Supporting Information

Gold Meets Enamine Catalysis in the Enantioselective α-Allylic Alkylation of Aldehydes with Alcohols

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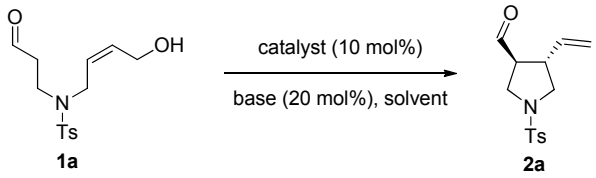
General Methods.

^{1}H-NMR spectra were recorded on Varian 200 (200 MHz), Varian 400 (400 MHz) spectrometers. Chemical shifts are reported in ppm from TMS with the solvent resonance as the internal standard (deuterochloroform: δ 7.27 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = duplet, , t = triplet, q = quartet, p = pseudo, b = broad, m = multiplet), coupling constants (Hz). ^{13}CNMR spectra were recorded on a Varian 200 (50 MHz), Varian 400 (100 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from TMS with the solvent as the internal standard (deuterochloroform: δ 77.0 ppm). GC-MS spectra were taken by EI ionization at 70 eV on a Hewlett-Packard 5971 with GC injection. They are reported as: *m/z* (rel. intense). LC-electrospray ionization mass spectra were obtained with Agilent Technologies MSD1100 single-quadrupole mass spectrometer. Chromatographic purification was done with 240-400 mesh silica gel. Anhydrous THF and DCM were distilled respectively from sodium-benzophenone and P_2O_5 prior to use; Other anhydrous solvents were supplied by Fluka or Sigma Aldrich in Sureseal® bottles and used without any further purification. Analytical high performance liquid chromatography (HPLC) was performed on a liquid chromatograph equipped with a variable wave-length UV detector (deuterium lamp 190-600 nm), using a Daicel Chiracel™ OD, OD-H, AD, IA, and IB column (0.46 cm I.D. x 25 cm) (Daicel Inc. HPLC grade isopropanol and hexane were used as the eluting solvents. Commercially available chemicals were purchased from Sigma Aldrich, Stream and TCI and used without any further purification. (*Z*)-allyl bromide **11** was obtained from commercially available (*Z*)-1,4-but-2-en-ol following a known procedure.[1]

[1] Oppolzer, W.; Moretti, R.; Zhou, C.; *Helv. Chim. Acta* **1994**, *77*, 2663-2668.

Catalytic system optimization.

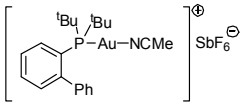
Table S1: Screening of gold catalysts and bases.



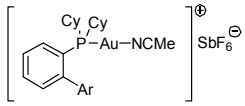
[a]:

Entry[a]	Catalyst	Solvent	Base	Yield% (time)[b]	*dr* (*trans:cis*)[c]
1	$AuCl_3$	DCM	pyrrolidine	21 (16h)	91:9
2	$[(PPh_3Au)_3O]BF_4$	THF	"	-	-
3	IPrAuOTf	DCM	"	-	-
4	$(PhO)_3PAu(OTf)$	THF	"	28 (4h)	76:24
5	**B**	THF	"	27 (4h)	95:5
6	$Ph_3PAuNTf_2$	THF	"	45 (4h)	93:7
7	**A**	THF	"	75 (4h)	95:5
8	**A**	DCM	"	45	93:7
9	**A**	THF	-	-	-
10[d]	**A**	THF	-	21 (11h)	95:5
11	**A**	THF	(Cy)NH(i-Pr)	15 (4h)	83:17
12	**A**	THF	$(i\text{-}Pr)_2NH$	15(4h)	84:16

Reaction conditions: **1a** (0.07 mmol) was dissolved in 0.4 mL of solvent, then metal catalyst (10 mol%) and the base (20 mol%) were added in sequence.



A



Ar: 2,4,6-tri-isopropylphenyl

B

[b]: Isolated yield after silica gel flash-chromatography.

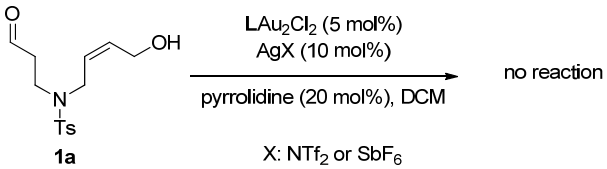
[c]: Determined after GC on the crude reaction mixture.

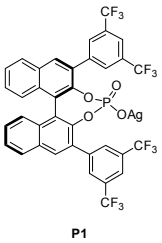
[d]: Reaction carried out at 60°C.

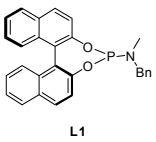
Typical reaction conditions for the gold catalyzed stereoselective cyclization (cationic gold chiral gold complexes were synthesized *in situ*)**.**

Reaction conditions: [AuCl(DMS)] (10 mol%) and the ligand (5 mol%) were dissolved in 0.5 mL of DCM. After stirring for 30 minutes the solvent was removed under vacuum. The gold complex was dissolved in 0.5 mL of DCM, the silver salt (10 mol%) was added and the reaction mixture was stirred for 30 minutes in the dark. A solution of **1a** (0.07 mmol) in 0.5 mL of DCM was added, followed by pyrrolidine (20 mol%). The reaction was stirred at rt and monitored by TLC and GC.

Table S2: Screening of chiral gold catalysts.







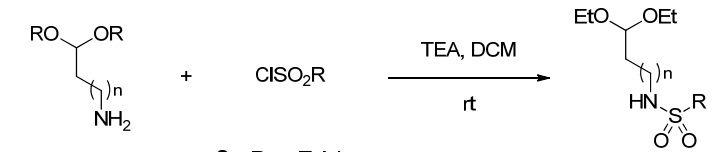
Entry	Ligand	Silver Salt	Yield%
1	(*R*)-OMe-BIPHEP	$AgNTf_2$	-
2	(*R*)-OMe-BIPHEP	$AgSbF_6$	-
3	(*S*)-DTBM-SEGPHOS	$AgSbF_6$	-
4	(*S*)-BINAP	$AgSbF_6$	-
5	PPh_3[a]	**P1**	-
6	**L1**[b]	$AgSbF_6$	-

[a]: Preformed Ph_3PAuCl was employed.

[b]: 10 mol% of ligand were employed.

Synthetic procedures and characterization of unknown compounds.

General procedure for the synthesis of sulfonamides 9a-c.

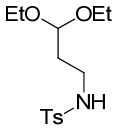


7a: R = Et, n =1
7b: R = Me, n =2

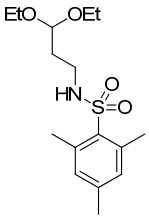
8a: R = *p*Tolyl
8b: R = Mesityl
8c: R = 2-thienyl

9a-c
9j

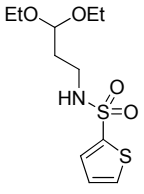
In an oven dried round bottom flask under nitrogen atmosphere 3,3-diethoxypropan-1-amine **7a-b** (5 mmol, 1 eq.) was dissolved in 20 mL of DCM and the solution was cooled to 0 °C. TEA (10 mmol, 2 eq.) and the appropriate sulfonyl chloride **8a-c** (6 mmol 1.2 eq.) were added. The reaction mixture was stirred at rt overnight and then quenched with saturated $NaHCO_3$ solution (20 mL). The organic phase was separated and the aqueous layer was extracted with DCM (2 x 20 mL). The combined organic phases were washed with brine and dried over Na_2SO_4. The volatiles were evaporated under reduced pressure and the residue was purified by flash-chromatography, eluting with cyclohexane ethyl acetate mixture, to afford the pure product as a clear oil in nearly quantitative yield.



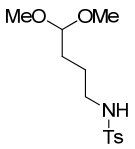
N*-(3,3-diethoxypropyl)-4-methylbenzenesulfonamide (9a)** was prepared from **7a** and **8a** according to the general procedure. Flash chromatography (c-Hex:AcOEt = 85:15). Yield = 90% (pale yellow oil)**.** ***^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 5.14 (t, *J* = 6.0 Hz, 1H), 4.49 (t, *J* = 4.8 Hz, 1H), 3.65-3.48 (m, 2H), 3.46-3.40 (m, 2H), 3.06 (q, *J* = 6.0 Hz, 2H), 2.43 (s, 3H), 1.77 (dt, *J* = 6.0 Hz, *J* = 4.8 Hz, 2H), 1.18 (t, *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 143.2, 136.9, 129.6 (2 C), 127.1 (2 C), 102.0, 62.1 (2 C), 39.2, 32.6, 21.4, 15.2 (2 C). ***ESI-MS*** (m/z): 625 $[2M+Na]^+$, 465, 419, 324 $[M+Na^+]$.



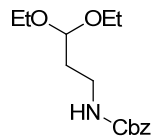
N*-(3,3-diethoxypropyl)-2,4,6-trimethylbenzenesulfonamide (9b)** was prepared from **7a** and **8b** according to the general procedure. Flash chromatography (c-Hex:AcOEt = 70:30). Yield = 91% (clear oil)**.** ***^{1}H-NMR (200 MHz, $CDCl_3$) δ 6.96 (s, 2H), 5.30 (bt, *J* = 5.8 Hz, 1H), 4.51 (t, *J* = 5.2 Hz, 1H), 3.70-3.55 (m, 2H), 3.52-3.37 (m, 2H), 3.04 (q, *J* = 5.8 Hz, 2H), 2.65 (s, 6H), 2.31 (s, 3H), 1.77 (pq, *J* = 5.6 Hz, 2H), 1.18 (t *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 141.9, 139.0 (2C), 133.7, 131.9 (2C), 102.2, 62.1 (2C), 38.5, 32.5, 22.9 (2C), 20.9, 15.2 (2C). ***ESI-MS*** (m/z): 681 $[2M+Na]^+$, 352 $[M+Na]^+$.



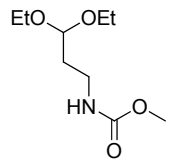
N*-(3,3-diethoxypropyl)thiophene-2-sulfonamide** (**9c**) was prepared from **7a** and **8c** according to the general procedure. Flash chromatography (c-Hex:AcOEt = from 8:2 to 6:4). Yield = 86% (clear oil)**.** ***^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.61-7.58 (m, 2H), 7.09 (dd, *J* = 5.0 Hz, *J* = 3.8 Hz, 1H), 5.34 (bs, 1H), 4.52 (t, *J* = 5.0 Hz, 1H), 3.68-3.56 (m, 2H), 3.53-3.38 (m, 2H), 3.16 (q, *J* = 5.8 Hz, 2H), 1.81 (pq, *J* = 5.8 Hz, 2H), 1.19 (t, *J* = 7.0 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 141.0, 132.0, 131.6, 127.3, 101.2, 62.2 (2 C), 39.5, 32.4, 15.2 (2 C). ***ESI-MS*** (m/z): 449, 316 $[M+Na]^+$, 219.



N*-(4,4-dimethoxybutyl)-4-methylbenzenesulfonamide** (**9j**) was prepared from **7b** and **8a** according to the general procedure. Flash chromatography (c-Hex:AcOEt = from 8:2). Yield = quantitative (clear oil). ***^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 2H), 7.31 (d, *J* = 7.6 Hz, 2H), 4.60 (bt, *J* = 6.0 Hz, 1H), 4.30 (t, *J* = 5.6 Hz, 1H), 3.29 (s, 6H), 2.97 (q, *J* = 6.0 Hz, 2H), 2.43 (s, 3H), 1.59-1.51 (m, 4H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 143.3, 135.4, 129.5 (2C), 127.0 (2C), 91.4, 54.9 (2C), 47.1, 32.3, 22.8, 21.2. ***ESI-MS*** (m/z): 597, 310 $[M+Na]^+$, 256 $[M-MeO]^+$, 224.

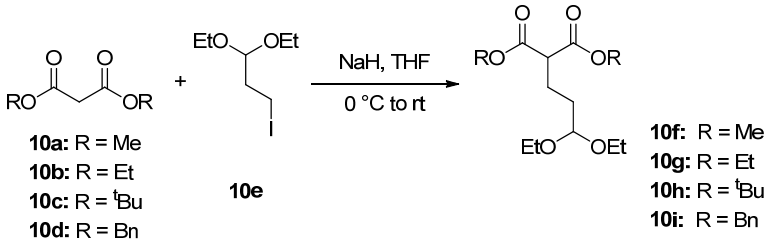


Benzyl (3,3-diethoxypropyl)carbamate (**9d**)**:** In an oven dried round bottom flask under nitrogen atmosphere 3,3-diethoxypropan-1-amine **7a** (3 mmol, 1 eq.) was dissolved in 15 mL of DCM. The solution was cooled to 0 °C, TEA (3.9 mmol, 1.3 eq.) and benzyl chloroformate (3.6 mmol, 1.2 eq.) were added. The reaction mixture was stirred at rt overnight and then quenched with 1M HCl solution (10 mL). The organic phase was then washed with $NaHCO_3$ saturated solution, brine and dried over Na_2SO_4. The volatiles were evaporated under reduced pressure and the residue was purified by flash-chromatography (c-Hex:AcOEt 7:3) affording the pure product as a clear oil in 81% yield. ***^{1}H-NMR*** (200 MHz, $CDCl_3$) δ 7.28-7.18 (m, 5H), 5.11 (bs, 1H), 5.02 (s, 2H), 4.48 (t, *J* = 5.4 Hz, 1H), 3.62-3.50 (m, 2H), 3.49-3.37 (m, 2H), 3.23 (pq, *J* = 6.0 Hz, 2H), 1.76 (pq, *J* = 6.0 Hz, 2H), 1.13 (t, *J* = 7.0 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 156.2, 136.2, 128.3 (3 C), 127.8 (2 C), 101.8, 66.3, 61.5 (2 C), 37.0, 33.3, 15.2 (2 C). ***ESI-MS*** (m/z): 304 $[M+Na]^+$, 236 $[M-EtO]^+$.

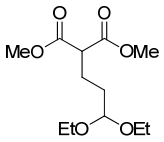


Methyl (3,3-diethoxypropyl)carbamate (**9e**): In an oven dried round bottom flask under nitrogen atmosphere 3,3-diethoxypropan-1-amine **7a** (3 mmol, 1 eq.) was dissolved in 15 mL of DCM. The solution was cooled to 0 °C, then diisopropyl ethyl amine (3.6 mmol, 1.2 eq.) and methyl chloroformate (3.6 mmol, 1.2 eq.) were added. The reaction mixture was stirred at rt overnight and then quenched with $NaHCO_3$ saturated solution (10 mL). The aqueous layer was extracted with DCM (3 x 10 mL) and the combined organic phases were washed with brine and dried over Na_2SO_4. After solvent evaporation the product was collected as a clear oil in quantitative yield and used in the following synthetic steps without further purification. ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 5.15 (bs, 1H), 4.55 (t, *J* = 5.6 Hz, 1H), 3.70-3.62 (m, 5H), 3.53-3.47 (m, 2H), 3.31-3.26 (m, 2H), 1.82 (q, *J* = 5.6 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 156.8, 101.6, 61.3, 51.5 (2C), 36.8, 33.2, 14.9 (2C). ***ESI-MS*** (m/z): 228 $[M+Na]^+$, 160.

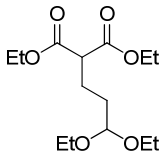
General procedure for the alkylation of malonates 10a-d.



In an oven dried Schlenk tube, under nitrogen atmosphere, 2.4 mmol (1.2 eq.) of malonate **10a-d** were dissolved in 15 ml of anhydrous THF and cooled to 0 °C. NaH (2.0 mmol, 1.0 eq, 60 % dispersion in mineral oil) was added portionwise and the solution was stirred for 30 minutes at rt. The iodoacetal **10e** (2 mmol, 1.0 eq.) was added at 0 °C and the reaction mixture was stirred overnight at rt. The reaction was quenched with water (15 mL) and extracted with ethyl acetate (3 x 15 ml). The combined organic layers were washed with brine (2 x 15 mL) and dried over Na_2SO_4. The solvent was evaporated at reduced pressure and the crude product was purified with flash chromatography on silica gel eluting with cyclohexane - ethyl acetate mixture affording the pure product as a clear oil in variable yield.

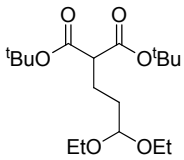


Dimethyl 2-(3,3-diethoxypropyl)malonate (**10f**)**:** Flash chromatography (c-Hex:AcOEt = 8:2). Yield = 32% (clear oil)**.** ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 4.50 (t, *J* = 5.6 Hz, 1H), 3.74 (s, 6H), 3.68-3.60 (m, 2H), 3.53-3.45 (m, 2H), 3.43 (t, *J* = 7.2 Hz, 1H), 2.01-1.95 (m, 2H), 1.68-1.63 (m, 2H), 1.21 (t, *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 169.6 (2C), 102.1, 61.1 (2C), 52.3 (2C), 51.1, 31.0, 23.9, 15.1 (2C). ***GC-MS*** (m/z): 231 (2) $[M\text{-}OMe]^+$, 217 (32) $[M\text{-}OEt]^+$, 185 (7), 156 (7), 125 (15), 103 (73), 85 (100), 59 (32).

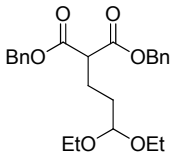


Diethyl 2-(3,3-diethoxypropyl)malonate (**10g**) was prepared according to literature reported procedure.[2] Flash chromatography (c-Hex:AcOEt = 8:2). Yield = 52% (clear oil)**.** ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 4.50 (t, *J* = 5.6 Hz, 1H), 4.24-4.16 (m, 4H), 3.68-3.60 (m, 2H), 3.53-3.45 (m, 2H), 3.37 (t, *J* = 7.6 Hz, 1H), 2.00-1.94 (m, 2H), 1.69-1.63 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 6H), 1.20 (t, *J* = 7.2 Hz, 6H). ***GC-MS*** (m/z): 245 (27) $[M\text{-}EtO]^+$, 170 (18), 125 (18), 103 (64), 85 (100), 57 (27).

[2] a) Segorbe, M. M.; Adrio, J.; Carretero, J. C. *Tetrahedron Lett.*, **2000**, *41,* 1983-1986. b) Carretero, J.C.; Adrio, J.; *Synthesis* **2001**, 1888–1896.

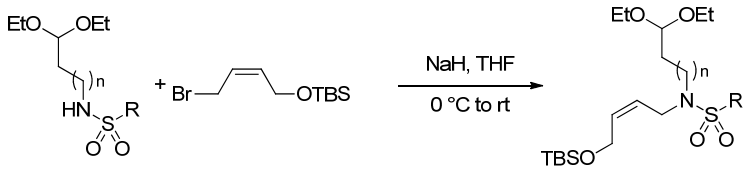


Di-*tert*-butyl 2-(3,3-diethoxypropyl)malonate (10h): Flash chromatography (c-Hex:AcOEt = 95:5). Yield = 66% (clear oil)**.** ***[1]H-NMR*** (400 MHz, $CDCl_3$) δ 4.50 (t, *J* = 5.6 Hz, 1H), 3.68-3.61 (m, 2H), 3.50-3.46 (m, 2H), 3.15 (t, *J* = 7.6 Hz, 1H), 1.90-1.84 (m, 2H), 1.67-1.62 (m, 2H), 1.46 (s, 18H), 1.21 (t, *J* = 7.2 Hz, 6H). ***[13]C-NMR*** (100 MHz, $CDCl_3$) δ 168.8 (2C), 102.4, 81.3 (2C), 61.0 (2C), 53.6, 31.1, 27.9 (6C), 23.9, 15.3 (2C). ***GC-MS*** (m/z): 289 (1) $[M-{}^tBu]^+$, 217 (15), 189 (36), 171 (32), 143 (11), 103 (91), 85 (24), 72 (23), 57 (100).

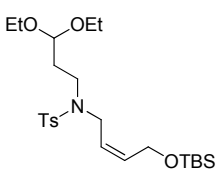


Dibenzyl 2-(3,3-diethoxypropyl)malonate (10i): Flash chromatography (c-Hex:AcOEt = 95:5). Yield = 36% (clear oil). ***[1]H-NMR*** (400 MHz, $CDCl_3$) δ 7.29-7.22 (m, 10H), 5.10 (d, *J* = 2.8 Hz, 4H), 4.42 (t, *J* = 6.4 Hz, 1H), 3.59-3.51 (m, 2H), 3.46 (t, *J* = 7.6 Hz, 1H), 3.44-3.36 (m, 2H), 2.00-1.94 (m, 2H), 1.62-1.57 (m, 2H), 1.13 (t, *J* = 7.2 Hz, 6H). ***[13]C-NMR*** (100 MHz, $CDCl_3$) δ 169.0 (2C), 135.3 (2C), 128.5 (4C), 128.3 (2C), 128.1 (4C), 102.2, 67.0 (2C), 61.1 (2C), 51.6, 31.1, 24.0, 15.2 (2C). ***GC-MS*** (m/z): 386 (4), 369 (14) $[M-EtO]^+$, 355 (9), 342 (5), 323 (5), 281 (6), 234 (6), 221 (6), 207 (18), 171 (32), 103 (100), 91 (100), 75 (100).

General procedure for the allylation of sulfonamides 9a-c and 9j.

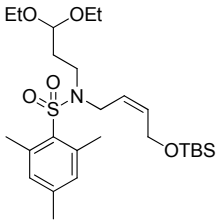


In an oven dried Schlenk tube sulfonamide **9** (2 mmol, 1 eq.) was dissolved in 10 mL of anhydrous THF and cooled to 0°C. NaH (2.1 mmol, 1.05 eq, 60 % dispersion in mineral oil) was added and the reaction mixture was stirred at rt for 30 minutes. The allyl bromide **11** (2.4 mmol, 1.2 eq.) was added at 0°C and the solution was stirred at rt overnight. The reaction was quenched with water (15 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4. The solvent was removed under vacuum and the residue was purified by flash-chromatography, eluting with cyclohexane ethyl acetate, to afford the pure product as a clear oil in moderate to good yields.

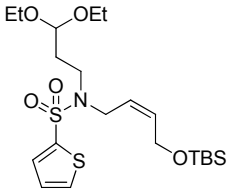


(*Z*)-*N*-(4-((tert-butyldimethylsilyl)oxy)but-2-en-1-yl)-*N*-(3,3-diethoxypropyl)-4-methylbenzenesulfonamide (12a'): Flash chromatography (c-Hex:AcOEt=

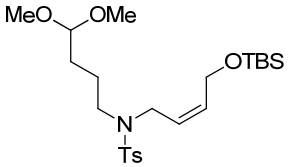
9:1). Yield = 80% (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.66-5.60 (m, 1H), 5.33-5.27 (m, 1H), 4.53 (t, *J* = 5.6 Hz, 1H), 4.20 (d, *J* = 6.4 Hz, 2H), 3.88 (d, *J* = 6.8 Hz, 2H), 3.67-3.59 (m, 2H), 3.53-3.45 (m, 2H), 3.18 (t, *J* = 7.2 Hz, 2H), 2.43 (s, 3H), 1.87 (dt, *J* = 7.2 Hz, *J* = 5.6 Hz, 2H), 1.20 (t, *J* = 7.2 Hz, 6H), 0.88 (s, 9H), 0.05 (s, 6H). ***GC-MS*** (m/z): 470 (3) $[M\text{-}Me]^+$, 428 $[M\text{-}^t Bu]^+$, 382 (6), 353 (11), 284 (6), 228 (8), 213 (9), 198 (6), 170 (6), 149 (6), 127 (14), 91 (34), 75 (41), 57 (23).



(*Z*)-*N*-(4-((tert-butyldimethylsilyl)oxy)but-2-en-1-yl)-*N*-(3,3-diethoxypropyl)-2,4,6-trimethylbenzenesulfonamide (12b'): Flash chromatography (c-Hex:AcOEt = 95:5). Yield = 64% (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 6.94 (s, 2H), 5.71-5.65 (m, 1H), 5.44-5.38 (m, 1H), 4.38 (t, *J* = 5.6 Hz, 1H), 4.17 (d, *J* = 6.0 Hz, 2H), 3.87 (d, *J* = 6.8 Hz, 2H), 3.56-3.49 (m, 2H), 3.40-3.32 (m, 2H), 3.22 (t, *J* = 7.6 Hz, 2H), 2.61 (s, 6H), 2.30 (s, 3H), 1.84-1.79 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 6H), 0.89 (s, 9H), 0.06 (s, 6H). ***GC-MS*** (m/z): 456 (100) $[M\text{-}^t Bu]^+$, 410 (9), 396 (10), 381 (23), 355 (4), 330 (9), 284 (11), 213 (9); 183 (13), 119 (36), 103 (27), 75 (54), 57 (50).

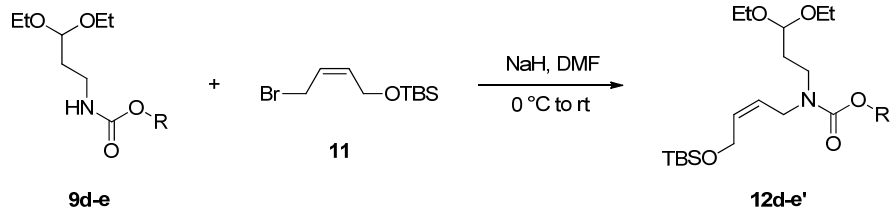


(*Z*)-*N*-(4-((tert-butyldimethylsilyl)oxy)but-2-en-1-yl)-*N*-(3,3-diethoxypropyl)thiophene-2-sulfonamide (12c'): Flash chromatography (c-Hex:AcOEt = 7:3). Yield = 56% (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 7.58-7.56 (m, 2H), 7.10 (t, *J* = 4.4 Hz, 1H), 5.70-5.64 (m, 1H), 5.39-5.33 (m, 1H), 4.55 (t, *J* = 5.6 Hz, 1H), 4.22 (d, *J* = 5.6 Hz, 2H), 3.92 (d, *J* = 6.8 Hz, 2H), 3.68-3.61 (m, 2H), 3.54-3.46 (m, 2H), 3.22 (t, *J* = 7.6 Hz, 2H), 1.92 (dt, *J* = 7.6 Hz, *J* = 5.6 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 6H), 0.89 (s, 9H), 0.06 (s, 6H). ***GC-MS*** (m/z): 462 (2) $[M\text{-}Me]^+$, 420 (100) $[M\text{-}^t Bu]^+$, 374 (9), 345 (9), 213 (13), 147 (30), 127 (23), 103 (40), 85 (91), 57 (73).



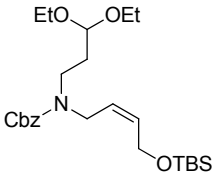
(*Z*)-*N*-(4-((tert-butyldimethylsilyl)oxy)but-2-en-1-yl)-*N*-(4,4-dimethoxybutyl)-4-methylbenzenesulfonamide (12j): Flash chromatography (c-Hex:AcOEt = from 95:5 to 7:3). Yield = 79% (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 5.65-5.59 (m, 1H), 5.30-5.24 (m, 1H), 4.36-4.33 (m, 1H), 4.19 (d, *J* = 6.0 Hz, 2H), 3.87 (d, *J* = 6.8 Hz, 2H), 3.31 (s, 6H), 3.14-3.11 (m, 2H), 2.43 (s, 3H), 1.60-1.58 (m, 4H), 0.88 (s, 9H), 0.05 (s, 6H). ***GC-MS*** (m/z): 456 (9) $[M\text{-}Me]^+$, 414 (86) $[M\text{-}^t Bu]^+$, 382 (9), 339 (23), 213 (27), 184 (32), 155 (27), 127 (23), 85 (100).

General procedure for the allylation of carbamates 9d-e.



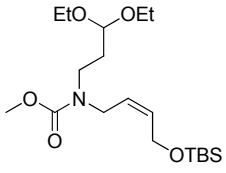
In an oven dried Schlenk tube carbamates **9d-e** (1 mmol, 1 eq.) was dissolved in 3 mL of anhydrous DMF and cooled to 0°C. NaH (1.2 mmol, 1.2 eq, 60 % dispersion in mineral oil) was added and the reaction mixture was stirred at rt for 30 minutes. The allyl bromide **11** (1.3 mmol, 1.3 eq.) was added at 0°C and the solution was stirred at rt overnight. The reaction was quenched with water (10 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was removed under vacuum and the residue was purified by flash-chromatography, eluting with cyclohexane ethyl acetate, to afford the pure product as a clear oil in moderate yields.

(*Z*)-benzyl(4-((tert-butyldimethylsilyl)oxy)but-2-en-1-yl)(3,3-diethoxypropyl)carbamate



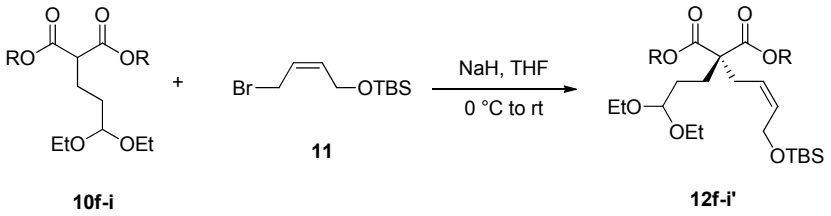
(12d'): Flash chromatography (c-Hex:AcOEt = 9:1). Yield = 28% (clear oil)**.** ***^{1}H-NMR*** (200 MHz, $CDCl_3$) δ 7.36-7.35 (m, 5H), 5.65 (bs, 1H), 5.45 (bs, 1H), 5.31 (s, 2H), 4.47 (bs, 1H), 4.23 (bs, 2H), 3.95 (bs, 2H), 3.71-3.40 (bs, 4H), 3.32 (bt, *J* = 7.0 Hz, 2H), 1.87 (bs, 2H), 1.17 (bt, *J* = 6.0 Hz, 6H), 0.90 (s, 9H), 0.07 (s, 6H). ***ESI-MS*** (m/z): 488 $[M+Na]^+$, 420 $[M-EtO]^+$.

(*Z*)-methyl(4-((tert-butyldimethylsilyl)oxy)but-2-en-1-yl)(3,3-diethoxypropyl)carbamate(12e'):



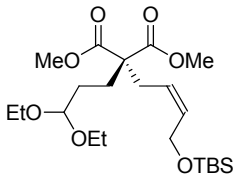
Flash chromatography (c-Hex:AcOEt = 8:2). Yield = 38% (clear oil)**.** ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 5.65 (bs, 1H), 5.44 (bs, 1H), 4.51 (bs, 1H), 4.26 (bd, *J* = 5.2 Hz, 2H), 3.92 (bs, 2H), 3.70 (s, 3H), 3.69-3.61 (m, 2H), 3.53-3.45 (m, 2H), 3.28 (m, 2H), 1.86 (bq, *J* = 6.4 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 6H), 0.91 (s, 9H), 0.08 (s, 6H). ***GC-MS*** (m/z): 374 (4) $[M-Me]^+$, 332 (100) $[M-{}^tBu]^+$, 257 (18), 216 (9), 182 (9), 127 (23), 103 (25), 85 (73), 57 (63).

General procedure for the alkylation of 2-allyl malonates 10f-i.



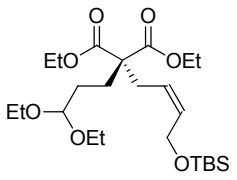
10f-i **11** **12f-i'**

In an oven dried Schlenk tube, under nitrogen atmosphere, **10f-i** (1 mmol, 1 eq.) was dissolved in 5 ml of anhydrous THF and cooled to 0°C. NaH (1.1 mmol, 1.1 eq, 60 % dispersion in mineral oil) was added portion-wise and the solution was stirred for 30 minutes at rt. Allyl bromide **11** (1.2 mmol, 1.2 eq.) was added at 0 °C and the reaction mixture was stirred overnight at rt. The reaction was quenched with water (5 mL) and extracted with ethyl acetate (3 x 10 ml). The combined organic layers were washed with brine (2 x 15 mL) and dried over $NaSO_4$. The solvent was evaporated at reduced pressure and the crude product was purified with flash chromatography on silica gel eluting with cyclohexane / ethyl acetate, to afford the pure product **12f-i'** as a clear oil in variable yield.



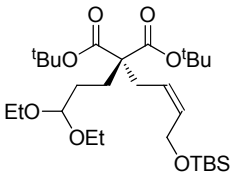
(Z)-Dimethyl 2-(4-((tert-butyldimethylsilyl)oxy)but-2-en-1-yl)-2-(3,3-diethoxypropyl)malonate (12f'):

Flash chromatography (c-Hex:AcOEt = 9:1). Yield = 46% (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 5.67-5.61 (m, 1H), 5.32-5.25 (m, 1H), 4.45 (t, *J* = 5.6 Hz, 1H), 4.22 (d, *J* = 6.4 Hz, 2H), 3.72 (s, 6H), 3.66-3.58 (m, 2H), 3.51-3.44 (m, 2H), 2.65 (d, *J* = 7.6 Hz, 2H), 1.96-1.92 (m, 2H), 1.54-1.49 (m, 2H), 1.20 (t, *J* = 7.2 Hz, 6H), 0.90 (s, 9H), 0.07 (s, 6H). ***GC-MS*** (m/z): 389 (23) $[M-{}^tBu]^+$, 343 (9), 269 (9), 237 (9), 209 (12), 189 (14), 163 (27), 129 (18), 103 (50), 85 (100), 57 (54).



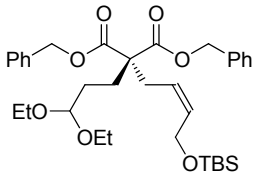
(*Z*)-Diethyl 2-(4-((tert-butyldimethylsilyl)oxy)but-2-en-1-yl)-2-(3,3-diethoxypropyl)malonate (12g'):

Flash chromatography (c-Hex:AcOEt = 95:5). Yield = 75% (clear oil). ***^{1}H-NMR*** (200 MHz, $CDCl_3$) δ 5.68-5.59 (m, 1H), 5.35-5.27 (m, 1H), 4.45 (t, *J* = 5.6 Hz, 1H), 4.23-4.16 (m, 6H), 3.70-3.37 (m, 4H), 2.64 (d, *J* = 6.6 Hz, 2H), 2.05-1.89 (m, 2H), 1.68-1.49 (m, 2H), 1.31-1.20 (m, 12H), 0.84 (s, 9H), 0.08 (s, 6H). ***GC-MS (m/z):*** 459 (1) $[M-Me]^+$, 417 (32) $[M-{}^tBu]^+$, 401 (3), 371 (5), 355 (5), 325 (3), 297 (9), 251 (10), 223 (9), 177 (27), 149 (9), 129 (18), 103 (36), 85 (100), 57 (30).



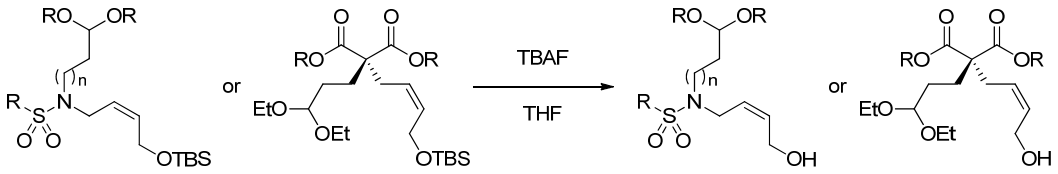
(*Z*)-Di-tert-butyl 2-(4-((tert-butyldimethylsilyl)oxy)but-2-en-1-yl)-2-(3,3-diethoxypropyl)malonate (12h'):

Flash chromatography (c-Hex:AcOEt = 95:5). Yield = 85% (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 5.63-5.59 (m, 1H), 5.31-5.25 (m, 1H), 4.43 (t, *J* = 5.6 Hz, 1H), 4.24 (d, *J* = 6.8 Hz, 2H), 3.65-3.58 (m, 2H), 3.51-3.43 (m, 2H), 2.54 (d, *J* = 7.2 Hz, 2H), 1.87-1.83 (m, 2H), 1.51-1.47 (m, 2H), 1.43 (s, 18H), 1.19 (t *J* = 7.2 Hz, 6H), 0.90 (s, 9H), 0.07 (s, 6H). ***GC-MS*** (m/z): 373 (2), 315 (33), 269 (27), 241 (14), 195 (14),103 (32), 85 (64), 57 (100).



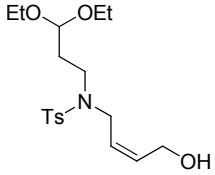
(*Z*)-Dibenzyl 2-(4-((tert-butyldimethylsilyl)oxy)but-2-en-1-yl)-2-(3,3-diethoxypropyl)malonate (12h'): Flash chromatography (c-Hex:AcOEt = 9:1). Yield = 54% (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 7.31-7.29 (m, 4H), 7.26-7.24 (m, 6H), 5.64-5.58 (m, 1H), 5.27-5.22 (m, 1H), 5.13 (d, *J* = 12.0 Hz, 2H), 5.07 (d, *J* = 12.0 Hz, 2H), 4.38 (t, *J* = 6.4 Hz, 1H), 4.16 (d, *J* = 6.0 Hz, 2H), 3.57-3.50 (m, 2H), 3.44-3.36 (m, 2H), 2.68 (d, *J* = 7.6 Hz, 2H), 1.99-1.95 (m, 2H), 1.50-1.45 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 6H), 0.88 (s, 9H), 0.04 (s, 6H). ***ESI-MS*** (m/z): 585, 282.

General procedure for the removal of TBS protecting group



12a-j' **12a-j**

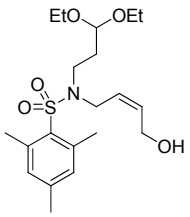
In a round bottom flask the *O*-TBS protected alcohol **12a-j'** (1 mmol, 1 eq.), was dissolved in 10 mL of THF. TBAF·$3H_2O$ (1.2 mmol, 1.2 eq.) was added to the solution at 0 °C and the reaction mixture was stirred at rt until complete consumption of the starting material (TLC, 4-6 hours). The solution was diluted with water (10 mL) and extracted with ethyl acetate (3 x 10 ml). The combined organic layers were washed with brine (2 x 10 mL) and dried over $NaSO_4$. The solvent was evaporated under reduced pressure and the crude product was purified with flash chromatography on silica gel eluting with cyclohexane / ethyl acetate, to afford the pure product as a clear oil.



(*Z*)-*N*-(3,3-diethoxypropyl)-*N*-(4-hydroxybut-2-en-1-yl)-4-methyl benzene-sulfonamide (12a): Flash chromatography (*c*-Hex:AcOEt = 6:4). Yield = 87%

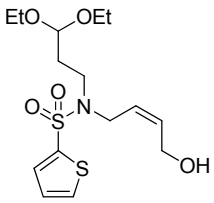
(clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 5.81-5.76 (m, 1H), 5.45-5.41 (m, 1H), 4.52 (t, *J* = 6.4 Hz, 1H), 4.16 (*b*d, 2H), 3.90 (d, *J* = 7.6 Hz, 2H), 3.67-3.60 (m, 2H), 3.53-3.45 (m, 2H), 3.22 (t, *J* = 7.6 Hz, 2H), 2.44 (s, 3H), 2.16 (*b*s, 1H), 1.91-1.86 (m, 2H), 1.20 (t, *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 143.2, 136.5, 132.7, 129.5 (2C), 126.9 (2C), 126.2, 100.6, 61.6 (2C), 57.5, 44.5, 43.4, 32.7, 21.5, 15.0 (2C). ***ESI-MS*** (m/z): 394 $[M+Na]^+$, 410 $[M+K]^+$. Anal. calcd for ($C_{18}H_{29}NO_5S$: 371,49): C, 58.20; H, 7.87; N, 3.77; Found: C, 58.11; H, 7.81; N, 3.70.

(*Z*)-*N*-(3,3-diethoxypropyl)-*N*-(4-hydroxybut-2-en-1-yl)-2,4,6-trimethylbenzenesulfonamide

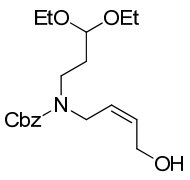


(**12b**)**:** Flash chromatography (c-Hex:AcOEt = 6:4). Yield = 90% (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 6.95 (s, 2H), 5.87-5.81 (m, 1H), 5.52-5.45 (m, 1H), 4.40 (t, *J* = 5.6 Hz, 1H), 4.17 (d, *J* = 6.8 Hz, 2H), 3.89 (d, *J* = 6.8 Hz, 2H), 3.60-3.53 (m, 2H), 3.43-3.35 (m, 2H), 3.24 (t, *J* = 7.6 Hz, 2H), 2.61 (s, 6H), 2.29 (s, 3H), 1.86-1.81 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 142.5, 140.3 (2 C), 133.2, 132.8, 131.9 (2 C), 126.3, 101.7, 61.7 (2 C), 57.7, 42.0, 41.3, 31.6, 22.8 (2 C), 20.9, 15.1 (2C). ***GC-MS*** (m/z): 356 (6), 281 (9), 212 (11), 183 (2) $[mesitylSO_2]^+$, 119 (100) $[mesityl]^+$, 91 (54), 68 (32). Anal. calcd for ($C_{20}H_{33}NO_5S$: 399,54): C, 60.12; H, 8.32; N, 3.51; Found: C, 60.23; H, 8.59; N, 3.44.

(*Z*)-*N*-(3,3-diethoxypropyl)-*N*-(4-hydroxybut-2-en-1-yl)thiophene-2-sulfonamide (**12c**): Flash

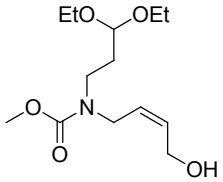


chromatography (c-Hex:AcOEt = 1:1). Yield = 79% (clear oil)**.** ***^{1}H-NMR*** (200 MHz, $CDCl_3$) δ 7.60-7.57 (m, 2H), 7.11 (dd, *J* = 4.4 Hz, *J* = 4.0 Hz, 1H), 5.85-5.76 (m, 1H), 5.53-5.40 (m, 1H), 4.45 (t, *J* = 5.4 Hz, 1H), 4.18 (bt, *J* = 6.4 Hz, 2H), 3.93 (d, *J* = 7.4 Hz, 2H), 3.73-3.42 (m, 4H), 3.26 (t, *J* = 7.6 Hz, 2H), 2.22 (bt, *J* = 6.4 Hz, 1H), 1.98-1.88 (m, 2H), 1.20 (t, *J* = 7.0 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 140.2, 133.0, 131.8, 131.6, 127.4, 126.3, 100.7, 61.9 (2 C), 57.8, 45.1, 44.1, 33.0, 15.2 (2 C). ***ESI-MS***: 386 $[M+Na]^+$. Anal. calcd for ($C_{15}H_{25}NO_5S_2$: 363,49): C, 49.56; H, 6.93; N, 3.85; Found: C, 49.61; H, 6.81; N, 3.77.



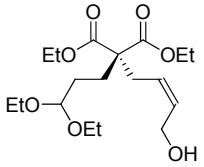
(*Z*)-benzyl (3,3-diethoxypropyl)(4-hydroxybut-2-en-1-yl)carbamate (**12d**): Flash chromatography (c-Hex:AcOEt = 1:1). Yield = 71% (clear oil)**.** ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 7.31-7.35 (m, 5H), 5.87 (bs, 0.6H), 5.74 (bs, 0.4 H), 5.31 (bs, 1H), 5.13 (s, 2H), 4.49 (bs, 1H), 4.20-4.10 (m, 2H), 3.98 (d, *J* = 7.2 Hz, 2H), 3.59 (bs, 2H), 3.43 (bs, 2H), 3.36 (t, *J* = 7.2 Hz, 2H), 1.89 (bs, 2H), 1.17 (bs, 6H). ***^{13}C-NMR*** (100 MHz,

$CDCl_3$) δ 156.2, 136.7, 132.0, 128.6, (2 C), 128.1, 128.0 (2 C), 127.2, 100.9, 67.4, 61.4 (2C), 57.8, 44.3, 43.6, 32.9, 15.3 (2 C). ***ESI-MS*** (m/z): 306 $[M\text{-}EtO]^+$. Anal. calcd for ($C_{19}H_{29}NO_5$: 351,44): C, 64.83; H, 8.32; N, 3.99; Found: C, 64.68; H, 8.21; N, 4.08.

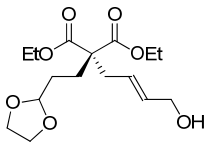


(*Z*)-methyl (3,3-diethoxypropyl)(4-hydroxybut-2-en-1-yl)carbamate (**12e**): Flash chromatography (c-Hex:AcOEt = from 1:1 to 0:100). Yield = quantitative (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 5.83 (bs, 1H), 5.53 (bs, 1H), 4.52 (t, *J* = 5.6 Hz, 1H), 4.19 (bd, *J* = 5.2 Hz, 2H), 3.93 (s, *J* = 7.2 Hz, 2H), 3.68 (s, 3H), 3.67-3.60 (m, 2H), 3.52-3.44 (m, 2H), 3.30 (t, *J* = 7.2 Hz, 2H), 3.08 (bs, OH), 1.89-1.84 (pq, 2H), 1.20 (t, *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 156.6, 131.9, 126.9, 100.7, 61.2 (2C), 57.5, 52.6, 44.3, 43.3, 32.6, 15.2 (2C). ***ESI-MS*** (m/z): 573, 298 $[M+Na]^+$, 230. Anal. calcd for ($C_{13}H_{25}NO_5$: 275,34): C, 56.71; H, 9.15; N, 5.09; Found: C, 56.50; H, 9.21; N, 5.19.

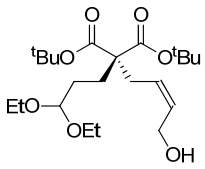
(*Z*)-Dimethyl 2-(3,3-diethoxypropyl)-2-(4-hydroxybut-2-en-1-yl)malonate (**12f**): Flash chromatography (c-Hex:AcOEt = 7:3). Yield = 74% (clear oil)**.** ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 5.76-5.70 (m, 1H), 5.32-5.25 (m, 1H), 4.41 (t, *J* = 5.6 Hz, 1H), 4.10 (d, *J* = 7.2 Hz, 2H), 3.69 (s, 6H), 3.61-3.56 (m, 2H), 3.47-3.42 (m, 2H), 2.66 (d, *J* = 7.6 Hz, 2H), 2.43 (bs, 1H), 1.93-1.88 (m, 2H), 1.48-1.43 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 171.4 (2 C), 132.6, 125.1, 102.4, 61.3 (2C), 57.8, 57.0, 52.4 (2C), 30.2, 28.5, 27.5, 15.1 (2C). ***ESI-MS*** (m/z): 355 $[M+Na]^+$, 287 $[M\text{-}OEt]^+$, 269 $[M\text{-}EtO\text{-}H_2O]^+$. Anal. calcd for ($C_{16}H_{28}O_7$: 332,39): C, 57.82; H, 8.49; Found: C, 57.63; H, 8.26.



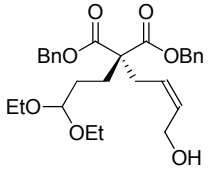
(*Z*)-Diethyl 2-(3,3-diethoxypropyl)-2-(4-hydroxybut-2-en-1-yl)malonate (**12g**): Flash chromatography (c-Hex:AcOEt = 1:1). Yield = 49% (clear oil)**.** ***^{1}H-NMR*** (200 MHz, $CDCl_3$) δ 5.84-5.72 (m, 1H), 5.42-5.28 (m, 1H), 4.46 (t, *J* = 5.6 Hz, 1H), 4.25-4.14 (m, 6H), 3.72-3.38 (m, 4H), 2.70 (d, *J* = 8.0 Hz, 2H), 2.18 (bs, 1H), 1.99-1.90 (m, 2H), 1.56-1.45 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 6H), 1.19 (t, *J* = 7.0 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 170.0 (2 C), 132.5, 125.4, 102.5, 61.3 (2 C), 57.9 (2 C), 56.7, 51.6, 30.0, 28.5, 27.3, 15.1 (2 C), 14.0 (2 C). ***ESI-MS*** (m/z): 383 $[M+Na]^+$. Anal. calcd for ($C_{18}H_{32}O_7$: 360,44): C, 59.98; H, 8.95; Found: C, 59.81; H, 8.79.



(*E*)-diethyl 2-(2-(1,3-dioxolan-2-yl)ethyl)-2-(4-hydroxybut-2-en-1-yl) malonate (*E*)-12g: was prepared according to literature reported procedure.[3]

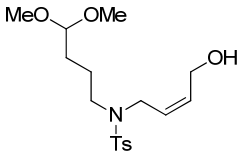


(*Z*)-di-tert-butyl 2-(3,3-diethoxypropyl)-2-(4-hydroxybut-2-en-1-yl)malonate (12h): Flash chromatography (c-Hex:AcOEt = 7:3). Yield = 69% (clear oil ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 5.81-5.75 (m, 1H), 5.37-5.30 (m, 1H), 4.45 (t, *J* = 5.6 Hz, 1H), 4.17 (d, *J* = 7.2 Hz, 2H), 3.68-3.51 (m, 2H), 3.53-3.45 (m, 2H), 2.62 (d, *J* = 7.6 Hz, 2H), 1.88-1.83 (m, 2H), 1.51-1.48 (m, 2H), 1.46 (s, 18H), 1.20 (t *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 170.3 (2C), 132.2, 125.8, 102.7, 81.4 (2C), 61.3 (2C), 57.9, 29.6, 28.4, 27.1, 27.8 (6C), 15.2 (2C). ***GC-MS*** (m/z): 417 (5), 373 (9), 281 (5), 258 (10), 241 (9), 212 (11), 184 (9), 156 (18), 137 (9), 96 (9), 79 (18), 57 (100).). Anal. calcd for ($C_{22}H_{40}O_7$: 416,55): C, 63.43; H, 9.68; Found: C, 63.22; H, 9.61.



(*Z*)-Dibenzyl 2-(3,3-diethoxypropyl)-2-(4-hydroxybut-2-en-1-yl)malonate (12i): Flash chromatography (c-Hex:AcOEt = 1:1. Yield = quantitative (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 7.29-7.21 (m, 10H), 5.72-5.66 (m, 1H), 5.25-5.20 (m, 1H), 5.09 (d, *J* = 12.4 Hz, 2H), 5.06 (d, *J* = 12.4 Hz, 2H), 4.34 (t, *J* = 5.6 Hz, 1H), 4.05 (d, *J* = 7.2 Hz, 2H), 3.54-3.49 (m, 2H), 3.41-3.36 (m, 2H), 2.69 (d, *J* = 8.0 Hz, 2H), 1.96-1.92 (m, 2H), 1.43-1.37 (m, 2H), 1.12 (t, *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 170.7 (2C), 135.2 (2C), 132.7, 128.5 (4C), 128.3 (2C), 128.2 (4C), 125.2, 102.4, 67.1 (2C), 61.3 (2C), 57.9, 57.0, 30.0, 28.4, 27.4, 15.2 (2C). ***ESI-MS*** (m/z): 439 $[M\text{-EtO}]^+$. Anal. calcd for ($C_{28}H_{36}O_7$: 484,58): C, 69.40; H, 7.49; Found: C, 69.55; H, 7.51.

(*Z*)-*N*-(4,4-diethoxybutyl)-*N*-(4-hydroxybut-2-en-1-yl)-4-methylbenzenesulfonamide (12j):

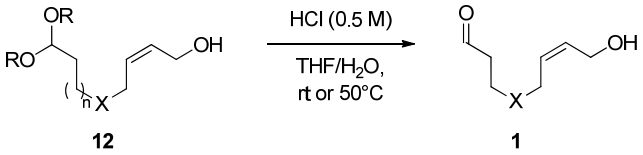


Flash chromatography (c-Hex:AcOEt = 1:1. Yield = 74% (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.80-5.73 (m, 1H), 5.45-5.39 (m, 1H), 4.35 (t, *J* = 5.2 Hz, 1H), 4.17 (bt, *J* = 6.0 Hz, 2H), 3.87 (d, *J* = 7.2 Hz, 2H), 3.30 (s, 6H), 3.17-3.12 (m, 2H), 2.44 (s, 3H), 2.19 (t, *J* = 6.0 Hz, OH), 1.61-1.59 (m, 4H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 143.2, 136.7, 132.4, 129.6 (2C), 127.0 (2C), 126.6, 103.9, 57.7, 52.9 (2C), 47.4, 44.3, 29.2, 23.1, 21.4. ***ESI-MS*** (m/z): 737, 556, 380

[3] Vulovic B.; Bihelovic F.; Matovic R.; Saicic R.; *Tetrahedron* **2009**, *50*, 10485-10494.

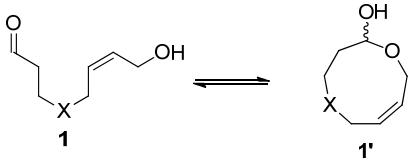
$[M+Na]^+$, 294. Anal. calcd for ($C_{19}H_{31}NO_5S$: 385,52): C, 59.19; H, 8.10; N, 3.63; Found: C, 59.21; H, 8.00; N, 3.21.

General procedure for the removal of dimethyl and diethyl acetals (method A).



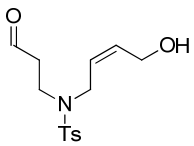
12 **1**

In a round bottom flask the acetal **12** (0.25 mmol, 1eq.) was dissolved in 2.5 mL of a 1:1 mixture of THF and water. Aqueous HCl (0.5 M, 2.5 mL) was added to the solution and the reaction mixture was stirred at rt or 50 °C for 2 hours. The aqueous layer was extracted with ethyl acetate (3 x 10 mL), the combined organic phases were washed with water (15 mL) and then dried over Na_2SO_4. The organic solvent was removed under reduced pressure and the crude product **1** was used in the following step without further purification. *[In some cases NMR spectra displayed the presence of a mixture of product **1** and cyclic hemiacetal **1'**]*.

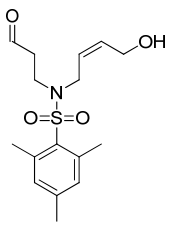


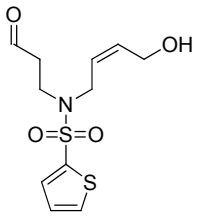
1 **1'**

(*Z*)-*N*-(4-hydroxybut-2-en-1-yl)-4-methyl-*N*-(3-oxopropyl)benzenesulfonamide (**1a**): Room temperature. Yield = 98 % (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.76 (t, *J* = 1.2 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 5.81-5.75 (m, 1H), 5.42-5.35 (m, 1H), 4.19 (d, *J* = 7.2 Hz, 2H), 3.89 (d, *J* = 7.2 Hz, 2H), 3.43 (t, *J* = 7.6 Hz, 2H), 2.85 (dt, *J* = 7.6 Hz, *J* = 1.2 Hz, 2H), 2.44 (s, 3H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 200.7, 143.7, 136.1, 132.8, 12938 (2C), 127.1 (2C), 126.5, 57.9, 45.6, 43.9, 41.2, 21.5 (2C). ***ESI-MS*** (m/z): 298 $[M+H]^+$, 320 $[M+Na]^+$, 338 $[M+K]^+$.

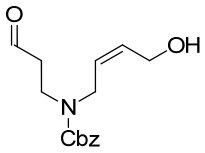


(*Z*)-*N*-(4-hydroxybut-2-en-1-yl)-2,4,6-trimethyl-*N*-(3-oxopropyl) benzenesulfonamide (**1b**): Room temperature. Yield = 74% (white sticky solid). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.65 (t, *J* = 1.2 Hz, 1H), 6.97 (s, 2H), 5.84-5.78 (m, 1H), 5.51-5.45 (m, 1H), 4.15 (d, *J* = 6.8 Hz, 2H), 3.86 (d, *J* = 6.8 Hz, 2H), 3.53 (t, *J* = 6.8 Hz, 2H), 2.77 (dt, *J* = 6.8 Hz, *J* = 1.2 Hz, 2H), 2.61 (s, 6H), 2.31 (s, 3H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 200.5, 142.9, 140.3 (2 C), 133.0, 132.1 (3 C), 126.4, 57.9, 43.2, 42.5, 39.3, 22.7 (2 C), 21.0. ***ESI-MS*** (m/z): 348 $[M+Na]^+$, 326 $[M+H]^+$.

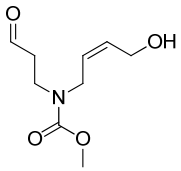




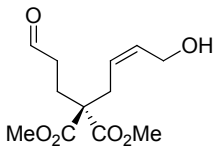
(*Z*)-*N*-(4-hydroxybut-2-en-1-yl)-*N*-(3-oxopropyl)thiophene-2-sulfonamide (1c): Room temperature. Yield = 98% (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.79 (t, *J* = 0.8 Hz, 1H), 7.62-7.59 (m, 2H), 7.13 (dd, *J* = 5.2 Hz, *J* = 4.0 Hz, 1H), 5.84-5.77 (m, 1H), 5.46-5.39 (m, 1H), 4.21 (d, *J* = 6.8 Hz, 2H), 3.94 (d, *J* = 7.2 Hz, 2H), 3.47 (t, *J* = 6.8 Hz, 2H), 2.89 (dt, *J* = 6.8 Hz, *J* = 0.8 Hz, 2H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 200.4, 139.4, 133.1, 132.8, 131.9, 127.5, 126.2, 58.0, 46.1, 44.1, 41.6. ***ESI-MS:*** 312 $[M+Na]^+$, 290 $[M+H]^+$, 272 $[M-OH]^+$.



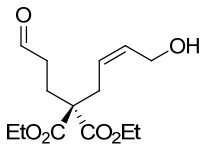
(*Z*)-benzyl (4-hydroxybut-2-en-1-yl)(3-oxopropyl)carbamate (1d): Room temperature. Yield = quantitative (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.76 (bs, 1H), 7.39-7.31 (m, 5H), 5.87 (bs, 0.5H), 5.73 (bs, 0.5 H), 5.53 (bs, 1H), 5.13 (s, 2H), 4.21 (bs, 2H), 4.00 (d, *J* = 6.0 Hz, 2H), 3.60 (t, *J* = 6.4 Hz, 2H), 2.75 (bs, 2H). ***^{13}C-NMR*** (50 MHz, $CDCl_3$) δ 200.6 156.0, 136.4, 132.3, 128.7 (2 C), 128.3, 128.1 (2 C), 127.0, 67.6, 58.0, 45.0, 43.6, 41.2. ***ESI-MS*** (m/z): 300 $[M+Na]^+$, 278 $[M+H]^+$.



(*Z*)-methyl (4-hydroxybut-2-en-1-yl)(3-oxopropyl)carbamate (1e): Room temperature. Yield = 79% (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$, mixture of conformers) δ 9.80 (s, 1H), 5.82 (bs, 0.6H), 5.68 (bs, 0.4 H), 5.52 (bs, 1H), 4.22 (bd, *J* = 6.8 Hz, 2H), 3.97 (bd, *J* = 6.8 Hz, 2H), 3.70 (s, 3H), 3.57 (t, *J* = 6.8 Hz, 2H), 2.77-2.74 (m, 2H). ***^{13}C-NMR*** (50 MHz, $CDCl_3$, mixture of conformers.) δ 200.5, 156.5, 132.0, 127.0, 57.9, 52.8, 44.8 (43.6), 41.0, 30.3 (29.6). ***ESI-MS*** (m/z): 425, 289, 224, 202, 184.

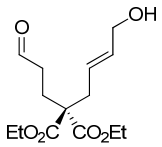


(*Z*)-dimethyl 2-(4-hydroxybut-2-en-1-yl)-2-(3-oxopropyl)malonate (1f): Room temperature. Yield = 74% (clear oil)**.** ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 5.79-5.73 (m, 1H), 5.41-5.35 (m, 1H), 4.16 (d, *J* = 6.8 Hz, 2H), 3.72 (s, 6H), 2.68 (d, *J* = 7.6 Hz, 2H), 2.49 (t, *J* = 7.6 Hz, 2H), 2.20 (t, *J* = 7.6 Hz, 2H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 200.7, 171.2 (2C), 132.7, 125.1, 58.1, 56.7, 52.6 (2C), 39.1, 31.5, 25.2. ***ESI-MS*** (m/z): 281 $[M+Na]^+$, 241 $[M-OH]^+$.

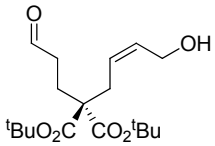


(*Z*)-Diethyl 2-(4-hydroxybut-2-en-1-yl)-2-(3-oxopropyl)malonate (*Z*)-1g: Room temperature .Yield = quantitative (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.75 (t, *J* = 1.2 Hz 1H), 5.81-5.74 (m, 1H), 5.46-5.39 (m, 1H), 4.25-4.18 (m, 6H),

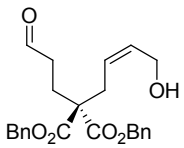
2.69 (d, *J* = 7.6 Hz, 2H), 2.51 (dt, *J* = 7.6 Hz, *J* 1.2 Hz, 2H), 2.21 (t, *J* = 7.6 Hz, 2H), 1.27 (t, *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (50 MHz, $CDCl_3$) δ 200.7, 170.8 (2C), 132.6, 125.3, 61.6 (2C), 58.2, 56.6, 39.1, 31.3, 25.1, 14.0 (2C). ***ESI-MS*** (m/z): 287 $[M+H]^+$, 269 $[M-OH]^+$.



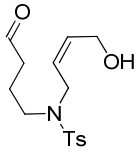
(*E*)-diethyl 2-(4-hydroxybut-2-en-1-yl)-2-(3-oxopropyl)malonate (*E*)-1g: 55 °C. Yield = 96% (clear oil). ***^{1}H-NMR*** (200 MHz, $CDCl_3$) δ 9.72 (s, 1H), 5.78-5.65 (m, 1H), 5.59-5.44 (m, 1H), 4.17 (q, *J* = 7.2 Hz, 4H), 4.06 (d, *J* = 5.4 Hz, 2H), 2.62 (d, *J* = 6.8 Hz, 2H), 2.48 (t, *J* = 7.6 Hz, 2H), 2.16 (t, *J* = 7.6 Hz, 2H), 1.2 (t, *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 200.8, 170.7 (2C), 134.0, 125.3, 63.1, 61.5 (2C), 56.6, 39.0, 36.3, 24.8, 14.0 (2C). ***ESI-MS*** (m/z): 327, 309 $[M+Na]^+$, 269 $[M-OH]^+$.



(*Z*)-Di-tert-butyl 2-(4-hydroxybut-2-en-1-yl)-2-(3-oxopropyl)malonate (1h): Yield = quantitative (white sticky solid)**.** ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 5.80-5.74 (m, 1H), 5.46-5.39 (m, 1H), 4.20 (d, *J* = 6.4 Hz, 2H), 2.60 (d, *J* = 8.0 Hz, 2H), 2.13 (t, *J* = 8.0 Hz, 2H), 2.13 (t, *J* = 8.0 Hz, 2H), 1.47 (s, 18H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 201.0, 169.9 (2C), 132.1, 125.8, 81.3 (2C), 58.3, 56.7, 39.1, 30.4, 27.9 (6C), 26.8. ***ESI-MS*** (m/z): 365 $[M+Na]^+$.

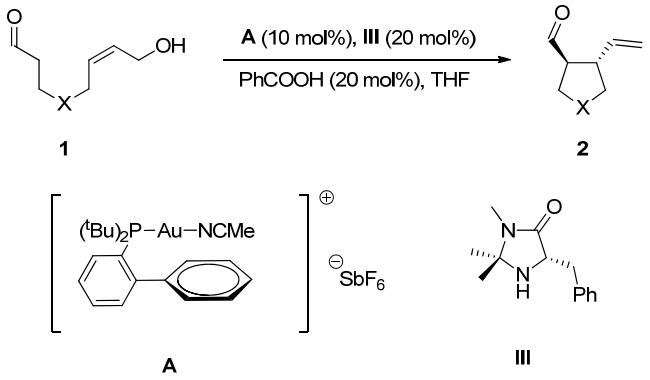


(*Z*)-Dibenzyl 2-(4-hydroxybut-2-en-1-yl)-2-(3-oxopropyl)malonate (1h): 60 °C. Yield = 88% (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.63 (s, 1H), 7.35-7.23 (m, 10H), 5.74-5.68 (m, 1H), 5.36-5.30 (m, 1H), 5.12 (s, 4H), 4.09 (d, *J* = 6.0 Hz, 2H), 2.70 (d, *J* = 8.0 Hz, 2H), 2.39 (t, *J* = 7.6 Hz 2H), 2.23 (t, *J* = 7.6 Hz, 2H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 200.4, 170.4 (2C), 135.2 (2C), 132.8, 128.6 (4C), 128.5 (2C), 128.2 (4C), 125.0, 67.3 (2C), 58.2 (2C), 56.0, 38.9, 31.3, 25.1. ***ESI-MS*** (m/z): 433 $[M+Na]^+$, 393 $[M-OH]^+$.

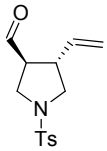


(*Z*)-*N*-(4-hydroxybut-2-en-1-yl)-*N*-(4-oxobutyl)-4-methylbenzenesulfonamide (1j): Room temperature. Yield 96% (clear oil). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 5.76-5.70 (m, 1H), 5.37-5.31 (m, 1H), 4.16 (d, *J* = 6.4 Hz, 2H), 3.85 (d, *J* = 7.2 Hz, 2H), 3.10 (t, *J* = 6.8 Hz, 2H), 2.55 (t, *J* = 6.8 Hz, 2H), 2.40 (s, 3H), 1.84 (quint, *J* = 6.8 Hz, 2H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 201.8, 143.4, 136.5, 132.7, 129.7 (2C), 127.0 (2C), 126.5, 57.8, 46.8, 44.7, 40.4, 21.4, 20.7. ***ESI-MS*** (m/z): 645 $[2M+Na]^+$, 334 $[M+Na]^+$, 312 $[M+H]^+$, 294 $[M-OH]^+$.

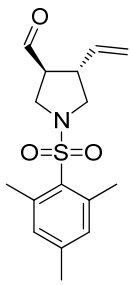
General procedure for the intramolecular gold-catalyzed α-allylic alkylation of 1.



In a screw-capped vials, with no exclusion of moisture or oxygen, **1** (0.07 mmol, 1 eq.) was dissolved in THF and gold catalyst **A** (0.007 mmol, 0.1 eq.), the organocatalyst **III** (0.014 mmol, 0.2 eq.) and benzoic acid (0.014 mmol, 0.2 eq.) were added in sequence. The reaction was monitored by TLC and stirred at rt until satisfactory conversion of the starting material was obtained. The crude reaction mixture was directly charged on the top of a silica gel column. Diastereoselection was determinate by GC or NMR on the crude reaction mixture, *ee* was determined by chiral HPLC analysis after suitable product derivatization.

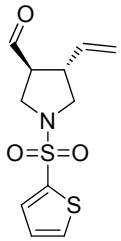


(3*S*,4*S*)-1-tosyl-4-vinylpyrrolidine-3-carbaldehyde (2a): Flash chromatography (*c*-Hex:AcOEt = 7:3). Yield 93% (38 hs, clear oil); *dr* (*trans:cis*) = 89:11; *ee* (*trans/cis*) 90/79. ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.53 (d, *J* = 1.6 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.36 (d *J* = 8.0 Hz, 2H), 5.66 (ddd, *J* = 16.8 Hz, *J* = 10.4 Hz, *J* = 7.6 Hz, 1H), 5.13 (d, *J* = 16.8 Hz, 1H), 5.12 (d, *J* = 10.4 Hz, 1H), 3.61-3.44 (m, 3H), 3.06 (dd, *J* = 10.0 Hz, *J* = 7.6 Hz, 1H), 2.46 (s, 3H), 2.96 (quint, *J* = 7.6 Hz, 1H), 2.76 (dq, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 198.7, 143.9, 135.3, 133.1, 129.8 (2 C), 127.6 (2C), 118.0, 55.2, 52.3, 46.7, 43.6, 21.6. ***ESI-MS*** (m/z): 280 $[M+H]^+$. The *ee* was determined by chiral HPLC analysis after reduction of the aldehyde with $NaBH_4$: Chiralcel® OD-H column, λ = 230 nm, *n*-Hexane: *i*-PrOH 96:4; flow rate 1.0 mL/min, *T* = 40°C. t_R (*trans*) = 46.45 min (*major*), 58.64 (*minor*) min. t_R (*cis*) = 50.75 min (*major*), 56.16 min (*minor*).

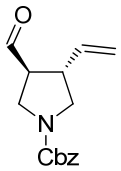


(3*S*,4*S*)-1-(mesitylsulfonyl)-4-vinylpyrrolidine-3-carbaldehyde (2b): Flash chromatography (*c*-Hex:AcOEt = 7:3). Yield 53% (32 hs, clear oil); *dr* (*trans:cis*) = 84:16; *ee* (*trans/cis*) 94/88. ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.64 (d, *J* = 2.0 Hz, 1H), 6.96 (s, 2H), 5.83-5.74 (m, 1H), 4.15 (d, *J* = 6.8 Hz, 2H), 3.86 (d, *J* = 6.8 Hz, 2H), 3.53 (t, *J* = 6.8 Hz, 2H), 2.77 (dt, *J* = 6.8 Hz, *J* = 1.2 Hz, 2H), 2.61 (s, 6H), 2.31 (s, 3H). ***^{13}C-***

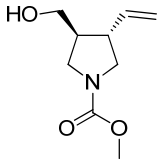
NMR (100 MHz, $CDCl_3$) δ 199.0, 142.8, 140.2 (2 C), 135.6, 132.0 (3 C), 118.0, 55.4, 51.2, 45.5, 44.0, 22.8 (2 C), 21.0. ***GC-MS*** (m/z): 307 (5) $[M]^+$, 279 (1), 212 (5), 183 (10), 119 (100), 91 (64), 67 (45). The *ee* was determined by chiral HPLC analysis after reduction of the aldehyde with $NaBH_4$: Chiralcel® OD-H column, λ = 230 nm, *n*-Hexane: *i*-PrOH 97:3; flow rate 1.0 mL/min, *T* = 40 °C. t_R (*trans*) = 41.24 min (*major*), 50.67 min (*minor*). t_R (*cis*) = 39.03 min (*major*), 44.24 min (*minor*).



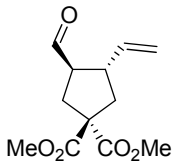
(3*S,4S*)-1-(thiophen-2-ylsulfonyl)-4-vinylpyrrolidine-3-carbaldehyde (2c): Flash chromatography (*c*-Hex:AcOEt = 7:3). Yield 76% (40 hours, clear oil); *dr* (*trans:cis*) = 95:5; *ee* (*trans/cis*) 84:65. ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.55 (d, *J* = 2.0 Hz, 1H), 7.65 (dd, *J* = 5.2 Hz, *J* = 1.2 Hz, 1H), 7.62 (dd, *J* = 4.0 Hz, *J* = 1.2 Hz, 1H), 7.18 (dd, *J* = 5.2 Hz, *J* = 4.0 Hz, 1H), 5.67 (ddd, *J* = 17.6 Hz, *J* = 10.0 Hz, *J* = 7.6 Hz, 1H), 5.15 (d, *J* = 17.6 Hz, 1H), 5.14 (d, *J* = 10.0 Hz, 1H), 3.64 (dd, *J* = 10.8 Hz, *J* = 7.6 Hz, 1H), 3.59-3.53 (m, 2H), 3.14 (dd, *J* = 10.0 Hz, *J* = 7.6 Hz, 1H), 2.98 (quint, *J* = 7.6 Hz, 1H), 2.83-2.77 (m, 1H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 198.4, 136.1, 135.1, 132.6, 132.2, 127.7, 118.1, 55.1, 52.4, 46.8, 43.3. ***GC-MS*** (m/z): 243 (5) $[M-CO]^+$, 215 (23), 176 (36), 147 (63), 124 (54), 99 (36), 84 (18), 67 (100), 57 (18). The *ee* was determined by chiral HPLC analysis after reduction of the aldehyde with $NaBH_4$: Chiralcel® OD-H column, λ = 254 nm, *n*-Hexane: *i*-PrOH 96:4; flow rate 1.0 mL/min, *T* = 40°C. t_R (*trans*) = 70.60 min (*major*), 85.29 min (*minor*). t_R (*cis*) = 79.42 min (*major*), 82.20 (*minor*).



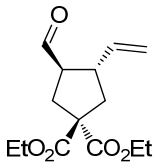
(3*S,4S*)-benzyl 3-formyl-4-vinylpyrrolidine-1-carboxylate (2d): Flash chromatography (*c*-Hex:AcOEt = 8:2). Yield 83% (43 hs, clear oil); *dr* (*trans:cis*) = 94:6; *ee* (*trans/cis*) 97/85. ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.66 (d, *J* = 1.2 Hz, 1H), 7.37-7.32 (m, 5H), 5.88-5.73 (m, 1H), 5.19-5.11 (m, 2H), 5.14 (s 2H), 3.77-3.64 (m, 3H), 3.33-3.25 (m, 1H), 3.16-3.05 (m, 1H), 2.91 (pquint, *J* = 8.4 Hz, 1H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 199.5, 167.3, 136.6, 135.7, 128.5 (2 C), 128.1, 127.9 (2 C), 117.8, 67.0, 55.6 (0.5 C), 54.8 (0.5 C), 50.7 (0.5 C), 50.3 (0.5 C), 45.4 (0.5 C), 44.8 (0.5 C), 43.8 (0.5 C), 43.1 (0.5 C). ***ESI-MS*** (m/z): 282 $[M+Na]^+$, 260 $[M+H]^+$. The *ee* was determined by chiral HPLC analysis after reduction of the aldehyde with $NaBH_4$: Chiralpak® IA column, λ = 214 nm, *n*-Hexane: *i*-PrOH 95:5; flow rate 1.0 mL/min, *T* = 40°C. t_R (*trans*) = 24.18 min (*major*), 28.17 min (*minor*). t_R (*cis*) = 26.41min (*major*), 37.22 (*minor*).



(*3S,4S*)-methyl 3-(hydroxymethyl)-4-vinylpyrrolidine-1-carboxylate (2e) was obtained from the corresponding aldehyde by *in situ* reduction with $NaBH_4$. Flash chromatography (*c*-Hex:AcOEt = 7:3). Yield 53% (24 hs, clear oil); *dr* (*trans:cis*) = 92:8; *ee* (*trans/cis*) 98/nd. ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 5.72 (ddd, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 8.4 Hz, 1H), 5.16 (d, *J* = 17.2 Hz, 1H), 5.11 (d, *J* = 10.4 Hz, 1H), 3.76 (dd, *J* = 11.2 Hz, *J* = 5.2 Hz, 1H), 3.71-3.57 (m, 3H), 3.70 (s, 3H), 3.27-3.13 (m, 2H), 2.68 (quint, *J* = 8.4 Hz, 1H), 2.18 (bs, OH), 1.72 (bs, 1H). ***^{13}C-NMR*** (50 MHz, $CDCl_3$, mixture of conformers) δ 155.4, 137.5, 117.1, 62.8, 52.3, 51.2 (50.8), 48.9 (48.6), 46.5 (45.7), 45.3 (44.5). ***ESI-MS*** (m/z): 393, 208 $[M+Na]^+$, 186 $[M+H]^+$.The *ee* was determined by chiral HPLC analysis after alcohol acylation with 3,5-dinitrobenzoyl chloride : Chiralpak® AD column, λ = 230 nm, *n*-Hexane: *i*-PrOH 92:8; flow rate 1.0 mL/min, *T* = 40°C. t_R (*trans*) = 39.10 min (*minor*), 42.24 min (*major*).

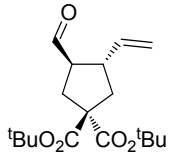


(*3R,4S*)-dimethyl 3-formyl-4-vinylcyclopentane-1,1-dicarboxylate (2f): Flash chromatography (*c*-Hex:AcOEt = 8:2). Yield 78% (24 hs, clear oil); *dr* (*trans:cis)* = 67:33; *ee* (*trans/cis*) 84/82. ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.62 (d, *J* = 2.4 Hz, 1H), 5.78 (ddd, *J* = 17.2 Hz, *J* = 10.0 Hz, *J* = 7.6 Hz, 1H), 5.13 (d, *J* = 17.2 Hz, 1H), 5.08 (d, *J* = 10.0 Hz, 1H), 3.75 (s, 6H), 2.93-2.84 (m, 1H), 2.74-2.67 (m, 1H), 2.61 (dd, *J* = 13.2 Hz, *J* = 7.6 Hz, 1H), 2.56-2.53 (m, 2H), 2.09 (dd, *J* = 13.2 Hz, *J* = 10.8 Hz, 1H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 201.4, 172.0 (2C), 138.1, 116.4, 59.0, 56.2 (2C), 53.0, 44.7, 40.3, 33.8. ***GC-MS*** (m/z): 209 (3), 180 (4), 162 (5), 145 (100), 113 (64), 91 (73), 59 (45). The *ee* was determined by chiral HPLC analysis after reduction of the aldehyde with $NaBH_4$ and acylation with 3,5-dinitrobenzoyl chloride: Chiralcel® OD column, λ = 230 nm, *n*-Hexane: *i*-PrOH 95:5; flow rate 1.0 mL/min, *T* = 40°C. t_R (*trans*) = 41.27 min (*major*), 45.67 min (*minor*). t_R (*cis*) = 48.17 min (*minor*), 50.71 min (*major*).

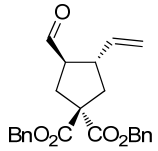


(*3R,4S*)-diethyl 3-formyl-4-vinylcyclopentane-1,1-dicarboxylate (2g): Flash chromatography (*c*-Hex:AcOEt = 8:2). Yield 71% (24, hs, clear oil); *dr* (*trans:cis)* = 70:30; *ee* (*trans/cis*) 96/85. ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.62 (d, *J* = 2.4 Hz 1H), 5.78 (ddd, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 7.6 Hz, 1H), 5.13 (d, *J* = 17.2 Hz, 1H), 5.07 (d, *J* = 10.4 Hz, 1H), 4.21 (q, *J* = 7.2 Hz, 4H), 2.93-2.84 (m, 1H), 2.73-2.66 (m, 1H), 2.59 (dd, *J* = 13.6 Hz, *J* =7.6 Hz, 1H), 2.54-2.51 (m, 2H), 2.09 (dd, *J* = 13.6 Hz, *J* = 10.8 Hz, 1H), 1.26 (t, *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 201.5, 171.6, 171.5, 138.2, 116.3, 61.7 (2C), 59.1, 56.3, 44.7, 40.2, 33.7, 14.0 (2C). ***GC-MS*** (m/z): 240 (4) $[M-CO]^+$, 223 (5), 194 (9), 173 (100), 148 (14), 127 (67), 93 (63), 77 (36). The *ee* was determined by chiral HPLC analysis after reduction of the aldehyde with

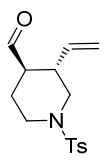
$NaBH_4$ and acylation with 3,5-dinitrobenzoyl chloride: Chiralcel® OD column, λ = 230 nm, *n*-Hexane: *i*-PrOH 95:5; flow rate 1.0 mL/min, *T* = 40°C. t_R (*trans*) = 22.24 min (*major*), 23.48 min (*minor*). t_R (*cis*) = 26.21 min (*minor*), 31.06 min (*major*).



(*3R,4S*)-di-*tert*-butyl 3-formyl-4-vinylcyclopentane-1,1-dicarboxylate (2h): Flash chromatography (*c*-Hex:AcOEt = 8:2). Yield 90% (40 hs, clear oil); *dr* (*trans:cis*) = 69:31; ee (*trans/cis*) 95/81. ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.61 (d , *J* = 2.4 Hz, 1H), 5.78 (ddd, *J* = 17.6 Hz, *J* = 10.0 Hz, *J* = 7.6 Hz, 1H), 5.11 (d, *J* = 17.6 Hz, 1H), 5.05 (d, *J* = 10.0 Hz, 1H), 2.86 (pquint, *J* = 9.2 Hz, 1H), 2.65 (dq, *J* = 9.2 Hz, *J* = 2.4 Hz, 1H), 2.48 (dd, *J* = 13.2 Hz, *J* = 7.6 Hz, 1H), 4.42 (m, 2H), 1.99 (d, *J* = 13.2 Hz, *J* = 10.8 Hz, 1H), 1.46 (s, 18H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 201.9, 170.9, 170.7, 138.6, 116.0, 81.6 (2C), 60.5, 56.3, 44.7, 40.8, 33.5, 27.8 (6C). ***GC-MS*** (m/z): 251 (2) $[M-{}^tBuO]^+$, 212 (5), 195 (6), 138 (9), 117 (10), 91 (8), 77 (5), 57 (100). The *ee* was determined by chiral HPLC analysis after reduction of the aldehyde with $NaBH_4$ and acylation with 3,5-dinitrobenzoyl chloride: Chiralpak® IB column, λ = 230 nm, *n*-Hexane: *i*-PrOH 95:5; flow rate 0.5 mL/min, *T* = 40 °C. t_R (*trans*) = 20.21 min (*major*), 21.13 min (*minor*). t_R (*cis*) = 22.16 min (*minor*), 23.27 (*major*).

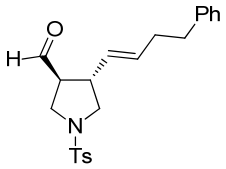


(*3R,4S)*-Dibenzyl 3-formyl-4-vinylcyclopentane-1,1-dicarboxylate (2i): Flash chromatography (*c*-Hex:AcOEt = 8:2). Yield 79% (38 hs, clear oil); *dr* (*trans:cis)* 67:33; *ee* (*trans/cis*) 89/83. ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.58 (d, *J* = 2.4 Hz, 1H), 7.34-7.31 (m, 6H), 7.27-7.24 (m, 4H), 5.74 (ddd, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 7.6 Hz, 1H), 5.12 (d, *J* = 2.0 Hz, 4H), 5.10 (d, *J* = 17.2 Hz, 1H), 5.05 (d, *J* = 10.4 Hz, 1H), 2.91-2.83 (m, 1H), 2.74-2.65 (m, 2H), 2.62 (dd, *J* = 13.6 Hz, *J* = 7.6 Hz, 1H), 2.57-2.53 (m, 1H), 2.10 (dd, *J* = 13.6 Hz, *J* = 10.8 Hz, 1H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 201.0, 171.3, 171.1, 138.1, 135.2 (2C), 128.6 (4C), 128.4 (2C), 128.1 (4C), 116.4, 67.5 (2C), 59.2, 56.2, 44.7, 40.2, 33.7. ***GC-MS*** (m/z): 355 (2), 312 (2), 299 (3), 207 (5), 195 (9), 181 (5), 137 (5), 121 (5), 107 (9), 91 (100), 65 (9). The *ee* was determined by chiral HPLC analysis after reduction of the aldehyde with $NaBH_4$: Chiralpak® OD column, λ = 214 nm, *n*-Hexane: *i*-PrOH 95:5; flow rate 0.7 mL/min, *T* = 40 °C. t_R (*trans*) = 23.64 min (*major*), 29.26 min (*minor*). t_R (*cis*) = 25.07 min (*major*), 26.71 (*minor*).



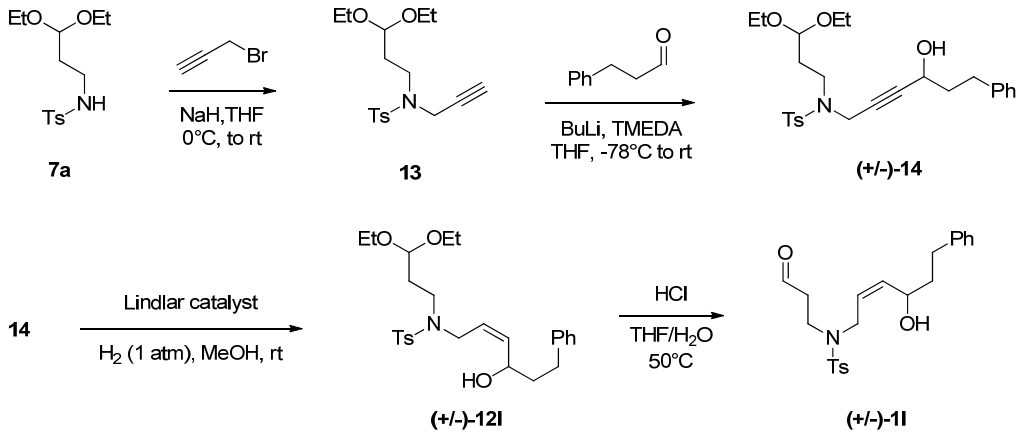
(*3S,4R*)-1-tosyl-3-vinylpiperidine-4-carbaldehyde (2j): Flash chromatography (*c*-Hex:AcOEt = 8:2). Yield 34% (8 hs at 60°C, clear oil); *dr* (*trans:cis)* 89:11; *ee* (*trans/cis*)

98/nd. Spectroscopic data matched with literature report.[4] The *ee* was determined by chiral HPLC analysis after reduction of the aldehyde with $NaBH_4$: Chiralcel® OD-H column, λ = 254 nm, *n*-Hexane: *i*-PrOH 95:5; flow rate 1.0 mL/min, *T* = 40°C. t_R (*trans*) = 34.97 min (*major*), 40.75 min (*minor*). [α]: -115° (c: 0.046, CH_2Cl_2), lit. -108.9°.[4]

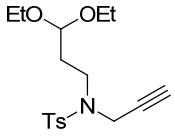


(*3S,4S*)-4-((*E*)-4-phenylbut-1-en-1-yl)-1-tosylpyrrolidine-3-carbaldehyde (2l): Flash chromatography (*c*-Hex:AcOEt = 7:3). ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.44 (d, *J* = 2.0 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.35-7.23 (m, 4H), 7.20-7.17 (m, 1H), 7.11 (d, *J* = 8.0 Hz, 2H), 5.58-5.48 (m, 1H), 5.19 (dd, *J* = 15.6 Hz, *J* = 8.0 Hz, 1H), 3.53 (dd, *J* = 10.4 Hz, *J* = 7.2 Hz, 1H), 3.47 (dd, *J* = 9.6 Hz, *J* = 7.2 Hz, 1H), 3.41 (dd, *J* = 10.4 Hz, *J* = 8.0 Hz, 1H), 2.95 (dd, *J* = 9.6 Hz, *J* = 7.2 Hz, 1H), 2.86 (bq, *J* = 8.0 Hz, 1H), 2.65-2.59 (m, 3H), 2.45 (s, 3H), 2.13-2.24 (m, 2H). ***^{13}C-NMR*** (50 MHz, $CDCl_3$) δ 199.0, 143.9, 141.2, 133.3, 133.2, 129.8 (2C), 128.4 (2C), 128.3 (2C), 127.8, 127.6 (2C), 125.6, 55.6, 52.7, 46.7, 43.0, 35.4, 34.0, 21.6. ***ESI-MS*** (m/z): 406 $[M+Na]^+$, 384 $[M+H]^+$. The *ee* was determined by chiral HPLC analysis after reduction of the aldehyde with $NaBH_4$ and olefin hydrogenation with $Pd(OH)_2/C$: Chiralpak® IB column, λ = 230 nm, *n*-Hexane: *i*-PrOH 90:10; flow rate 1.0 mL/min, *T* = 40°C. t_R (*trans*) = 17.90 min (*major*), 20.80 min (*minor*). t_R (*cis*) = 19.35 min (*major*), 24.42 (*minor*).

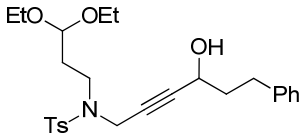
Synthesis of racemic secondary allylic alcohol 1l.



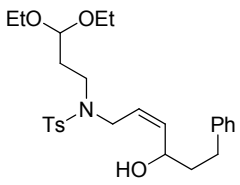
[4] Pham, P.V.; Ashton, K.; MacMillan, D.W.C.; *Chem. Sci.* **2011**, *2*, 1470-1473.



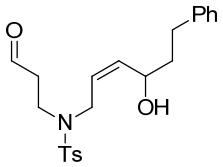
N*-(3,3-diethoxypropyl)-*N*-(prop-2-yn-1-yl)-4-methylbenzenesulfonamide (13):** In an oven dried Schlenk tube sulfonamide **7a** (2 mmol, 1 eq.) was dissolved in 10 mL of anhydrous THF and cooled to 0°C. NaH (2.1 mmol, 1.05 eq, 60 % dispersion in mineral oil) was added and the reaction mixture was stirred at rt for 30 minutes. propargyl bromide (80% w/w solution in toluene, 2.4 mmol, 1.2 eq.) was added at 0°C and the solution was stirred at rt overnight. The reaction was quenched with water (15 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4. The solvent was removed under vacuum and the residue was purified by flash-chromatography on silica gel, (c-Hex:AcOEt = 8:2) to afford the pure product as a pale yellow solid in 98% yield. ***Mp = 55-57 °C. ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 4.58 (t, *J* = 5.6 Hz, 1H), 4.14 (d, *J* = 2.8 Hz, 2H), 3.70-3.62 (m, 2H), 3.56-3.48 (m, 2H), 3.28 (t, *J* = 7.2 Hz, 2H), 2.42 (s, 3H), 2.03 (t, *J* = 2.4 Hz, 1H), 1.93-1.88 (pq, 2H), 1.21 (t, *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 143.5, 135.8, 129.4 (2C), 127.7 (2C), 100.7, 76.6, 73.7, 61.7 (2C), 42.7, 36.7, 32.1, 21.5, 13.3 (2C); ***ESI-MS***: (m/z): 362 $[M+Na]^+$, 265, 222.



N*-(3,3-diethoxypropyl)-*N*-(4-hydroxy-6-phenylhex-2-yn-1-yl)-4-methylbenzenesulfonamide (14):** In an oven dried two-necked round bottom flask the alkyne **13** (2 mmol, 1eq.) and TMEDA (2.6 mmol, 1.3 eq.) were dissolved in 5 ml of anhydrous THF and cooled to -78 °C. BuLi (2.5 M solution in hexane, 2.4 mmol, 1.2 eq.) was added and the solution was stirred for 30 minutes letting the temperature to rise up to -30 °C. Then 3-phenylpropanaldehyde was added dropwise and the orange-brown solution was stirred at room temperature overnight. The reaction was quenched with saturated NH_4Cl solution (2 ml) and diluted with water (10 ml). Aqueous phase were extracted with ethyl acetate (3 x 10 ml) and the combined organic phases were washed with brine and dried over Na_2SO_4. The solvent was evaporated under vacuum and the crude product was purified with flash-chromatography on silica gel (c-Hex:AcOEt 6:4) affording the desired product s a pale yellow oil in 89% of yield. ***^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.0 Hz, 2H), 7.27 (t, *J* = 7.2 Hz, 4H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 4.63 (t, *J* = 5.6 Hz, 1H), 4.17 (s, 2H), 4.12 (bq, *J* = 6.0 Hz, 1H), 3.70-3.62 (m, 2H), 3.56-3.49 (m, 2H), 3.30 (t, *J* = 7.2 Hz, 2H), 2.61 (t, *J* = 8.0 Hz, 2H), 2.32 (s, 3H), 1.96-1.91 (pq, 2H), 1.86-1.70 (m, 2H+OH), 1.21 (t, *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (50 MHz, $CDCl_3$) δ 143.6, 141.0, 135.8, 129.5 (2C), 128.4 (2C), 128.3 (2C), 127.8 (2C), 126.0, 100.6, 86.8, 78.1, 61.6, 61.3 (2C), 42.9, 38.9, 37.1, 32.3, 31.2, 21.4, 15.3 (2C). ***ESI-MS*** (m/z): 496 $[M+Na]^+$, 428 $[M-EtO]^+$, 410, 328. Anal. calcd for ($C_{26}H_{35}NO_5S$: 473,62): C, 65.93; H, 7.45; N, 2.96; Found: C, 65.88; H, 7.55; N, 2.90.

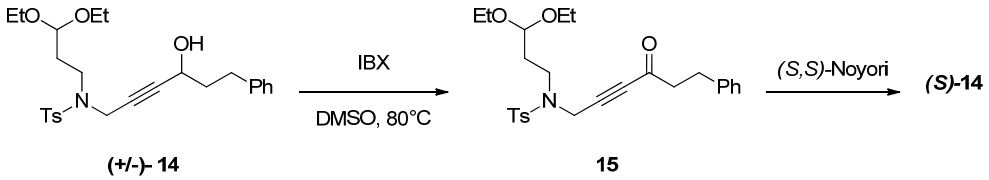


(*Z*)-*N*-(3,3-diethoxypropyl)-*N*-(4-hydroxy-6-phenylhex-2-en-1-yl)-4-methylbenzenesulfonamide (12l): In a two-necked round bottom flask **14** (300 mg, 0.63 mmol, 1 eq.) was dissolved in 5 ml of anhydrous methanol and Lindlar catalyst was added (5 % of $Pd/CaCO_3$, 0.031 mmol, 0.05 eq). The reaction flask was evacuated and backfilled with hydrogen 3 times. The reaction mixture was then stirred under atmospheric pressure of hydrogen for three hours. The solution was filtered through a Celite® pad, washing the solid with DCM. The filtrate was concentrated under vacuum and the crude product was purified with flash chromatography on silica gel (c-Hex:AcOEt 7:3) affording the product in 76% of yield as a clear oil. ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.4 Hz, 2H), 7.32-7.26 (m, 4H), 7.20-7.17 (m, 1H), 7.18 (d, *J* = 8.4 Hz, 2H), 5.61 (dd, *J* = 10.8 Hz, *J* = 9.2 Hz, 1H), 5.42-5.35 (m, 1H), 4.50 (t, *J* = 5.2 Hz, 1H), 4.42-4.36 (pq, 1H), 3.85 (dd, *J* = 15.2 Hz, *J* = 5.6 Hz, 1H), 3.77(dd, *J* = 15.2 Hz, *J* = 8.8 Hz, 1H) 3.67-3.58 (m, 2H), 3.53-3.44 (m, 2H), 3.27-3.14 (m, 2H), 2.67 (t, *J* = 7.2 Hz, 2H), 2.58 (bs, 1H), 2.44 (s, 3H), 1.99-1.90 (m, 1H), 1.88-1.84 (pq, 2H), 1.78-1.69 (m, 1H), 1.19 (t, *J* = 7.2 Hz, 6H). ***^{13}C-NMR*** (50 MHz, $CDCl_3$) δ 143.2, 141.5, 136.6, 129.6 (2C), 128.3 (3C), 128.2 (2C), 127.0 (2C), 125.8, 125.7, 100.7, 65.8, 61.8, 61.7, 44.8, 43.6, 38.1, 32.8, 31.4, 21.4, 15.1 (2C). ***ESI-MS*** (m/z): 498 $[M+Na]^+$, 430 $[M-EtO]^+$, 412, 384, 358. Anal. calcd for ($C_{26}H_{37}NO_5S$: 473,62): C, 65.65; H, 7.84; N, 2.94; Found: C, 65.70; H, 7.61; N, 2.91.

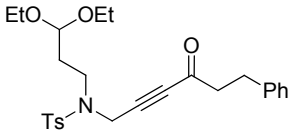


(*Z*)-*N*-(4-hydroxy-6-phenylhex-2-en-1-yl)-*N*-(3-oxopropyl)-4-methylbenzene-sulfonamide (1l): In a round bottom flask **12l** (0.25 mmol, 1eq.) was dissolved in 5 mL of a 1:1 mixture of THF and water. Aqueous HCl (0.5 M, 2.5 mL) was added to the solution and the reaction mixture was stirred at 50 °C until complete consumption of the starting material was observed by TLC (2 hours). The aqueous layer was extracted with ethyl acetate (3 x 10 mL), the combined organic phases were washed with water (10 mL) and then dried over Na_2SO_4. The organic solvent was removed under reduced pressure affording **1l** as a clear oil in 94% of yield. **1l** was used for the catalytic cyclization without further purification. ***^{1}H-NMR*** (400 MHz, $CDCl_3$) δ 9.70 (s, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.30-7.23 (m, 4H), 7.17-7.14 (m, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 5.57 (dd, *J* = 10.8 Hz, *J* = 8.8 Hz, 1H), 5.34-5.28 (m, 1H), 4.38-4.33 (pq, 1H), 3.79 (d, *J* = 8.8 Hz, 2H), 3.37 (t, *J* = 8.8 Hz, 2H), 2.76 (t, *J* = 8.8 Hz, 2H), 2.64-2.62 (m, 2H), 2.02 (s, 3H), 1.95-1.85 (m, 1H), 1.75-1.66 (m, 1H). ***^{13}C-NMR*** (50 MHz, $CDCl_3$) δ 200.7, 143.6, 141.4, 136.6, 136.1, 129.8 (2C), 128.3 (3C), 127.1 (3C), 125.9 (2C), 66.2, 45.8, 43.8, 41.2, 38.4, 31.4, 21.4. ***ESI-MS*** (m/z): 498, 384 $[M-OH]^+$.

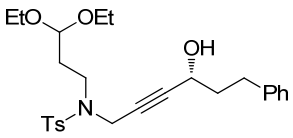
Synthesis of enantiomerically enriched secondary allylic alcohol 1l.



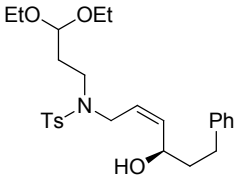
(+/-)- 14 15



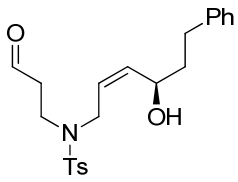
N*-(3,3-diethoxypropyl)-*N*-(4-oxo-6-phenylhex-2-yn-1-yl)-4-methylbenzene-sulfonamide 15:** In an oven-dried two-necked round bottom flask under nitrogen atmosphere, of **14** (300 mg, 0.63 mmol, 1 eq.) was dissolved in 5 ml of anhydrous DMSO and IBX was added (0.76 mmol, 1.2 eq.). The reaction mixture was heated at 60°C until complete consumption of alcohol **14** (TLC, 2 hours). The solution was diluited with water (10 ml) and extracted with ethyl acetate (3 x 5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified with flash-chromatography (c-Hex:AcOEt 8:2) to afford the pure ketone as a clear oil in 81% of yield. ***^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.31-7.24 (m, 5H), 7.13 (d, *J* = 8.0 Hz, 2H), 4.59 (t, *J* = 5.6 Hz, 1H), 4.32 (s, 2H), 3.72-3.47 (m, 4H), 3.29 (t, *J* = 7.2 Hz, 2H), 2.82 (t, *J* = 6.8 Hz, 2H), 2.60 (t, *J* = 6.8 Hz, 2H), 2.31 (s, 3H), 1.95-1.87 (pq, 2H), 1.21 (t, *J* = 7.2 Hz, 6H).***^{13}C-NMR*** (100 MHz, $CDCl_3$) δ 185.3, 143.9, 139.8, 135.3, 129.6 (2C), 128.5 (2C), 128.1 (2C), 127.6 (2C), 126.3, 100.6, 84.9, 84.0, 61.8 (2C), 46.6, 43.0, 36.8, 32.2, 29.4, 21.3, 15.2 (2C). ***ESI-MS*** (m/z): 494 $[M+Na]^+$, 426 $[M-EtO]^+$, 380. Anal. calcd for ($C_{26}H_{33}NO_5S$: 471,61): C, 66.22; H, 7.05; N, 2.97; Found: C, 66.12; H, 7.00; N, 3.05.



(*R*)-13. In an oven-dried Schlenk tube ketone **15** (100 mg, 0.2 mmol, 1.0 eq.) was dissolved in 1:1 mixture of DCM and water. Sodium formate (2 mmol, 10 eq.), TBAC (0.06 mmol, 0.3 eq.) and (*S,S*)-Noyori catalyst [(*R,R*)-TsDIPEN-RuCl(*p*-cymene)] were added. The reaction was allowed to stir at room temperature for 24 hours, then it was diluited with water (2 ml) and extracted with DCM (3 x 5 ml). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified with flash-chromatography (c-Hex:AcOEt 8:2) to afford the desired product as a brown oil in 33% of yield and 86% of *ee*. [α]: -1.9 ° (*c*: 0.42, $CHCl_3$). The *ee* was determined by chiral HPLC analysis: Chiralcel® OD column, λ = 230 nm, *n*-Hexane: *i*-PrOH 90:10; flow rate 0.5 mL/min, *T* = 40 °C. t_R = 29.62 min (*minor*), 32.23 min (*major*). [(*S*)-**13** was prepared following the same procedure using the (*S,S*)-Noyori catalyst].



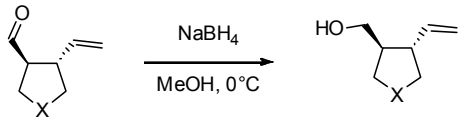
(*R*)-12l was prepared with Lindlar reduction as (+/-)-**12l.** [α]:+ 291° ($CHCl_3$, c = 0.67). The *ee* was confirmed by chiral HPLC analysis: Chiralcel® OD column, λ = 230 nm, *n*-Hexane:*i*-PrOH 90:10; flow rate 0.8 mL/min, *T* = 40°C. t_R = 17.04 min (*major*), 20.88 min (*minor*). [(*S*)-**12l** was prepared in the same way and *ee* was confirmed by HPLC analysis].



(***R*)-1l** was prepared from (***R*)-12l** as **(+/-)-1l**. [α]: +25° ($CHCl_3$, c: 0.60). [**(*S*)-1l** was prepared from (***S*)-12l**].

HPLC Derivatization.

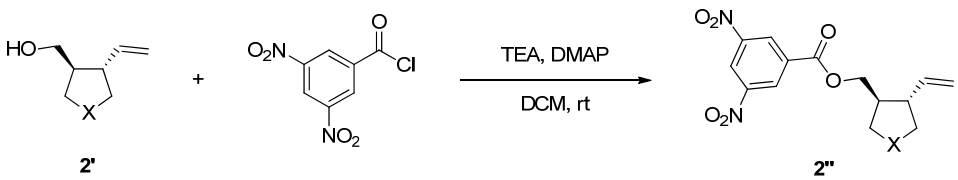
General procedure for the reduction of 2:



2 **2'**

Under air atmosphere, aldehyde **2** (1 eq.) was dissolved in 0.5 ml of MeOH. The solution was cooled to 0 °C and $NaBH_4$ (5 eq.) was added. The reaction mixture was stirred for 30 minutes at 0°C and then quenched with water (1 mL). The aqueous layer was extracted with ethyl acetate (3 x 3 mL). The combined organic phases were washed with brine (5 mL), dried over Na_2SO_4 and concentrated under vacuum to afford the alcohol **2'** as a clear oil which was submitted without further purification, either to chiral HPLC analysis or to further derivatization.

General procedure for the acylation of alcohols 2':

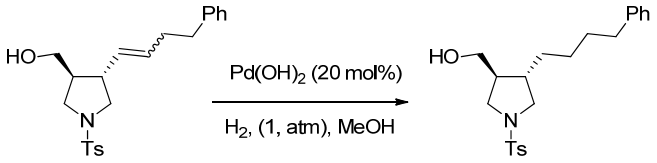


2' **2"**

Under air atmosphere, alcohol **2'** (1 eq.) was dissolved in 1 mL of DCM. The solution was cooled to 0 °C and triethylamine (4 eq.), 3,5-dinitrobenzoyl chloride (2 eq.) and DMAP (0.1 eq.) were added. The reaction mixture was stirred at rt until complete consumption of the starting material (TLC, 2 hours). Then the reaction was quenched with $NaHCO_3$ saturated solution (2 ml) and the

aqueous layer was extracted with DCM (3 x 3 mL). The combined organic phases were dried over Na_2SO_4 ad the organic solvent was removed under reduced pressure. The crude product was purified by flash-chromatography on a short pad of silica gel (c-Hex:AcOEt 8:2).

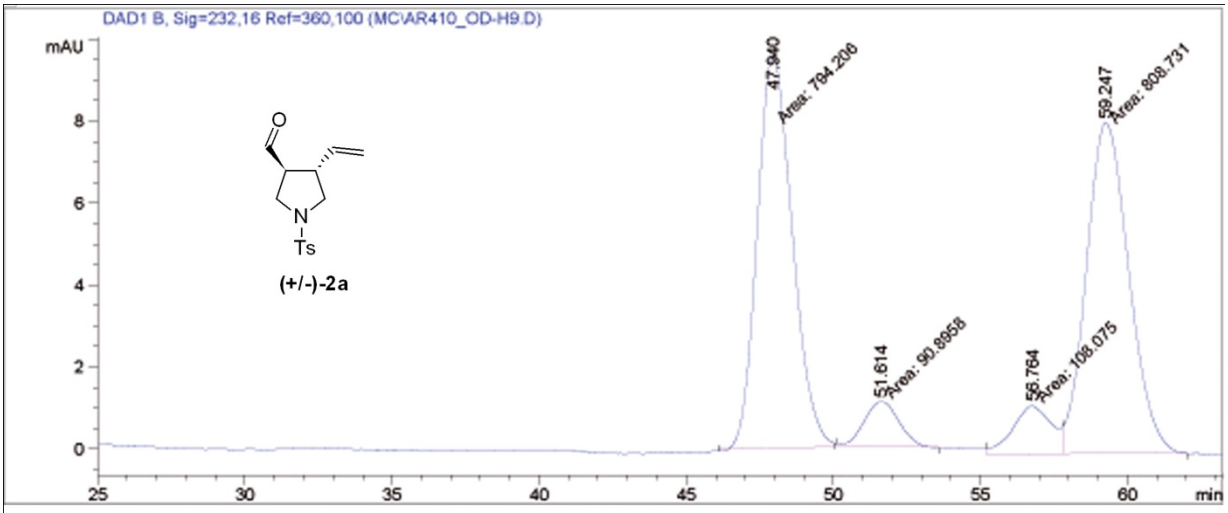
General procedure for the reduction of olefins 2l':



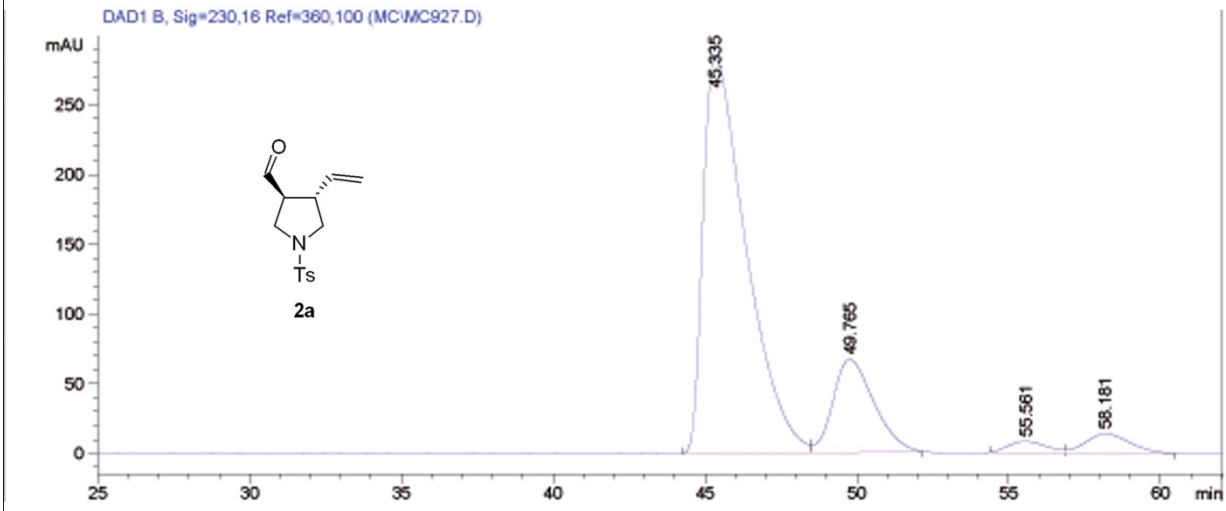
2l' **2l''**

In a two necked round bottom flask alcohols **2l'** (10 mg, 26 µmol, 1 eq.) was dissolved in 0.5 mL of anhydrous methanol and 7 mg of $Pd(OH)_2$ (10% w/w dispersion on charcoal, 0.2 eq) were added. The reaction flask was evacuated and backfilled with hydrogen 3 times and the reaction mixture was stirred overnight under hydrogen atmosphere. The solution was filtered through a short pad of Celite® washing with ethyl acetate (5 mL) and the solvent was removed under reduced pressure to afford the desired product which was subjected to chiral HPLC analysis without further purification.

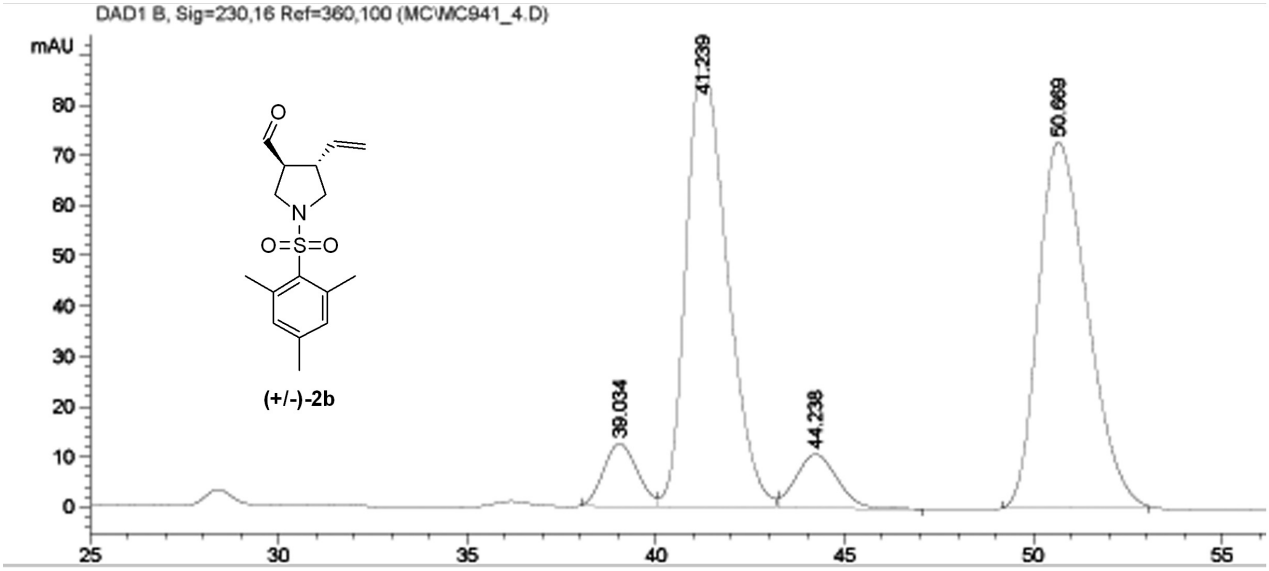
HPLC spectra.



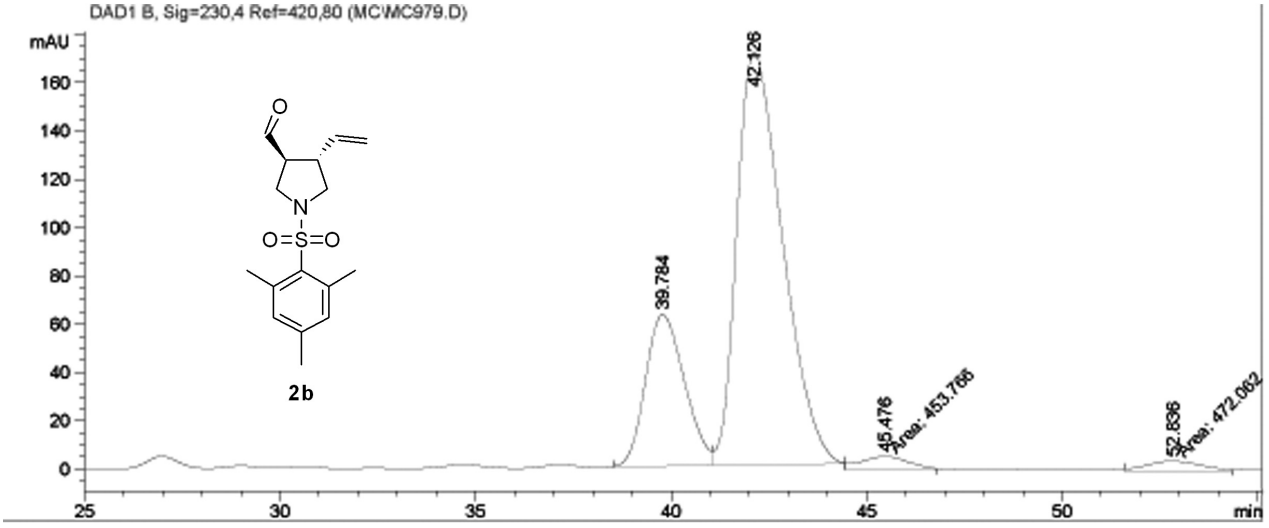
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	47.940	MM	1.3874	794.20618	9.54060	44.0758
2	51.614	MM	1.3783	90.89584	1.09914	5.0444
3	56.764	MF	1.5369	108.07489	1.17200	5.9978
4	59.247	FM	1.6742	808.73138	8.05088	44.8819



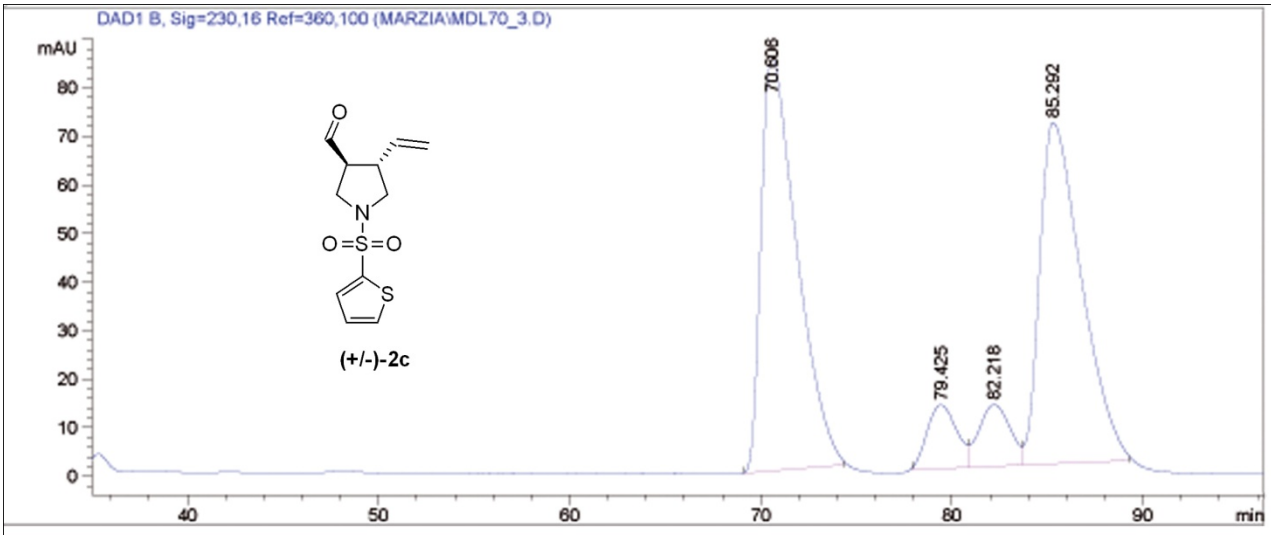
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	45.335	BB	1.4679	2.80039e4	285.10358	77.0712
2	49.765	BB	1.4128	6243.83643	66.65603	17.1840
3	55.561	BV	1.2533	693.78717	8.06721	1.9094
4	58.181	VB	1.4387	1393.60132	13.84074	3.8354



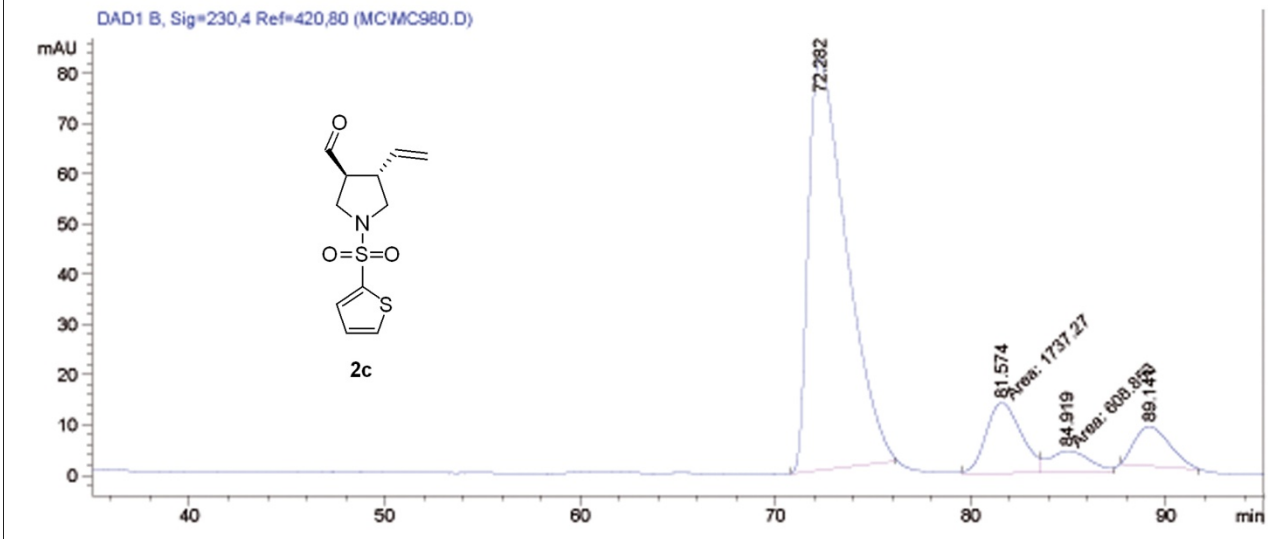
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	39.034	BV	0.9761	777.49463	12.45813	5.2195
2	41.239	VB	1.1565	6705.41211	89.45301	45.0148
3	44.238	BB	1.1067	820.15009	10.69441	5.5058
4	50.669	BB	1.3801	6592.94922	72.83155	44.2598



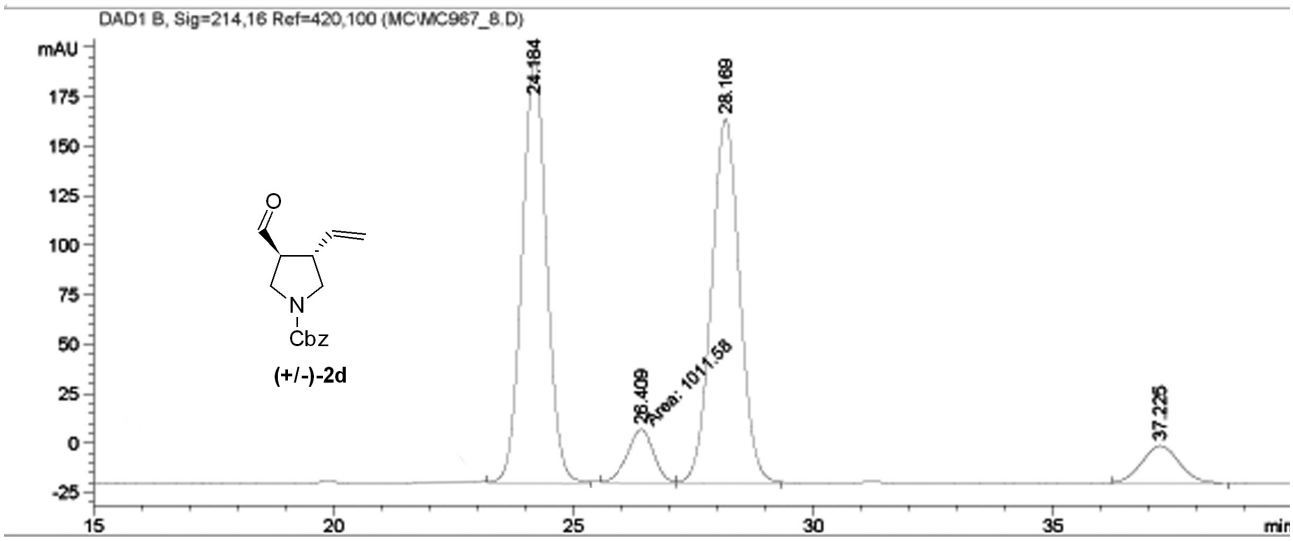
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	39.784	BV	1.0757	4350.94580	62.69361	22.7000
2	42.126	VB	1.2455	1.38903e4	170.67711	72.4697
3	45.476	MM	1.4404	453.76636	5.25064	2.3674
4	52.836	MM	1.7271	472.06158	4.55556	2.4629



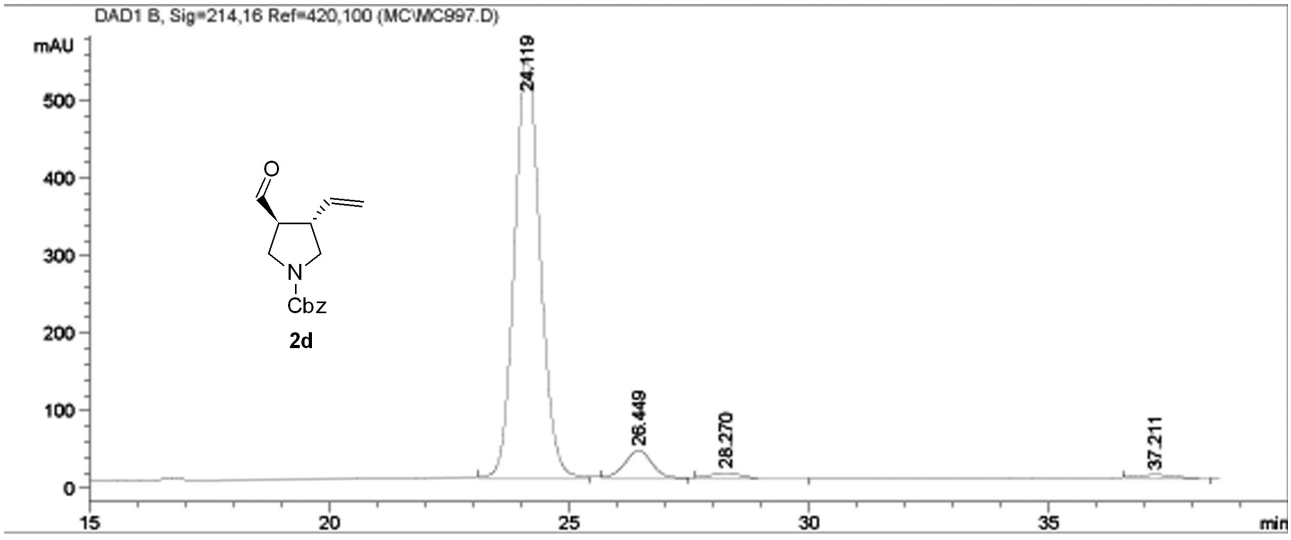
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	70.606	BB	1.9113	1.10717e4	84.90718	44.9824
2	79.425	BV	1.5180	1404.91028	13.07114	5.7079
3	82.218	VV	1.6082	1446.24597	12.70375	5.8758
4	85.292	VB	2.1380	1.06906e4	70.22620	43.4338



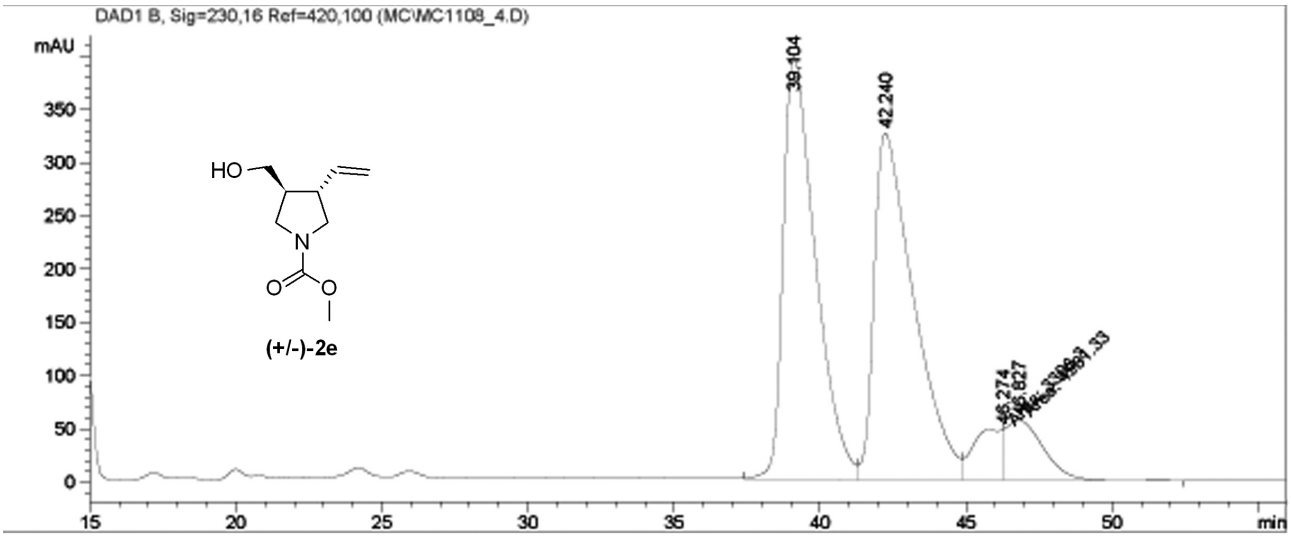
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	72.282	BB	1.8855	1.11047e4	81.81365	76.9366
2	81.574	MF	2.0727	1737.26575	13.96946	12.0363
3	84.919	FM	2.4069	608.85303	4.21610	4.2183
4	89.141	BB	1.4685	982.74036	7.85016	6.8087



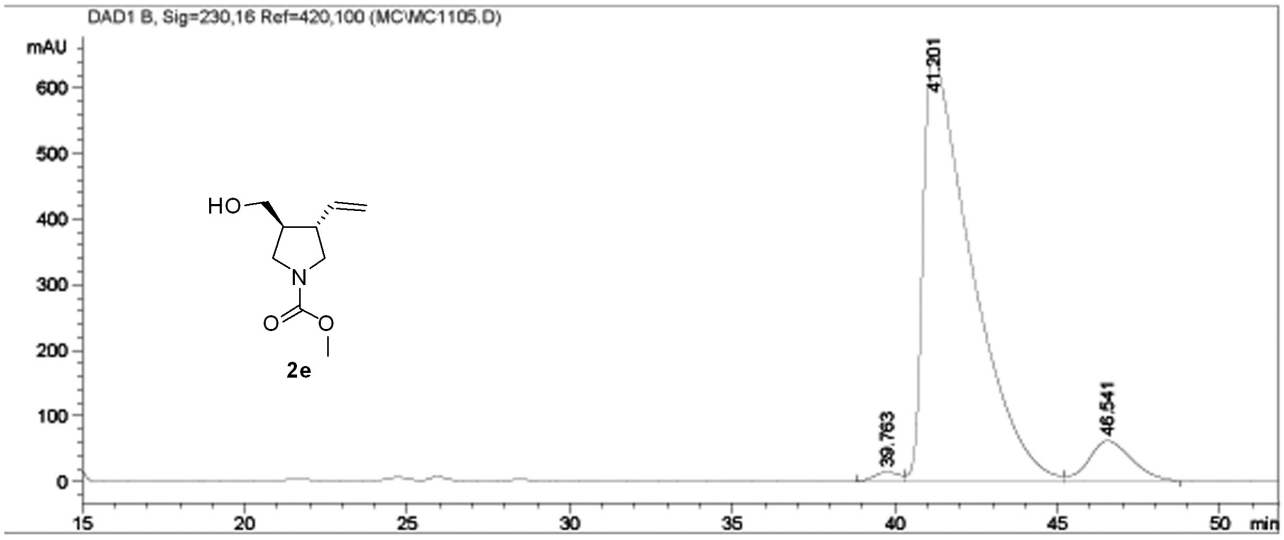
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.184	VB	0.5489	7604.75244	213.86201	44.3284
2	26.409	FM	0.6236	1011.58002	27.03625	5.8965
3	28.169	VB	0.6282	7503.64502	183.82829	43.7390
4	37.225	BB	0.8469	1035.51111	18.84862	6.0360



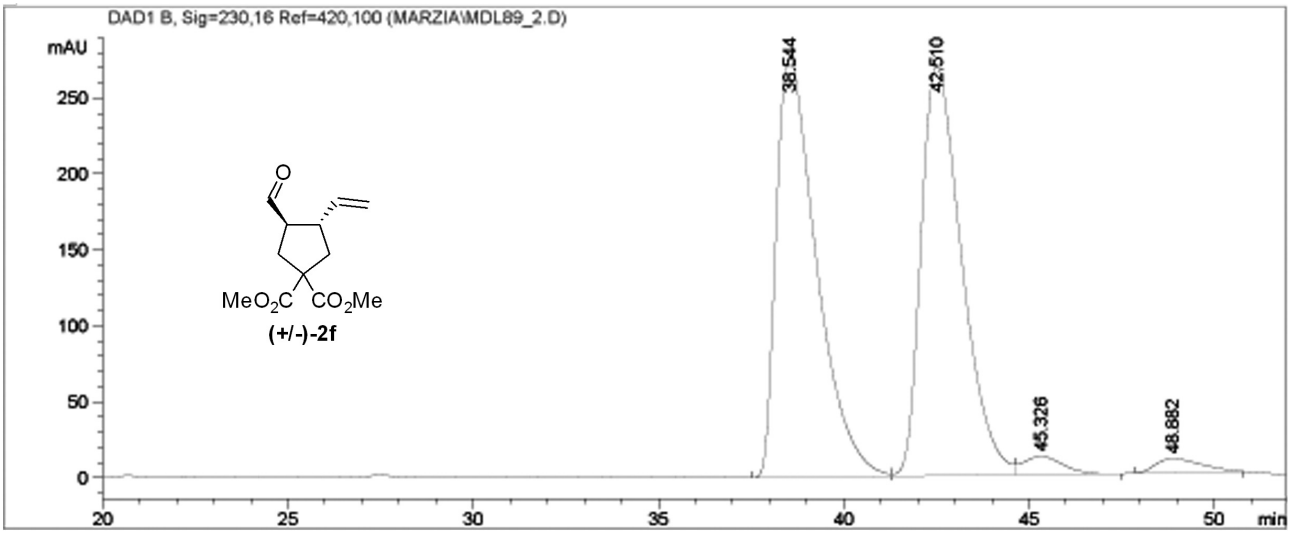
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.119	VB	0.5725	2.02928e4	544.87268	91.1581
2	26.449	BB	0.6267	1457.19324	35.81544	6.5459
3	28.270	BB	0.6755	332.72617	7.35943	1.4946
4	37.211	BB	0.7227	178.38824	3.67263	0.8013



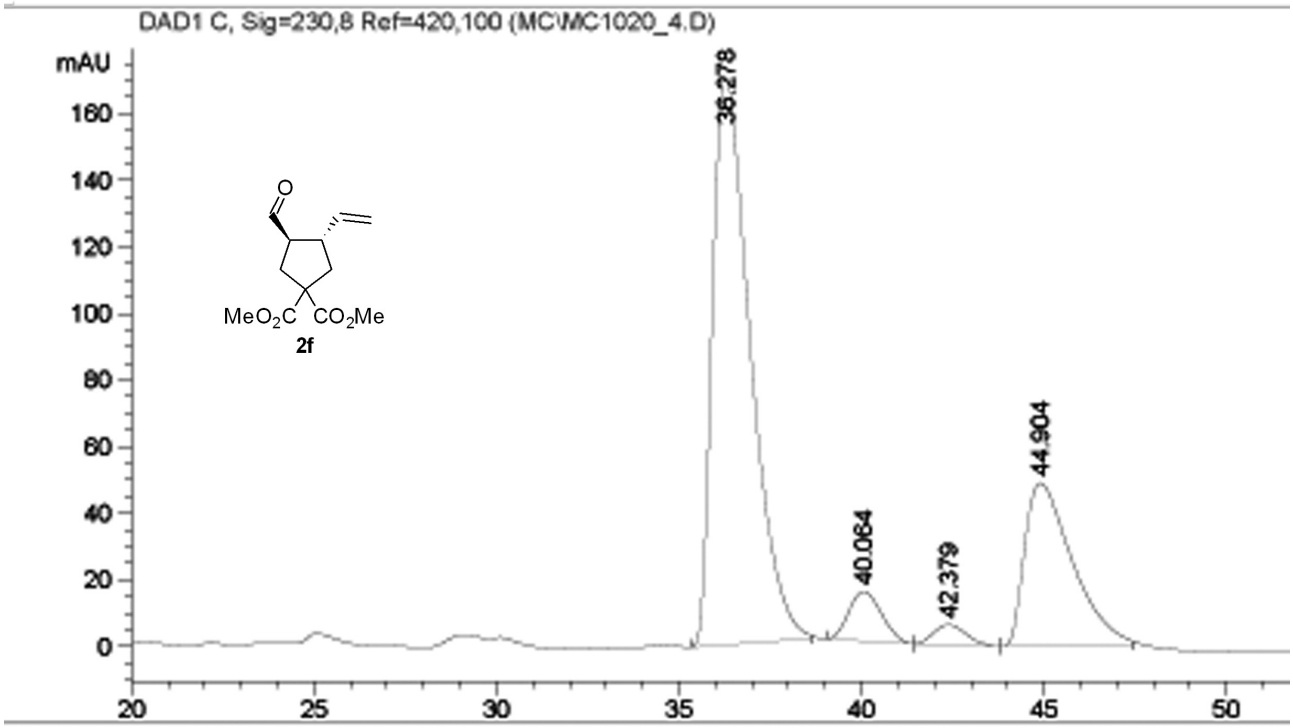
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	39.104	VV	1.1568	3.06803e4	397.33609	43.9476
2	42.240	VV	1.3769	3.08432e4	325.66959	44.1809
3	46.274	MF	1.1633	3306.30322	47.37077	4.7361
4	46.827	FM	1.4827	4981.32812	55.99429	7.1354



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	39.763	BV	0.8211	758.74493	14.20555	1.0332
2	41.201	VB	1.4667	6.70871e4	645.43152	91.3497
3	46.541	BB	1.3791	5594.04492	61.27642	7.6172



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	38.544	BB	1.1496	2.08574e4	276.03241	48.3829
2	42.510	BB	1.1726	2.05367e4	269.61823	47.6388
3	45.326	BB	1.0887	874.09369	12.01636	2.0276
4	48.882	BB	1.3165	840.90326	9.46488	1.9506



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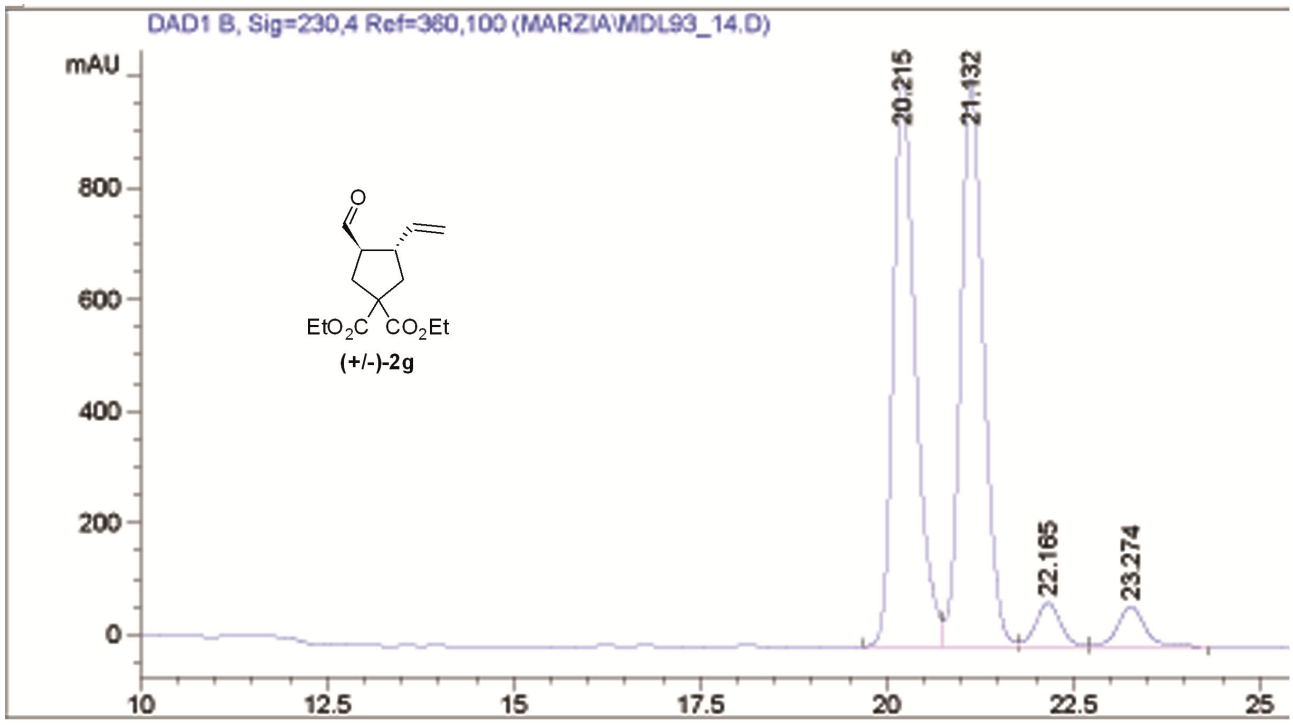
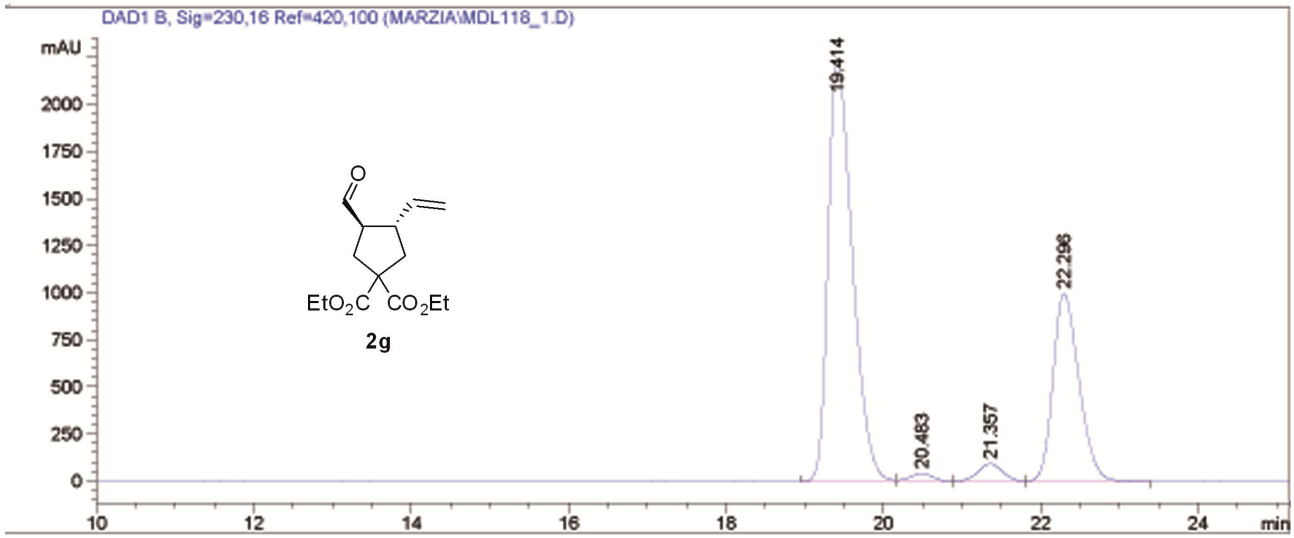
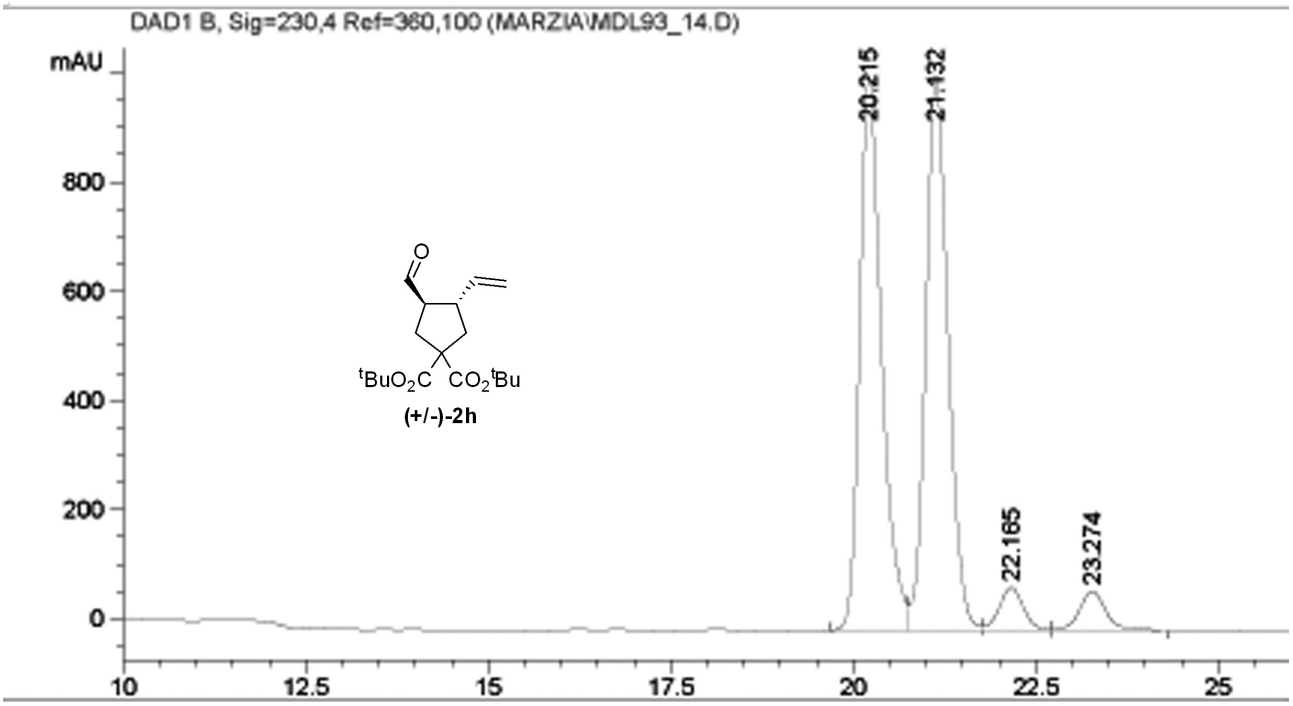
1	36.278	BB	1.1040	1.22859e4	170.24001	68.4141
2	40.064	BV	0.9294	927.63641	14.87744	5.1656
3	42.379	VV	0.8678	367.46085	5.98947	2.0462
4	44.904	VB	1.3250	4377.13672	48.68304	24.3741



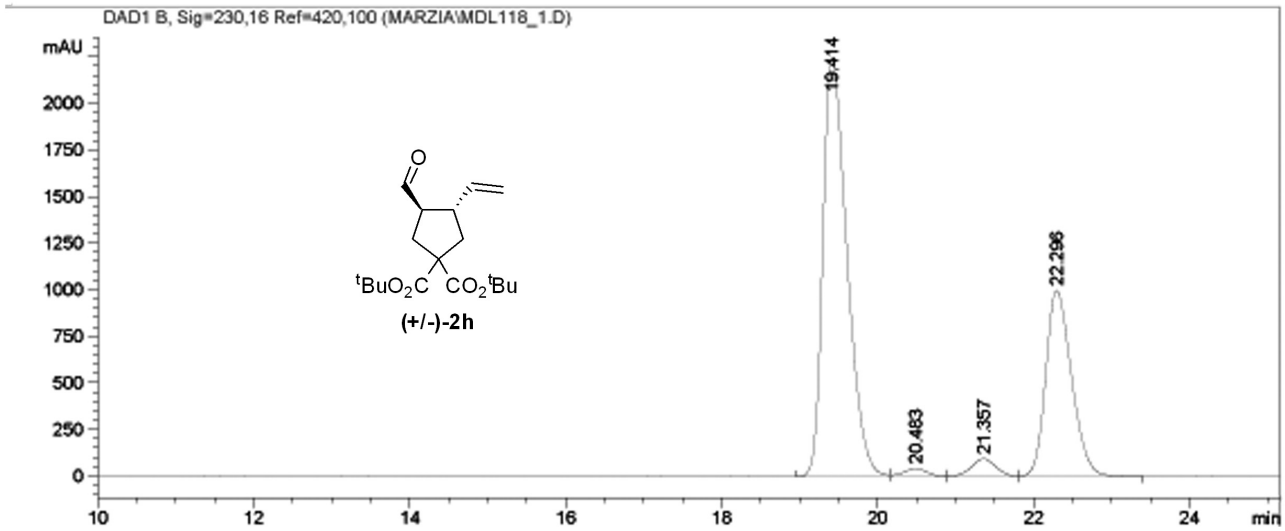
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.215	BV	0.3138	2.12213e4	1015.40509	45.6639
2	21.132	VV	0.3216	2.15590e4	1015.64124	46.3905
3	22.165	VV	0.3539	1819.57849	78.66660	3.9154
4	23.274	VB	0.3897	1872.97925	72.41776	4.0303



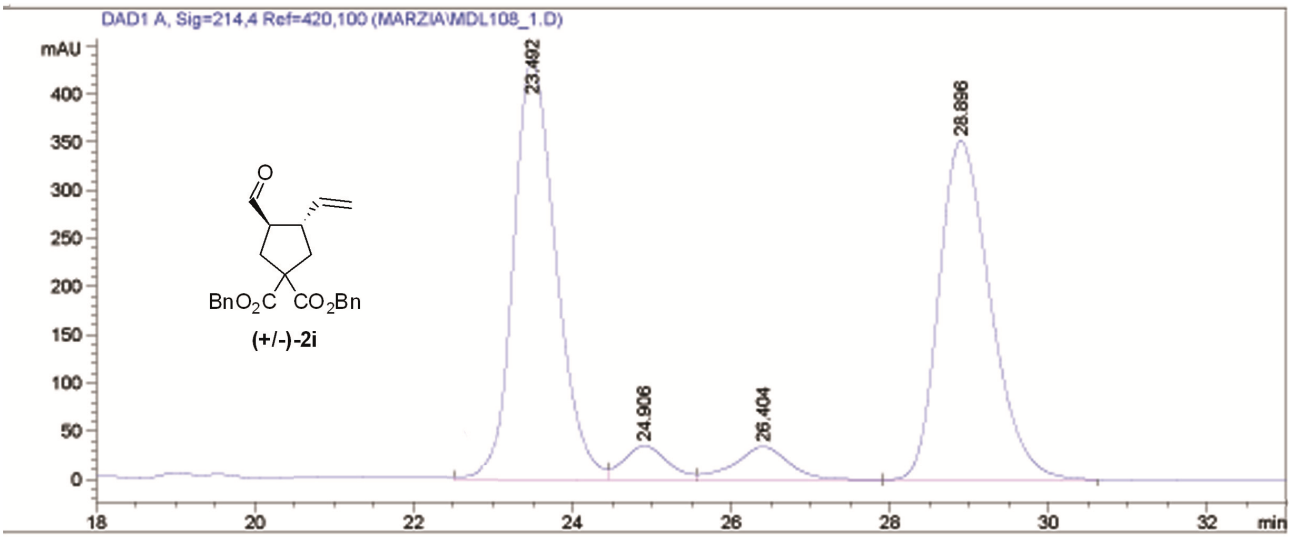
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.414	BV	0.3301	4.81908e4	2247.97461	64.9748
2	20.483	VV	0.3248	906.50781	42.85817	1.2222
3	21.357	VV	0.3415	2115.91919	95.12052	2.8529
4	22.296	VB	0.3521	2.29552e4	999.07977	30.9501



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.215	BV	0.3138	2.12213e4	1015.40509	45.6639
2	21.132	VV	0.3216	2.15590e4	1015.64124	46.3905
3	22.165	VV	0.3539	1819.57849	78.66660	3.9154
4	23.274	VB	0.3897	1872.97925	72.41776	4.0303



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.414	BV	0.3301	4.81908e4	2247.97461	64.9748
2	20.483	VV	0.3248	906.50781	42.85817	1.2222
3	21.357	VV	0.3415	2115.91919	95.12052	2.8529
4	22.296	VB	0.3521	2.29552e4	999.07977	30.9501



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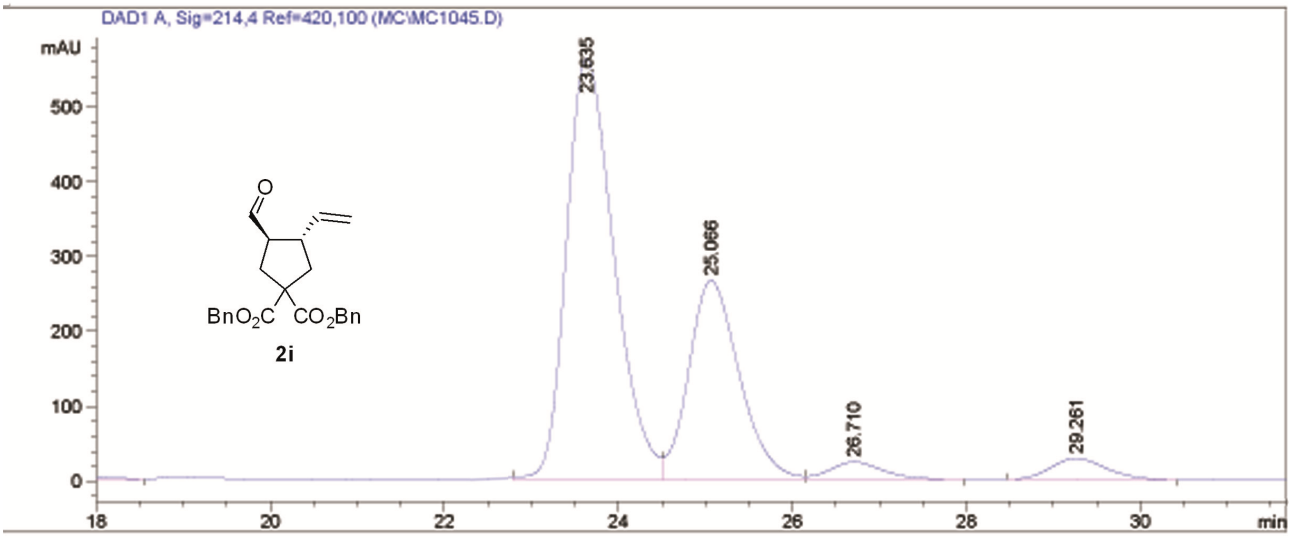
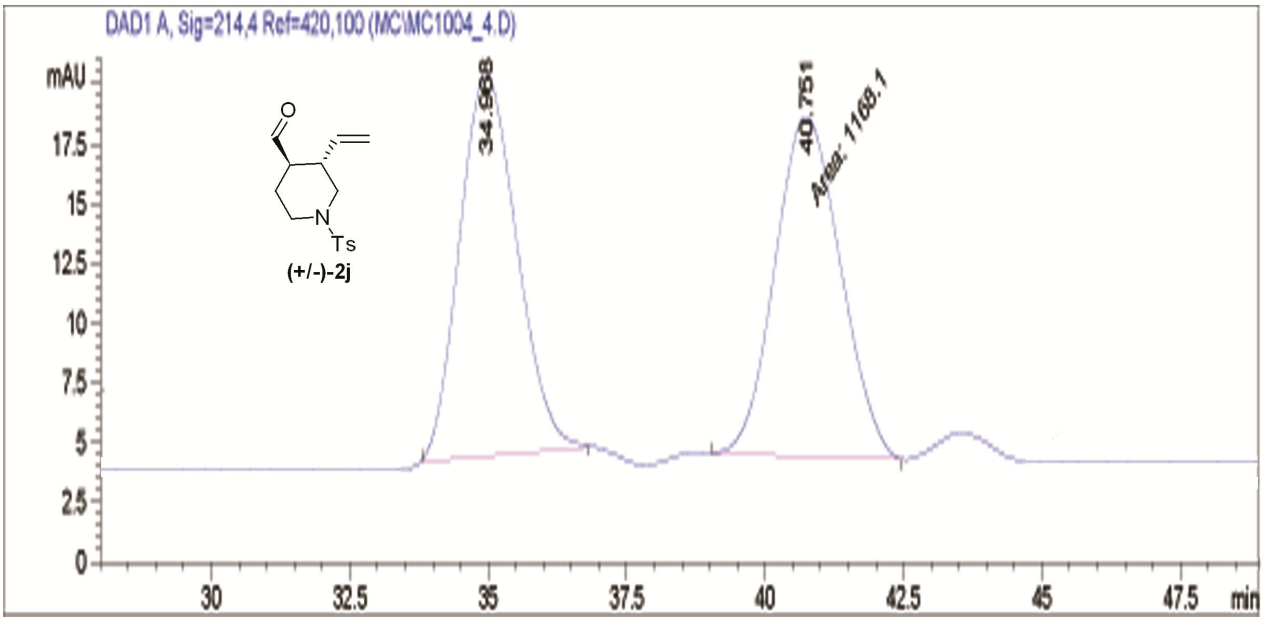
1	23.492	VV	0.5661	1.60552e4	435.55353	45.9688
2	24.906	VV	0.5867	1350.40735	34.95952	3.8664
3	26.404	VV	0.7028	1643.79321	34.32207	4.7065
4	28.896	VB	0.6984	1.58769e4	351.88626	45.4583



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
3	23.635	VV	0.5894	2.13677e4	562.26788	57.4020
4	25.066	VV	0.6199	1.07542e4	265.86685	28.8900
5	26.710	VB	0.6469	989.48730	23.23217	2.6581
6	29.261	BB	0.6738	1251.78516	28.20258	3.3628



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.968	BB	1.0242	1147.77075	15.90054	49.5611
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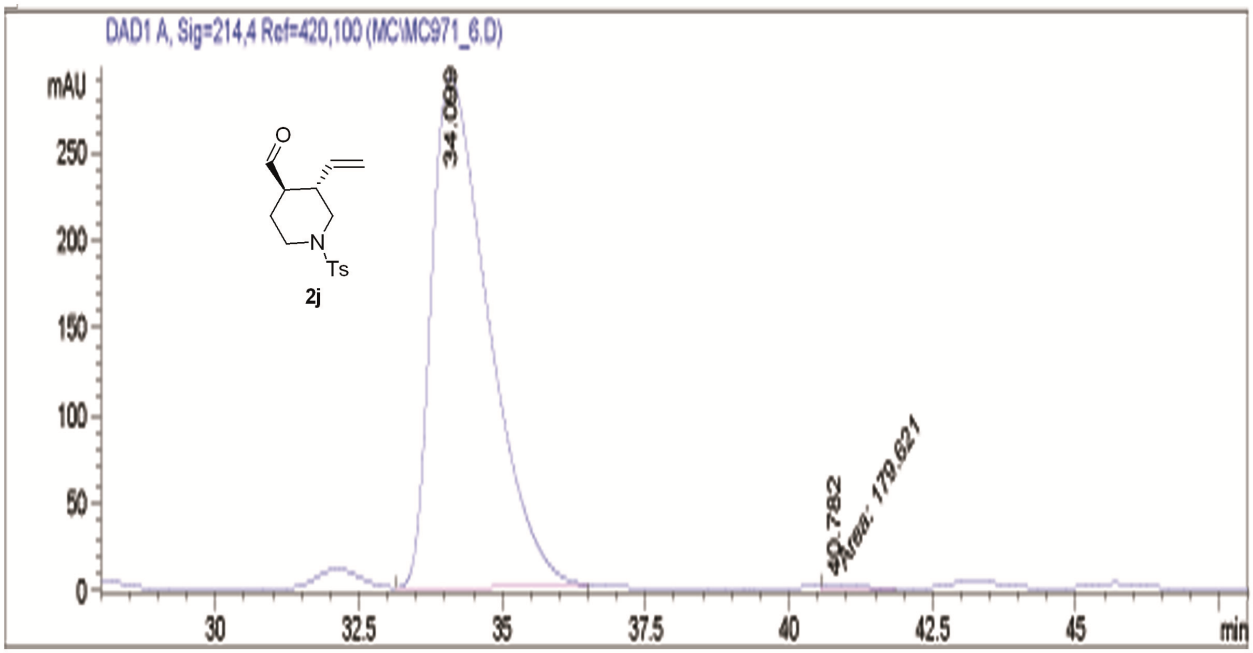

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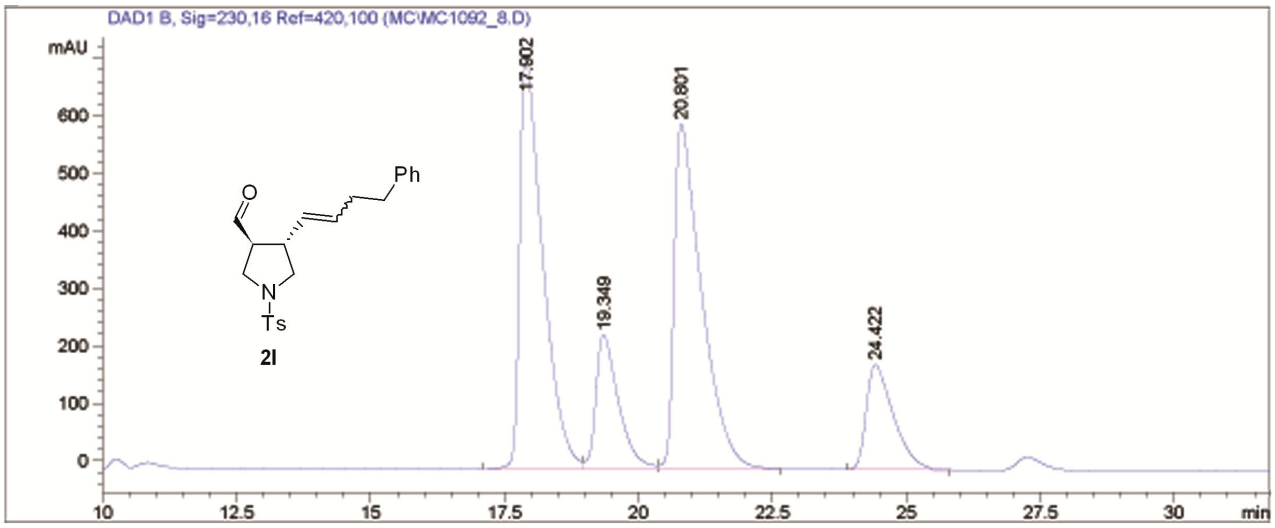
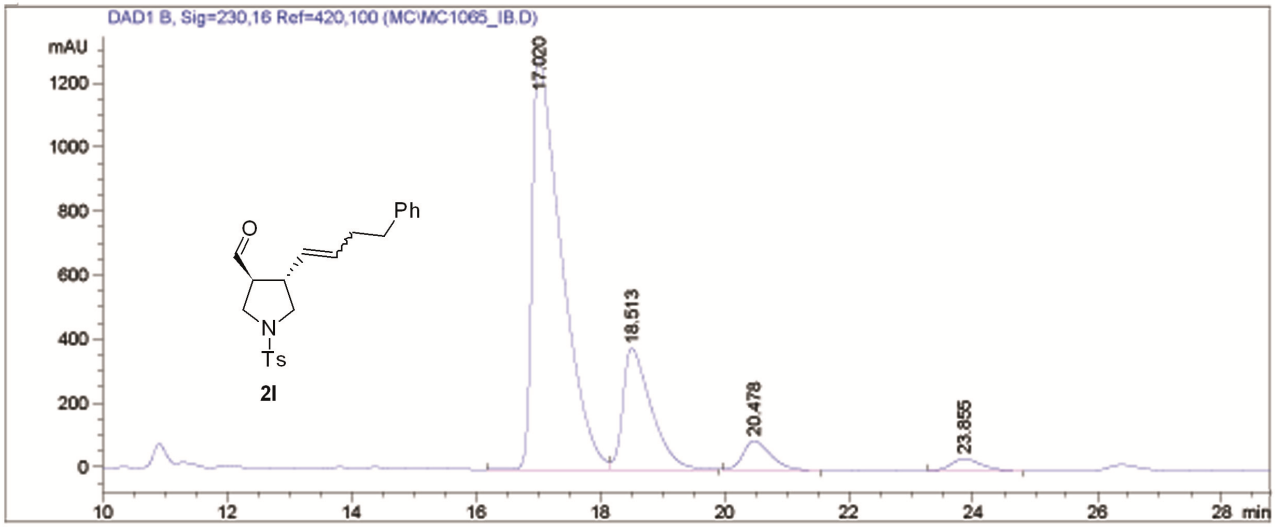
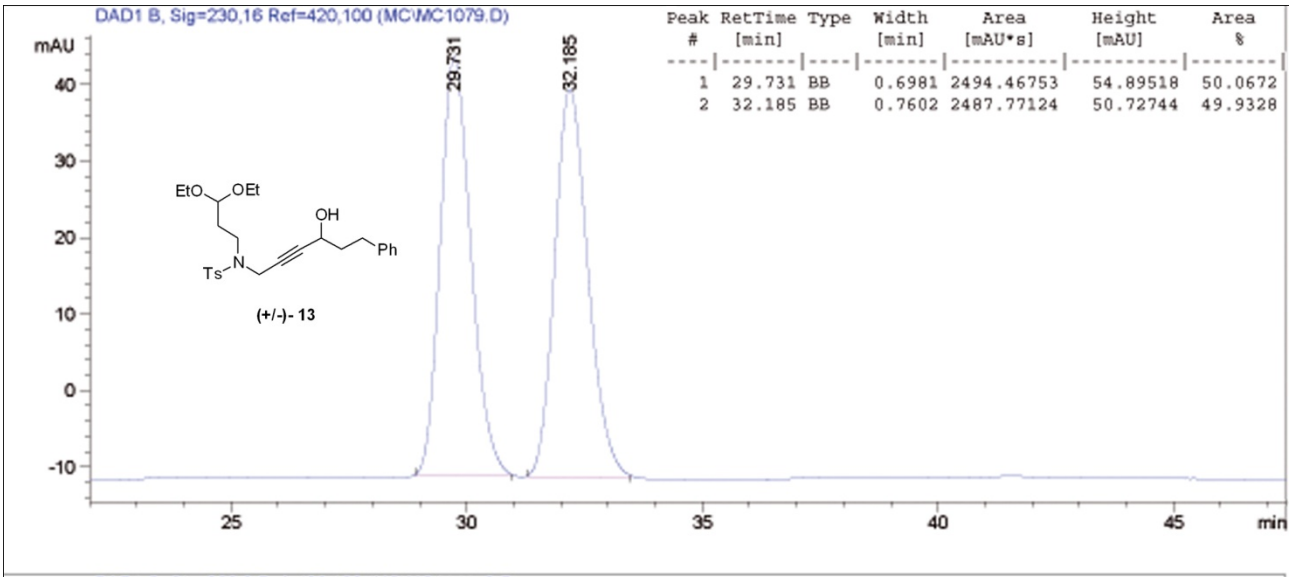
1	34.099	VB	1.0446	2.01729e4	291.06061	99.1175
2	40.782	MM	0.8962	179.62080	3.34037	0.8825



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.902	VV	0.4392	2.14036e4	715.00415	38.1905
2	19.349	VV	0.4365	6841.22607	233.02049	12.2068
3	20.801	VB	0.5186	2.14092e4	599.62347	38.2005
4	24.422	BB	0.5278	6390.23535	181.91318	11.4021



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.020	BV	0.4792	4.23116e4	1288.33618	72.2526
2	18.513	VB	0.4777	1.21612e4	379.66013	20.7669
3	20.478	BB	0.4721	2860.33643	91.64367	4.8844
4	23.855	BB	0.5113	1227.44995	36.59459	2.0960



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.731	BB	0.6981	2494.46753	54.89518	50.0672
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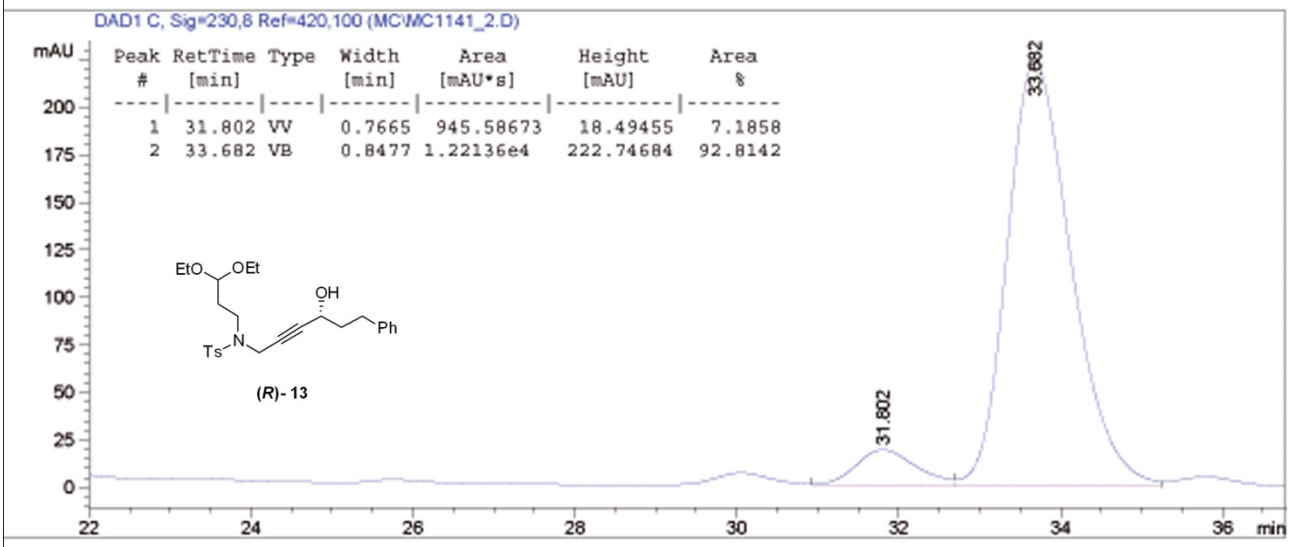
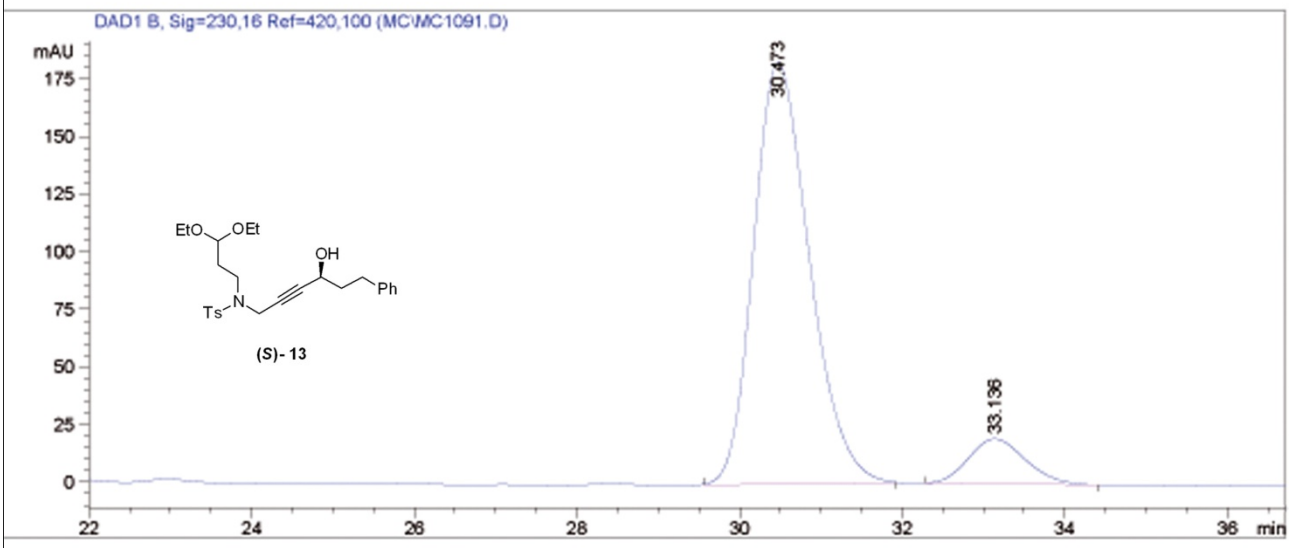
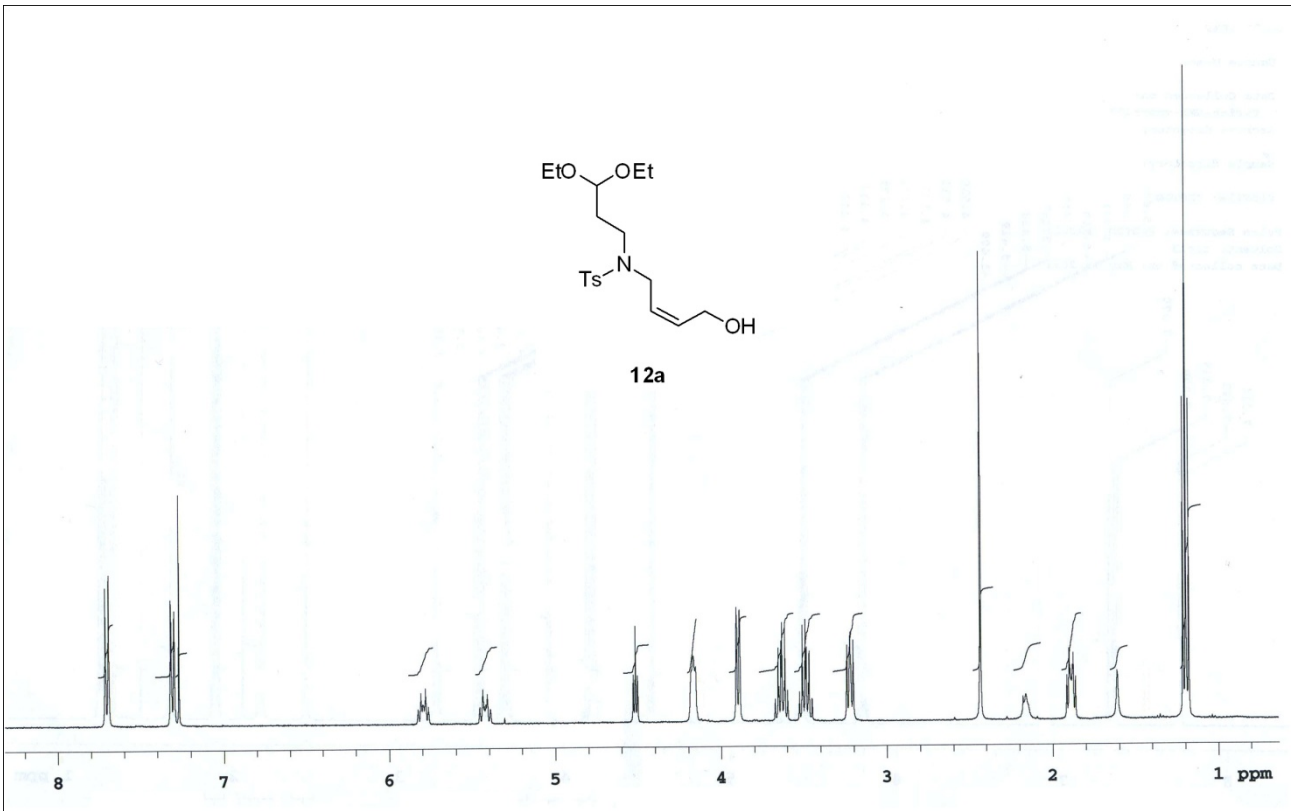


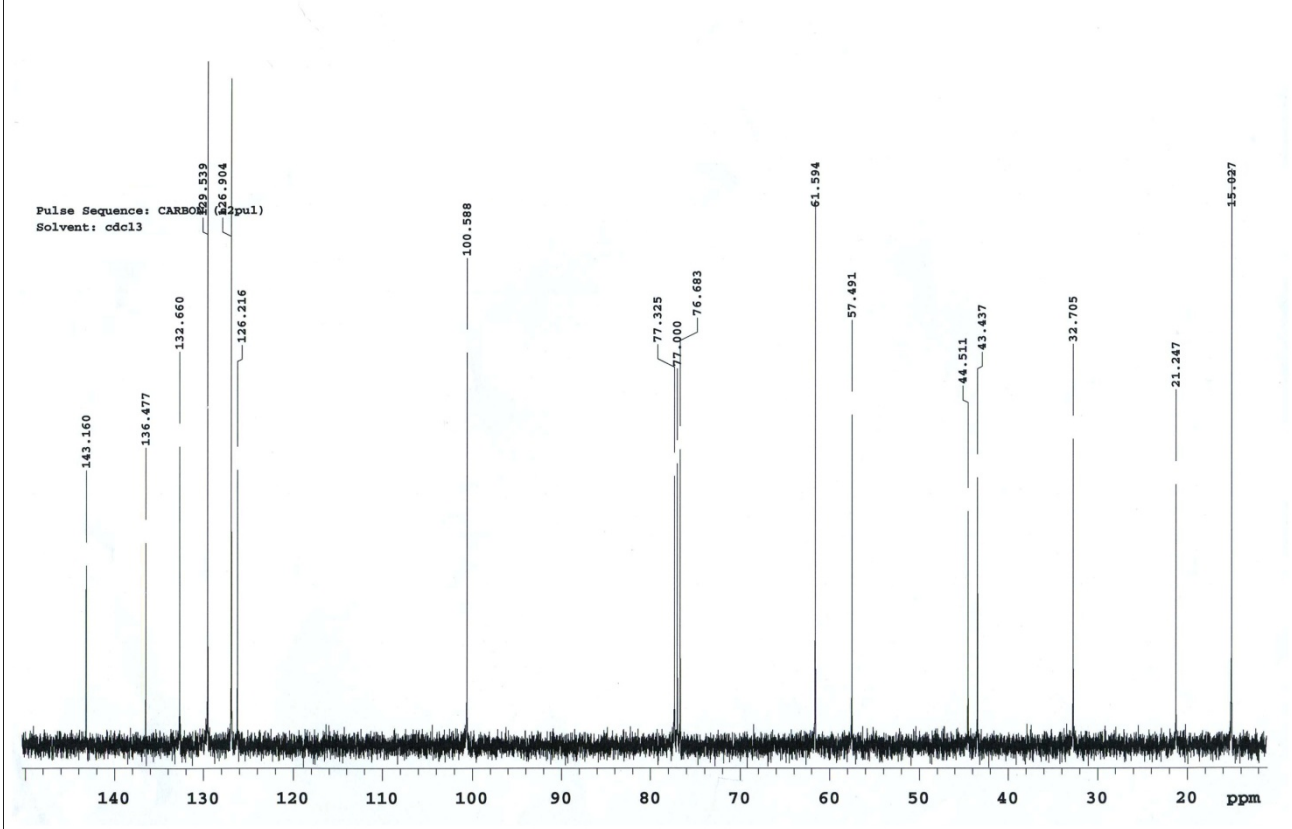
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.802	VV	0.7665	945.58673	18.49455	7.1858
2	33.682	VB	0.8477	1.22136e4	222.74684	92.8142

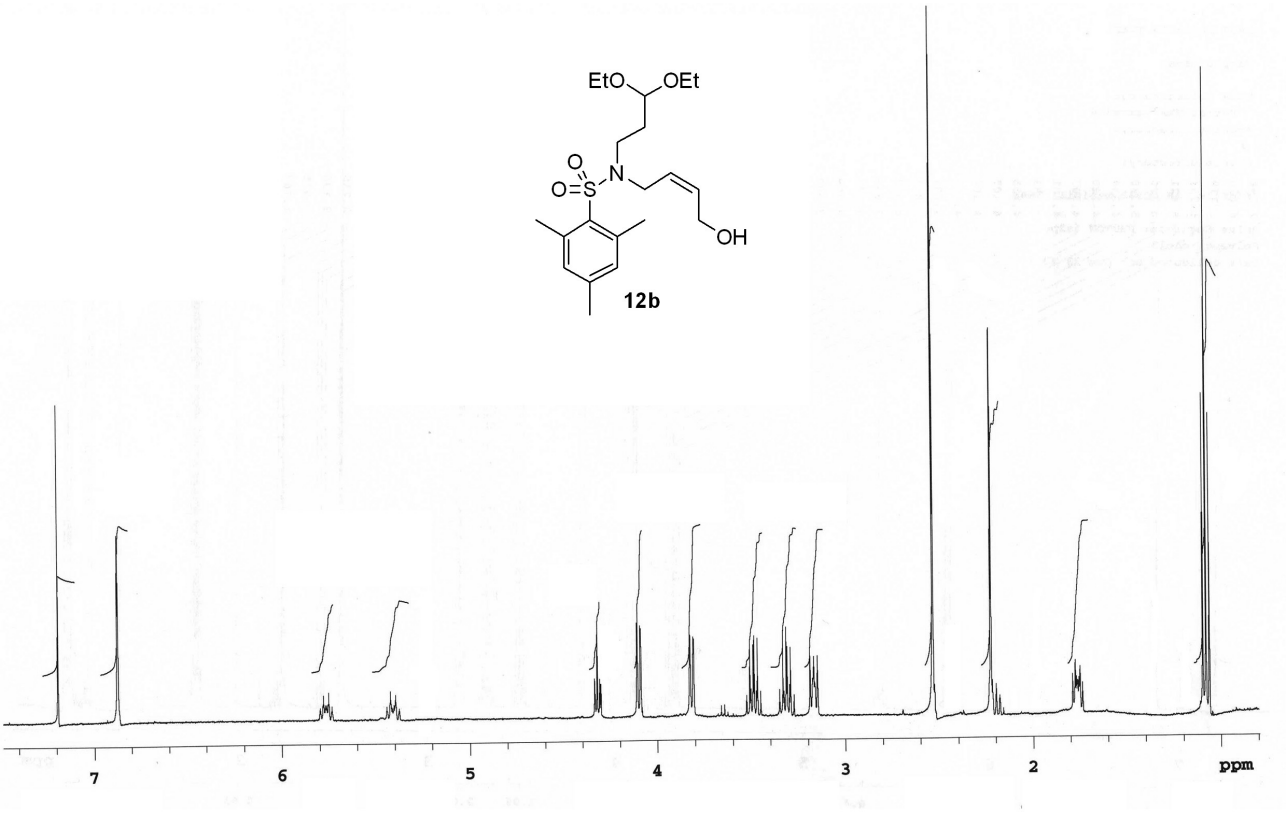


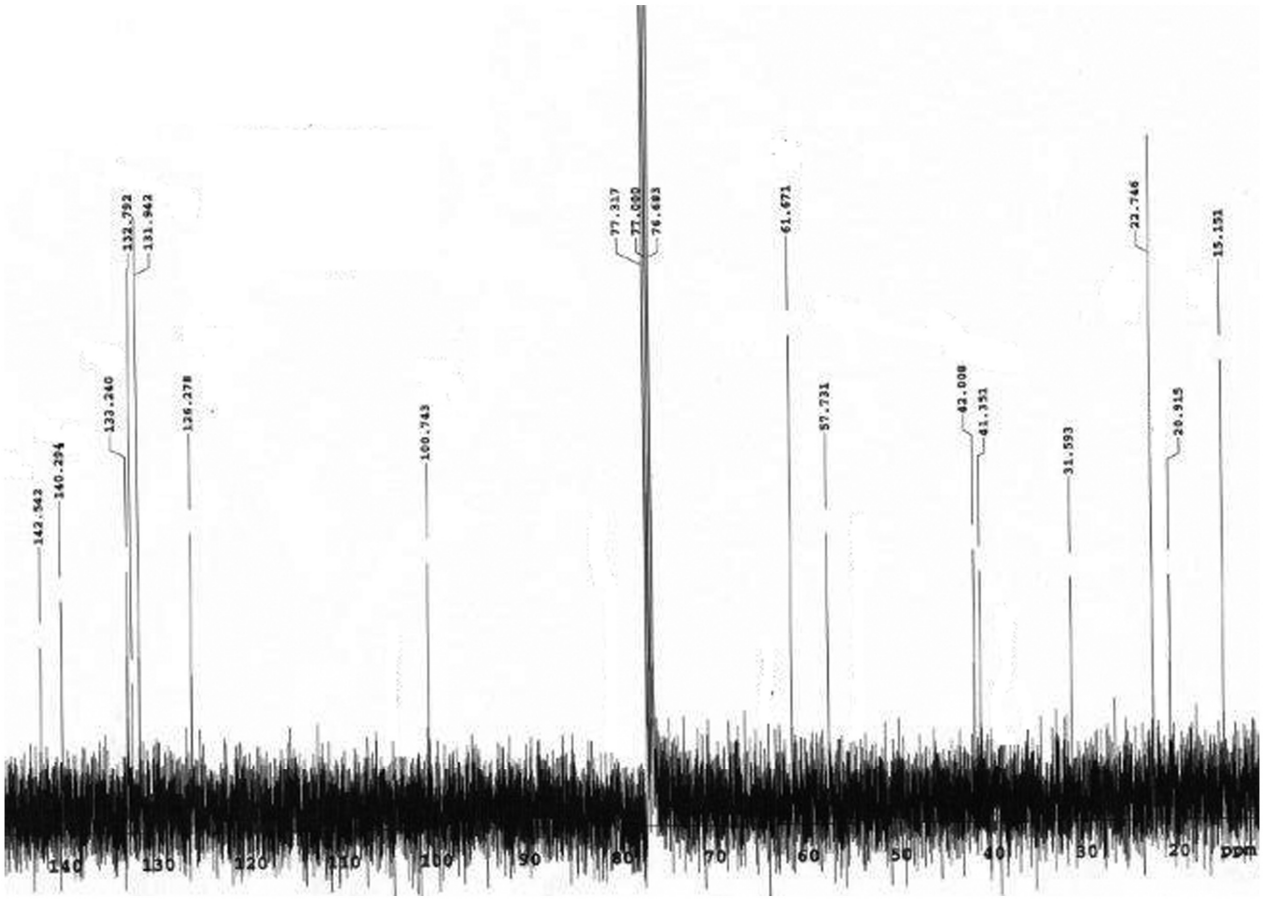
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.473	BB	0.7384	8724.35254	182.94391	90.1911
2	33.136	BB	0.7379	948.83783	19.49320	9.8089

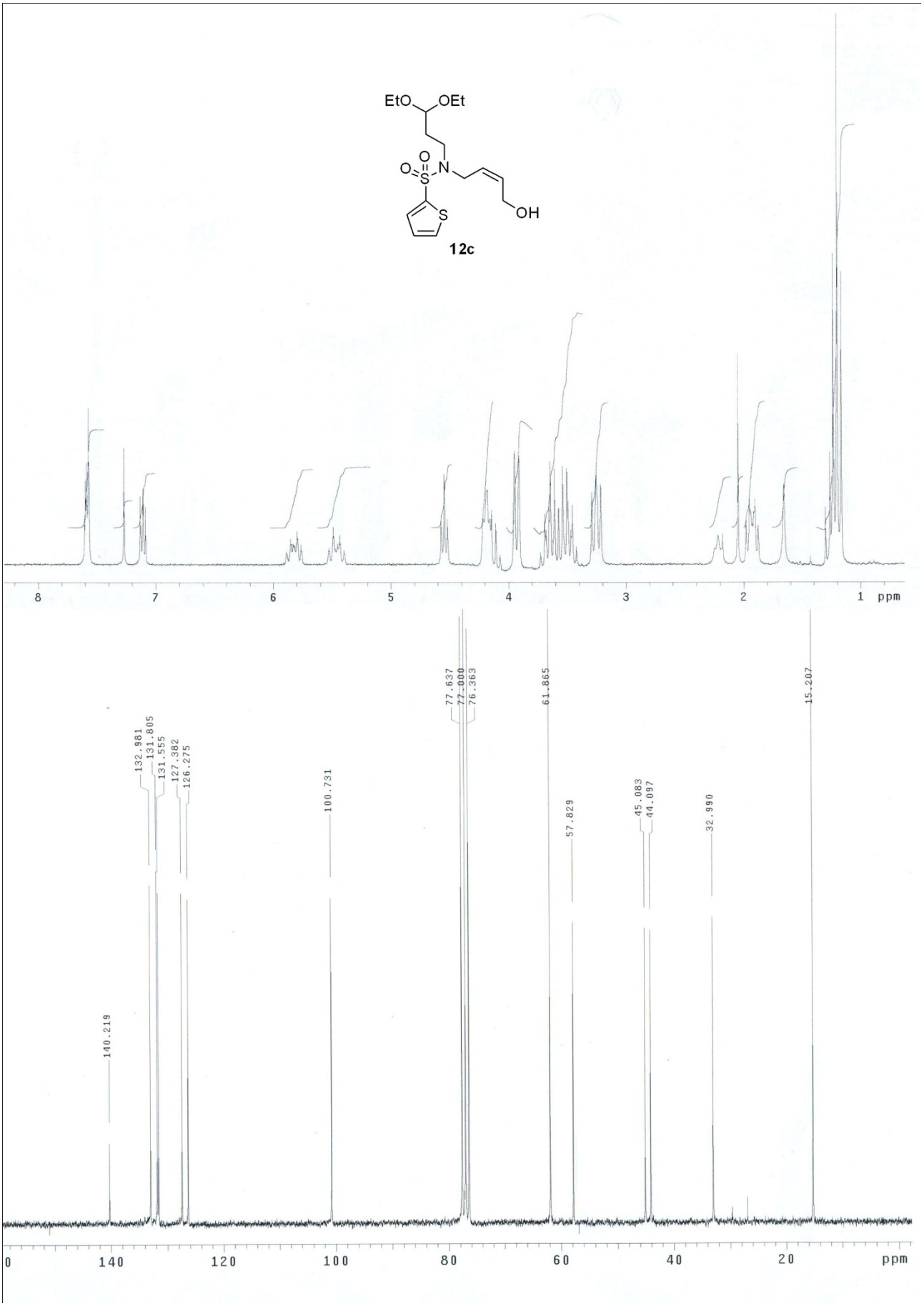
NMR spectra.

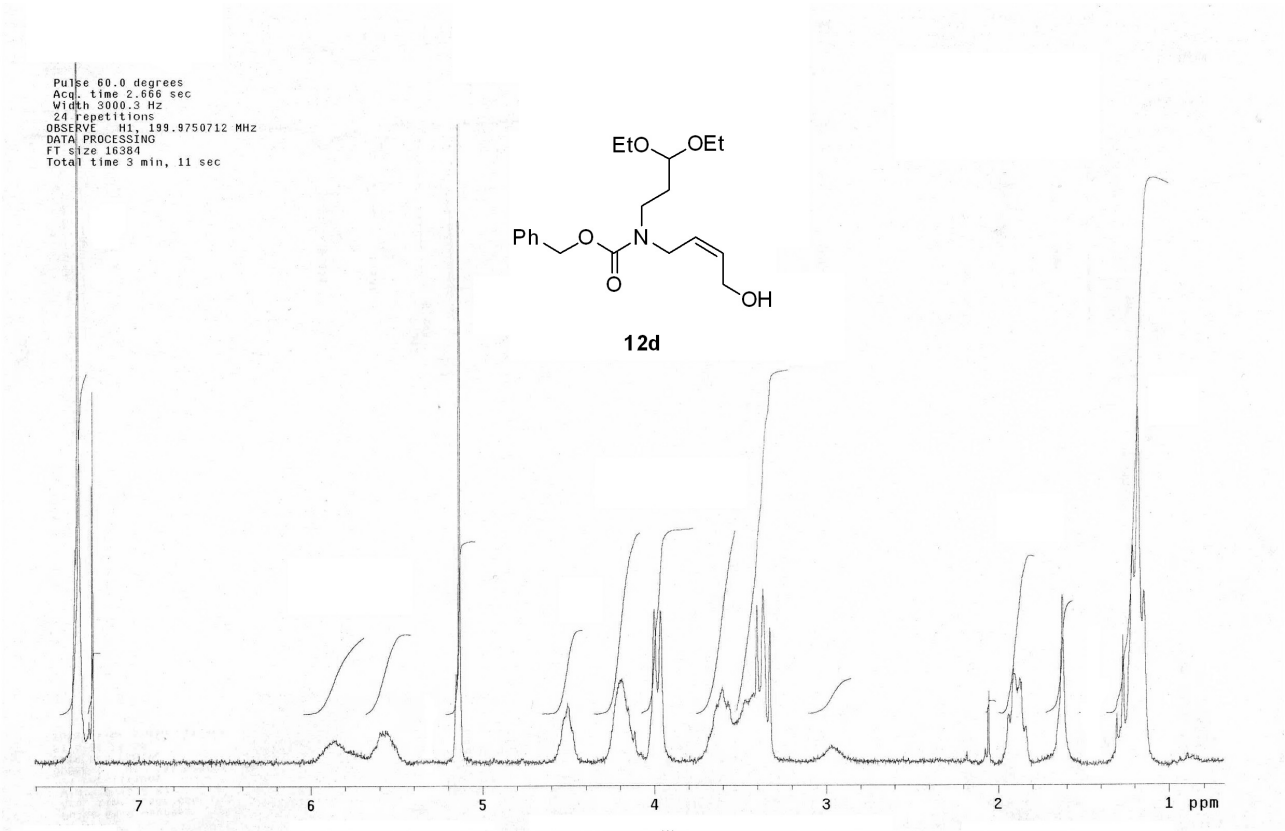








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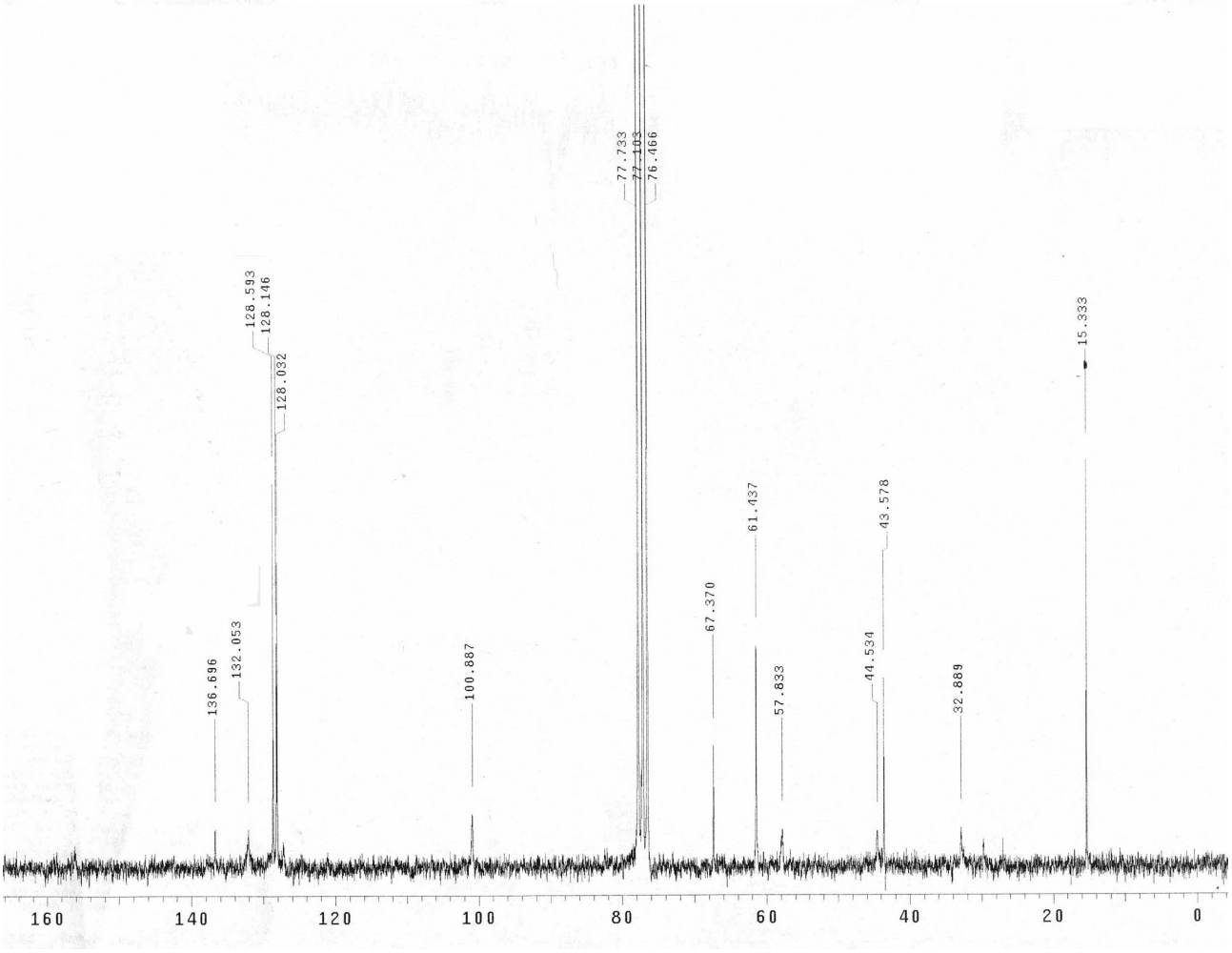
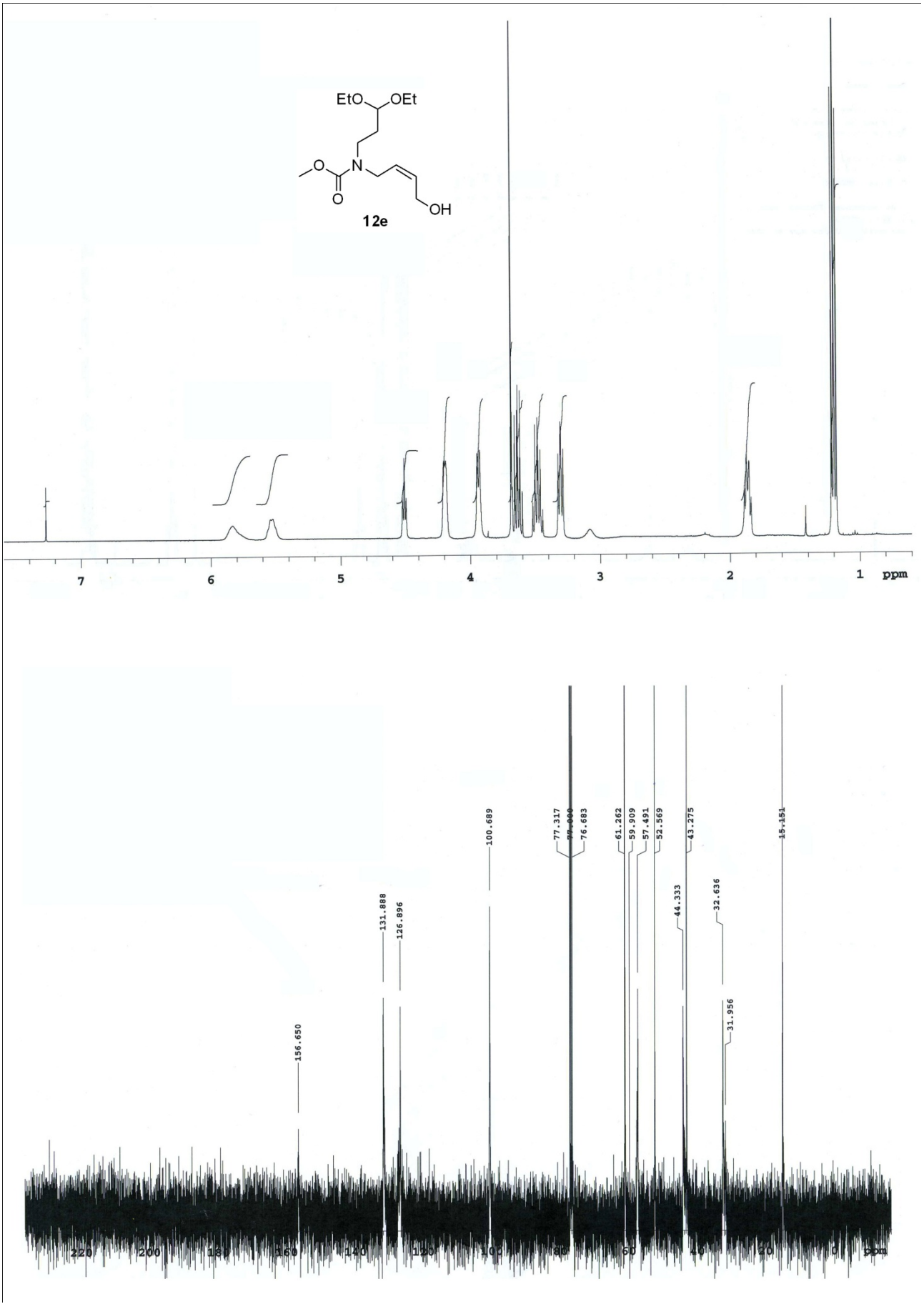
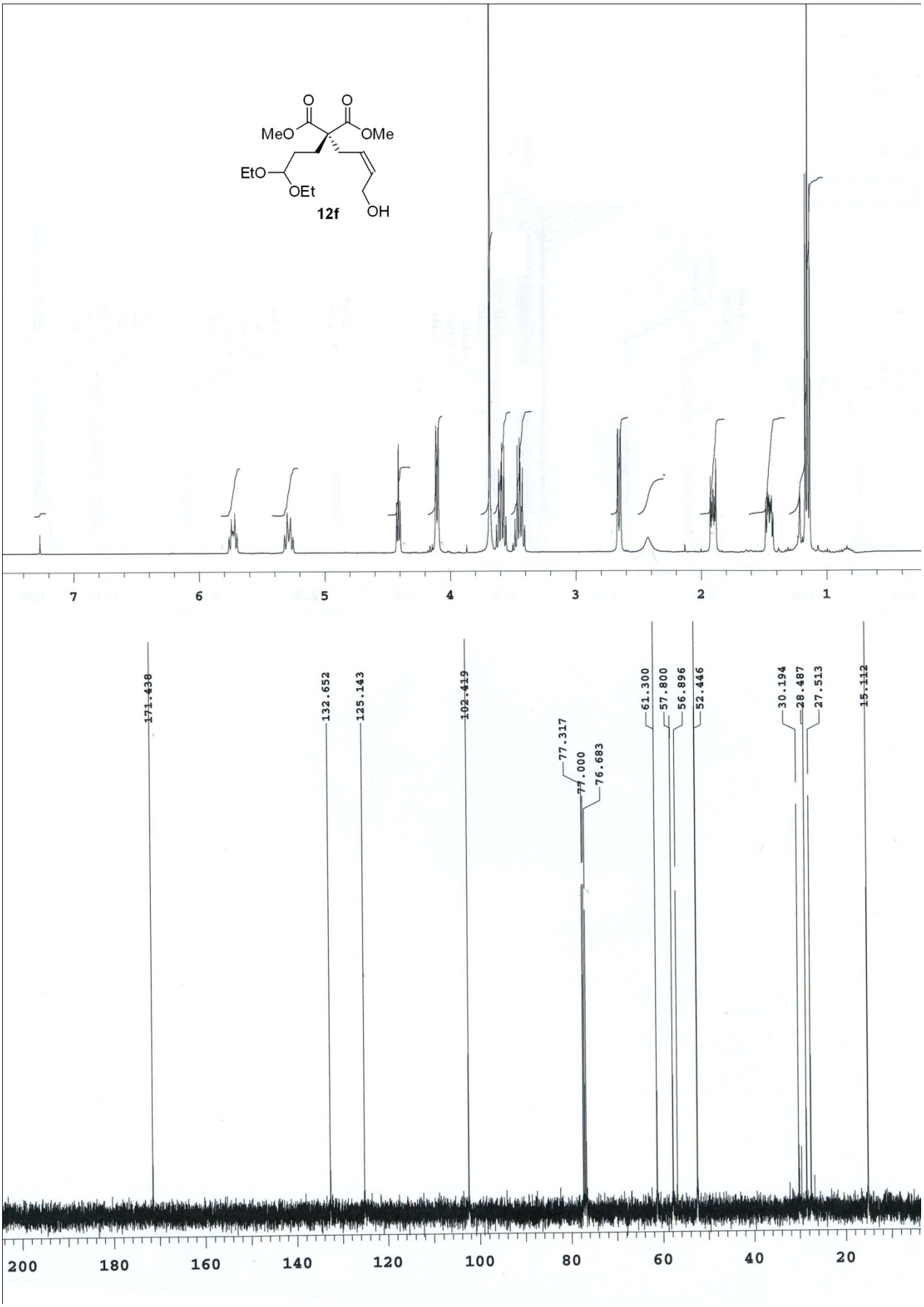
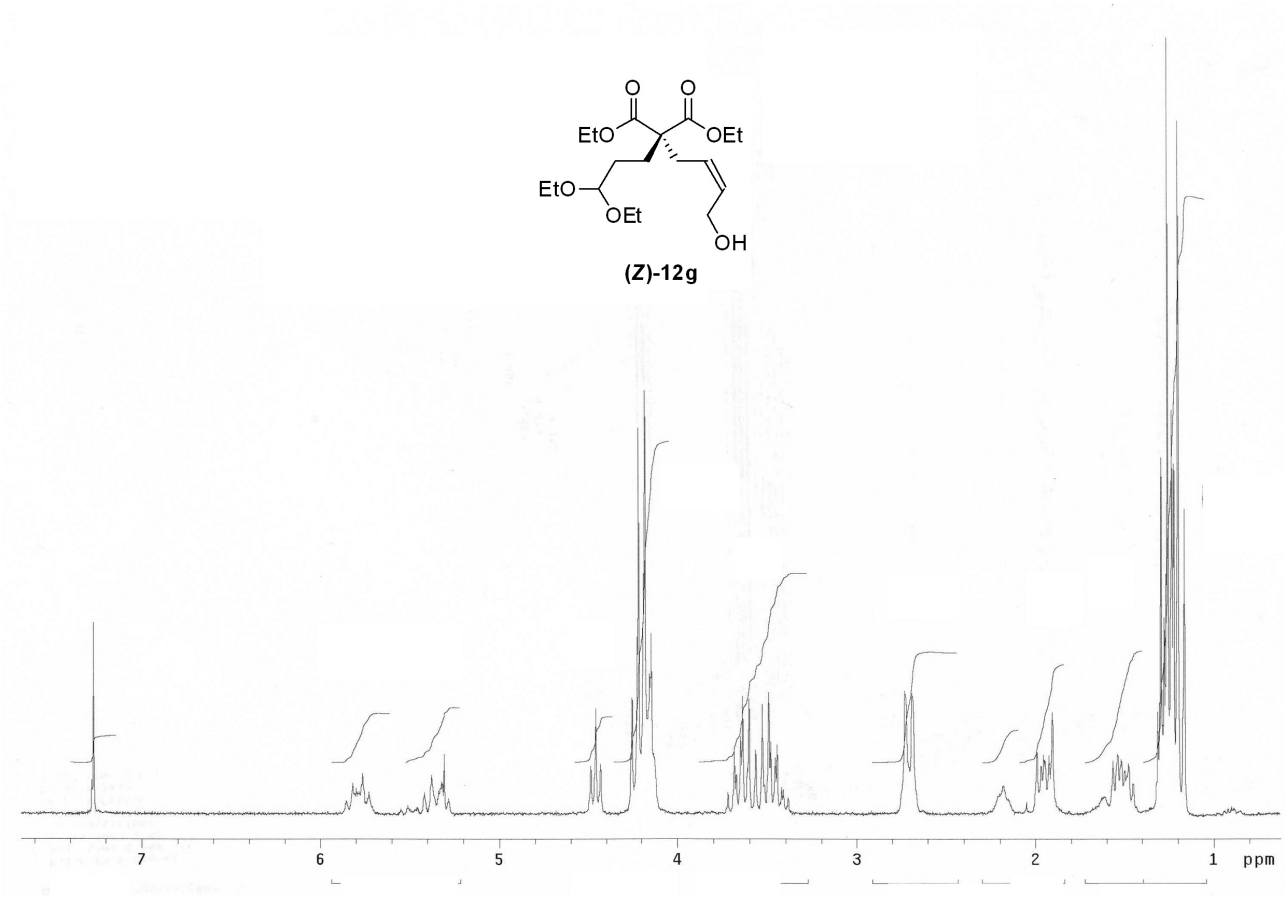
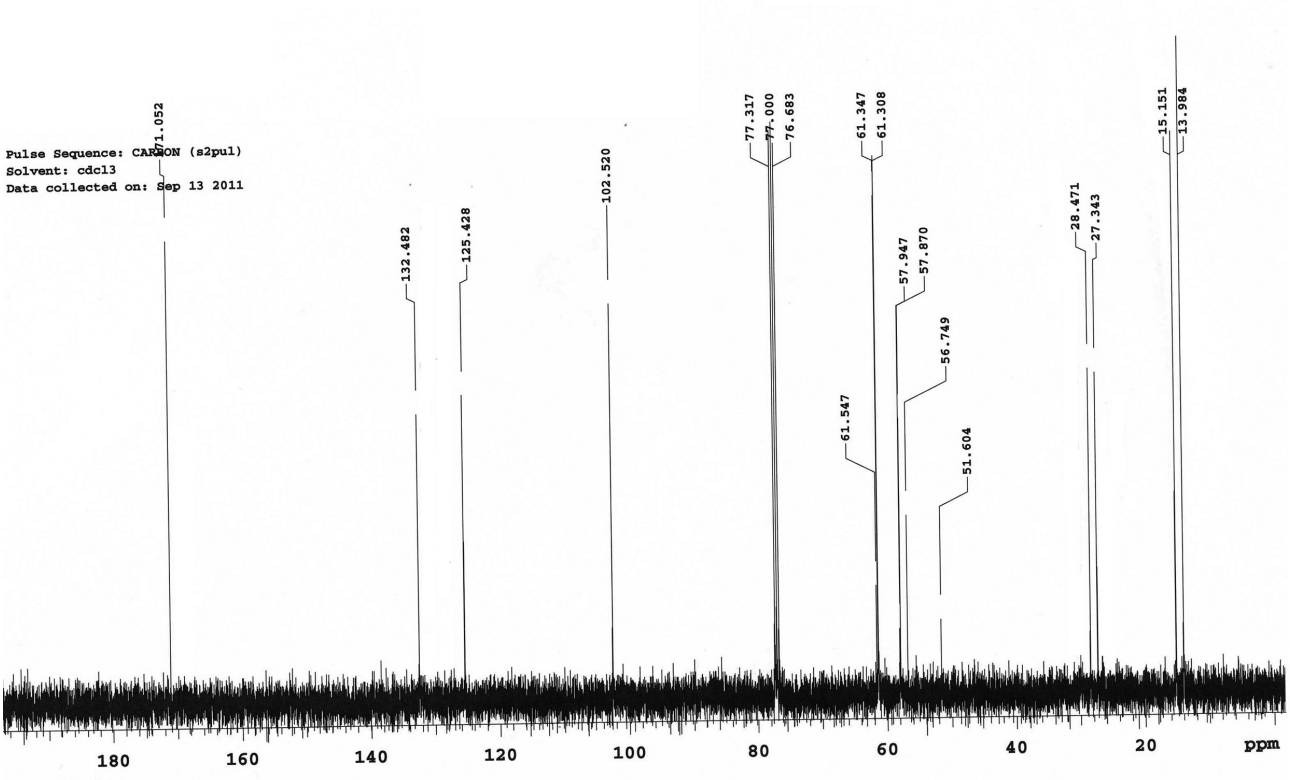
Acq. time 2.666 sec
Width 3000.3 Hz
24 repetitions
OBSERVE H1, 199.9750712 MHz
DATA PROCESSING
FT size 16384
Total time 3 min, 11 sec
EtO
OEt
Ph
O
N
O
OH
12d
7
6
5
4
3
2
1 ppm

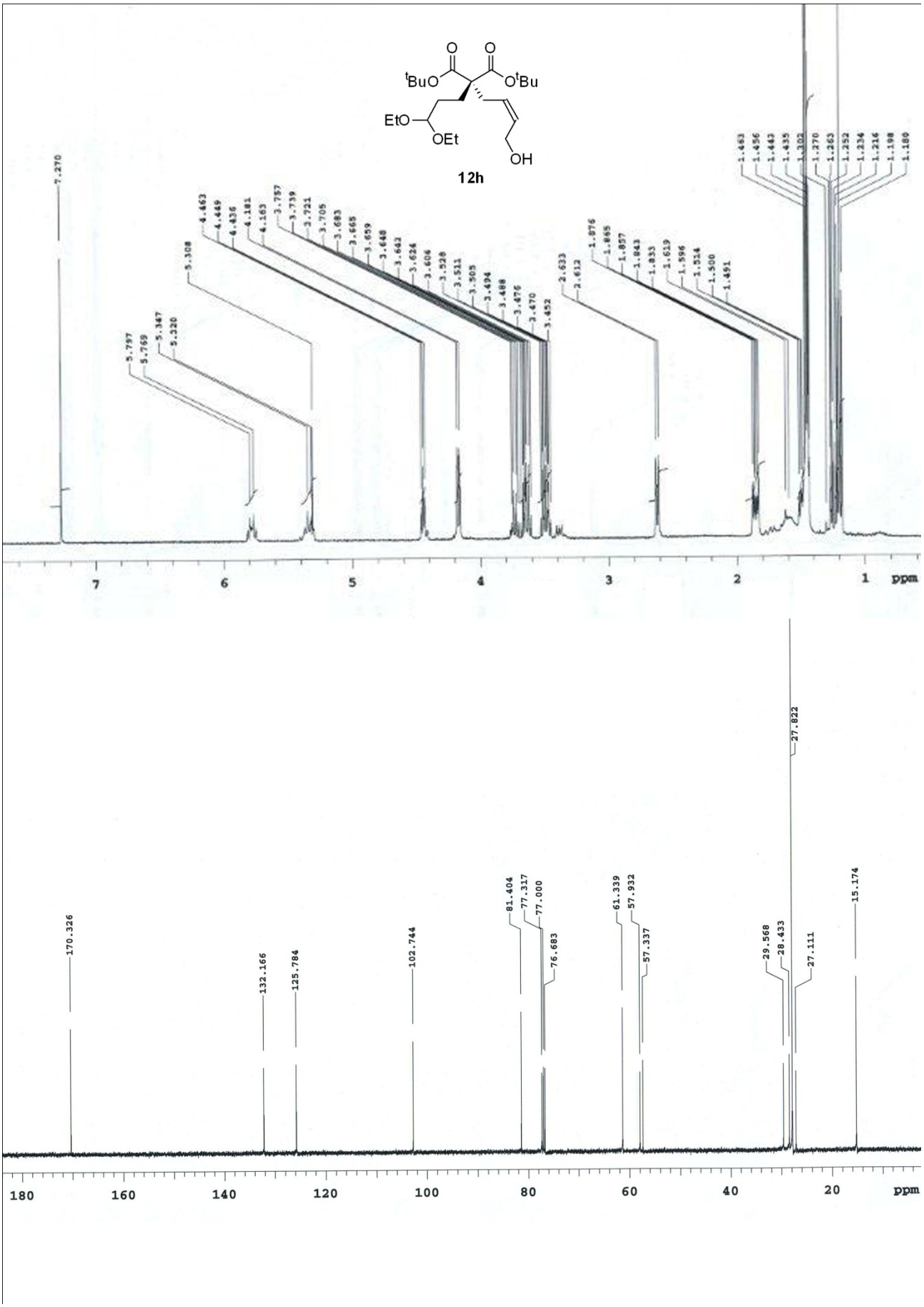

77.733
77.103
76.466
128.593
128.146
128.032
136.696
132.053
100.887
67.370
61.437
57.833
44.534
43.578
32.889
15.333
160
140
120
100
80
60
40
20
0

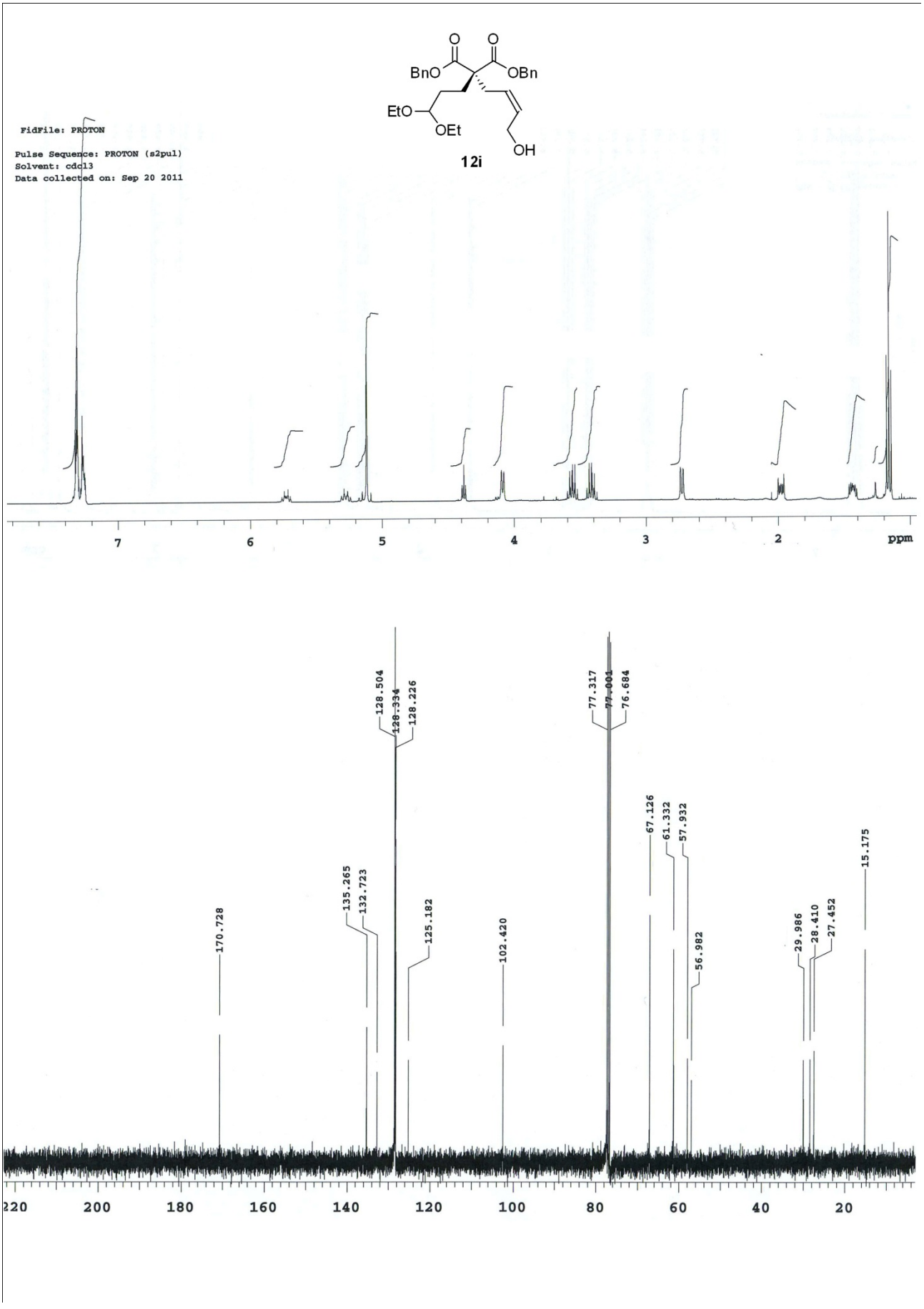


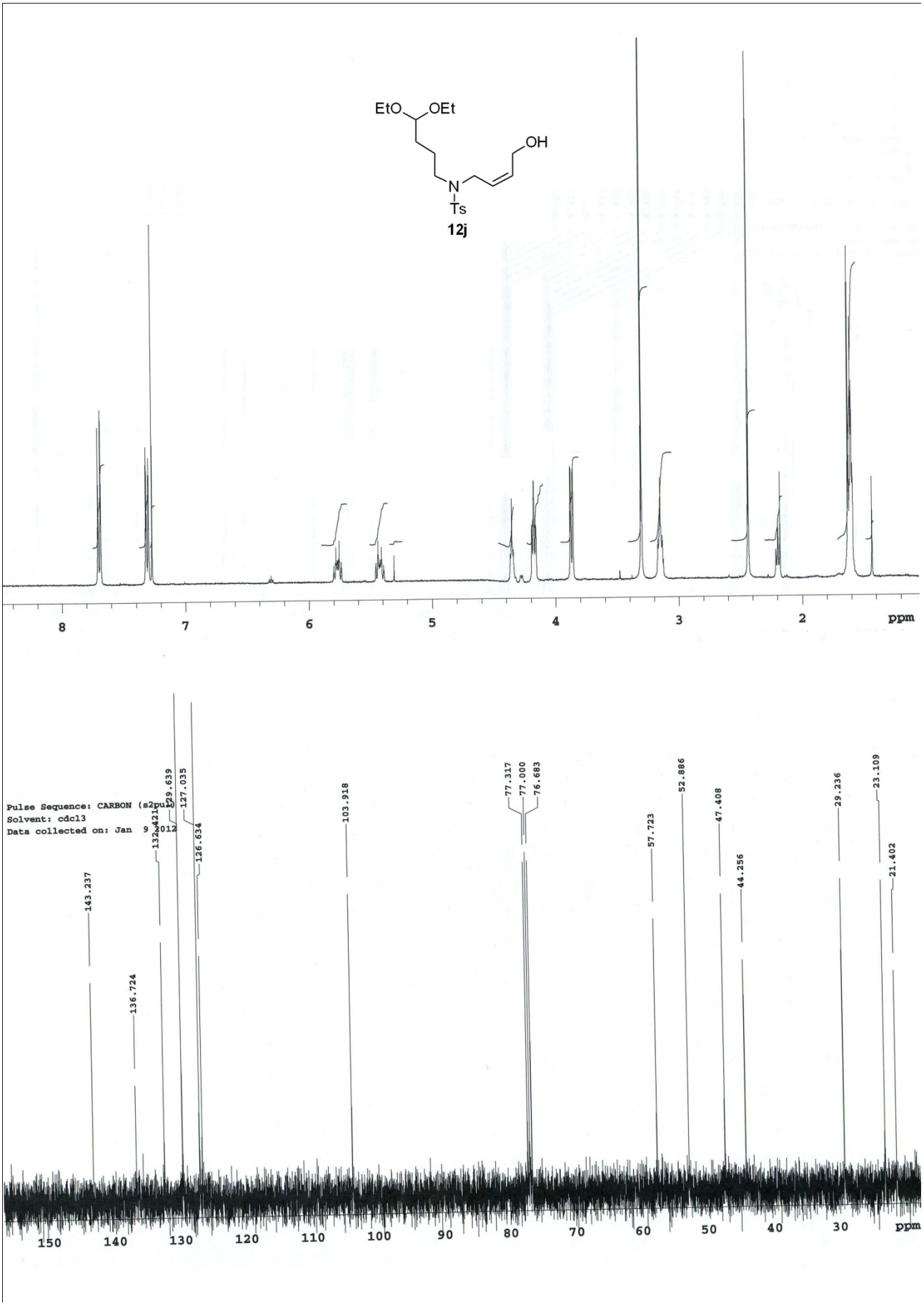

MeO
OMe
EtO
OEt
OH
12f
7
6
5
4
3
2
1
171.438
132.652
125.143
102.419
77.317
77.000
76.683
61.300
57.800
56.896
52.446
30.194
28.487
27.513
15.112
200
180
160
140
120
100
80
60
40
20

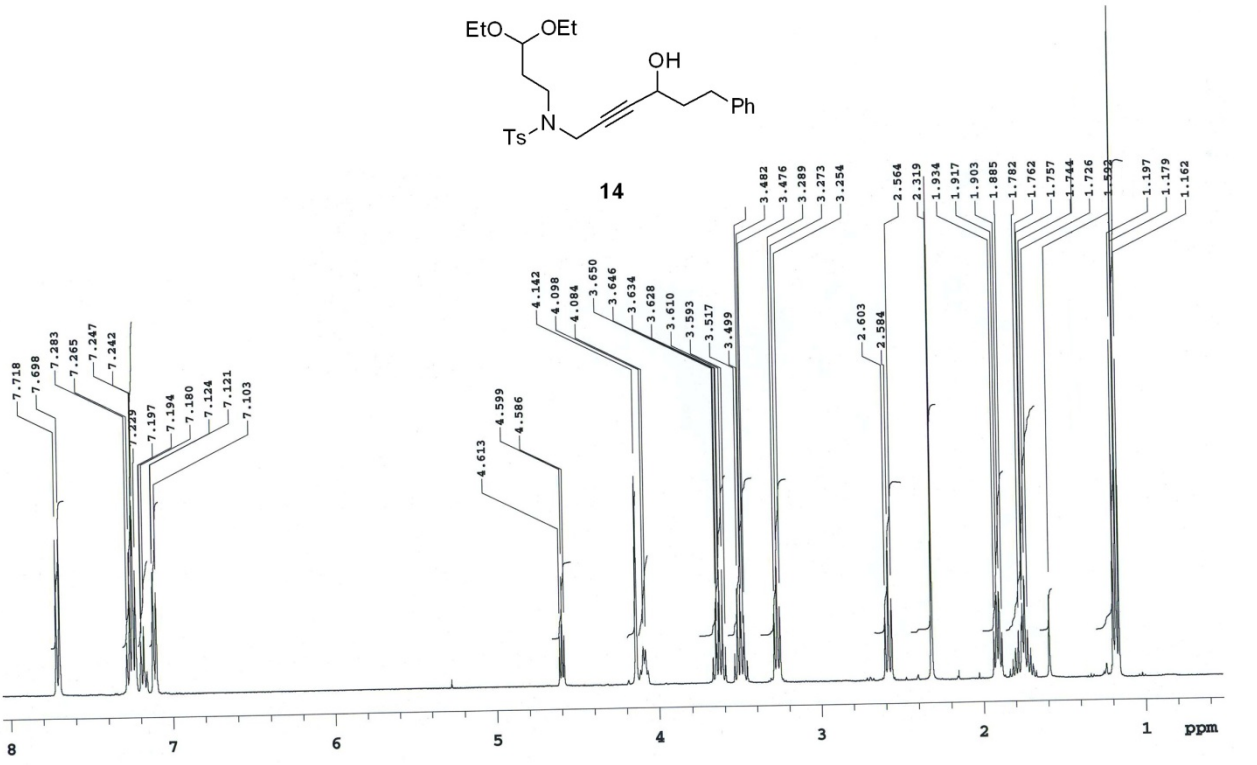

EtO
OEt
EtO
OEt
OH
(Z)-12g
7
6
5
4
3
2
1
ppm

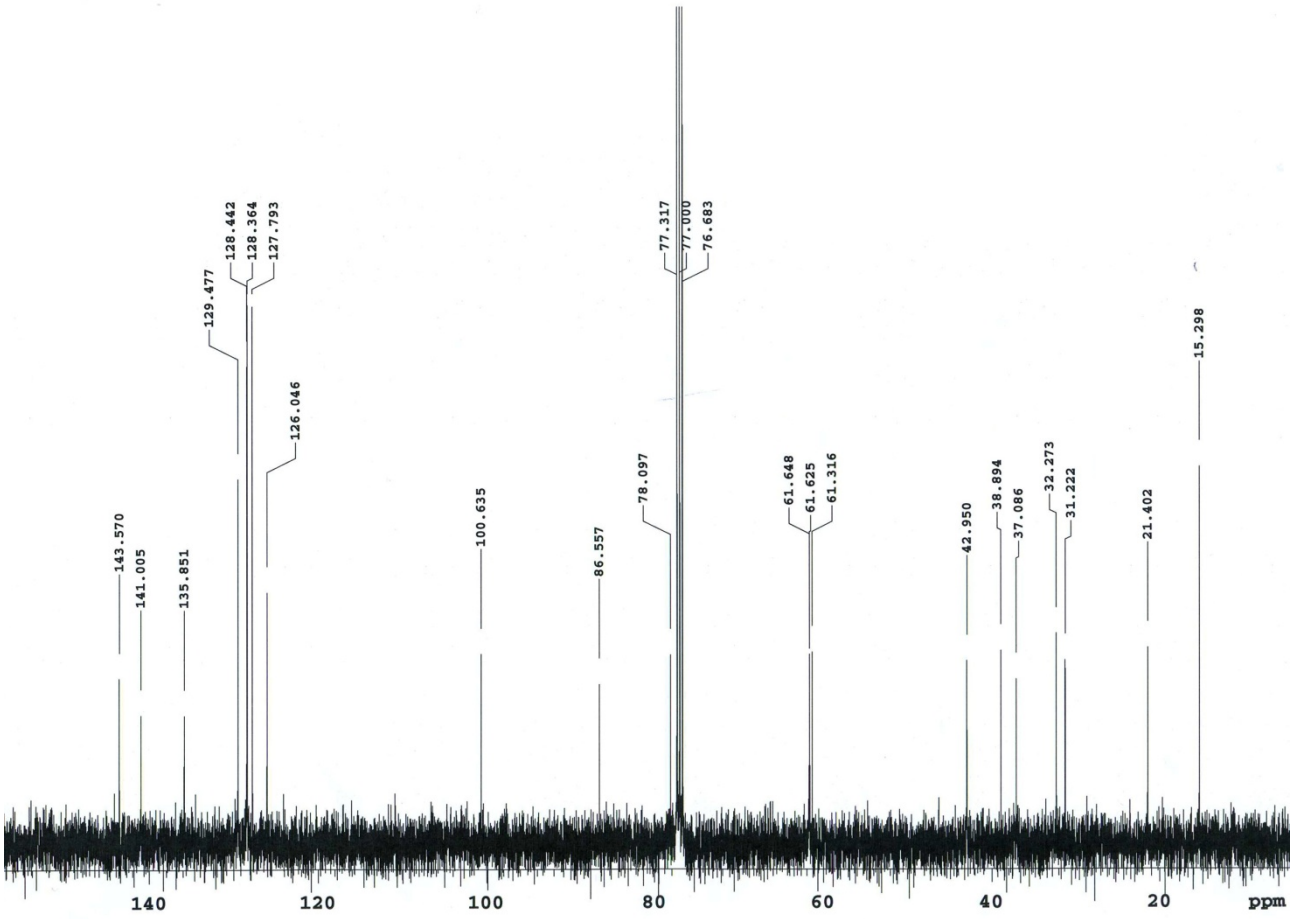

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 13 2011
171.052
132.482
125.428
102.520
77.317
77.000
76.683
61.347
61.308
61.547
57.947
57.870
56.749
51.604
28.471
27.343
15.151
13.984
180
160
140
120
100
80
60
40
20
ppm

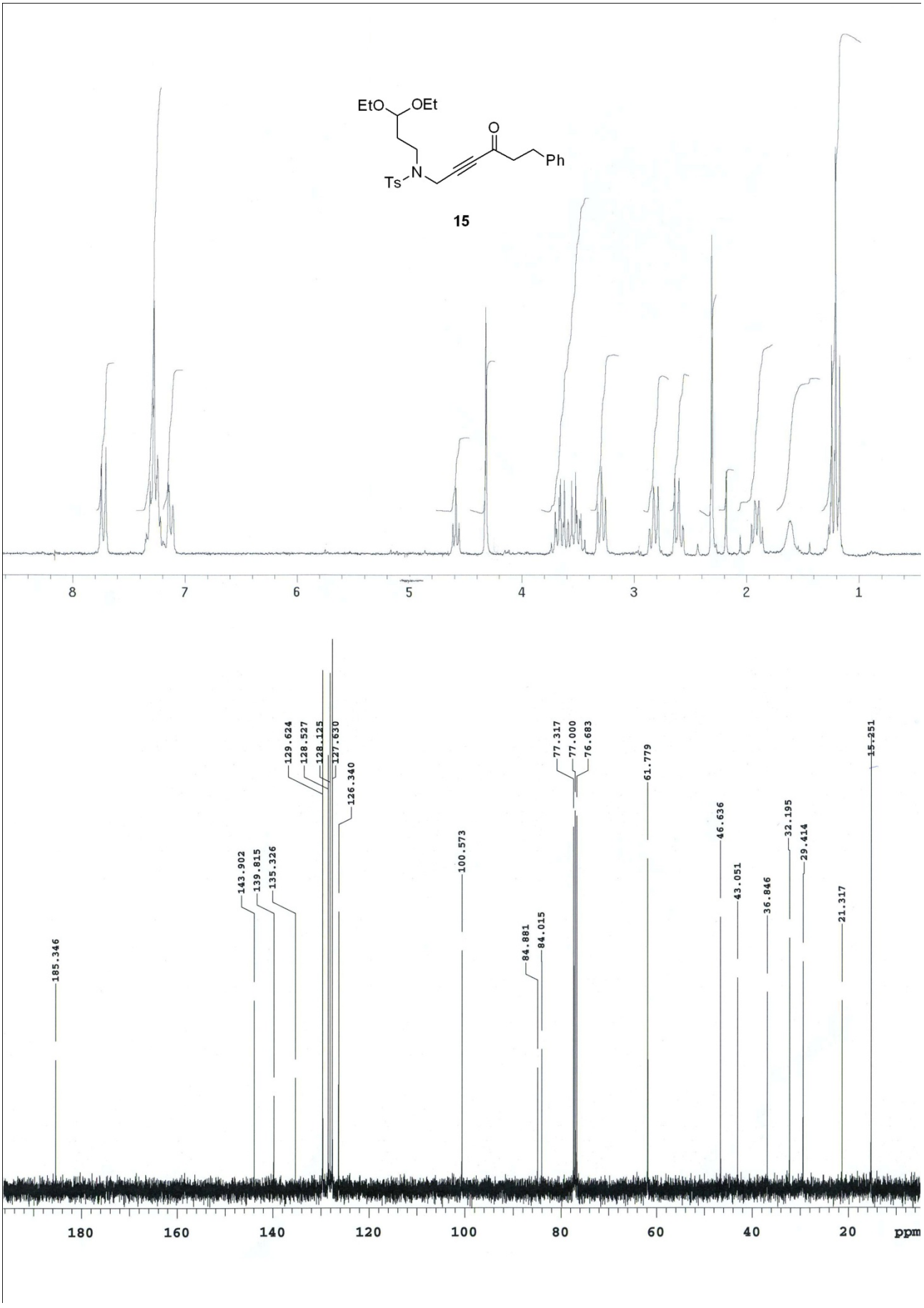


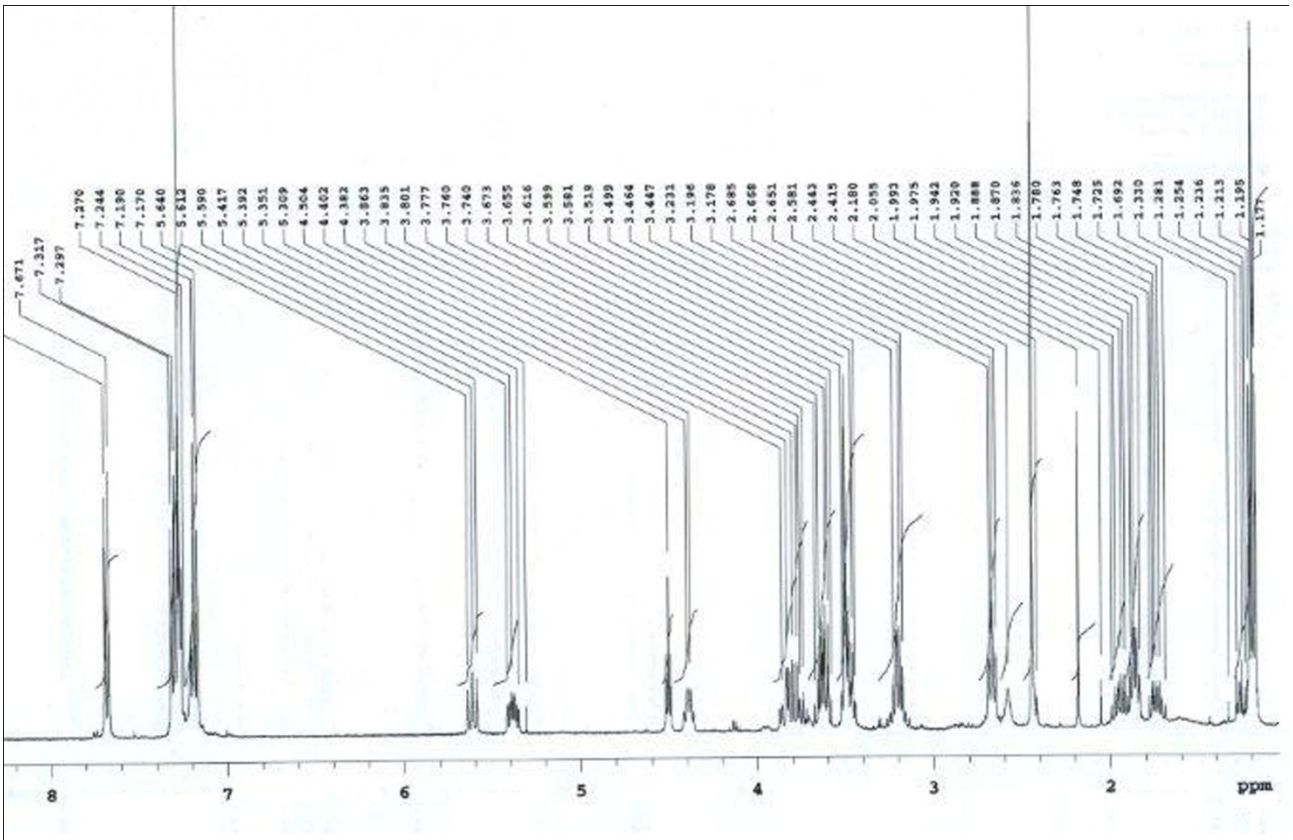

BnO
OBn
EtO
OEt
OH
12i
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 20 2011
7
6
5
4
3
2
ppm
170.728
135.265
132.723
128.504
128.334
128.226
125.182
102.420
77.317
77.001
76.684
67.126
61.332
57.932
56.982
29.986
28.410
27.452
15.175
220
200
180
160
140
120
100
80
60
40
20

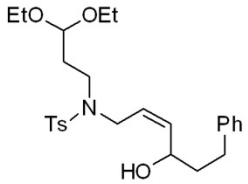




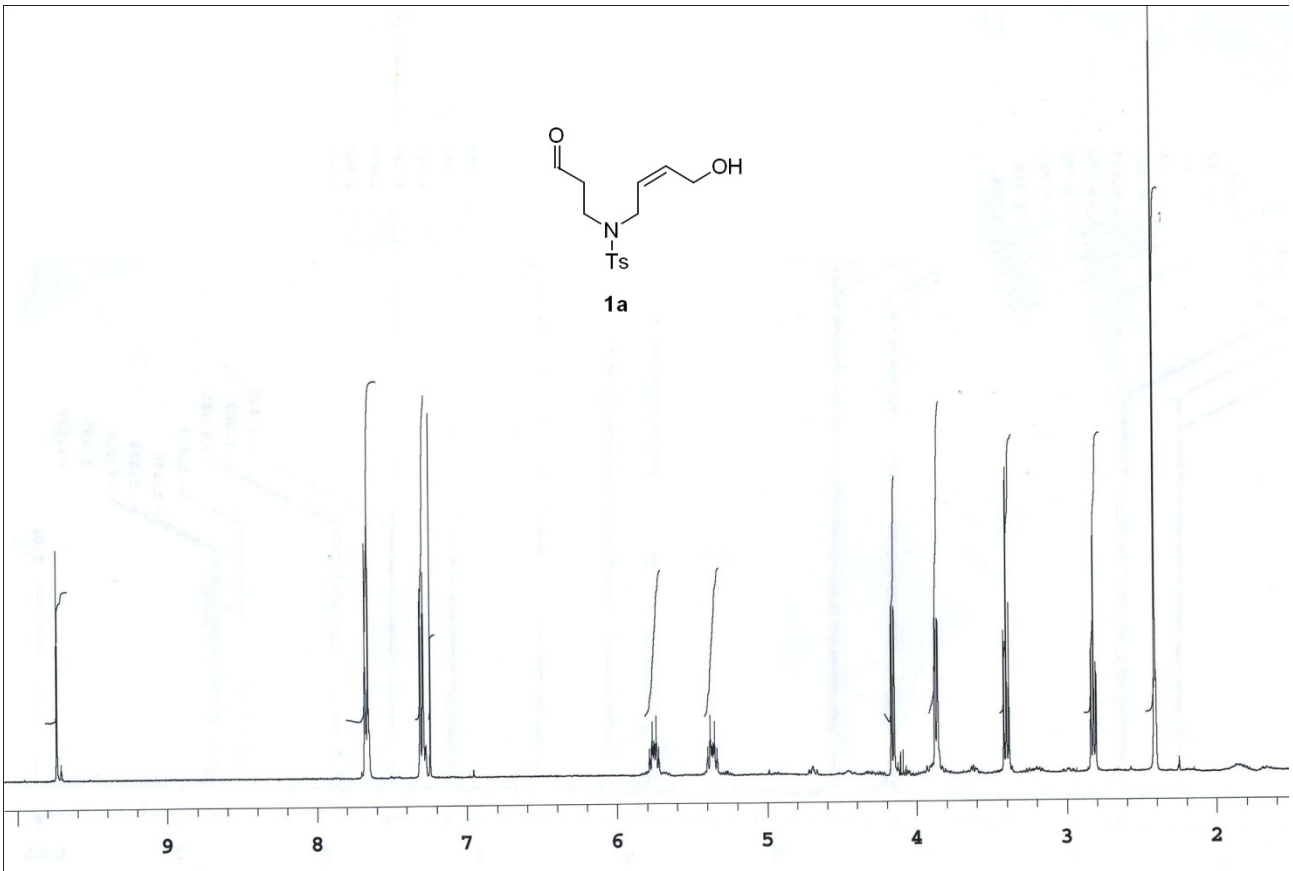



EtO
OEt
O
Ph
Ts
N
15
8
7
6
5
4
3
2
1
185.346
143.902
139.815
135.326
129.624
128.527
128.125
127.630
126.340
100.573
84.881
84.015
77.317
77.000
76.683
61.779
46.636
43.051
36.846
32.195
29.414
21.317
15.251
180
160
140
120
100
80
60
40
20
ppm

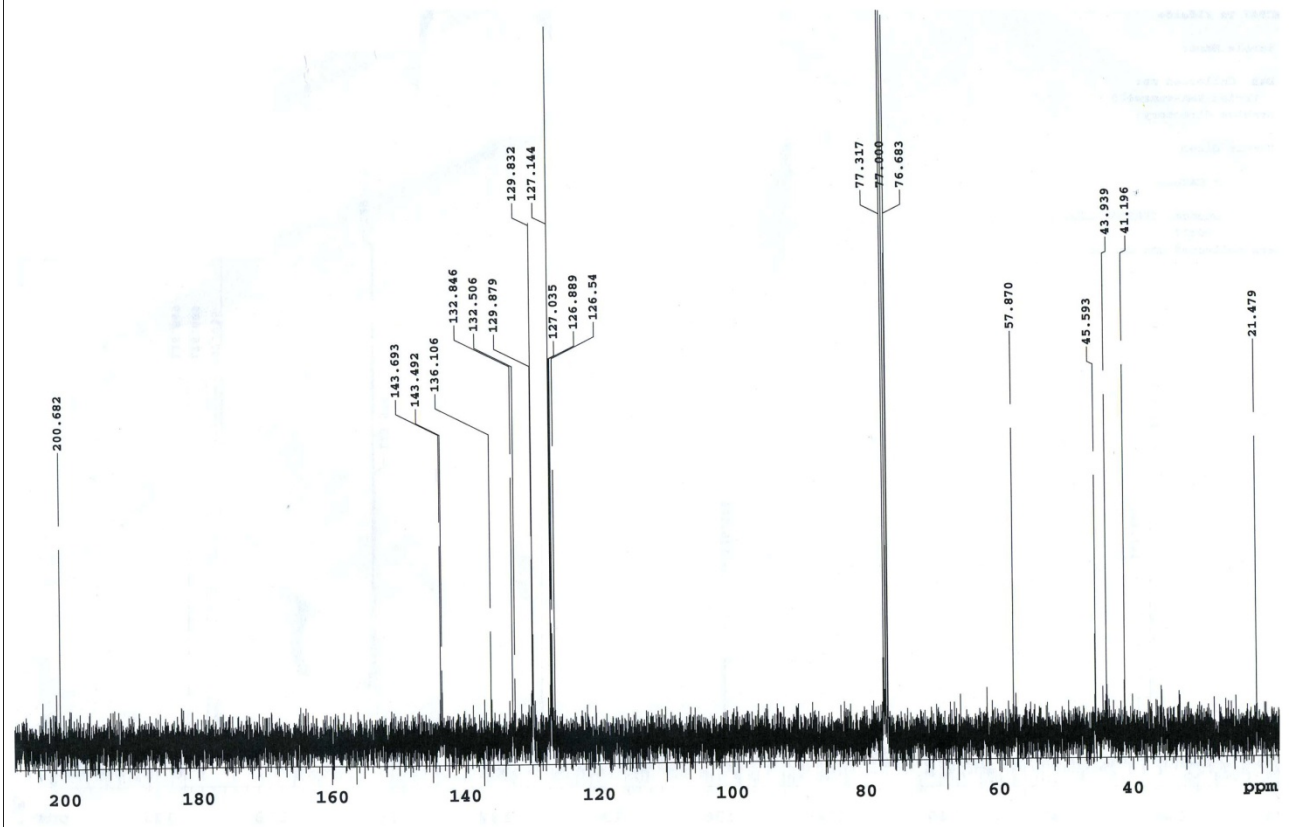


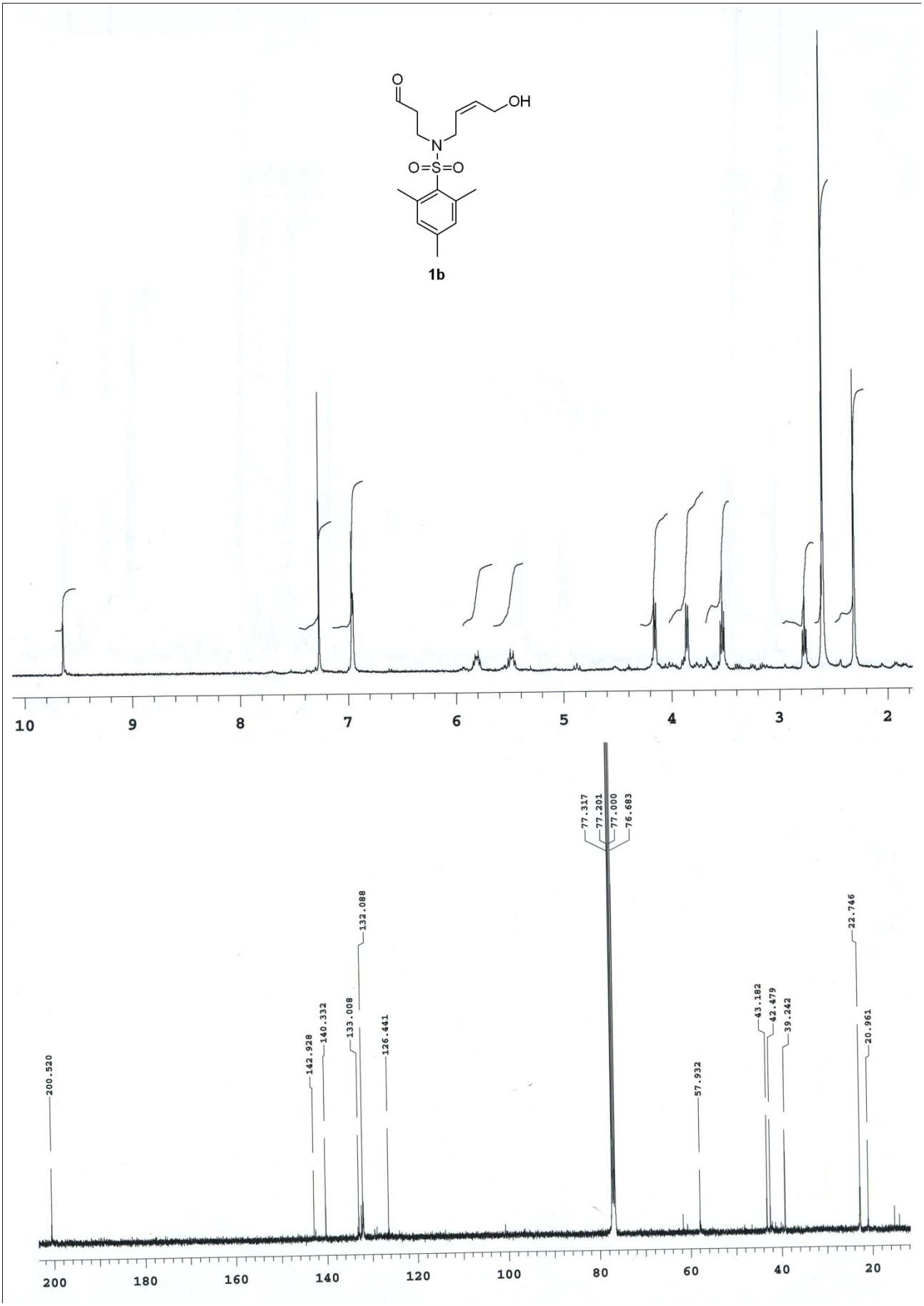


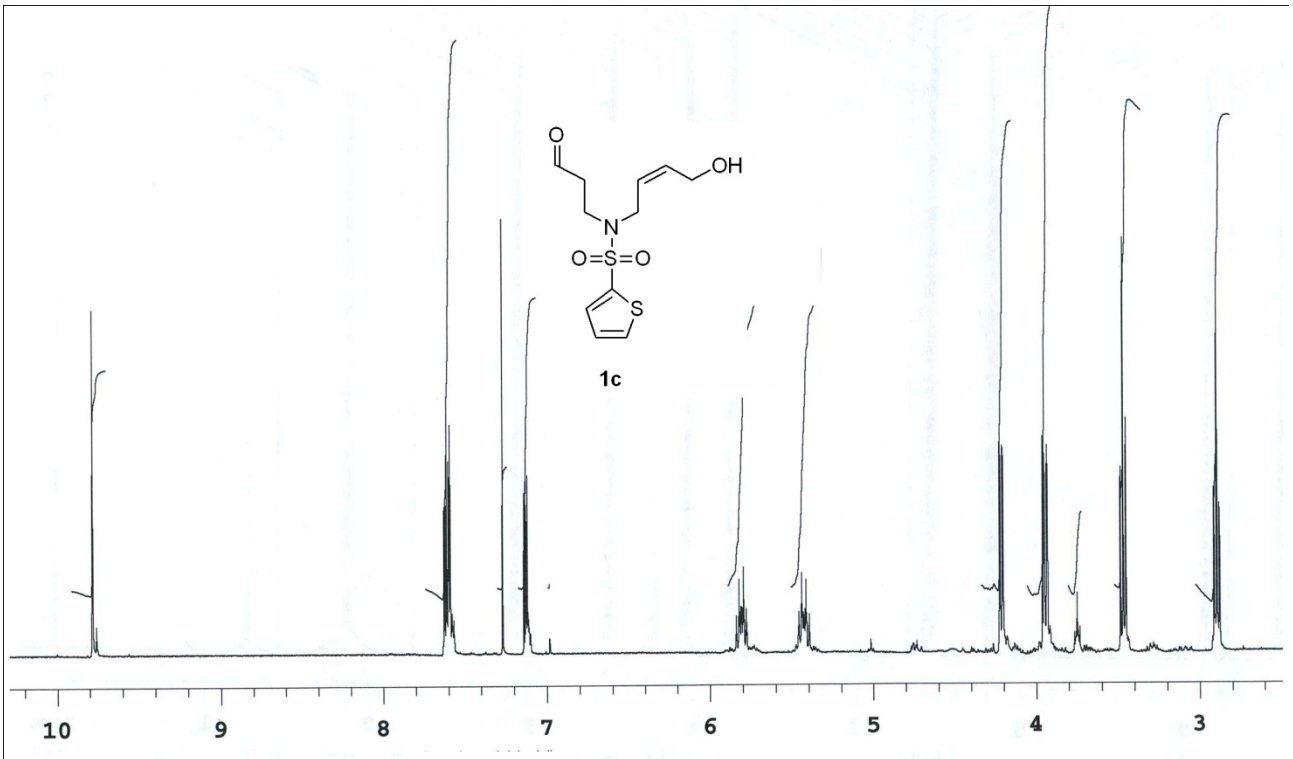
12l


O
OH
N
Ts
9
8
7
6
5
4
3
2

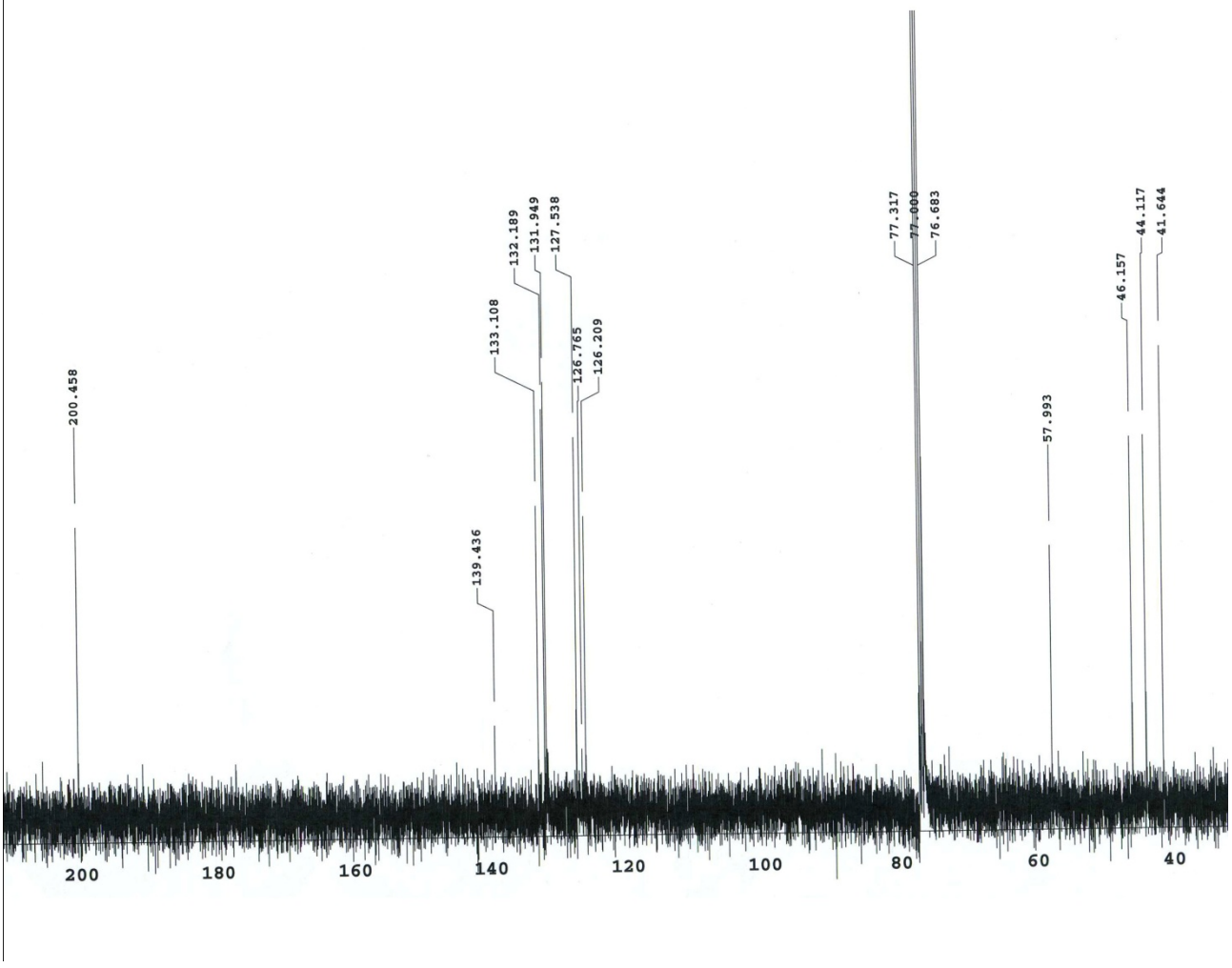
1a

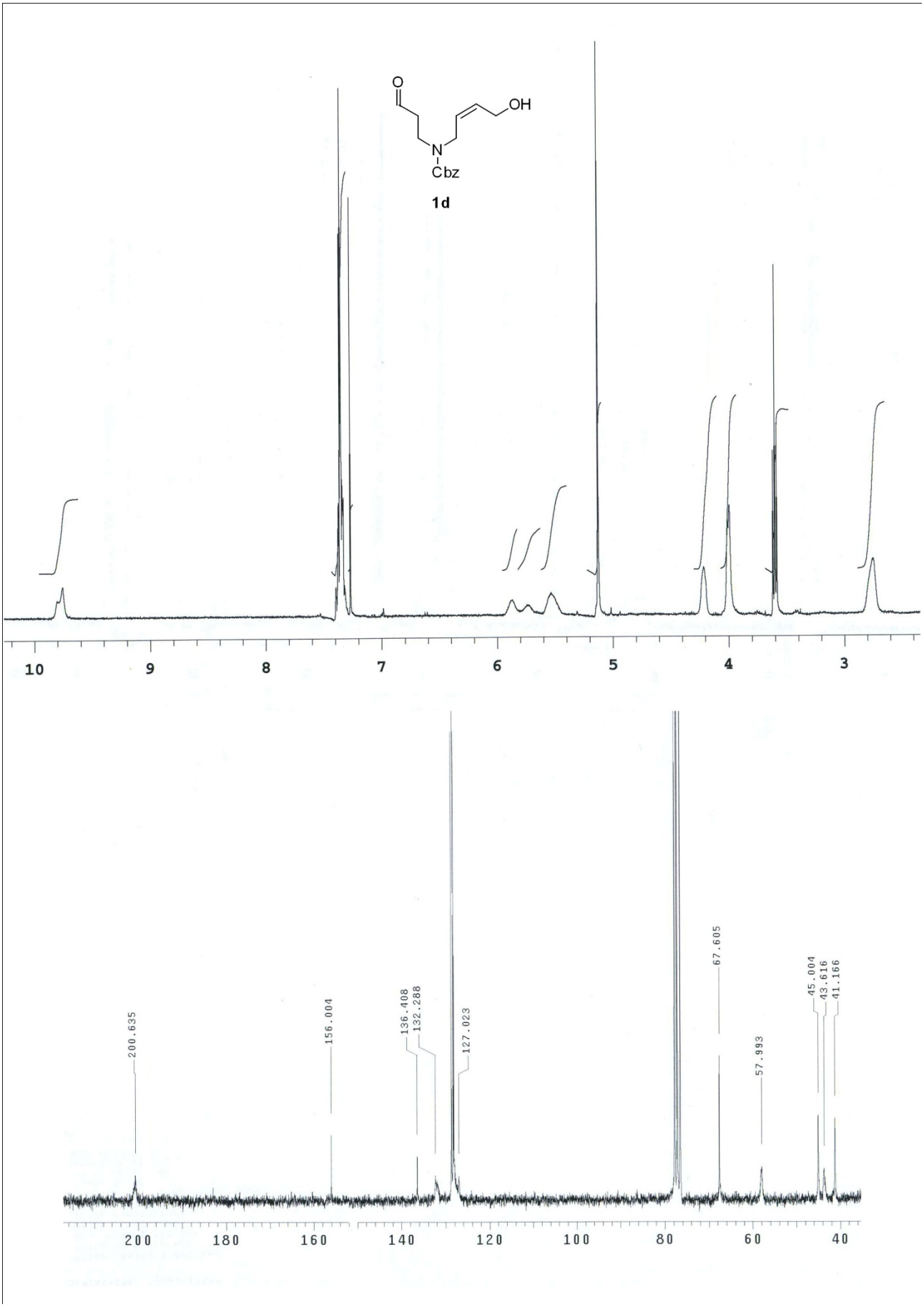

200.682
143.693
143.492
136.106
132.846
132.506
129.879
129.832
127.144
127.035
126.889
126.54
77.317
77.000
76.683
57.870
45.593
43.939
41.196
21.479
200
180
160
140
120
100
80
60
40
ppm

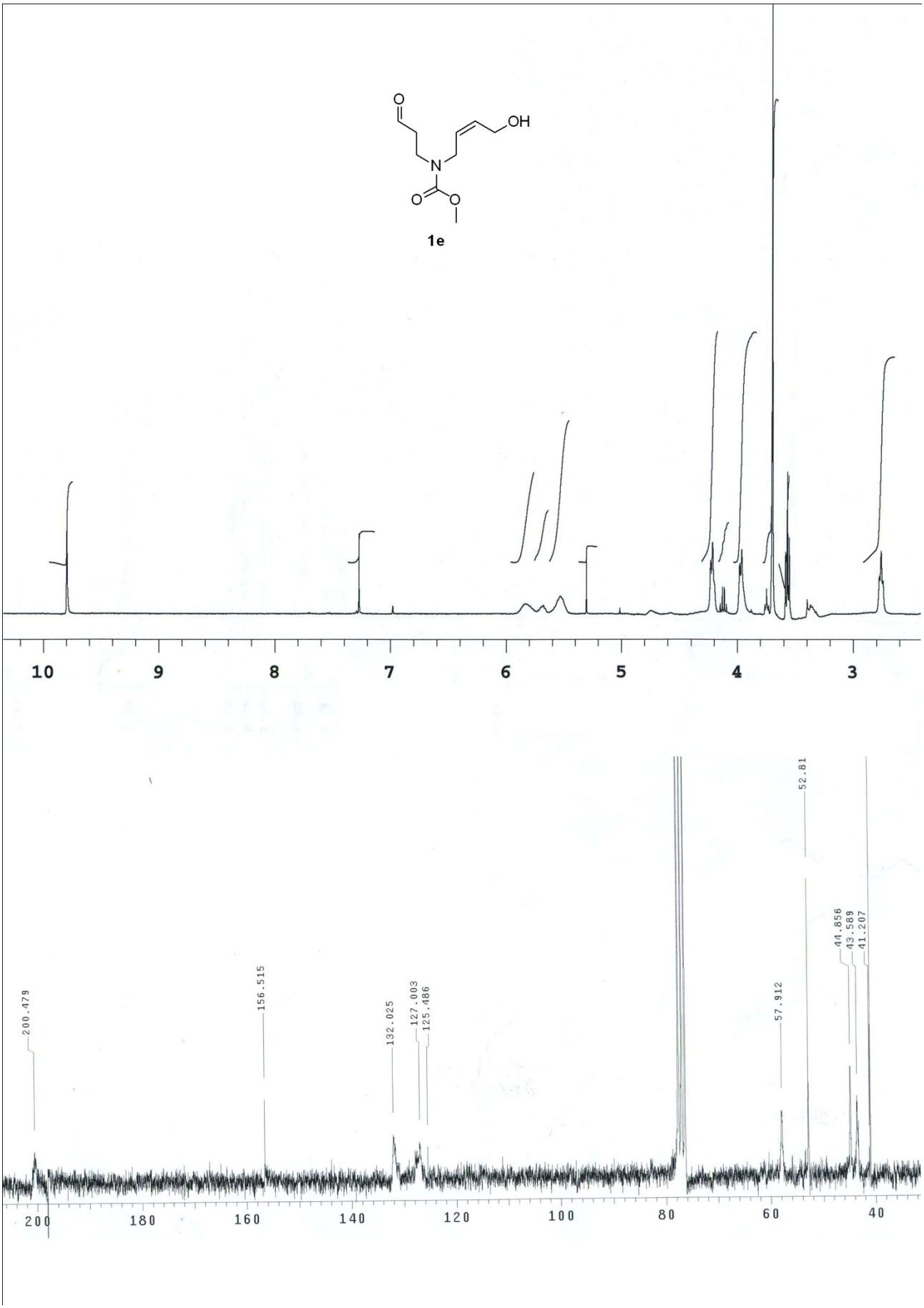


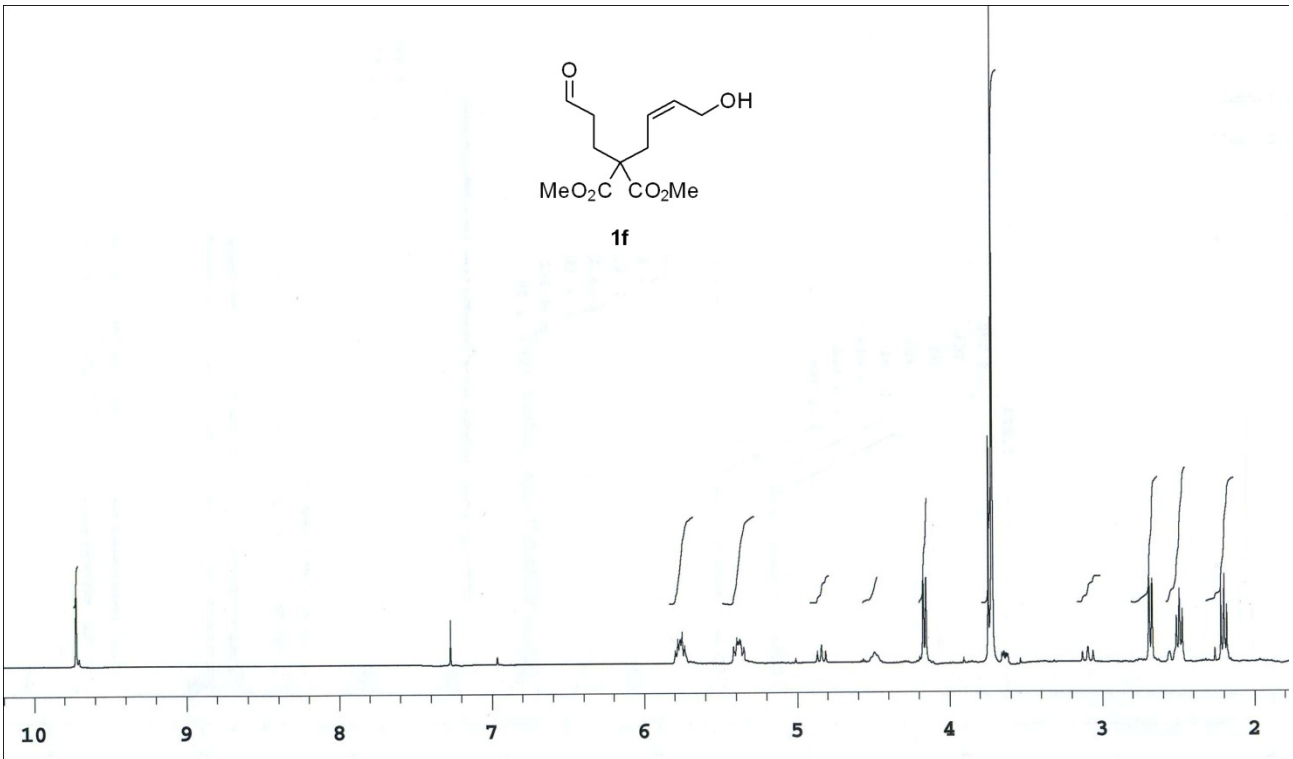


1c

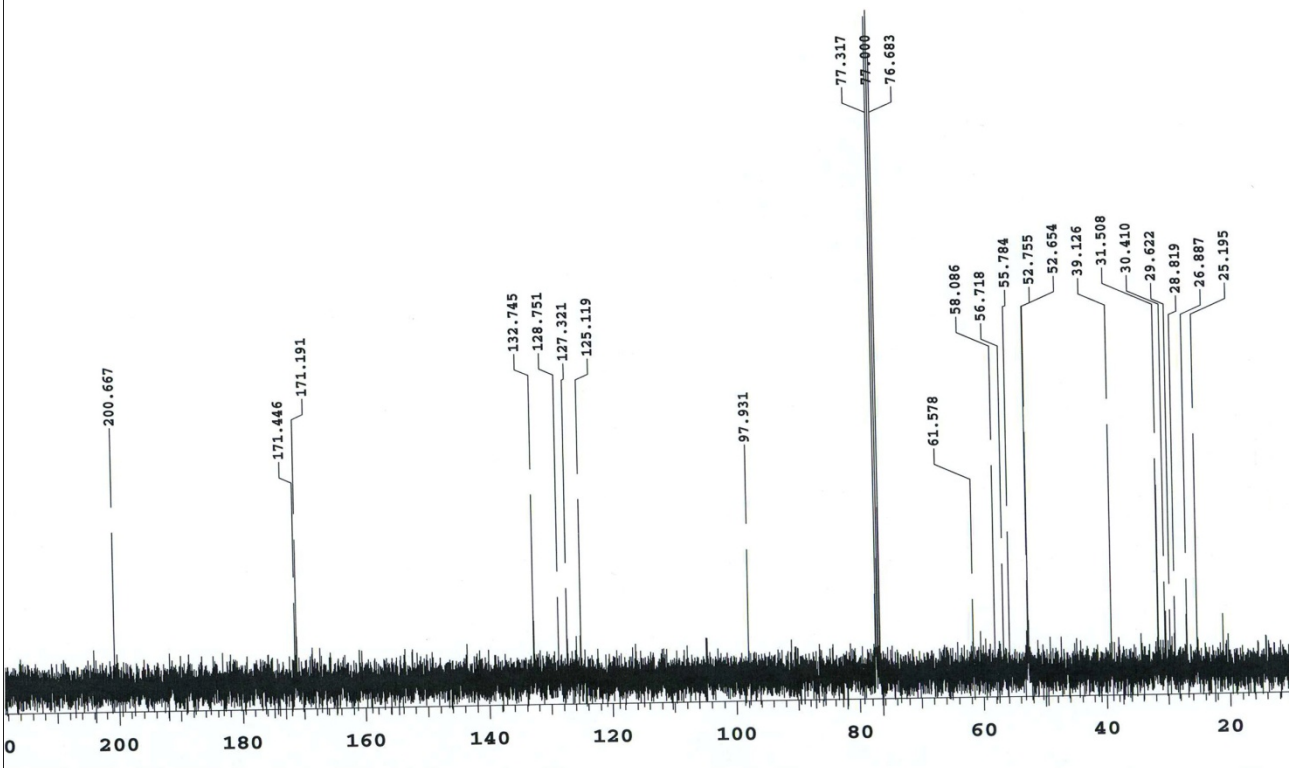


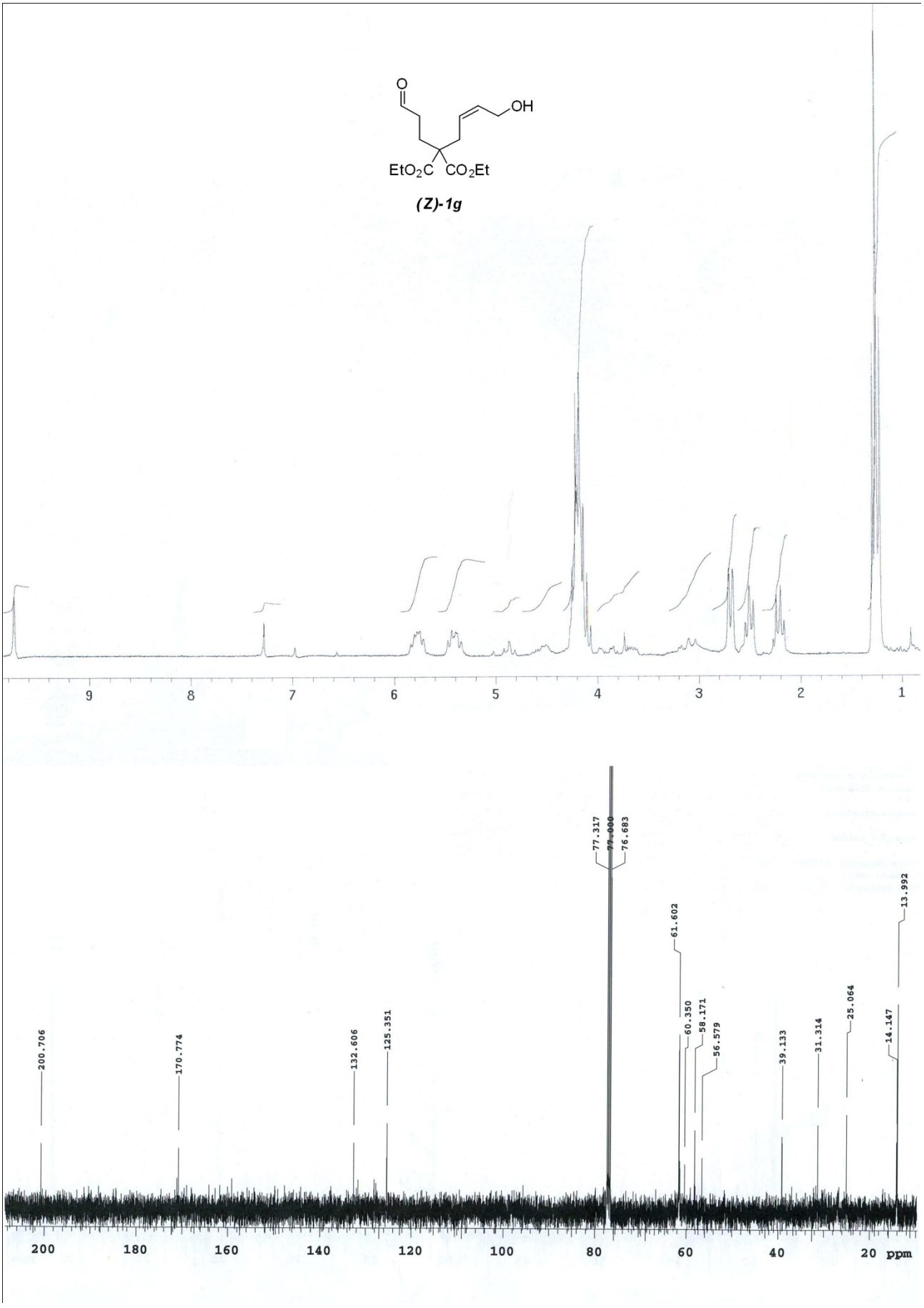


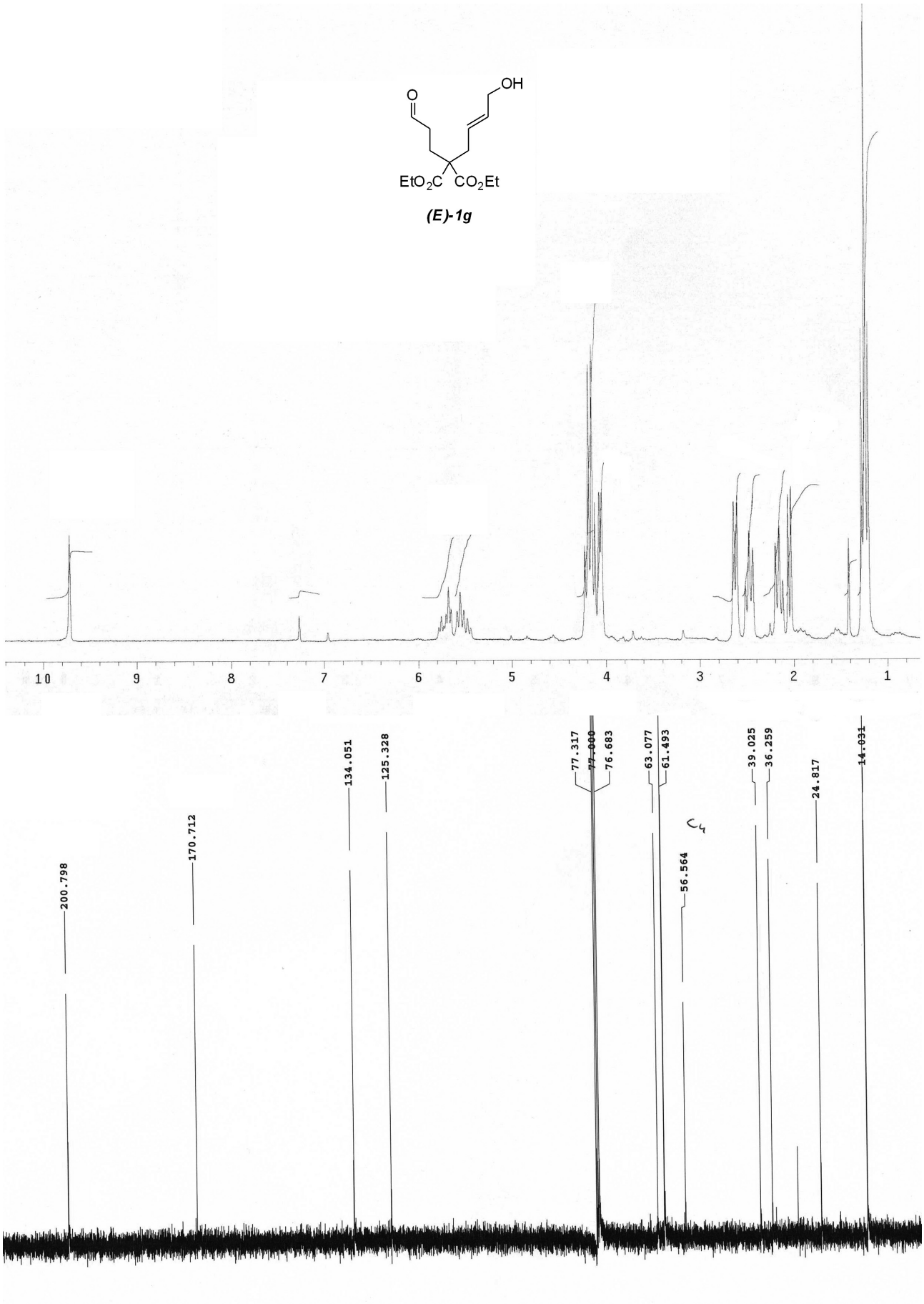


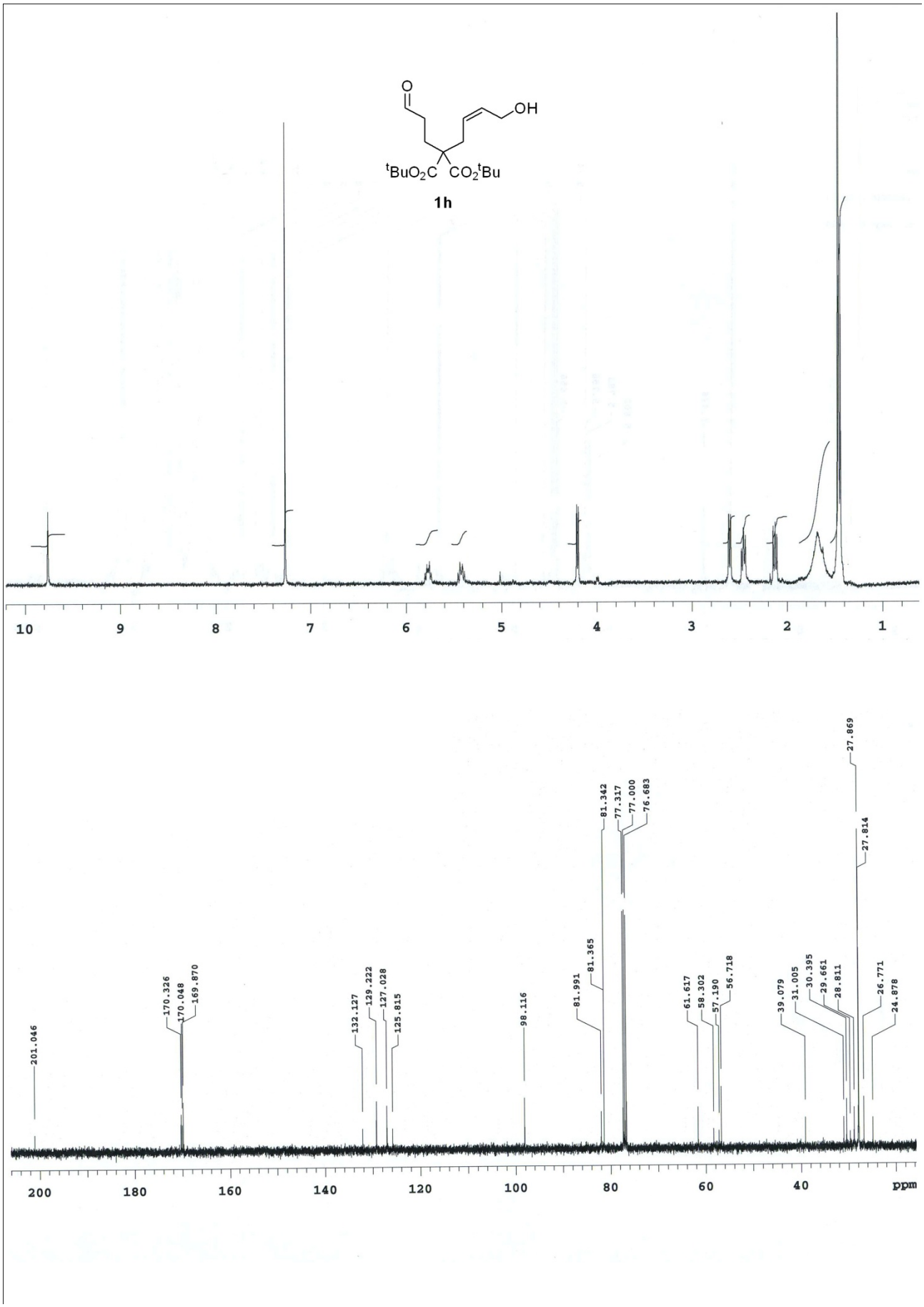

O
OH
MeO2C CO2Me
10
9
8
7
6
5
4
3
2

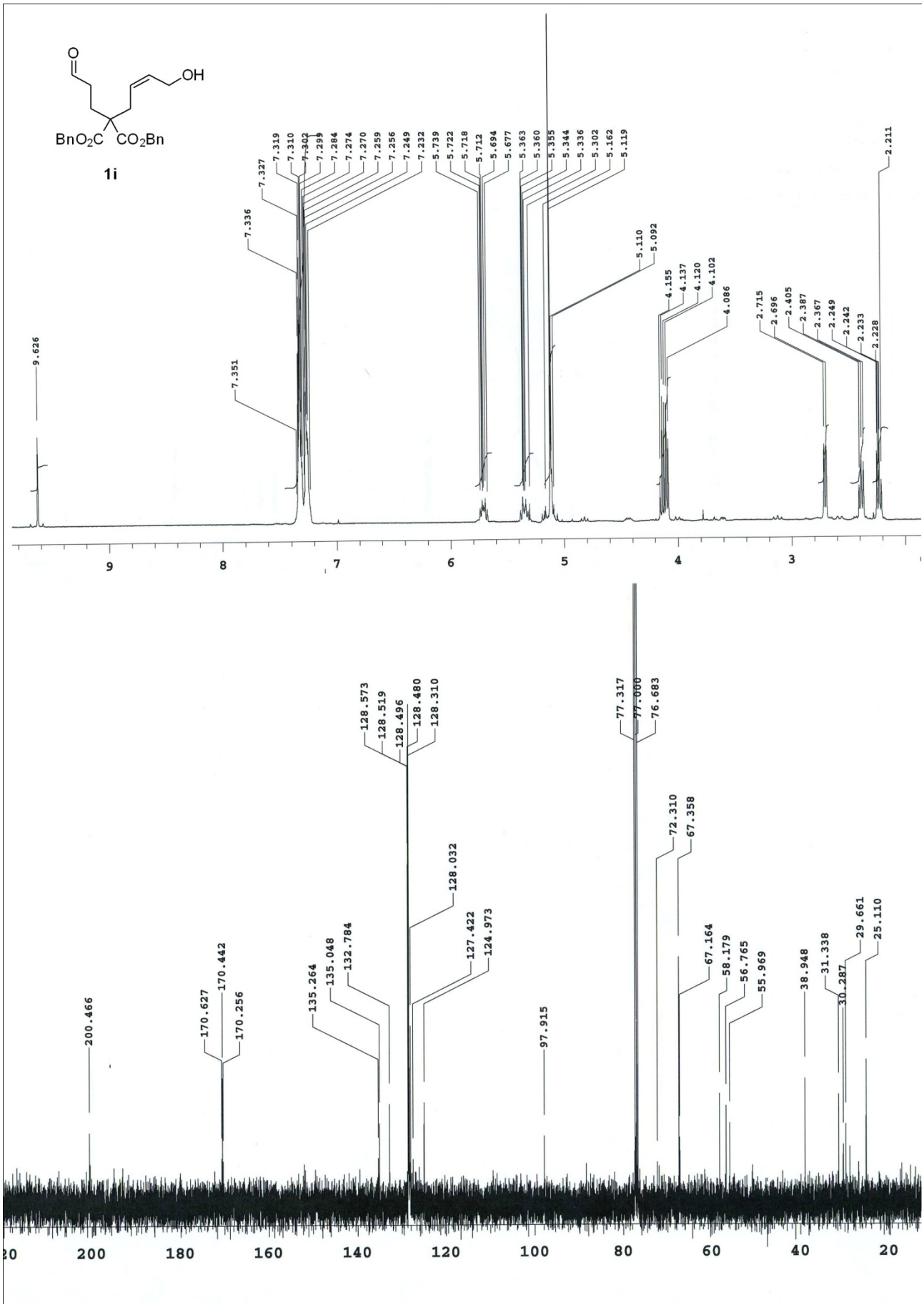
1f

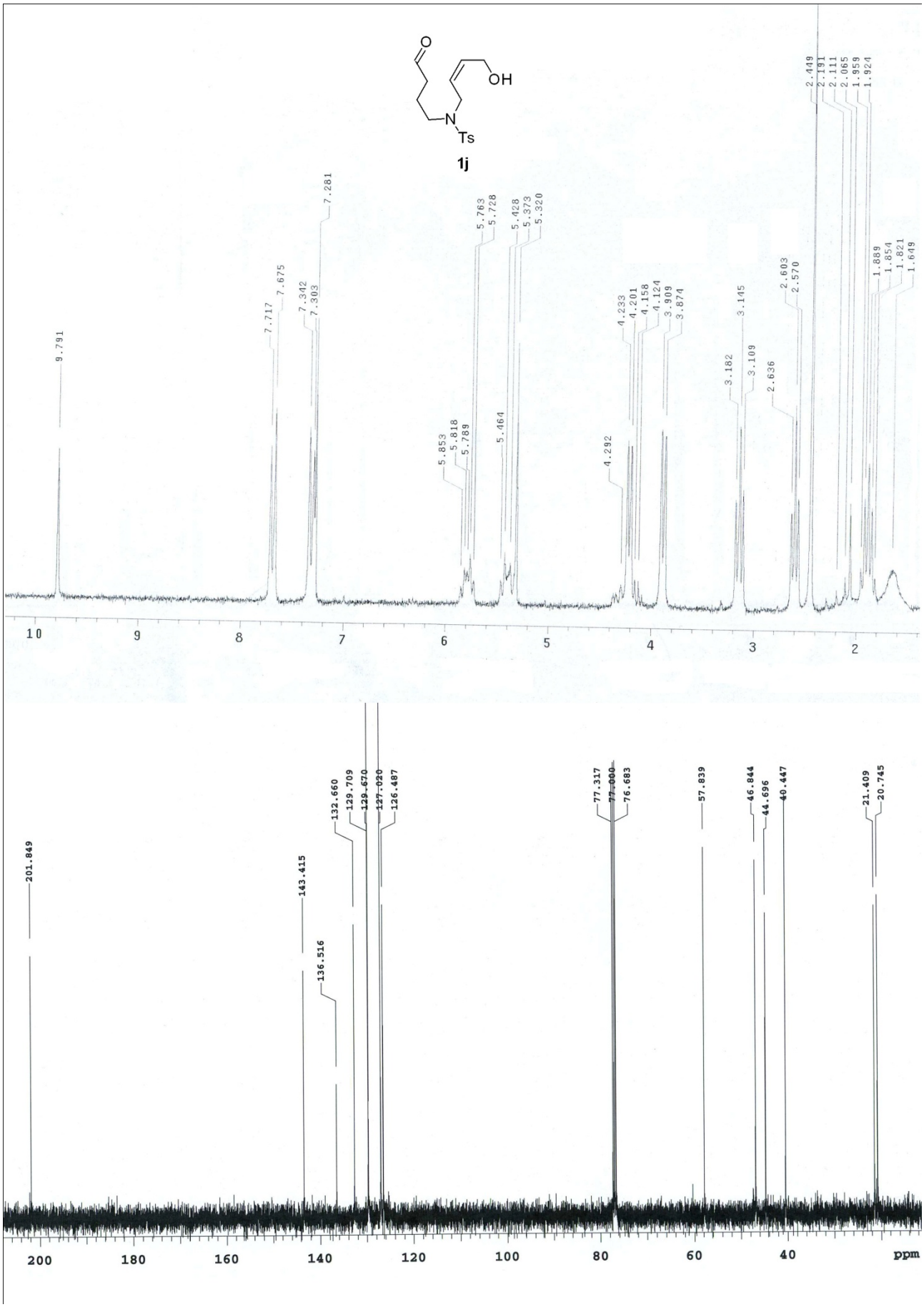

77.317
77.000
76.683
200.667
171.446
171.191
132.745
128.751
127.321
125.119
97.931
61.578
58.086
56.718
55.784
52.755
52.654
39.126
31.508
30.410
29.622
28.819
26.887
25.195
200
180
160
140
120
100
80
60
40
20

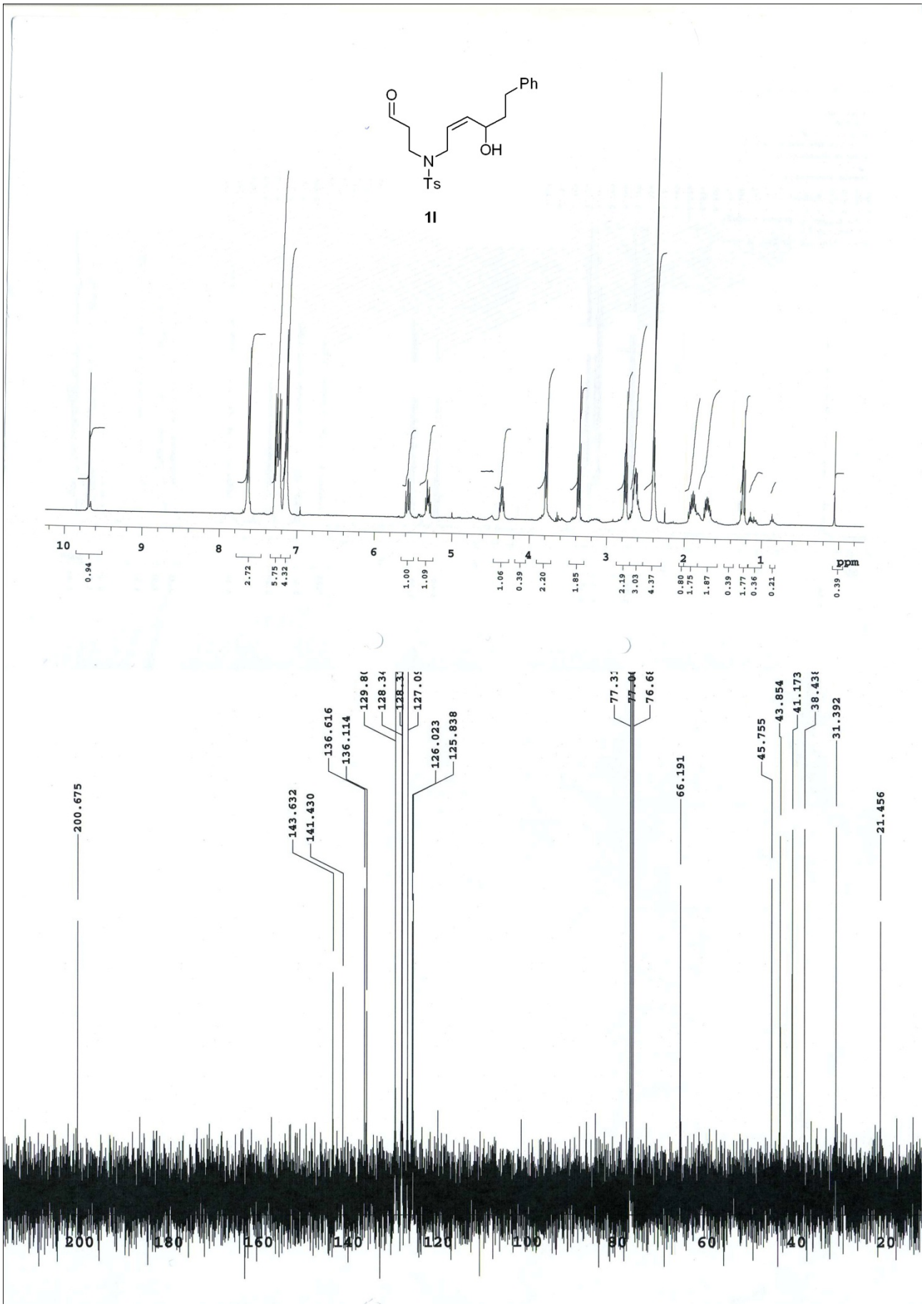

O
OH
EtO2C CO2Et
(Z)-1g
9
8
7
6
5
4
3
2
1
77.317
77.000
76.683
61.602
60.350
58.171
56.579
39.133
31.314
25.064
14.147
13.992
200.706
170.774
132.606
125.351
200
180
160
140
120
100
80
60
40
20 ppm

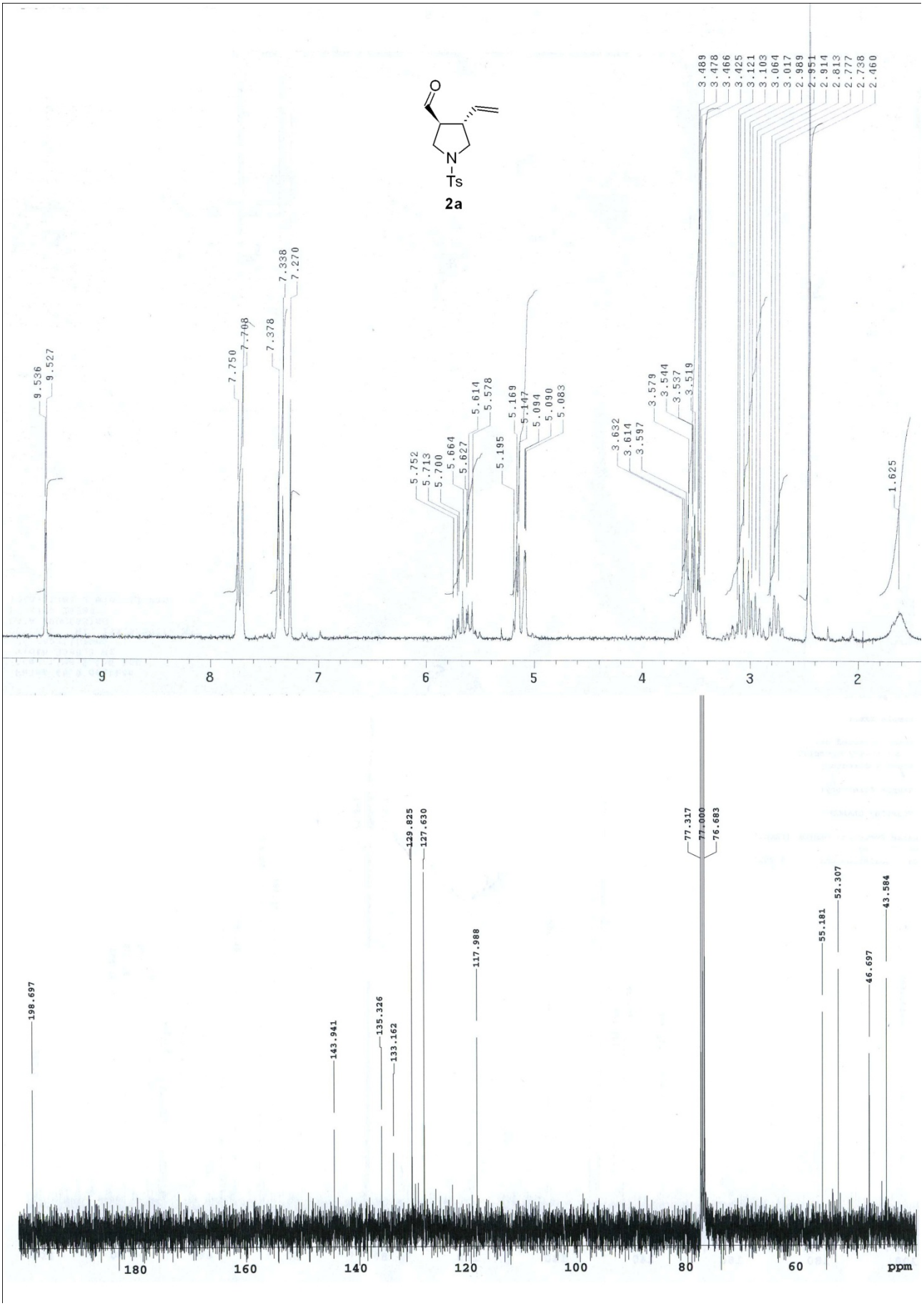


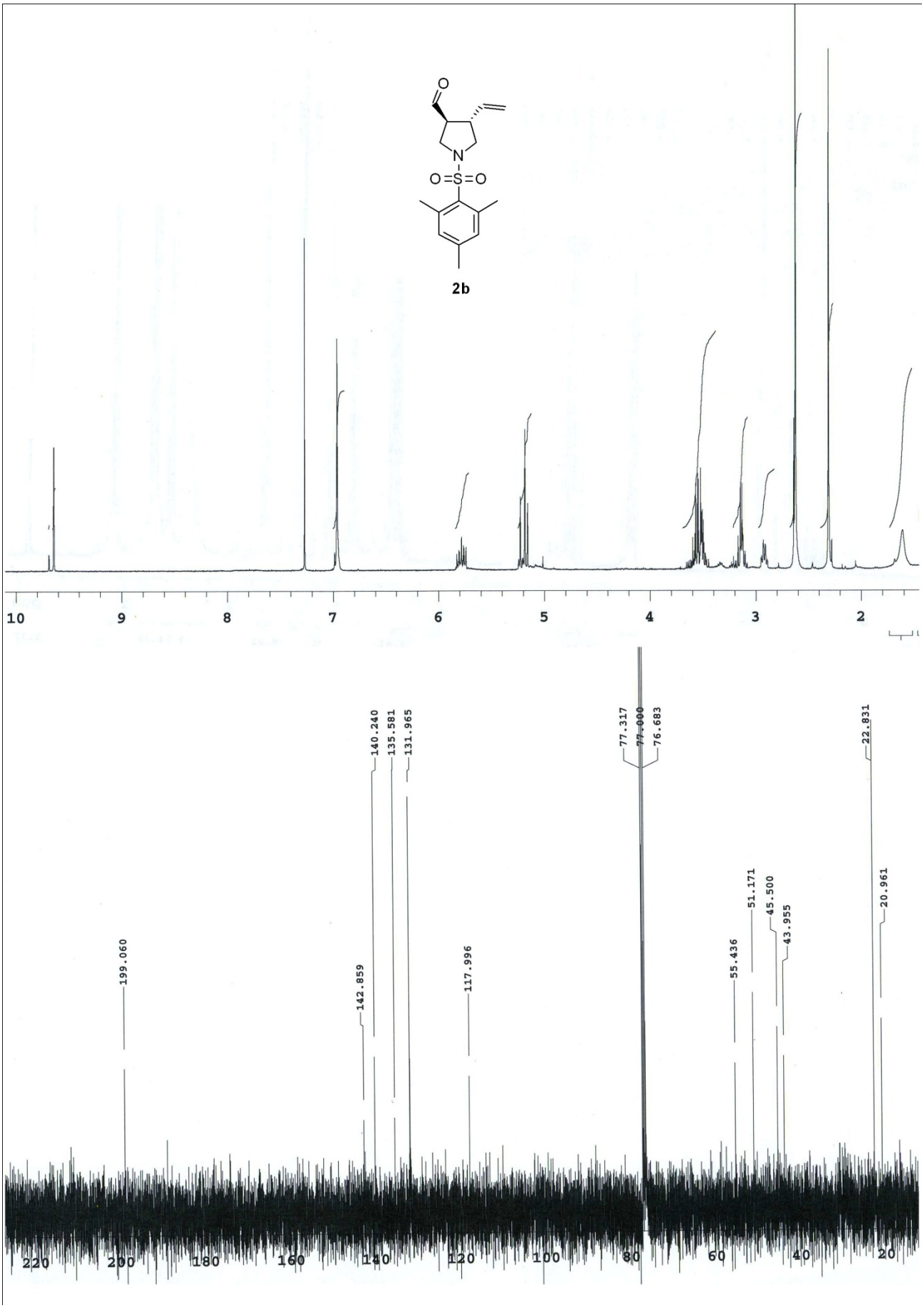

O
OH
$^{t}BuO_2C$ $CO_2{}^{t}Bu$
1h
10
9
8
7
6
5
4
3
2
1
201.046
170.326
170.048
169.870
132.127
129.222
127.028
125.815
98.116
81.991
81.365
81.342
77.317
77.000
76.683
61.617
58.302
57.190
56.718
39.079
31.005
30.395
29.661
28.811
27.869
27.814
26.771
24.878
200
180
160
140
120
100
80
60
40
ppm

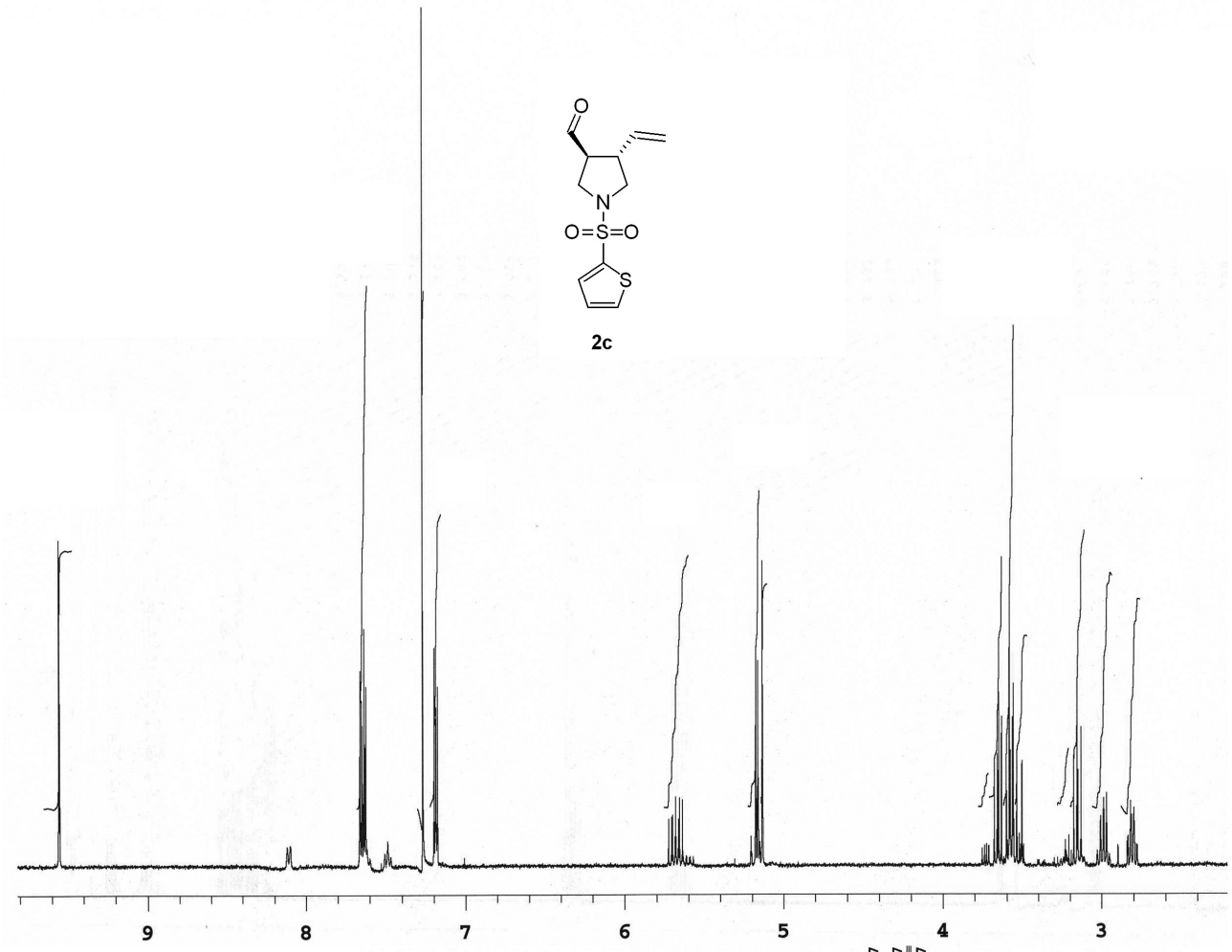

O
OH
BnO2C CO2Bn
1i
9.626
7.351
7.336
7.327
7.319
7.310
7.302
7.299
7.284
7.274
7.270
7.259
7.256
7.249
7.232
5.739
5.722
5.718
5.712
5.694
5.677
5.363
5.360
5.355
5.344
5.336
5.302
5.162
5.119
5.110
5.092
4.155
4.137
4.120
4.102
4.086
2.715
2.696
2.405
2.387
2.367
2.249
2.242
2.233
2.228
2.211
9
8
7
6
5
4
3
200.466
170.627
170.442
170.256
135.264
135.048
132.784
128.573
128.519
128.496
128.480
128.310
128.032
127.422
124.973
97.915
77.317
77.000
76.683
72.310
67.358
67.164
58.179
56.765
55.969
38.948
31.338
30.287
29.661
25.110
200
180
160
140
120
100
80
60
40
20


O
OH
N
Ts
1j
9.791
7.717
7.675
7.342
7.303
7.281
5.853
5.818
5.789
5.763
5.728
5.464
5.428
5.373
5.320
4.292
4.233
4.201
4.158
4.124
3.909
3.874
3.182
3.145
3.109
2.636
2.603
2.570
2.449
2.191
2.111
2.065
1.959
1.924
1.889
1.854
1.821
1.649
10
9
8
7
6
5
4
3
2
201.849
143.415
136.516
132.660
129.709
129.670
127.020
126.487
77.317
77.000
76.683
57.839
46.844
44.696
40.447
21.409
20.745
200
180
160
140
120
100
80
60
40
ppm

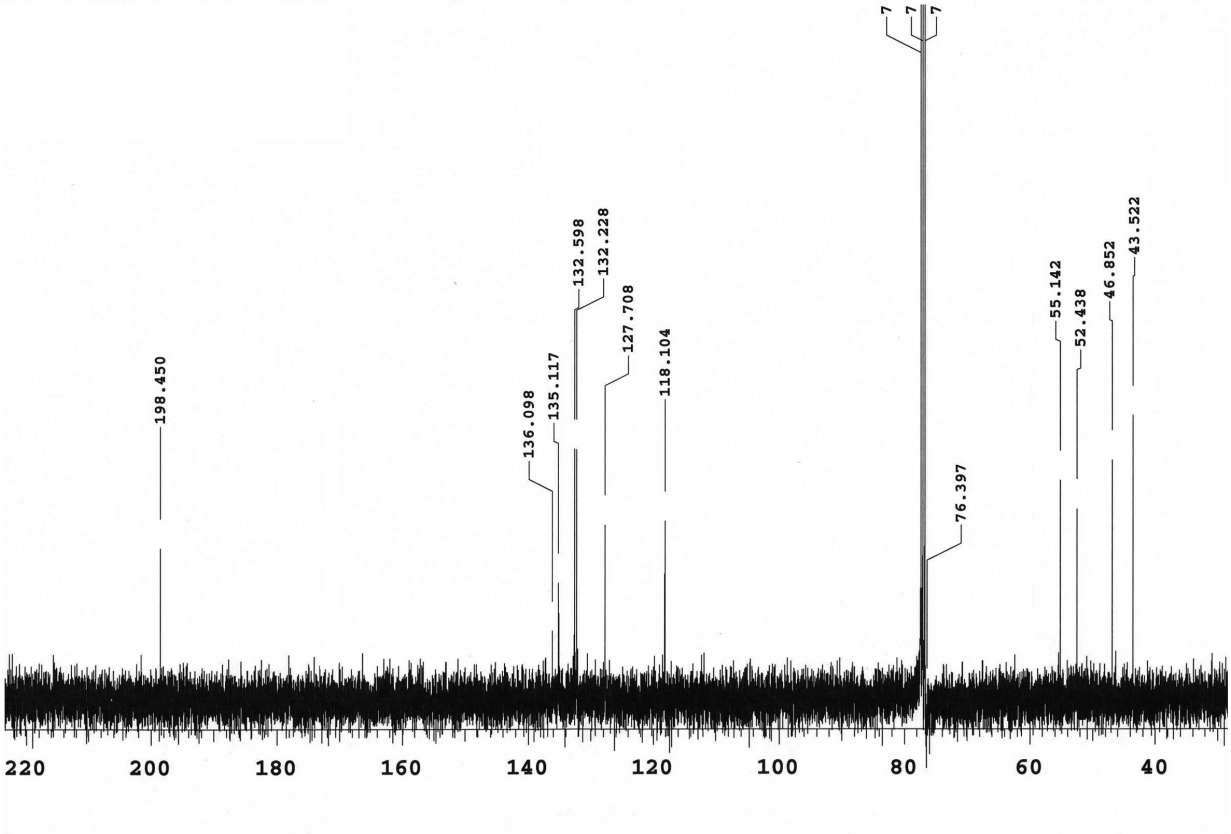


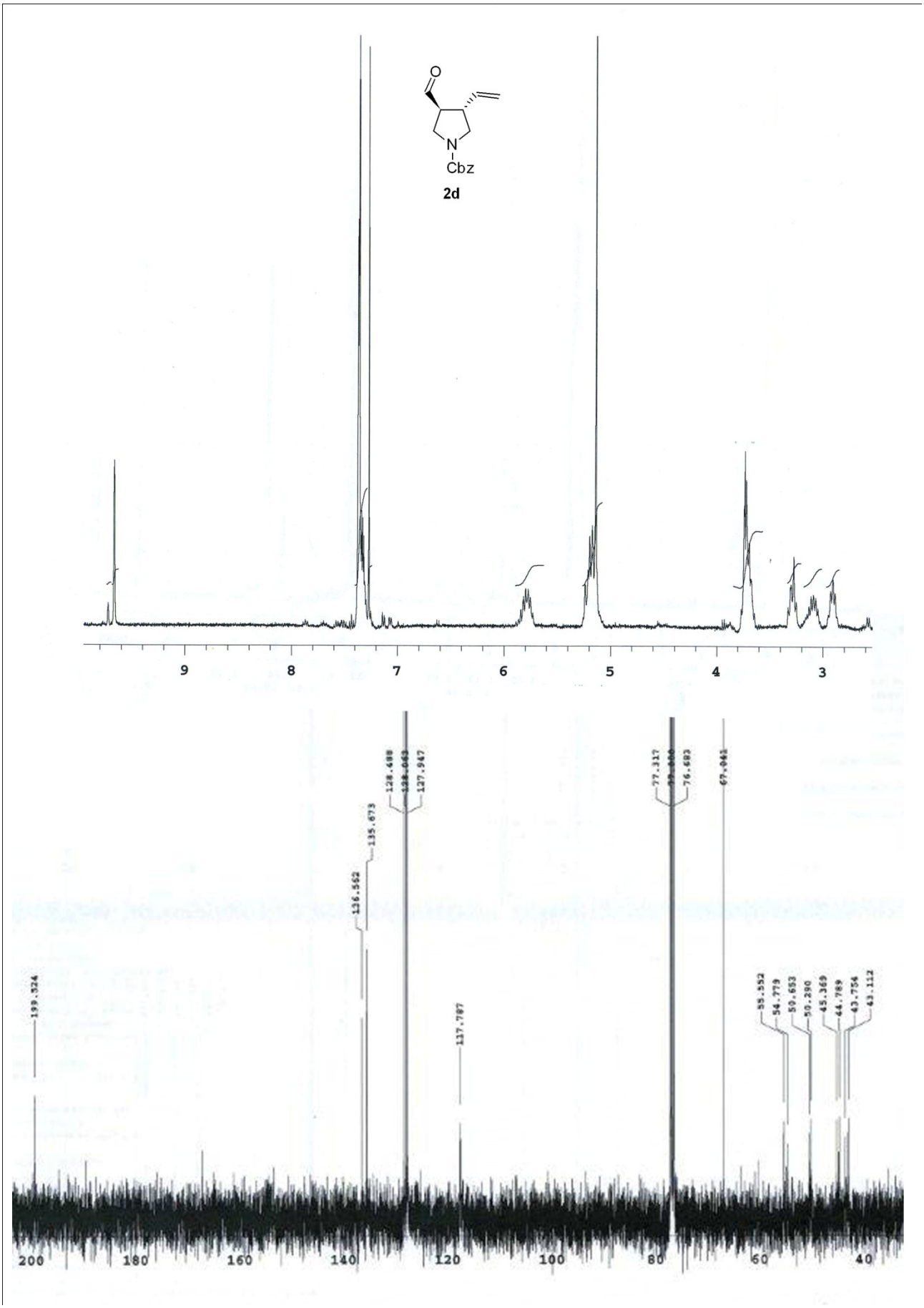

O
N
Ts
2a
9.536
9.527
7.750
7.708
7.378
7.338
7.270
5.752
5.713
5.700
5.664
5.627
5.614
5.578
5.195
5.169
5.147
5.094
5.090
5.083
3.632
3.614
3.597
3.579
3.544
3.537
3.519
3.489
3.478
3.466
3.425
3.121
3.103
3.064
3.017
2.989
2.951
2.914
2.813
2.777
2.738
2.460
1.625
9
8
7
6
5
4
3
2
198.697
143.941
135.326
133.162
129.825
127.630
117.988
77.317
77.000
76.683
55.181
52.307
46.697
43.584
180
160
140
120
100
80
60
ppm

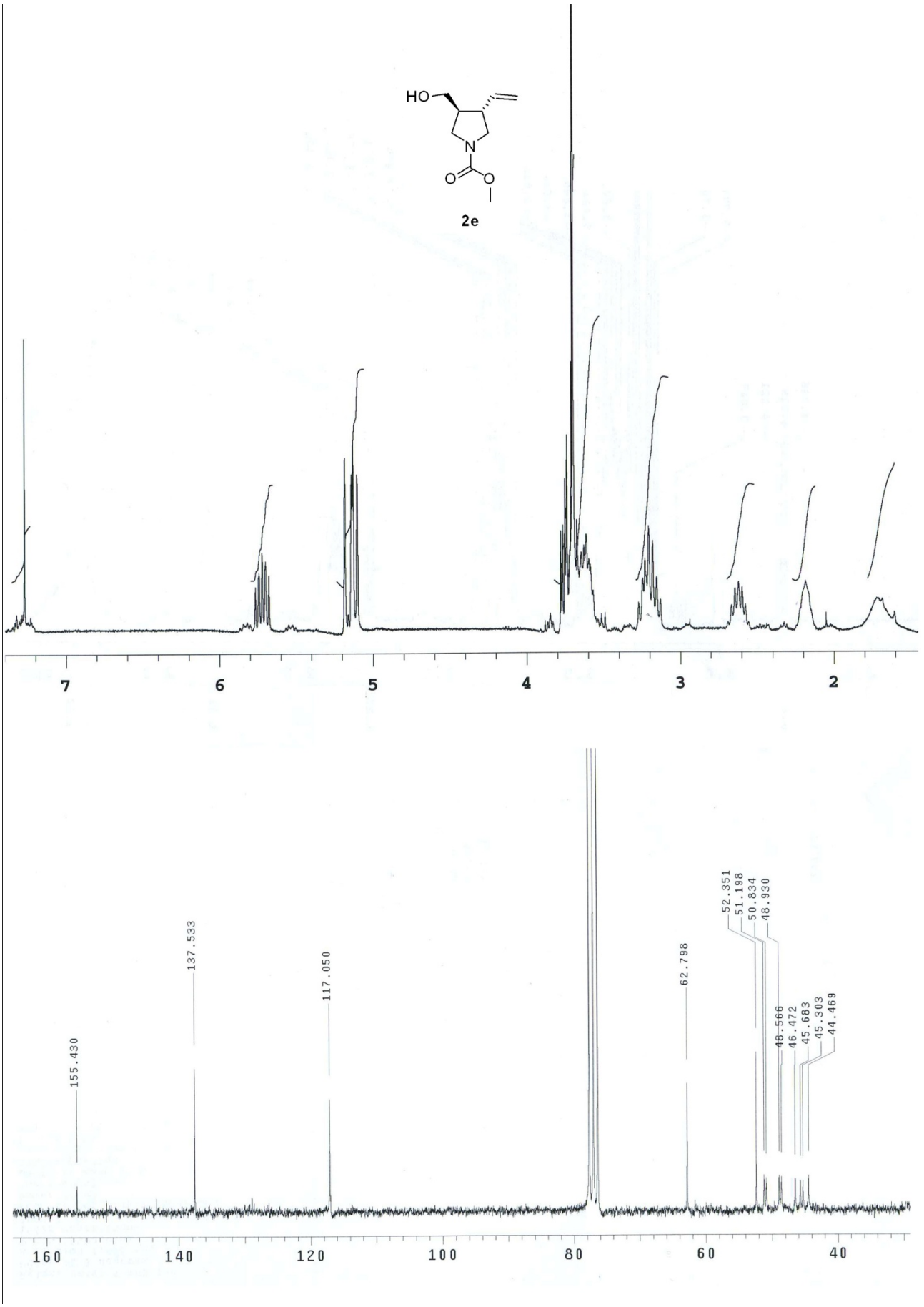

O
N
O=S=O
2b
10
9
8
7
6
5
4
3
2
199.060
142.859
140.240
135.581
131.965
117.996
77.317
77.000
76.683
55.436
51.171
45.500
43.955
22.831
20.961
220
200
180
160
140
120
100
80
60
40
20

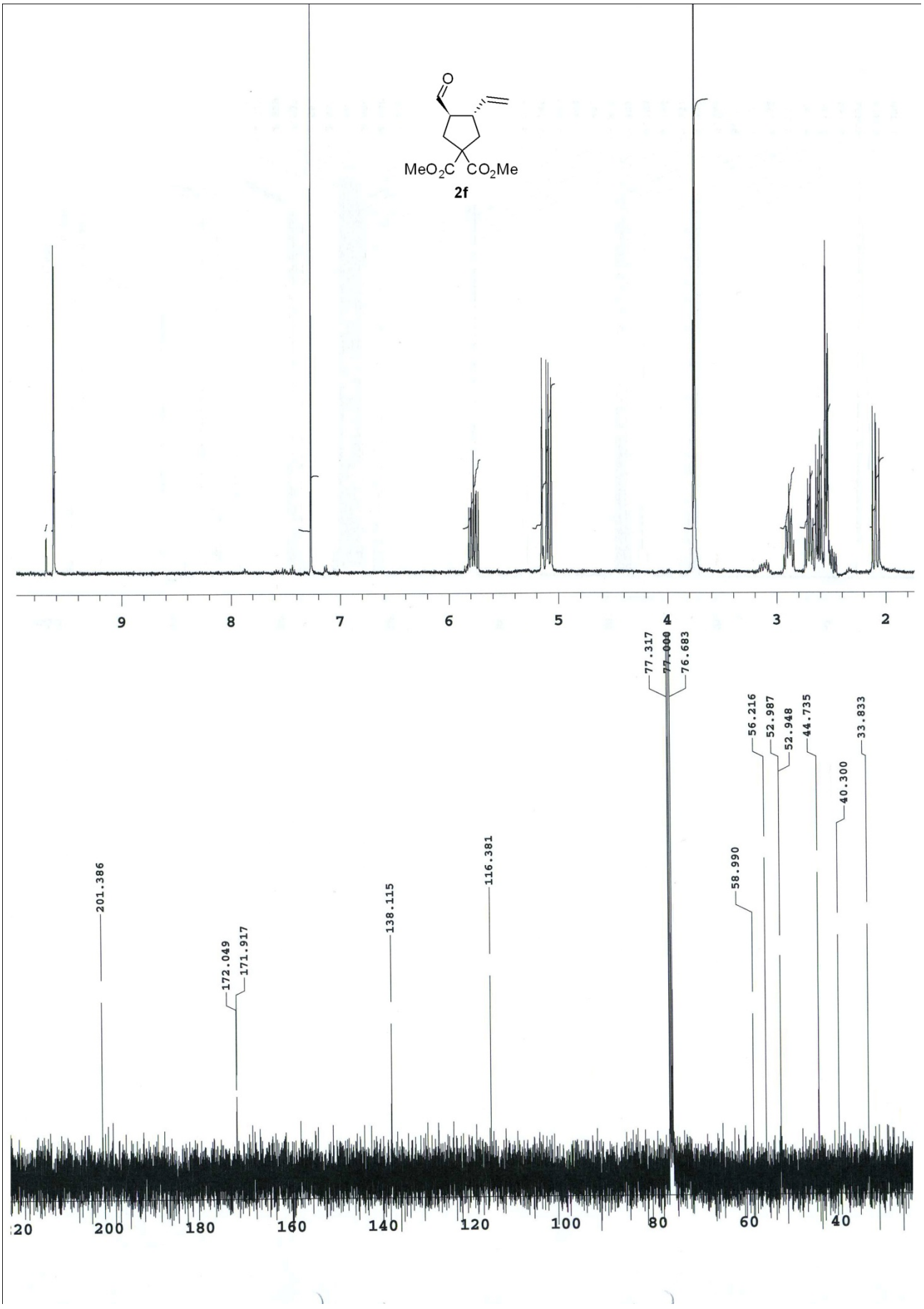


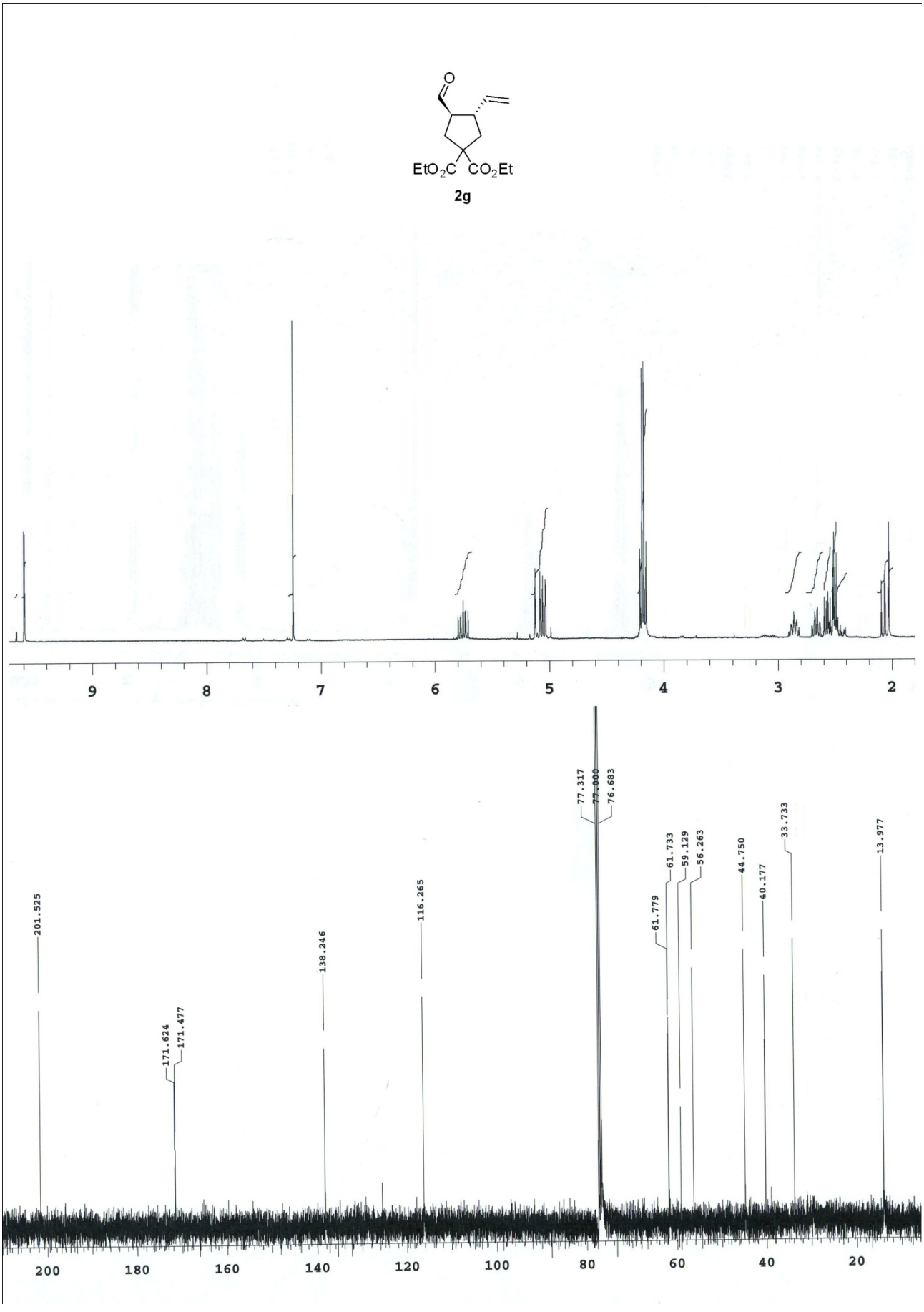
2c



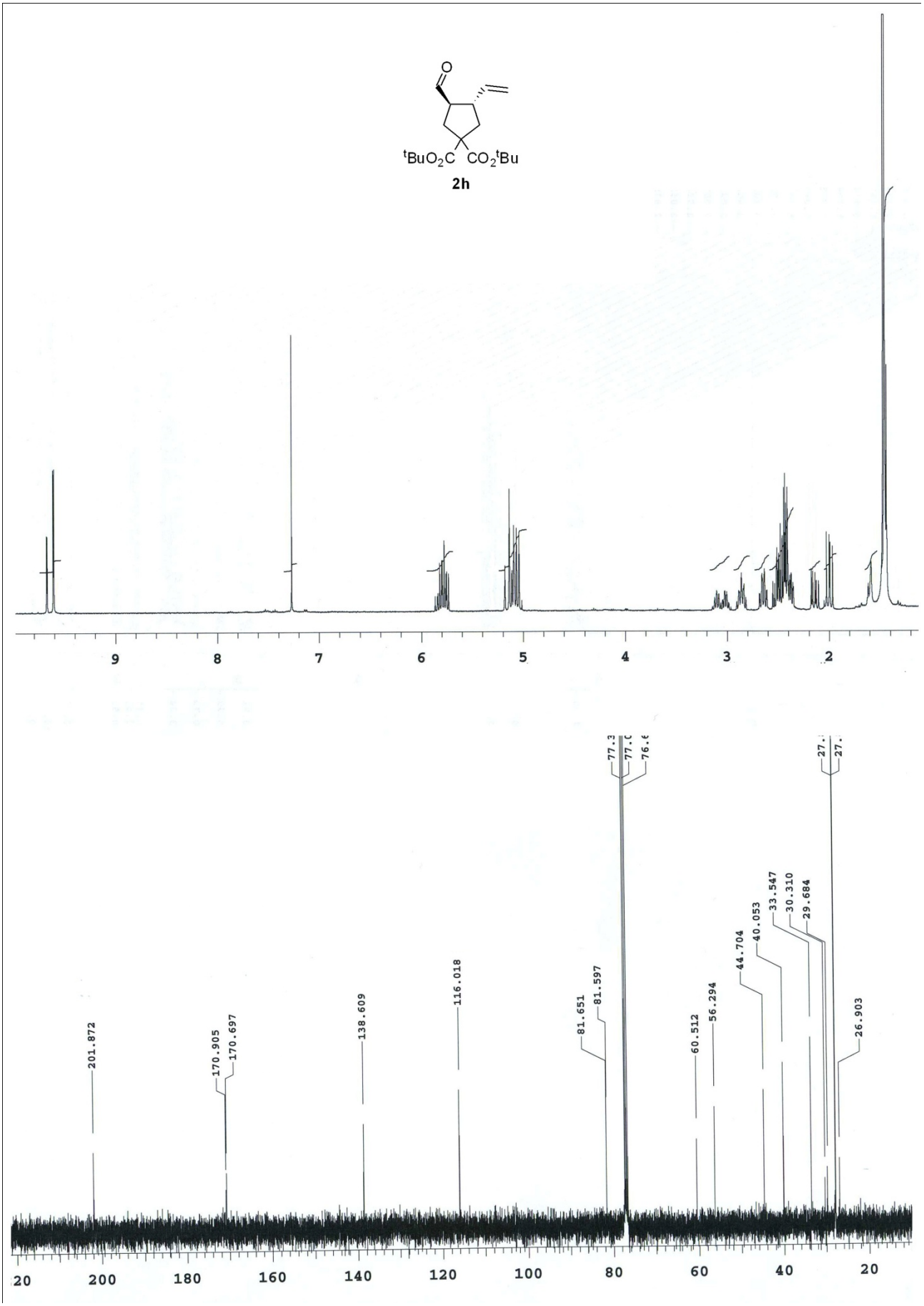


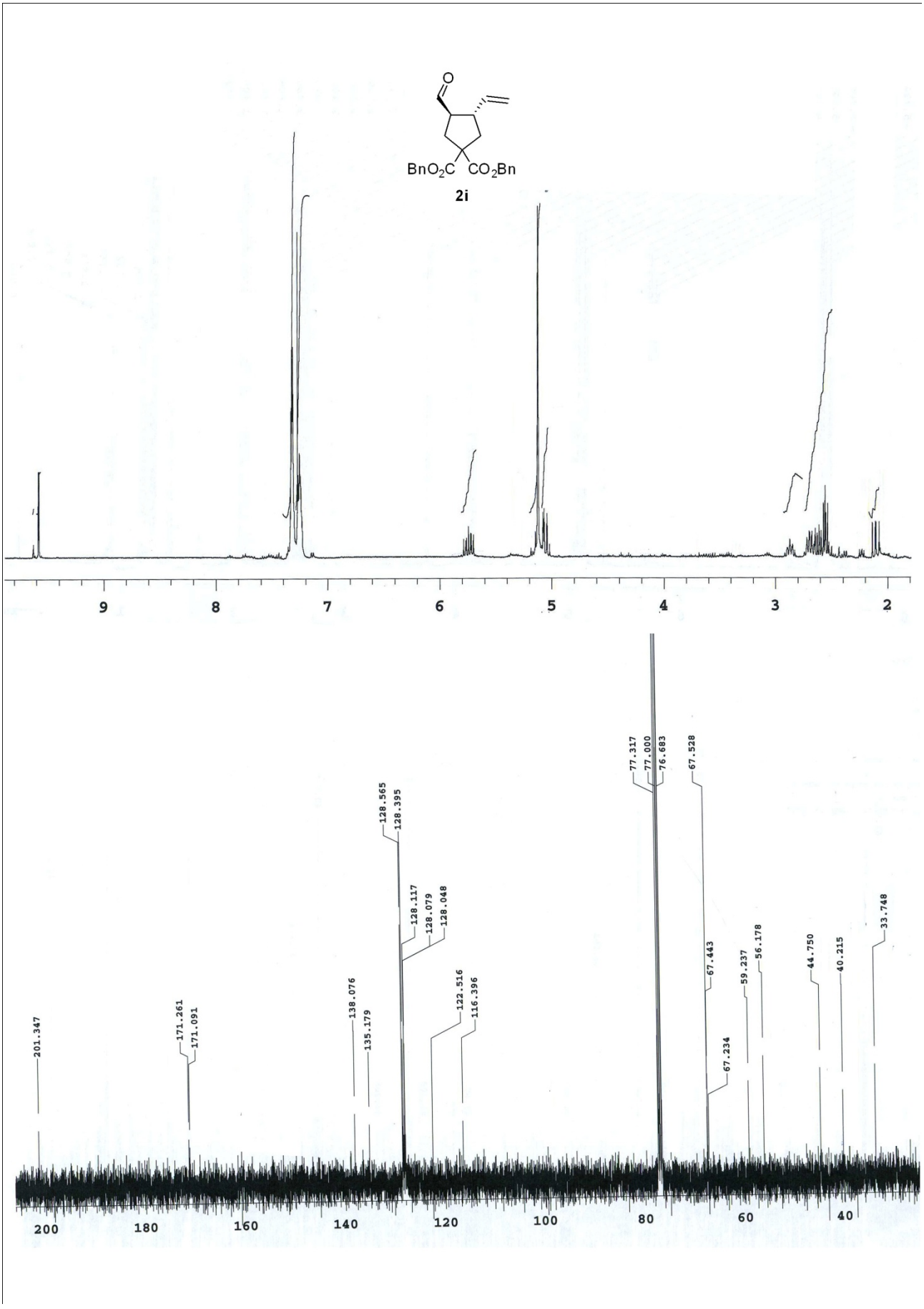






v


O
tBuO2C CO2tBu
2h
9
8
7
6
5
4
3
2
77.3
77.0
76.6
27.
27.
201.872
170.905
170.697
138.609
116.018
81.651
81.597
60.512
56.294
44.704
40.053
33.547
30.310
29.684
26.903
20
200
180
160
140
120
100
80
60
40
20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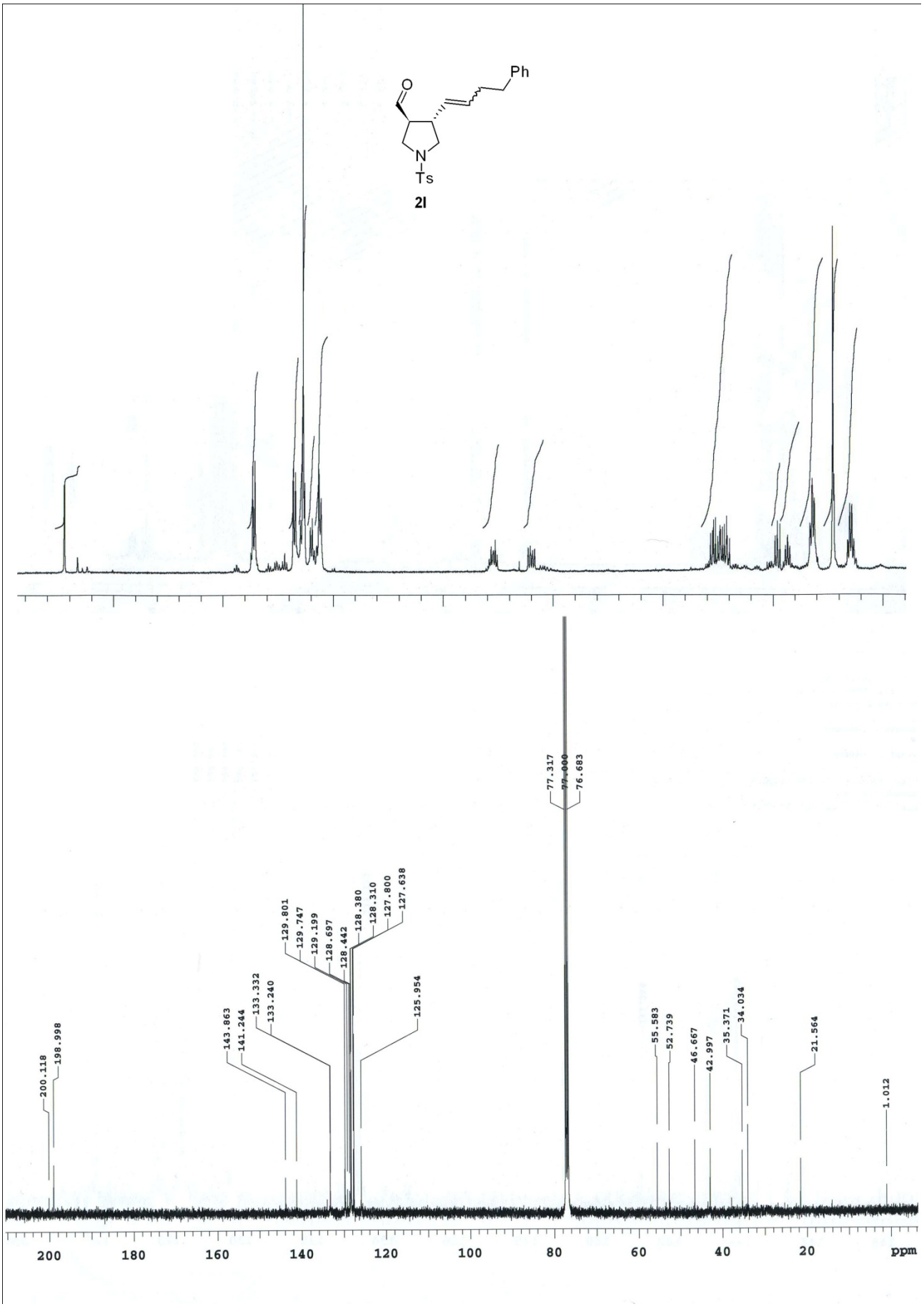
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