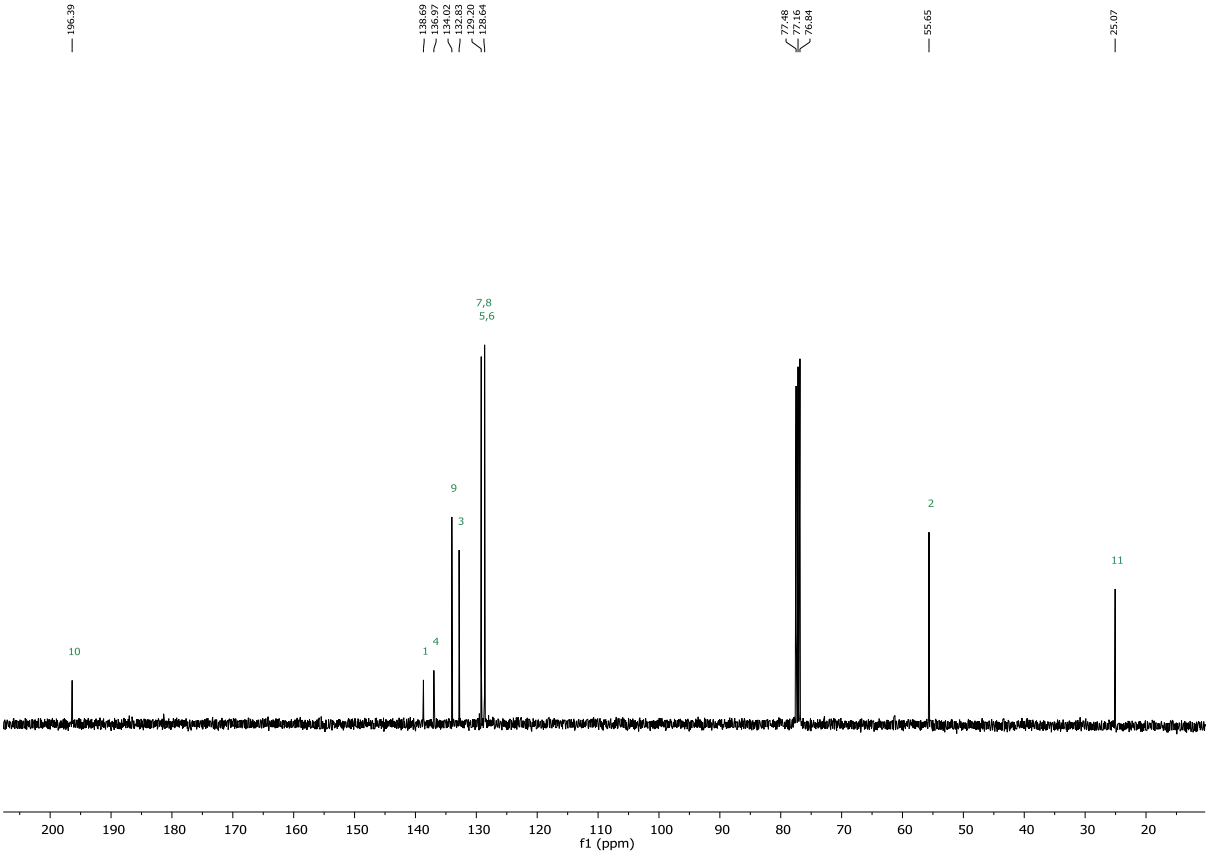
15

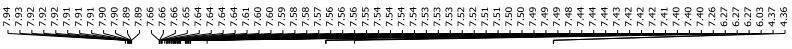


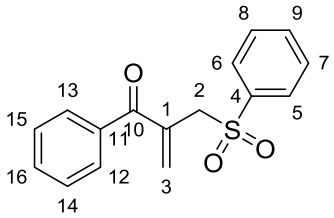



7.86
7.86
7.85
7.85
7.84
7.84
7.83
7.66
7.65
7.65
7.64
7.64
7.63
7.62
7.62
7.62
7.56
7.56
7.55
7.55
7.53
7.53
7.53
7.53
7.52
7.51
7.51
7.26
6.37
6.28
6.27
6.27
4.16
4.16
2.24
11
2
3trans
3cis
5,6
7,8
9
1.70
0.96
1.98
0.98
1.00
2.04
2.95
f1 (ppm)

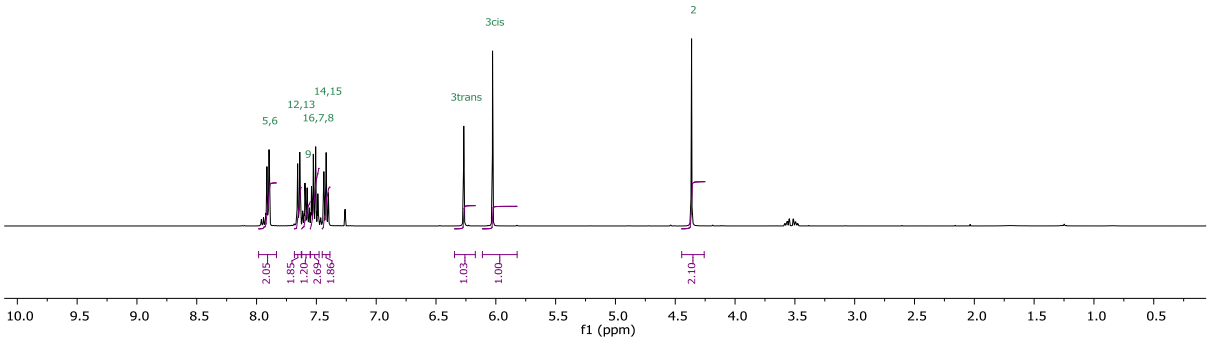
16

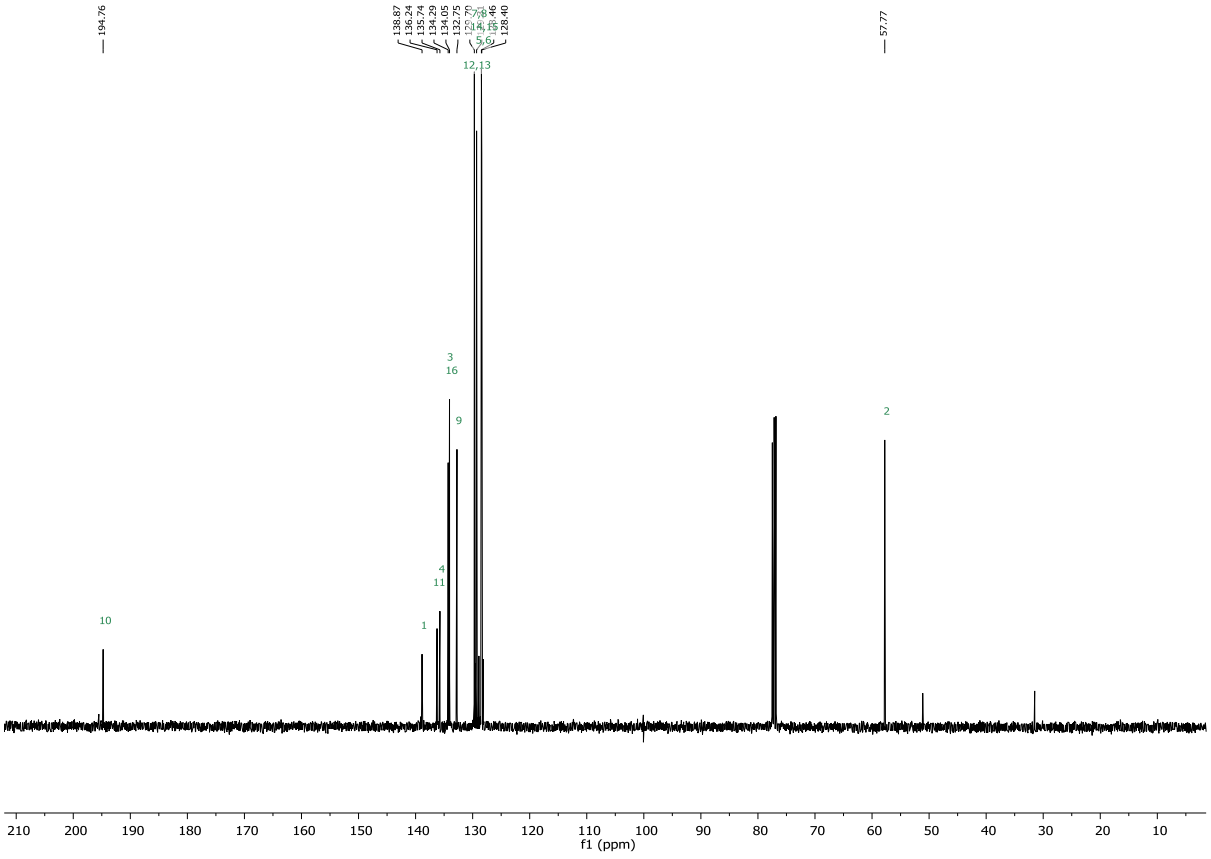

196.39
138.69
136.97
134.02
132.83
129.20
128.64
77.48
77.16
76.84
55.65
25.07
7,8
5,6
9
3
2
11
10
1
4
f1 (ppm)

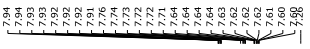




17


3cis
2
14,15
12,13
5,6
16,7,8
3trans
9
2.05
1.85
1.20
2.69
1.86
1.03
1.00
2.10
f1 (ppm)


194.76
57.77
12,13
3
16
9
2
4
11
10
1
f1 (ppm)


7.94
7.94
7.93
7.93
7.92
7.92
7.92
7.91
7.76
7.74
7.73
7.72
7.72
7.71
7.64
7.64
7.64
7.64
7.63
7.62
7.62
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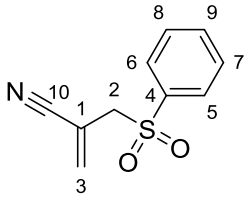
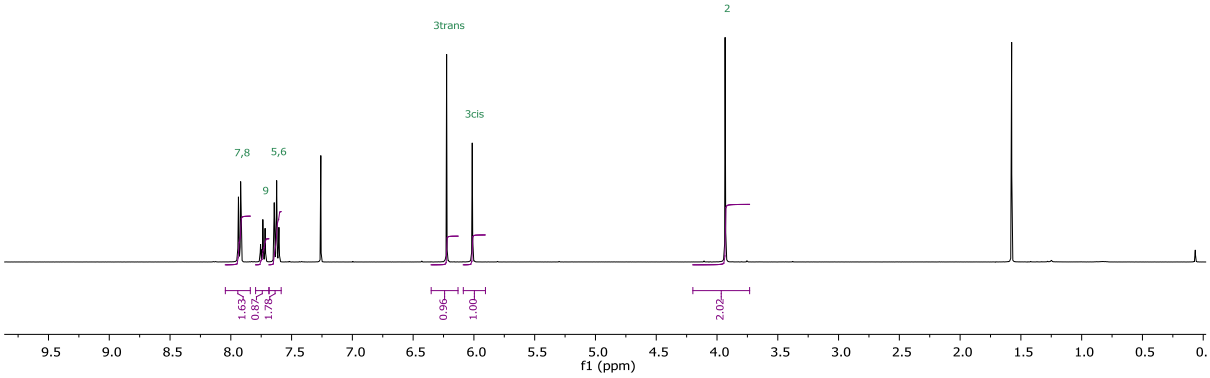
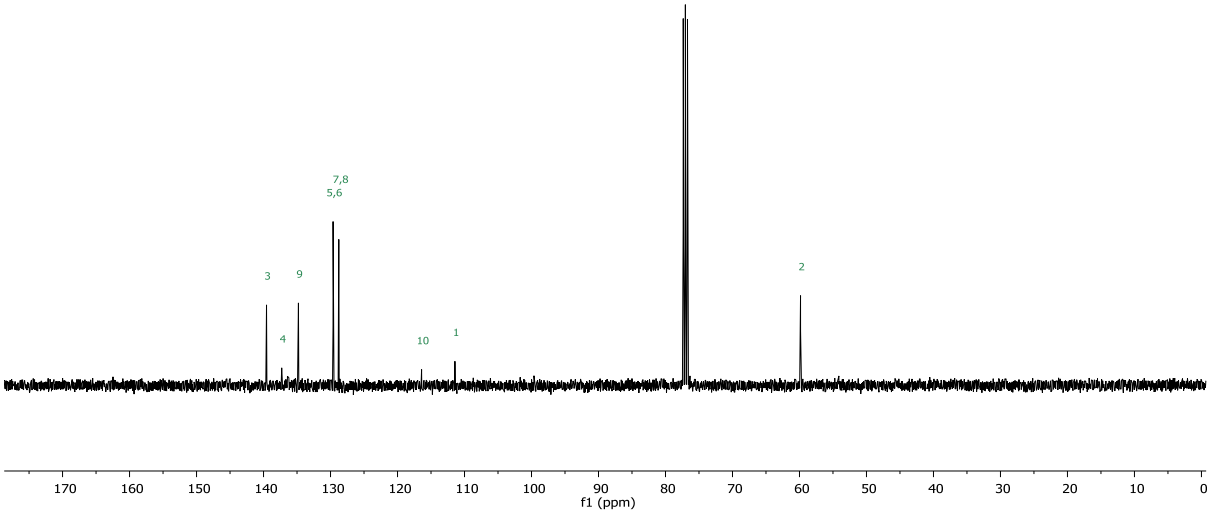
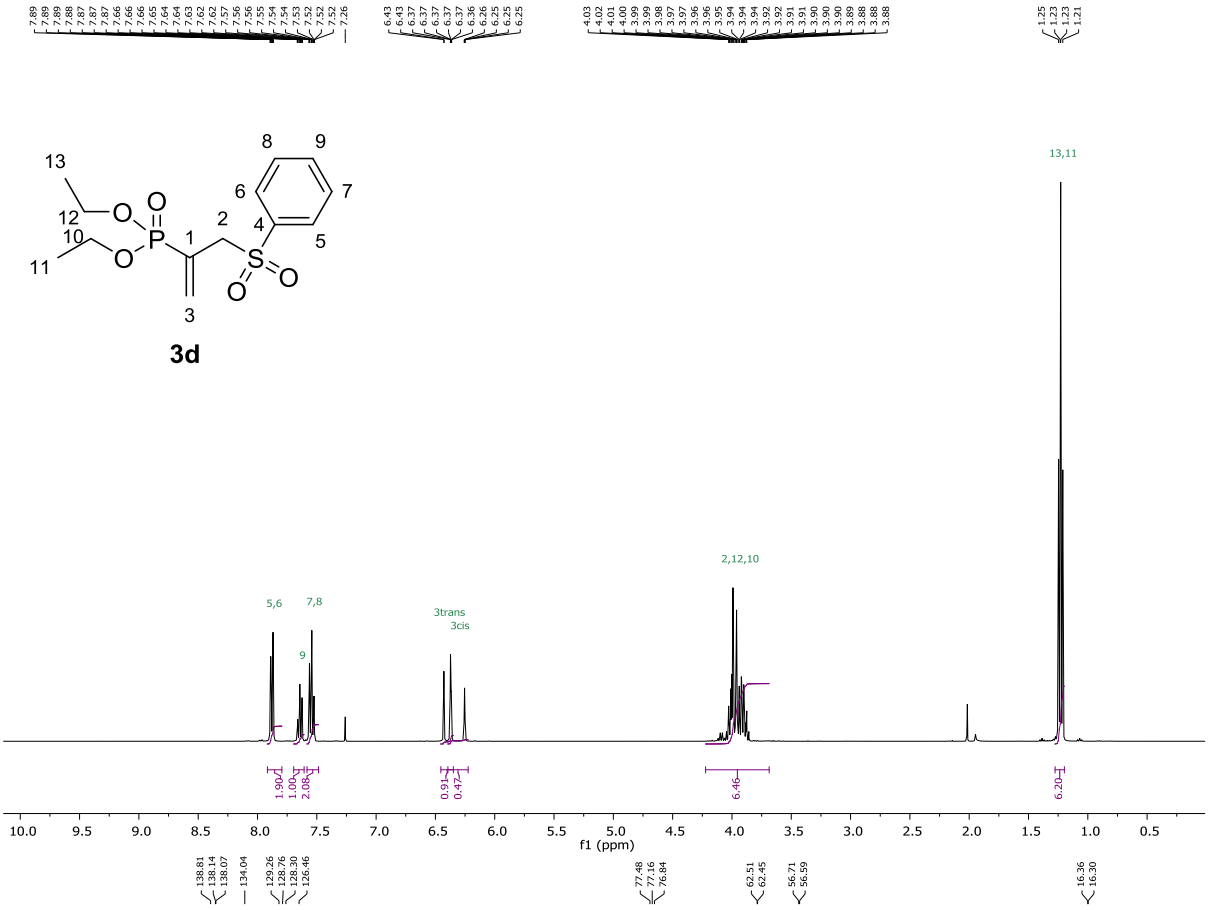
7.60
7.60
7.28
6.22
6.02
6.01
6.01
3.93
3.93

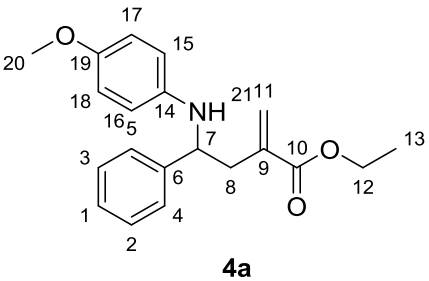

8
9
6
7
N
10
2
1
4
5
S
O
O
3

3c

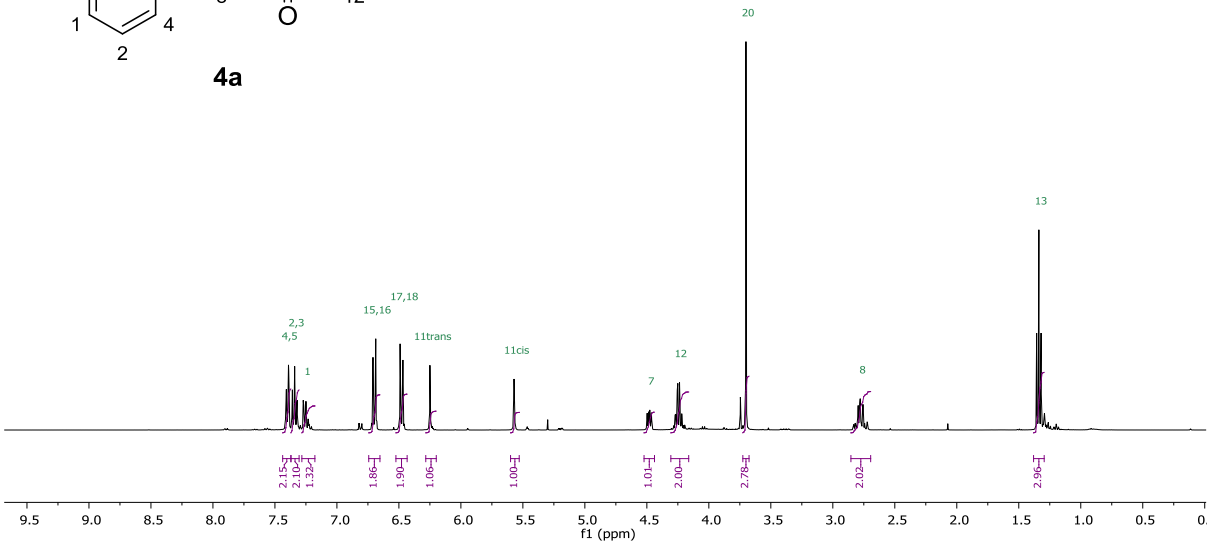

3trans
2
3cis
7,8
5,6
9
1.63
0.87
1.78
0.96
1.00
2.02
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

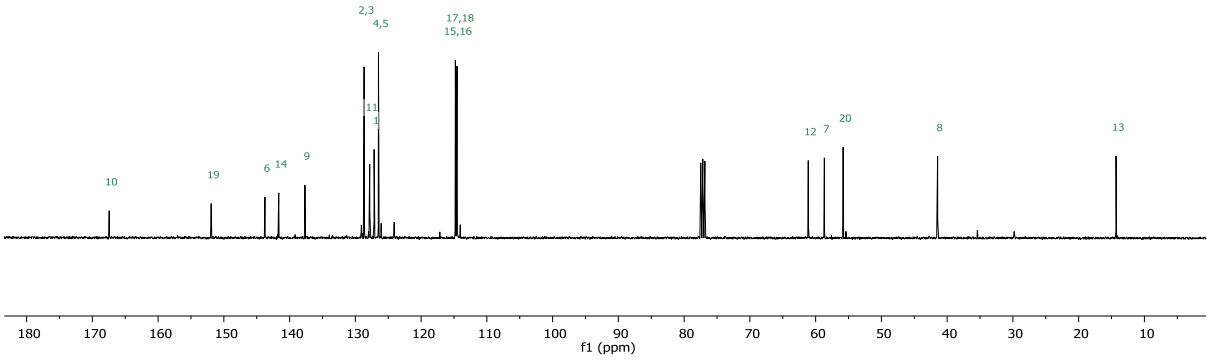

7,8
5,6
3
9
4
10
1
2
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

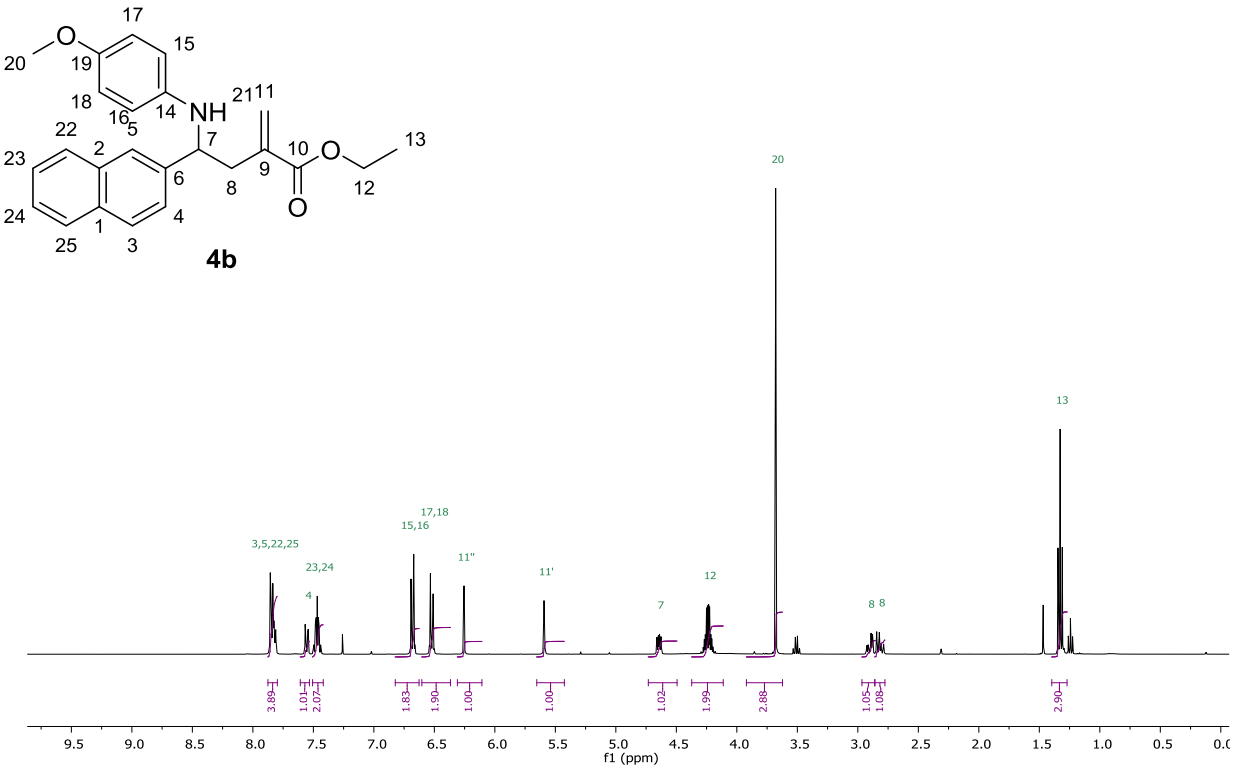

7.89 7.89 7.89 7.88 7.87 7.87 7.87 7.66 7.66 7.66 7.65 7.64 7.64 7.63 7.62 7.57 7.56 7.56 7.55 7.54 7.54 7.53 7.52 7.52 7.52 7.26
6.43 6.43 6.37 6.37 6.37 6.37 6.36 6.36 6.25 6.25 6.25 6.25
4.03 4.02 4.01 4.00 3.99 3.99 3.98 3.97 3.97 3.96 3.96 3.95 3.94 3.94 3.94 3.92 3.91 3.91 3.90 3.90 3.90 3.89 3.88 3.88 3.88
1.25 1.23 1.23 1.21
13 12 10 11 O O P O 1 2 3 S O O 4 5 6 7 8 9
3d
13,11
2,12,10
5,6
7,8
9
3trans
3cis
1.90
1.00
2.08
0.91
0.47
6.46
6.20
f1 (ppm)
138.81 138.14 138.07 134.04 129.26 128.76 128.30 126.46 77.48 77.16 76.84 63.51 62.45 56.71 56.59 16.36 16.30
7,8
5,6
9
3
4
1
12,10
2
11
13
f1 (ppm)

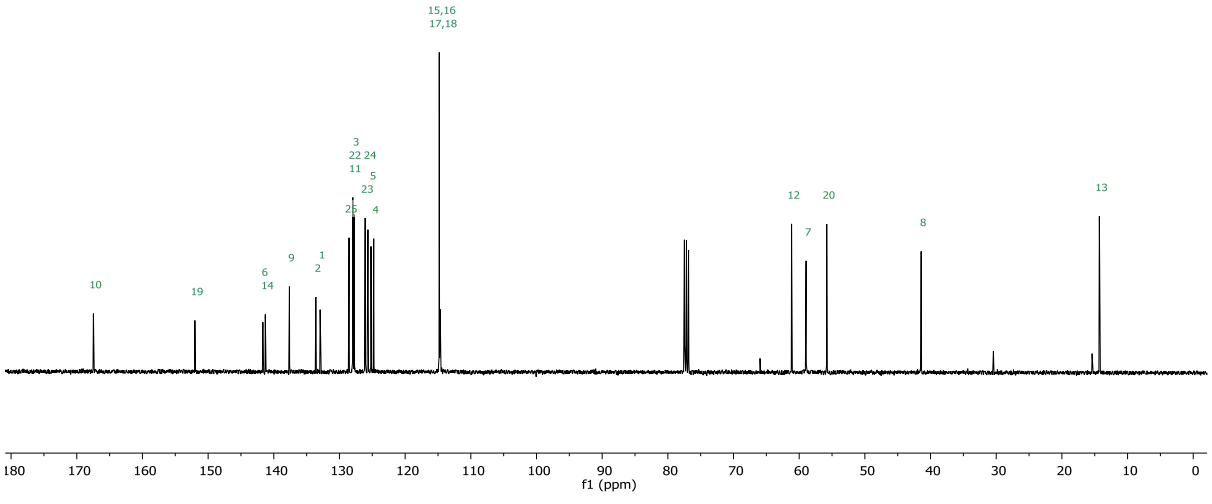


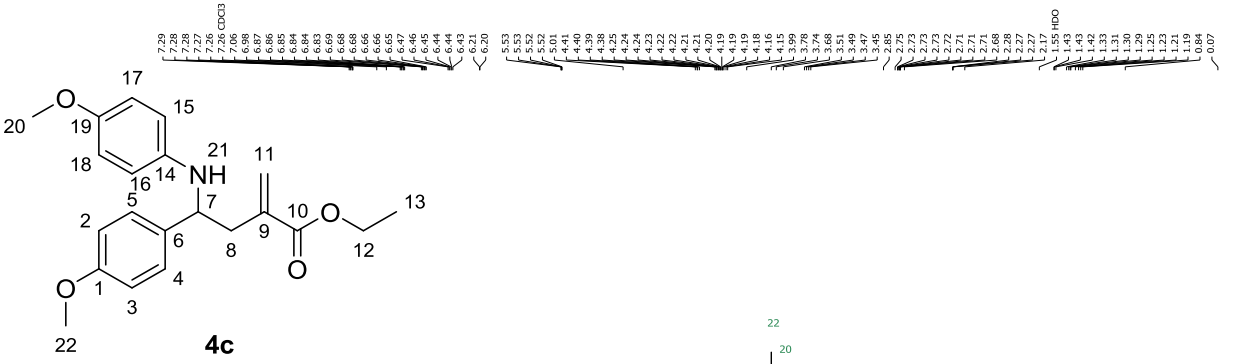
4a


20
13
17,18
15,16
2,3
4,5
11trans
11cis
1
12
7
8
f1 (ppm)

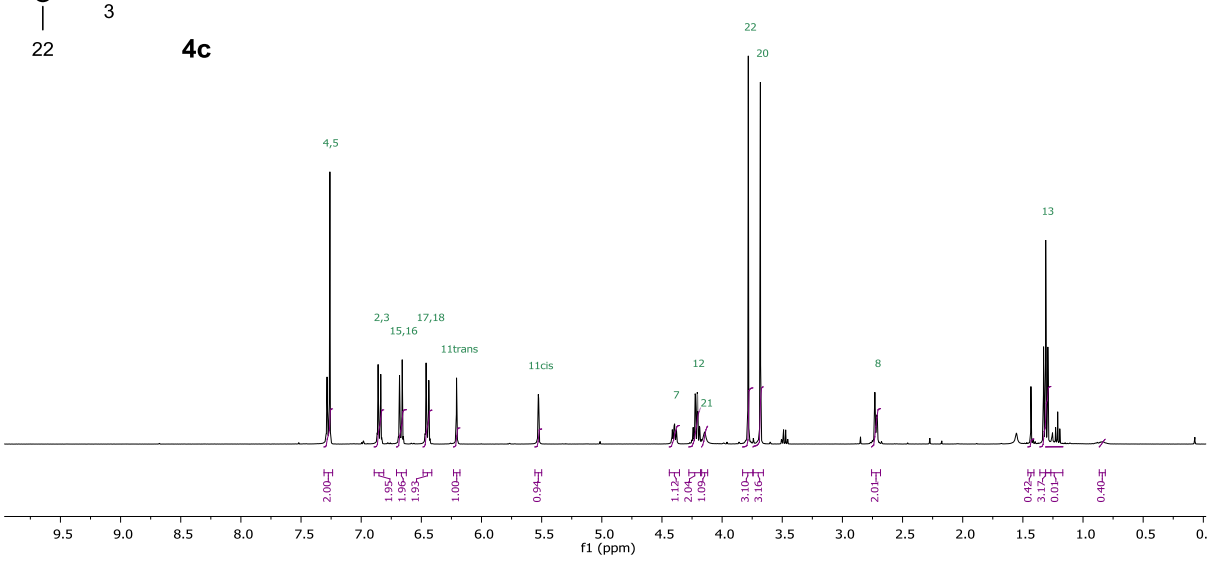

2,3
4,5
17,18
15,16
10
19
6
14
9
11
1
12
7
20
8
13
f1 (ppm)

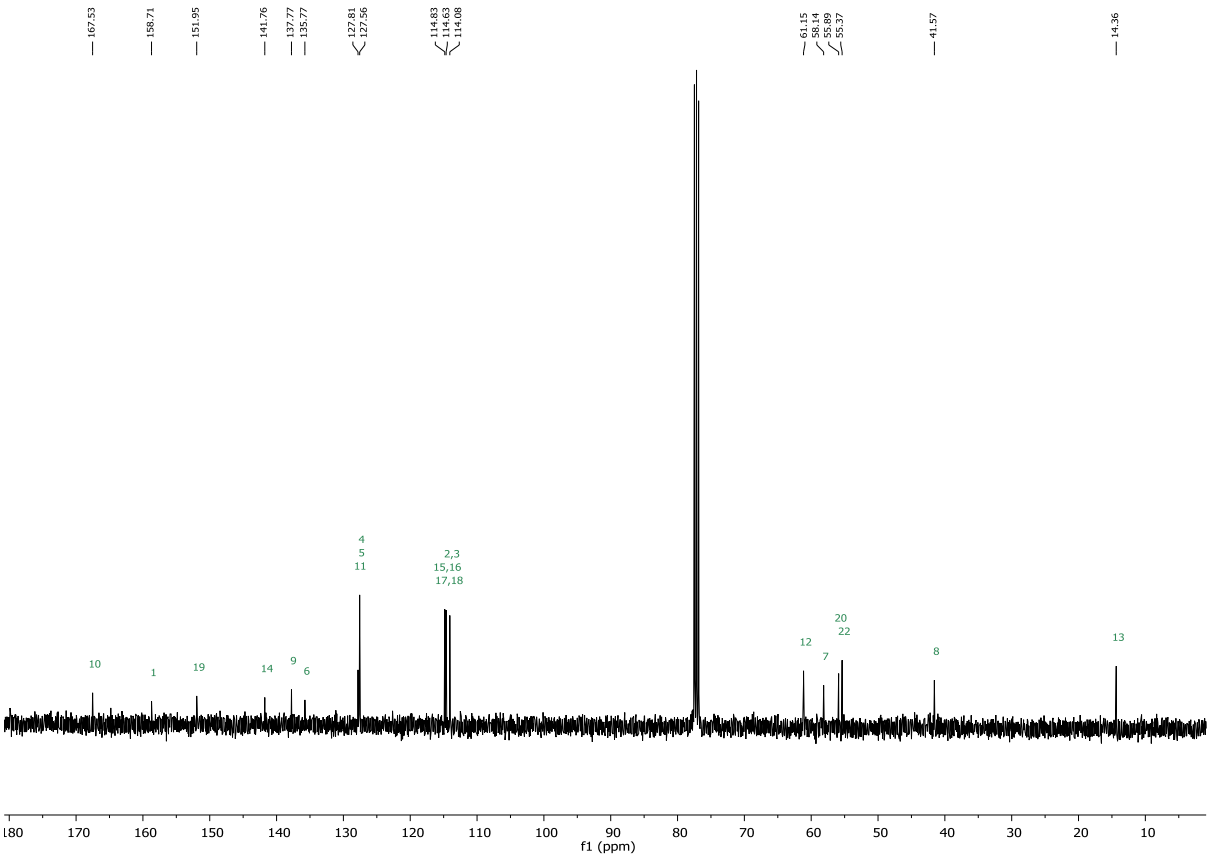

4b
f1 (ppm)

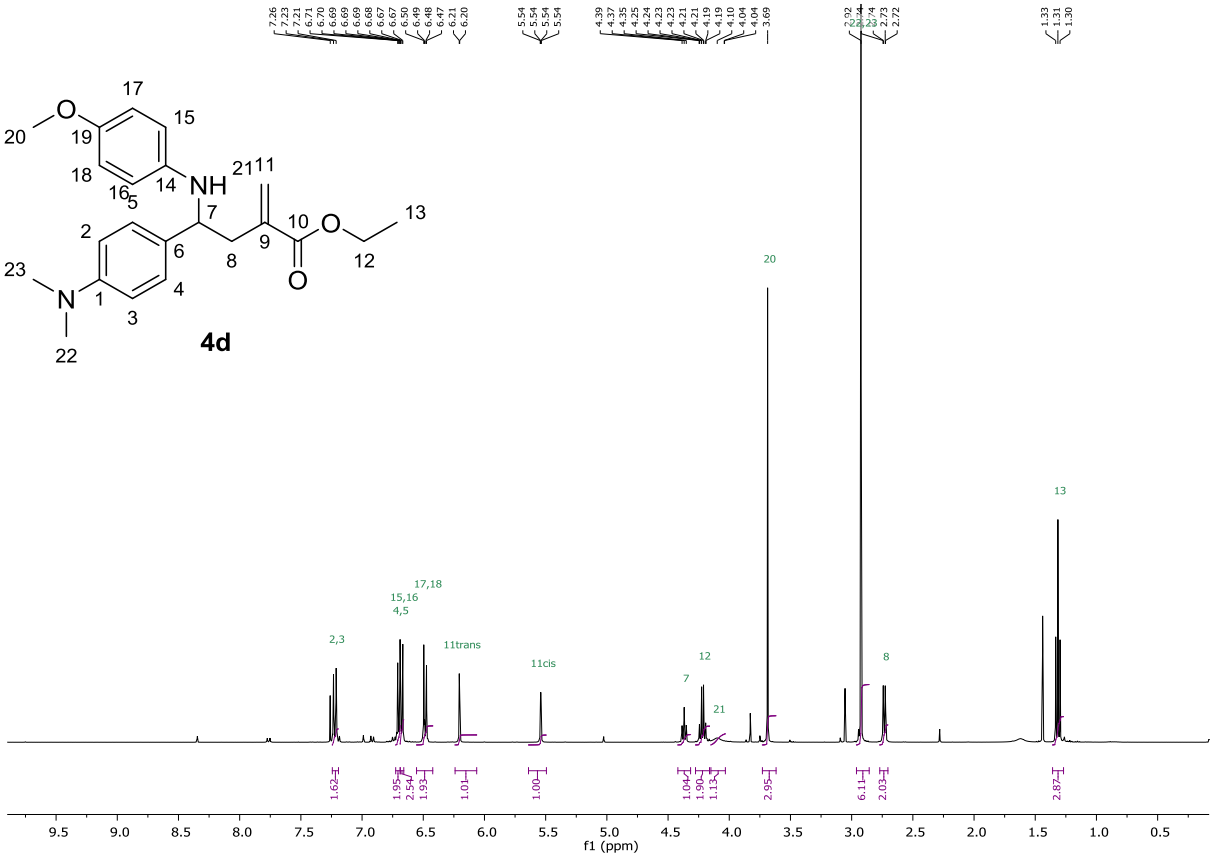

f1 (ppm)

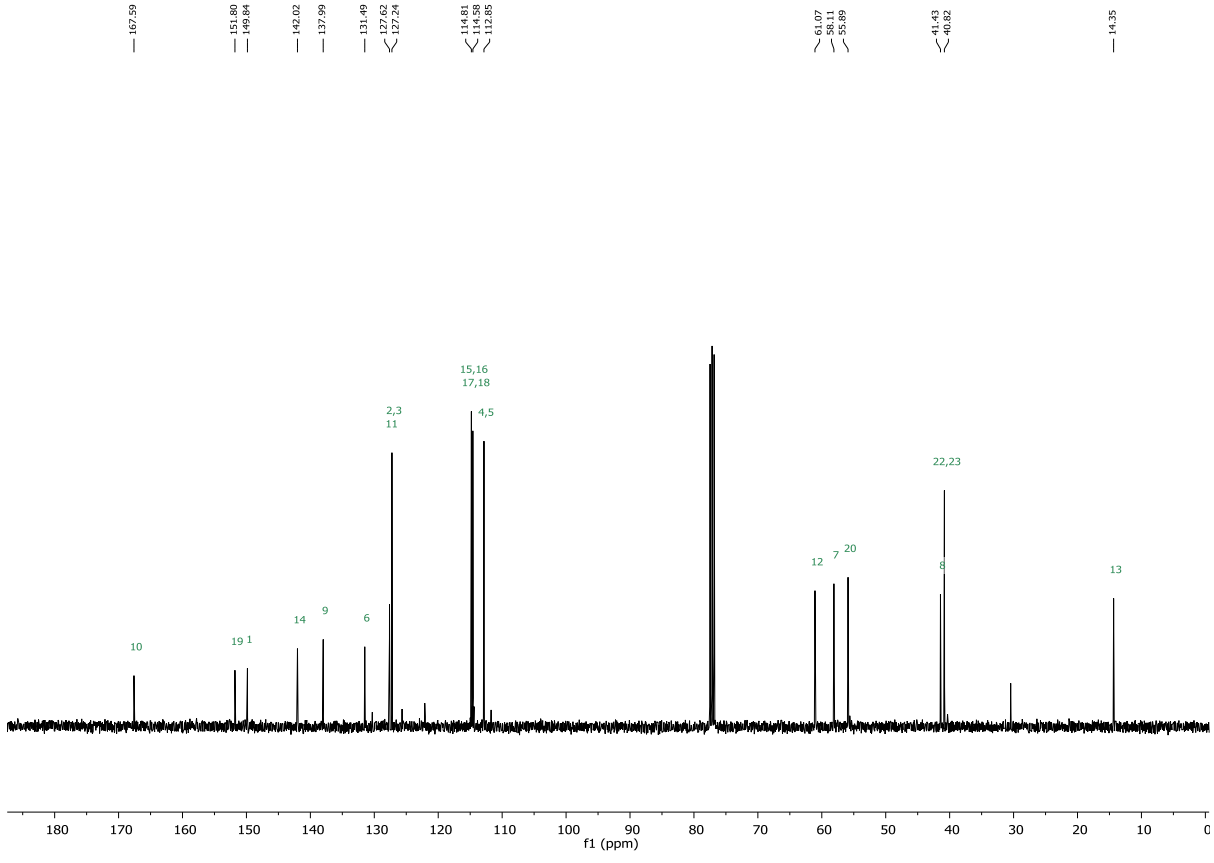


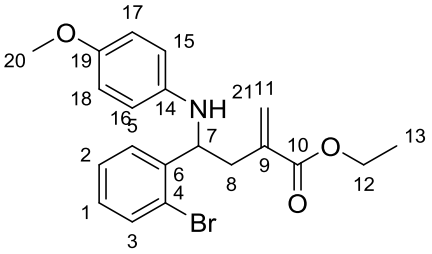
4c





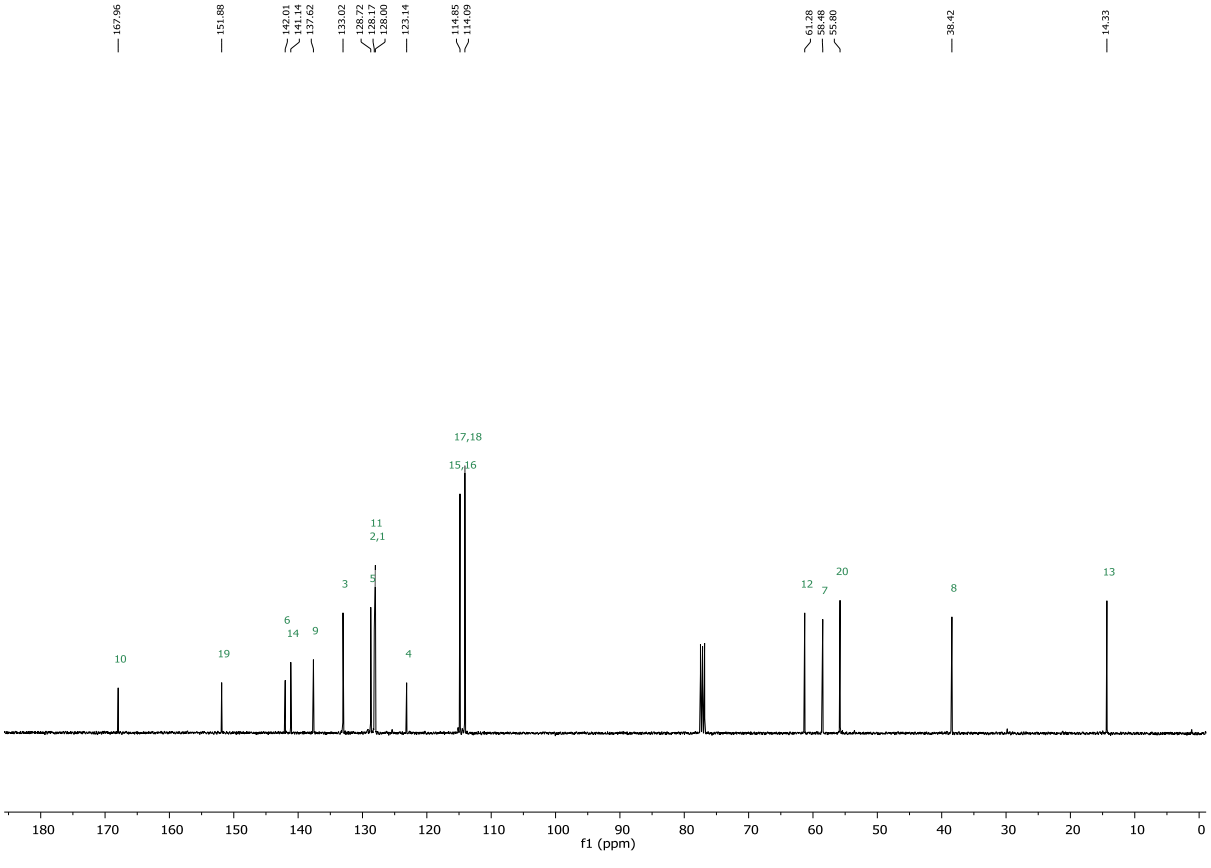

4d
f1 (ppm)

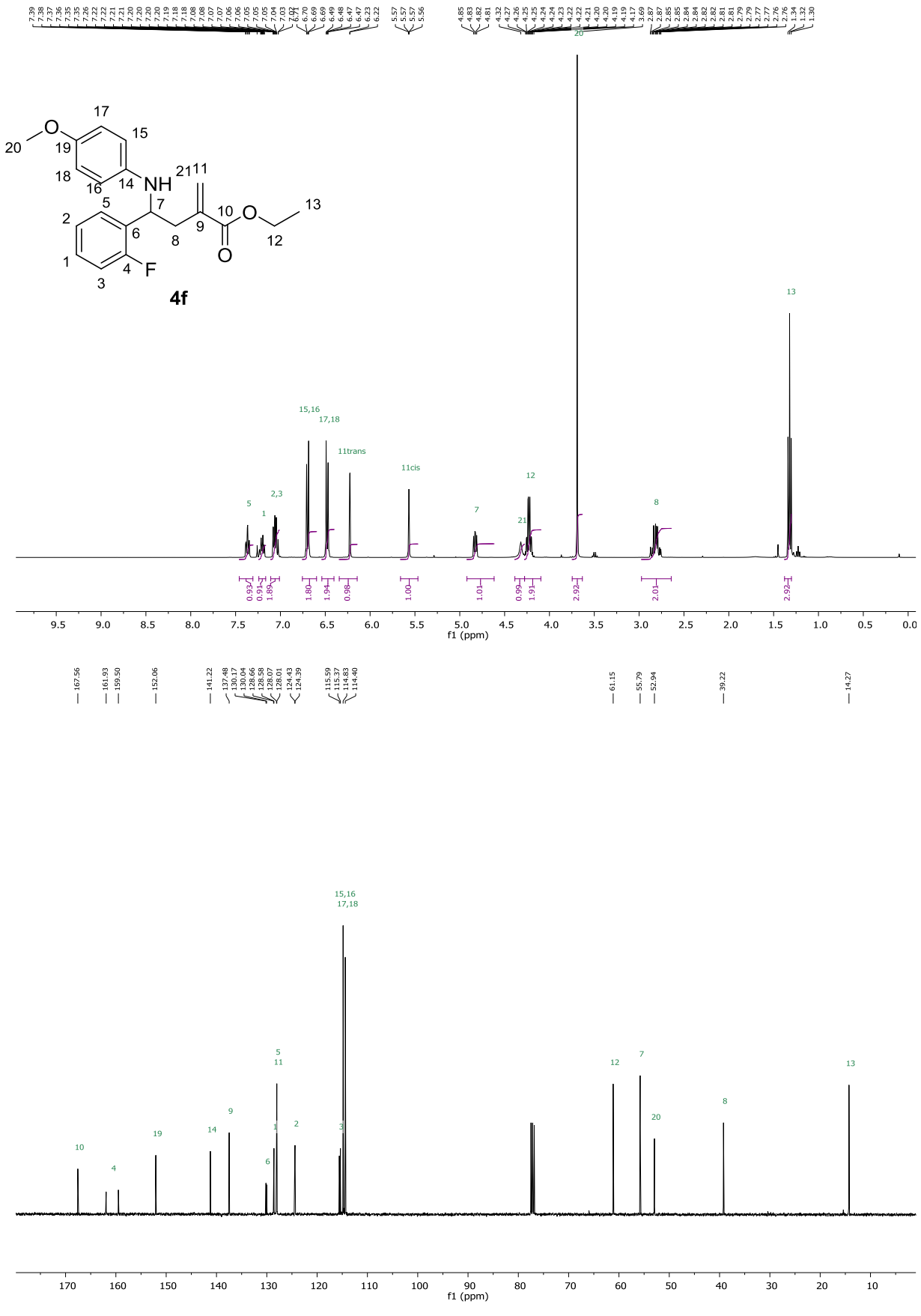

f1 (ppm)

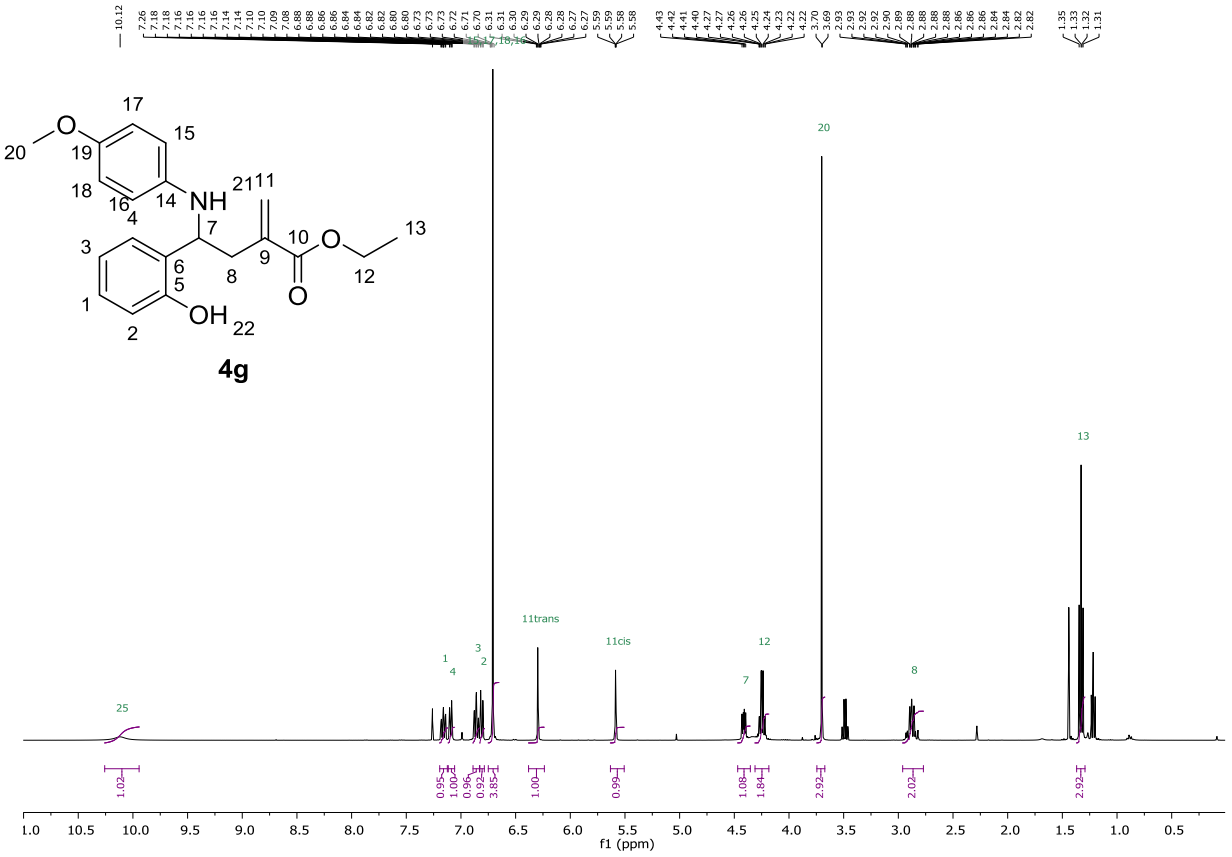

17
15
O
20
19
18
16
14
NH
21
11
5
7
10
O
13
2
9
6
4
8
12
1
O
Br
3

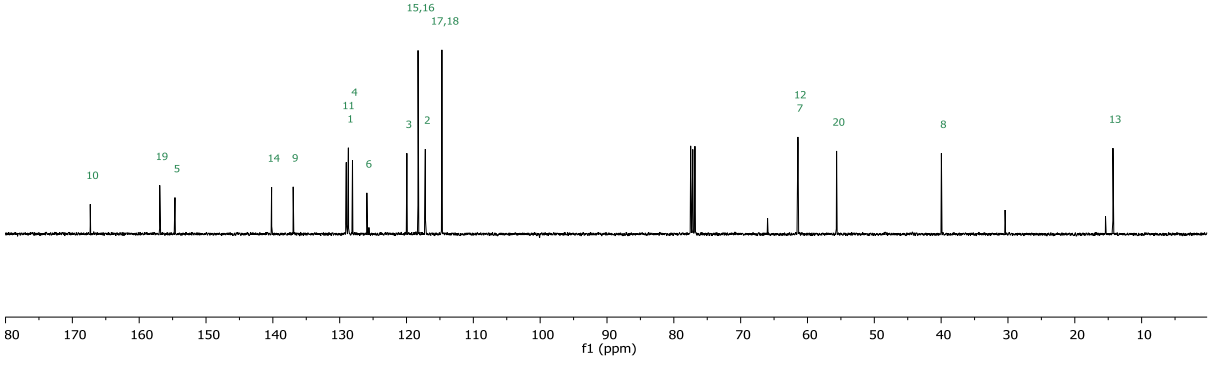
4e

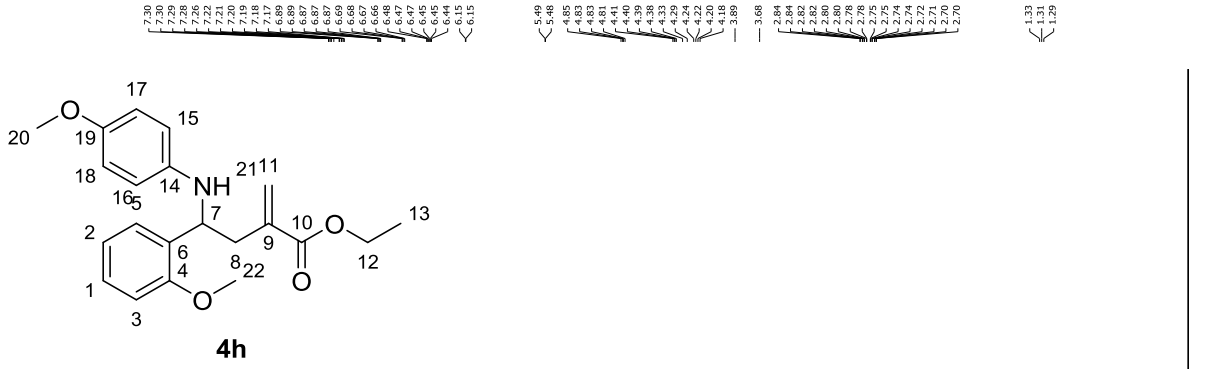
20
13
15,16
17,18
11trans
11cis
12
3
1
2
5
7
21
8
8
f1 (ppm)


17,18
15,16
11
2,1
20
12
7
8
13
3
5
6
14
9
10
19
4
f1 (ppm)

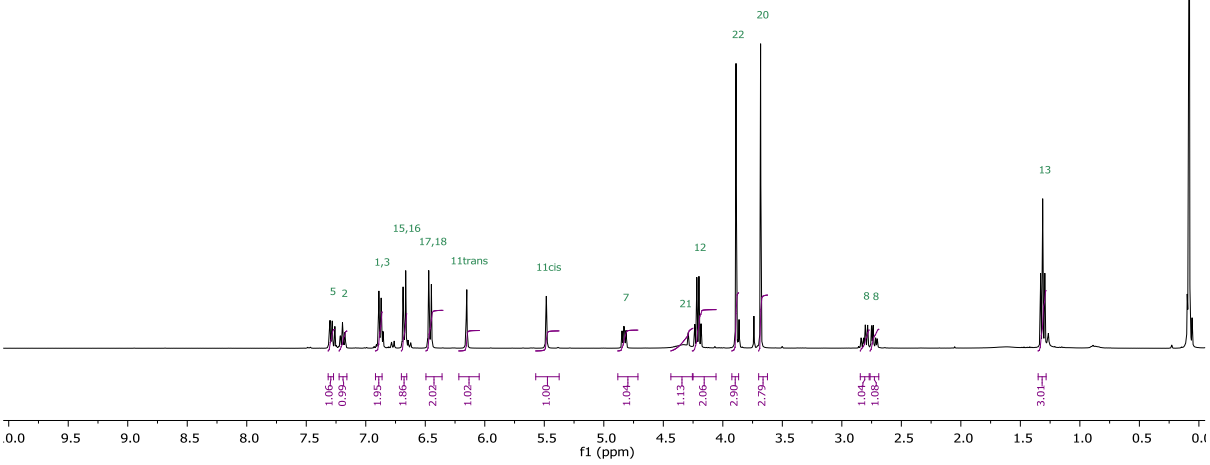

4f
f1 (ppm)
f1 (ppm)

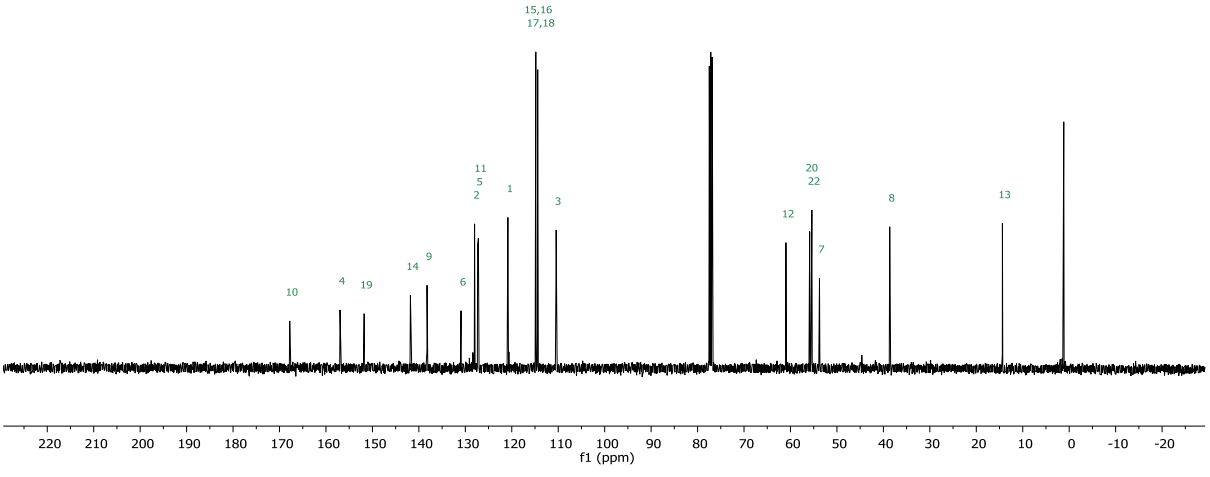

4g
f1 (ppm)

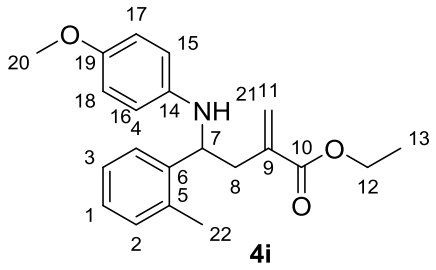

f1 (ppm)



4h

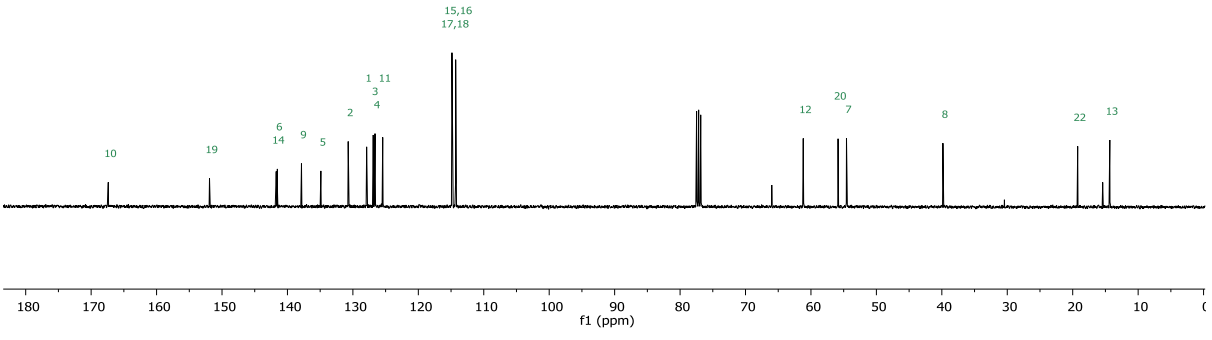


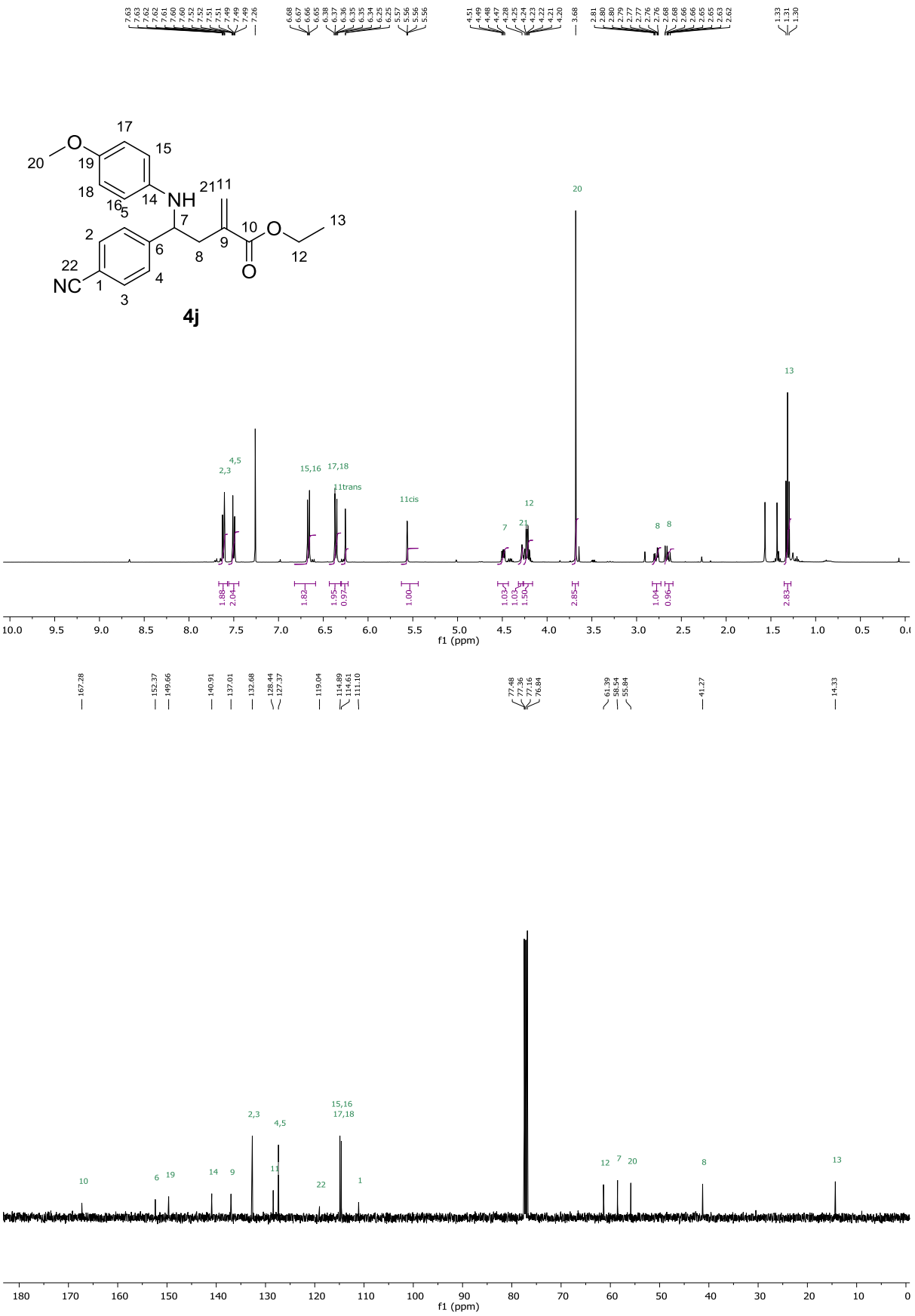


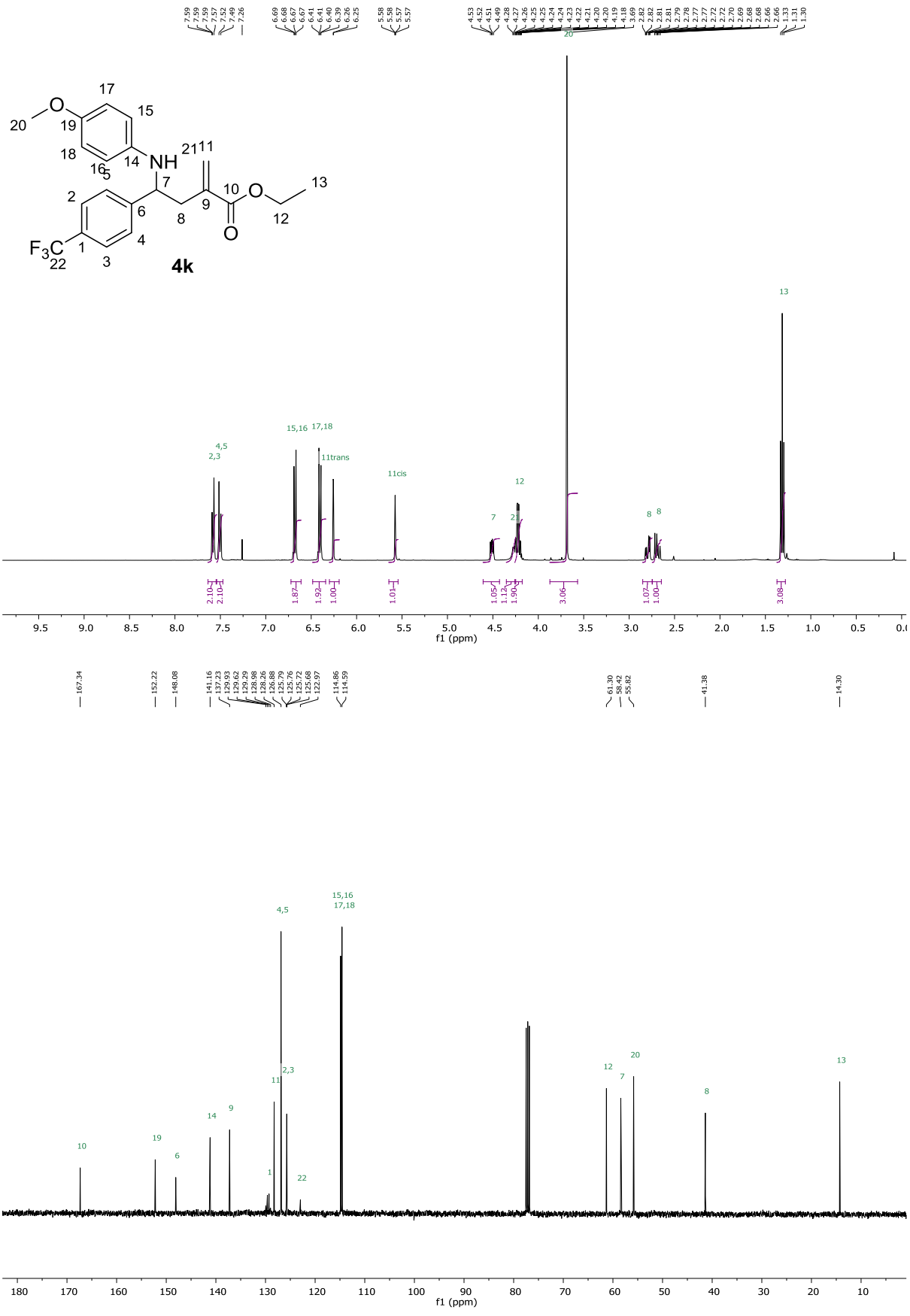


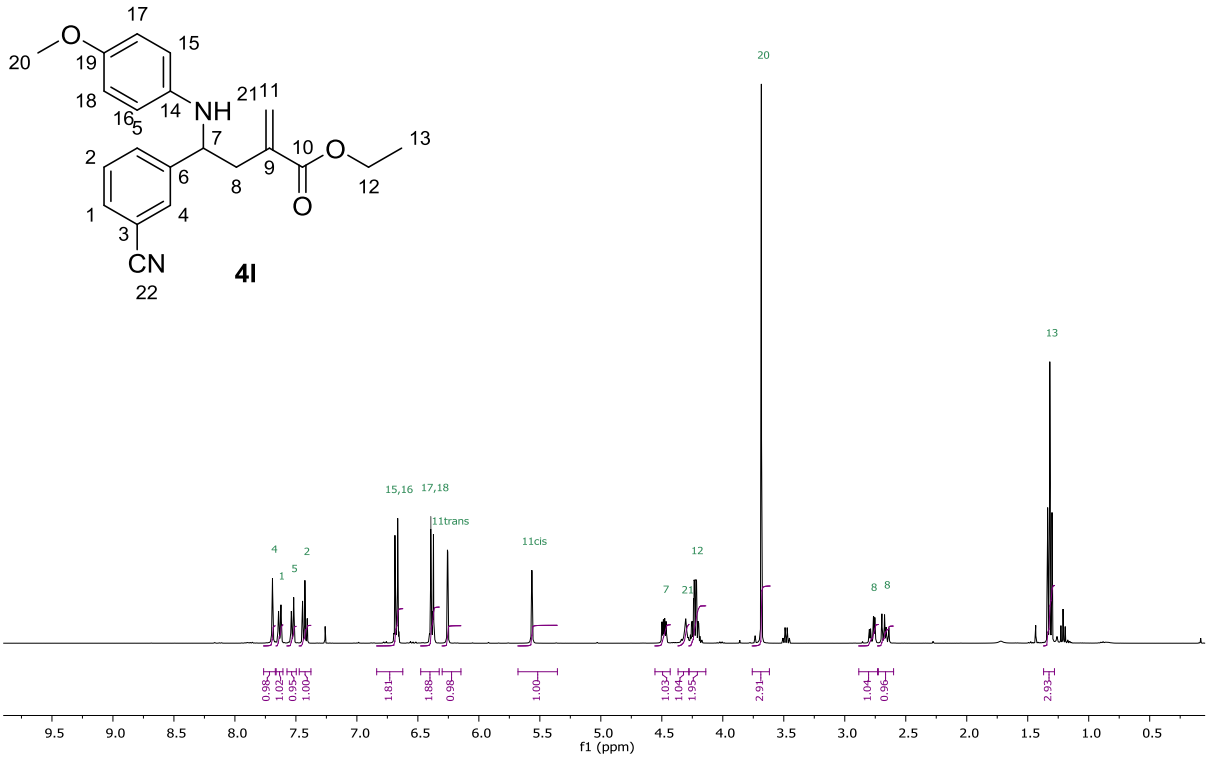
4i

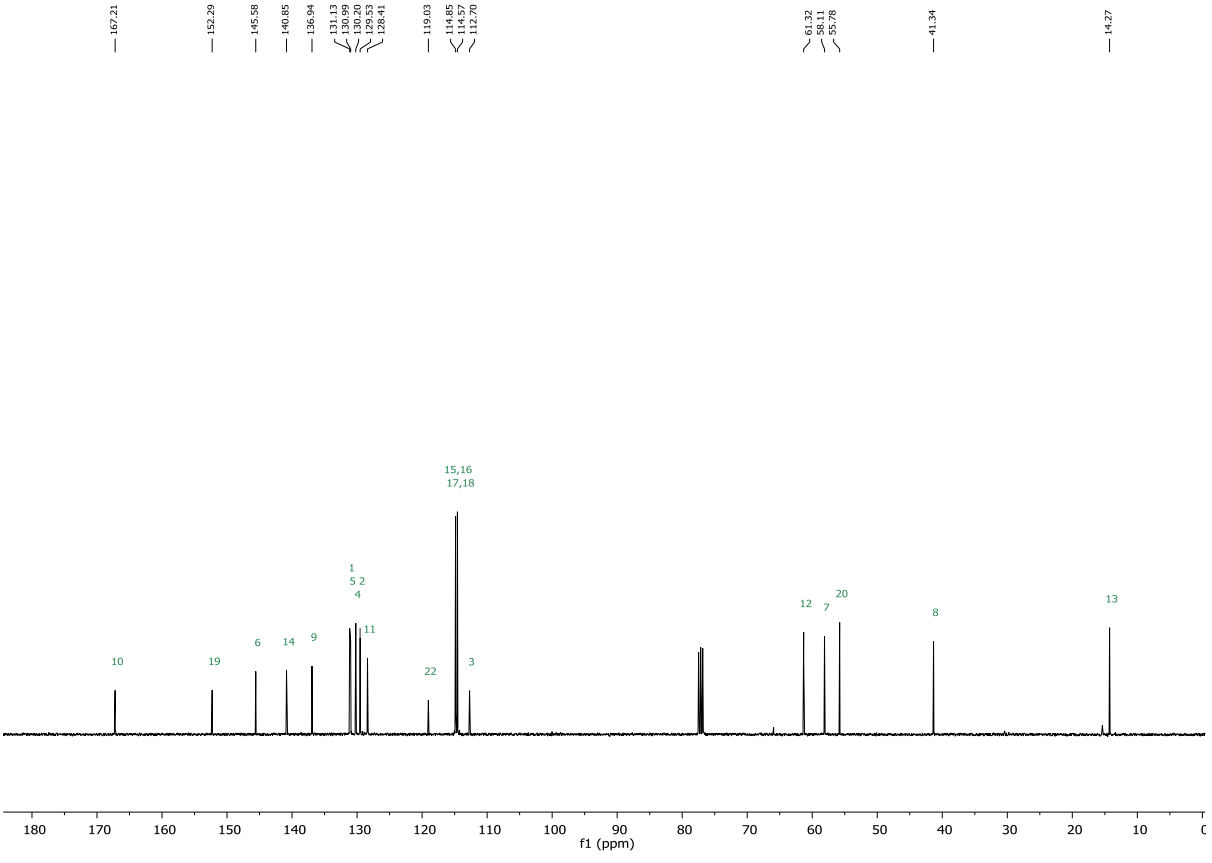
20
22
13
15,16
17,18
1,3,4
11trans
11cis
12
2
7
21
8'
8"
1.02
3.06
1.88
1.95
1.00
1.07
1.05
2.00
1.03
3.12
1.09
0.99
3.03
3.12
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

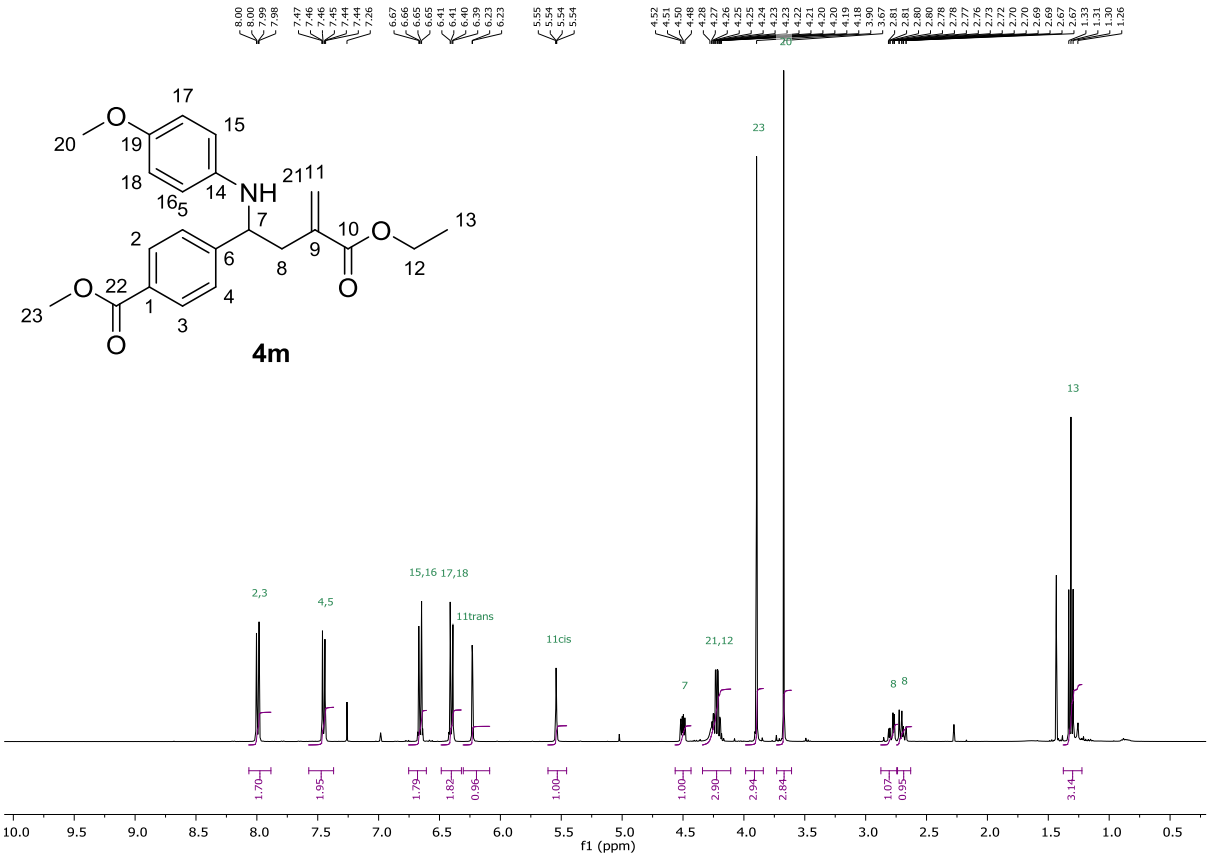

15,16
17,18
1
11
3
4
2
6
14
9
5
10
19
12
20
7
8
22
13
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

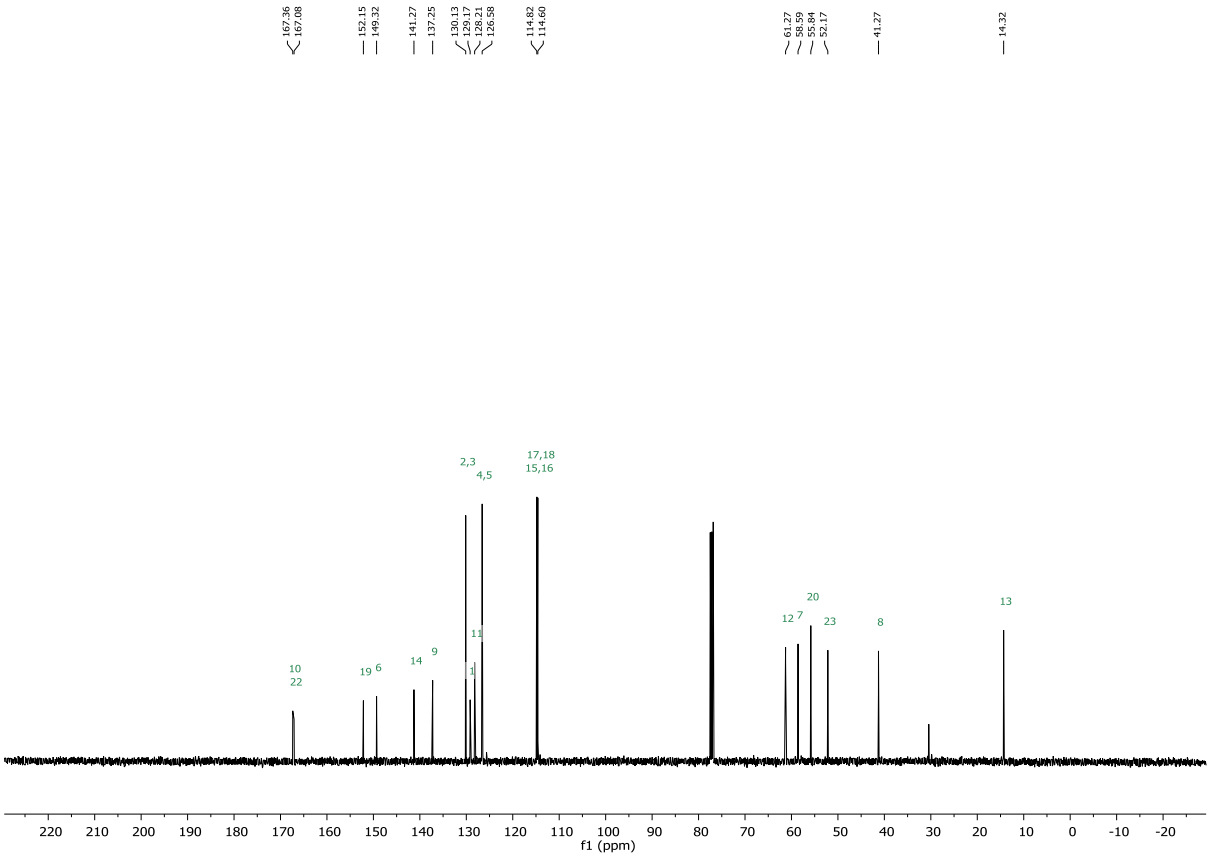

4j
f1 (ppm)
f1 (ppm)

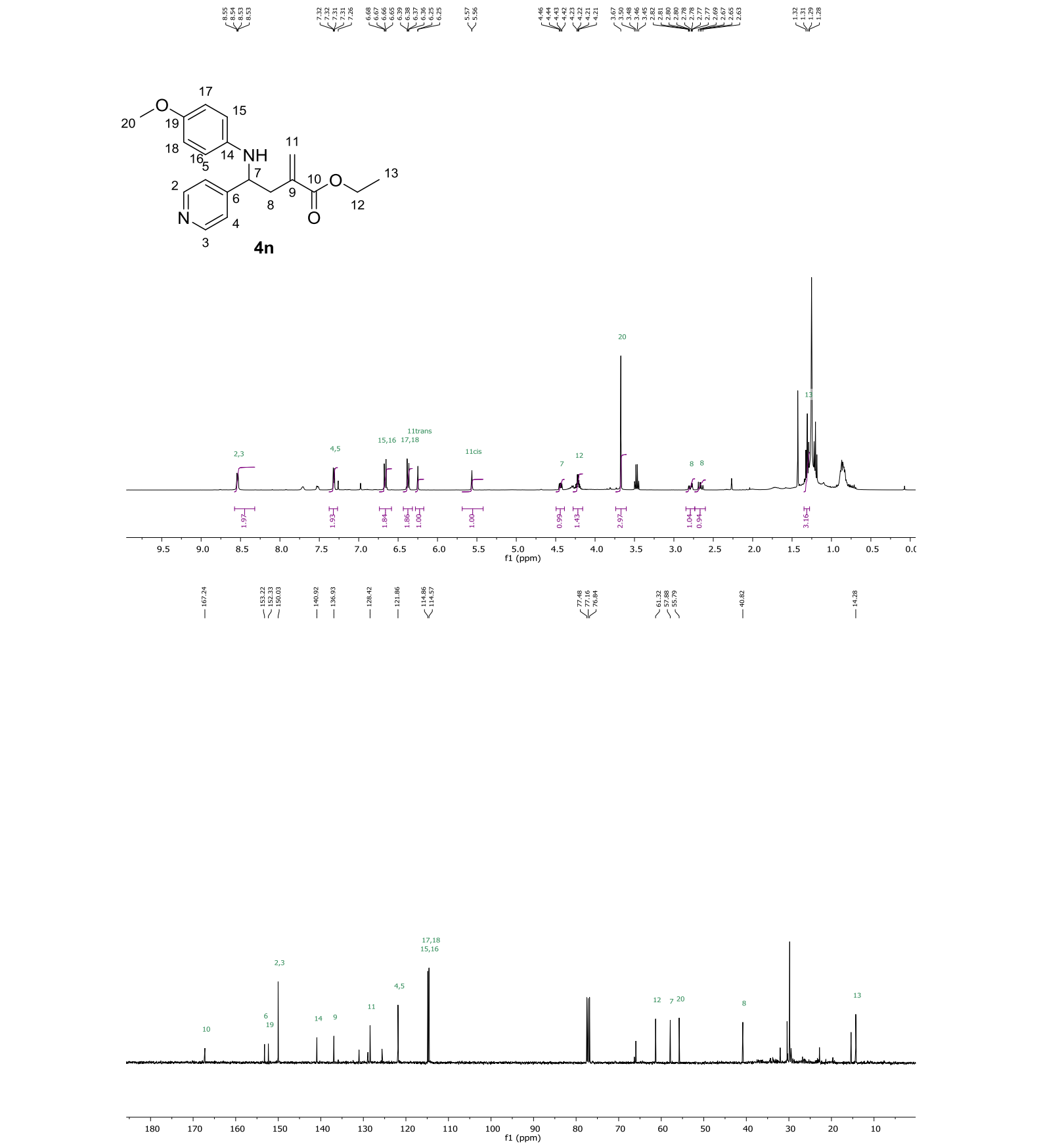

4k
f1 (ppm)
f1 (ppm)

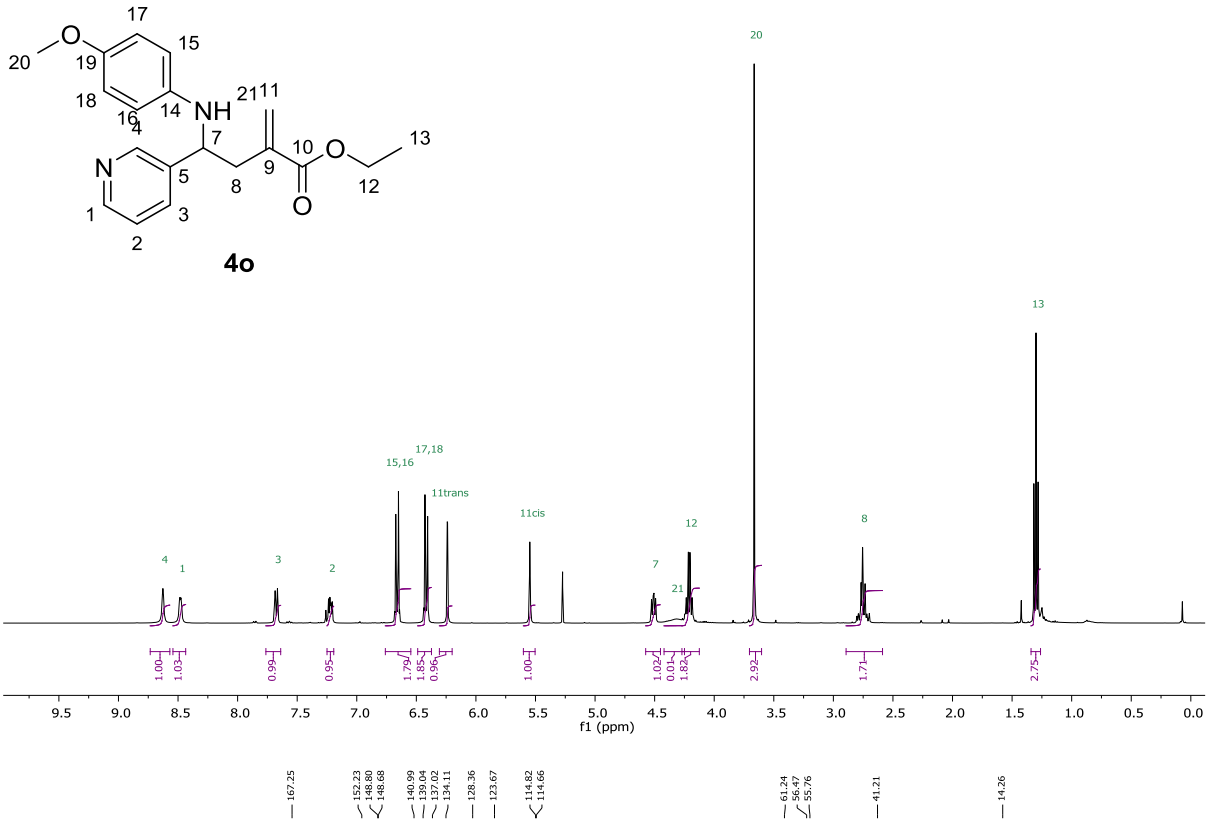

4l
f1 (ppm)

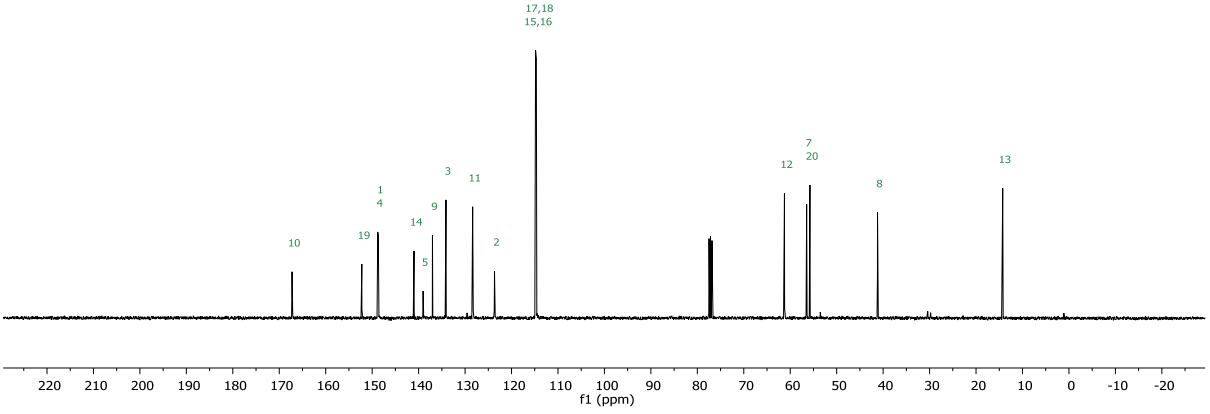

f1 (ppm)

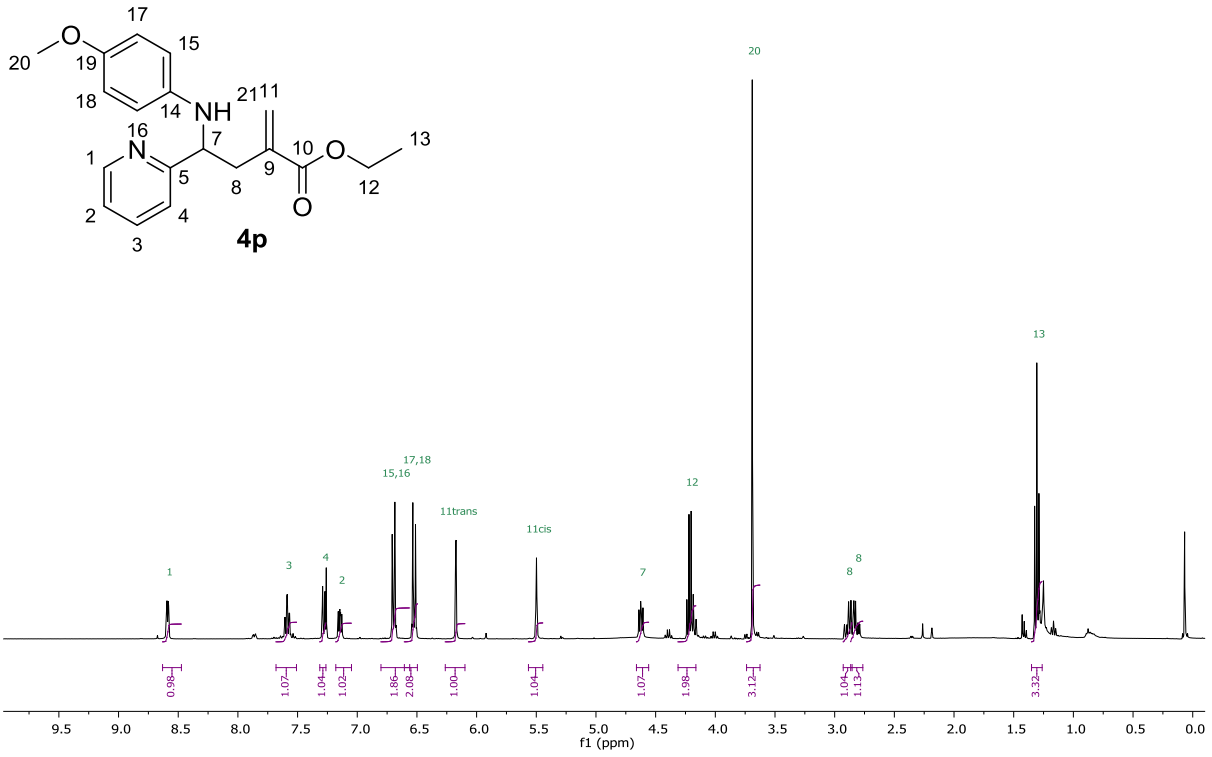

4m
f1 (ppm)

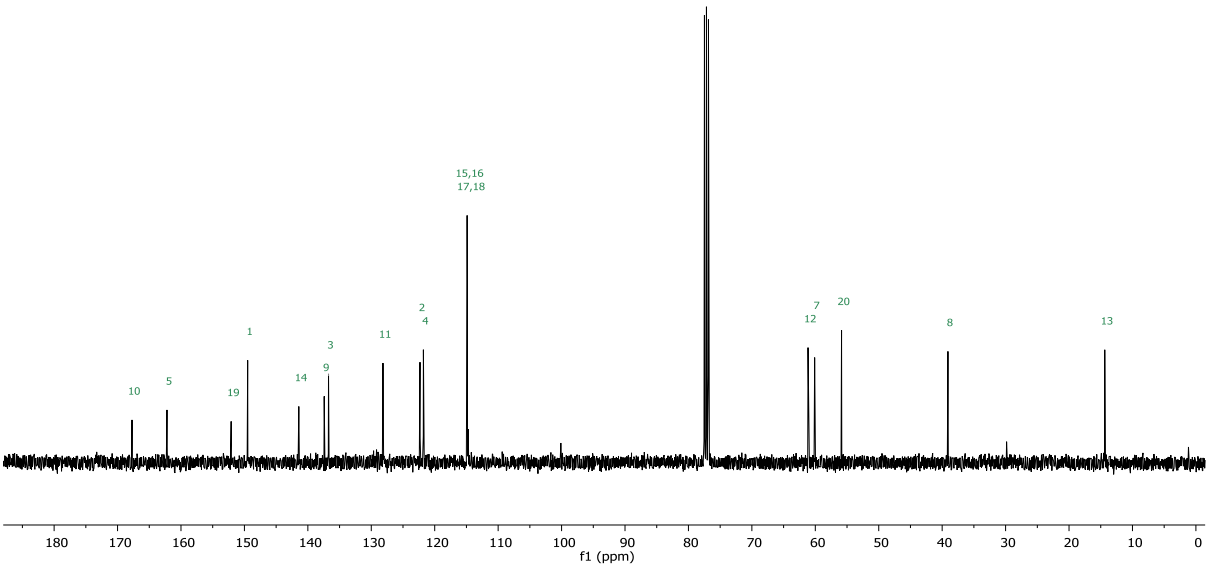

f1 (ppm)

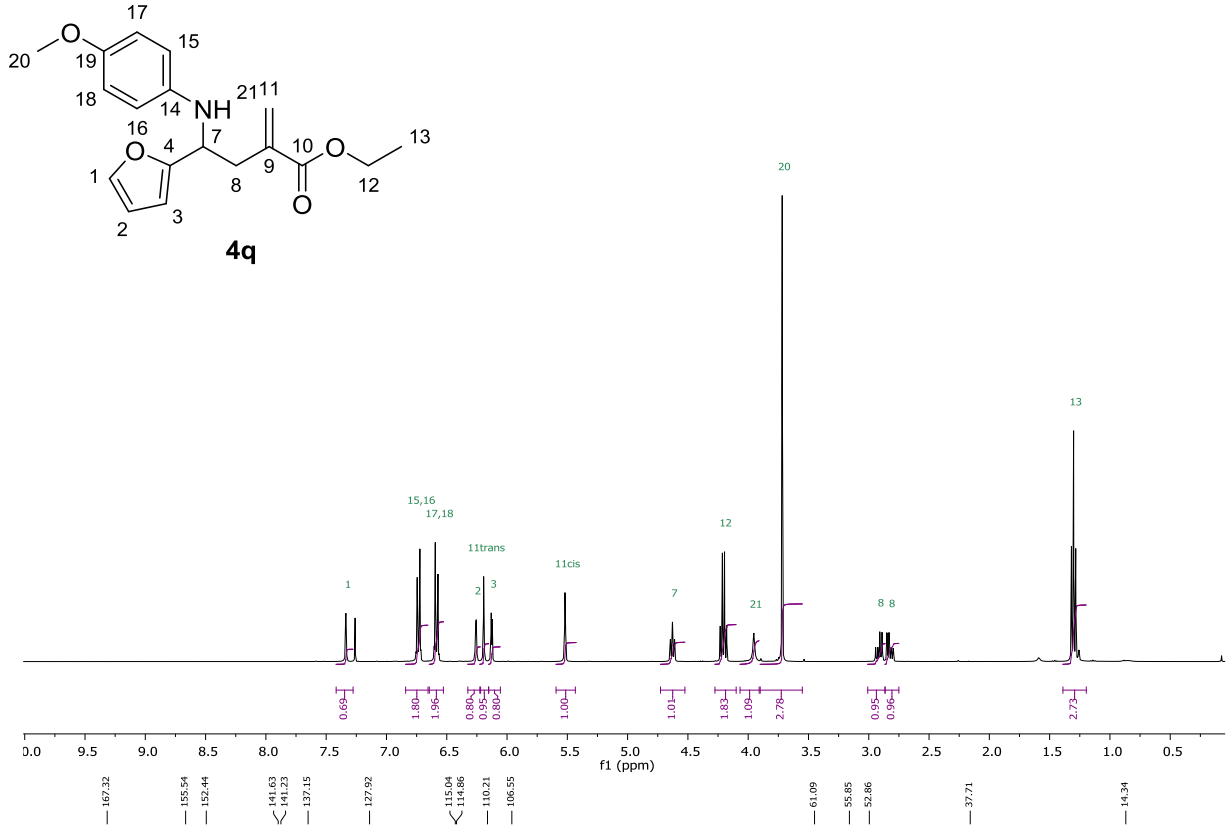

8.55 8.54 8.53 8.53
7.32 7.32 7.31 7.31 7.26
6.68 6.67 6.66 6.65 6.39 6.38 6.37 6.36 6.35 6.25
5.57 5.56
4.46 4.44 4.43 4.42 4.23 4.22 4.21 4.21
3.67 3.50 3.48 3.46 3.45 2.82 2.81 2.80 2.80 2.78 2.78 2.77 2.77 2.69 2.67 2.65 2.63
1.32 1.31 1.29 1.28
O
N
NH
4n
2,3
4,5
15,16 17,18
11trans
11cis
7
12
20
8 8
13
1.97
1.93
1.84
1.86
1.00
1.00
0.99
1.43
2.97
1.04
0.94
3.16
f1 (ppm)
167.24
153.22 152.33 150.03
140.92
136.93
128.42
121.86
114.86 114.57
77.48 77.16 76.84
61.32 57.88 55.79
40.82
14.28
17,18 15,16
2,3
4,5
6 19
10
14
9
11
12
7
20
8
13
f1 (ppm)

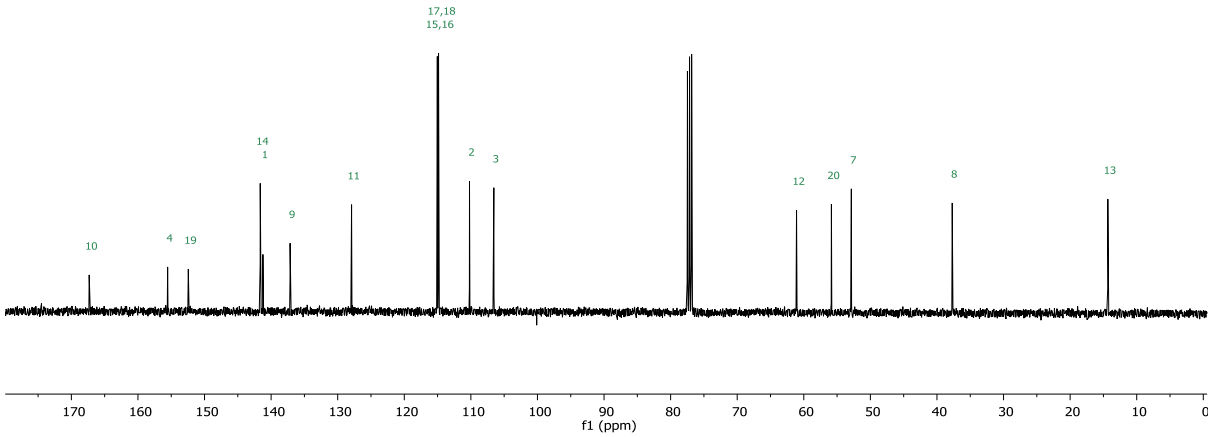

4o
f1 (ppm)

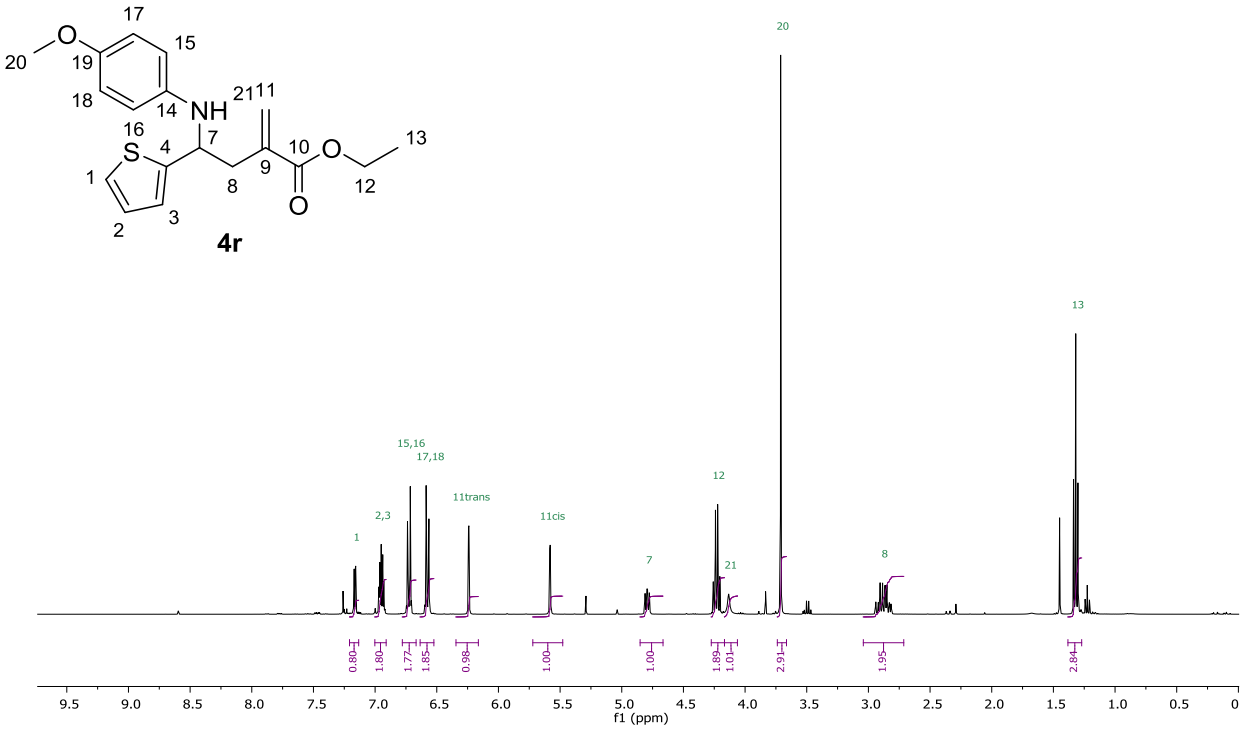

f1 (ppm)

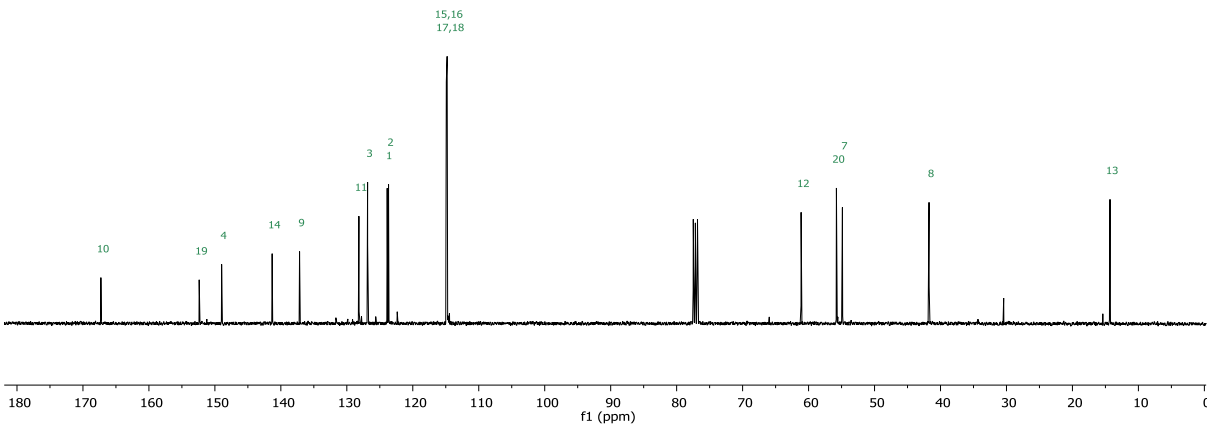

4p
f1 (ppm)

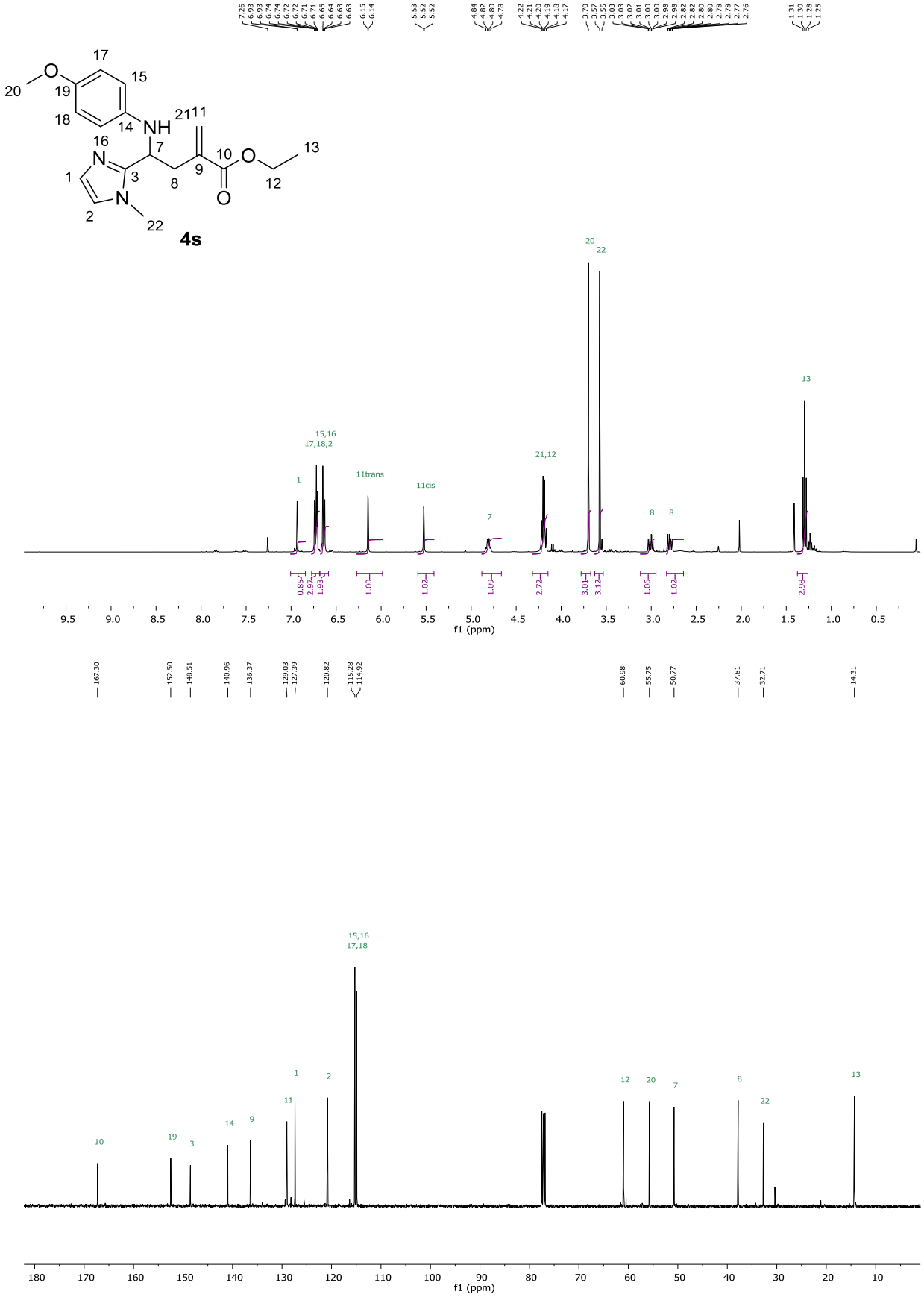

f1 (ppm)

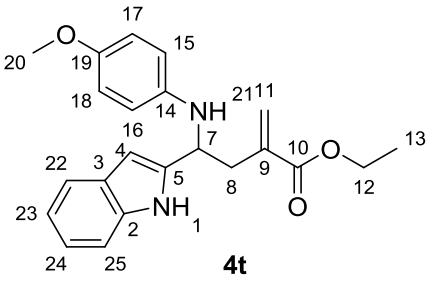

4q
f1 (ppm)


f1 (ppm)

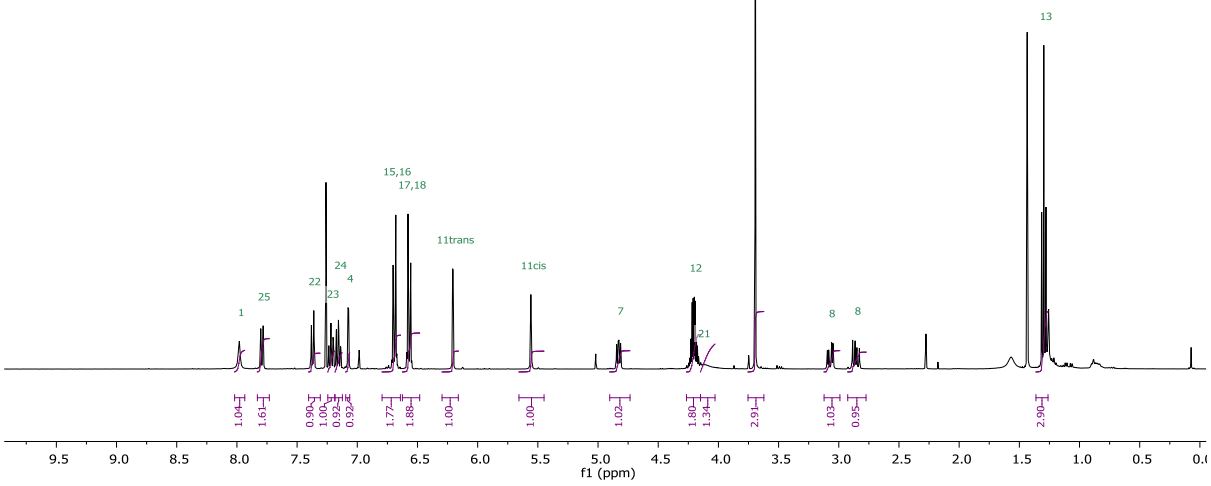

4r
f1 (ppm)

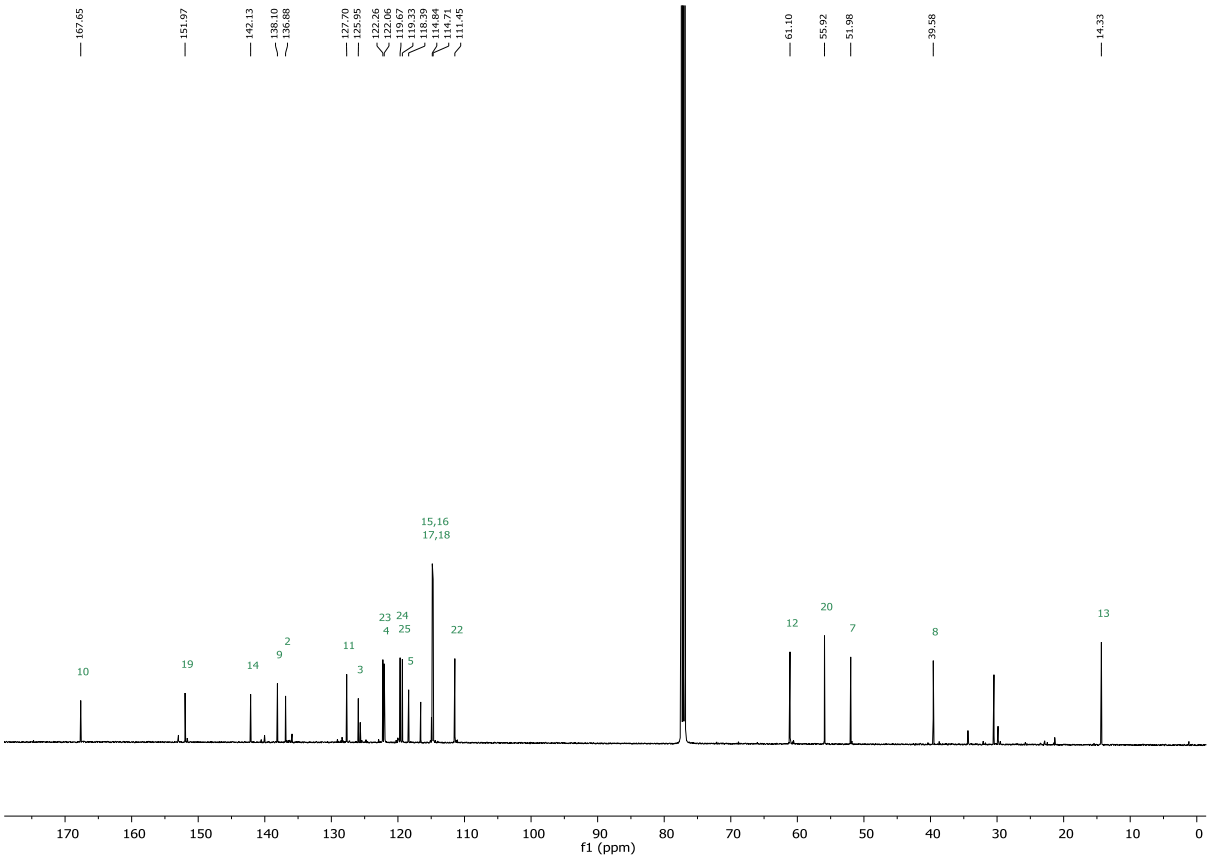

f1 (ppm)

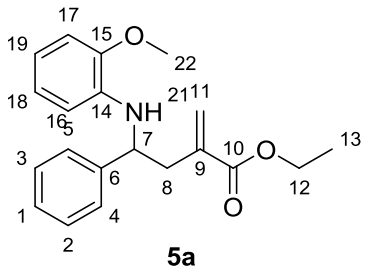

4s
f1 (ppm)
f1 (ppm)


17
O
15
20
19
18
14
NH
21
11
16
7
10
O
13
22
3
4
9
12
5
8
23
NH
1
O
2
24
25

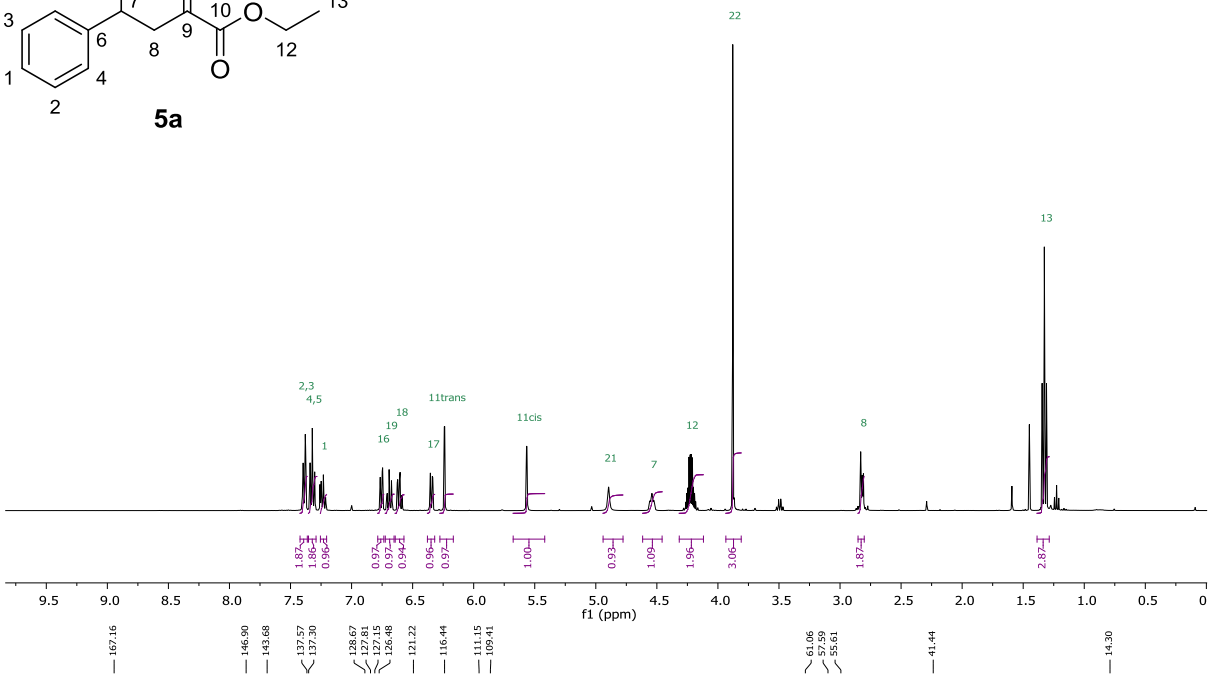
4t

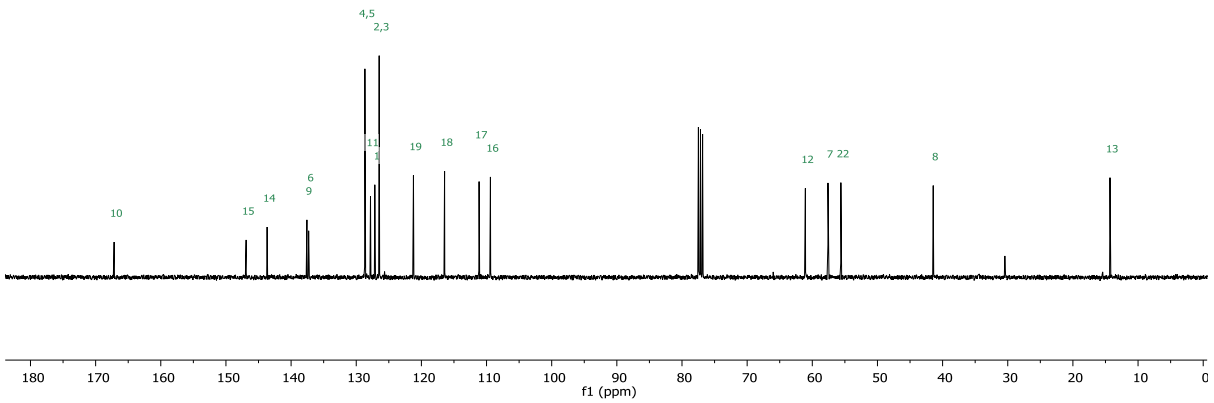

13
15,16
17,18
11trans
11cis
12
24
4
22
23
25
1
7
8
8
21
1.04
1.61
0.90
1.00
0.92
0.92
1.77
1.88
1.00
1.00
1.02
1.80
1.34
2.91
1.03
0.95
2.90
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

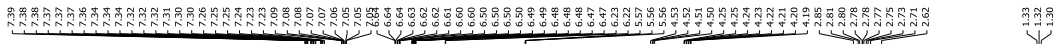

167.65
151.97
142.13
138.10
136.88
127.70
125.95
122.26
119.67
119.33
118.39
114.84
114.71
111.45
61.10
55.92
51.98
39.58
14.33
15,16
17,18
10
19
14
9
2
11
3
23
4
24
25
5
22
12
20
7
8
13
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

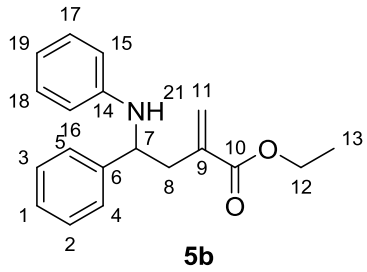


5a

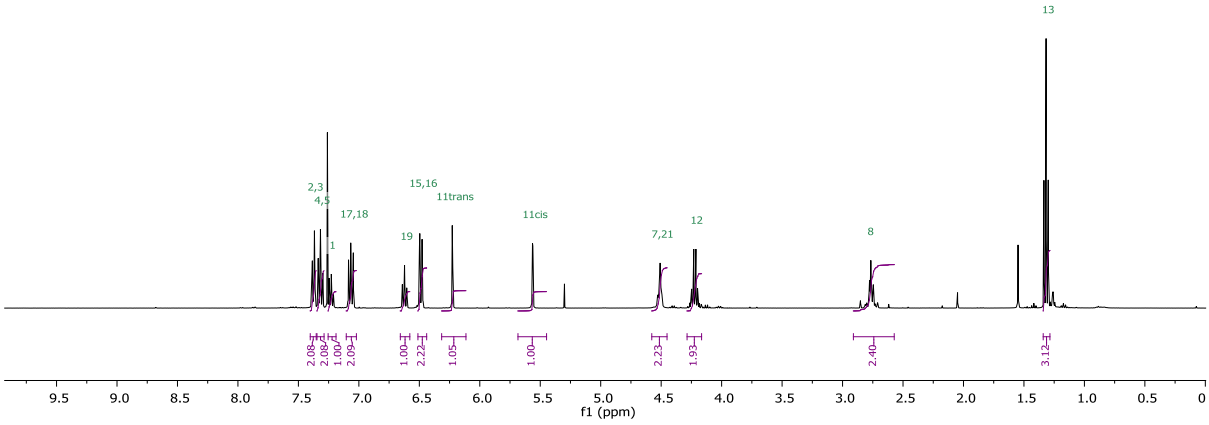

22
13
2,3
4,5
11trans
11cis
18
19
16
17
1
21
7
12
8
f1 (ppm)

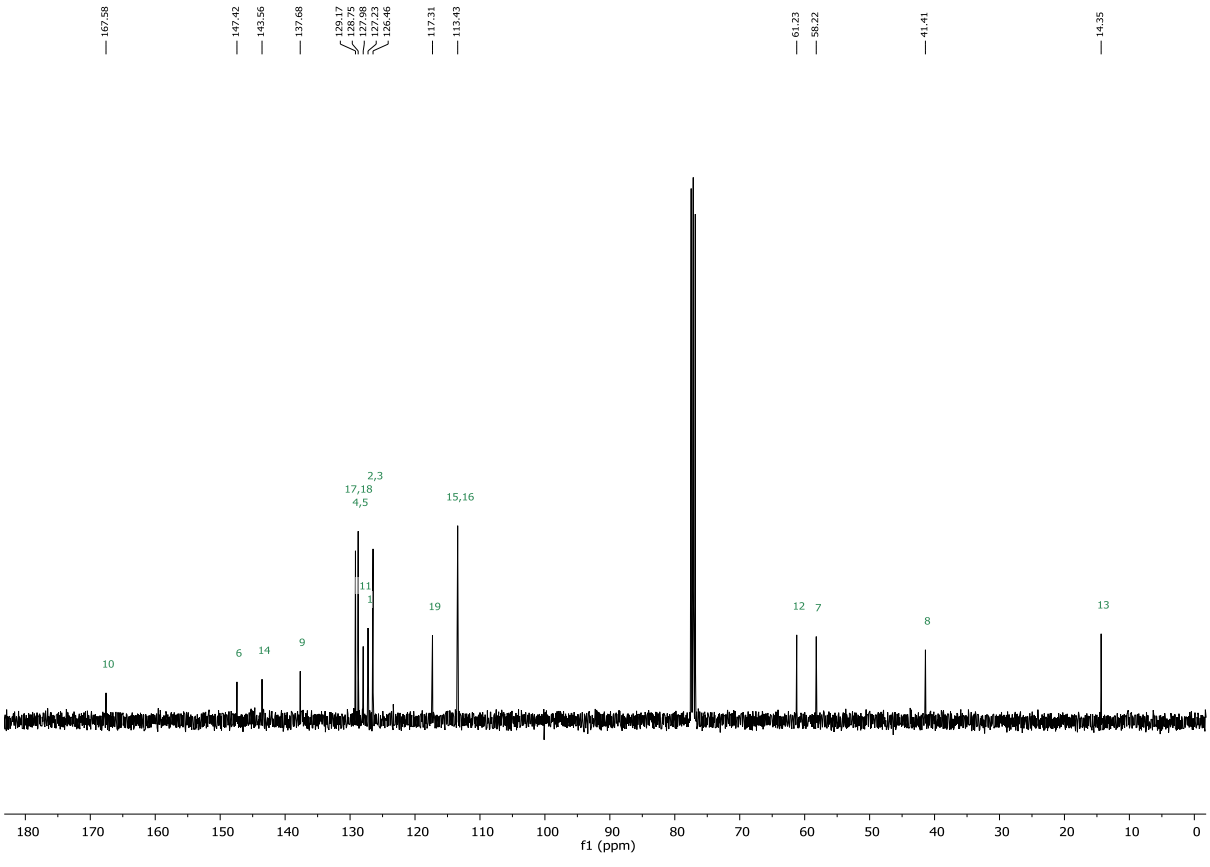

4,5
2,3
10
15
14
6
9
11
1
19
18
17
16
12
7 22
8
13
f1 (ppm)

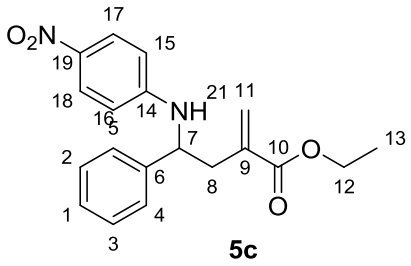



17
19
15
18
21
11
14
NH
16
5
7
10
O
13
3
6
9
8
12
1
4
O
2

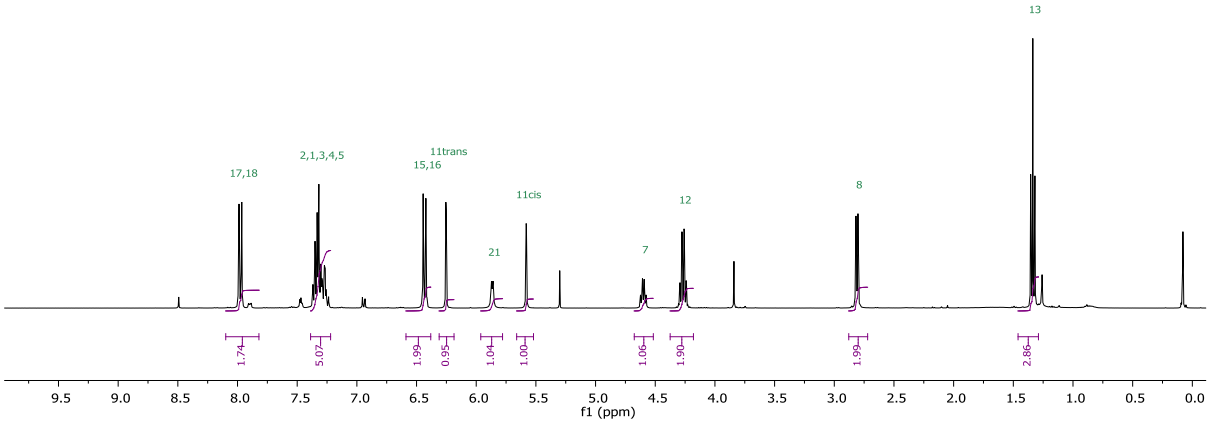
5b

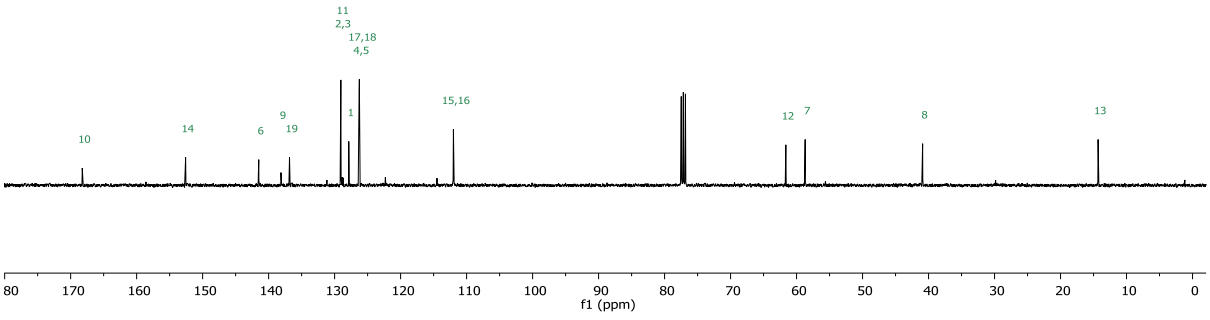

13
2,3
4,5
15,16
11trans
17,18
11cis
19
1
7,21
12
8
2.08
2.08
1.00
2.09
1.00
2.22
1.05
1.00
2.23
1.93
2.40
3.12
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

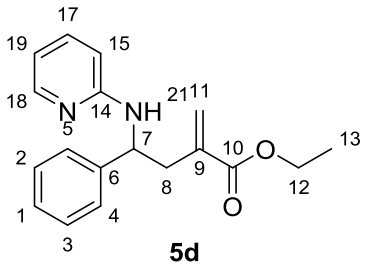

167.58
147.42
143.56
137.68
129.17
128.75
127.98
127.23
126.46
117.31
113.43
61.23
58.22
41.41
14.35
2,3
17,18
4,5
15,16
11
1
10
6
14
9
19
12
7
8
13
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


17
O_2N
15
19
18
21
11
NH
14
16
5
7
13
2
10
O
6
9
8
12
O
1
4
3

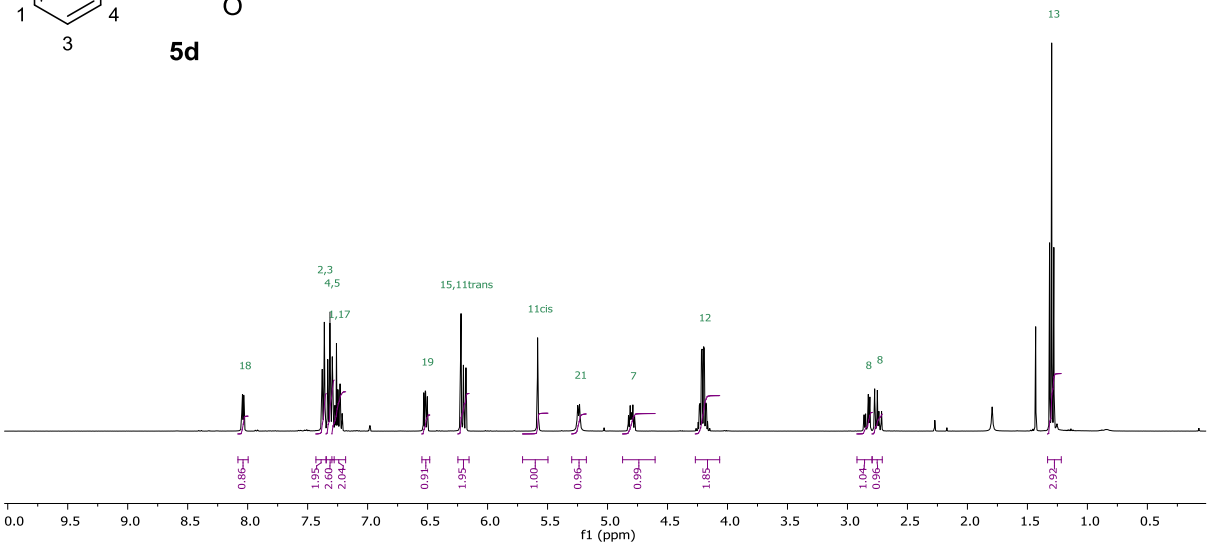
5c


13
17,18
2,1,3,4,5
11trans
15,16
11cis
21
12
8
7
1.74
5.07
1.99
0.95
1.04
1.00
1.06
1.90
1.99
2.86
f1 (ppm)

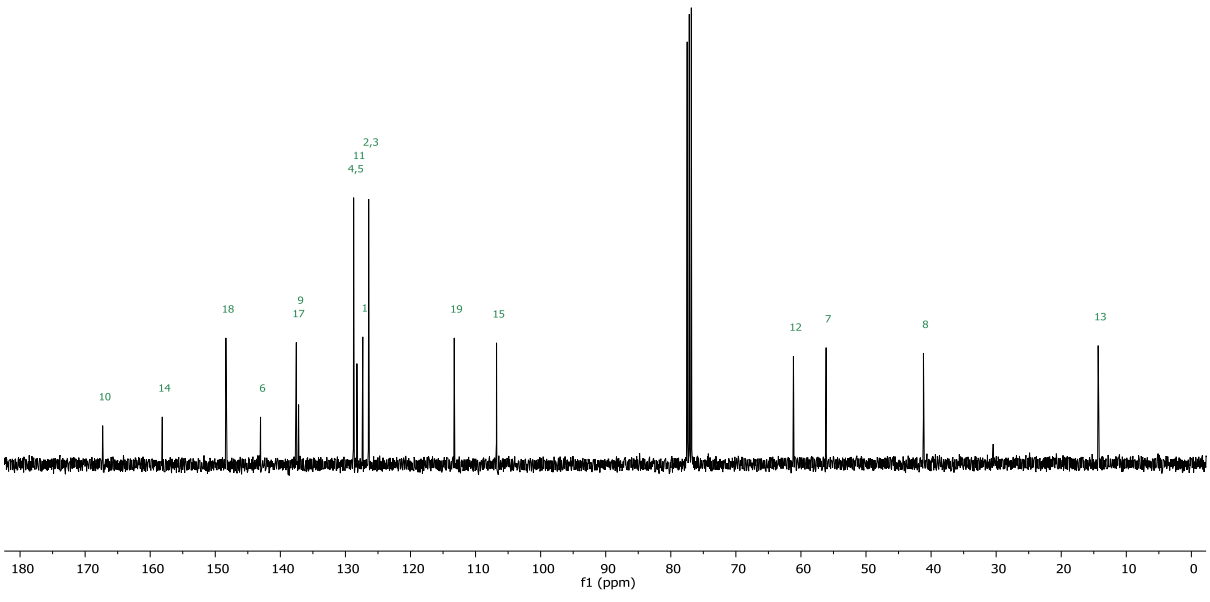

11
2,3
17,18
4,5
15,16
10
14
6
9
19
1
12
7
8
13
f1 (ppm)

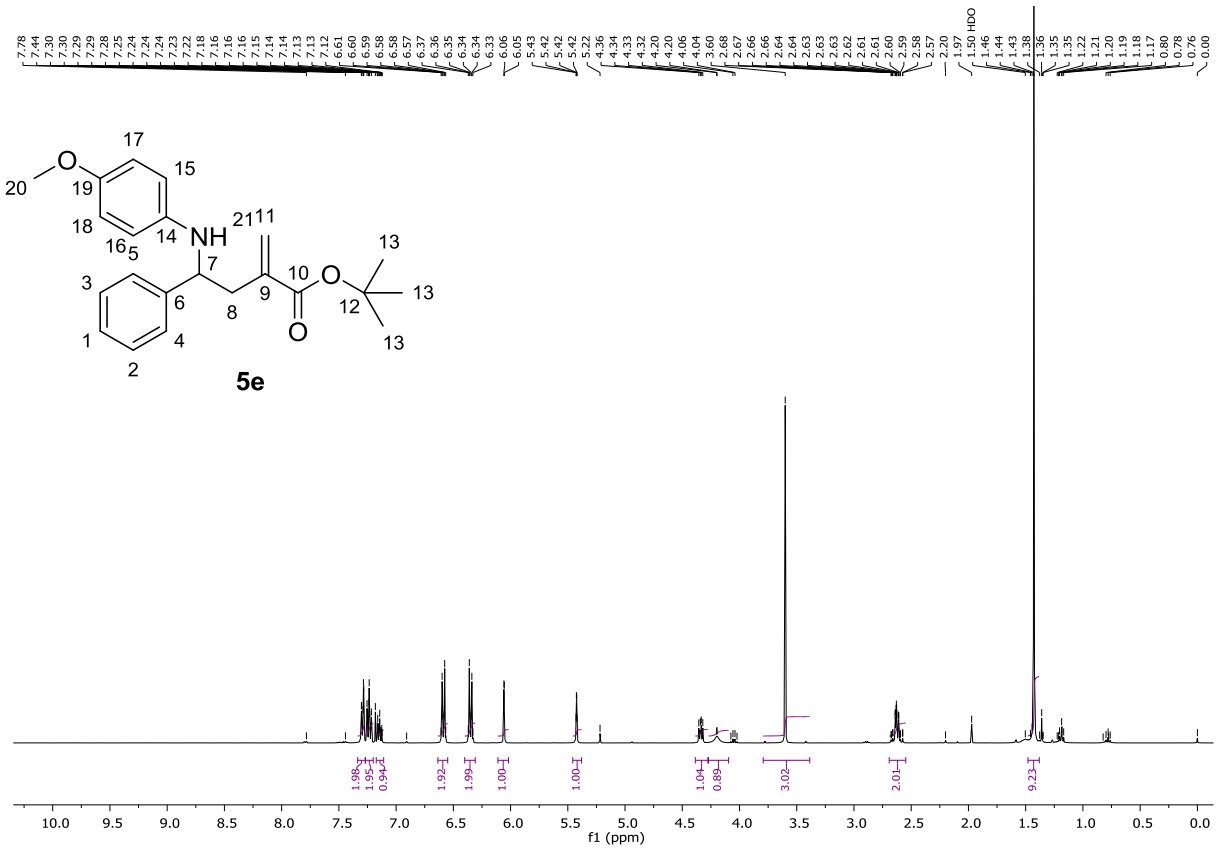

17
19
15
18
N
5
14
NH
21
11
7
10
O
13
2
6
9
8
12
1
4
O
3

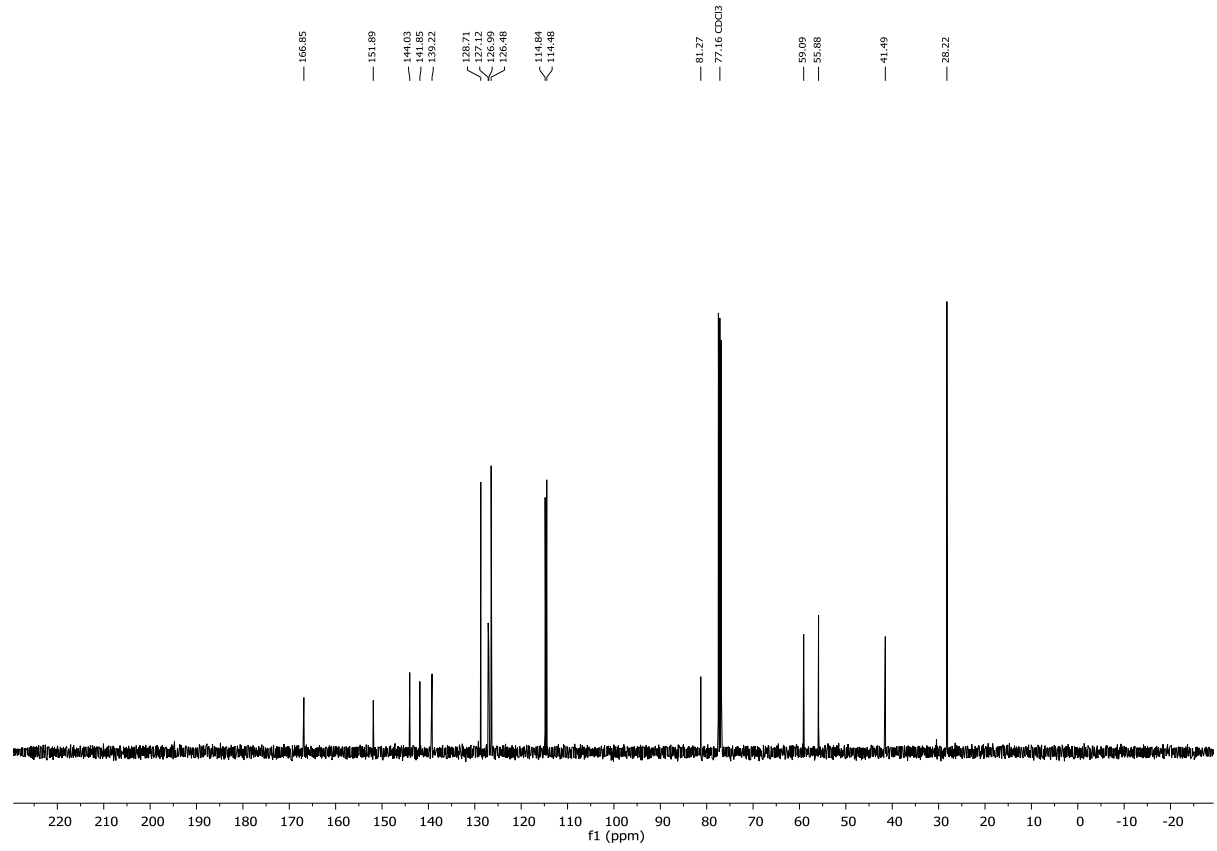
5d

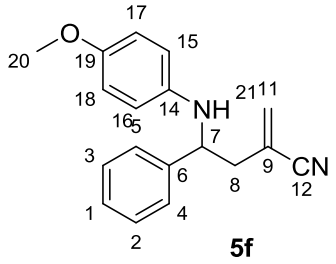

13
2,3
4,5
15,11trans
11cis
12
18
19
21
7
8
8
0.86
1.95
2.60
2.04
0.91
1.95
1.00
0.96
0.99
1.85
1.04
0.96
2.92
f1 (ppm)


167.31
158.15
148.37
143.05
137.55
137.20
128.74
128.23
127.33
126.43
113.28
106.78
61.15
56.13
41.17
14.32

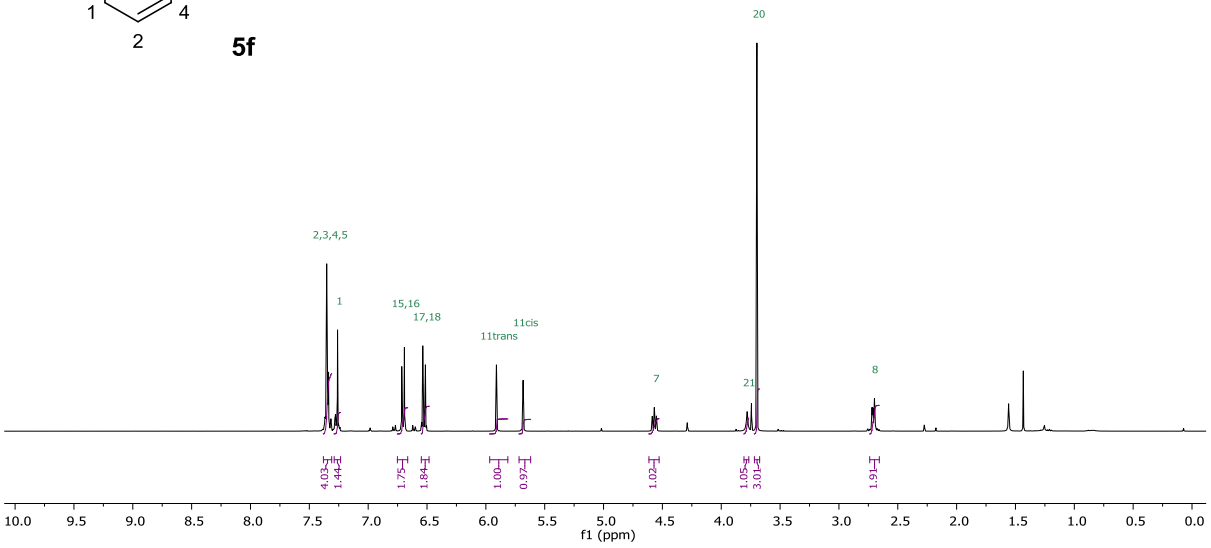

2,3
11
4,5
10
14
18
6
9
17
1
19
15
12
7
8
13
f1 (ppm)

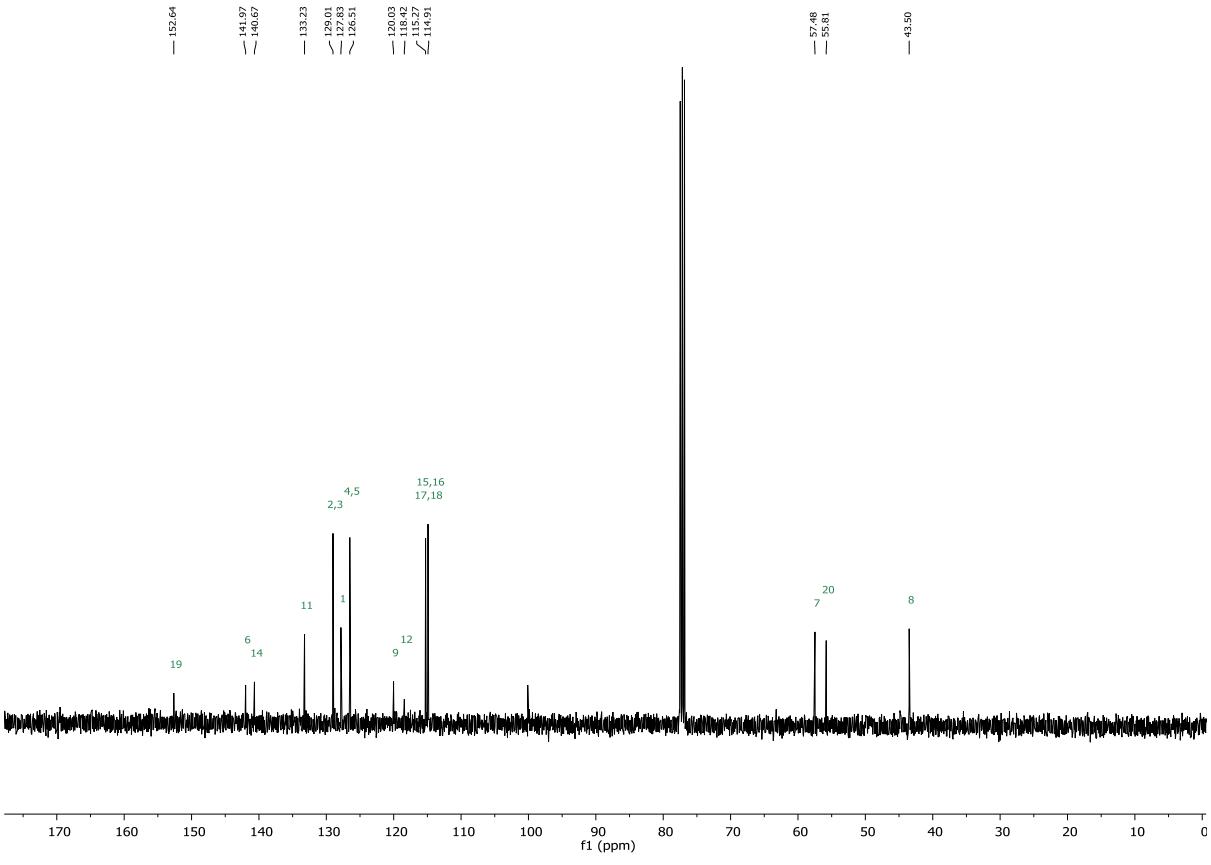

5e
f1 (ppm)

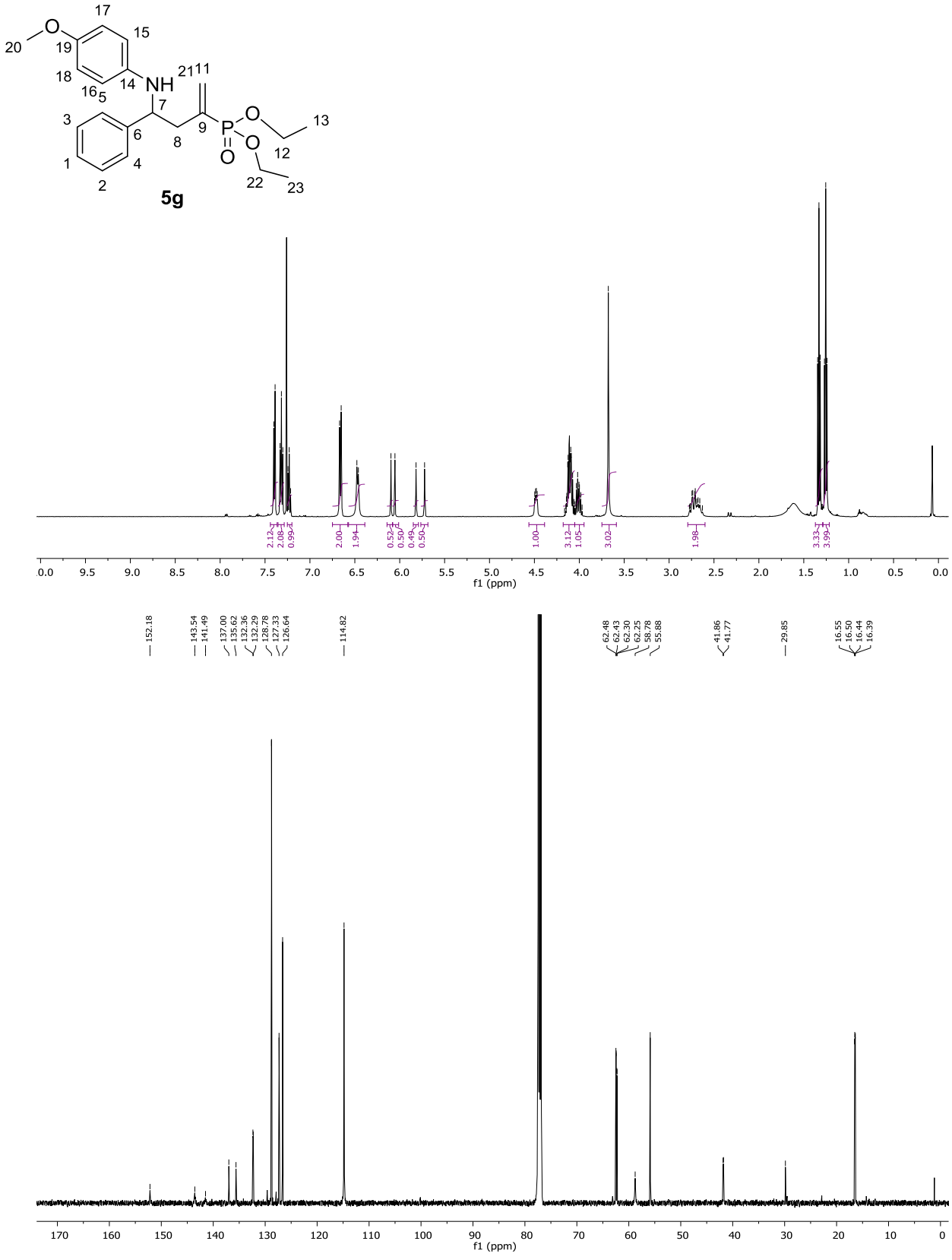

f1 (ppm)

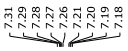

17
O
15
20
19
18
16
5
14
NH
21
11
7
3
6
9
CN
8
12
1
4
2

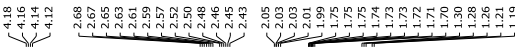
5f

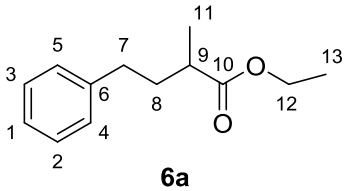

20
2,3,4,5
1
15,16
17,18
11cis
11trans
7
21
8
4.03
1.44
1.75
1.84
1.00
0.97
1.02
1.05
3.01
1.91
f1 (ppm)


152.64
141.97
140.67
133.23
129.01
127.83
126.51
120.03
118.42
115.27
114.91
57.48
55.81
43.50
2,3
4,5
15,16
17,18
11
1
6
14
19
9
12
7
20
8
f1 (ppm)

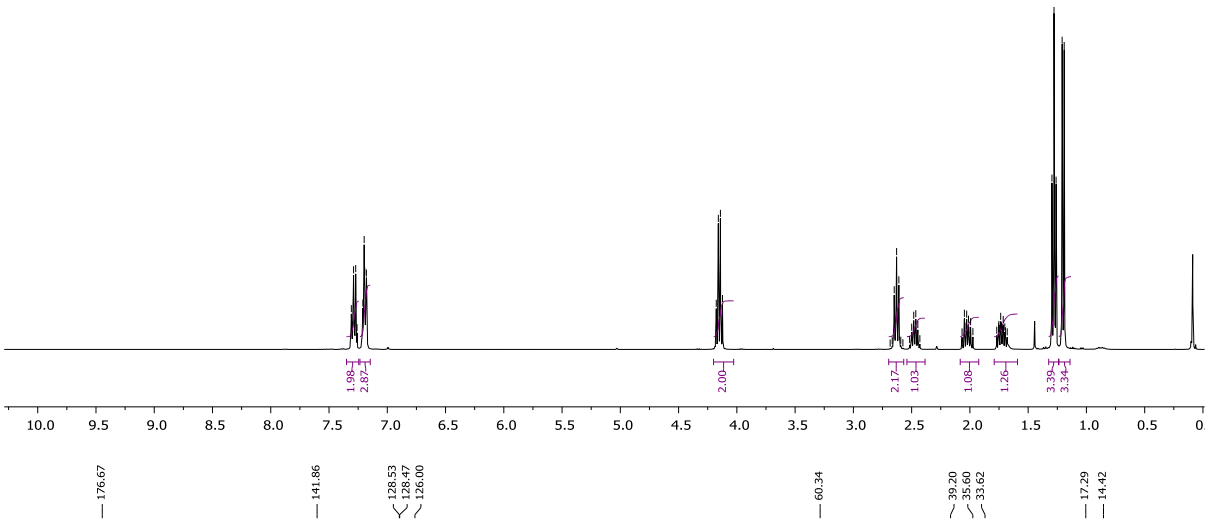

7.40 7.39 7.33 7.32 7.30 7.25 7.23 7.22 6.67 6.65 6.48 6.46 6.10 6.05 5.82 5.72
4.50 4.49 4.48 4.47 4.15 4.14 4.14 4.13 4.12 4.10 4.10 4.10 4.09 4.08 4.07 4.06 4.05 4.03 4.03 4.02 4.01 4.00 4.00 3.99 3.98 3.97 3.68 2.77 2.77 2.74 2.74 2.71 2.71 2.69 2.68 2.66 1.35 1.33 1.32 1.27 1.26
O 17 15 20 19 18 16 5 14 NH 21 11 7 3 6 8 9 P O 13 O 12 1 4 2 22 23
5g
2.12 2.08 0.99 2.00 1.94 0.52 0.50 0.49 0.50 1.00 3.12 1.05 3.02 1.98 3.33 3.99
f1 (ppm)
152.18 143.54 141.49 137.00 135.62 132.36 132.29 128.78 127.33 126.64 114.82 62.48 62.43 62.30 62.25 58.78 55.88 41.86 41.77 29.85 16.55 16.50 16.44 16.39
f1 (ppm)


7.31
7.29
7.28
7.27
7.26
7.21
7.20
7.19
7.18

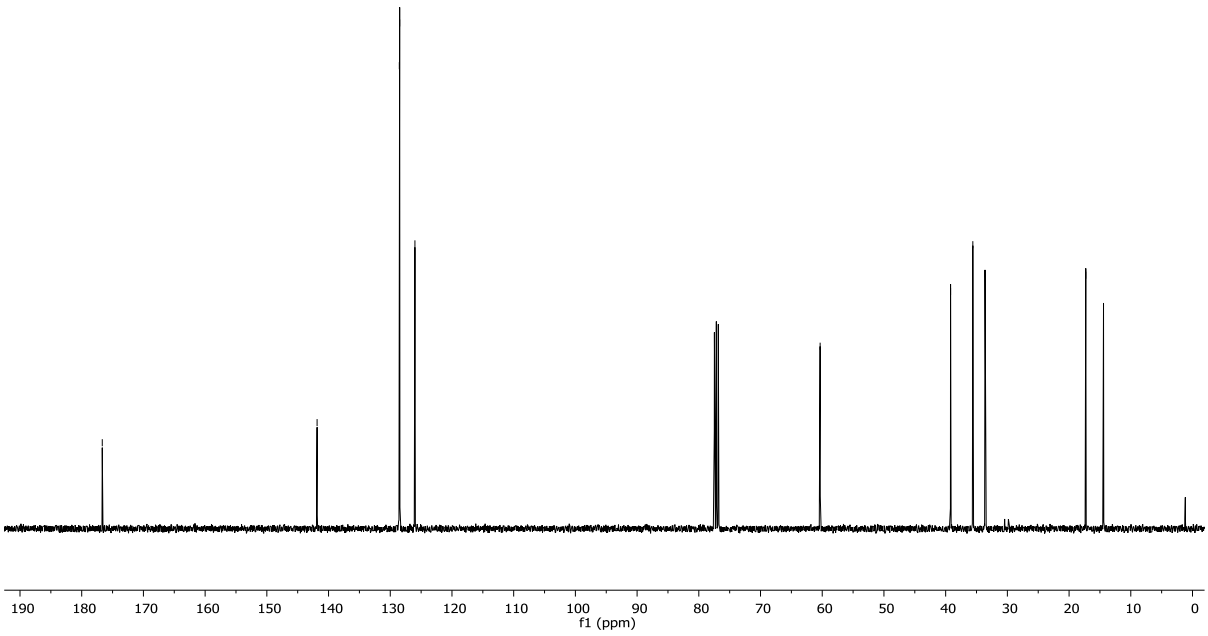

4.18
4.16
4.14
4.12
2.68
2.67
2.65
2.63
2.61
2.59
2.57
2.52
2.50
2.48
2.46
2.45
2.43
2.05
2.03
2.03
2.01
1.99
1.75
1.75
1.75
1.74
1.73
1.73
1.72
1.71
1.70
1.30
1.28
1.26
1.21

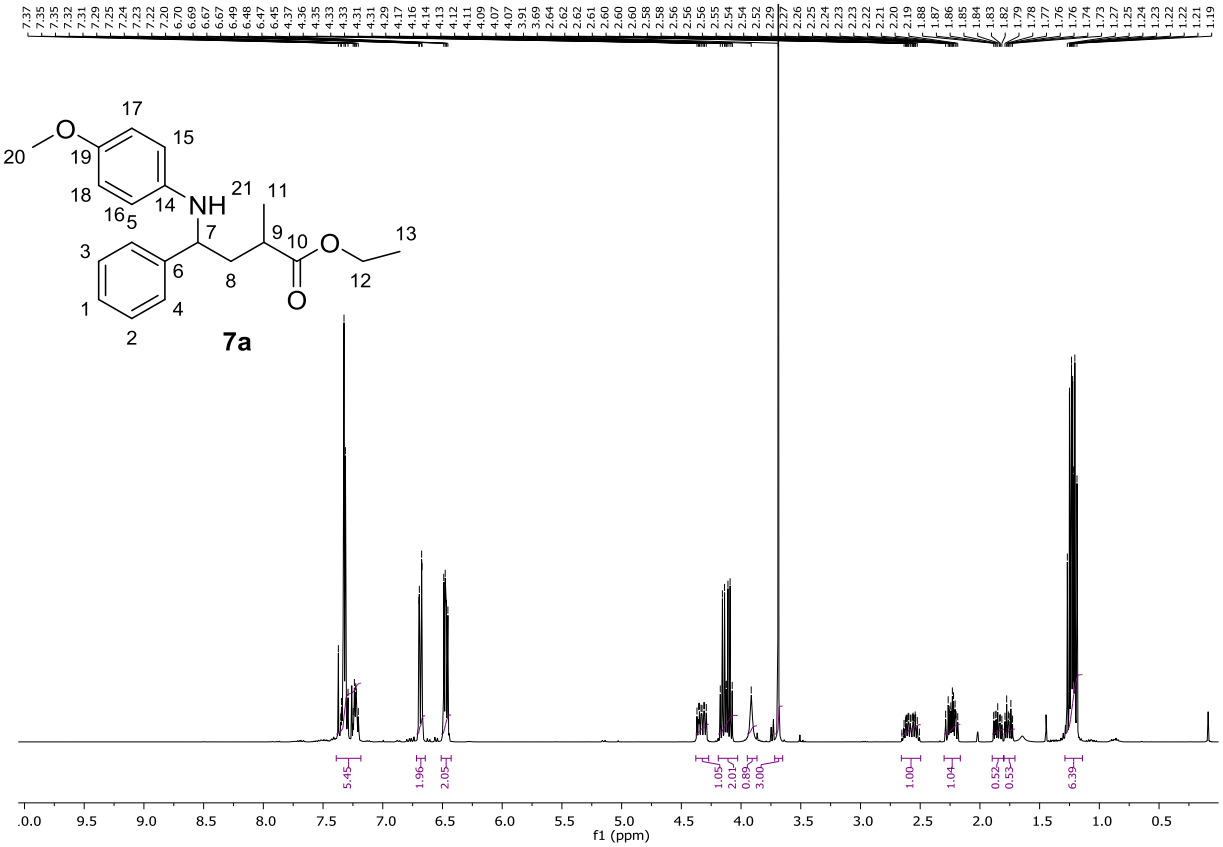

11
5
7
9
10
O
13
3
6
8
12
1
4
O
2

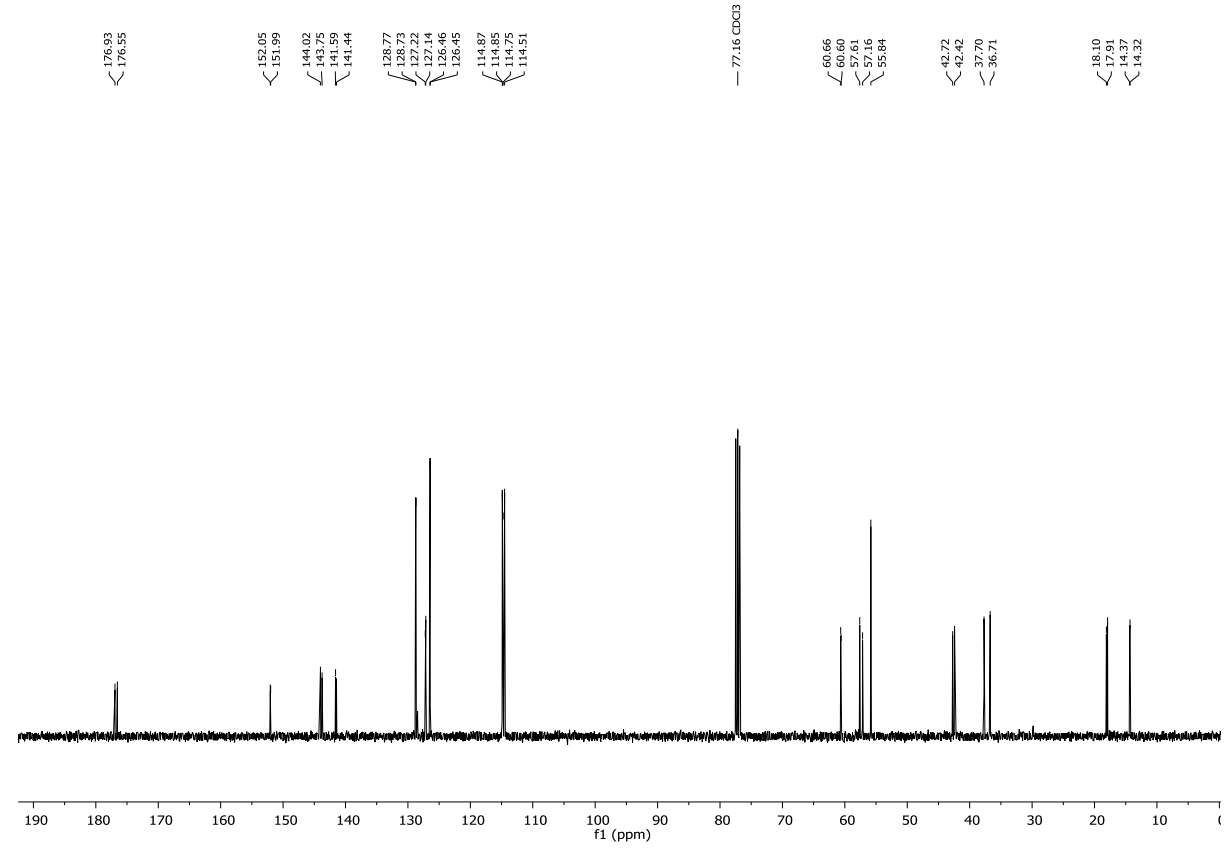
6a

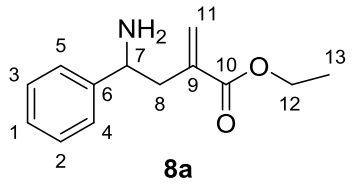

1.98
2.87
2.00
2.17
1.03
1.08
1.26
3.39
3.34
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0

176.67
141.86
128.53
128.47
126.00
60.34
39.20
35.60
33.62
17.29
14.42


190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

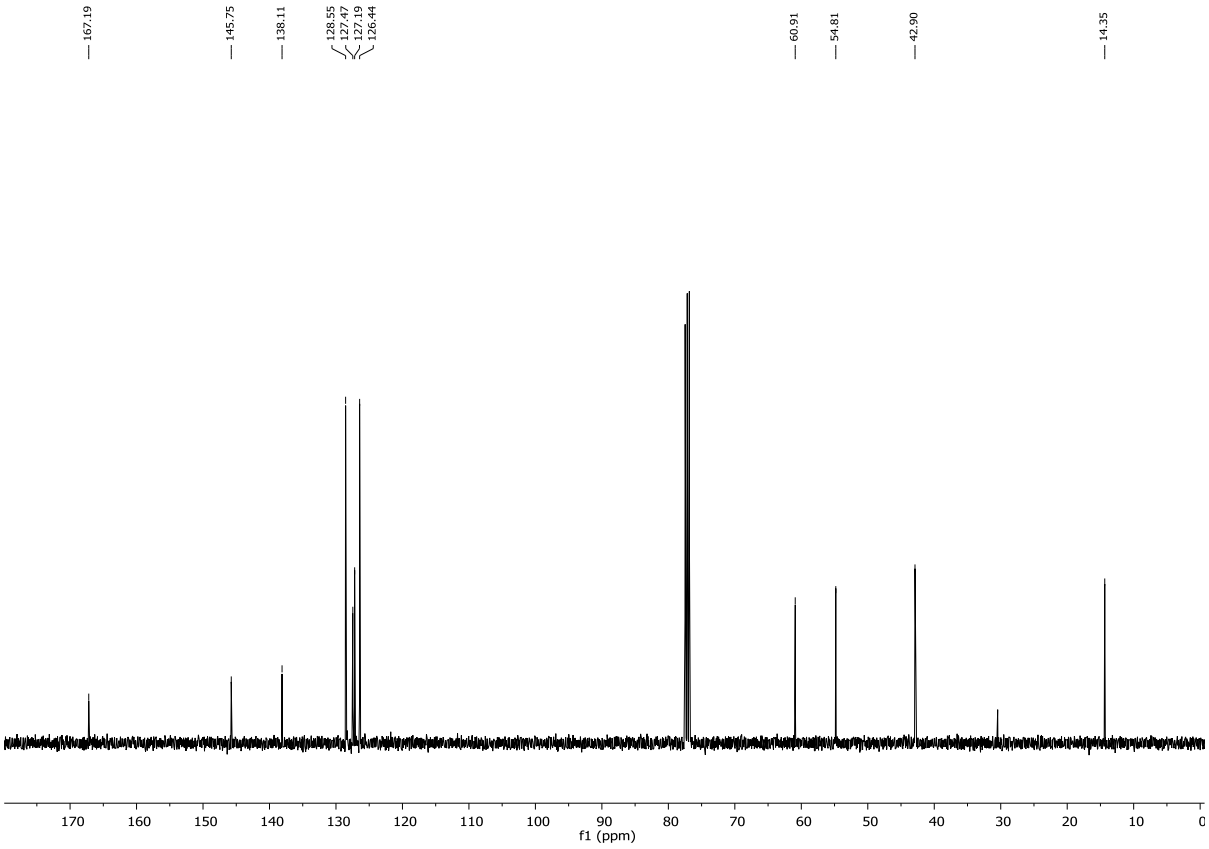

7a
f1 (ppm)

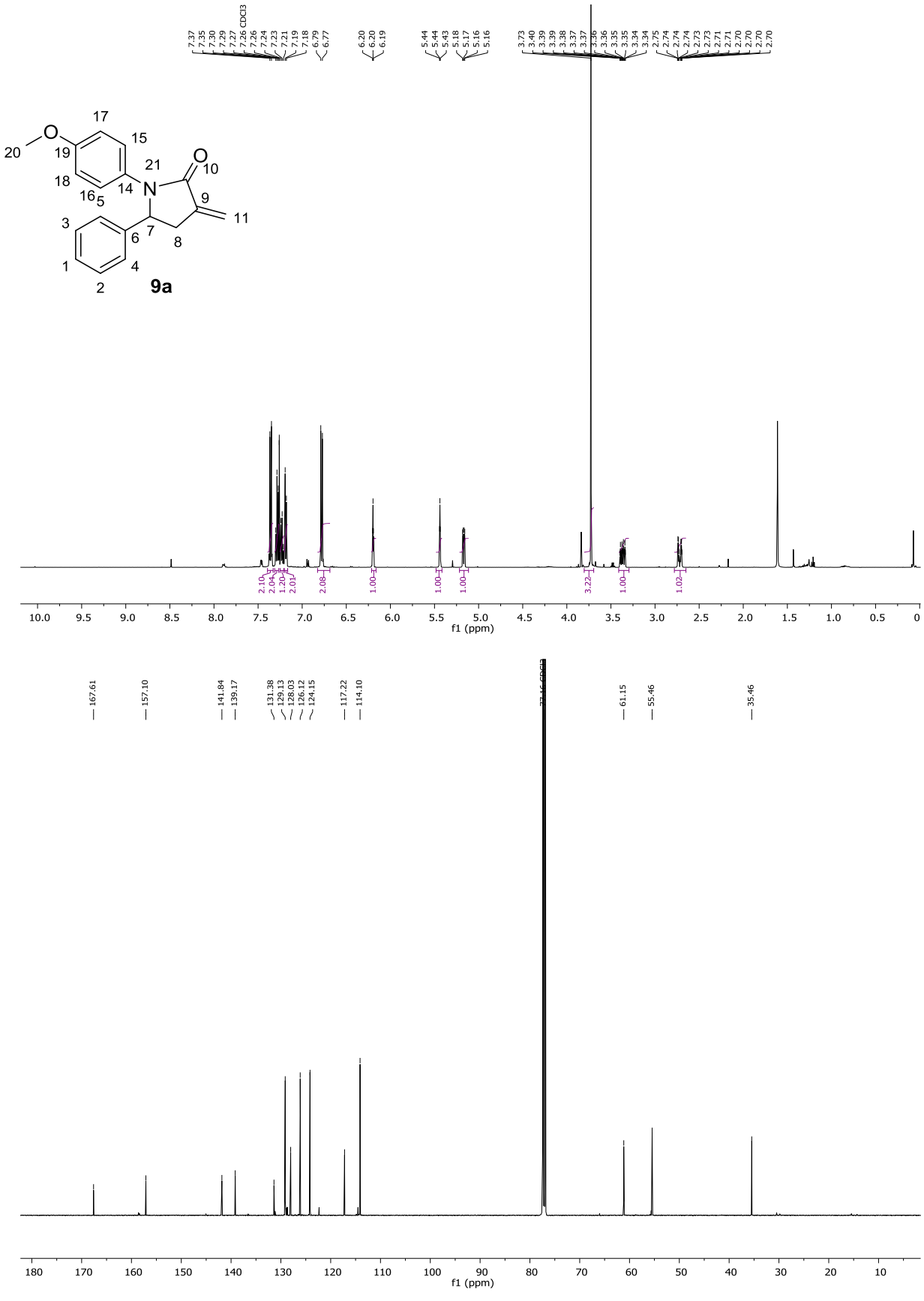

f1 (ppm)

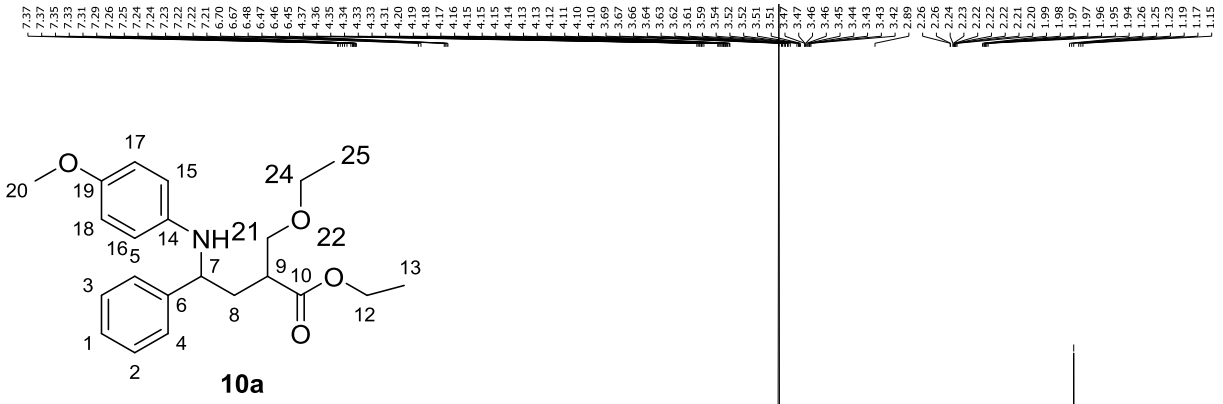

NH2
11
5
7
10
O
13
3
6
9
8
12
1
4
O
2

8a

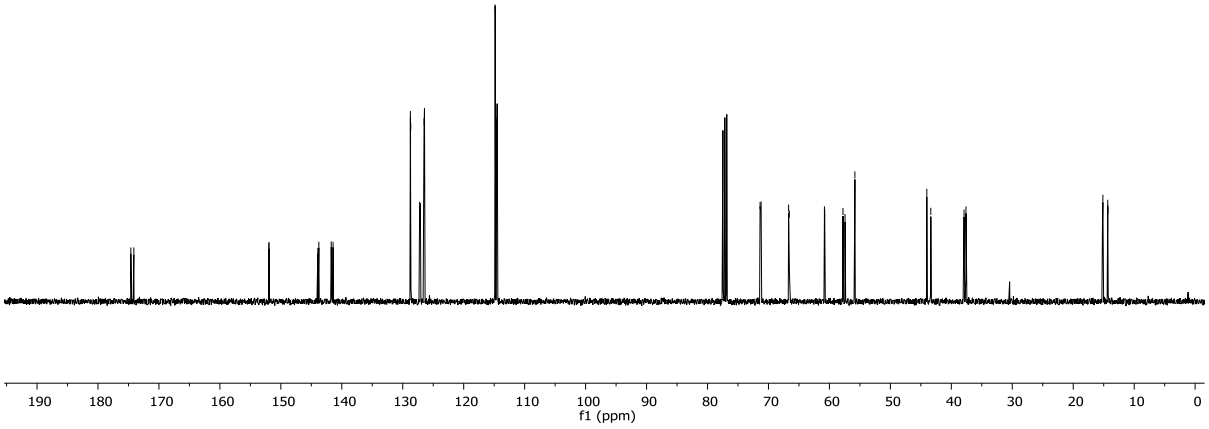
7.29
7.27
7.25
7.24
7.19
7.17
7.15
6.13
5.46
4.16
4.14
4.12
4.10
4.08
4.06
2.69
2.68
2.66
2.65
2.49
2.47
2.45
2.43
1.49
1.26
1.24
1.22
4.86
1.00
0.99
2.87
1.02
1.00
1.87
3.18
f1 (ppm)


167.19
145.75
138.11
128.55
127.47
127.19
126.44
60.91
54.81
42.90
14.35
f1 (ppm)


9a
f1 (ppm)
f1 (ppm)


10a

f1 (ppm)


f1 (ppm)

11. X-ray structure of compound **4m**