Electronic Supplementary Material (ESI) for ChemComm.

Development of an Enantioselective Amine-Silver Co-Catalyzed Conia-Ene Reaction

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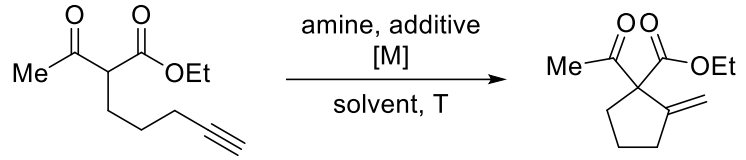
General remarks

Solvents were distilled using standard procedures. Flash column chromatography was performed with silica gel SIL G-25 UV254 (size 0.040-0.063 mm) from *Machery&Nagel*. For the TLC silica gel 60 F254 plates from *Merck*, Darmstadt, were used. The compounds on the TLC plates were identified under UV light (254 nm) and by staining with anisaldehyde staining reagent (solution of 3.2 g of *p*-methoxy benzaldehyde and 1 ml conc. H_2SO_4 in 100 ml ethanol). ^{1}H, ^{13}C, and ^{19}F NMR spectra were measured with *Varian Gemini 300*, *Varian Mercury 300*, *Varian Inova 400*, and *Varian Inova 600* at ambient temperature. Specifically assigned hydrogen and carbon atoms are written in italics. Mass spectra were recorded with the spectrometer *SSQ7000* from *Finnigan* at 70 eV, whereas HRMS data (ESI) were collected with a *ThermoFisher Scientific LTQ-Orbitrap XL* apparatus. Using the ATR technique IR spectra were measured on a *Perkin-Elmer FT-IR Spectrum 100*. The elemental analyses were conducted at *Vario EL* element analyzer. Melting points were measured with a *MPM-H2*. For determining the enantiomeric excess the HPLC data were collected with either *Hewlett-Packard 1050*, *Agilent 1100*, or *Agilent 1260* instruments using *Chiracel* (OD, OJ), *Chiralpak* (AD, AS, IA, IC) columns from *Daicel*. Optical rotation was determined on a *Perkin-Elmer P241* polarimeter. The absolute configuration was determined by comparison of the optical rotation with known optical rotations from the literature.

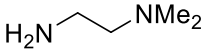
Optimization

Table S1. Optimization of the Conia-ene reaction.[a]



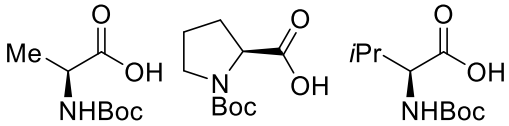
1a **2a**

amine



A

additives



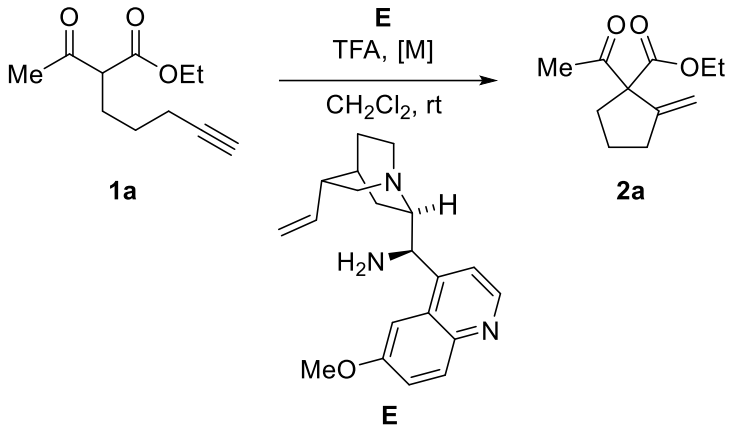
B **C** **D**

entry	[M] (mol%)	amine (mol%)	additive (mol%)	solvent	T [°C]	*t* [h]	yield[b] [%]
1	Ag_2CO_3 (10)	-	TFA (20)	CH_2Cl_2	25	65	20
2	Ag_2O (10)	-	TFA (20)	CH_2Cl_2	25	65	32
3	Ag_2CO_3 (10)	*t*BuNH$_2$ (20)	TFA (20)	CH_2Cl_2	25	154	trace
4	Ag_2O (10)	*t*BuNH$_2$ (20)	TFA (20)	CH_2Cl_2	25	154	trace
5	Ag_2CO_3 (10)	**A** (20)	TFA (20)	CH_2Cl_2	25	24	80
6	Ag_2O (10)	**A** (20)	TFA (20)	CH_2Cl_2	25	24	81
7	$AgNTf_2$·MeCN (10)	**A** (20)	TFA (20)	CH_2Cl_2	25	24	84
8	$AgSbF_6$ (10)	**A** (20)	TFA (20)	CH_2Cl_2	25	30	80
9	$AgNTf_2$·MeCN (10)	**A** (20)	TFA (20)	$CHCl_3$	25	24	84
10	$AgNTf_2$·MeCN (10)	**A** (20)	TFA (20)	CCl_4	25	24	74
11	$AgNTf_2$·MeCN (10)	**A** (20)	TFA (20)	1,2-DCE	25	24	78
12	$AgNTf_2$·MeCN (10)	**A** (20)	TFA (20)	Et_2O	25	24	67
13	$AgNTf_2$·MeCN (10)	**A** (20)	TFA (20)	THF	25	24	72
14	$AgNTf_2$·MeCN (10)	**A** (20)	TFA (20)	dioxane	25	24	29
15	$AgNTf_2$·MeCN (10)	**A** (20)	TFA (20)	MeCN	25	24	80
16	$AgNTf_2$·MeCN (10)	**A** (20)	TFA (20)	EtOAc	25	24	69
17	$AgNTf_2$·MeCN (10)	**A** (20)	TFA (20)	DMF	25	24	69
18	$AgNTf_2$·MeCN (10)	**A** (20)	TFA (20)	toluene	25	24	78
19	$AgNTf_2$·MeCN (10)	**A** (20)	TFA (20)	MeOH	25	24	43
20	$AgNTf_2$·MeCN (10)	**A** (20)	*p*TSA (20)	$CHCl_3$	25	20	85
21	$AgNTf_2$·MeCN (10)	**A** (20)	**B** (20)	$CHCl_3$	25	20	86
22	$AgNTf_2$·MeCN (10)	**A** (20)	**C** (20)	$CHCl_3$	25	21	86
23	$AgNTf_2$·MeCN (10)	**A** (20)	**D** (20)	$CHCl_3$	25	21	86
24	**$AgNTf_2$·MeCN (10)**	**A (10)**	**B (10)**	**$CHCl_3$**	**25**	**20**	**89**
25	$AgNTf_2$·MeCN (10)	**A** (40)	**B** (40)	$CHCl_3$	25	20	80
26	$AgNTf_2$·MeCN (10)	**A** (5)	**B** (5)	$CHCl_3$	25	20	49

27	$AgNTf_2$·MeCN (10)	**A** (20)	**B** (40)	$CHCl_3$	25	20	63
28	$AgNTf_2$·MeCN (5)	**A** (20)	**B** (20)	$CHCl_3$	25	70	78
29	$AgNTf_2$·MeCN (1)	**A** (20)	**B** (20)	$CHCl_3$	25	70	82
30	$AgNTf_2$·MeCN (10)	**A** (20)	**B** (20)	$CHCl_3$	40	6	80
31	$AgNTf_2$·MeCN (5)	**A** (20)	**B** (20)	$CHCl_3$	40	6	91[c] (80)
32	$AgNTf_2$·MeCN (1)	**A** (20)	**B** (20)	$CHCl_3$	40	6	77[c] (55)

[a] The reactions were carried out with β-ketoester **1a** (0.25 mmol), [M], amine, and additive in 0.25 mL of the given solvent (*c* = 1 M) at the given temperature. [b] Yield of the isolated products. [c] Not reproducible.

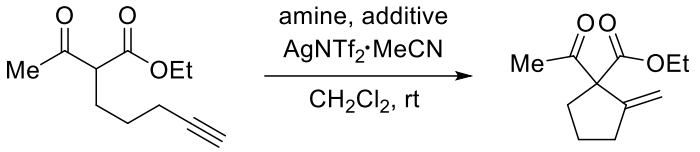
Table S2. Screening of different metal sources for the enantioselective Conia-ene reaction.[a]



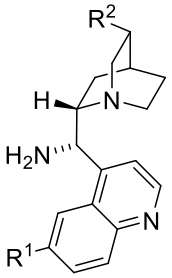
entry	[M]	*t* [h]	yield[b] [%]	*ee*[c] [%]
1	$[Ph_3PAu]NTf_2$	24	94	0
2	Cu(OTf)·4 MeCN	44	trace	-[e]
3	$Cu(OTf)_2$	44	trace	-[e]
4	$Yb(OTf)_3·H_2O$	154	nr[d]	-[e]
5	$In(OTf)_3$	48	78	1
6	$Sc(OTf)_3$	154	nr[d]	-[e]
7	$Bi(OTf)_3$	154	nr[d]	-[e]
8	$PtCl_2$	154	nr[d]	-[e]
9	**$AgNTf_2$·MeCN**	**20**	**63**	**75**
10	AgOTf	44	45	72
11	$AgSbF_6$	42	35	74
12	$AgBF_4$	42	38	74
13	$AgNO_3$	48	47	0
14	AgOAc	120	nr[d]	-[e]
15	AgF	65	45	67
16	Ag_2SO_4	72	24	62
17	AgO	135	55	27
18	AgOCN	135	18	49
19	Ag_2CO_3	48	84	43
20	Ag_2O	48	65	0

[a] The reactions were carried out with β-ketoester **1a** (0.25 mmol), [M] (10 mol%), *epi*-quinidine amine **E** (20 mol%), and TFA (20 mol%) in 0.25 mL CH_2Cl_2 (*c* = 1 M) at ambient temperature. [b] Yield of the isolated products. [c] Determined by HPLC with a chiral stationary phase. [d] No reaction. [e]Not determined.

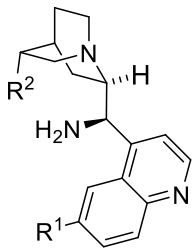
Table S3. Further Optimization of the enantioselective Conia-ene reaction.[a]



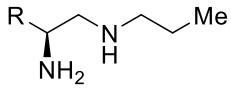
sub:2a **sub:1a**



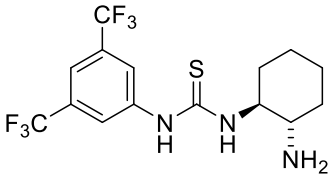
R^1 = H, R^2 = vinyl **F**
R^1 = OMe, R^2 = vinyl **G**
R^1 = H, R^2 = Et **H**



R^1 = H, R^2 = vinyl **I**
R^1 = OMe, R^2 = vinyl **E**
R^1 = OMe, R^2 = Et **J**

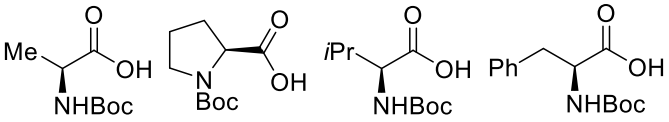


R = *i*Bu **K**
R = Bn **L**
R = Ph **M**



N

additives

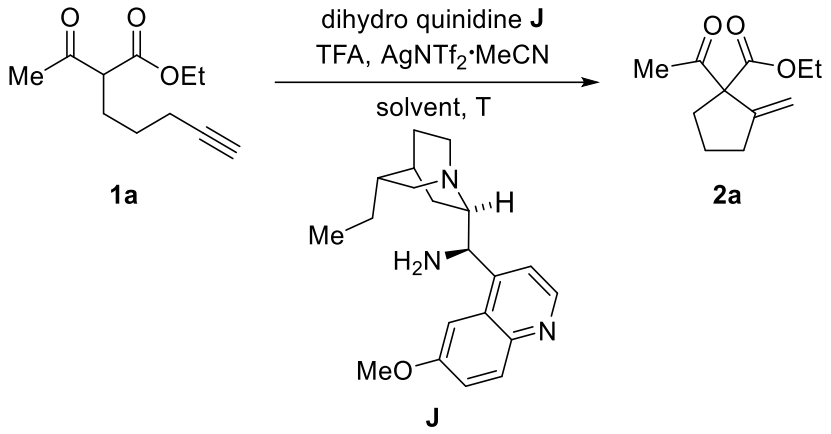


B **C** **D** **O**

entry	amine	additive	*t* [h]	yield[b] [%]	*ee*[c] [%]
1	**F**	TFA	20	31	32
2	**G**	TFA	20	63	−16
3	**H**	TFA	20	67	−26
4	**I**	TFA	20	80	−22
5	**E**	TFA	20	63	75
6	**J**	**TFA**	**20**	**61**	**78**
7	**K**	TFA	20	78	−1
8	**L**	TFA	20	trace	-[e]
9	**M**	TFA	20	45	6
10	**N**	TFA	20	nr[d]	-[e]
11	**J**	*p*TSA	20	21	−67
12	**J**	*rac*-**B**	20	10	−37
13	**J**	**B**	20	69	−27
14	**J**	**C**	20	83	−54
15	**J**	**D**	20	38	−43
16	**J**	**O**	20	32	22

[a] The reactions were carried out with β-ketoester **1a** (0.25 mmol), [M] (10 mol%), amine (20 mol%), and additive (20 mol%) in 0.25 mL CH_2Cl_2 (*c* = 1 M) at ambient temperature. [b] Yield of the isolated products. [c] Determined by HPLC with a chiral stationary phase. [d] No reaction. [e]Not determined.

Table S4. Final Optimization of the enantioselective Conia-ene reaction.[a]



entry	solvent	amine [mol%]	additive [mol%]	Ag [mol%]	T [°C]	yield [%][b]	*ee* [%][c]
1	$CHCl_3$	20	20	10	25	69	48
2	CCl_4	20	20	10	25	35	69
3	1,2-DCE	20	20	10	25	45	60
4	Et_2O	20	20	10	25	8	50
5	THF	20	20	10	25	43	34
6	dioxane	20	20	10	25	40	17
7	MeCN	20	20	10	25	11	35
8	EtOAc	20	20	10	25	57	80
9	DMF	20	20	10	25	63	86
10	toluene	20	20	10	25	14	80
11	MeOH	20	20	10	25	76	90
12	MeOH	20	20	10	40	85	90
13	MeOH	20	20	10	60	81	85
14	MeOH	20	20	10	0	82	91
15	MeOH	20	20	10	−20	28	89
16	MeOH	40	40	10	0	85	91
17	MeOH	20	40	10	0	57	90
18	MeOH	10	10	10	0	46	85
19	MeOH	5	5	10	0	43	77
20	MeOH	20	20	5	0	84	93
21	**MeOH**	**20**	**20**	**2.5**	**0**	**86**	**95**
22	MeOH	20	20	1	0	46	−22
23[d]	MeOH	20	20	10	0	89	90
24[e]	MeOH	20	20	10	0	61	95

[a] The reactions were carried out for 20 h with β-ketoester **1a** (0.25 mmol), $AgNTf_2$·MeCN, dihydro quinidine **J**, and TFA in 0.25 mL of the given solvent (*c* = 1 M) at the given temperature. [b] Yield of the isolated products. [c] Determined by HPLC with a chiral stationary phase. [d] 0.13 mL of MeOH (*c* = 2 M) were used. [e] 0.5 mL of MeOH (*c* = 0.5 M) were used.

General Procedure A

To a suspension of potassium carbonate (2.0 eq.) in acetone (c = 0.2 M) ethyl acetoacetate or another C-H acidic compound (2.0 mmol) and 5-iodopent-1-yne (1.1 eq.) were added and the resulting mixture heated to reflux for 16 h. After the completion of the reaction the mixture was cooled to ambient temperature and the solvent removed under reduced pressure. The residue was dissolved in dichloromethane and water, the layers were separated, and the water layer was extracted with dichloromethane. Subsequent drying over sodium sulfate, removal of the solvent under reduced pressure and purification by flash chromatography (*n*-pentane/Et_2O or *n*-pentane/EtOAc) yielded the alkylated compounds.

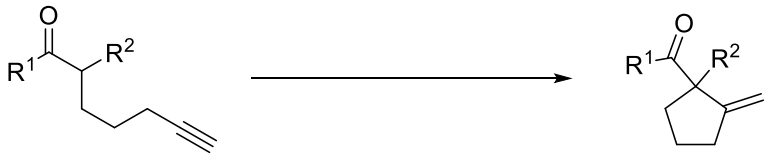
General Procedure B (Non-Asymmetric Protocol)

To a solution of **1** (0.25 mmol), $AgNTf_2$·MeCN (10 mol%), and *N*-Boc-alanine (10 mol%) in $CHCl_3$ (c_1 = 1 M) was *N*,*N*-dimethylethylenediamine **A** (10 mol%) added. The resulting mixture was stirred at ambient temperature until TLC showed the consumption of the starting material. Subsequently, the crude product was purified by flash chromatography (*n*-pentane/Et_2O).

General Procedure C (Enantioselective Protocol)

$AgNTf_2$·MeCN (2.5 mol%), **1** (0.25 mmol), primary amine **J** (20 mol%), and trifluoroacetic acid (20 mol%) were dissolved in cold methanol (c_1 = 1 M) and stirred at 0 °C or the given temperature until the reaction was completed as observed by TLC. The pure title compounds were obtained after flash chromatography (*n*-pentane/Et_2O) of the crude reaction mixture.

Table S5. Substrate scope of the silver-catalyzed Conia-ene reaction following the racemic and enantioselective protocol.[a]

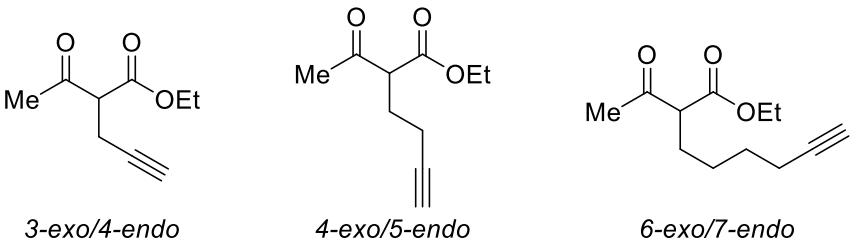


1 **2**

2	R^1	R^2	General Procedure B	General Procedure C	
			yield[b] [%]	yield[b][%]	*ee*[c] [%]
a	Me	COOEt	89	89	95
b	Me	COOMe	77	97	93
c	Me	COOBu	86	91	93
d	Me	COOallyl	77	94	87
e	Me	COO*i*Pr	75	92	93
f	Me	COO*t*Bu	89	97	91
g	Me	COOBn	97	93	88
h	Et	COOMe	95[d]	93[d]	11
i	Et	COOEt	78	97[d]	27
j	Pr	COOEt	46[d]	32[d]	51
k	*i*Pr	COOEt	54[e]	20[f]	0
l	Ph	COOEt	54[e]	55[d]	65
m	Me	COMe	67	-	-
n	Me	COPh	90[d]	86[d]	70
o	Me	SO_2Me	93[e]	-	-
p	Me	SO_2Ph	39[e]	46[f]	11

[a] The reactions were carried out according the the general procedures B and C. [b] Yield of the isolated product. [c] Determined by HPLC with a chiral stationary phase. [d] Synthesized at 40 °C. [e] Synthesized in toluene at 80 °C. [f] Synthesized at 60 °C.

substrates for other ring sizes



3-exo/4-endo *4-exo/5-endo* *6-exo/7-endo*

other not suitable substrates

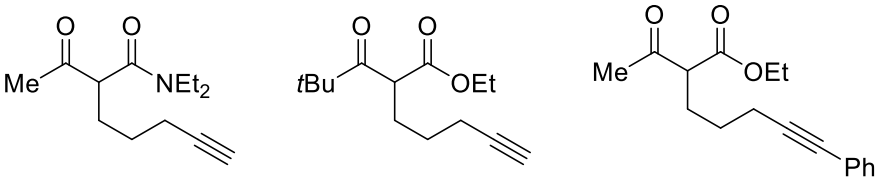
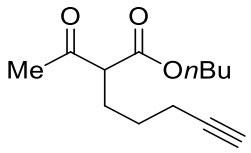


Figure S1. Substrates that were not suitable for the enamine-silver co-catalyzed Conia-ene reaction.

Analytical Data

Butyl 2-acetylhept-6-ynoate (1c)



Prepared according to General Procedure A with butyl 3-oxobutanoate (513 mg, 3.25 mmol).

Yield: 221 mg (0.99 mmol, 30%, colorless oil), .

Molecular Formula: $C_{13}H_{20}O_3$.

Molecular Weight: 224.30 g/mol.

***R_f*:** 0.51 (*n*-Pentane/Et_2O = 2:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.94 (t, ^3J = 7.4 Hz, 3H, $(CH_2)_3CH_3$), 1.32-1.44 (m, 2H, $CH_2CH_2CH_2CH_3$), 1.46-1.57 (m, 2H, $CH_2CH_2CH_2$), 1.59-1.69 (m, 2H, $CH_2CH_2CH_2CH_3$), 1.91-2.02 (m, 3H, C≡C*H*, $CHCH_2CH_2$), 2.19-2.29 (m, 5H, $CH_2C{\equiv}CH$, $H_3CC{=}O$), 3.44 (t, ^3J = 7.4 Hz, 1H, $CH(C{=}O)_2$), 4.09-4.21 (m, 2H, $CH_2CH_2CH_2CH_3$) ppm.

^{13}C NMR (151 MHz, $CDCl_3$): δ = 13.8 ($(CH_2)_3CH_3$), 18.3 ($CH_2C{\equiv}CH$), 19.2 ($CH_2CH_2CH_2CH_3$), 26.3 ($CH_2CH_2CH_2$), 27.2 ($CHCH_2CH_2$), 29.0 ($H_3CC{=}O$), 30.6 ($CH_2CH_2CH_2CH_3$), 59.5 ($CH(C{=}O)_2$), 65.5 ($CH_2CH_2CH_2CH_3$), 69.1 (C≡*C*H), 83.6 (*C*≡CH), 169.8 (*C*OOBu), 203.0 ($H_3CC{=}O$) ppm.

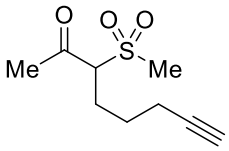
IR (ATR): ν_{max} = 3430, 3288, 2955, 2873, 2324, 2113, 1994, 1930, 1716, 1644, 1457, 1357, 1201, 1149, 1061, 954, 840, 741, 676 cm^{-1}.

MS (EI, 70 eV): *m/z* = 225 (42) $[M]^{+\cdot}$, 182 (11) $[M-Ac]^+$, 158 (20), 151 (21) $[M-BuO]^+$, 150 (38) $[M-BuOH]^{+\cdot}$, 126 (29), 122 (36) $[M\text{-}HCOOBu]^{+\cdot}$, 107 (20), 103 (23), 81 (100) $[C_6H_9]^+$, 79 (42) $[C_6H_7]^+$, 57 (50) $[Bu]^+$.

MS (CI, methane): *m/z* = 253 (9) $[M+Et]^+$, 225 (100) $[M+H]^+$.

HRMS (ESI): calculated for $C_{13}H_{21}O_3^+$ $[M+H]^+$ *m/z* = 225.1485, **found** 225.1478.

3-(Methylsulfonyl)oct-7-yn-2-one (1o)



Prepared according to General Procedure A with 1-(methylsulfonyl)propan-2-one.

Yield: 279 mg (1.38 mmol, 67%, colorless solid).

Molecular Formula: $C_{14}H_{17}O_3S$.

Molecular Weight: 202.27 g/mol.

***R_f*:** 0.18 (*n*-Pentane/EtOAc = 3:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.50-1.65 (m, 2H, $CH_2CH_2CH_2$), 2.02 (t, ^3J = 2.8 Hz, 1H, C≡C*H*), 2.14-2.24 (m, 2H, $CHCH_2CH_2$), 2.27 (td, $^3J_1$ = 6.9 Hz, $^4J_2$ = 2.8 Hz, 2H, $CH_2C{\equiv}CH$), 2.46 (s, 3H, $H_3CC{=}O$), 2.86 (s, 3H, SO_2CH_3), 3.98 (dd, $^3J_1$ = 9.7 Hz,$^3J_2$ = 5.1 Hz, 1H, $CH(C{=}O)SO_2CH_3$) ppm.

^{13}C NMR (151 MHz, $CDCl_3$): δ = 18.3 ($CH_2C{\equiv}CH$), 25.9 ($CH_2CH_2CH_2$), 26.4 ($CHCH_2CH_2$), 32.4 ($H_3CC{=}O$), 37.5 (SO_2CH_3), 69.9 (C≡*C*H), 74.1 ($C(C{=}O)SO_2CH_3$), 82.7 (*C*≡CH), 201.9 ($H_3CC{=}O$) ppm.

IR (ATR): ν_{max} = 3288, 3015, 2935, 2660, 2294, 2097, 1925, 1713, 1426, 1292, 1188, 1130, 1024, 970, 890, 808, 756, 662 cm^{-1}.

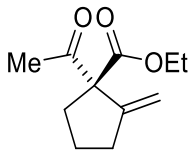
MS (EI, 70 eV): *m/z* = 202 (83) $[M]^{+\cdot}$, 160 (9), 136 (13), 123 (100) $[M{-}SO_2Me]^+$, 107 (14), 95 (11), 81 (23) $[C_6H_9]^+$, 79 (38) $[SO_2Me]^+$, 77 (10).

MS (CI, methane): *m/z* = 203 (44) $[M+H]^+$.

m.p.: 52-53 °C

HRMS (ESI): calculated for $C_9H_{14}O_3SNa^+$ $[M+Na]^+$ *m/z* = 225.0556, **found** 225.0550.

Ethyl 1-acetyl-2-methylenecyclopentanecarboxylate (2a)[1]



Synthesized according to General Procedure C with 50 mg (0.254 mmol) **1a**. Racemate synthesized according to General Procedure B with 49 mg (0.252 mmol) **1a**.

Yield: 43 mg (0.219 mmol, 86%, colorless oil); by General Procedure B: 44 mg (0.224 mmol, 89%).

Molecular Formula: $C_{11}H_{16}O_3$.

Molecular Weight: 196.25 g/mol.

***R_f*:** 0.49 (*n*-Pentane/Et_2O = 5:1).

HPLC (CHIRALPAK IC, *n*-heptane/*i*-PrOH 97:3, flow rate = 0.500 ml/min): 95% *ee*

t_{major} = 13.7 min

t_{minor} = 13.0 min.

$[\alpha]_D^{22}$ = +93.9 (*c* 1.02, $CHCl_3$, 95% *ee*); lit. $[\alpha]_D^{22}$ = +89.6 (c 0.63, $CHCl_3$, 89% *ee*)[2].

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.27 (t, ^3J = 7.2 Hz, 3H, CH_2CH_3), 1.64-1.79 (m, 2H, $CH_2CH_2CH_2$), 2.18 (dt, $^3J_1$ = 13.4 Hz, $^3J_2$ = 6.7 Hz, 1H, $CH_2C(C{=}O)_2$), 2.22 (s, 3H, $H_3CC{=}O$), 2.36-2.51 (m, 3H, $CH_2C(C{=}O)_2$, $CH_2C{=}CH_2$), 4.17-4.26 (m, 2H, CH_2CH_3), 5.24 (dd, $^2J_1$ = 2.1 Hz, $^4J_2$ =2.1 Hz, 1H, C=CH_2), 5.29 (dd, $^2J_1$ = 2.1 Hz, $^4J_2$ =2.1 Hz, 1H, C=CH_2) ppm.

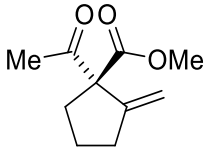
^{13}C NMR (151 MHz, $CDCl_3$): δ = 14.2 (CH_2CH_3), 24.2 ($CH_2CH_2CH_2$), 26.8 (H_3CC=O), 34.2 (CH_2C=CH_2), 35.2 (CH_2C(C=O)$_2$), 61.7 (CH_2CH_3), 70.6 (C(C=O)$_2$), 112.2 (C=CH_2), 148.9 (C=CH_2), 171.3 (COOEt), 203.7 (H_3CC=O) ppm.

IR (ATR): ν_{max} = 3416, 3088, 2967, 2323, 2091, 1994, 1938, 1712, 1651, 1441, 1357, 1231, 1138, 1093, 1018, 900, 855, 761 cm^{-1}.

MS (ESI): *m/z* = 229 (100) [M+MeOH+H]$^+$, 219 (74) [M+Na]$^+$, 197 (42) [M+H]$^+$.

MS (CI, methane): *m/z* = 197 (100) [M+H]$^+$.

Methyl 1-acetyl-2-methylenecyclopentane-1-carboxylate (2b)[3]



Synthesized according to General Procedure C with 47 mg (0.250 mmol) **1b**. Racemate synthesized according to General Procedure B with 88 mg (0.483 mmol) **1b**.

Yield: 44 mg (0.241 mmol, 97%, colorless oil); by General Procedure B: 68 mg (0.373 mmol, 77%).

Molecular Formula: $C_{10}H_{14}O_3$.

Molecular Weight: 182.22 g/mol.

***R*$_f$:** 0.50 (*n*-Pentane/Et_2O = 5:1).

GC (CHIRASIL-dex CB, N_2): 93% *ee*

t_{major} = 37.9 min

t_{minor} = 38.8 min.

$[\alpha]_D^{22}$ = +65.7 (*c* 0.46, $CHCl_3$, 93% *ee*); lit. $[\alpha]_D^{22}$ = +92.1 (c 0.95, $CHCl_3$, 97% *ee*)[2].

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.66-1.79 (m, 2H, $CH_2CH_2CH_2$), 2.16-2.23 (m, 4H, CH_2C(C=O)$_2$, H_3CC=O), 2.38-2.50 (m, 3H, CH_2C(C=O)$_2$, CH_2C=CH_2), 3.75 (s, 3H, OCH_3), 5.22 (dd, $^2J_1$ = 2.2 Hz, $^4J_2$ = 2.2 Hz, 1H, C=CH_2), 5.30 (dd, $^2J_1$ = 2.2 Hz, $^4J_2$ =2.2 Hz, 1H, C=CH_2) ppm.

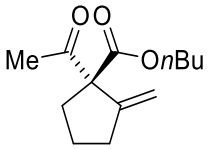
^{13}C NMR (151 MHz, $CDCl_3$): δ = 24.3 ($CH_2CH_2CH_2$), 26.8 (H_3CC=O), 34.1 (CH_2C=CH_2), 35.2 (CH_2C(C=O)$_2$), 52.8 (OCH_3), 70.6 (C(C=O)$_2$), 112.4 (C=CH_2), 148.8 (C=CH_2), 171.8 (COOMe), 203.7 (H_3CC=O) ppm.

IR (ATR): ν_{max} = 3431, 2956, 2323, 2091, 1716, 1436, 1231, 900, 776 cm^{-1}.

MS (ESI): *m/z* = 205 (100) [M+Na]$^+$, 183 (21) [M+H]$^+$.

MS (CI, methane): *m/z* = 183 (100) [M+H]$^+$.

Butyl 1-acetyl-2-methylenecyclopentane-1-carboxylate (2c)



Synthesized according to General Procedure C with 58 mg (0.256 mmol) **1c**. Racemate synthesized according to General Procedure B with 56 mg (0.250 mmol) **1c**.

Yield: 52 mg (0.232 mmol, 91%, colorless oil); by General Procedure B: 48 mg (0.214 mmol, 86%).

Molecular Formula: $C_{13}H_{20}O_3$.

Molecular Weight: 224.30 g/mol.

***R*$_f$:** 0.43 (*n*-Pentane/Et_2O = 5:1).

HPLC (CHIRALPAK IC, *n*-heptane/EtOH 99:1, flow rate = 1.000 ml/min): 93% *ee*

t_{major} = 16.7 min

t_{minor} = 15.5 min.

$[\alpha]_D^{22}$ = +78.3 (*c* 1.04, $CHCl_3$, 93% *ee*).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.92 (t, ^3J = 7.4 Hz, 3H, $(CH_2)_3CH_3$), 1.37 (sxt, ^3J = 7.4 Hz, 2H, $(CH_2)_2CH_2CH_3$), 1.59-1.80 (m, 4H, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2$), 2.17 (dt, $^3J_1$ = 13.1 Hz, $^3J_2$ = 6.8 Hz, 1H, $CH_2C(C=O)_2$), 2.22 (s, 3H, $H_3CC=O$), 2.36-2.50 (m, 3H, $CH_2C(C=O)_2$, $CH_2C=CH_2$), 4.11-4.18 (m, 2H, $CH_2(CH_2)_2CH_3$), 5.23 (dd, $^2J_1$ = 2.0 Hz, $^4J_2$ =2.0 Hz, 1H, $C=CH_2$), 5.29 (dd, $^2J_1$ = 2.0 Hz, $^4J_2$ =2.0 Hz, 1H, $C=CH_2$) ppm.

^{13}C NMR (151 MHz, $CDCl_3$): δ = 13.8 ($(CH_2)_3CH_3$), 19.3 ($(CH_2)_2CH_2CH_3$), 24.2 ($CH_2CH_2CH_2$), 26.9 ($H_3CC=O$), 30.6 ($CH_2CH_2CH_2CH_3$), 34.1 ($CH_2C=CH_2$), 35.2 ($CH_2C(C=O)_2$), 65.6 ($CH_2(CH_2)_2CH_3$), 70.6 ($C(C=O)_2$), 112.2 ($C=CH_2$), 148.9 ($C=CH_2$), 171.4 (*C*O*n*Bu), 203.7 ($H_3CC=O$) ppm.

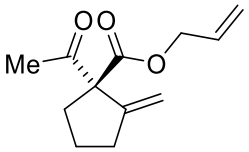
IR (ATR): ν_{max} = 3422, 2957, 2878, 2324, 2103, 1994, 1920, 1714, 1454, 1354, 1232, 1137, 1064, 955, 900, 841, 738 cm^{-1}.

MS (EI, 70 eV): *m/z* = 225 (6) $[M+H]^+$, 182 (20) $[M-Ac+H]^+$, 150 (35) $[M-BuOH]^{+\cdot}$, 147 (5), 126 (100), 123 (17), 111 (10), 108 (52) $[M-Ac-BuO]^+$, 105 (18), 81 (99) $[C_6H_9]^+$, 79 (66) $[C_6H_7]^+$, 77 (35) $[C_6H_5]^+$, 67 (10), 57 (27), 53 (15).

MS (CI, methane): *m/z* =253 (3) $[M+Et]^+$, 225 (86) $[M+H]^+$.

HRMS (ESI): calculated for $C_{13}H_{21}O_3^+$ $[M+H]^+$ *m/z* = 225.1485, **found** 225.1477.

Allyl 1-acetyl-2-methylenecyclopentane-1-carboxylate (2d)[1]



Synthesized according to General Procedure C with 56 mg (0.267 mmol) **1d**. Racemate synthesized according to General Procedure B with 48 mg (0.230 mmol) **1d**.

Yield: 52 mg (0.250 mmol, 94%, colorless oil); by General Procedure B: 37 mg (0.178 mmol, 77%).

Molecular Formula: $C_{12}H_{16}O_3$.

Molecular Weight: 208.26 g/mol.

***R*$_f$:** 0.46 (*n*-Pentane/Et_2O = 5:1).

HPLC (CHIRALPAK IC, *n*-heptane/EtOH 99:1, flow rate = 1.000 ml/min): 87% *ee*

t_{major} = 17.1 min

t_{minor} = 16.3 min.

$[\alpha]_D^{22}$ = +75.6 (*c* 1.02, $CHCl_3$, 87% *ee*).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.66-1.80 (m, 2H, $CH_2CH_2CH_2$), 2.15-2.28 (m, 4H, $CH_2C(C=O)_2$, $H_3CC=O$), 2.38-2.51 (m, 3H, $CH_2C(C=O)_2$, $CH_2C=CH2$), 4.64 (d, ^3J = 5.9 Hz, 2H, $CH_2CH=CH_2$), 5.22-5.36 (m, 4H, $CH=CH_2$, $C=CH_2$), 5.85-5.96 (m, 1H, $CH=CH_2$) ppm.

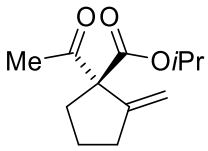
^{13}C NMR (151 MHz, $CDCl_3$): δ = 24.3 ($CH_2CH_2CH_2$), 26.8 ($H_3CC=O$), 34.1 ($CH_2C=CH_2$), 35.2 ($CH_2C(C=O)_2$), 66.2 ($CH_2CH=CH_2$), 70.6 ($C(C=O)_2$), 112.4 ($C=CH_2$), 118.9 ($CH=CH_2$), 131.7 ($CH=CH_2$), 148.7 ($C=CH_2$), 171.0 (*C*OOallyl), 203.6 ($H_3CC=O$) ppm.

IR (ATR): ν_{max} = 3526, 2956, 2087, 1717, 1436, 1354, 1227, 1141, 921, 760 cm^{-1}.

MS (EI, 70 eV): *m/z* = 209 (22) $[M+H]^+$, 208 (1) $[M]^{+\cdot}$, 167 (42) $[M-allyl]^+$, 166 (29) $[M-Ac+H]^+$, 150 (71) $[M-allylOH]^{+\cdot}$, 137 (49), 123 (28) $[M-CO_2-allyl]^+$, 121 (41), 108 (64) $[M-Ac-allylO]^+$, 97 (20), 79 (100) $[C_6H_7]^+$, 77 (31) $[C_6H_5]^+$, 52 (17).

MS (CI, methane): *m/z* = 209 (100) $[M+H]^+$.

iso-Propyl 1-acetyl-2-methylenecyclopentane-1-carboxylate (2e)[3]



Synthesized according to General Procedure C with 53 mg (0.252 mmol) **1e**. Racemate synthesized according to General Procedure B with 51 mg (0.243 mmol) **1e**.

Yield: 49 mg (0.233 mmol, 92%, colorless oil); by General Procedure B: 38 mg (0.181 mmol, 75%).

Molecular Formula: $C_{12}H_{18}O_3$.

Molecular Weight: 210.27 g/mol.

***R*$_f$:** 0.45 (*n*-Pentane/Et_2O = 5:1).

HPLC (CHIRALPAK IC, *n*-heptane/EtOH 98:2, flow rate = 1.000 ml/min): 93% *ee*

t_{major} = 10.5 min

t_{minor} = 11.0 min.

$[\alpha]_D^{22}$ = +85.8 (*c* 0.53, $CHCl_3$, 93% *ee*).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.25 (d, ^3J = 6.3 Hz, 6H, $CH(CH_3)_2$), 1.62-1.81 (m, 2H, $CH_2CH_2CH_2$), 2.15 (dt, $^2J_1$ = 13.1 Hz, $^3J_2$ = 6.8 Hz, 1H, $CH_2C(C=O)_2$), 2.22 (s, 3H, $H_3CC=O$), 2.35-2.50 (m, 3H, $CH_2C(C=O)_2$, $CH_2C=CH_2$), 5.08 (spt, ^3J = .3 Hz, 1H, $CH(CH_3)_2$), 5.23 (dd, $^2J_1$ = 2.1 Hz, $^4J_2$ = 2.1 Hz, 1H, $C=CH_2$), 5.29 (dd, $^2J_1$ = 2.1 Hz, $^4J_2$ =2.1 Hz, 1H, $C=CH_2$) ppm.

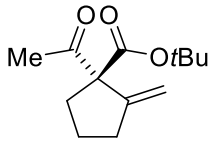
^{13}C NMR (151 MHz, $CDCl_3$): δ = 21.6 ($CH(CH_3)_2$), 21.7 ($CH(CH_3)_2$), 24.2 ($CH_2CH_2CH_2$), 26.9 ($H_3CC=O$), 34.2 ($CH_2C=CH_2$), 35.1 ($CH_2C(C=O)_2$), 69.2 ($CH(CH_3)_2$), 70.5 ($C(C=O)_2$), 112.0 ($C=CH_2$), 148.9 ($C=CH_2$), 170.7 (*C*OO*i*Pr), 203.6 ($H_3CC=O$) ppm.

IR (ATR): ν_{max} = 3846, 3424, 2959, 2333, 2090, 1715, 1453, 1376, 1231, 1092, 896, 690 cm^{-1}.

MS (EI, 70 eV): *m/z* = 211 (31) $[M+H]^+$, 210 (2) $[M]^{+\cdot}$, 169 (43) $[M-C_3H_6]^+$, 168 (31) $[M-C_3H_7]^+$, 150 (60) $[M-i\text{PrOH}]^{+\cdot}$, 126 (100), 123 (39) $[M-\text{COO}i\text{Pr}]^+$, 108 (100) $[M-\text{Ac}-\text{O}i\text{Pr}]^+$, 81 (98) $[C_6H_9]^+$, 79 (34) $[C_6H_7]^+$, 77 (13) $[C_6H_5]^+$.

MS (CI, methane): *m/z* = 211 (43) $[M+H]^+$, 197 (1) $[M-C_3H_6+Et]^+$, 169 (49) $[M-C_3H_6+H]^+$.

tert-Butyl 1-acetyl-2-methylenecyclopentane-1-carboxylate (2f)[4]



Synthesized according to General Procedure C with 59 mg (0.262 mmol) **1f**. Racemate synthesized according to General Procedure B with 95 mg (0.424 mmol) **1f**.

Yield: 57 mg (0.254 mmol, 97%, colorless oil); by General Procedure B: 85 mg (0.379 mmol, 89%).

Molecular Formula: $C_{13}H_{20}O_3$.

Molecular Weight: 224.30 g/mol.

***R*$_f$:** 0.65 (*n*-Pentane/Et_2O = 5:1).

HPLC (CHIRALPAK IC, *n*-heptane/EtOH 98:2, flow rate = 1.000 ml/min): 91% *ee*

t_{major} = 8.1 min

t_{minor} = 7.7 min.

$[\alpha]_D^{22}$ = +81.7 (*c* 1.04, $CHCl_3$, 91% *ee*); lit. $[\alpha]_D^{22}$ = +99.3 (c 0.22, CH_2Cl_2, 97% *ee*)[5].

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.46 (s, 9H, $C(CH_3)_3$), 1.60-1.68 (m, 1H, $CH_2CH_2CH_2$), 1.69-1.77 (m, 1H, $CH_2CH_2CH_2$), 2.08-2.15 (m, 1H, $CH_2C(C=O)_2$), 2.21 (s, 3H, $H_3CC=O$), 2.31-2.48 (m, 3H, $CH_2C(C=O)_2$, $CH_2C=CH_2$), 5.23 (dd, $^2J_1$ = 2.1 Hz, $^4J_2$ =2.1 Hz, 1H, $C=CH_2$), 5.28 (dd, $^2J_1$ = 2.1 Hz, $^4J_2$ = 2.1 Hz, 1H, $C=CH_2$) ppm.

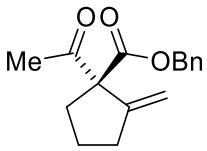
^{13}C NMR (151 MHz, $CDCl_3$): δ = 24.1 ($CH_2CH_2CH_2$), 26.9 (H_3CC=O), 28.0 (3C, $C(CH_3)_3$), 34.3 (CH_2C=CH_2), 35.1 ($CH_2C(C{=}O)_2$), 71.2 ($C(C{=}O)_2$), 82.0 ($C(CH_3)_3$), 111.8 (C=CH_2), 149.0 (C=CH_2), 170.2 (COO*t*Bu), 203.8 (H_3CC=O) ppm.

IR (ATR): ν_{max} = 3428, 2963, 2327, 2084, 1713, 1451, 1367, 1249, 1141, 841 cm^{-1}.

MS (EI, 70 eV): *m/z* = 225 (1) $[M]^{+\cdot}$, 182 (1) $[M-Ac]^+$, 168 (9) $[M-C_4H_9]^+$, 151 (5) $[M-O$*t*$Bu]^+$, 126 (12), 123 (16) $[M-CO_2-C_4H_9]^+$, 108 (89) $[M-Ac-O$*t*$Bu]^+$, 81 (16), 79 (30), 77 (11), 60 (77) $[C_3H_7O]^+$, 57 (5) $[$*t*$Bu]^+$, 48 (100) 47 (42).

MS (CI, methane): *m/z* = 197 (5) $[M+Et-C_4H_8]^+$, 169 (30) $[M+H-C_4H_8]^+$.

Benzyl-1-acetyl-2-methylenecyclopentane-1-carboxylate (2g)[3]



Synthesized according to General Procedure C with 64 mg (0.249 mmol) **1g**. Racemate synthesized according to General Procedure B with 80 mg (0.310 mmol) **1g**.

Yield: 60 mg (0.232 mmol, 93%, colorless oil); by General Procedure B: 78 mg (0.302 mmol, 97%).

Molecular Formula: $C_{16}H_{18}O_3$.

Molecular Weight: 258.32 g/mol.

***R_f*:** 0.37 (*n*-Pentane/Et_2O = 5:1).

HPLC (CHIRACEL OJ, *n*-heptane/*i*-PrOH 97:3, flow rate = 0.500 ml/min): 88% *ee*

t_{major} = 26.7 min

t_{minor} = 31.6 min.

$[\alpha]_D^{22}$ = +63.2 (*c* 1.07, $CHCl_3$, 88% *ee*); lit. $[\alpha]_D^{22}$ = +62.3 (c 0.13, $CHCl_3$, 86% ee)[2]

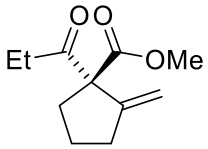
^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.65-1.79 (m, 2H, $CH_2CH_2CH_2$), 2.16-2.23 (m, 4H, $CH_2C(C{=}O)_2$, H_3CC=O), 2.38-2.51 (m, 3H, $CH_2C(C{=}O)_2$, CH_2C=CH_2), 5.18 (s, 2H, CH_2Ph), 5.21 (dd, $^2J_1$ = 2.2 Hz, $^4J_2$ = 2.2 Hz, 1H, C=CH_2), 5.26-5.31 (m, 1H, C=CH_2), 7.29-7.40 (m, 5H, H_{Ar}) ppm.

^{13}C NMR (151 MHz, $CDCl_3$): δ = 24.3 ($CH_2CH_2CH_2$), 26.8 (H_3CC=O), 34.1 (CH_2C=CH_2), 35.2 ($CH_2C(C{=}O)_2$), 67.4 (CH_2Ph), 70.6 ($C(C{=}O)_2$), 112.5 (C=CH_2), 128.3 (2C, CH_{Ar}), 128.5 (CH_{Ar}), 128.7 (2C, CH_{Ar}), 135.5 (C_{Ar}), 148.6 (C=CH_2), 171.1 (COOBn), 203.5 (H_3CC=O) ppm.

IR (ATR): ν_{max} = 3422, 2956, 2329, 2101, 1712, 1498, 1448, 1357, 1225, 1136, 1061, 980, 902, 824, 742, 697 cm^{-1}.

MS (ESI): *m/z* = 259 (36) $[M+H]^+$, 281 (100) $[M+Na]^+$, 295 (48) $[M+K]^+$.

Methyl 2-methylene-1-propionylcyclopentane-1-carboxylate (2h)[6]



Synthesized according to General Procedure C at 40 °C with 50 mg (0.253 mmol) **1h**. Racemate synthesized according to General Procedure B at 40 °C with 59 mg (0.301 mmol) **1h**.

Yield: 46 mg (0.234 mmol, 93%, colorless oil); by General Procedure B: 56 mg (0.285 mmol, 95%).

Molecular Formula: $C_{11}H_{16}O_3$.

Molecular Weight: 196.25 g/mol.

***R_f*:** 0.50 (*n*-Pentane/Et_2O = 5:1).

HPLC (CHIRALPAK IC, *n*-heptane/EtOH 99:1, flow rate = 1.000 ml/min): 11% *ee*

t_{major} = 17.5 min

t_{minor} = 16.5 min.

$[\alpha]_D^{22}$ = +11.7 (*c* 1.03, $CHCl_3$, 11% *ee*); lit. $[\alpha]_D^{22}$ = +86.3 (c 0.66, $CHCl_3$, 84% *ee*)[2].

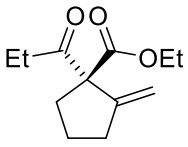
^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.06 (t, ^3J = 7.2 Hz, 3H, H_3CCH_2C=O), 1.64-1.78 (m, 2H, $CH_2CH_2CH_2$), 2.18 (dt, $^3J_1$ = 13.4 Hz, $^3J_2$ = 6.7 Hz, 1H, $CH_2C(C{=}O)_2$), 2.36-2.65 (m, 5H, $CH_2C(C{=}O)_2$, $CH_2C{=}CH_2$, H_3CCH_2C=O), 3.73 (s, 3H, OCH_3), 5.21 (dd, $^2J_1$ = 2.1 Hz, $^4J_2$ = 2.1 Hz, 1H, C=CH_2), 5.28 (dd, $^2J_1$ = 2.1 Hz, $^4J_2$ = 2.1 Hz, 1H, C=CH_2) ppm.

^{13}C NMR (151 MHz, $CDCl_3$): δ = 8.7 (H_3CCH_2C=O), 24.3 ($CH_2CH_2CH_2$), 32.4 ($CH_2C{=}CH_2$), 34.1 (H_3CCH_2C=O), 35.3 ($CH_2C(C{=}O)_2$), 52.8 (OCH_3), 70.4 ($C(C{=}O)_2$), 112.2 (C=CH_2), 148.8 ($C{=}CH_2$), 172.0 (COOMe), 206.8 (H_3CCH_2C=O) ppm.

IR (ATR): ν_{max} = 3442, 2955, 2323, 2094, 1940, 1713, 1440, 1342, 1229, 1117, 999, 897, 835, 774, 704 cm^{-1}.

MS (ESI): *m/z* = 229 (100) $[M+MeOH+H]^+$, 219 (56) $[M+Na]^+$, 197 (21) $[M+H]^+$.

Ethyl 2-methylene-1-propionylcyclopentane-1-carboxylate (2i)[2]



Synthesized according to General Procedure C at 40 °C with 53 mg (0.251 mmol) **1i**. Racemate synthesized according to General Procedure B with 90 mg (0.428 mmol) **1i**.

Yield: 51 mg (0.243 mmol, 97%, colorless oil); by General Procedure B: 70 mg (0.333 mmol, 78%).

Molecular Formula: $C_{12}H_{18}O_3$.

Molecular Weight: 210.27 g/mol.

***R_f*:** 0.63 (*n*-Pentane/Et_2O = 5:1).

HPLC (CHIRALPAK IC, *n*-heptane/EtOH 99:1, flow rate = 1.0 ml/min): 27% *ee*

t_{major} = 15.3 min

t_{minor} = 16.4 min.

$[\alpha]_D^{22}$ = +29.3 (*c* 1.02, $CHCl_3$, 27% *ee*); lit. $[\alpha]_D^{22}$ = +85.7 (c 0.66, $CHCl_3$, 83% *ee*)[2].

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.07 (t, ^3J = 7.2 Hz, 3H, H_3CCH_2C=O), 1.26 (t, ^3J = 7.0 Hz, 3H, H_3CCH_2O), 1.62-1.79 (m, 2H, $CH_2CH_2CH_2$), 2.18 (dt, ^2J = 13.1 Hz, ^3J = 6.8 Hz, 1H, $CH_2C(C{=}O)_2$), 2.35-2.55 (m, 4H, H_3CCH_2C=O, $CH_2C(C{=}O)_2$, $CH_2C{=}CH_2$), 2.56-2.66 (m, 1H, $CH_2C{=}CH_2$), 4.15-4.25 (m, 2H, H_3CCH_2O), 5.22 (dd, $^2J_1$ = 2.1 Hz, $^4J_2$ = 2.1 Hz, 1H, C=CH_2), 5.28 (dd, $^2J_1$ = 2.1 Hz, $^4J_2$ = 2.1 Hz, 1H, C=CH_2) ppm.

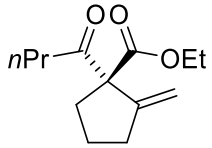
^{13}C NMR (151 MHz, $CDCl_3$): δ = 8.7 (H_3CCH_2C=O), 14.2 (H_3CCH_2O), 24.2 ($CH_2CH_2CH_2$), 32.5 ($CH_2C{=}CH_2$), 34.2 (H_3CCH_2C=O), 35.2 ($CH_2C(C{=}O)_2$), 61.6 (H_3CCH_2O), 70.3 ($C(C{=}O)_2$), 112.1 (C=CH_2), 148.9 ($C{=}CH_2$), 171.4 (*C*OOEt), 206.7 (H_3CCH_2C=O) ppm.

IR (ATR): ν_{max} = 3087, 2975, 2657, 2327, 2089, 1992, 1957, 1712, 1649, 1454, 1368, 1341, 1226, 1174, 1116, 1022, 898, 856, 804, 757, 694 cm^{-1}.

MS (EI, 70 eV): *m/z* = 211 (29) $[M+H]^+$, 177 (9), 164 (100) $[M-EtOH]^+$, 155 (38) $[M-COEt]^+$, 154 (39) $[M-COEt-H]^+$, 137 (11) $[M-CO_2-Et]^+$, 125 (21) $[M-COEt-CO]^+$, 108 (15), 79 (14) $[C_6H_7]^+$, 77 (6), 59 (17) $[C_3H_7O]^+$.

MS (CI, methane): *m/z* = 239 (2) $[M+Et]^+$, 211 (100) $[M+H]^+$.

Ethyl 1-butyryl-2-methylenecyclopentane-1-carboxylate (2j)[7]



Synthesized according to General Procedure C at 40 °C with 56 mg (0.251 mmol) **1j**. Racemate synthesized according to General Procedure B at 40 °C with 54.5 mg (0.243 mmol) **1j**.

Yield: 18 mg (0.080 mmol, 32%, colorless oil); by General Procedure B: 25 mg (0.111 mmol, 46%).

Molecular Formula: $C_{13}H_{20}O_3$.

Molecular Weight: 224.30 g/mol.

***R_f*:** 0.57 (*n*-Pentane/Et_2O = 5:1).

HPLC (CHIRAPAK IC, *n*-heptane/*i*-PrOH 97:3, flow rate = 0.500 ml/min): 51% *ee*

t_{major} = 9.8 min

t_{minor} = 9.1 min.

$[\alpha]_D^{22}$ = +51.0 (c 0.31, $CHCl_3$, 51% *ee*).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.89 (t, ^3J = 7.4 Hz, 3H, $H_3C(CH_2)_2C$=O), 1.26 (t, ^3J = 7.2 Hz, 3H, OCH_2CH_3), 1.58-1.79 (m, 4H, $CH_2CH_2CH_2$, $H_3CCH_2CH_2C$=O), 2.17 (dt, $^3J_1$ = 13.1 Hz, $^3J_2$ = 6.8 Hz, 1H, $CH_2C(C=O)_2$), 2.35-2.59 (m, 5H, $CH_2C(C=O)_2$, $CH_2C=CH_2$, $H_3CCH_2CH_2C$=O), 4.14-4.25 (m, 2H, OCH_2CH_3), 5.23 (dd, $^2J_1$ = 2.1 Hz, $^4J_2$ = 2.1 Hz, 1H, C=CH_2), 5.28 (dd, $^2J_1$ = 2.1 Hz, $^4J_2$ = 2.1 Hz, 1H, C=CH_2) ppm.

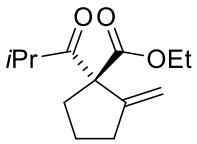
^{13}C NMR (151 MHz, $CDCl_3$): δ = 13.8 ($H_3C(CH_2)_2C$=O), 14.2 (OCH_2CH_3), 17.7 ($H_3CCH_2CH_2C$=O), 24.2 ($CH_2CH_2CH_2$), 34.2 ($CH_2C=CH_2$), 35.1 ($CH_2C(C=O)_2$), 41.0 ($H_3CCH_2CH_2C$=O), 61.6 (OCH_2CH_3), 70.4 ($C(C=O)_2$), 112.1 (C=CH_2), 148.7 ($C=CH_2$), 171.4 (COOEt), 205.8 ($H_3C(CH_2)_2C$=O) ppm.

IR (ATR): ν_{max} = 3415, 2962, 2324, 2084, 1714, 1455, 1363, 1233, 1117, 1022, 896, 753 cm^{-1}.

MS (EI, 70 eV): *m/z* = 225 (5) $[M+H]^+$, 178 (46) $[M-EtOH]^+$, 154 (27) $[M-PrCO+H]^+$, 151 (6), 125 (31) $[M-PrCO-C_2H_4]^+$, 108 (34) $[M-PrCO-OEt]^+$, 81 (31) $[C_6H_9]^+$, 79 (39) $[C_6H_7]^+$, 77 (16) $[C_6H_5]^+$, 71 (100) $[PrCO]^+$, 52 (8).

MS (CI, methane): *m/z* = 253 (5) $[M+Et]^+$, 225 (59) $[M+H]^+$.

Ethyl 1-isobutyryl-2-methylenecyclopentane-1-carboxylate (2k)[8]



Synthesized according to General Procedure C at 60 °C with 40 mg (0.178 mmol) **1k**. Racemate synthesized according to General Procedure B at 80 °C in toluene with 56 mg (0.250 mmol) **1k**.

Yield: 8 mg (0.036 mmol, 20%, colorless oil); by General Procedure B: 30 mg (0.134 mmol, 54%).

Molecular Formula: $C_{13}H_{20}O_3$.

Molecular Weight: 224.30 g/mol.

***R_f*:** 0.69 (*n*-Pentane/Et_2O = 5:1).

HPLC (CHIRALPAK IC, *n*-heptane/*i*-PrOH 97:3, flow rate = 0.500 ml/min): 0% *ee*

t_1 = 8.0 min

t_2 = 8.7 min.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.08 (d, ^3J = 6.4 Hz, 3H, $(H_3C)_2CH$), 1.12 (d, ^3J = 6.4 Hz, 3H, $(H_3C)_2CH$), 1.27 (t, ^3J = 7.4 Hz, 3H, CH_2CH_3), 1.60-1.80 (m, 2H, $CH_2CH_2CH_2$), 2.26 (dt, $^2J_1$ = 13.1 Hz, $^3J_2$ = 6.8 Hz, 1H, $CH_2C(C=O)_2$), 2.34-2.52 (m, 3H, $CH_2C(C=O)_2$, $CH_2C=CH_2$), 2.99 (spt, ^3J = 6.7 Hz, 1H, $(H_3C)_2CH$), 4.14-4.28 (m, 2H, CH_2CH_3), 5.25 (dd, $^2J_1$ = 2.3 Hz, $^4J_2$ = 2.3 Hz, 1H, C=CH_2), 5.30 (dd, $^2J_1$ = 2.3 Hz, $^4J_2$ = 2.3 Hz, 1H, C=CH_2) ppm.

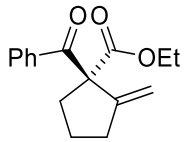
^{13}C NMR (151 MHz, $CDCl_3$): δ = 14.2 (CH_2CH_3), 20.8 ($CH(CH_3)_2$), 20.9 ($CH(CH_3)_2$), 24.1 ($CH_2CH_2CH_2$), 34.0 ($CH_2C=CH_2$), 34.8 ($CH_2C(C=O)_2$), 37.6 ($CH(CH_3)_2$), 61.6 (CH_2CH_3), 71.0 ($C(C=O)_2$), 112.3 (C=CH_2), 148.6 ($C=CH_2$), 171.4 (COOEt), 210.4 (*i*Pr*C*=O) ppm.

IR (ATR): ν_{max} = 3288, 2971, 2324, 2113, 1990, 1935, 1717, 148, 1368, 1202, 1158, 1100, 1018, 925, 855, 663 cm^{-1}.

MS (EI, 70 eV): *m/z* = 225 (1) $[M+H]^+$, 179 (23) $[M-EtOH]^{+\cdot}$, 155 (8) $[M-(H_3C)_2CHCO+H]^+$, 125 (9), 108 (35) [M−*i*Pr−COOEt]$^+$, 81 (30) $[M-(H_3C)_2CHCO-COOEt+H]^+$, 79 (36) $[C_6H_7]^+$, 71 (100) $[(H_3C)_2CHCO]^+$, 52 (9).

MS (CI, methane): *m/z* = 225 (100) $[M+H]^+$.

Ethyl 1-benzoyl-2-methylenecyclopentane-1-carboxylate (2l)[2]



Synthesized according to General Procedure C at 40 °C with 65 mg (0.252 mmol) **1l**. Racemate synthesized according to General Procedure B at 80 °C in toluene with 61 mg (0.236 mmol) **1l**.

Yield: 36 mg (0.139 mmol, 55%, colorless oil); by General Procedure B: 33 mg (0.128 mmol, 54%).

Molecular Formula: $C_{16}H_{18}O_3$.

Molecular Weight: 258.32 g/mol.

***R_f*:** 0.45 (*n*-Pentane/Et_2O = 5:1).

HPLC (CHIRAPAK IC, *n*-heptane/*i*-PrOH 97:3, flow rate = 1.000 ml/min): 65% *ee*

t_{major} = 17.1 min

t_{minor} = 8.9 min.

$[\alpha]_D^{22}$ = −40.5 (*c* 0.37, $CHCl_3$, 65% *ee*); lit. $[\alpha]_D^{22}$ = +152.8 (c 0.72, $CHCl_3$, −86% *ee*)[2].

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.06 (t, ^3J = 7.2 Hz, 3H, CH_2CH_3), 1.66-1.74 (m, 1H, $CH_2CH_2CH_2$), 1.80-1.91 (m, 1H, $CH_2CH_2CH_2$), 2.14-2.23 (m, 1H, $CH_2C(C=O)_2$), 2.47-2.55 (m, 2H, $CH_2C(C=O)_2$, $CH_2C=CH_2$), 2.81-2.90 (m, 1H, $CH_2C=CH_2$), 4.07-4.18 (m, 2H, CH_2CH_3), 5.21 (dd, $^2J_1$ = 2.0 Hz, $^4J_2$ = 2.0 Hz, 1H, $C=CH_2$), 5.36 (dd, $^2J_1$ = 2.0 Hz, $^4J_2$ = 2.0 Hz, 1H, $C=CH_2$), 7.42 (t, ^3J = 7.8 Hz, 2H, H_{Ar}), 7.52 (t, ^3J = 7.4 Hz, 1H, H_{Ar}), 7.84 (d, ^3J = 7.4 Hz, 2H, H_{Ar}) ppm.

^{13}C NMR (151 MHz, $CDCl_3$): δ = 13.9 (CH_2CH_3), 24.5 ($CH_2CH_2CH_2$), 34.5 ($CH_2C=CH_2$), 36.9 ($CH_2C(C=O)_2$), 61.7 (CH_2CH_3), 67.6 ($C(C=O)_2$), 111.9 ($C=CH_2$), 128.5 (2C, CH_{Ar}), 129.0 (2C, CH_{Ar}), 132.8 (CH_{Ar}), 135.5 (C_{Ar}), 149.6 ($C=CH_2$), 172.0 (*C*OOEt), 195.6 (Ph*C*=O) ppm.

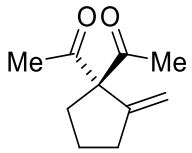
IR (ATR): ν_{max} = 3067, 2966, 2328, 2104, 1991, 1921, 1819, 1728, 1685, 1584, 1447, 1381, 1237, 1160, 1080, 1017, 889, 785, 699 cm^{-1}.

MS (EI, 70 eV): *m/z* = 258 (1) $[M]^{+\cdot}$, 212 (32) $[M-EtOH]^{+\cdot}$, 185 (15) $[M-CO_2-Et]^+$, 105 (100) $[PhCO]^+$, 79 (12) $[C_6H_7]^+$, 77 (60) $[C_6H_5]^+$, 51 (10).

MS (CI, methane): *m/z* = 287 (7) $[M+Et]^+$, 259 (32) $[M+H]^+$.

MS (ESI): *m/z* = 281 (100) $[M+Na]^+$.

1,1'-(2-Methylenecyclopentane-1,1-diyl)diethanone (2m)[9]



Synthesized according to General Procedure B with 69 mg (0.415 mmol) **1m**.

Yield: 46 mg (0.277 mmol, 67%, colorless oil).

Molecular Formula: $C_{10}H_{14}O_2$.

Molecular Weight: 166.22 g/mol.

***R*$_f$:** 0.44 (*n*-Pentane/Et_2O = 5:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.73 (quin, ^3J = 7.4 Hz, 2H, $CH_2CH_2CH_2$), 2.20 (s, 6H, H_3CC=O), 2.28 (t, ^3J = 6.9 Hz, 2H, $CH_2C(C=O)_2$), 2.45 (tt, $^3J_1$ = 7.4 Hz, $^4J_2$ = 2.1 Hz, 2H, $CH_2C=CH_2$), 5.14 (dd, $^2J_1$ = 2.3 Hz, $^4J_2$ = 2.3 Hz, 1H, C=CH_2), 5.34 (dd, $^2J_1$ = 2.3 Hz, $^4J_2$ = 2.3 Hz, 1H, C=CH_2) ppm.

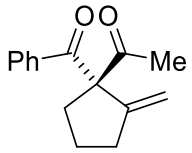
^{13}C NMR (151 MHz, $CDCl_3$): δ = 24.5 ($CH_2CH_2CH_2$), 27.0 (2C, H_3CC=O), 34.1 ($CH_2C=CH_2$), 34.2 ($CH_2C(C=O)_2$), 112.7 (C=CH_2), 149.6 (C=CH_2), 205.9 (2C, H_3CC=O) ppm.

IR (ATR): ν_{max} = 3828, 3405, 2954, 2322, 2093, 1699, 1430, 1354, 1214, 1134, 1027, 897, 754 cm^{-1}.

MS (EI, 70 eV): *m/z* = 166 (2) $[M]^{+\cdot}$, 156 (31), 138 (18), 127 (11), 123 (100) $[M-MeCO]^+$, 111 (32), 109 (50) $[M-MeCO-Me]^+$, 105 (48), 95 (71) $[M-MeCO-CO]^+$, 81 (58), 79 (76) $[C_6H_7]^+$, 77 (72) $[C_6H_5]^+$, 67 (61), 55 (55).

MS (CI, methane): *m/z* = 195 (7) $[M+Et]^+$, 167 (100) $[M+H]^+$.

1-(1-Benzoyl-2-methylenecyclopentyl)ethanone (2n)[3]



Synthesized according to General Procedure C at 40 °C with 57 mg (0.251 mmol) **1n**. Racemate synthesized according to General Procedure B with 54.5 mg (0.239 mmol) **1n**.

Yield: 49 mg (0.215 mmol, 86%, yellow oil); by General Procedure B: 49 mg (0.215 mmol, 90%).

Molecular Formula: $C_{15}H_{16}O_2$.

Molecular Weight: 228.29 g/mol.

***R*$_f$:** 0.41 (*n*-Pentane/Et_2O = 5:1).

HPLC (CHIRACEL OJ, *n*-heptane/*i*-PrOH 97:3, flow rate = 0.500 ml/min): 70% *ee*

t_{major} = 34.6 min

t_{minor} = 46.6 min.

$[\alpha]_D^{22}$ = −55.2 (c 0.27, $CHCl_3$, 70% *ee*).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.71-1.86 (m, 2H, $CH_2CH_2CH_2$), 2.19-2.28 (m, 4H, $CH_2C(C=O)_2$, $H_3CC=O$), 2.46-2.60 (m, 2H, $CH_2C=CH_2$), 2.74 (dt, $^3J_1$ = 13.3 Hz, $^3J_2$ = 6.5 Hz, 1H, $CH_2C(C=O)_2$), 5.13 (dd, $^2J_1$ = 2.1 Hz, $^4J_2$ = 2.1 Hz, 1H, $C=CH_2$), 5.41 (dd, $^2J_1$ = 2.1 Hz, $^4J_2$ = 2.1 Hz, 1H, $C=CH_2$), 7.39-7.46 (m, 2H, H_{Ar}), 7.49-7.56 (m, 1H, H_{Ar}), 7.75-7.80 (m, 2H, H_{Ar}) ppm.

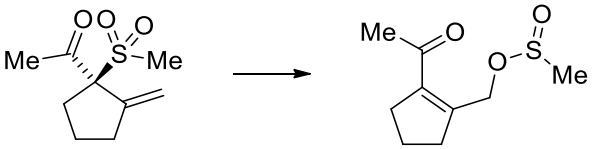
^{13}C NMR (151 MHz, $CDCl_3$): δ = 24.4 ($CH_2CH_2CH_2$), 27.4 ($H_3CC=O$), 34.5 ($CH_2C=CH_2$), 36.0 ($CH_2C(C=O)_2$), 75.6 ($C(C=O)_2$), 113.4 ($C=CH_2$), 128.6 (2C, CH_{Ar}), 129.5 (2C, CH_{Ar}), 132.9 (CH_{Ar}), 135.6 (C_{Ar}), 149.1 ($C=CH_2$), 198.1 ($PhC=O$), 204.7 ($H_3CC=O$) ppm.

IR (ATR): ν_{max} = 3372, 3068, 2958, 2327, 2097, 1993, 1916, 1817, 1682, 1591, 1438, 1355, 1234, 1150, 1073, 1000, 892, 780, 699 cm^{-1}.

MS (EI, 70 eV): *m/z* = 228 (4) $[M]^{+\cdot}$, 185 (58) $[M-Ac]^+$, 167 (4), 157 (14) $[M-Ac-Ph]^+$, 129 (10), 105 (100) $[PhCO]^+$, 91 (5), 79 (12) $[C_6H_7]^+$, 77 (71) $[C_6H_5]^+$, 51 (15).

MS (CI, methane): *m/z* = 257 (15) $[M+Et]^+$, 229 (81) $[M+H]^+$.

1-(2-Methylene-1-(methylsulfonyl)cyclopentyl)ethan-1-one (2o)



Synthesized according to General Procedure B with 65 mg (0.321 mmol) **1o**. The sulfone **2o** spontaneously underwent a Mislow-Evans-type rearrangement to form the corresponding sulfonate and thus contains a growing amount of that impurity.

Yield: 60 mg (0.297 mmol, 93%, colorless oil).

Molecular Formula: $C_9H_{14}O_3S$.

Molecular Weight: 202.27 g/mol.

***R_f*:** 0.24 (*n*-Pentane/Et_2O = 2:1).

^{1}H NMR (600 MHz, C_6D_6): δ = 1.07-1.19 (m, 1H, $CH_2CH_2CH_2$), 1.54-1.61 (m, 1H, $CH_2CH_2CH_2$), 1.88 (s, 3H, $H_3CC=O$), 1.93-2.05 (m, 2H, $CH_2C=CH_2$, $CH_2C(C=O)SO_2Me$), 2.26-2.39 (m, 2H, $CH_2C=CH_2$, $CH_2C(C=O)SO_2Me$), 2.47-2.55 (m, 3H, SO_2CH_3), 5.01 (s, 1H, $C=CH_2$), 5.40 (s, 1H, $C=CH_2$) ppm.

^{13}C NMR (151 MHz, C_6D_6): δ = 23.7 ($H_3CC=O$), 27.2 ($CH_2CH_2CH_2$), 32.6 ($CH_2C(C=O)SO_2Me$), 34.4 ($CH_2C=CH_2$), 37.1 (SO_2CH_3), 69.6 ($C(C=O)SO_2Me$), 114.9 ($C=CH_2$), 145.5 ($C=CH_2$), 201.3 ($H_3CC=O$) ppm.

IR (ATR): ν_{max} = 3889, 3531, 2942, 2325, 2096, 1687, 1419, 1295, 1126, 946, 757 cm^{-1}.

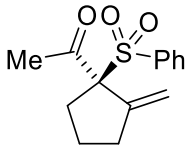
MS (EI, 70 eV): *m/z* = 202 (11) $[M]^{+\cdot}$, 160 (4), 123 (33) $[M-SO_2Me]^+$, 108 (14), 79 (100) $[C_6H_7]^+$, 77 (25) $[C_6H_5]^+$, 52 (31).

MS (CI, methane): *m/z* = 203 (59) $[M+H]^+$.

MS (ESI): *m/z* = 225 (81) $[M+Na]^+$.

HRMS (ESI): calculated for $C_9H_{15}O_3S^+$ $[M+H]^+$ *m/z* = 203.0736, **found** 203.0728.

1-(2-Methylene-1-(phenylsulfonyl)cyclopentyl)ethan-1-one (2p)[5]



Synthesized according to General Procedure C at 60 °C with 68 mg (0.256 mmol) **1p**. Racemate synthesized according to General Procedure B at 80 °C in toluene with 83 mg (0.314 mmol) **1p**.

Yield: 31 mg (0.117 mmol, 46%, pale yellow oil); by General Procedure B: 32 mg (0.121 mmol, 39%).

Molecular Formula: $C_{14}H_{16}O_3S$.

Molecular Weight: 264.34 g/mol.

***R_f*:** 0.65 (*n*-Pentane/EtOAc = 5:1).

HPLC (CHIRAPAK IA, *n*-heptane/*i*-PrOH 97:3, flow rate = 0.500 ml/min): 11% *ee*

t_{major} = 31.5 min

t_{minor} = 27.2 min.

$[\alpha]_D^{22}$ = +2.7 (c 0.17, $CHCl_3$, 11% *ee*); lit. $[\alpha]_D^{25}$ = +45.8 (c 0.22, $CHCl_3$, 92% *ee*)[5].

^{1}H NMR (600 MHz, $CDCl_3$): (major) δ = 1.52-1.59 (m, 1H, $CH_2CH_2CH_2$), 1.70 (m, 1H, $CH_2CH_2CH_2$), 2.41-2.47 (m, 4H, CH_2CSO_2Ph, $CH_2C=CH_2$), 2.49 (s, 3H, $H_3CC=O$), 5.50 (s, 1H, $C=CH_2$), 5.63 (s, 1H, $C=CH_2$), 7.49-7.55 (m, 2H, H_{Ar}), 7.64 (t, ^3J = 7.4 Hz, 1H, H_{Ar}), 7.87 (d, ^3J = 8.3 Hz, 2H, H_{Ar}) ppm.

^{13}C NMR (151 MHz, $CDCl_3$): (major) δ = 23.7 ($CH_2CH_2CH_2$), 28.2 ($H_3CC=O$), 34.1 ($CH_2C=CH_2$), 35.1 (CH_2CSO_2Ph), 110.1 ($C(C=O)SO_2Ph$), 116.8 ($C=CH_2$), 128.6 (2C, CH_{Ar}), 130.9 (2C, CH_{Ar}), 134.1 (CH_{Ar}), 136.8 (C_{Ar}), 144.7 ($C=CH_2$), 200.1 ($H_3CC=O$) ppm.

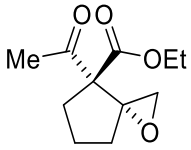
IR (ATR): ν_{max} = 3853, 3488, 2944, 2328, 2094, 1696, 1302, 1142, 922, 738 cm^{-1}.

MS (EI, 70 eV): *m/z* = 264 (19) $[M]^{+\cdot}$, 143 (9), 139 (29) $[M-SOPh]^+$, 125 (11), 123 (79) $[M-SO_2Ph]^+$, 122 (55), 107 (21), 95 (26), 79 (60) $[C_6H_7]^+$, 77 (100) $[C_6H_5]^+$, 67 (15), 55 (12), 51 (40).

MS (CI, methane): *m/z* = 265 (100) $[M+H]^+$.

MS (ESI): *m/z* = 287 (96) $[M+Na]^+$, 265 (95) $[M+H]^+$.

Ethyl 4-acetyl-1-oxaspiro[2.4]heptane-4-carboxylate (3)



To a solution of alkene **2a** (201 mg, 1.02 mmol) in 4 mL CH_2Cl_2 (*c* = 0.25 M) $NaHCO_3$ (97 mg, 1.15 mmol, 1.1 eq.) was added and the resulting suspension cooled to 0 °C. Subsequently, a solution of *m*CPBA (280 mg, 1.18 mmol, 1.2 eq.) in 5 mL CH_2Cl_2 (c = 0.24 M) was added and the reaction mixture stirred at 0 °C. After 30 min the ice bath was removed and the reaction continued for 3 h. The white turbid solution was washed with sat. aq. Na_2CO_3 solution (2x, 30 mL) and sat. aq. $Na_2S_2O_3$ solution. The combined organic layers were dried over Na2SO4, the solvent removed in vacuo and the crude product purified by flash column chromatography (*n*-pentane/Et_2O) to obtain the epoxide **3** as a diastereomeric mixture.

Yield: 212 mg (1.0 mmol, quant., *dr* = 1.5:1, colorless oil).

Molecular Formula: $C_{11}H_{16}O_4$.

Molecular Weight: 212.25 g/mol.

***R*$_f$:** 0.21 (*n*-Pentane/Et_2O = 5:1).

^{1}H NMR (600 MHz, $CDCl_3$): (major) δ = 1.18-1.31 (m, 3H, CH_2CH_3), 1.66-1.79 (m, 2H, $CH_2CC(O)(CH_2)$), 1.88-2.00 (m, 2H, $CH_2CH_2CH_2$), 2.08-2.25 (m, 4H, $H_3CC{=}O$, $CH_2C(C{=}O)_2$), 2.70-2.79 (m, 1H, $CH_2C(C{=}O)_2$), 2.97-3.09 (m, 2H, OCH_2C_q), 4.12-4.25 (m, 2H, CH_2CH_3) ppm.

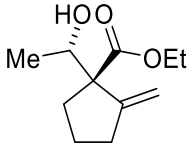
^{13}C NMR (151 MHz, $CDCl_3$): (major) δ = 14.2 (CH_2CH_3), 22.6 ($CH_2CH_2CH_2$), 26.8 ($H_3CC{=}O$), 33.2 ($CH_2C(C{=}O)_2$), 34.6 ($CH_2CC(O)(CH_2)$), 50.3 (OCH_2C_q), 61.8 (CH_2CH_3), 65.7 ($C(C{=}O)_2$), 69.3 ($CH_2CC(O)(CH_2)$), 168.0 (*C*OOEt), 201.7 ($H_3CC{=}O$) ppm.

IR (ATR): ν_{max} = 3419, 2973, 2324, 2095, 1996, 1906, 1712, 1447, 1359, 1241, 1148, 1091, 1018, 911, 848, 752 cm^{-1}.

MS (CI, isobutane): *m/z* = 213 (61) $[M+H]^+$, 195 (100) $[M-H_2O+H]^+$.

HRMS (ESI): calculated for $C_{11}H_{17}O_4^+$ $[M+H]^+$ m/z = 213.1121, **found** 213.1114.

Ethyl 1-(1-hydroxyethyl)-2-methylenecyclopentane-1-carboxylate (4)



Sodium borohydride (59 mg, 1.56 mmol, 1.6 eq.) was added to a solution of β-ketoester **2a** (197 mg, 1.0 mmol) in 1 mL dry EtOH (*c* = 1 M) and the resulting suspension stirred for 16 h at ambient temperature. After the addition of 1 mL water and 0.1 mL conc. acetic acid the mixture was extracted with Et_2O (3x, 20 mL), the combined organic layers dried other Na_2SO_4, and the solvent removed under reduced pressure. Flash column chromatography of the crude product yielded two diastereomers of the alcohol **4** as pale yellow oils.

Yield: 189 mg (0.95 mmol, 95%, *dr* = 1.4:1, pale yellow oil).

Molecular Formula: $C_{11}H_{18}O_3$.

Molecular Weight: 198.26 g/mol.

***R*$_f$:** 0.14 (major), 0.10 (minor) (*n*-Pentane/Et_2O = 5:1).

^{1}H NMR (600 MHz, $CDCl_3$): (major) δ = 1.13 (d, ^3J = 6.4 Hz, 3H, H_3CCHOH), 1.24 (t, ^3J = 7.3 Hz, 3H, CH_2CH_3), 1.71-1.81 (m, 2H, $CH_2CH_2CH_2$), 1.83-1.96 (m, 1H, CH_2C(C=O)(CHOH)), 2.11 (br. s., 1H, O*H*), 2.16-2.24 (m, 1H, CH_2C(C=O)(CHOH)), 2.25-2.36 (m, 1H, $CH_2C=CH_2$), 2.39-2.52 (m, 1H, $CH_2C=CH_2$), 4.13 (q, ^3J = 7.3 Hz, 2H, CH_2CH_3), 4.37 (qd, $^3J_1$ = 6.3 Hz, $^4J_2$ = 2.3 Hz, 1H, H_3CCHOH), 5.19-5.23 (m, 1H, $C=CH_2$), 5.24 (dd, $^3J_1$ = 2.3 Hz, $^4J_2$ = 2.3 Hz, 1H, $C=CH_2$) ppm.

^{13}C NMR (151 MHz, $CDCl_3$): (major) δ = 14.1 (CH_2CH_3), 18.2 (H_3CCHOH), 24.7 ($CH_2CH_2CH_2$), 29.7 (CH_2C(C=O)(CHOH)), 35.1 ($CH_2C=CH_2$), 60.9 (CH_2CH_3), 62.1 (*C*(C=O)(CHOH)), 71.0 (H_3CCHOH), 108.9 ($C=CH_2$), 153.3 ($C=CH_2$), 174.3 (*C*OOEt) ppm.

^{1}H NMR (600 MHz, $CDCl_3$): (minor) δ = 1.10 (d, ^3J = 6.4 Hz, 3H, H_3CCHOH), 1.25 (t, ^3J = 6.9 Hz, 3H, CH_2CH_3), 1.65-1.77 (m, 1H, $CH_2CH_2CH_2$), 1.78-1.89 (m, 1H, $CH_2CH_2CH_2$), 1.91-2.01 (m, 1H, CH_2C(C=O)(CHOH)), 2.18 (dt, $^2J_1$ = 13.1 Hz, $^3J_2$ = 6.8 Hz, 1H, CH_2C(C=O)(CHOH)), 2.30-2.40 (m, 1H, $CH_2C=CH_2$), 2.41-2.53 (m, 1H, $CH_2C=CH_2$), 2.92 (br. s., 1H, O*H*), 4.10-4.22 (m, 2H, CH_2CH_3), 4.24-4.33 (m, 1H, H_3CCHOH), 4.88-4.98 (m, 1H, $C=CH_2$), 5.05 (s, 1H, $C=CH_2$) ppm.

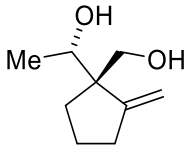
^{13}C NMR (151 MHz, $CDCl_3$): (minor) δ = 14.1 (CH_2CH_3), 17.4 (H_3CCHOH), 25.1 ($CH_2CH_2CH_2$), 30.9 (CH_2C(C=O)(CHOH)), 35.2 ($CH_2C=CH_2$), 61.1 (CH_2CH_3), 61.2 (*C*(C=O)(CHOH)), 71.8 (H_3CCHOH), 108.2 ($C=CH_2$), 153.3 ($C=CH_2$), 176.6 (*C*OOEt) ppm.

IR (ATR): ν_{max} = 3306, 2957, 2289, 2090, 1978, 1715, 1647, 1448, 1232 1090, 1026, 893, 727 cm^{-1}.

MS (CI, isobutane): *m/z* = 199 (48) $[M+H]^+$, 197 (21) $[M-H]^+$, 181 (24) $[M-H_2O+H]^+$, 155 (100) $[M-EtOH+H]^+$.

HRMS (ESI): calculated for $C_{11}H_{17}O_4^+$ $[M-H_2O+H]^+$ m/z = 181.1223, **found** 181.1223

(1-(1-(Hydroxymethyl)-2-methylenecyclopentyl)ethan-1-ol (5)



Under argon a solution of β-ketoester **2a** (208 mg, 1.06 mmol) in 5.0 mL THF (*c* = 0.2 M) was cooled to −78 °C and treated with a 2.4 M solution of $LiAlH_4$ in THF (2.2 mL, 5.3 mmol, 5 eq.). The reaction was allowed to warm up to room temperature and stirred for 16 h. After re-cooling to 0 °C 0.2 mL water, 0.2 mL 15% aq. NaOH, and 0.6 mL water were added in that order and the resulting mixture stirred for 30 min at room temperature. Subsequently, $MgSO_4$ was added, the stirring was continued for additional 15 min, and the precipitate was filtered off. The pure diol **5** was obtained as a diastereomeric

mixture after removal of the volatiles in vacuo and flash column chromatography (*n*-pentane/Et_2O) of the residue.

Yield: 163 mg (1.01 mmol, 98%, *dr* = 1.4:1, white crystalline solid).

Molecular Formula: $C_9H_{16}O_2$.

Molecular Weight: 156.23 g/mol.

***R*$_f$:** 0.40 (Et_2O).

^{1}H NMR (600 MHz, $CDCl_3$): (major) δ = 1.20 (d, ^3J = 6.4 Hz, 3H, H_3CCHOH), 1.54-1.73 (m, 3H, $CH_2CH_2CH_2$, CH_2C(CHOH)(CH_2OH)), 1.83-1.89 (m, 1H, $CH_2CH_2CH_2$), 1.93-2.10 (m, 2H, CHO*H*, CH_2O*H*), 2.34-2.49 (m, 2H, $CH_2C{=}CH_2$), 3.48-3.56 (m, 2H, CH_2OH), 4.01 (q, ^3J = 6.4 Hz, 1H, H_3CHOH), 4.98 (s, 1H, C=CH_2), 5.18 (s, 1H, C=CH_2) ppm.

^{13}C NMR (151 MHz, $CDCl_3$): (major) δ = 17.9 (H_3CCHOH), 23.3 ($CH_2CH_2CH_2$), 31.3 ($CH_2C{=}CH_2$), 35.7 (CH_2C(CHOH)(CH_2OH)), 55.5 (*C*(CHOH)(CH_2OH)), 67.3 (CH_2OH), 70.6 (H_3CCHOH), 107.6 (C=CH_2), 155.0 (*C*=CH_2) ppm.

IR (ATR): ν_{max} = 3304, 2950, 2879, 2705, 2325, 2094, 1985, 1927, 1793, 1645, 1443, 1299, 1240, 1187, 1026, 893, 725 cm^{-1}.

MS (CI, isobutane): *m/z* = 157 (15) $[M+H]^+$, 139 (100) $[M-H_2O+H]^+$.[1]

[1] The confirmation of the sum formula by HRMS was even under APCI conditions not possible.

Deuterium-Labelling Experiments

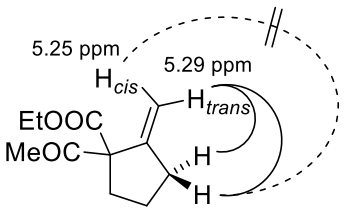
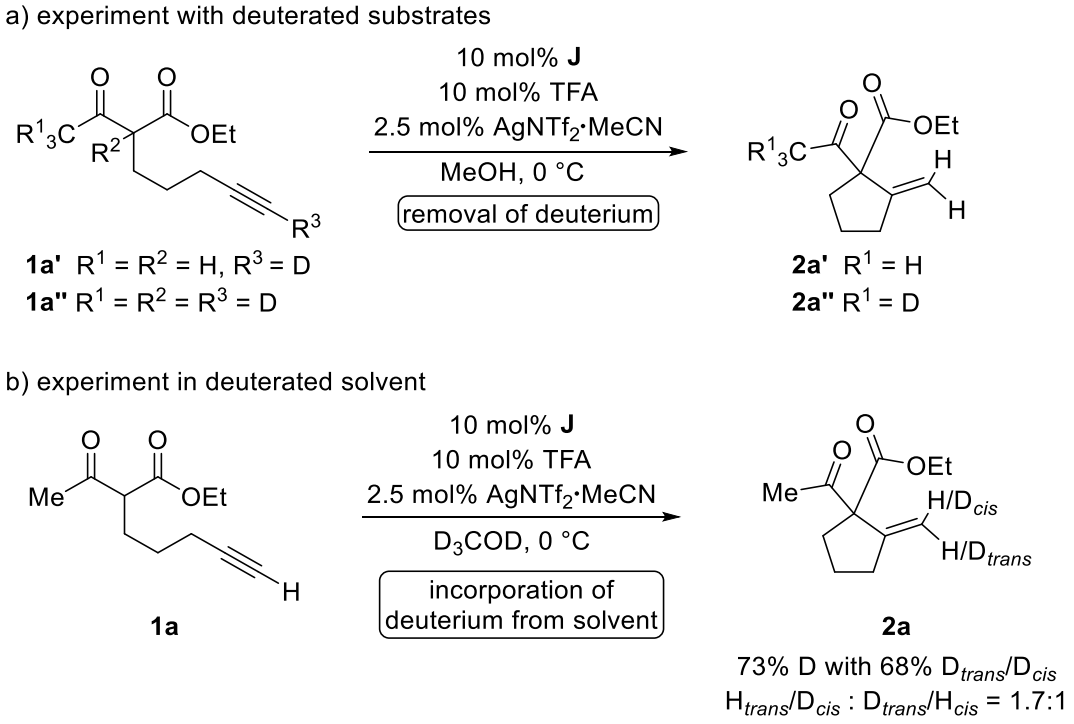


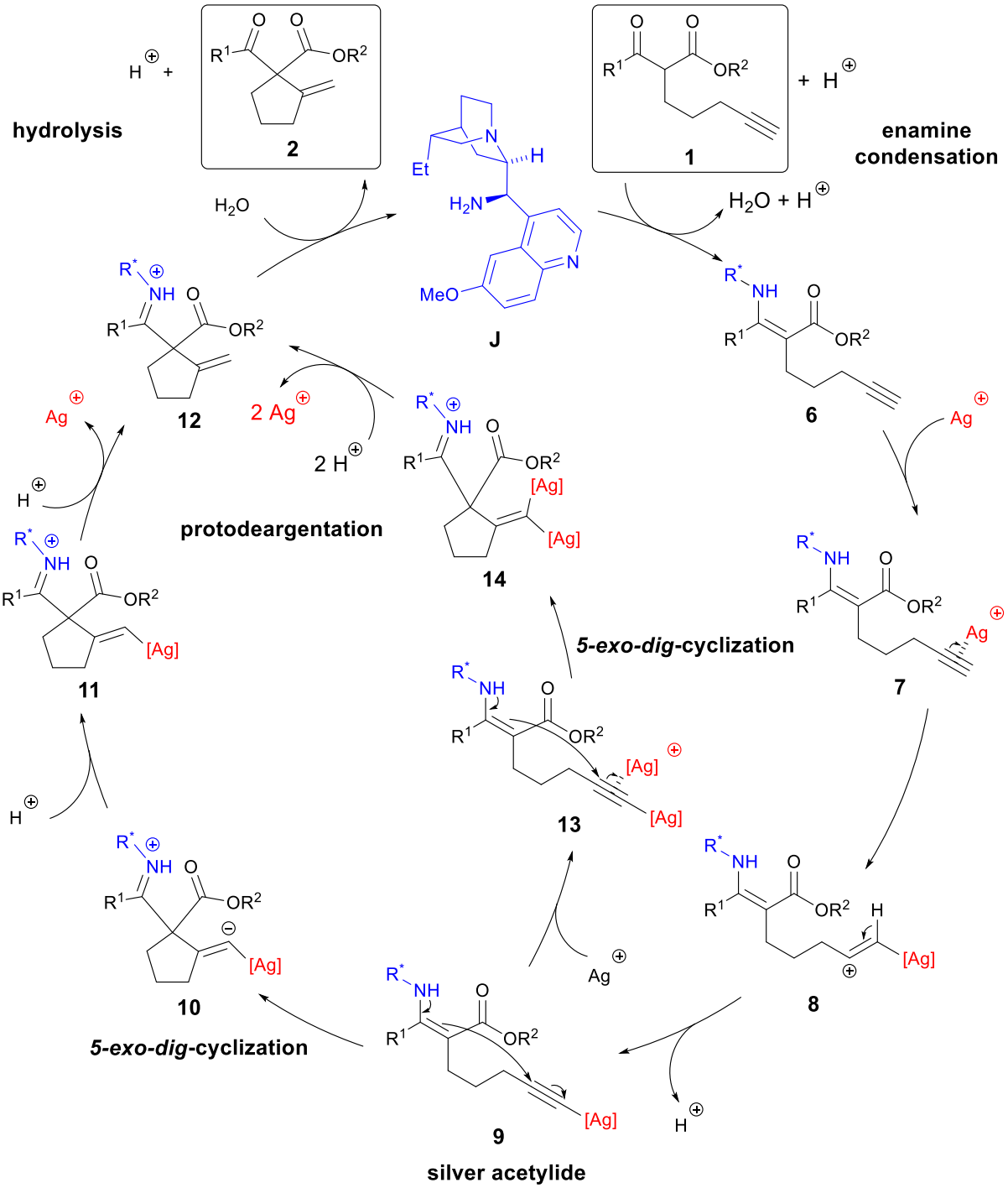
Figure S2. Assignement of *cis*- and *trans*-proton *via* NOESY study.

First the *cis*- and *trans*-proton of the exocyclic double bond were assigned using NMR spectroscopy (Figure S2). In contrast to the *trans*-proton with a chemical shift of 5.29 ppm no NOE contact to the adjacent methylene group was observed for the *cis*-proton with a chemical shift of 5.25 ppm. When deuterium-labeled substrates **1a'** and **1a''** were subjected to the optimized reaction conditions complete removal of the deuterium form the alkyne and the 2-position of the β-ketoester were observed. Thus, we conclude the formation of a silver acetylide intermediate **9** (Scheme S2, a). In contrast to a H/D-exchange on the stage of the starting material, the silver acetylide formation could also explain, why the reaction failed when internal alkynes were used. In the second set of deuterium-labelling experiment we investigated the reaction in deuterated solvent, to gain deeper insight in the *cis*/*trans*-fashion of the cyclization step (Scheme S1, b). We found that cyclized product **2a** mainly contained the species with deuterium in *cis*- and *trans*-position. Furthermore, the ratio of both mono-deuterated species H_{trans}/D_{cis}-**2a** and D_{trans}/H_{cis}-**2a** was found to be close to 1:1; thus, the reaction may occur via both, *cis*- and *trans*-addition, and a definite proof is impossible.



Scheme S1. Deuterium-labelling experiments.

Mechanism



Scheme S2. Proposed mechanism of the novel enamine-silver co-catalyzed Conia-ene reaction.

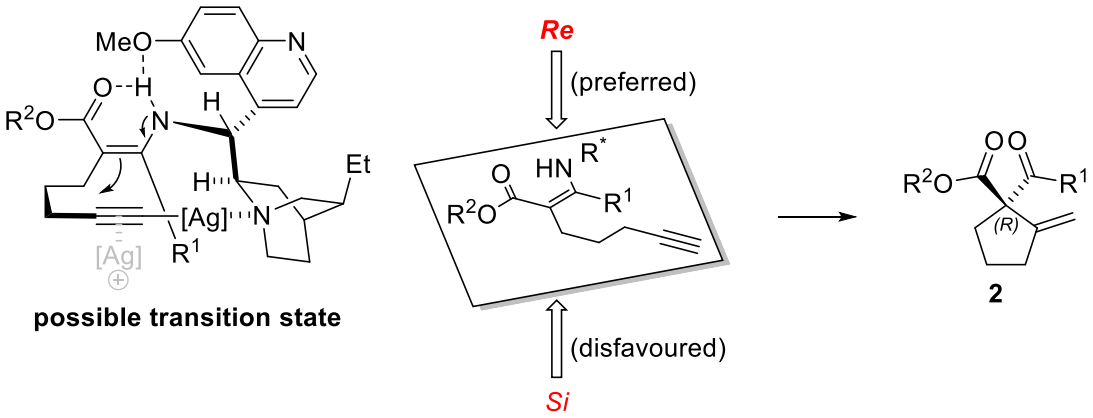


Figure 3. Possible transition state and model for the enantioselective enamine-silver co-catalyzed Conia-ene reaction.

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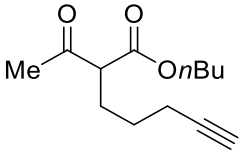
Spectra and HPLC data



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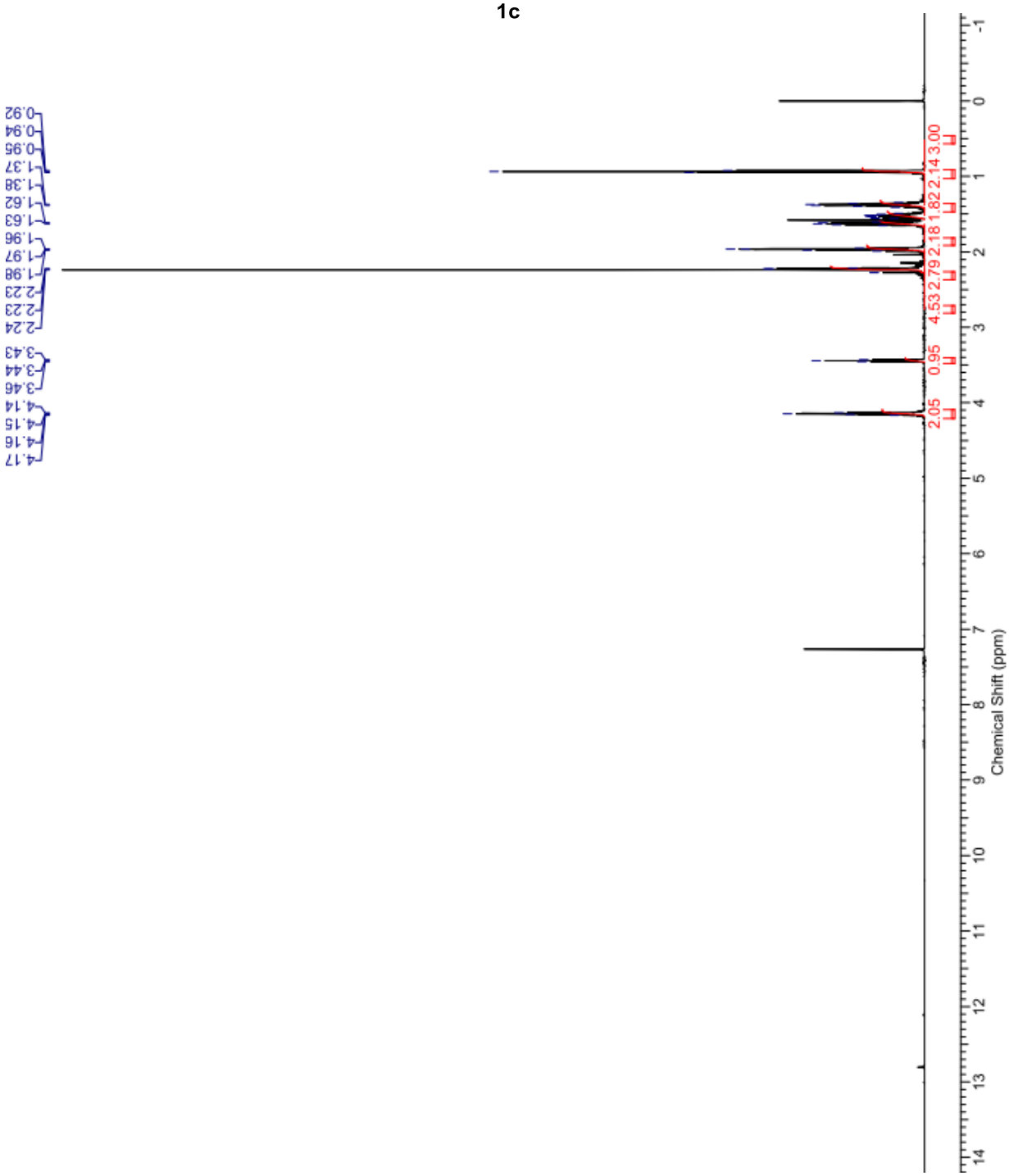

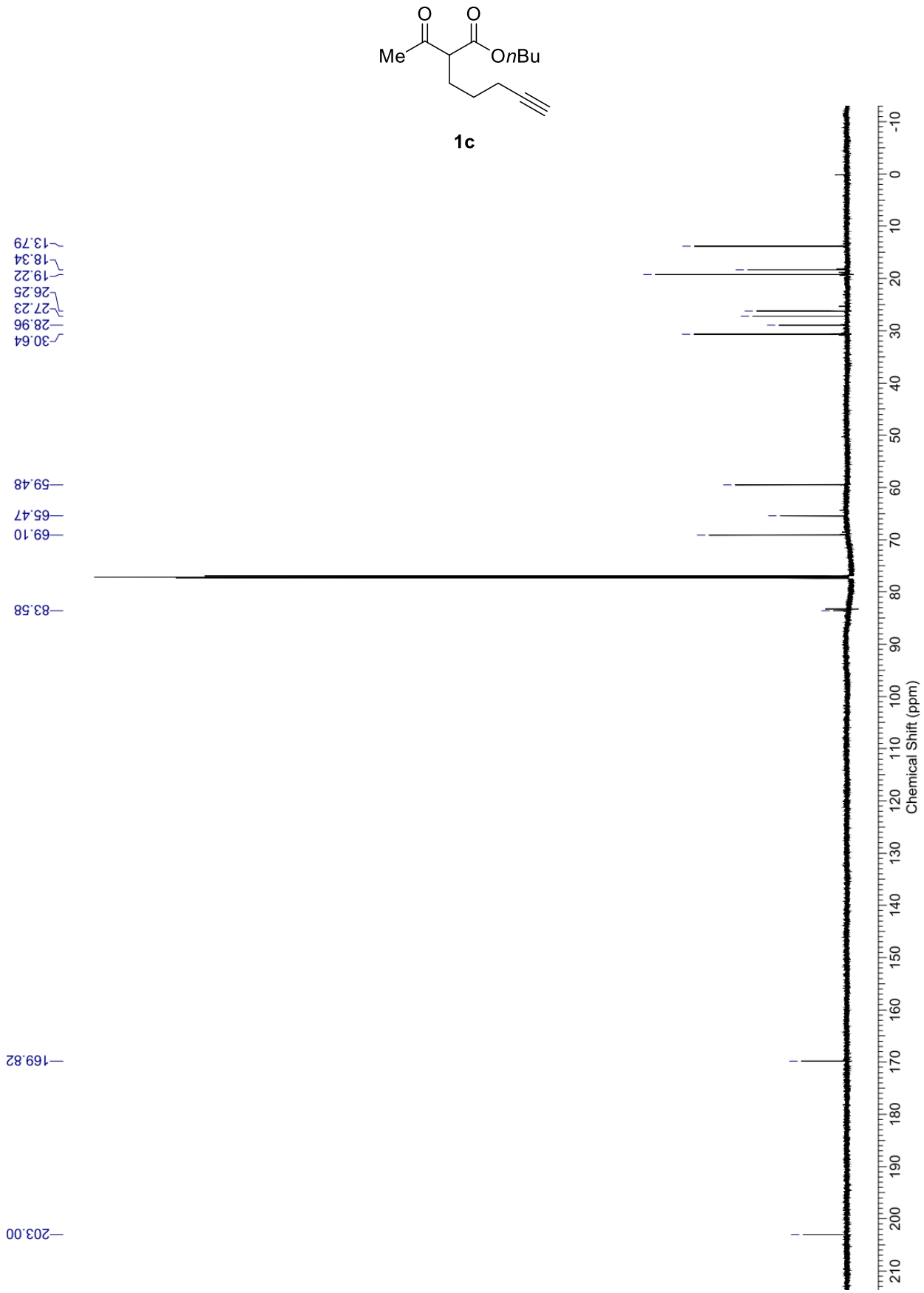
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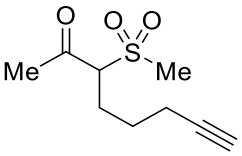
65.47
69.10
83.58
169.82
203.00
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
Chemical Shift (ppm)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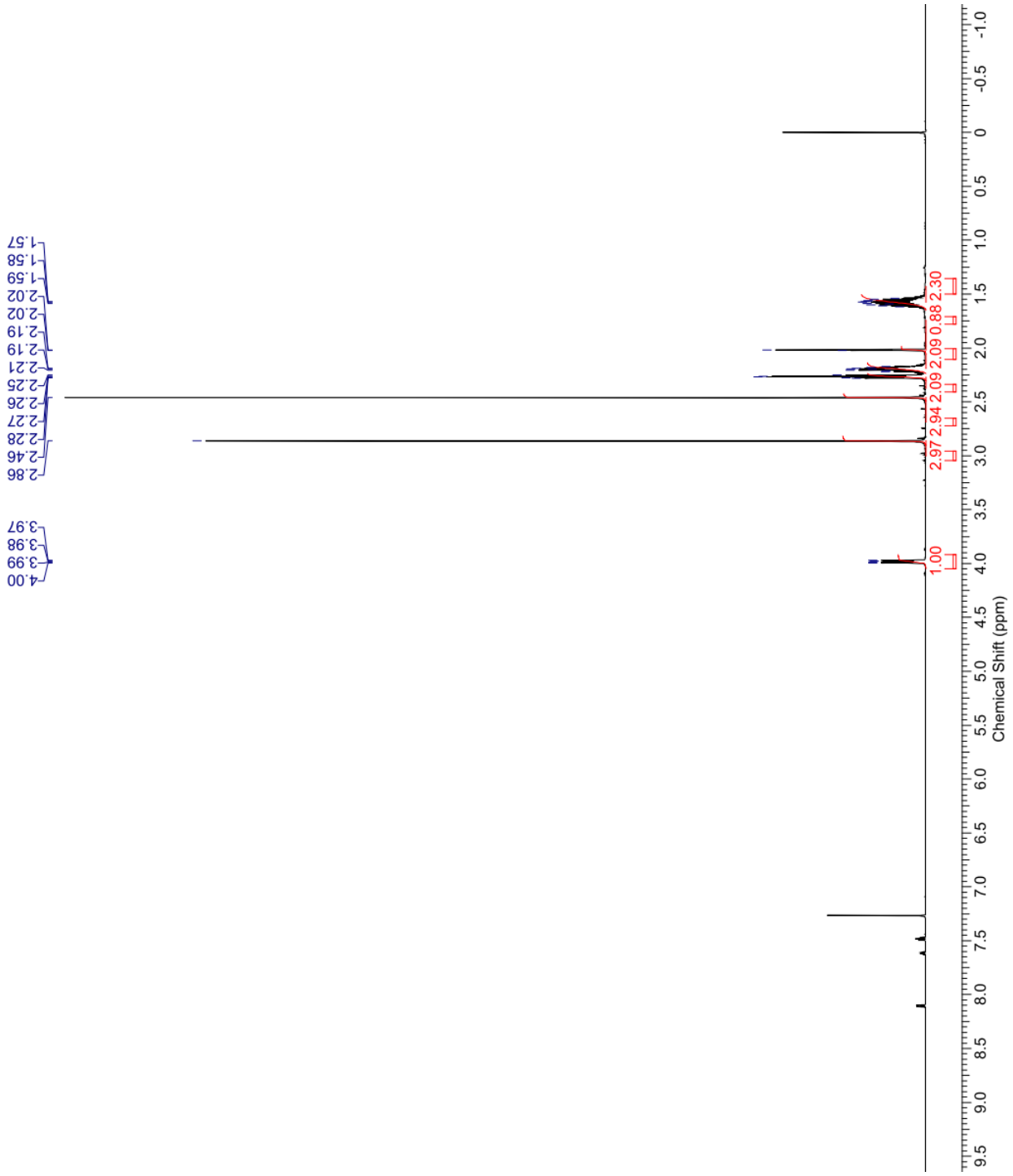
S
Me
Me

1o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2.02
2.19
2.19
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2.25
2.26
2.27
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2.86
3.97
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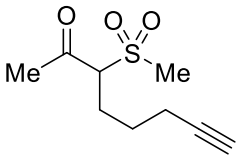
Chemical Shift (ppm)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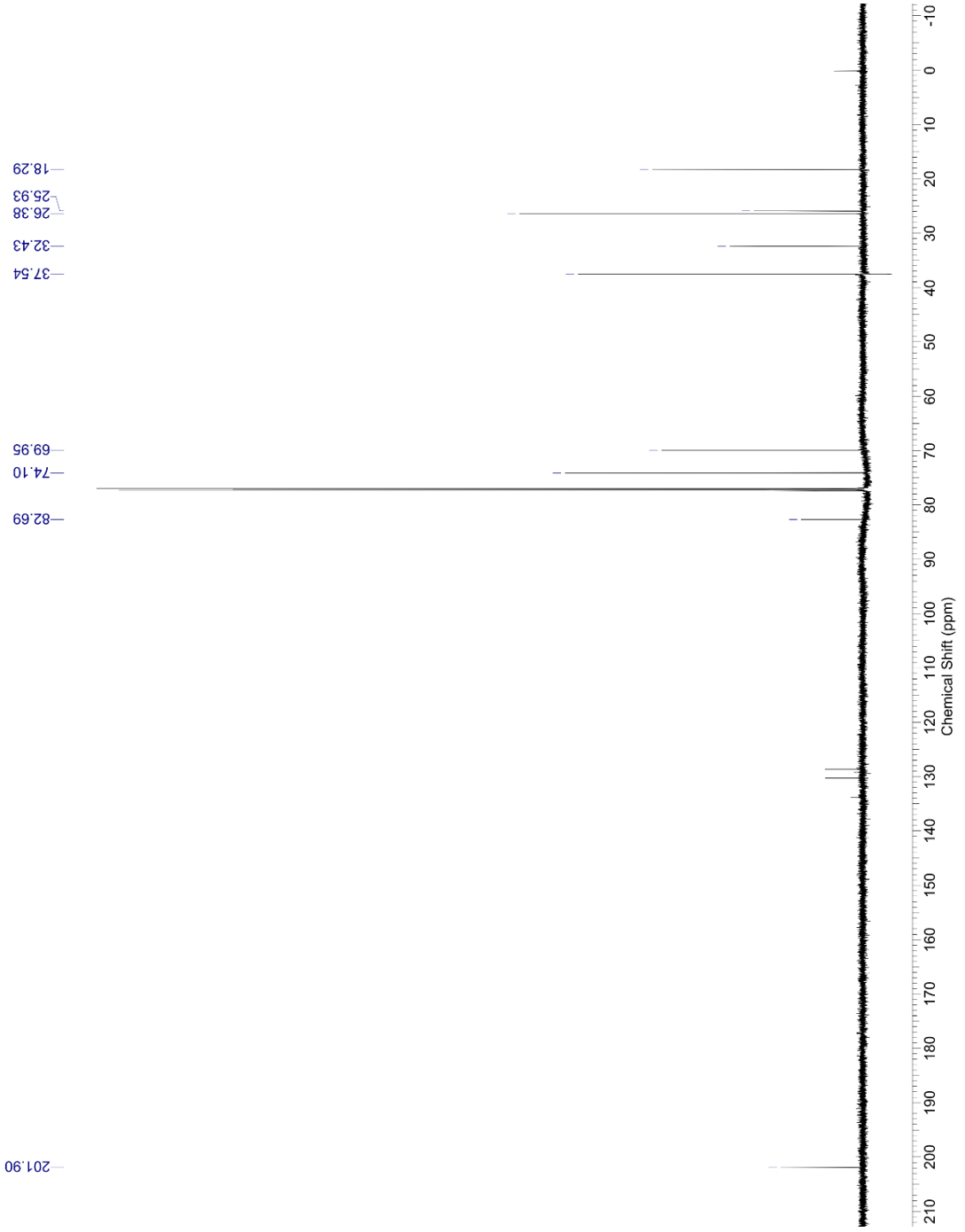
Me
Me

1o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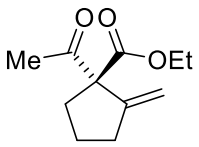
Chemical Shift (ppm)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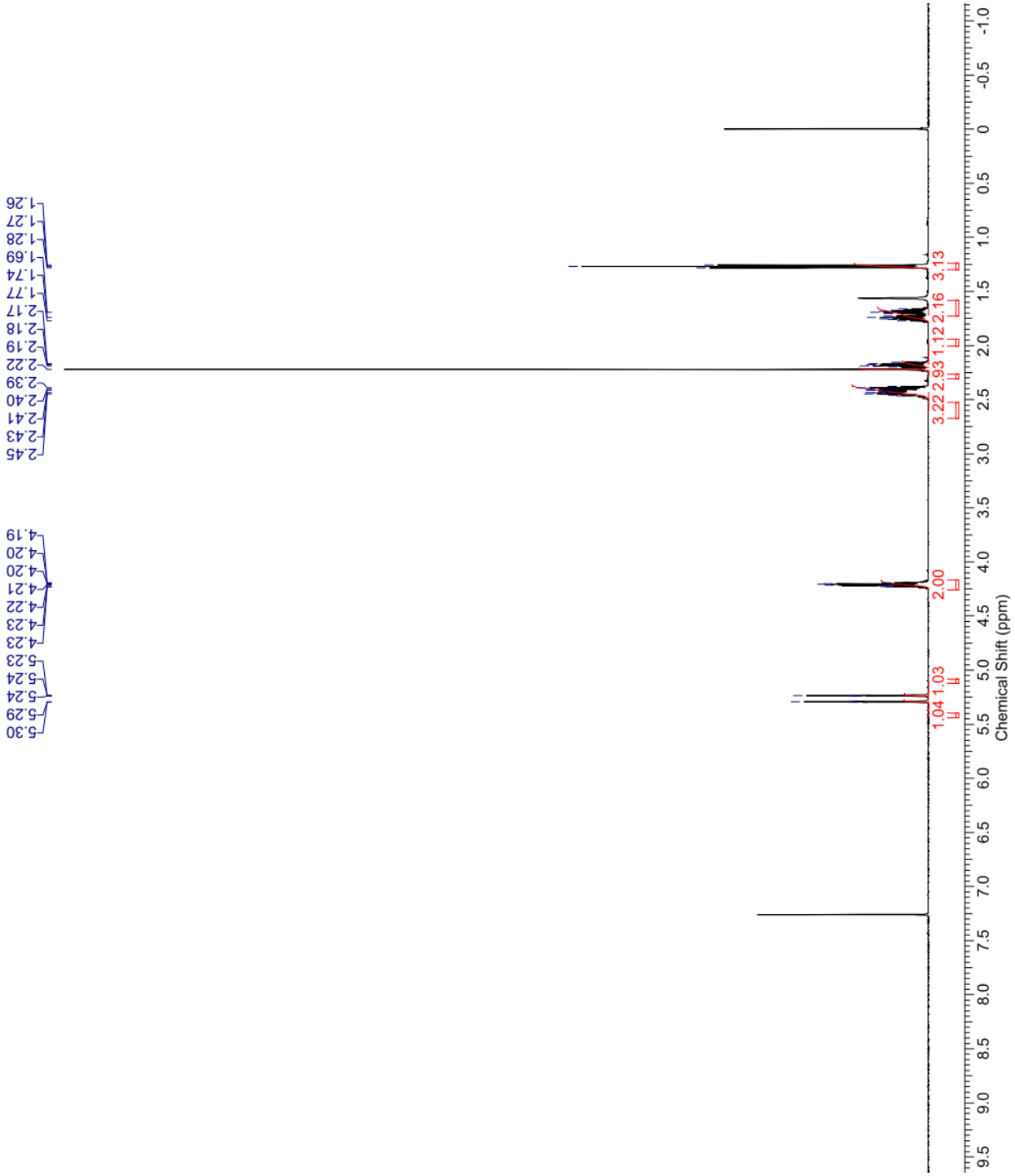
OEt

2a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5.30
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2.16
3.13
2.00
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1.03
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1.0
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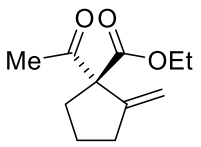
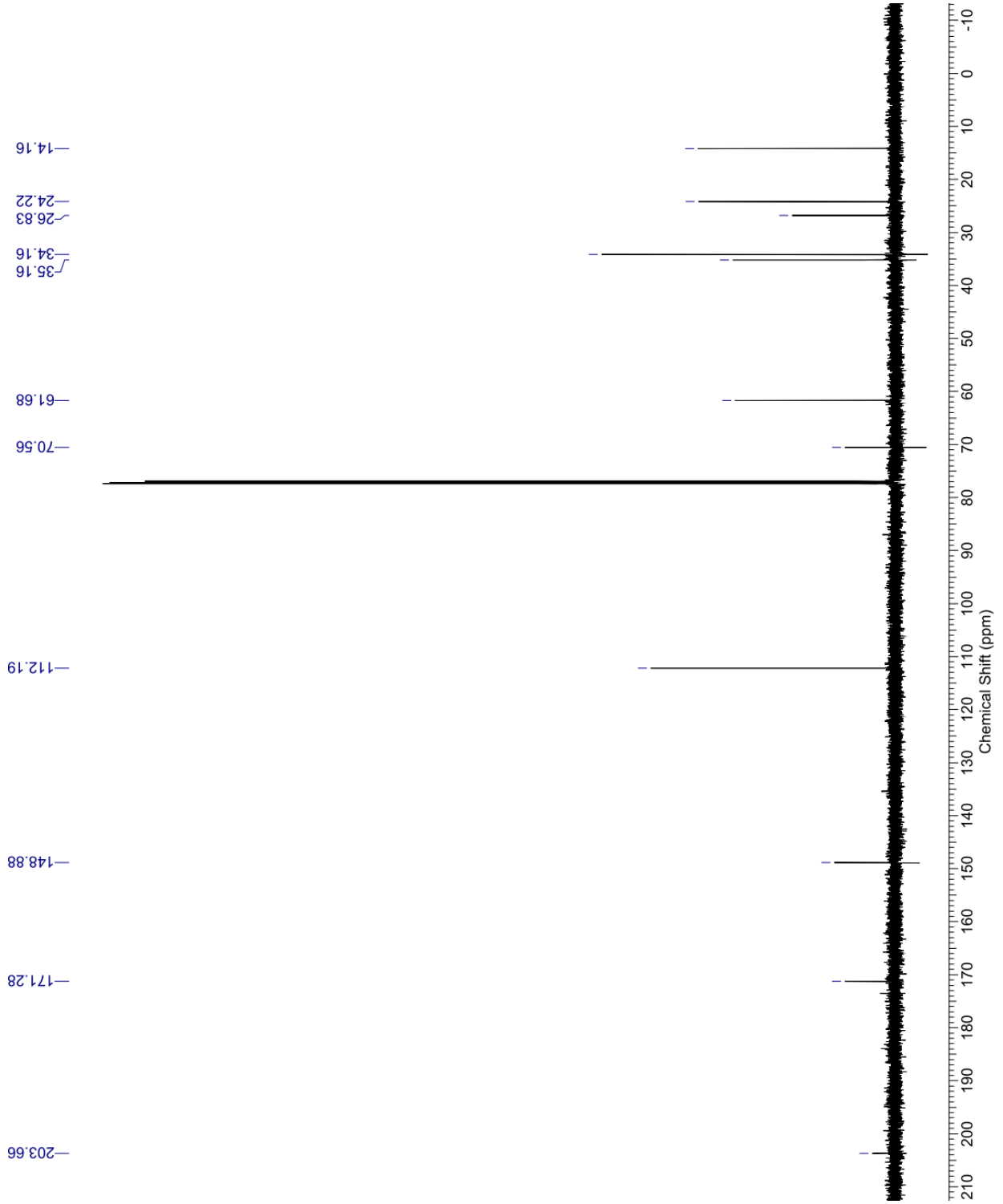
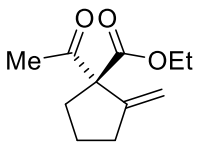
9.5
Chemical Shift (ppm)


O
O
Me
OEt

2a


14.16
24.22
26.83
34.16
35.16
61.68
70.56
112.19
148.88
171.28
203.66
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
Chemical Shift (ppm)



2a

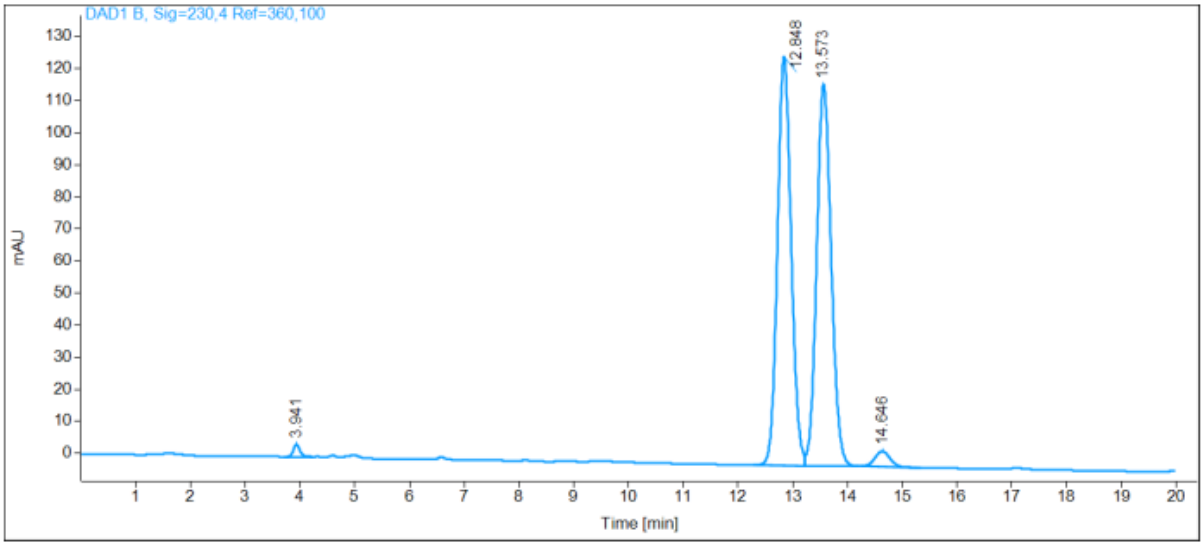
Sample name: **MB G 2A rac**

Data file: C:\SNOOPY\MB\MB G 2A RAC 1IC.D
Description: Laufmittel: n-Heptan/iPrOH 97:3 ; Die Probe ist DCM/LM gelöst.

Injection date: 5/5/2015 10:16:08 AM
Acq. Analysis method: CHIRALPAKIC1-6LNP.M

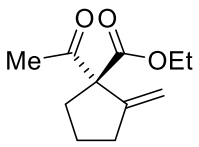
Column: Chiralpak IC, (150 x 4,6) mm, 5µ, SN: IC00CD-QF015

Pressure at start: 18 bar **Start flow:** 0.500 ml/min **Column oven:** 30 °C



Name MB G 2A rac

RT [min]	Type	Area%	Area	Height	Width [min]
3.94	BB	0.70	31.82	3.78	0.13
12.85	BV	48.84	2215.90	127.49	0.27
13.57	VB	48.42	2196.84	118.93	0.29
14.65	BB	2.04	92.75	4.83	0.30
	Sum	100.00	4537.31		



2a

Sample name: **LR195**

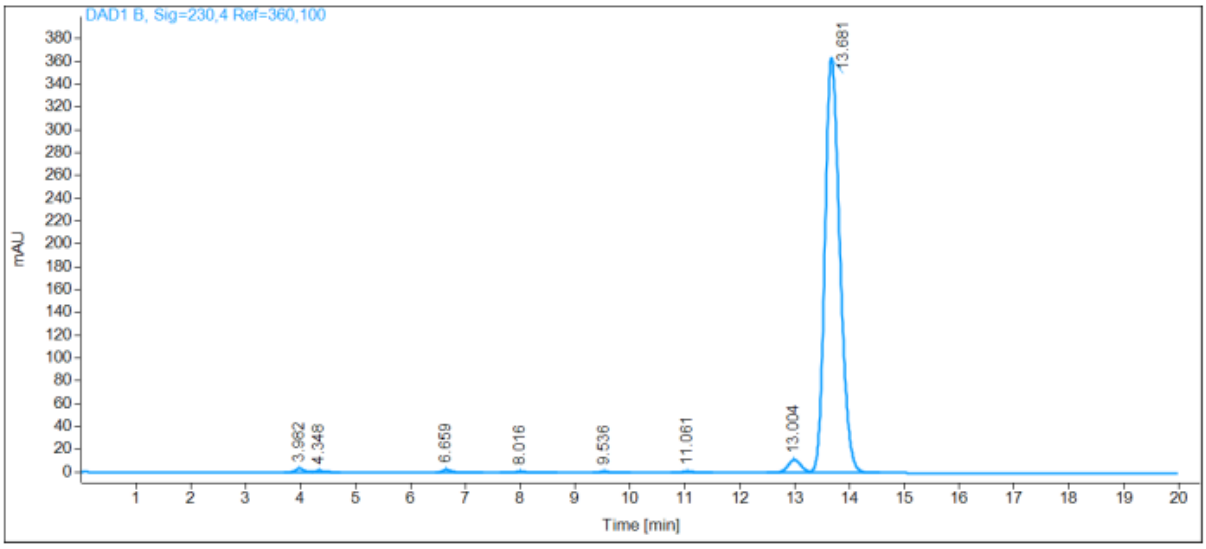
Data file: C:\SNOOPY\LR\195IC.D
Description: Mobile phase: n-Heptane/i-PrOH 97:3 ;
The sample is solved in DCM/MP

Injection date: 8/5/2016 7:34:21 AM

Acq. Analysis method: CHIRALPAKIC1-6LNP.M

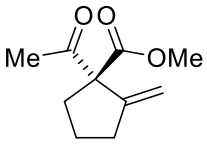
Column: Chiralpak IC, (150 x 4,6) mm, 5µ, SN: IC00CD-QF015

Pressure at start: 24 bar **Start flow:** 0.500 ml/min **Column oven:** 29.99 °C

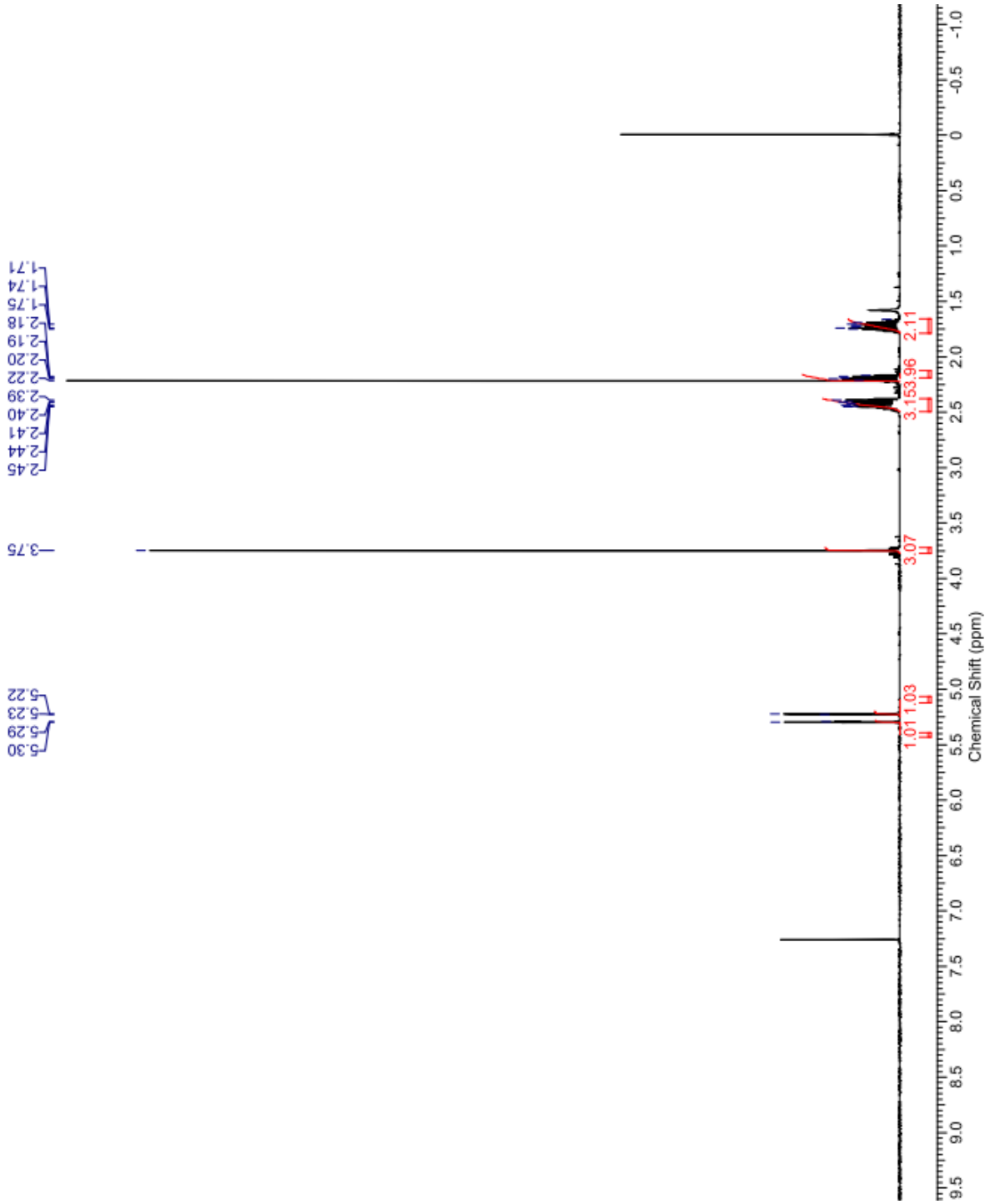


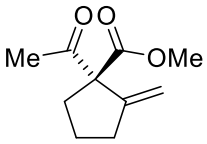
Name LR195

RT [min]	Type	Area%	Area	Height	Width [min]
3.98	BV	0.49	34.91	3.45	0.15
4.35	VB	0.22	16.05	1.37	0.16
6.66	BB	0.38	27.24	2.52	0.16
8.02	BB	0.18	13.22	1.06	0.19
9.54	VB	0.15	10.90	0.86	0.20
11.06	BB	0.22	15.44	1.00	0.23
13.00	BV	2.66	190.90	11.37	0.26
13.68	VB	95.70	6871.52	363.52	0.29
	Sum	100.00	7180.18		

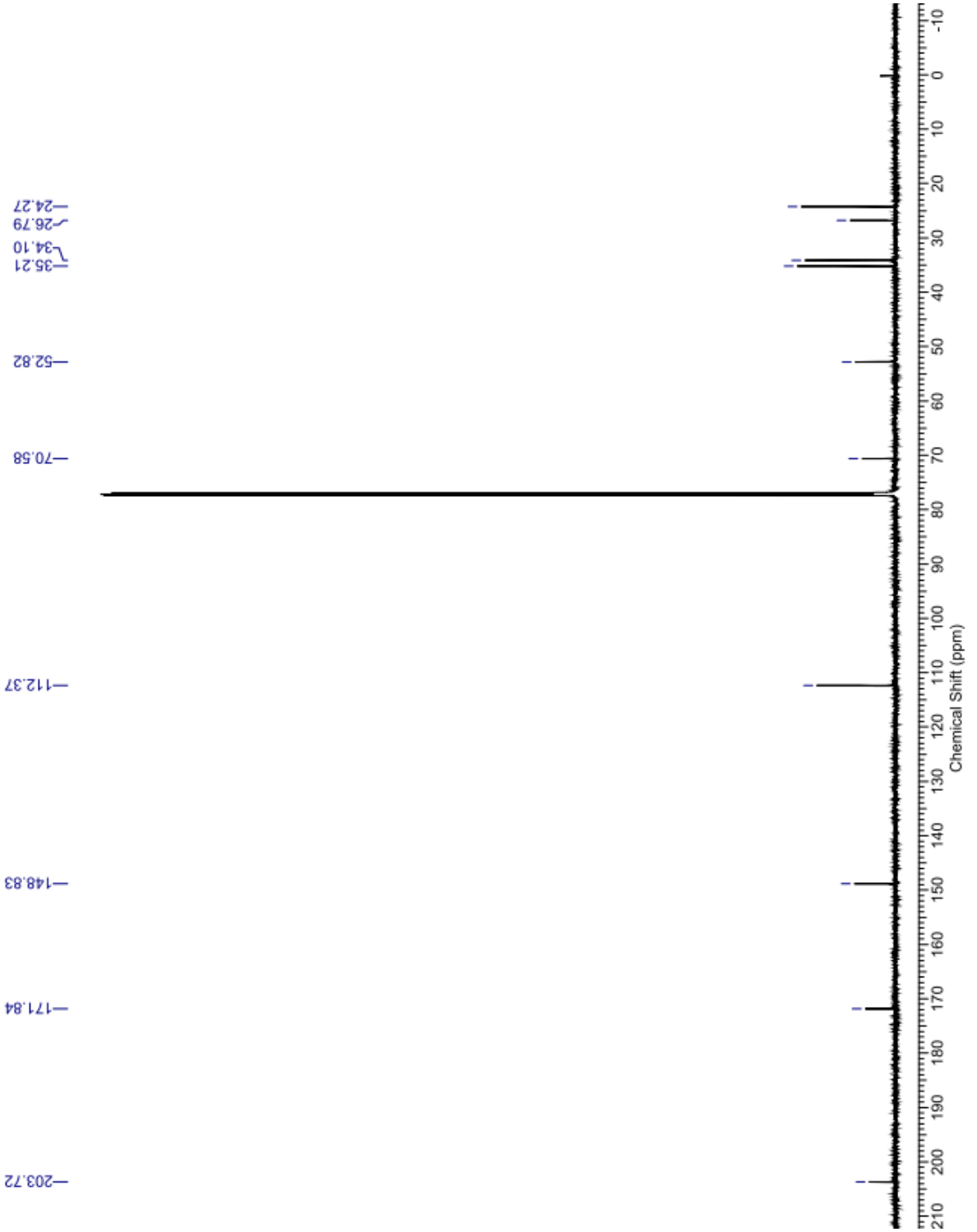

O
O
Me
OMe

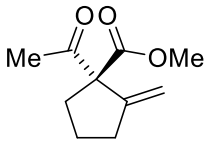
2b


1.71
1.74
1.75
2.18
2.19
2.20
2.22
2.39
2.40
2.41
2.44
2.45
3.75
5.22
5.23
5.29
5.30
2.11
3.15
3.96
3.07
1.01
1.03
Chemical Shift (ppm)


O
O
Me
OMe

2b

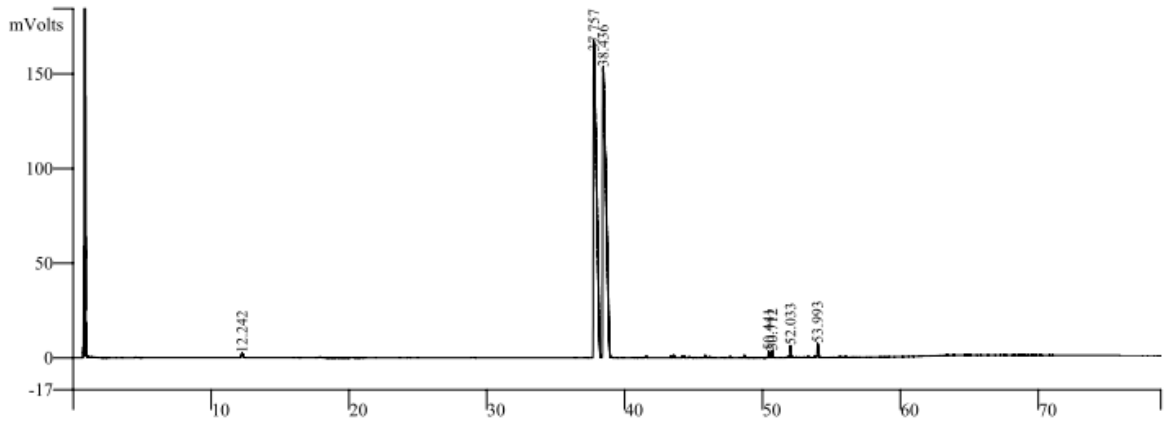

24.27
26.79
34.10
35.21
52.82
70.58
112.37
148.83
171.84
203.72
Chemical Shift (ppm)



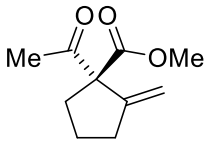
2b

Data File:	c:\star\data\lr 188 rac.run	Channel:	**Middle = FID RESULTS**
Operator:	Analytics lab	Run Mode:	Analysis
Injection Method:	c:\star\odie\60-10iso-1-80-3-180-odie.m	Peak Measurement:	Peak Area
Run Time (min):	78,907	Calculation Type:	Percent
Instrument (Inj):	Odie		19.08.2016 11:04:30

Temp.-Progr.: 60-10iso-1-80-3-180-30iso 11,6 PSI H2
Channel Front: CP-Chirasil-dex CB 25 m x 0,25 mm ID
Channel Middel: Lipodex E 25 m x 0.25 mm ID



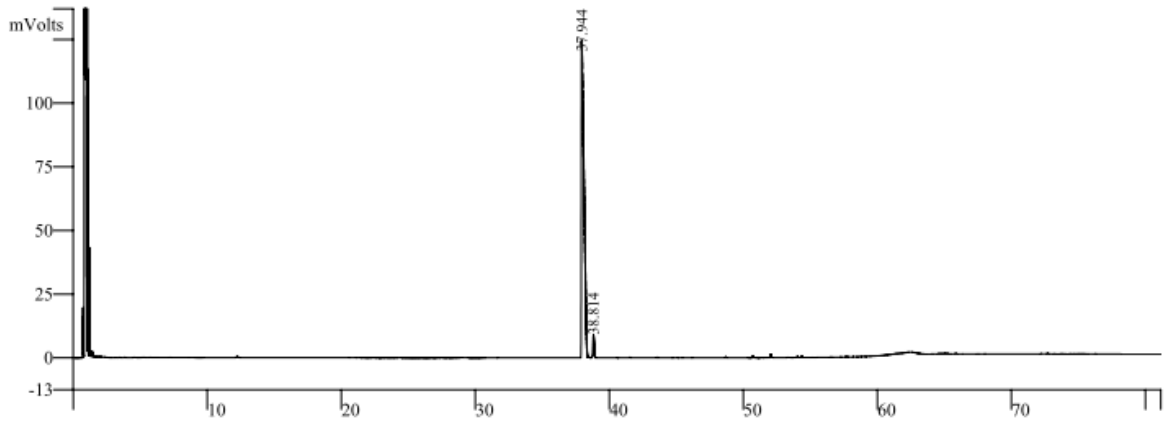
Peak No	Peak Name	Ret Time (min)	Result ()	Peak Area (counts)	Sep. Code	Peak Height (counts)	Width 1/2 (sec)
1		12.24	0.35	18904	BB	2314	7.48
2		37.76	49.00	2613923	BV	167183	15.77
3		38.44	48.85	2605908	VB	153356	16.99
4		50.44	0.26	13842	BV	3374	3.63
5		50.71	0.26	13772	VB	3514	3.58
6		52.03	0.45	23774	BB	6153	3.44
7		53.99	0.83	44267	VB	7346	6.51
	Totals		**100.00**	**5334390**		**343240**	



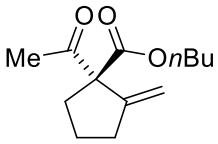
2b

Data File:	c:\star\data\lr 199.run	Channel:	**Middle = FID RESULTS**
Operator:	Analytics lab	Run Mode:	Analysis
Injection Method:	c:\star\odie\60-10iso-1-80-3-180-odie.m	Peak Measurement:	Peak Area
Run Time (min):	81,165	Calculation Type:	Percent
Instrument (Inj):	Odie		19.08.2016 12:30:36

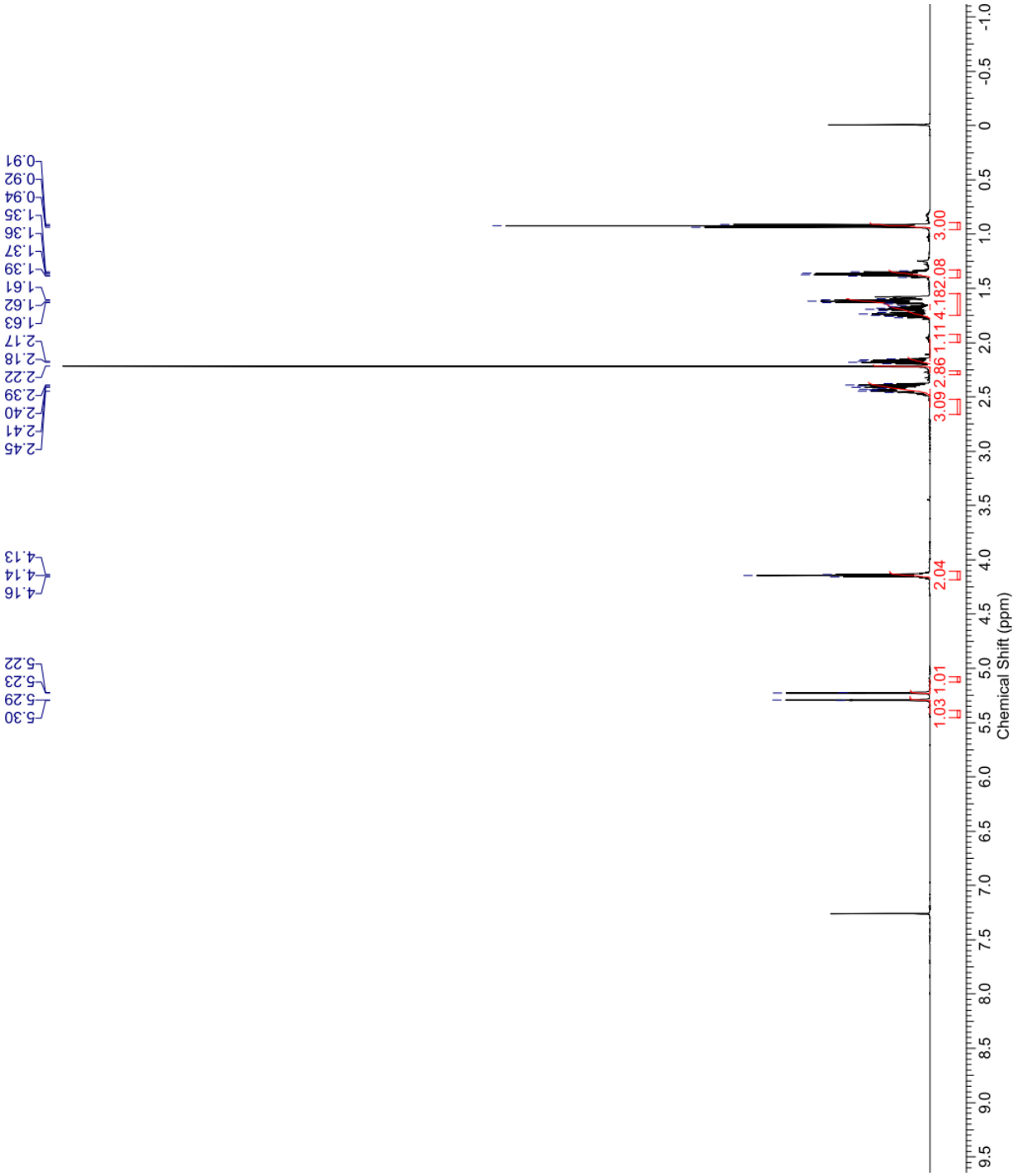
Temp.-Progr.: 60-10iso-1-80-3-180-30iso 11,6 PSI H2
Channel Front: CP-Chirasil-dex CB 25 m x 0,25 mm ID
Channel Middel: Lipodex E 25 m x 0.25 mm ID

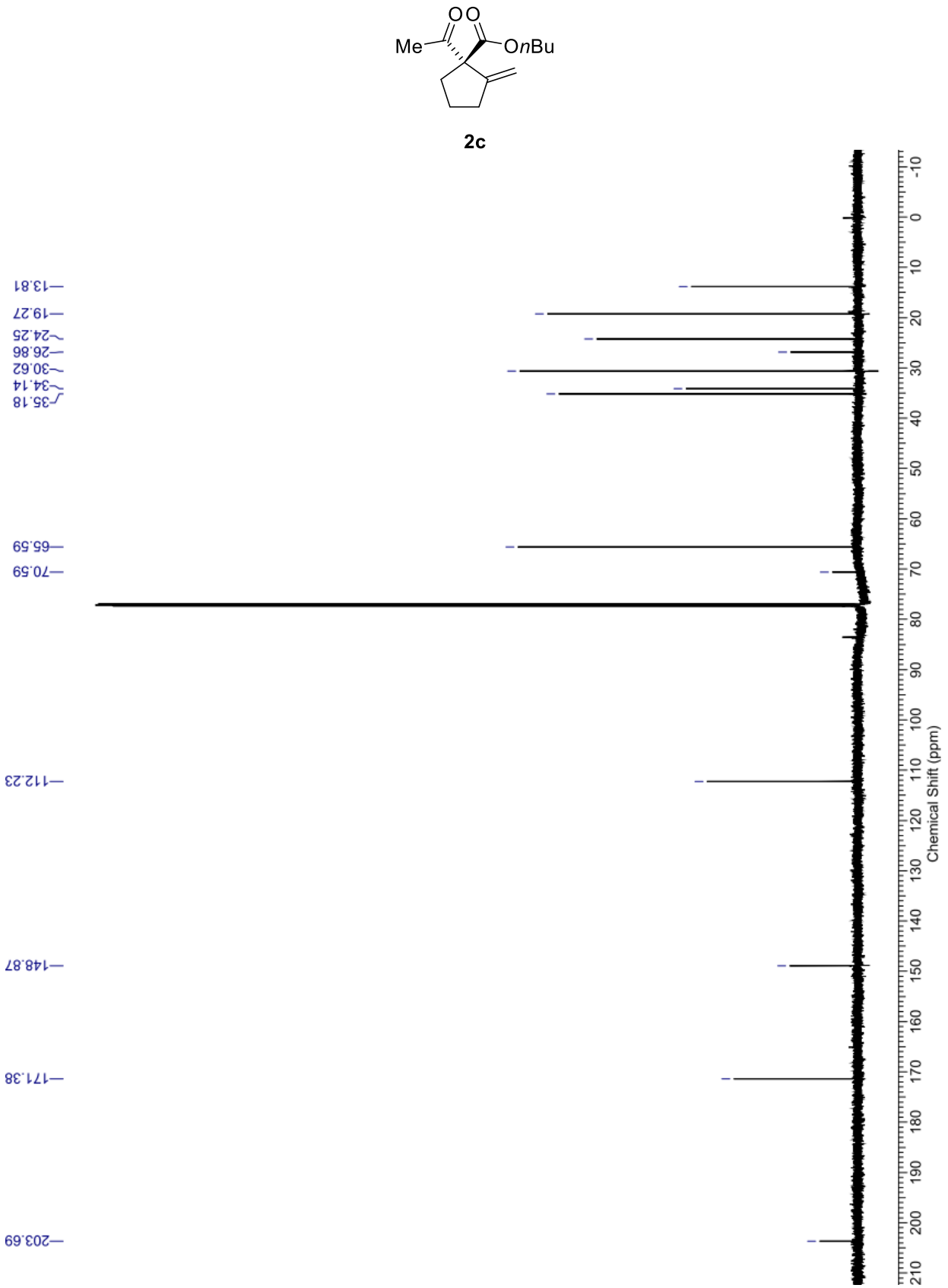


Peak No	Peak Name	Ret Time (min)	Result ()	Peak Area (counts)	Sep. Code	Peak Height (counts)	Width 1/2 (sec)
1		37.94	96.74	1667861	BB	122793	13.32
2		38.81	3.26	56239	BB	8839	6.09
	Totals		**100.00**	**1724100**		**131632**	

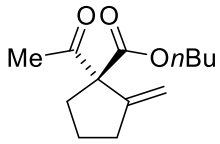

O
O
Me
OnBu

2c


0.91
0.92
0.94
1.35
1.36
1.37
1.39
1.61
1.62
1.63
2.17
2.18
2.22
2.39
2.40
2.41
2.45
4.13
4.14
4.16
5.22
5.23
5.29
5.30
3.00
2.08
4.18
1.11
2.86
3.09
2.04
1.01
1.03
Chemical Shift (ppm)

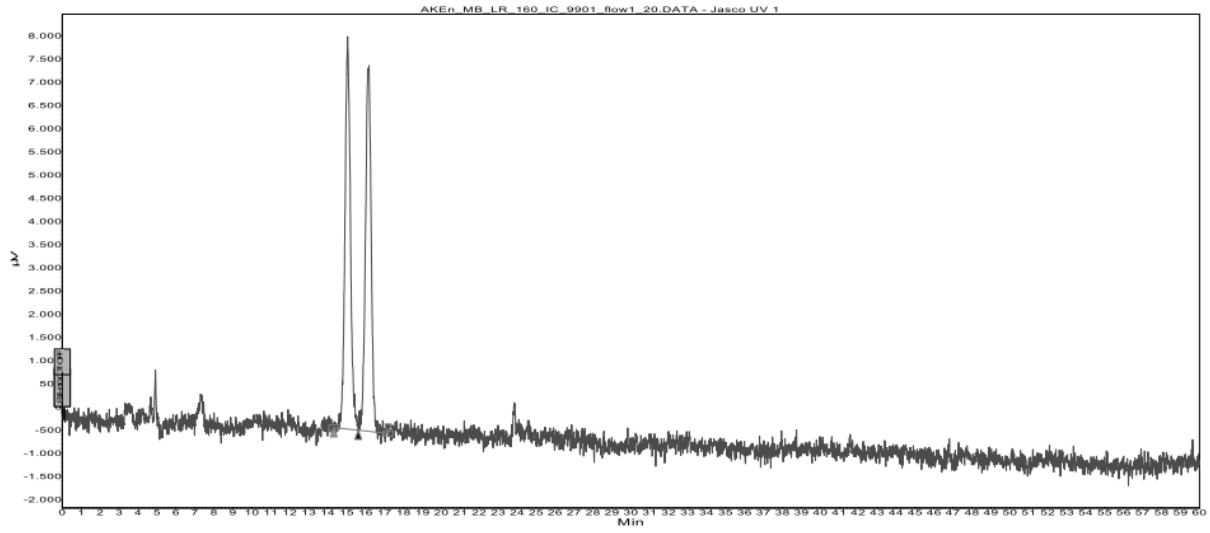

Me
O
O
OnBu
13.81
19.27
24.25
26.86
30.62
34.14
35.18
65.59
70.59
112.23
148.87
171.38
203.69
Chemical Shift (ppm)

2c



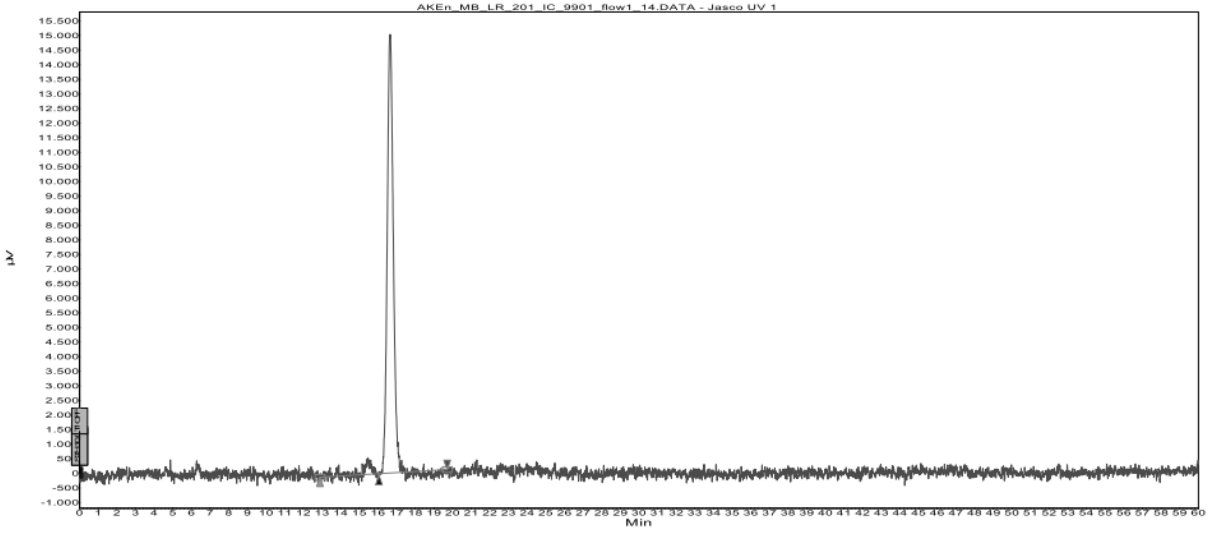
2c

Data file: AKEn_MB_LR_160_IC_9901_flow1_20.DATA
Method: HPLC1_IC_9901_flow1_acq_60
Date: 03.11.2016 21:57:45

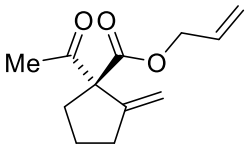


Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	14,323	15,050	15,617	50,256
2	15,617	16,142	17,190	49,744
Total				100,000

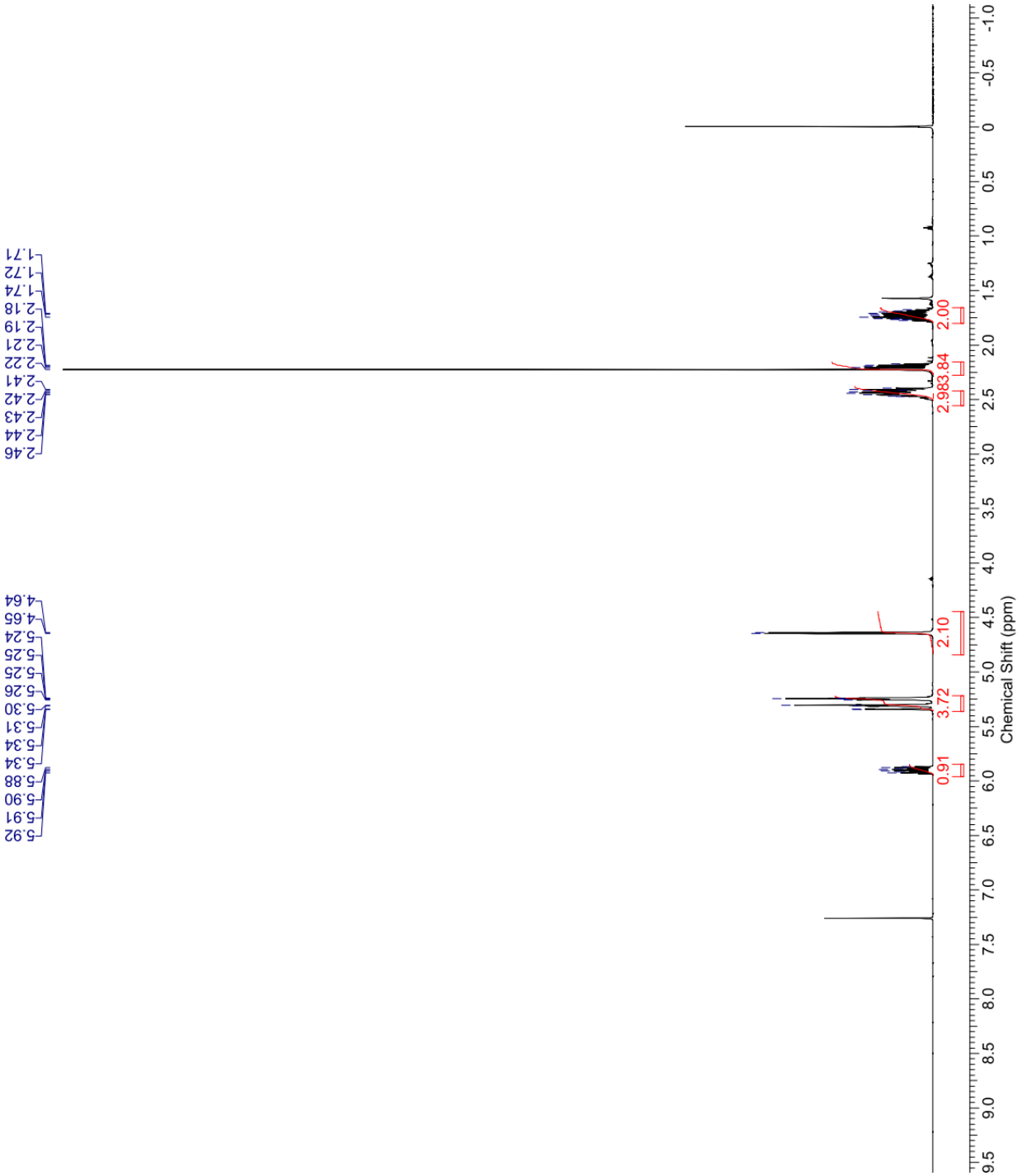
Data file: AKEn_MB_LR_201_IC_9901_flow1_14.DATA
Method: HPLC1_IC_9901_flow1_acq_60
Date: 08.11.2016 03:22:35

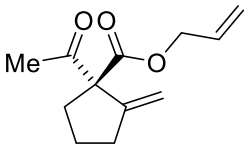


Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	12,893	15,475	16,054	3,756
2	16,054	16,650	19,711	96,244
Total				100,000

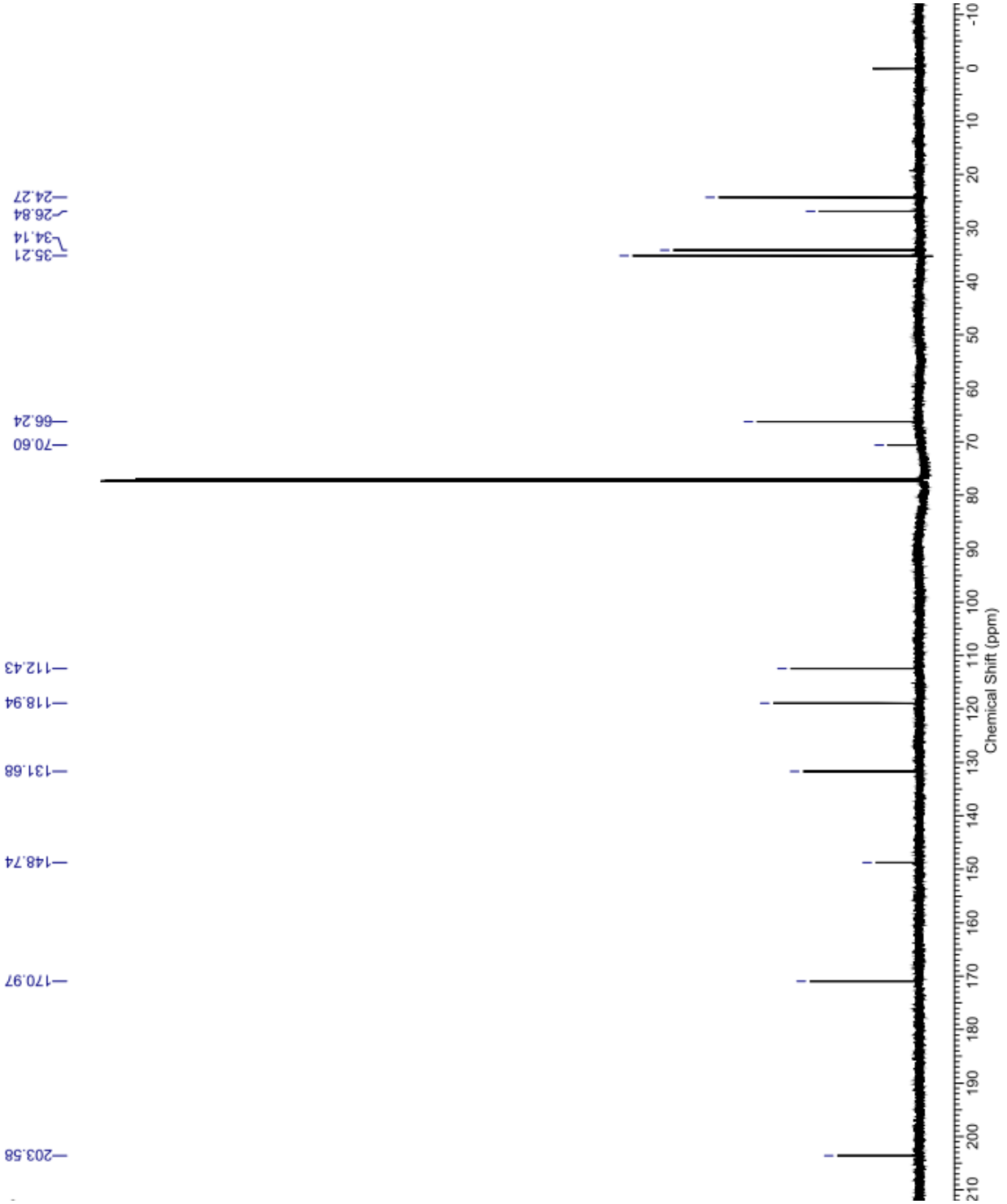

O
O
Me
O

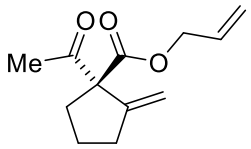
2d


1.71
1.72
1.74
2.18
2.19
2.21
2.22
2.41
2.42
2.43
2.44
2.46
4.64
4.65
5.24
5.25
5.25
5.26
5.30
5.31
5.34
5.34
5.88
5.90
5.91
5.92
2.00
2.98
3.84
2.10
3.72
0.91
Chemical Shift (ppm)


O
O
Me
O

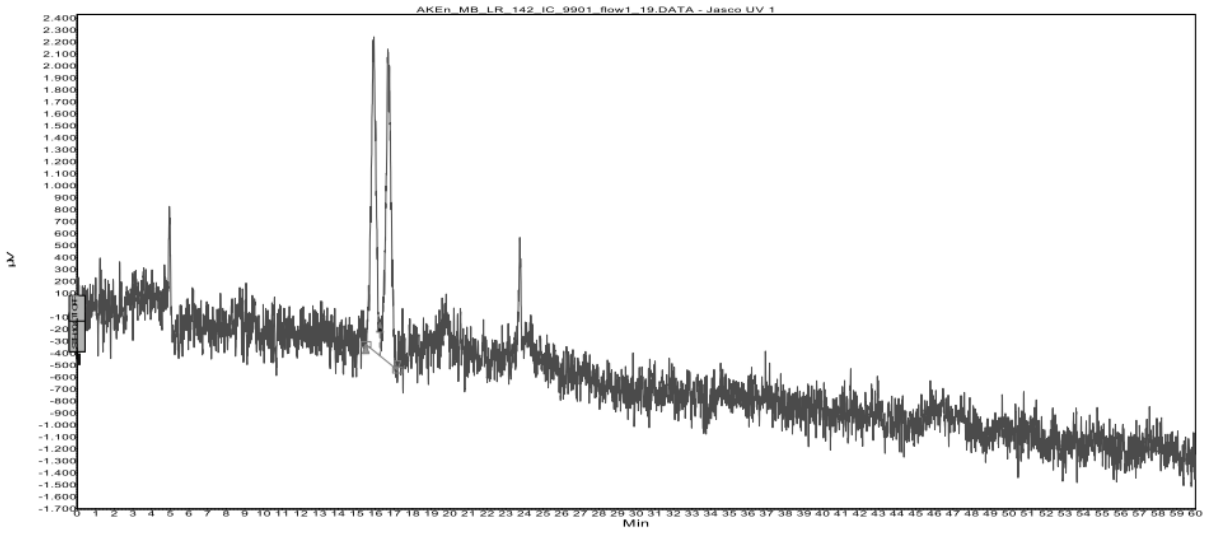
2d


24.27
26.84
34.14
35.21
66.24
70.60
112.43
118.94
131.68
148.74
170.97
203.58
Chemical Shift (ppm)



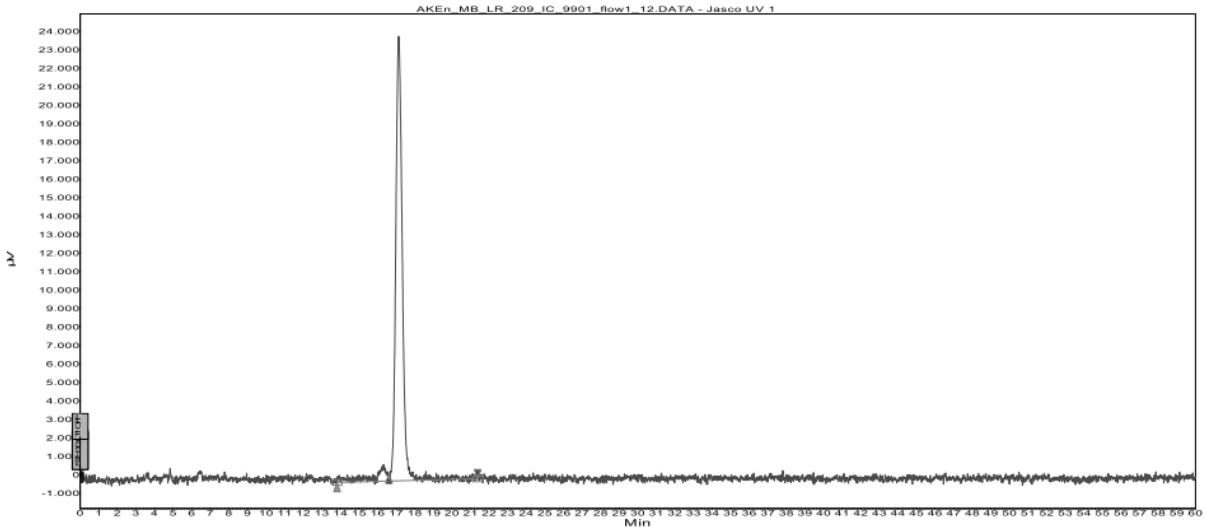
2d

Data file: AKEn_MB_LR_142_IC_9901_flow1_19.DATA
Method: HPLC1_IC_9901_flow1_acq_60
Date: 03.11.2016 20:55:04

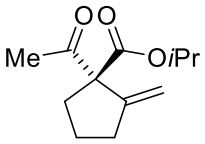


Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	15,490	15,892	16,253	48,282
2	16,253	16,683	17,191	51,718
Total				100,000

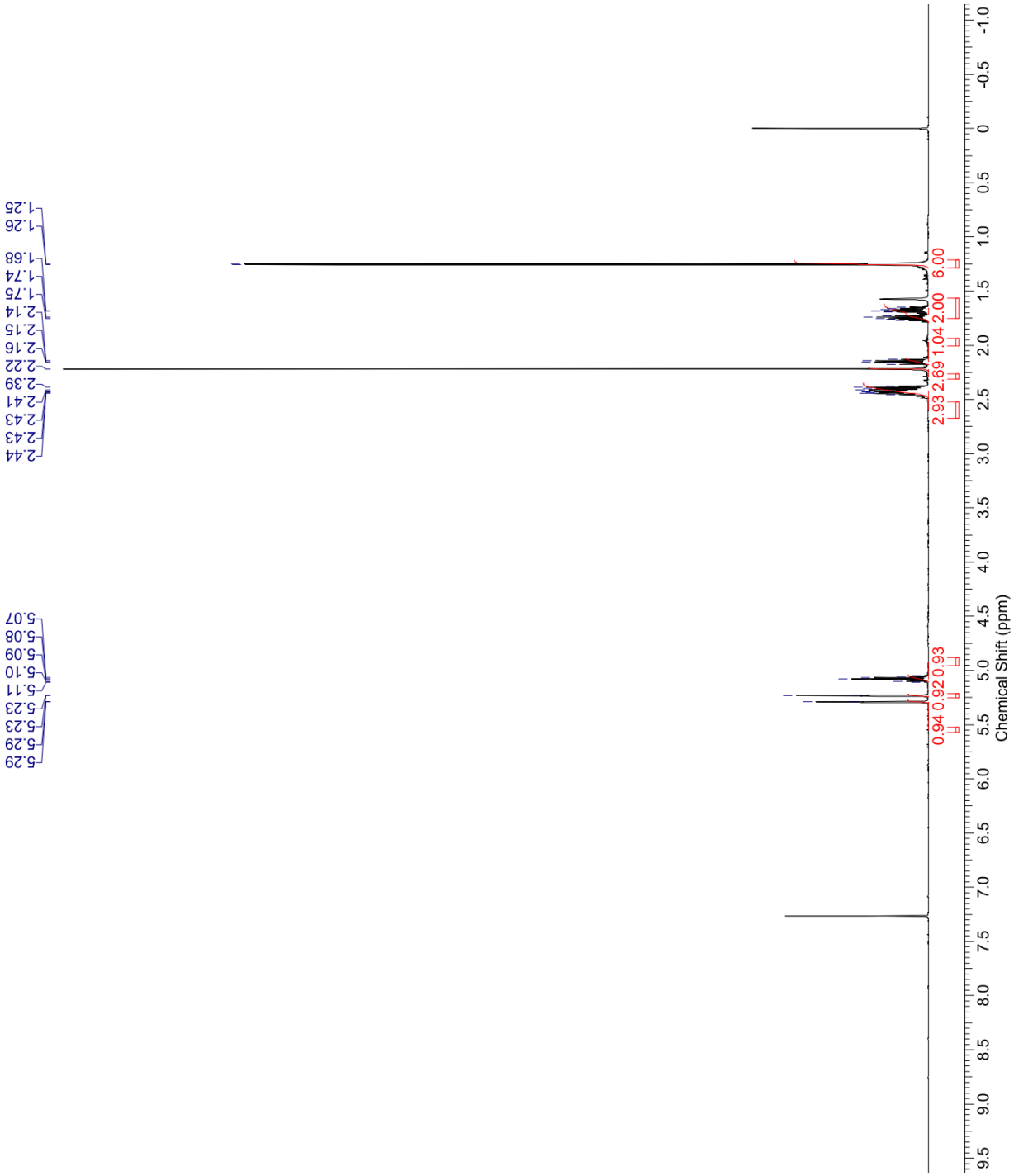
Data file: AKEn_MB_LR_209_IC_9901_flow1_12.DATA
Method: HPLC1_IC_9901_flow1_acq_60
Date: 08.11.2016 01:17:16

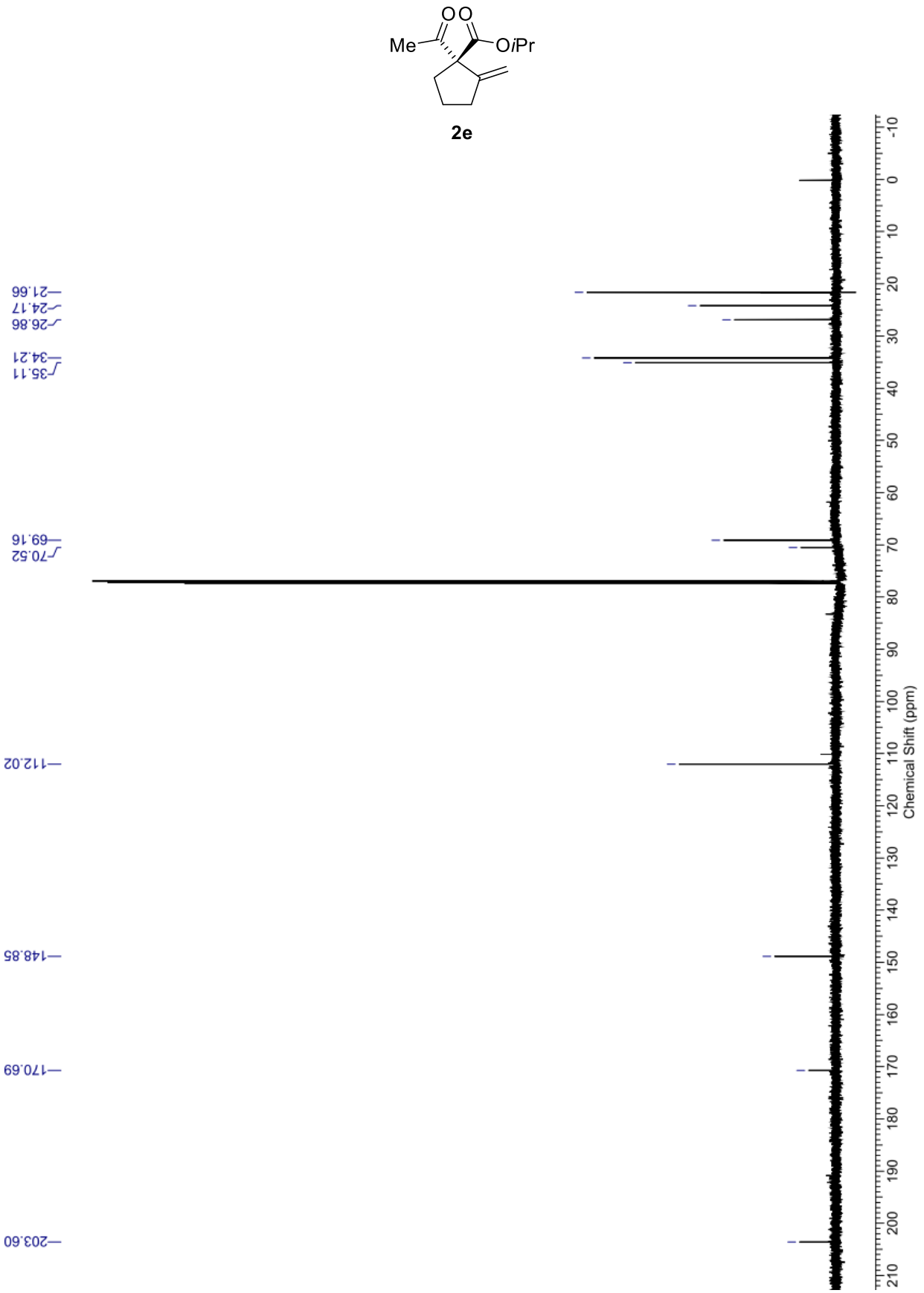


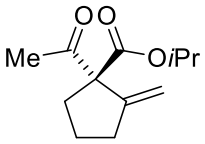
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	13,822	16,317	16,612	6,647
2	16,612	17,133	21,384	93,353
Total				100,000


O
O
Me
O*i*Pr

2e

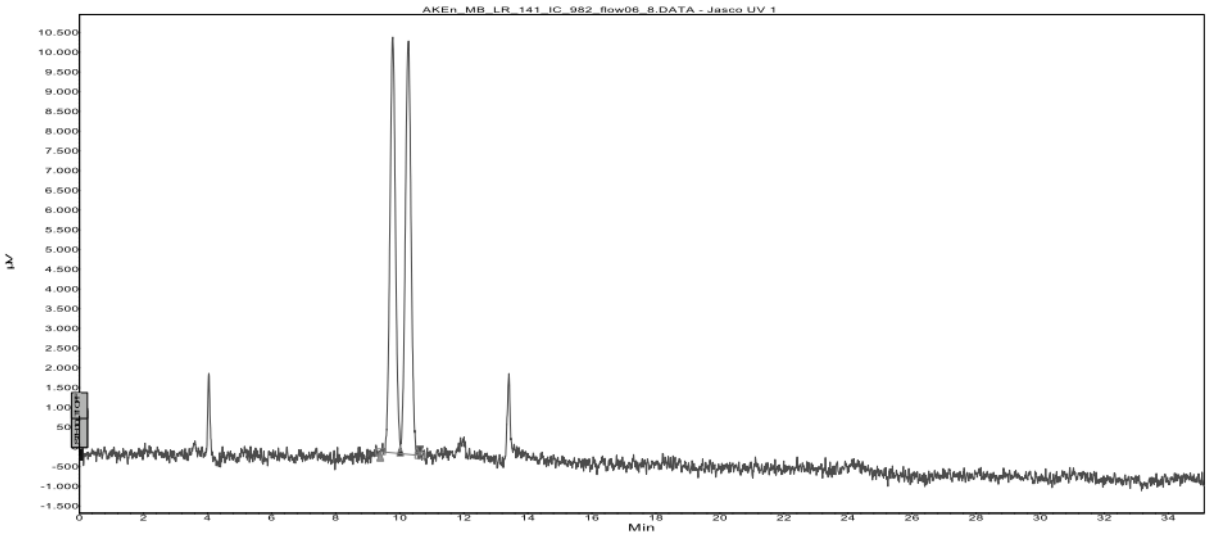

1.25
1.26
1.68
1.74
1.75
2.14
2.15
2.16
2.22
2.39
2.41
2.43
2.43
2.44
5.07
5.08
5.09
5.10
5.11
5.23
5.23
5.29
5.29
6.00
2.00
1.04
2.69
2.93
0.93
0.92
0.94
Chemical Shift (ppm)


Me
O
O
OiPr
2e
21.66
24.17
26.86
34.21
35.11
69.16
70.52
112.02
148.85
170.69
203.60
Chemical Shift (ppm)



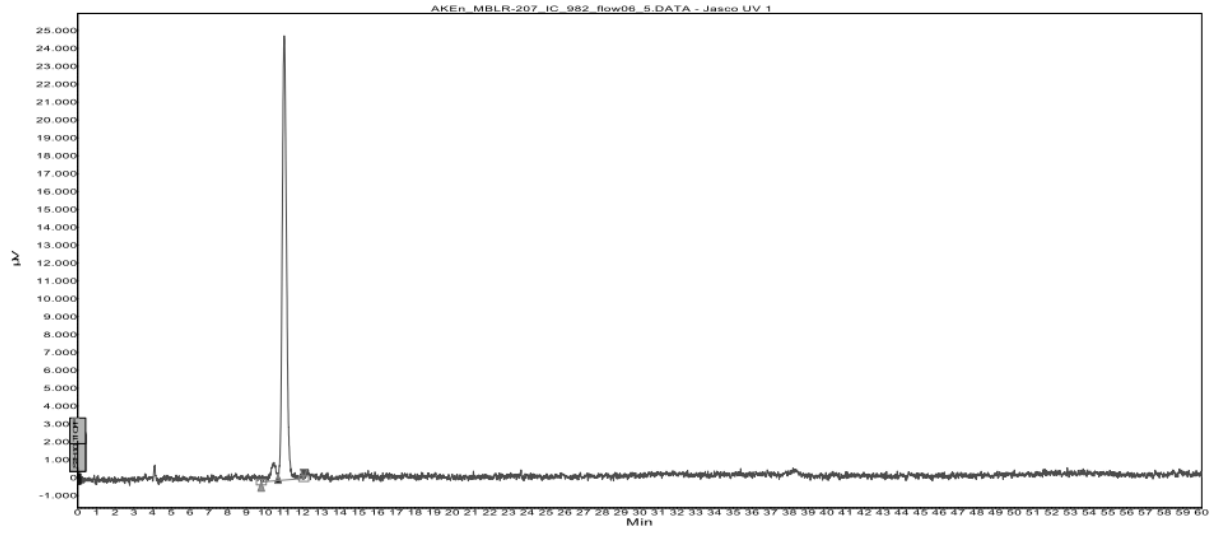
2e

Data file: AKEn_MB_LR_141_IC_982_flow06_8.DATA
Method: HPLC1_IC_982_flow1_acq_60
Date: 03.11.2016 15:27:06

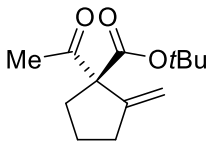


Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	9,395	9,783	10,017	49,232
2	10,017	10,267	10,631	50,768
Total				100,000

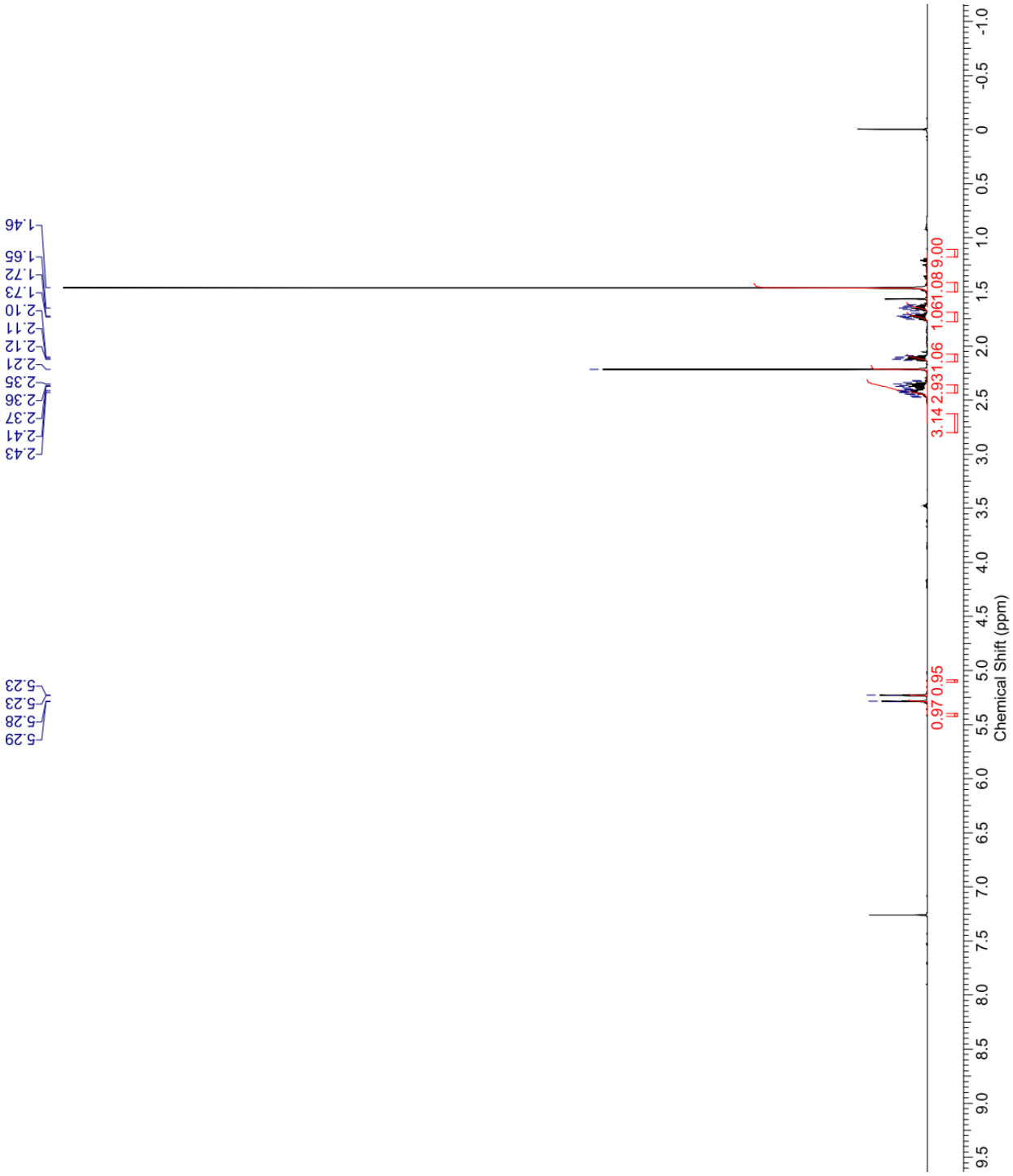
Data file: AKEn_MBLR-207_IC_982_flow06_5.DATA
Method: HPLC1_IC_982_flow1_acq_60
Date: 07.11.2016 18:28:40

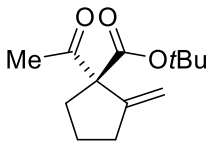


Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	9,793	10,475	10,698	5,452
2	10,698	11,025	12,062	94,548
Total				100,000

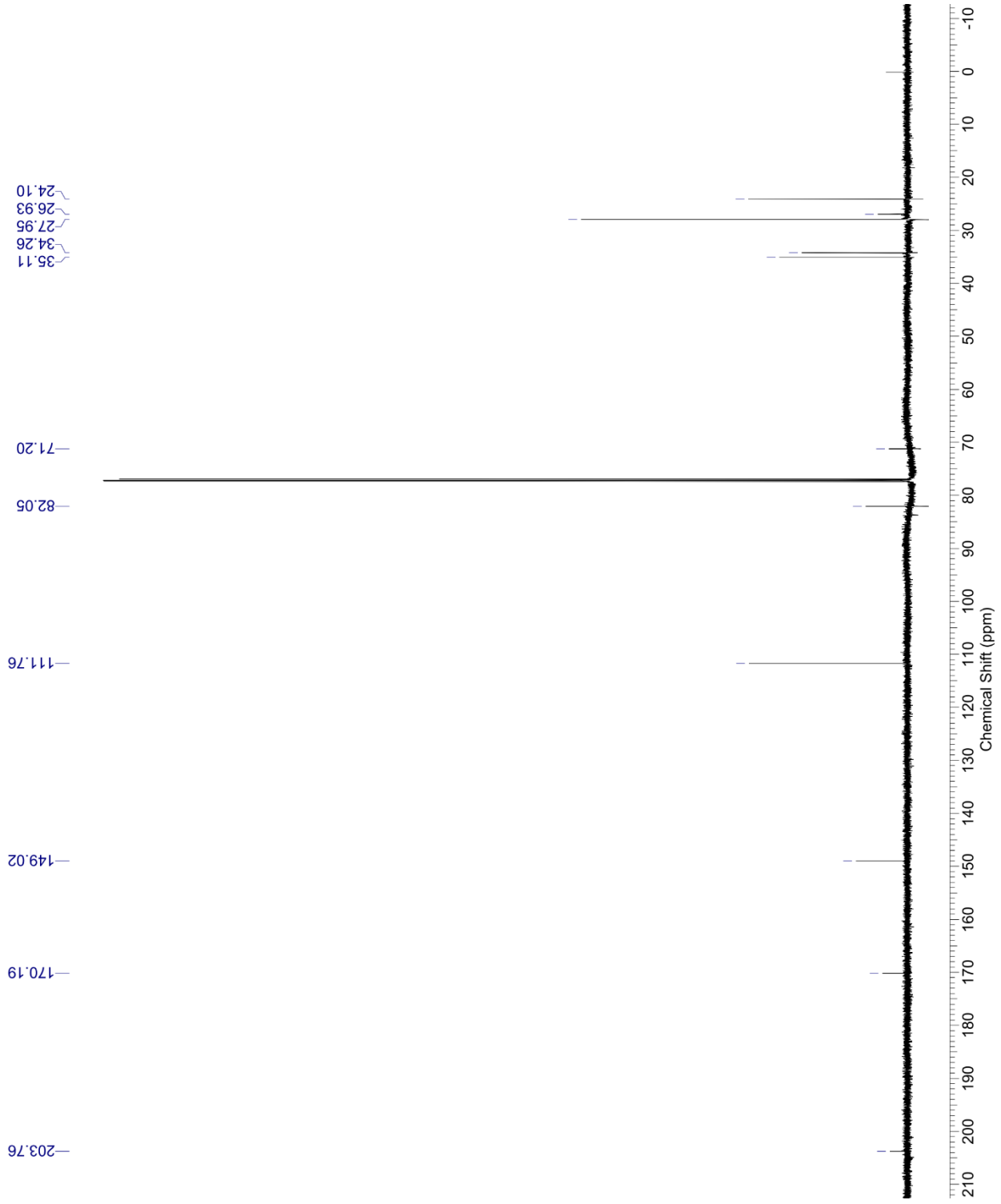

O
O
Me
O*t*Bu

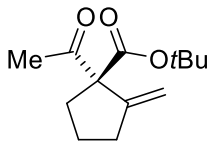
2f


1.46
1.65
1.72
1.73
2.10
2.11
2.12
2.21
2.35
2.36
2.37
2.41
2.43
5.23
5.23
5.28
5.29
3.14
2.93
1.06
1.06
1.08
9.00
0.97
0.95
Chemical Shift (ppm)


O
O
Me
O*t*Bu

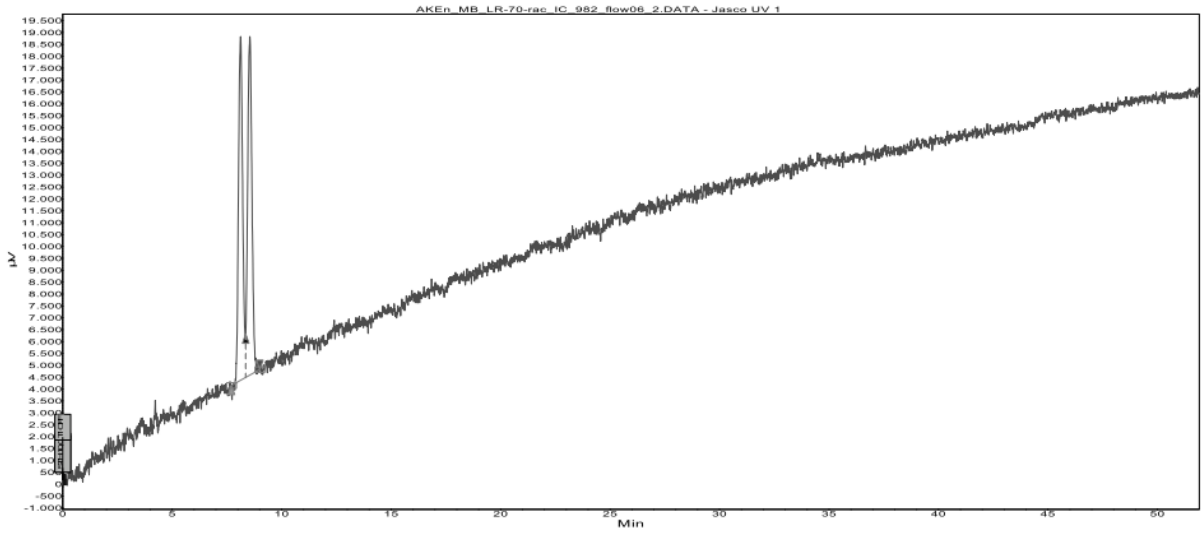
2f


24.10
26.93
27.95
34.26
35.11
71.20
82.05
111.76
149.02
170.19
203.76
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
Chemical Shift (ppm)



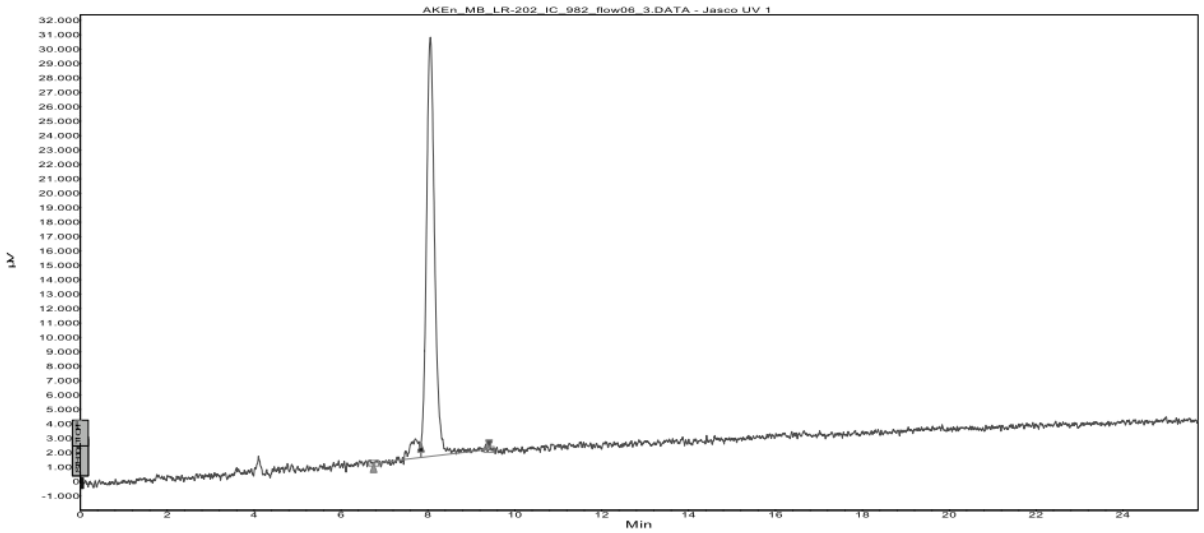
2f

Data file: AKEn_MB_LR-70-rac_IC_982_flow06_2.DATA
Method: HPLC1_IC_982_flow1_acq_60
Date: 07.11.2016 16:03:40

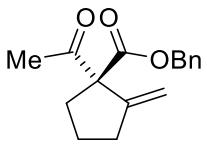


Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	7,707	8,125	8,358	49,289
2	8,358	8,550	9,001	50,711
Total				100,000

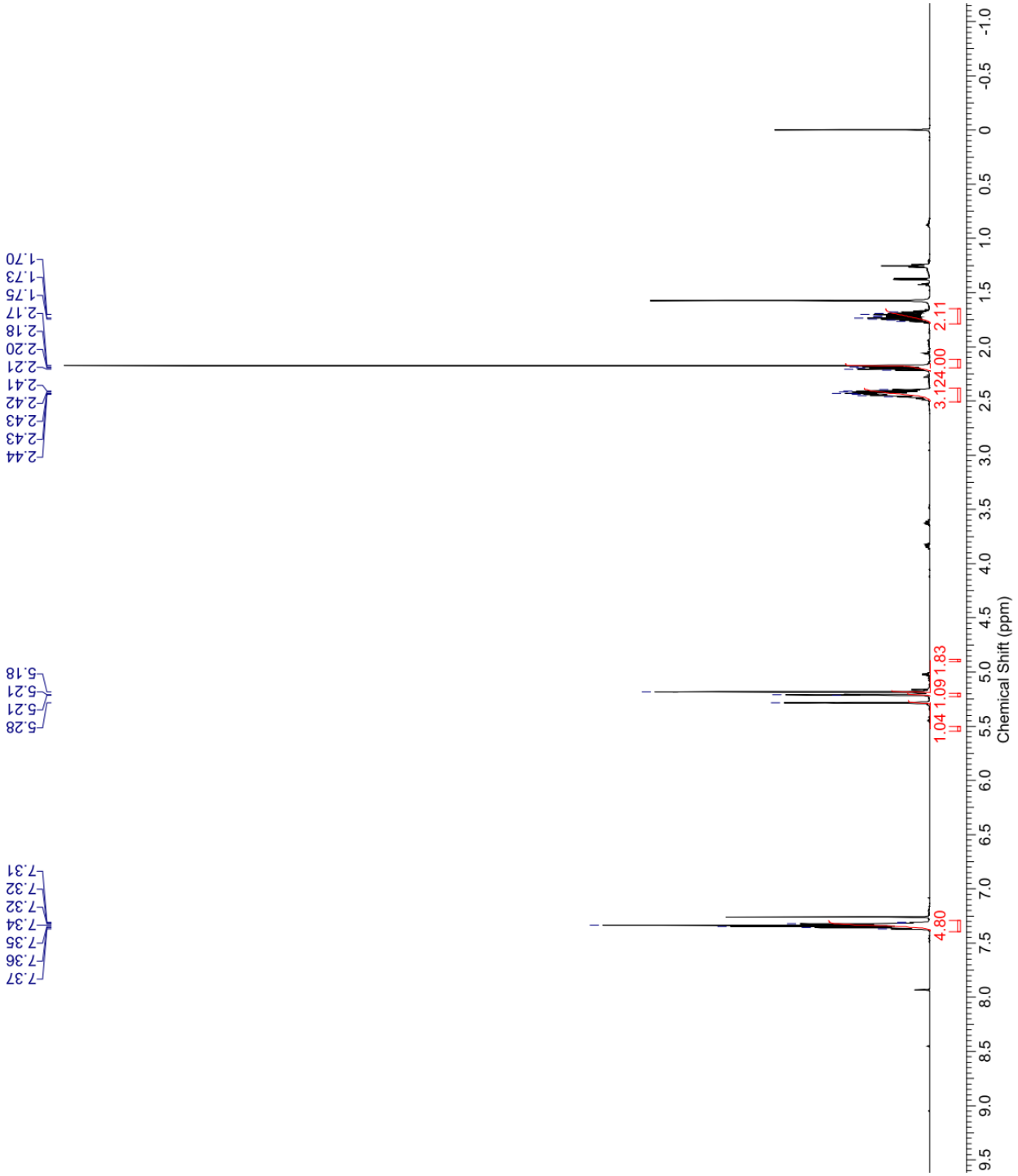
Data file: AKEn_MB_LR-202_IC_982_flow06_3.DATA
Method: HPLC1_IC_982_flow1_acq_60
Date: 07.11.2016 16:57:58

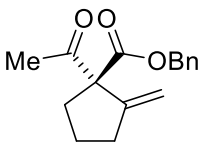


Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	6,750	7,708	7,840	4,601
2	7,840	8,058	9,408	95,399
Total				100,000

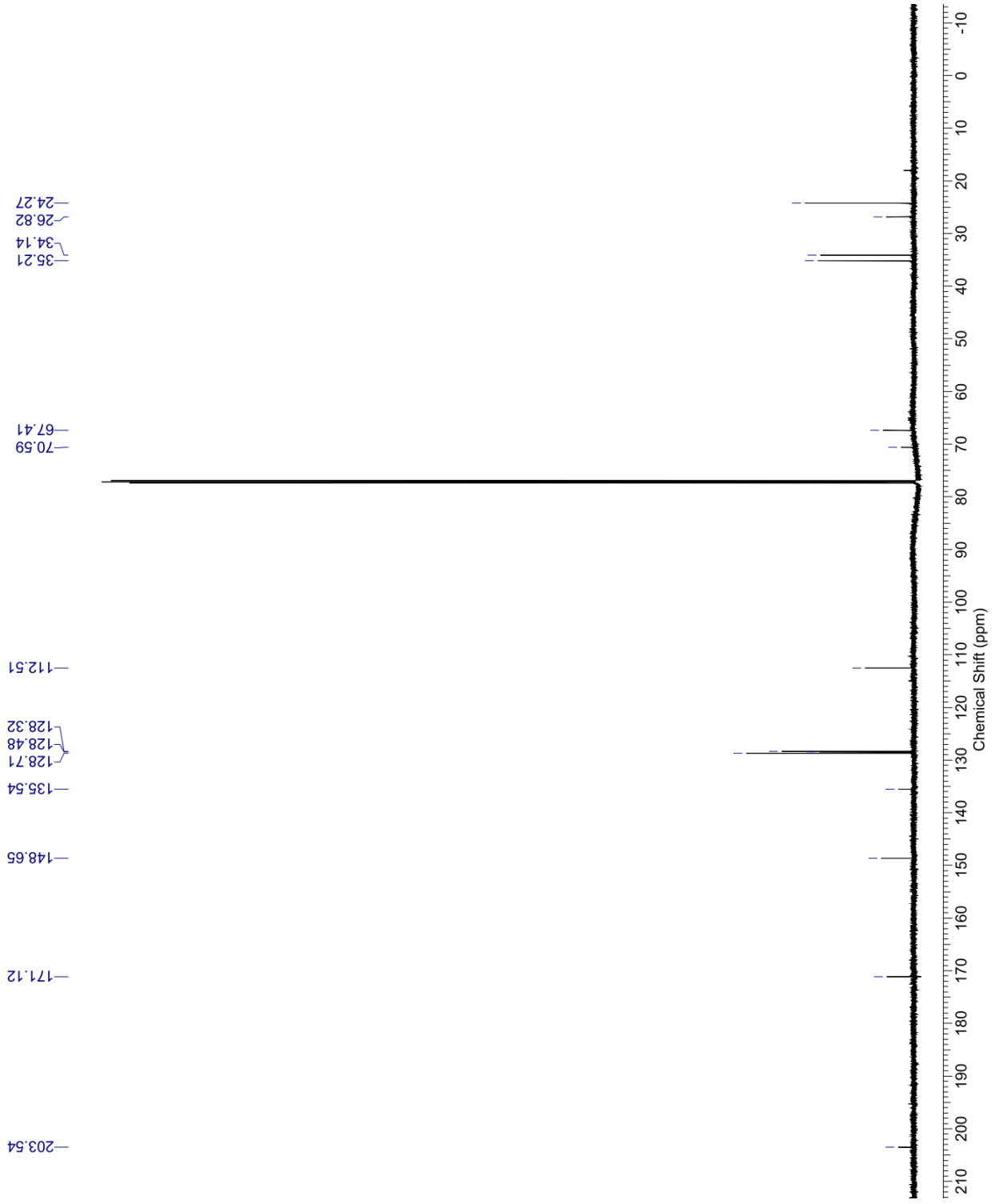

O
O
Me
OBn

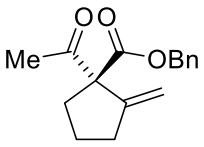
2g


7.37
7.36
7.35
7.34
7.32
7.32
7.31
5.28
5.21
5.21
5.18
2.44
2.43
2.43
2.42
2.41
2.21
2.20
2.18
2.17
1.75
1.73
1.70
4.80
1.04
1.09
1.83
3.12
4.00
2.11
Chemical Shift (ppm)


O
O
Me
OBn

2g

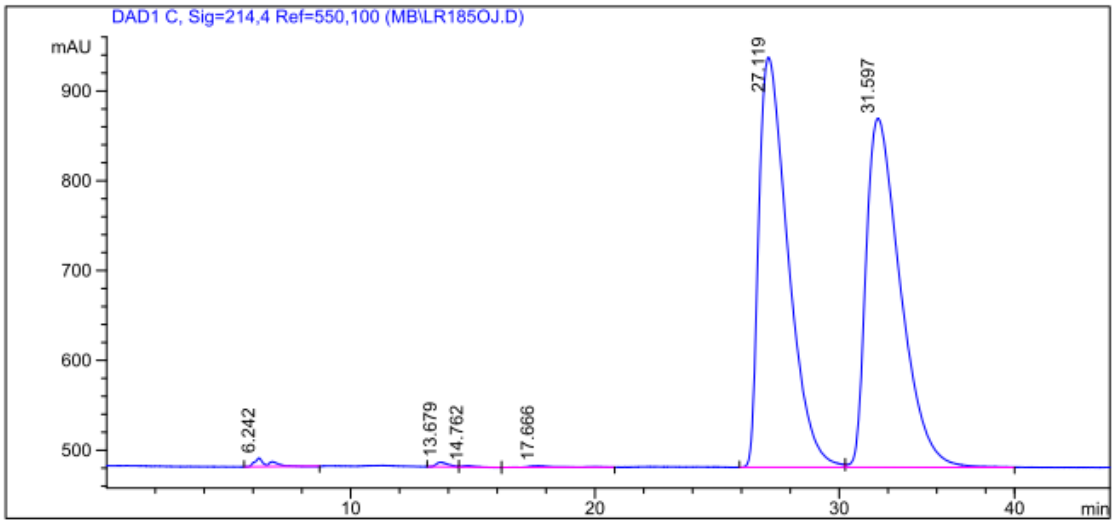

24.27
26.82
34.14
35.21
67.41
70.59
112.51
128.32
128.48
128.71
135.54
148.65
171.12
203.54
Chemical Shift (ppm)



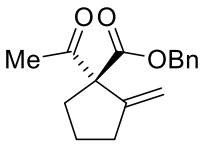
2g

Agilent Technologies

```
Sample Name:      LR185
Data file:        D:\ERNIE\MB\LR185OJ.D
Sample Info:      Mobile phase: n-Heptane/iPrOH 97:3 ;
                  The sample is solved in DCM/LM

Column:           DAICELOJ.M
Column info:      Chiralcel OJ (250 x 4.6) mm 5µ

Operator:         Analytical Lab AKEN

Injektion Time:       11:03:53
Injektion Date:       02.09.2016

Instrument Conditions:    At Start              At Stop

Temperature in°C:         30.0                    30.0
Pressure in bar:          20.0                    20.0
Flow in ml/min:           0.5                     0.5
```



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.24	0.49	9.59	367.90	0.48
2	13.68	0.54	5.11	175.94	0.23
3	14.76	0.47	1.56	52.54	0.07
4	17.67	0.86	1.72	103.04	0.13
5	27.12	1.29	456.53	37803.90	49.49
6	31.60	1.49	388.42	37882.87	49.59
Total				76386.19	100.00



2g

Sample Name: LR200
Data file: D:\ERNIE\MB\LR200OJ.D
Sample Info: Mobile phase: n-Heptane/iPrOH 97:3 ;
The sample is solved in DCM/LM

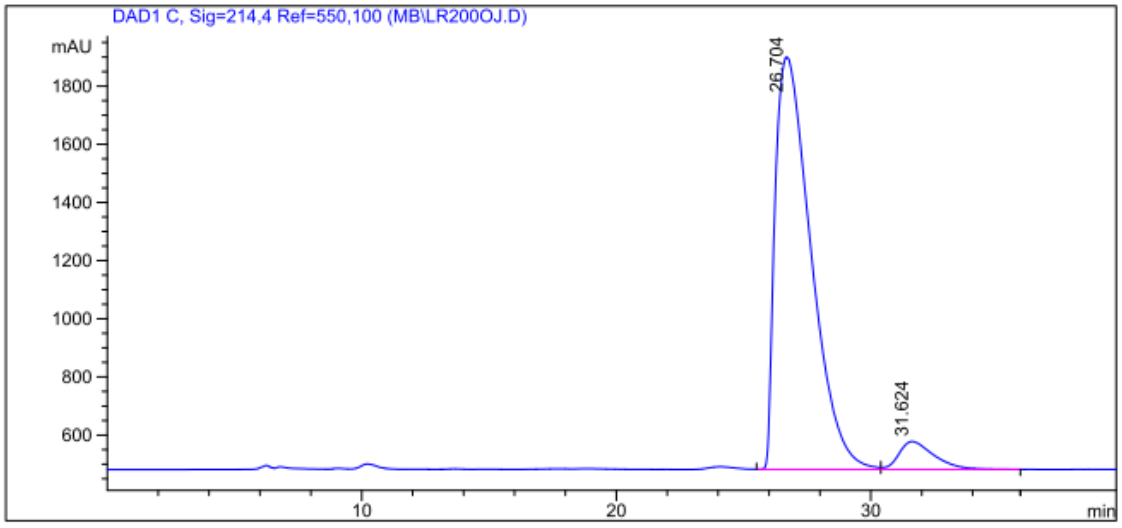
Agilent Technologies

Column: DAICELOJ.M
Column info: Chiralcel OJ (250 x 4.6) mm 5µ

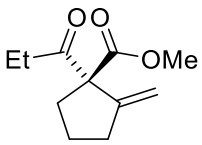
Operator: Analytical Lab AKEN

Injektion Time: 11:45:56
Injektion Date: 02.09.2016

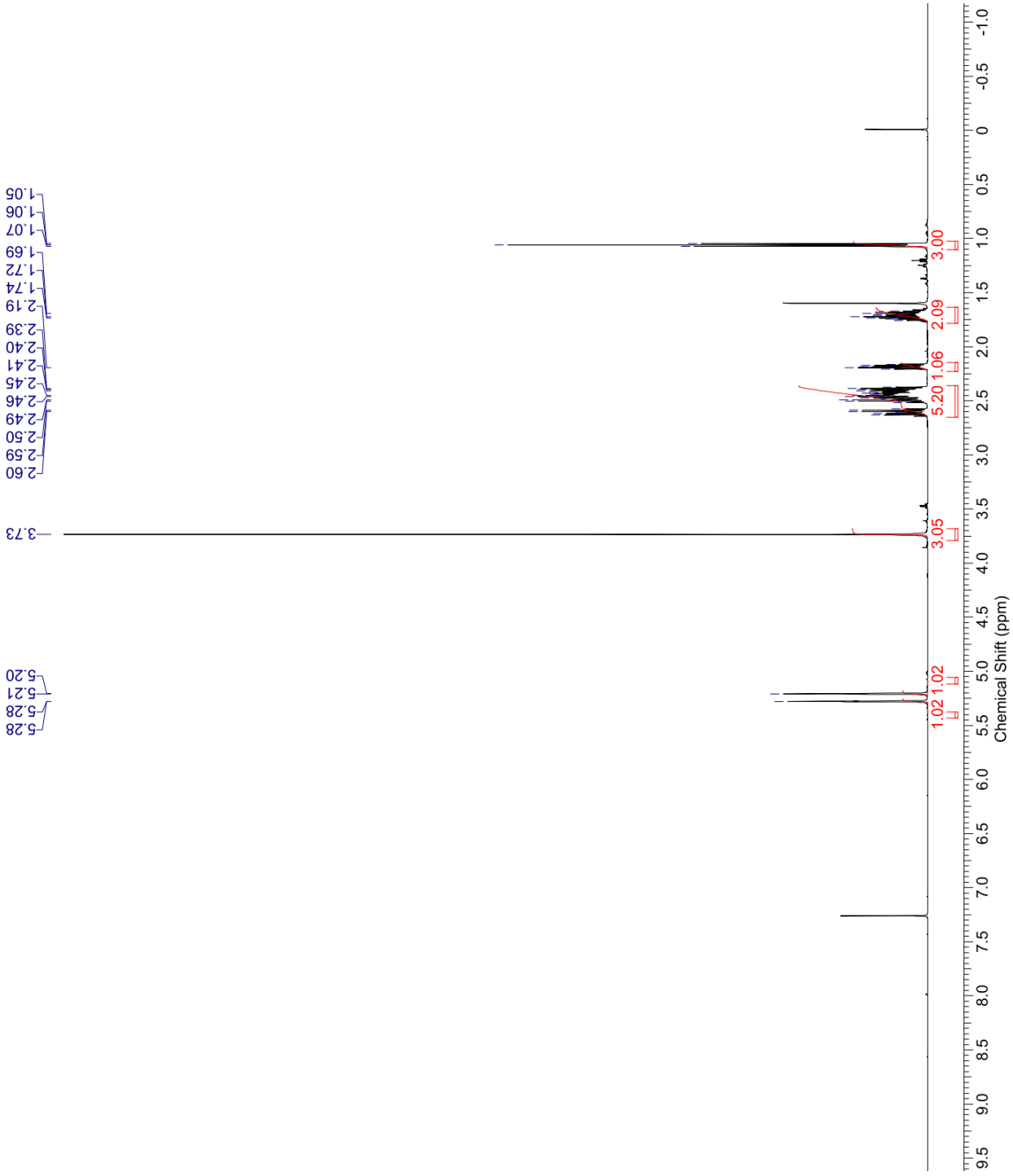
Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	20.4	19.8
Flow in ml/min:	0.5	0.5

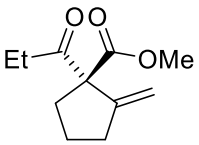


#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	26.70	1.55	1418.38	138449.31	93.75
2	31.62	1.44	96.02	9232.45	6.25
Total				147681.77	100.00

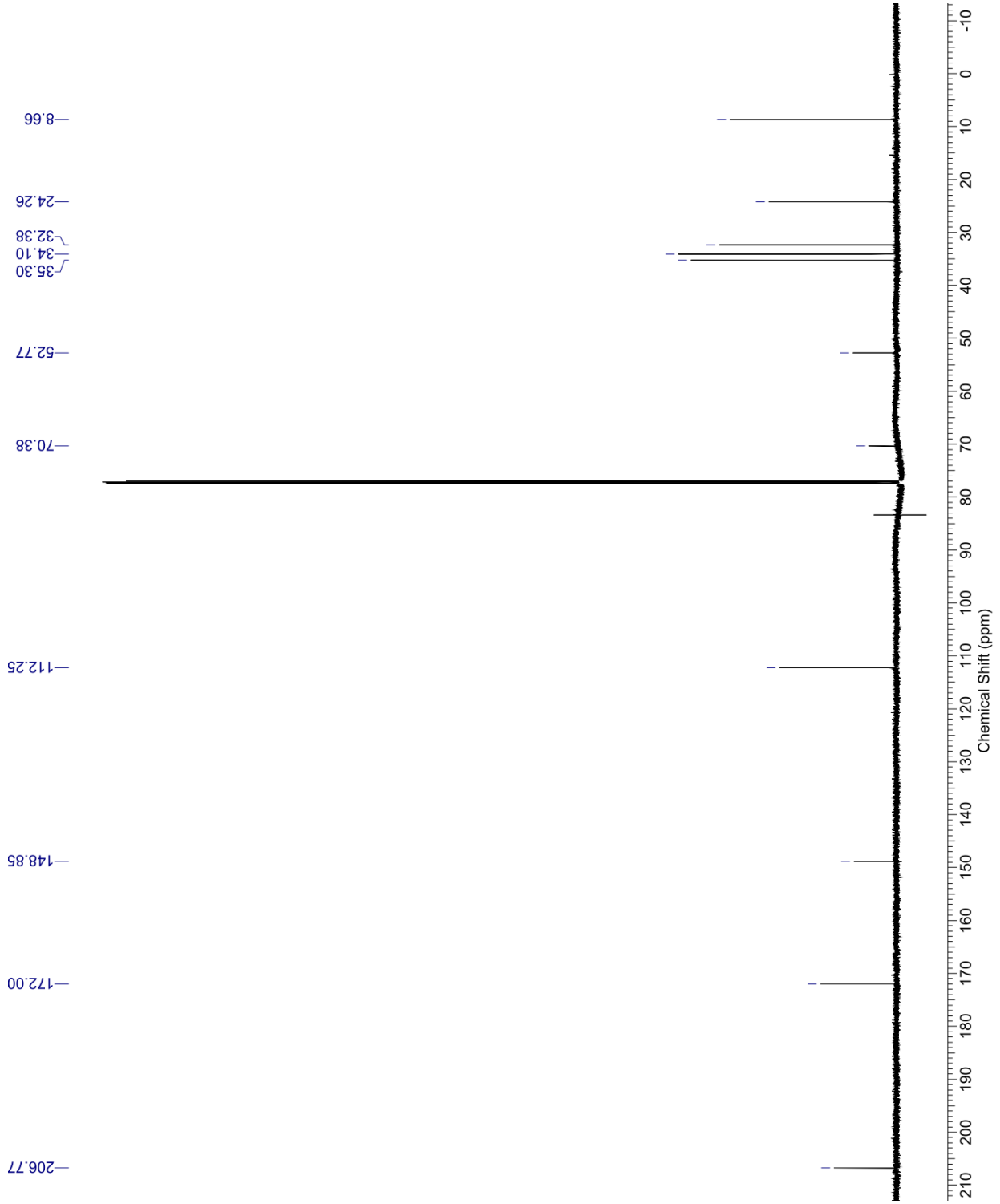

O
O
Et
OMe

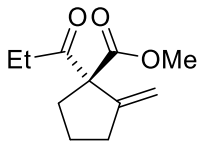
2h


1.05
1.06
1.07
1.69
1.72
1.74
2.19
2.39
2.40
2.41
2.45
2.46
2.49
2.50
2.59
2.60
3.73
5.20
5.21
5.28
5.28
3.00
2.09
1.06
5.20
3.05
1.02
1.02
-1.0
-0.5
0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
Chemical Shift (ppm)


O
O
Et
OMe

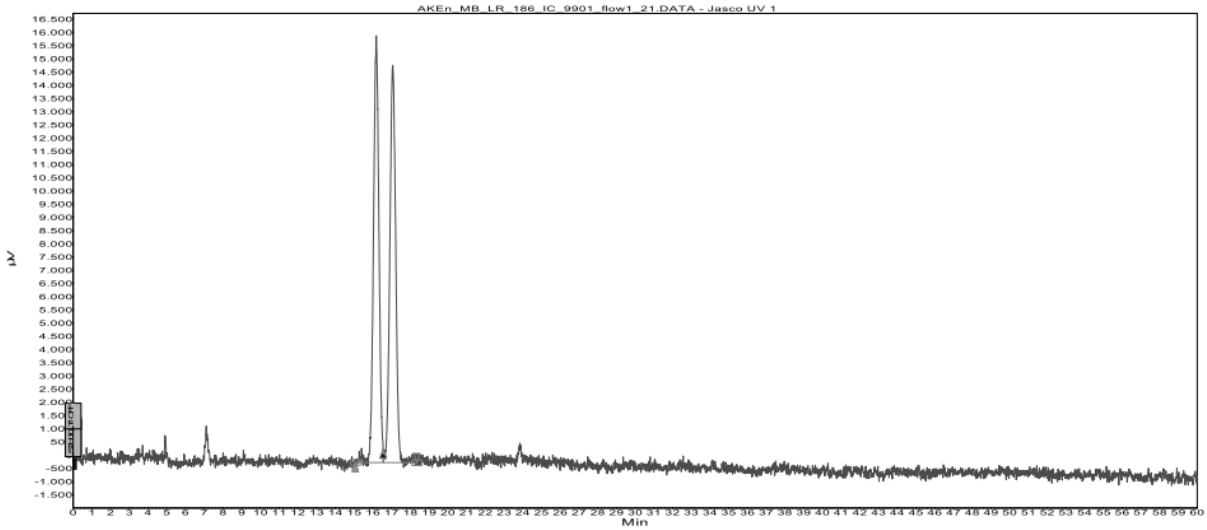
2h


8.66
24.26
32.38
34.10
35.30
52.77
70.38
112.25
148.85
172.00
206.77
Chemical Shift (ppm)



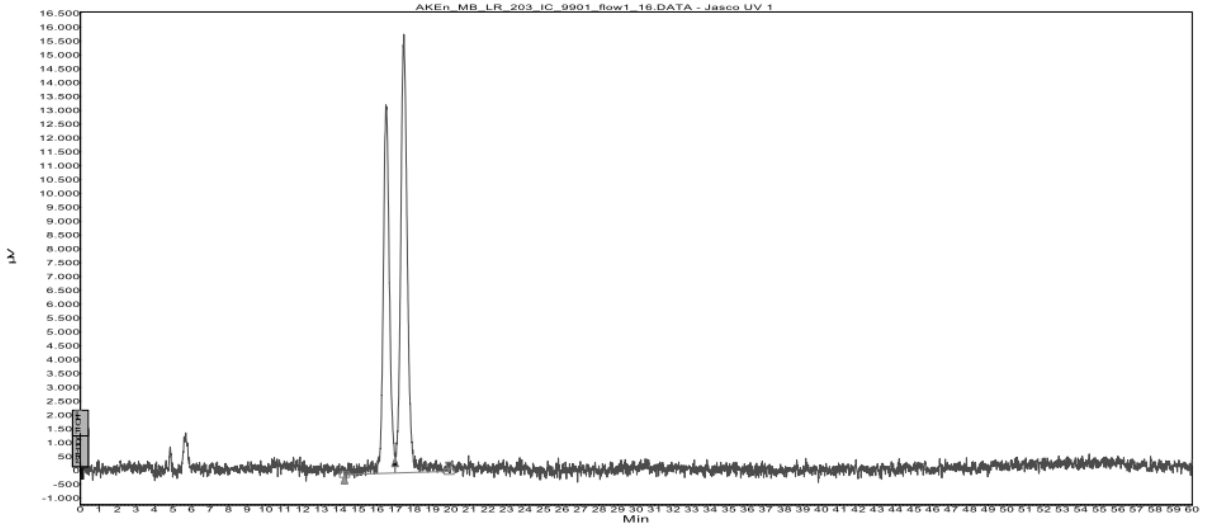
2h

Data file: AKEn_MB_LR_186_IC_9901_flow1_21.DATA
Method: HPLC1_IC_9901_flow1_acq_60
Date: 03.11.2016 23:00:26

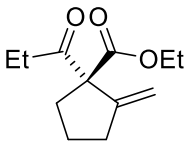


Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	15,062	16,183	16,550	49,924
2	16,550	17,058	18,347	50,076
Total				100,000

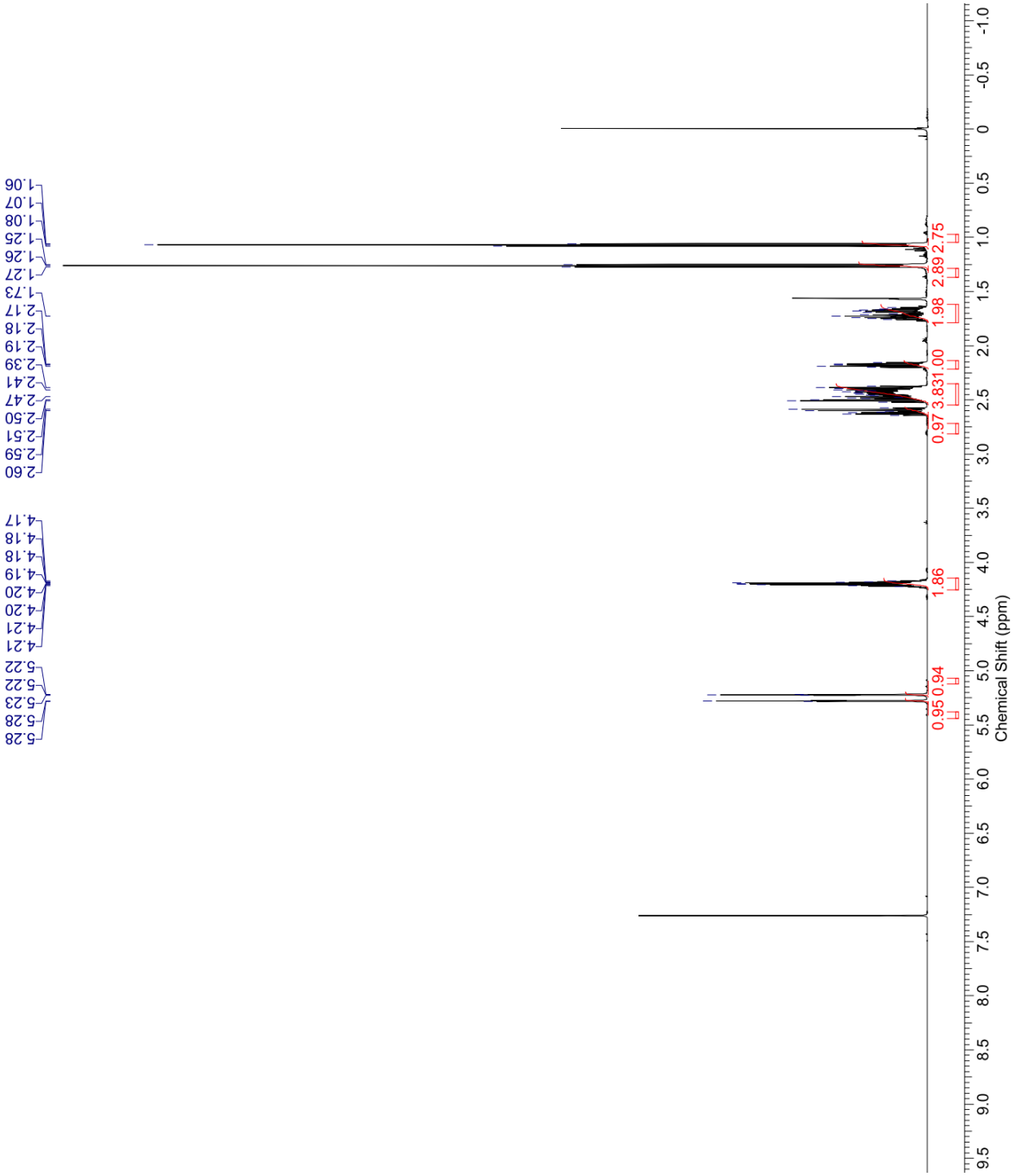
Data file: AKEn_MB_LR_203_IC_9901_flow1_16.DATA
Method: HPLC1_IC_9901_flow1_acq_60
Date: 08.11.2016 05:27:54

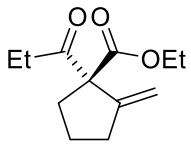


Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	14,256	16,483	16,983	44,274
2	16,983	17,458	19,897	55,726
Total				100,000

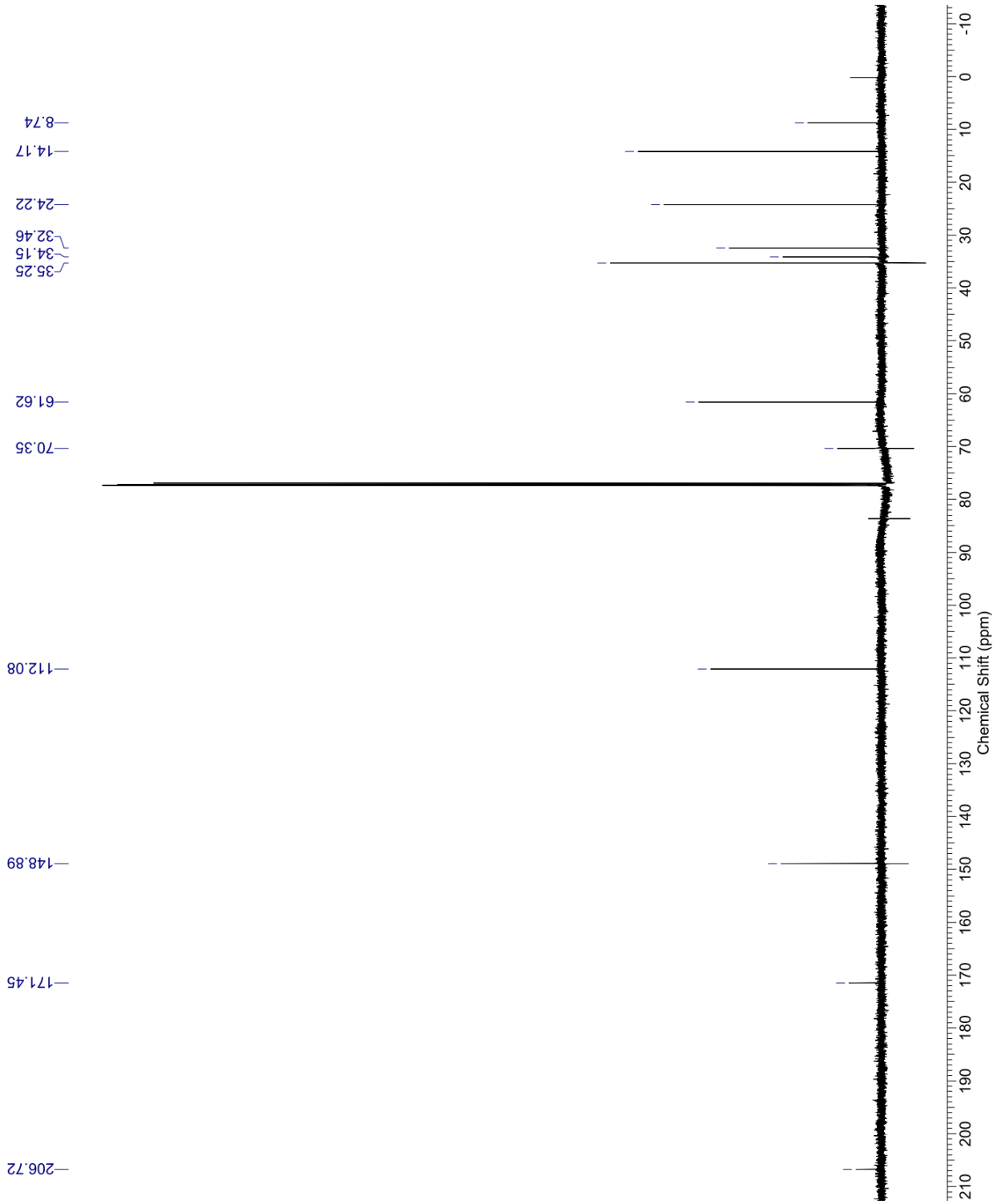

O
O
Et
OEt

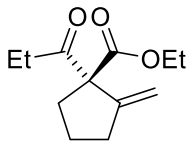
2i


1.06
1.07
1.08
1.25
1.26
1.27
1.73
2.17
2.18
2.19
2.39
2.41
2.47
2.50
2.51
2.59
2.60
4.17
4.18
4.18
4.19
4.20
4.20
4.21
4.21
5.22
5.22
5.23
5.28
5.28
2.75
2.89
1.98
1.00
3.83
0.97
1.86
0.94
0.95
-1.0
-0.5
0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
Chemical Shift (ppm)


O
O
Et
OEt

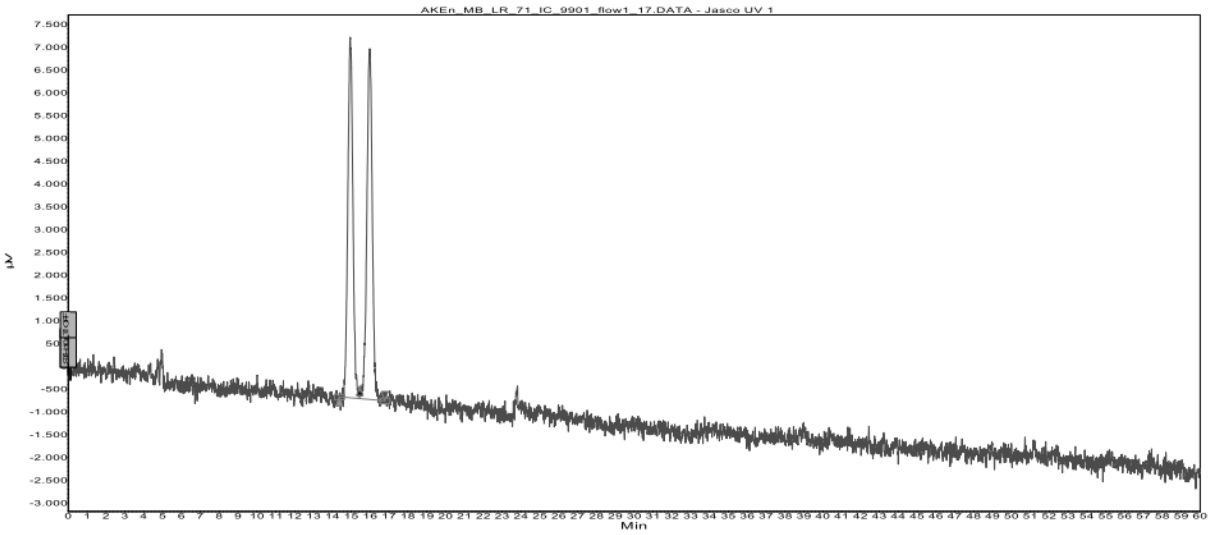
2i


8.74
14.17
24.22
32.46
34.15
35.25
61.62
70.35
112.08
148.89
171.45
206.72
Chemical Shift (ppm)



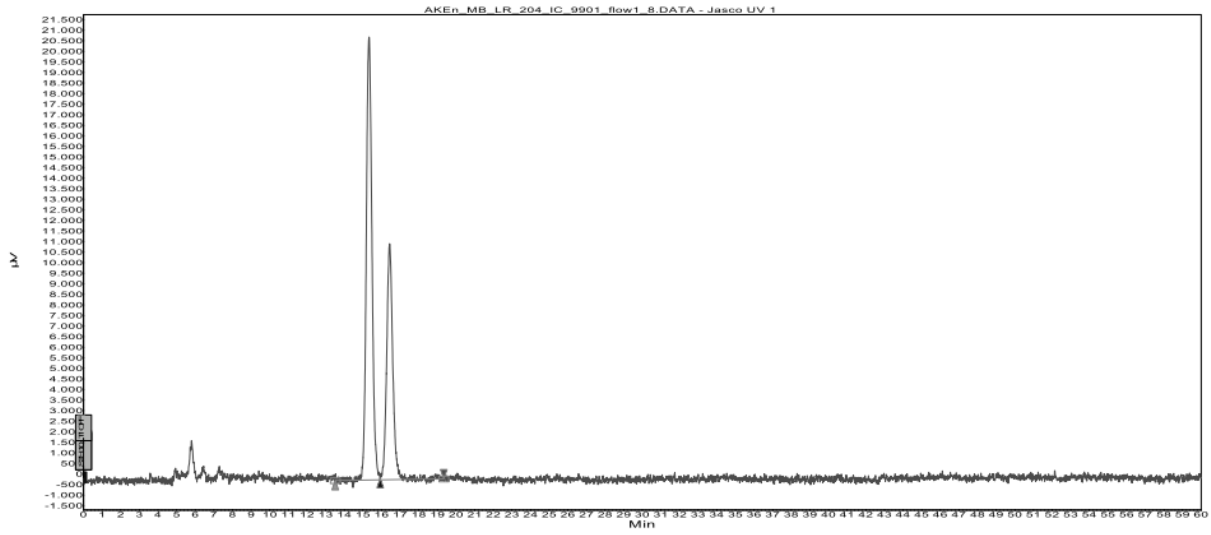
2i

Data file: AKEn_MB_LR_71_IC_9901_flow1_17.DATA
Method: HPLC1_IC_9901_flow1_acq_60
Date: 03.11.2016 18:49:44

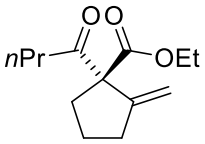


Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	14,372	14,942	15,457	48,930
2	15,457	15,983	16,783	51,070
Total				100,000

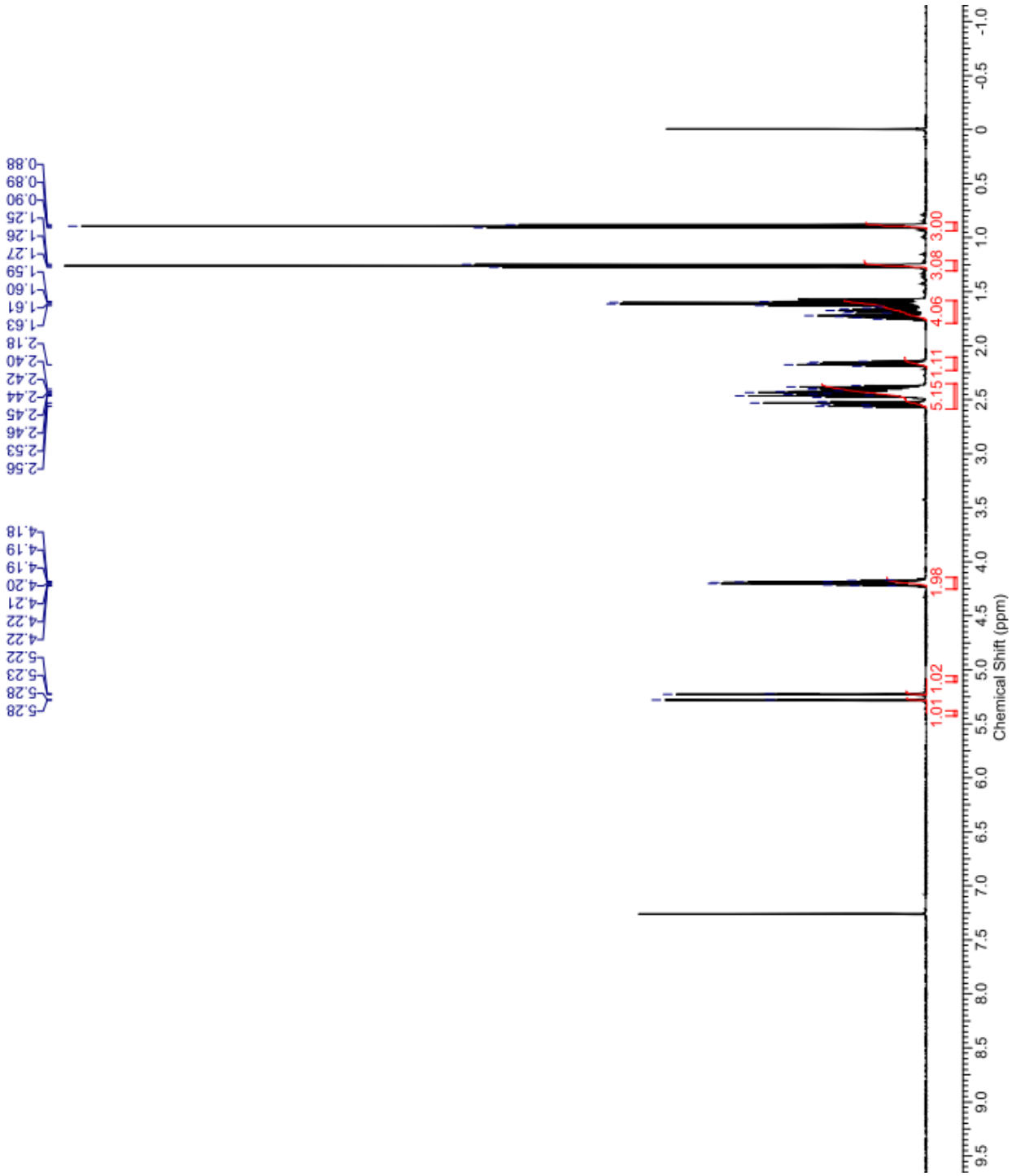
Data file: AKEn_MB_LR_204_IC_9901_flow1_8.DATA
Method: HPLC1_IC_9901_flow1_acq_60
Date: 07.11.2016 21:06:39

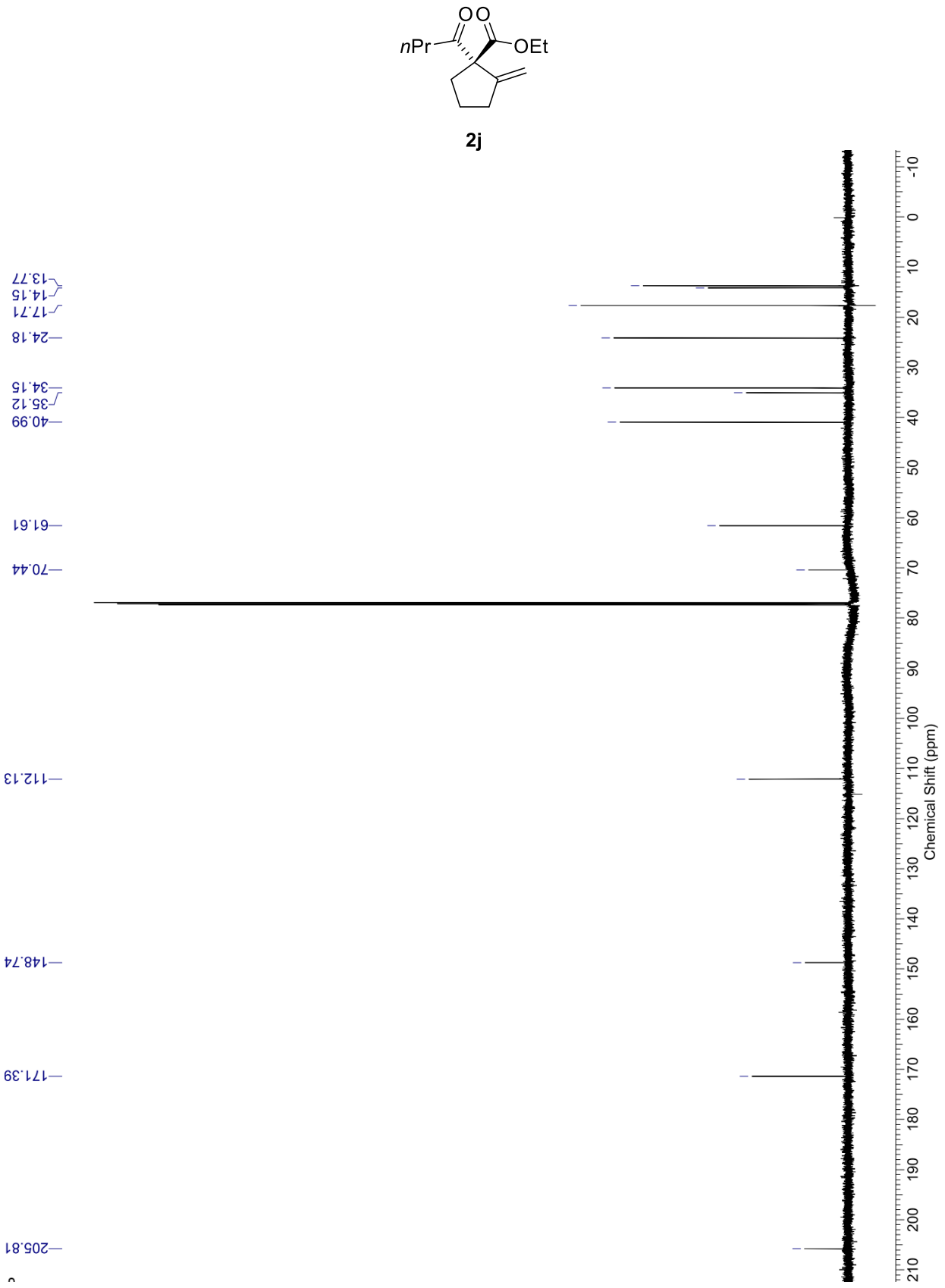


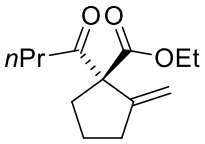
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	13,512	15,325	15,930	63,642
2	15,930	16,433	19,339	36,358
Total				100,000


O
O
nPr
OEt

2j


0.88
0.89
0.90
1.25
1.26
1.27
1.59
1.60
1.61
1.63
2.18
2.40
2.42
2.44
2.45
2.46
2.53
2.56
4.18
4.19
4.19
4.20
4.21
4.22
4.22
5.22
5.23
5.28
5.28
3.00
3.08
4.06
5.15
1.11
1.98
1.01
1.02
Chemical Shift (ppm)


nPr
O
O
OEt
2j
13.77
14.15
17.71
24.18
34.15
35.12
40.99
61.61
70.44
112.13
148.74
171.39
205.81
Chemical Shift (ppm)



2j

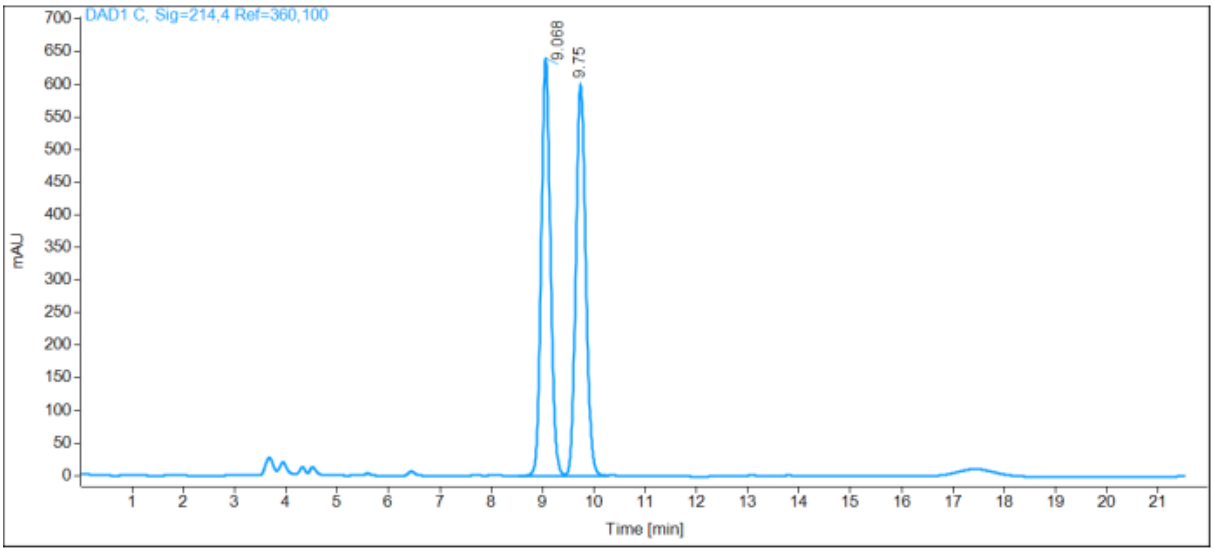
Sample name: **LR161**

Data file: C:\SNOOPY\MB\LR161 IC.D
Description: Mobile phase: n-Heptane/i-PrOH97:3 ;
The sample is solved in DCM/MP

Injection date: 9/21/2016 2:56:54 PM
Acq. Analysis method: CHIRALPAKIC1-6LNP.M

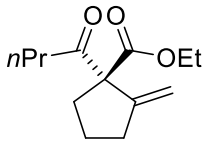
Column: Chiralpak IC, (150 x 4,6) mm, 5µ, SN: IC00CD-QF015

Pressure at start: 18 bar **Start flow:** 0.500 ml/min **Column oven:** 30 °C



Name LR161

RT [min]	Type	Area%	Area	Height	Width [min]
9.07	BV	49.82	7988.07	640.44	0.19
9.75	VV	50.18	8045.83	598.94	0.21
	Sum	100.00	16033.90		



2j

Sample name: **LR205**

Data file: C:\SNOOPY\MB\L205IC.D

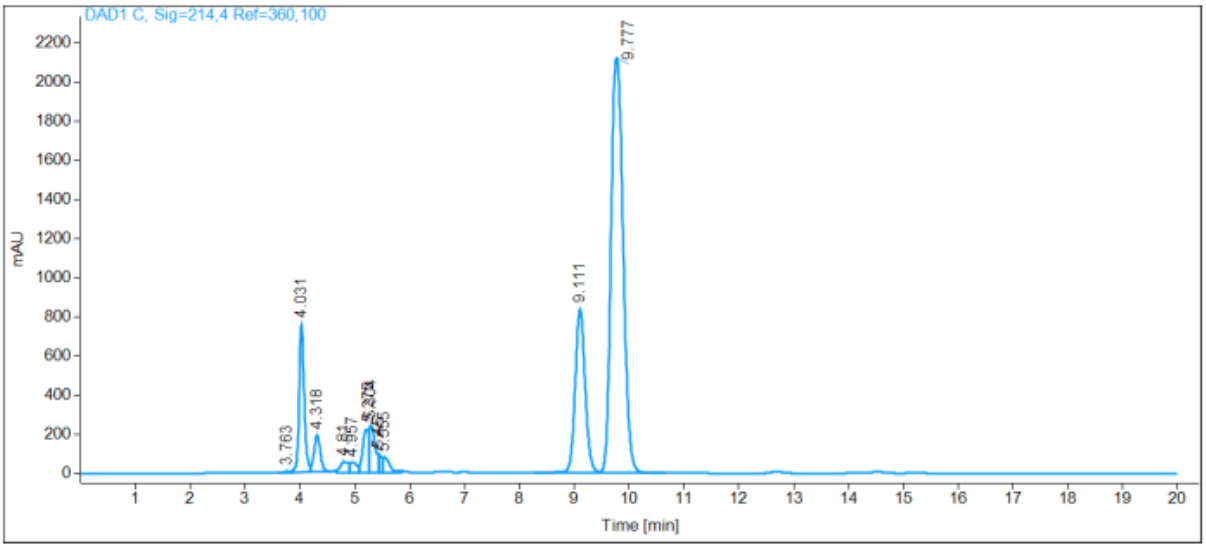
Description: Mobile phase: n-Heptane/i-PrOH 97:3 ;
The sample is solved in DCM/MP

Injection date: 9/21/2016 3:20:54 PM

Acq. Analysis method: CHIRALPAKIC1-6LNP.M

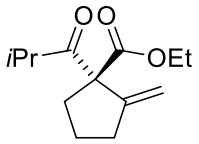
Column: Chiralpak IC, (150 x 4,6) mm, 5µ, SN: IC00CD-QF015

Pressure at start: 19 bar **Start flow:** 0.500 ml/min **Column oven:** 29.99 °C

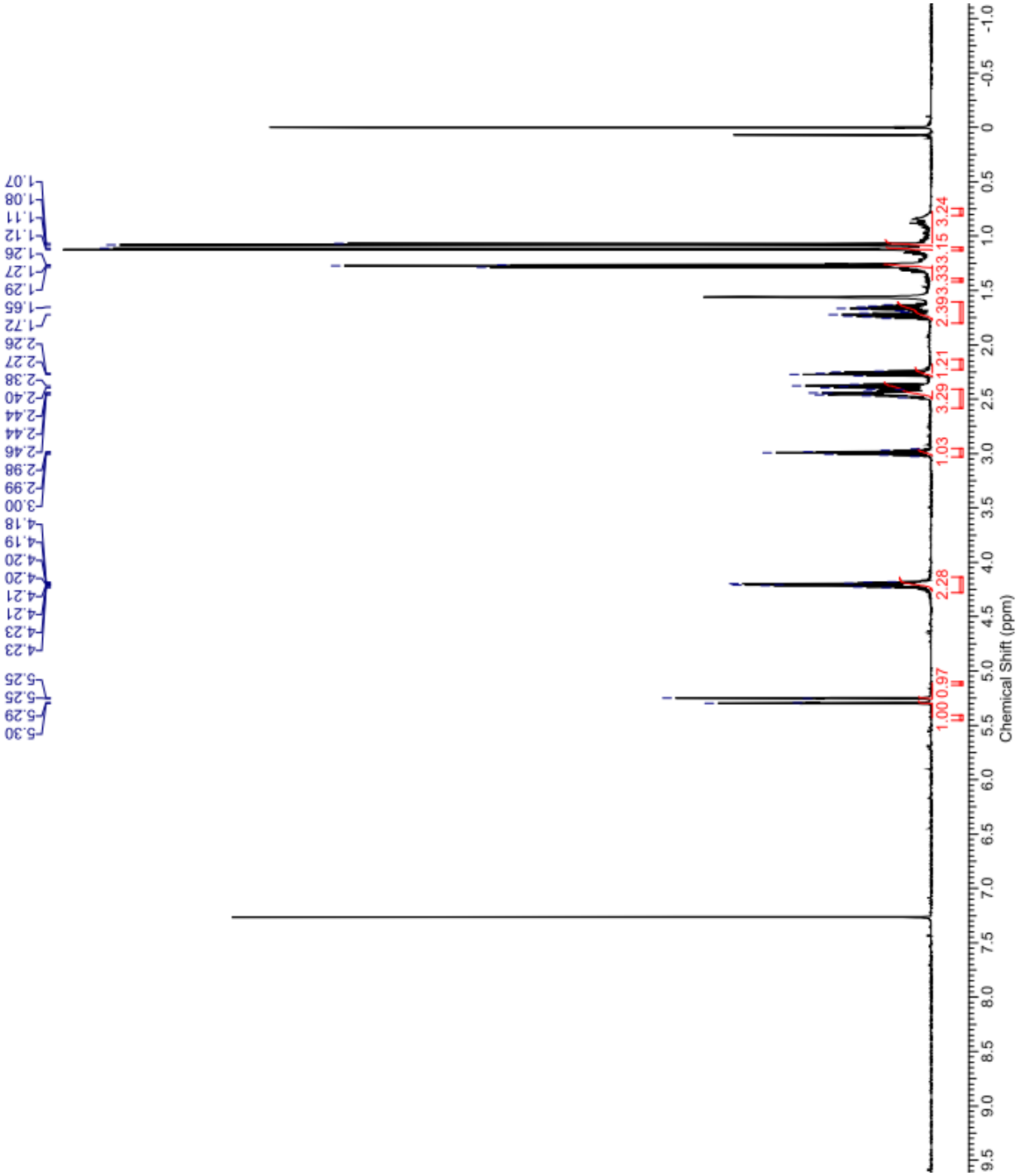


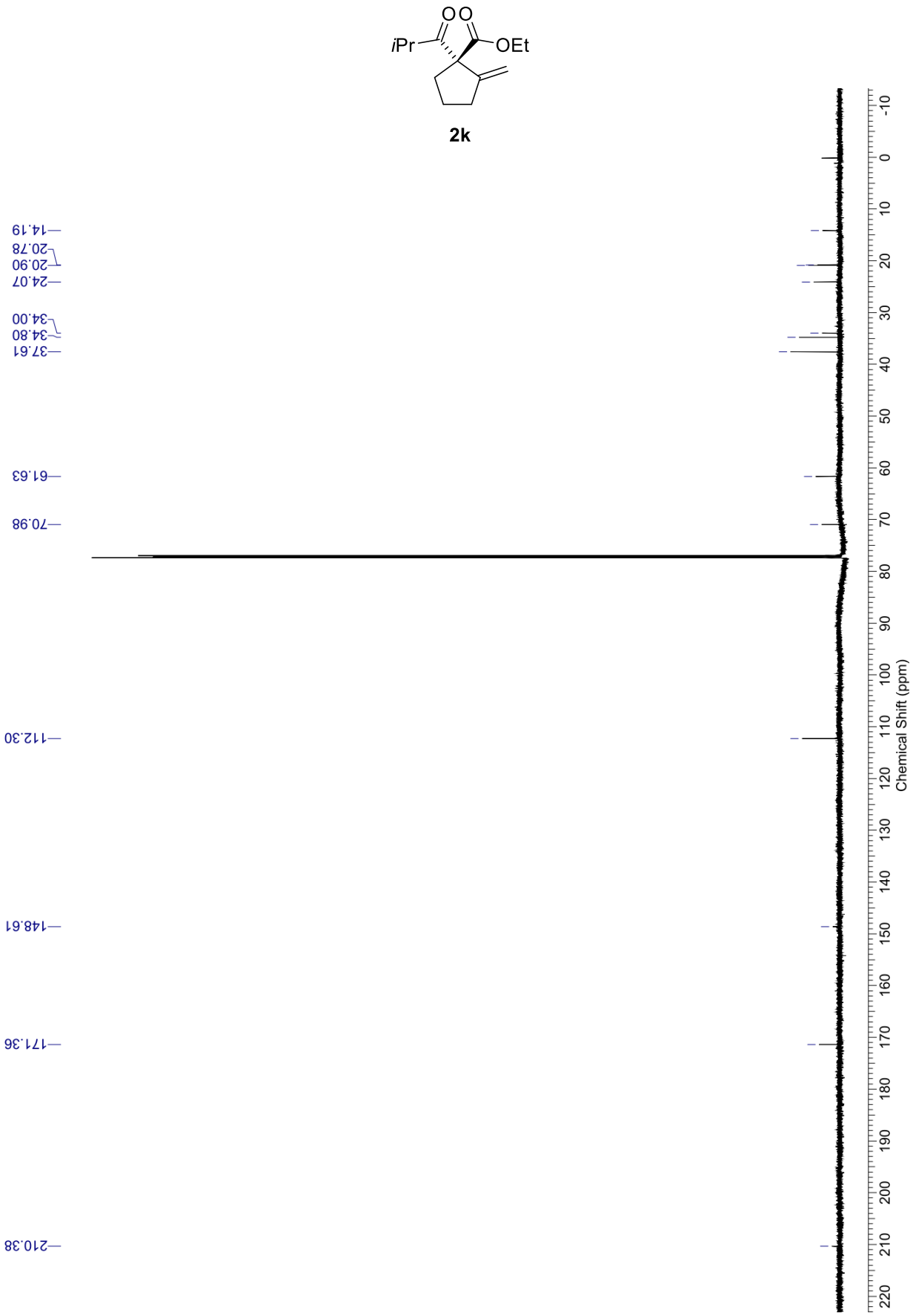
Name LR205

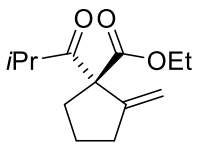
RT [min]	Type	Area%	Area	Height	Width [min]
3.76	BV	0.07	36.71	5.84	0.10
4.03	VV	8.92	4892.54	759.50	0.10
4.32	VB	2.74	1504.14	186.67	0.13
4.81	MF	1.10	603.23	52.76	0.19
4.96	FM	0.83	456.95	51.47	0.15
5.28	MF	3.30	1807.83	224.71	0.13
5.30	MF	3.04	1665.53	240.17	0.12
5.45	MF	0.66	359.36	87.41	0.07
5.56	FM	1.14	623.75	73.77	0.14
9.11	BV	19.32	10595.71	836.95	0.20
9.78	VV	58.88	32287.12	2121.15	0.24
	Sum	100.00	54832.86		


O
O
iPr
OEt

2k


1.07
1.08
1.11
1.12
1.26
1.27
1.29
1.65
1.72
2.26
2.27
2.38
2.40
2.44
2.44
2.46
2.98
2.99
3.00
4.18
4.19
4.20
4.20
4.21
4.23
4.23
5.25
5.25
5.29
5.30
1.00
0.97
2.28
1.03
3.29
1.21
2.39
3.33
3.15
3.24
Chemical Shift (ppm)


O
O
iPr
OEt
2k
14.19
20.78
20.90
24.07
34.00
34.80
37.61
61.63
70.98
112.30
148.61
171.36
210.38
Chemical Shift (ppm)



2k

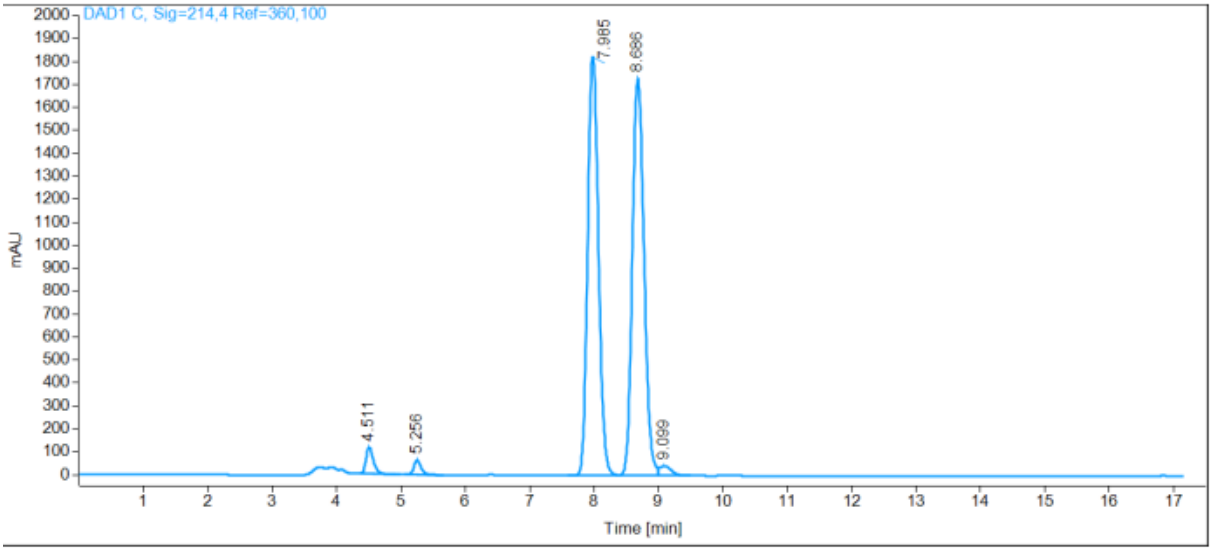
Sample name: **LR130**

Data file: C:\SNOOPY\MB\LR130 IC.D
Description: Mobile phase: n-Heptane/i-PrOH97:3 ;
The sample is solved in DCM/MP

Injection date: 9/22/2016 7:50:01 AM
Acq. Analysis method: CHIRALPAKIC1-6LNP.M

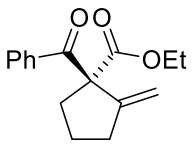
Column: Chiralpak IC, (150 x 4,6) mm, 5µ, SN: IC00CD-QF015

Pressure at start: 19 bar **Start flow:** 0.500 ml/min **Column oven:** 30.01 °C

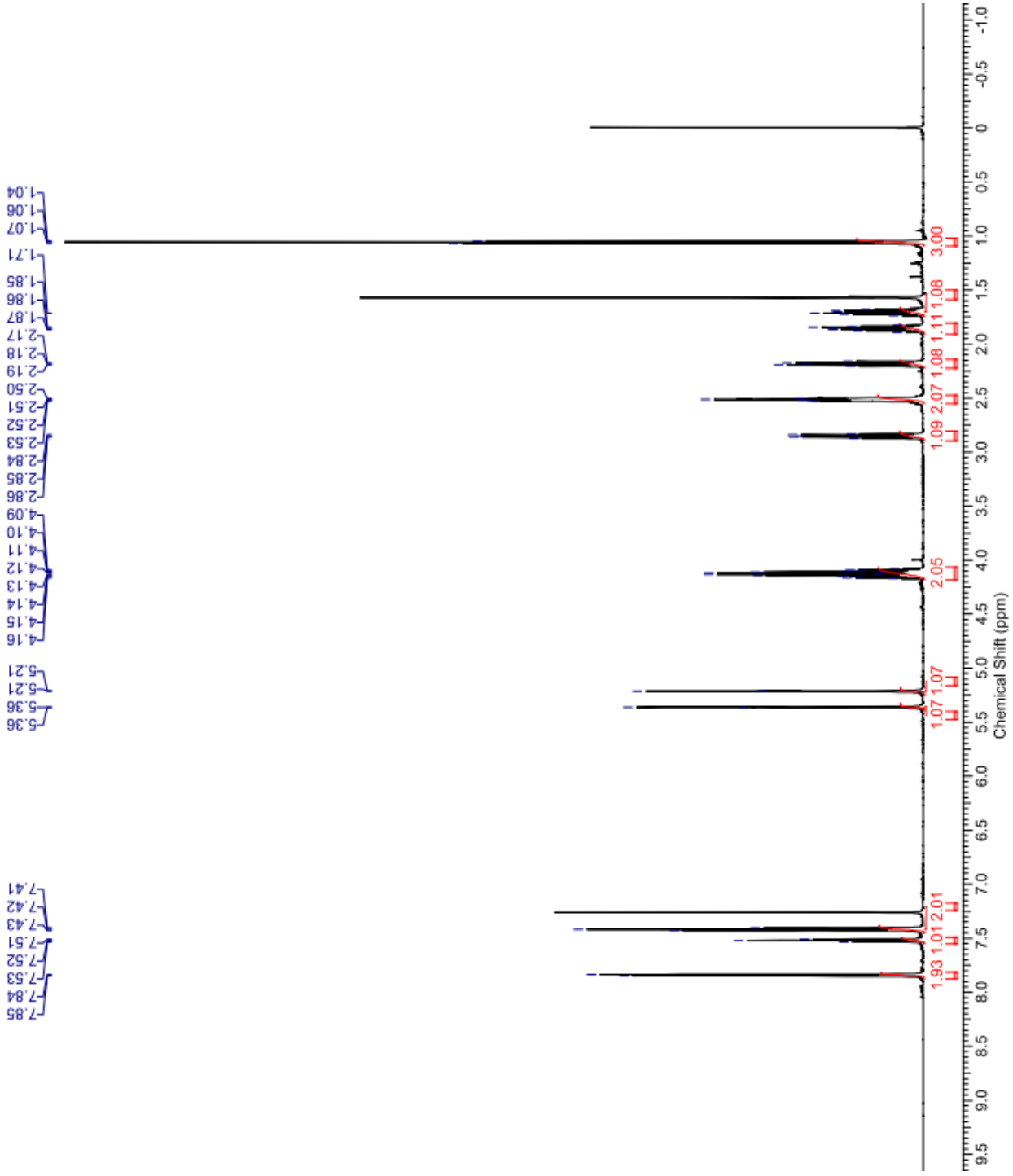


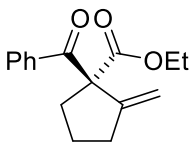
Name LR130

RT [min]	Type	Area%	Area	Height	Width [min]
4.51	BB	2.04	916.03	115.23	0.12
5.26	BB	1.11	501.39	63.32	0.12
7.98	BB	47.22	21237.03	1823.24	0.18
8.69	BV	48.47	21799.21	1726.61	0.20
9.10	VB	1.16	520.58	41.61	0.19
	Sum	100.00	44974.25		

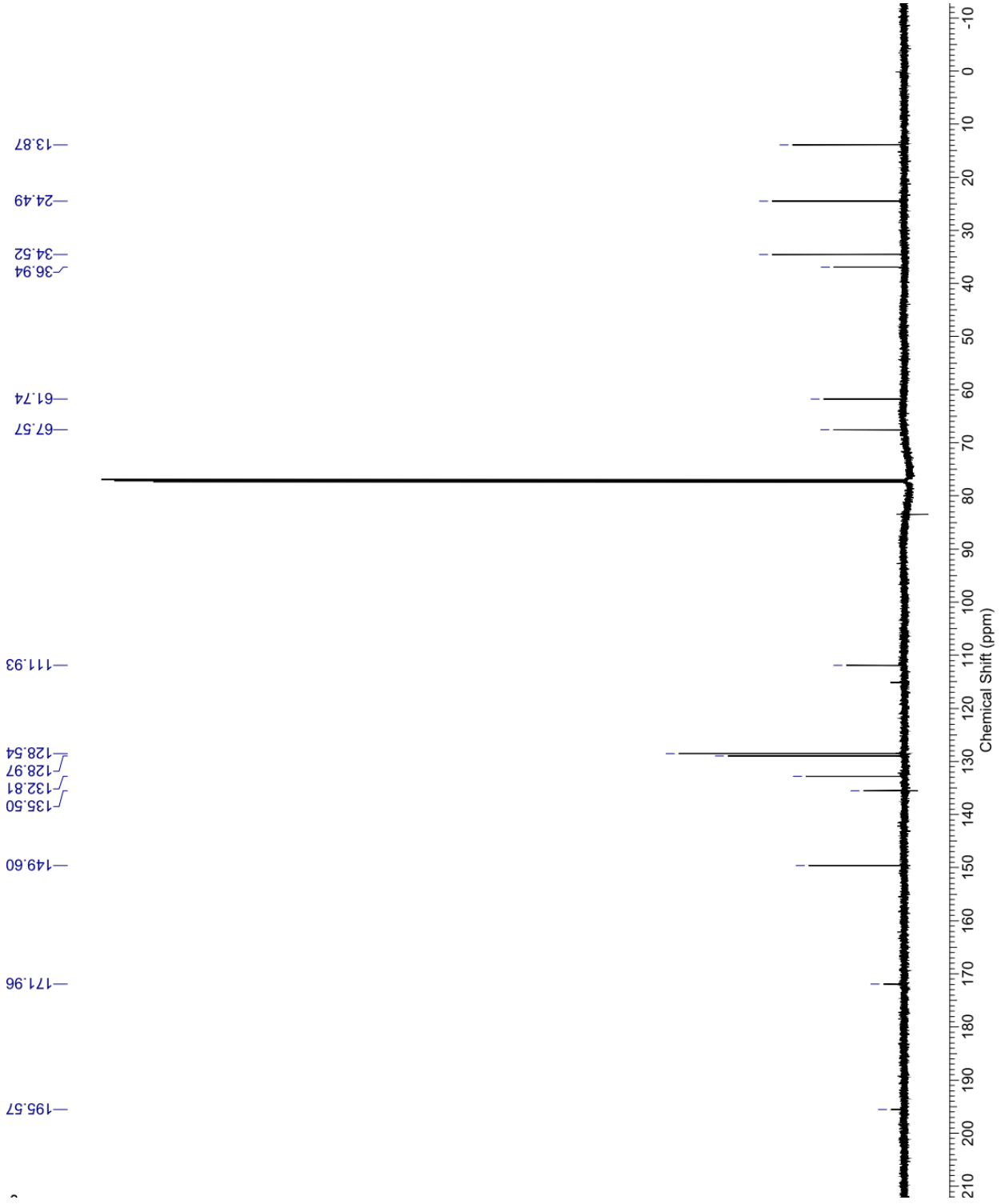

O
O
Ph
OEt

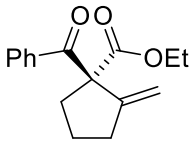
2l


1.04
1.06
1.07
1.71
1.85
1.86
1.87
2.17
2.18
2.19
2.50
2.51
2.52
2.53
2.84
2.85
2.86
4.09
4.10
4.11
4.12
4.13
4.14
4.15
4.16
5.21
5.21
5.36
5.36
7.41
7.42
7.43
7.51
7.52
7.53
7.84
7.85
3.00
1.08
1.11
1.08
2.07
1.09
2.05
1.07
1.07
2.01
1.01
1.93
Chemical Shift (ppm)


O
O
Ph
OEt

2l


13.87
24.49
34.52
36.94
61.74
67.57
111.93
128.54
128.97
132.81
135.50
149.60
171.96
195.57
Chemical Shift (ppm)



2l

Sample Name: LR158
Data file: D:\ERNIE\MB\LR158AD.D
Sample Info: Mobile phase: n-Heptane/iPrOH 97:3 ;
The sample is solved in DCM/LM

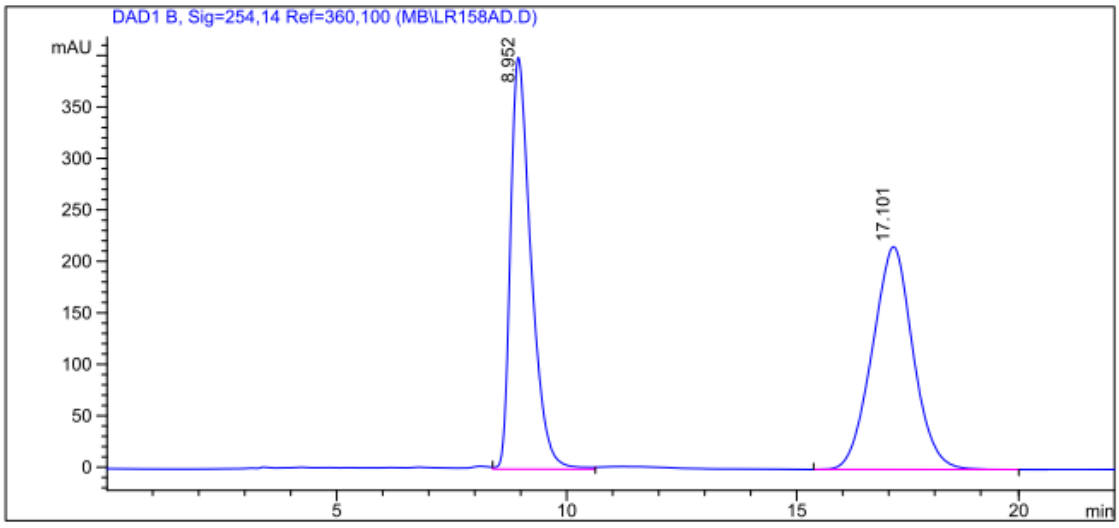
Agilent Technologies

Column: DAICELOJ.M
Column info: Chiralcel OJ (250 x 4.6) mm 5µ

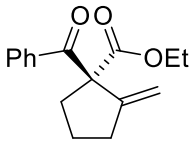
Operator: Analytical Lab AKEN

Injektion Time: 09:44:54
Injektion Date: 15.09.2016

Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.1
Pressure in bar:	38.4	38.1
Flow in ml/min:	1.0	1.0



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	8.95	0.48	398.93	12446.01	48.40
2	17.10	0.96	216.06	13266.52	51.60
Total				25712.53	100.00



2l

Sample Name: LR214
Data file: D:\ERNIE\MB\LR214AD.D
Sample Info: Mobile phase: n-Heptane/iPrOH 97:3 ;
The sample is solved in DCM/LM

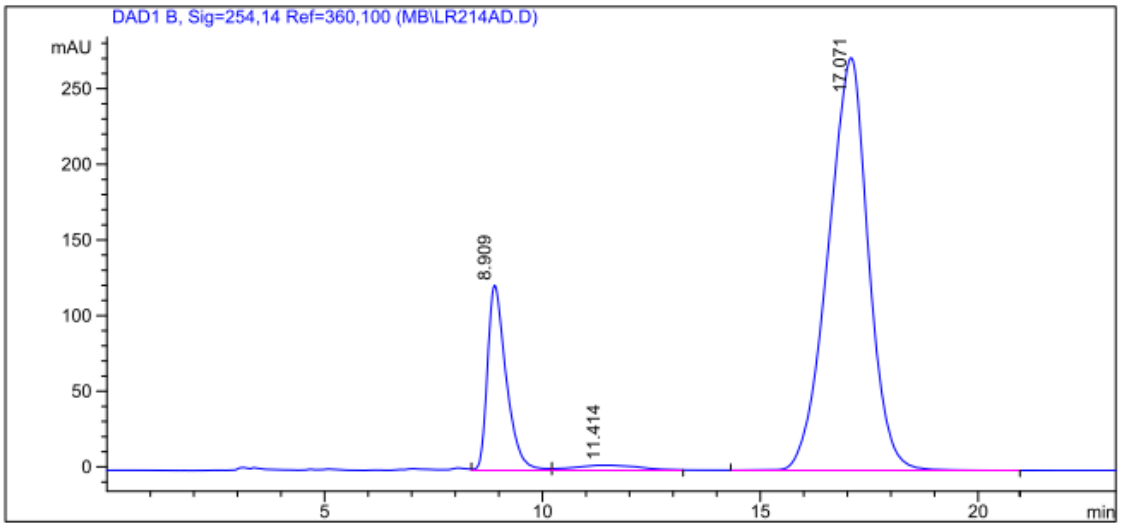
Agilent Technologies

Column: DAICELOJ.M
Column info: Chiralcel OJ (250 x 4.6) mm 5µ

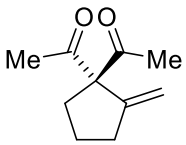
Operator: Analytical Lab AKEN

Injektion Time: 10:07:37
Injektion Date: 15.09.2016

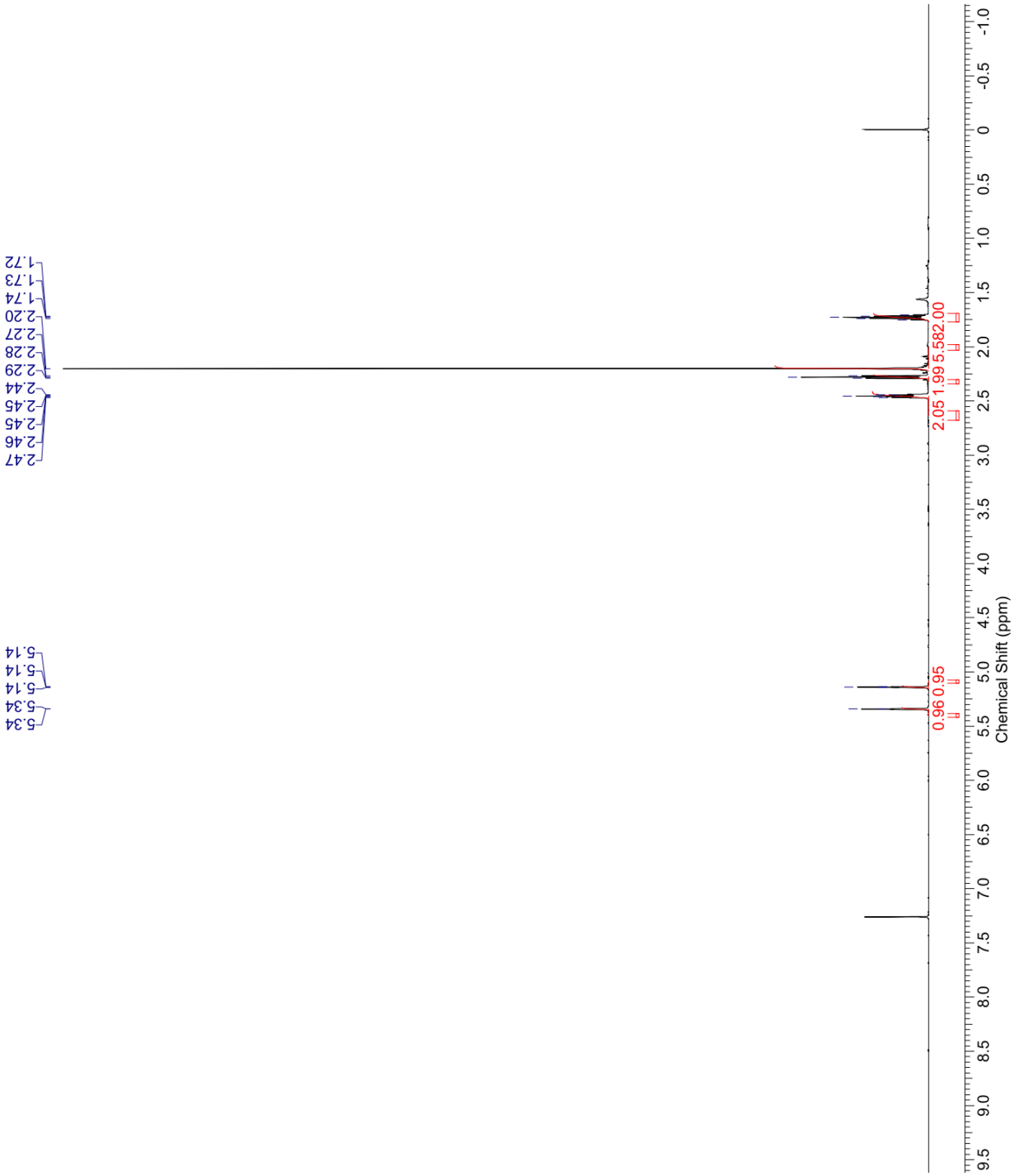
Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.1	30.3
Pressure in bar:	38.5	38.2
Flow in ml/min:	1.0	1.0

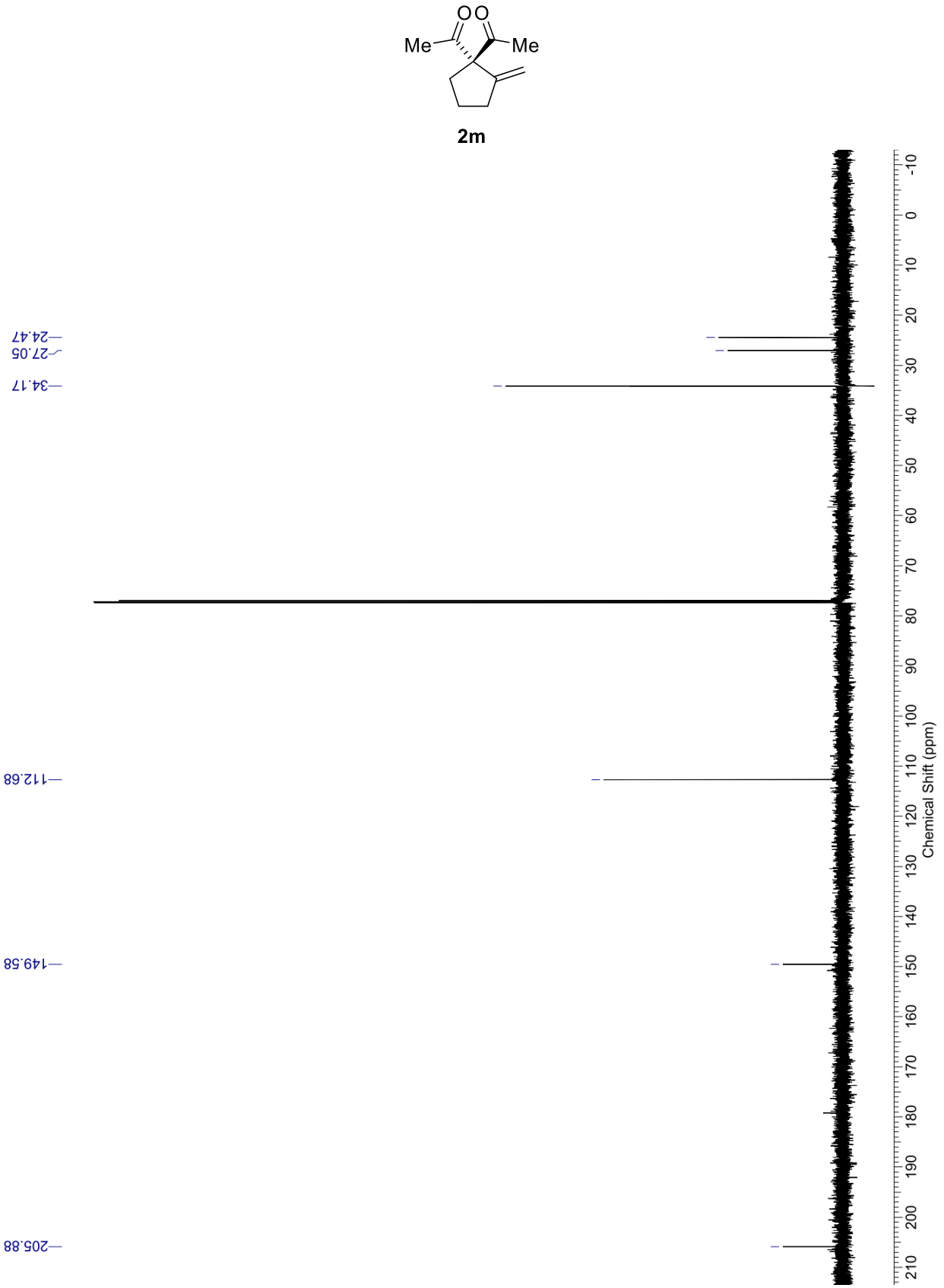


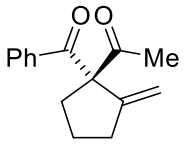
#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	8.91	0.45	122.24	3660.20	16.99
2	11.41	1.45	3.43	360.65	1.67
3	17.07	0.99	271.66	17518.38	81.33
Total				21539.23	100.00


O
O
Me
Me

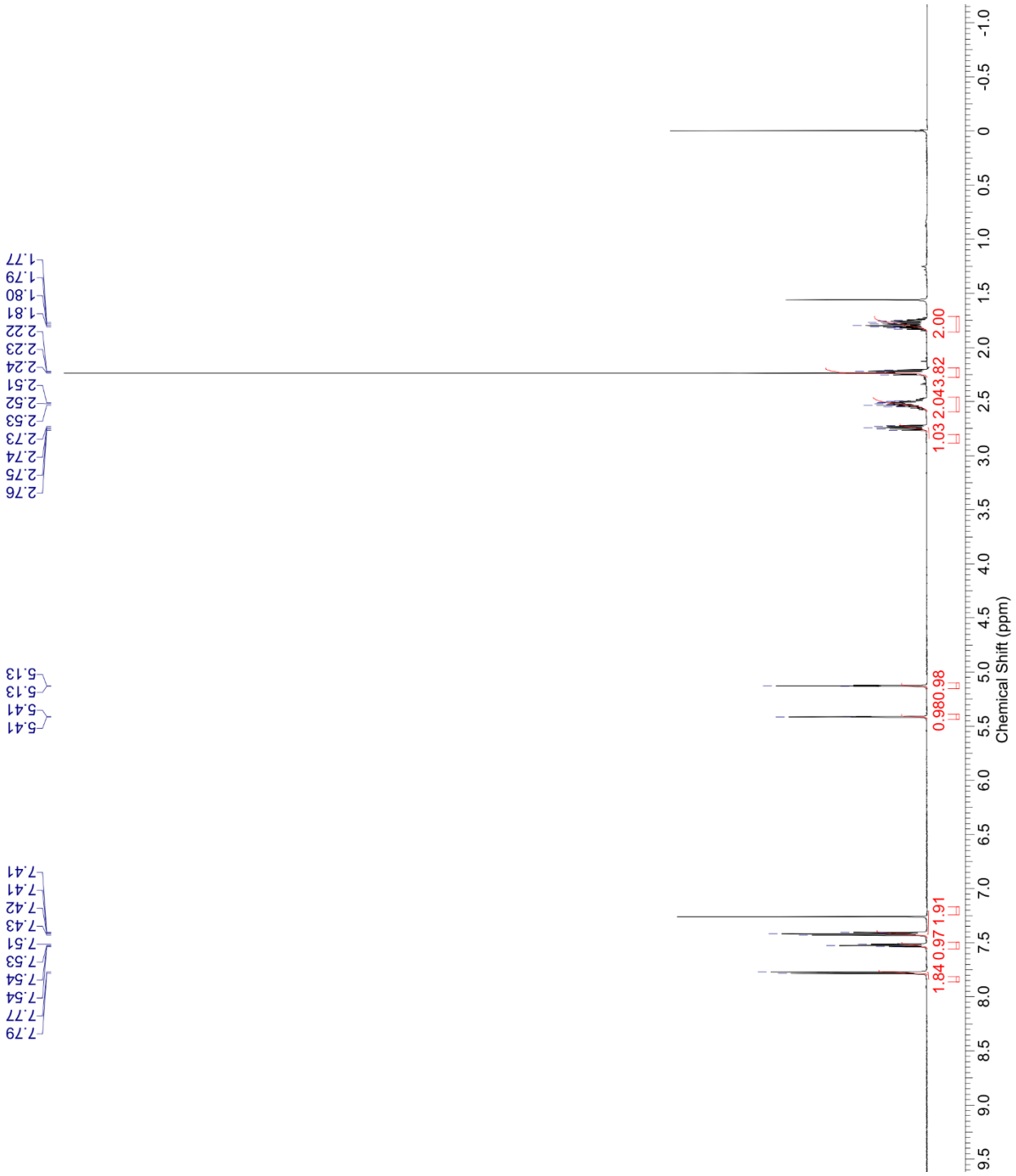
2m

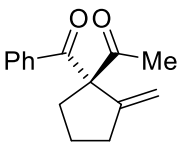

1.72
1.73
1.74
2.20
2.27
2.28
2.29
2.44
2.45
2.45
2.46
2.47
5.14
5.14
5.14
5.34
5.34
2.05
1.99
5.58
2.00
0.96
0.95
Chemical Shift (ppm)


O
O
Me
Me
2m
24.47
27.05
34.17
112.68
149.58
205.88
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
Chemical Shift (ppm)

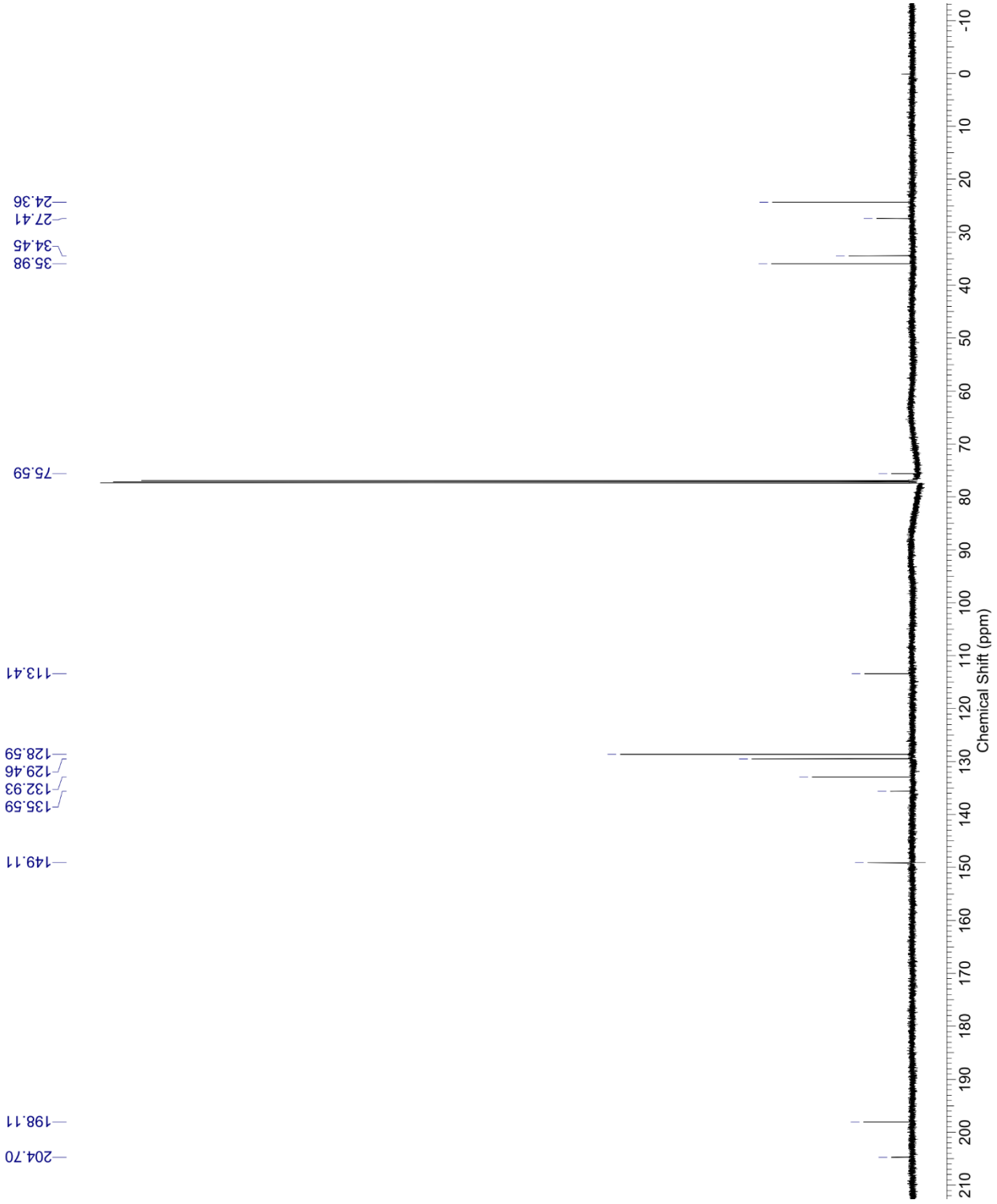

O
O
Ph
Me

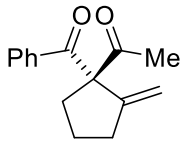
2n


1.77
1.79
1.80
1.81
2.22
2.23
2.24
2.51
2.52
2.53
2.73
2.74
2.75
2.76
5.13
5.13
5.41
5.41
7.41
7.41
7.42
7.43
7.51
7.53
7.54
7.54
7.77
7.79
2.00
2.04
3.82
1.03
0.98
0.98
1.91
0.97
1.84
-1.0
-0.5
0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
Chemical Shift (ppm)


O
O
Ph
Me

2n


24.36
27.41
34.45
35.98
75.59
113.41
128.59
129.46
132.93
135.59
149.11
198.11
204.70
Chemical Shift (ppm)



2n

Agilent Technologies

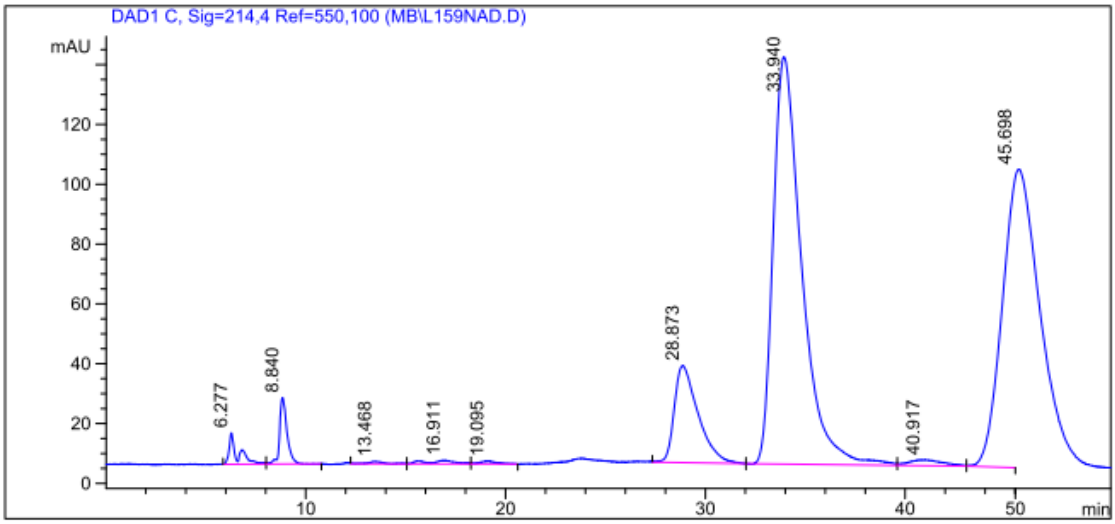
Sample Name: LR159
Data file: D:\ERNIE\MB\L159NAD.D
Sample Info: Mobile phase: n-Heptane/iPrOH 97:3 ;
The sample is solved in DCM/LM

Column: DAICELOJ.M
Column info: Chiralcel OJ (250 x 4.6) mm 5µ

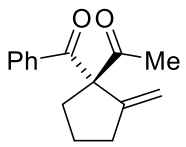
Operator: Analytical Lab AKEN

Injektion Time: 11:11:12
Injektion Date: 15.09.2016

Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.6	31.0
Pressure in bar:	18.2	18.0
Flow in ml/min:	0.5	0.5



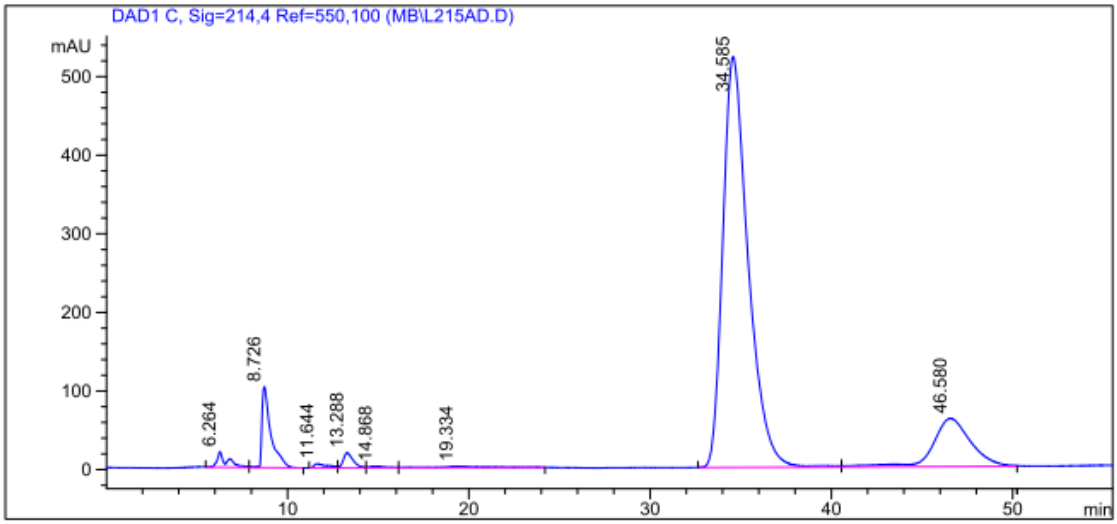
#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.28	0.40	10.52	315.86	1.04
2	8.84	0.39	22.16	565.34	1.86
3	13.47	0.87	0.79	44.84	0.15
4	16.91	1.36	1.19	118.69	0.39
5	19.10	0.88	0.94	55.35	0.18
6	28.87	1.22	32.41	2683.74	8.82
7	33.94	1.51	135.89	13466.42	44.24
8	40.92	1.81	1.88	229.46	0.75
9	45.70	2.00	99.39	12961.19	42.58
Total				30440.89	100.00



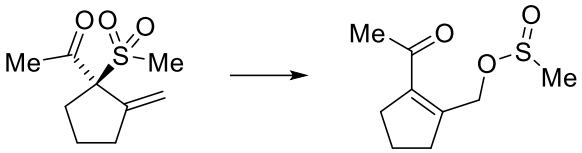
2n

Agilent Technologies

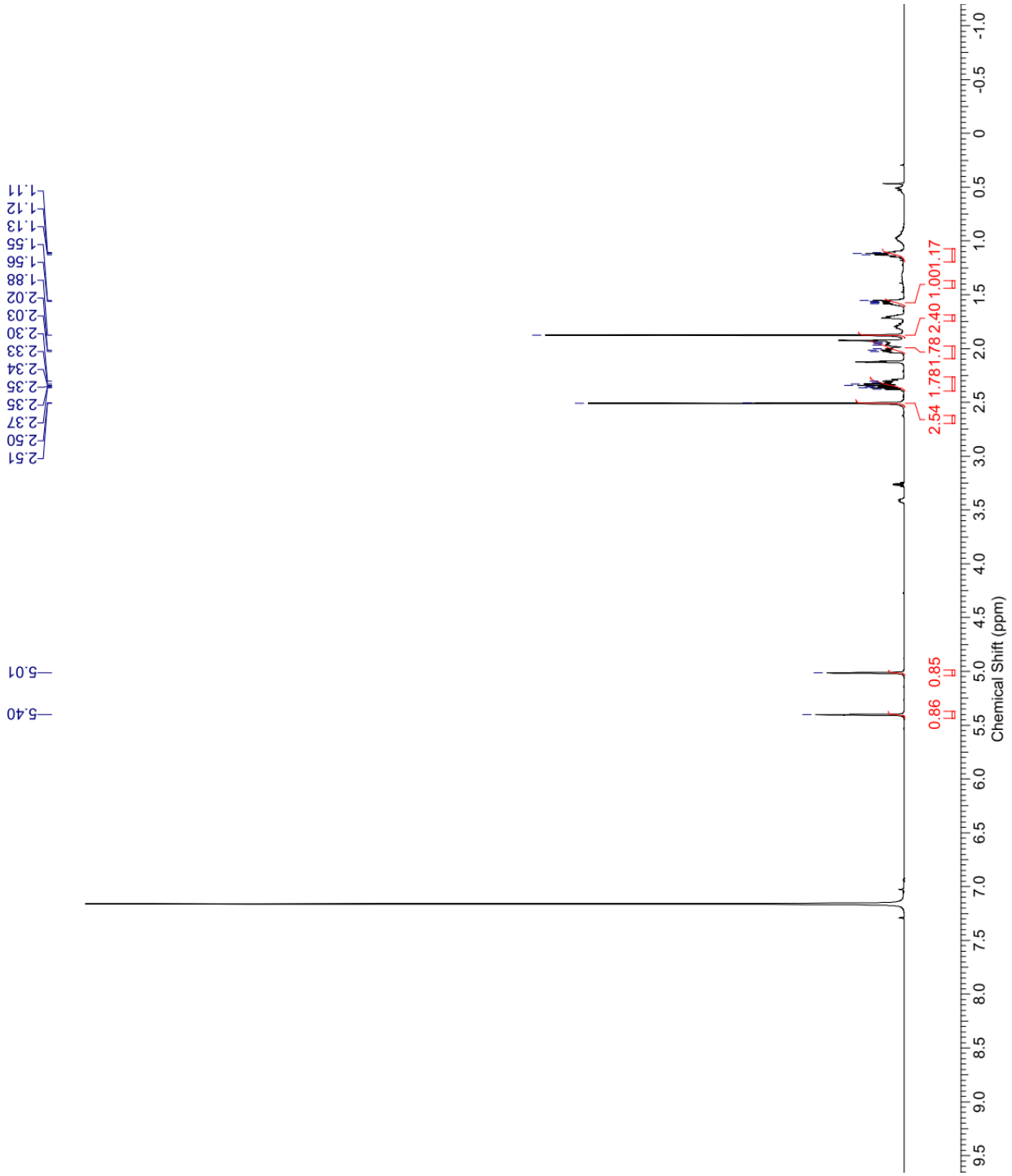
```
Sample Name:      LR215
Data file:        D:\ERNIE\MB\L215AD.D
Sample Info:      Mobile phase: n-Heptane/iPrOH 97:3 ;
                  The sample is solved in DCM/LM

Column:           DAICELOJ.M
Column info:      Chiralcel OJ (250 x 4.6) mm 5µ

Operator:         Analytical Lab AKEN

Injektion Time:       08:40:57
Injektion Date:       15.09.2016

Instrument Conditions:    At Start              At Stop

Temperature in°C:         30.0                    30.0
Pressure in bar:          19.2                    18.8
Flow in ml/min:           0.5                     0.5
```

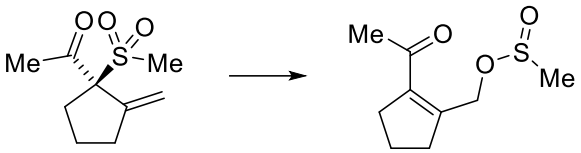


#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.26	0.50	19.89	766.86	1.17
2	8.73	0.49	102.91	3506.77	5.37
3	11.64	0.75	5.42	279.81	0.43
4	13.29	0.55	19.25	723.82	1.11
5	14.87	0.84	2.06	117.19	0.18
6	19.33	2.06	1.84	284.99	0.44
7	34.59	1.45	521.30	50632.75	77.55
8	46.58	2.19	61.19	8974.93	13.75
Total				65287.14	100.00

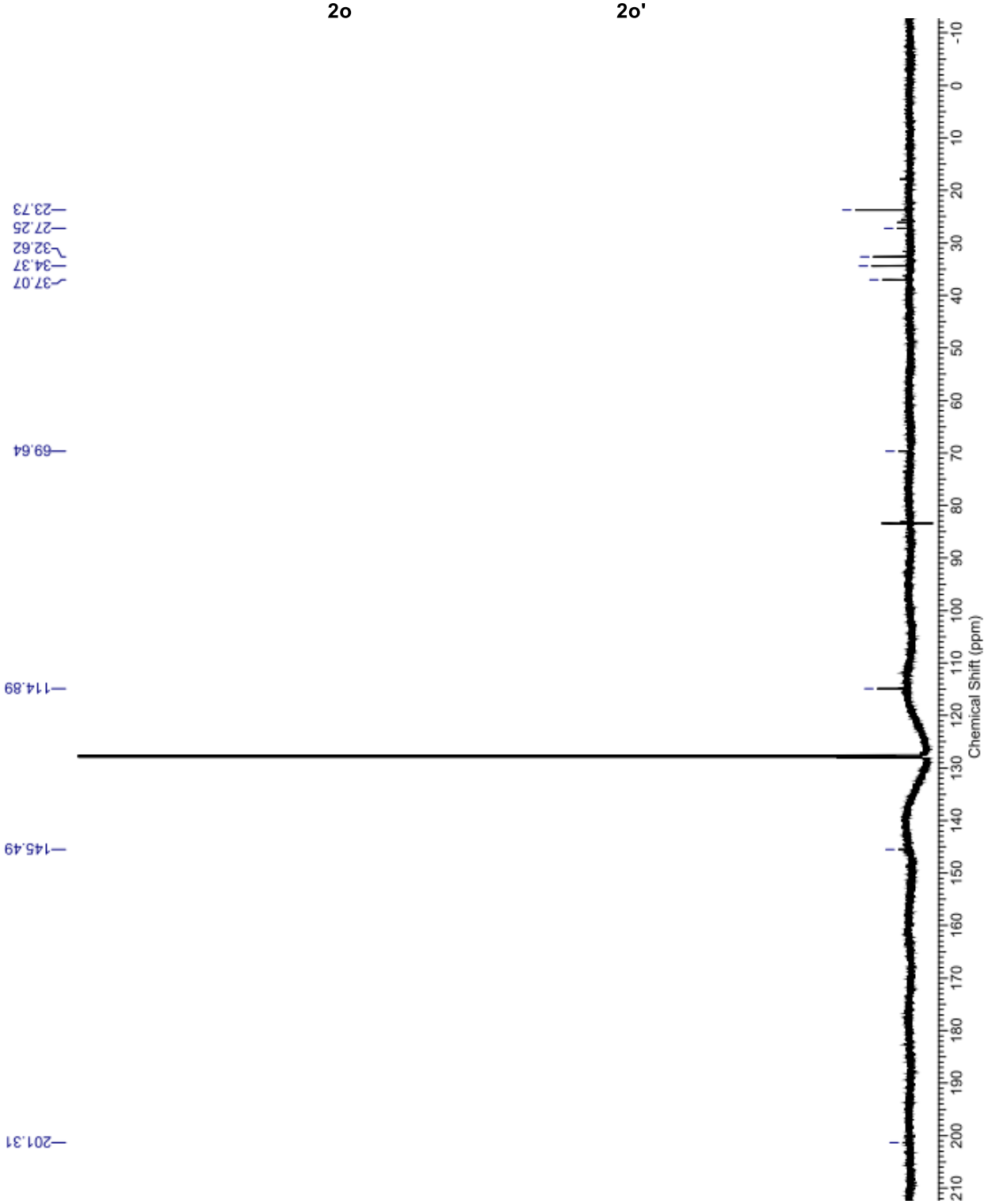

Me
S
Me
Me
O
O
S
Me

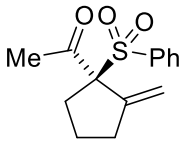
2o **2o'**


1.11
1.12
1.13
1.55
1.56
1.88
2.02
2.03
2.30
2.33
2.34
2.35
2.35
2.37
2.50
2.51
5.01
5.40
2.54 1.78 2.40 1.00 1.17
0.86 0.85
Chemical Shift (ppm)

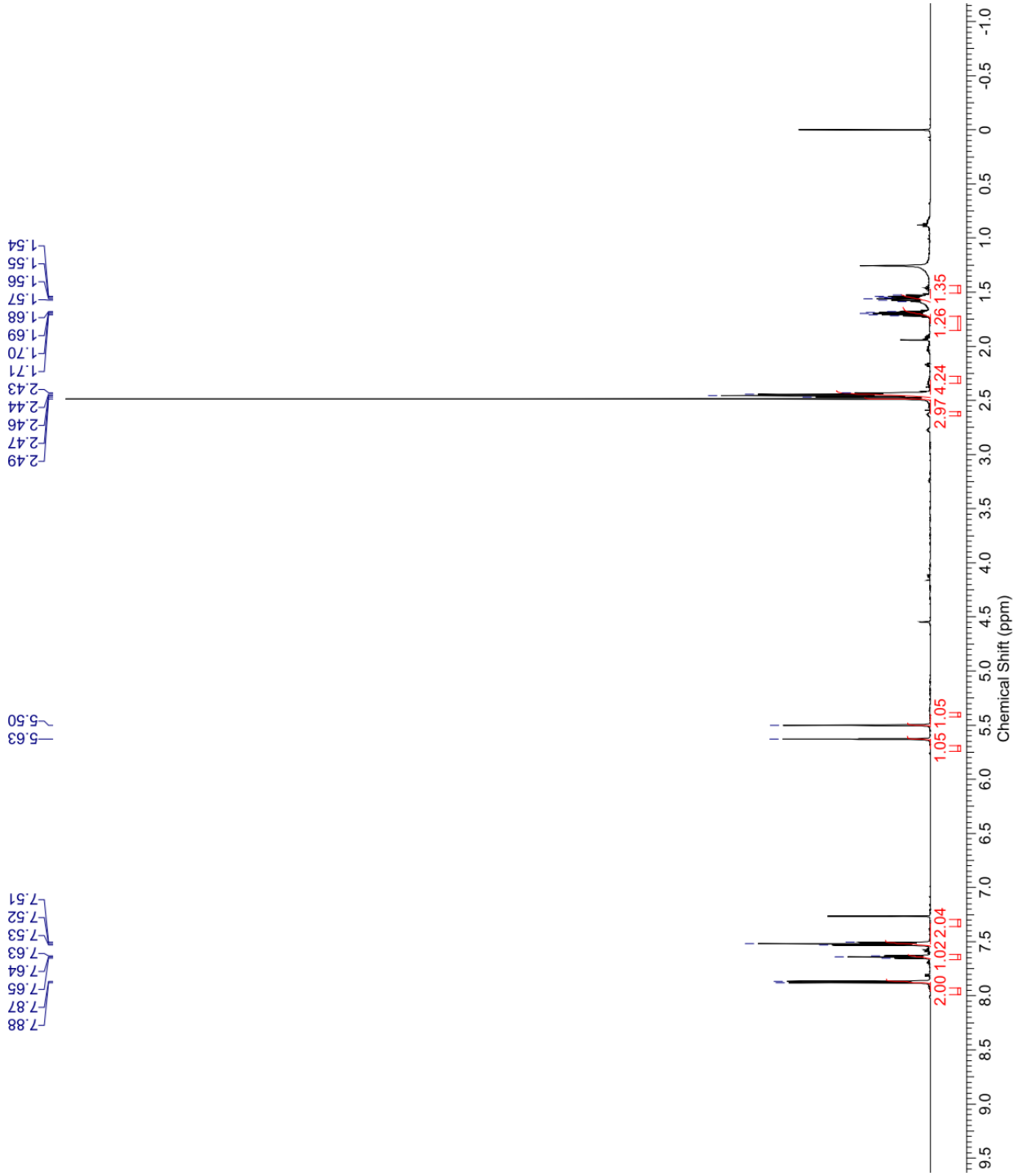

Me
O
O
O
S
Me
Me
O
O
S
Me

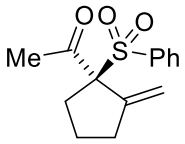
2o **2o'**


23.73
27.25
32.62
34.37
37.07
69.64
114.89
145.49
201.31
Chemical Shift (ppm)

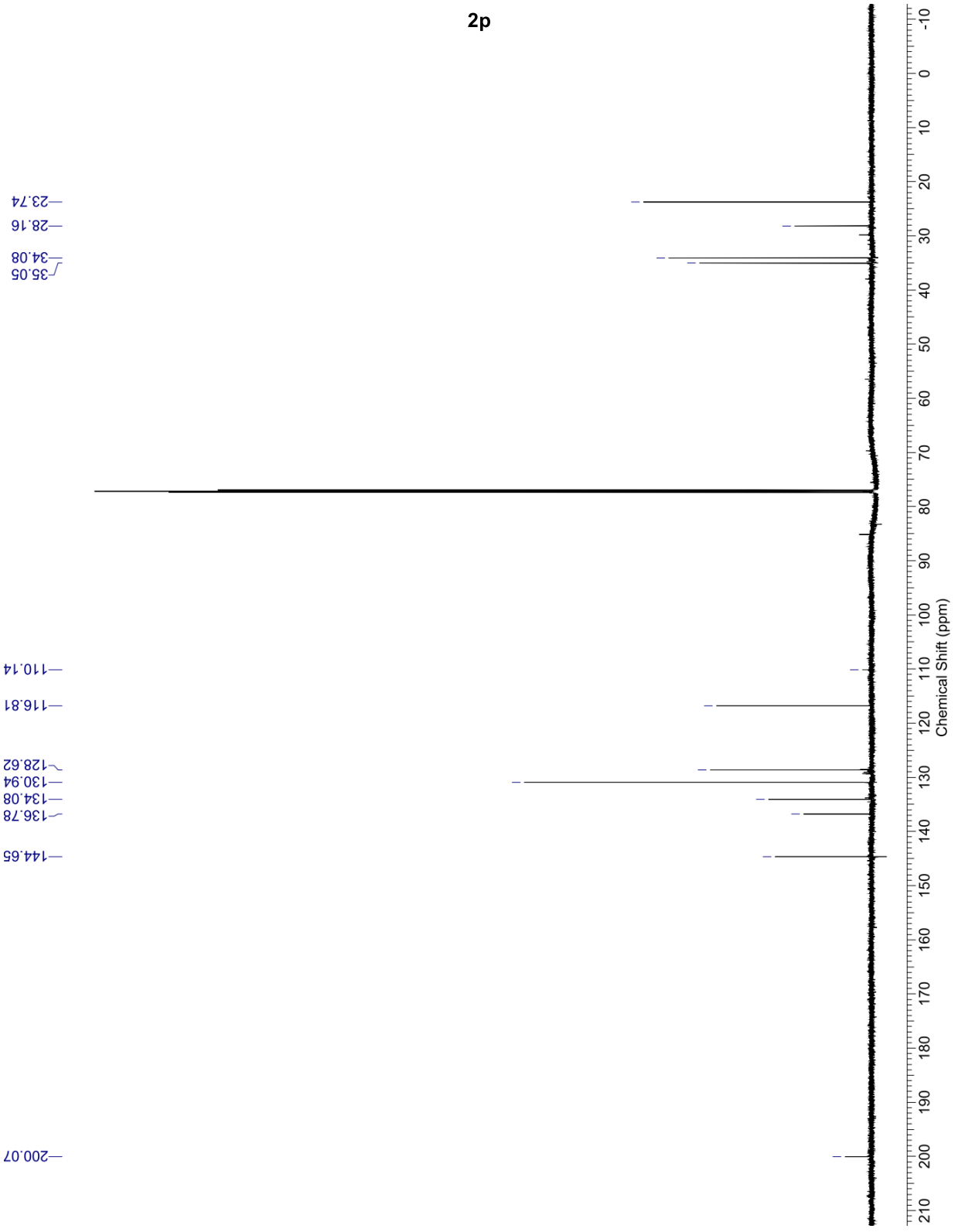

O
O
O
Me
S
Ph

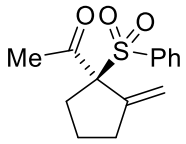
2p


1.54
1.55
1.56
1.57
1.68
1.69
1.70
1.71
2.43
2.44
2.46
2.47
2.49
5.50
5.63
7.51
7.52
7.53
7.63
7.64
7.65
7.87
7.88
2.97 4.24
1.26 1.35
1.05 1.05
2.00 1.02 2.04
Chemical Shift (ppm)


O
O
O
Me
S
Ph

2p


23.74
28.16
34.08
35.05
110.14
116.81
128.62
130.94
134.08
136.78
144.65
200.07
Chemical Shift (ppm)



2p

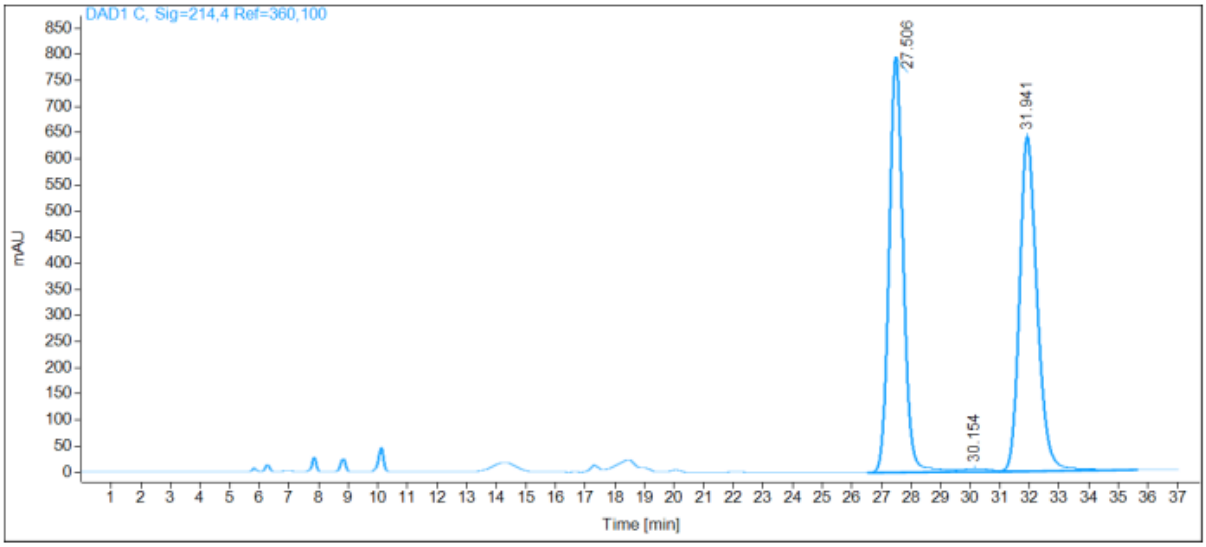
Sample name: **LR122**

Data file: C:\SNOOPY\MB\LR122 2 IA.D
Description: Mobile phase: n-Heptane/i-PrOH 97:3
The sample is solved in DCM/MP

Injection date: 9/14/2016 12:23:58 PM
Acq. Analysis method: CHIRALPAKIARNP.M

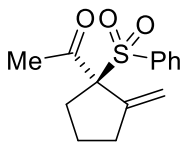
Column: Chiralpak IA, (250 x 4,6) mm, 5µ, SN: IA00CE-RC036

Pressure at start: 27 bar **Start flow:** 0.500 ml/min **Column oven:** 30 °C



Name LR122

RT [min]	Type	Area%	Area	Height	Width [min]
27.51	BV	49.69	26349.34	795.16	0.51
30.15	VV	0.64	339.59	5.77	0.76
31.94	VB	49.67	26340.73	640.06	0.62
	Sum	100.00	53029.66		



2p

Sample name: **LR212**

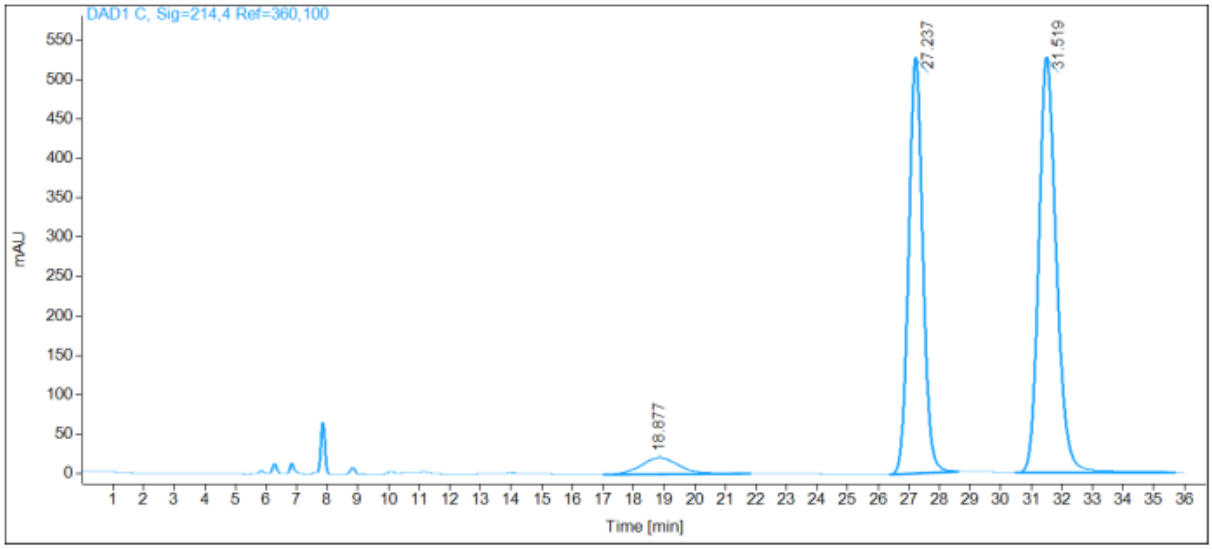
Data file: C:\SNOOPY\MB\L212IA.D
Description: Mobile phase: n-Heptane/iPrOH 97:3;
The sample is solved in DCM/MP

Injection date: 9/14/2016 1:14:08 PM

Acq. Analysis method: CHIRALPAKIARNP.M

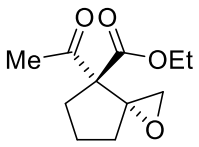
Column: Chiralpak IA, (250 x 4,6) mm, 5µ, SN: IA00CE-RC036

Pressure at start: 26 bar **Start flow:** 0.500 ml/min **Column oven:** 30.01 °C

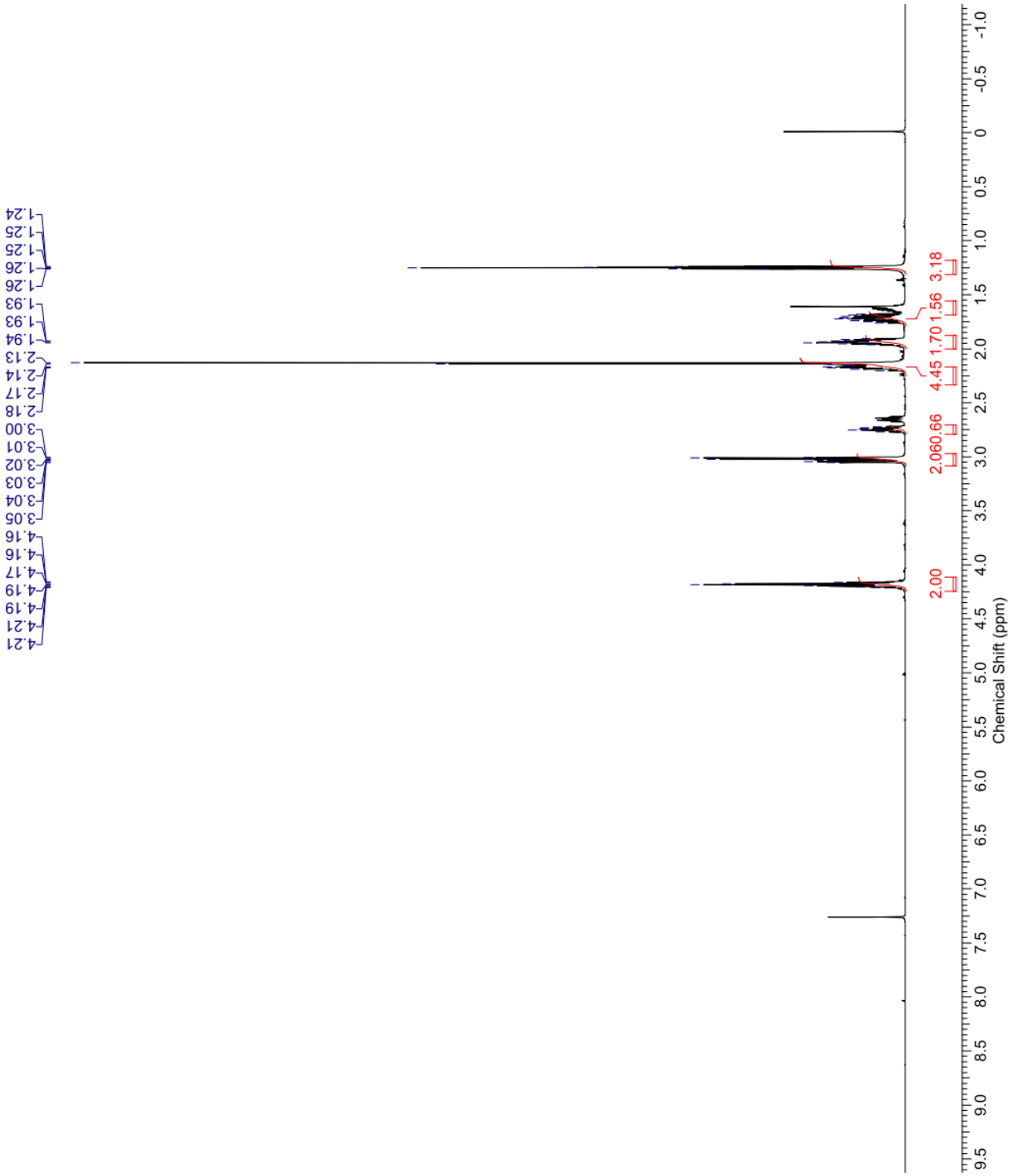


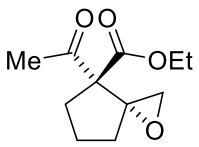
Name LR212

RT [min]	Type	Area%	Area	Height	Width [min]
18.88	BB	4.55	1814.23	20.58	1.25
27.24	BB	42.43	16933.62	527.70	0.49
31.52	BB	53.03	21165.72	527.81	0.61
	Sum	100.00	39913.57		

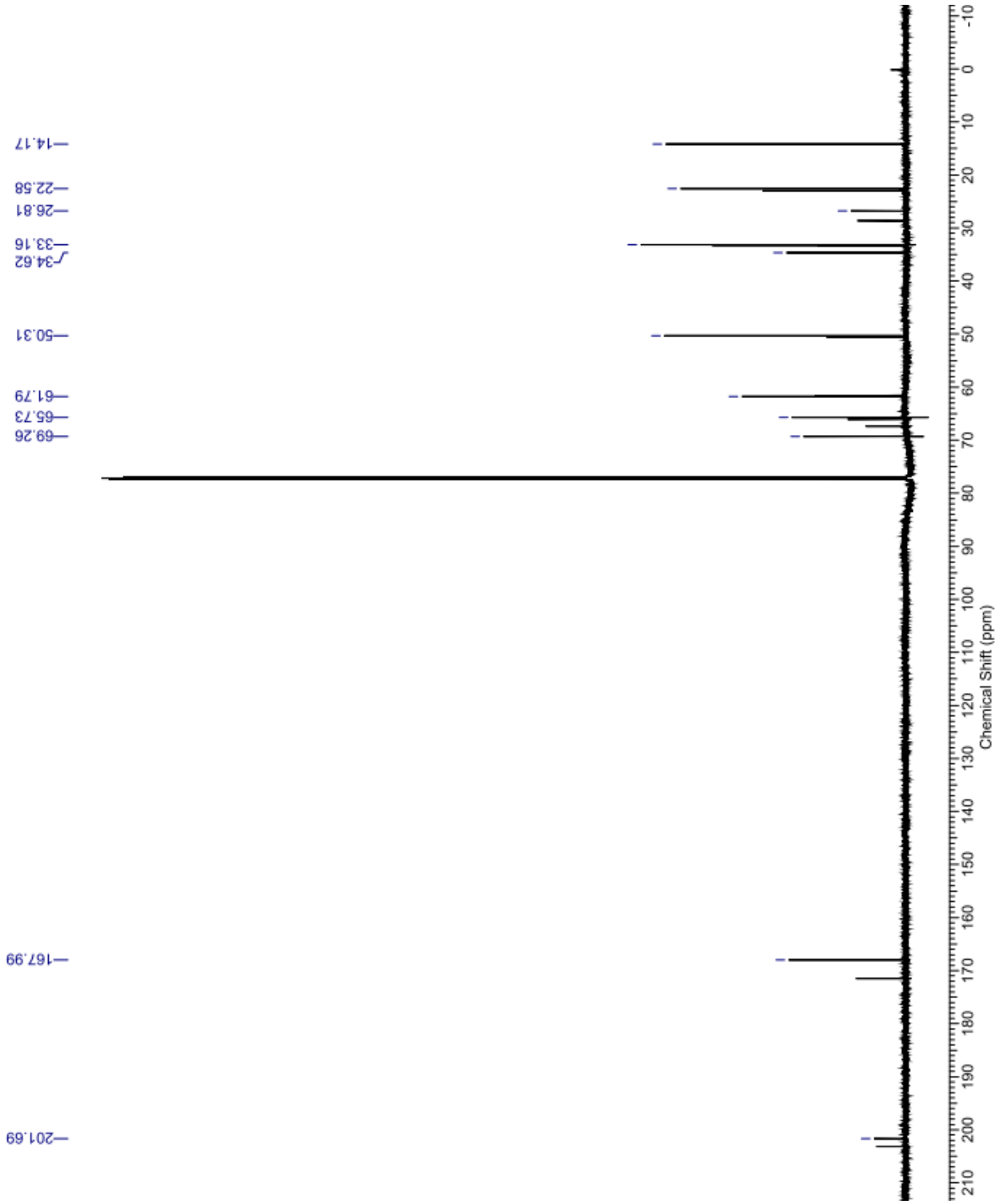

O
O
Me
OEt
O

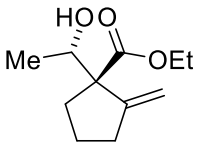
3


1.24
1.25
1.25
1.26
1.26
1.93
1.93
1.94
2.13
2.14
2.17
2.18
3.00
3.01
3.02
3.03
3.04
3.05
4.16
4.16
4.17
4.19
4.19
4.21
4.21
2.00
2.06
0.66
4.45
1.70
1.56
3.18
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
-1.0
Chemical Shift (ppm)

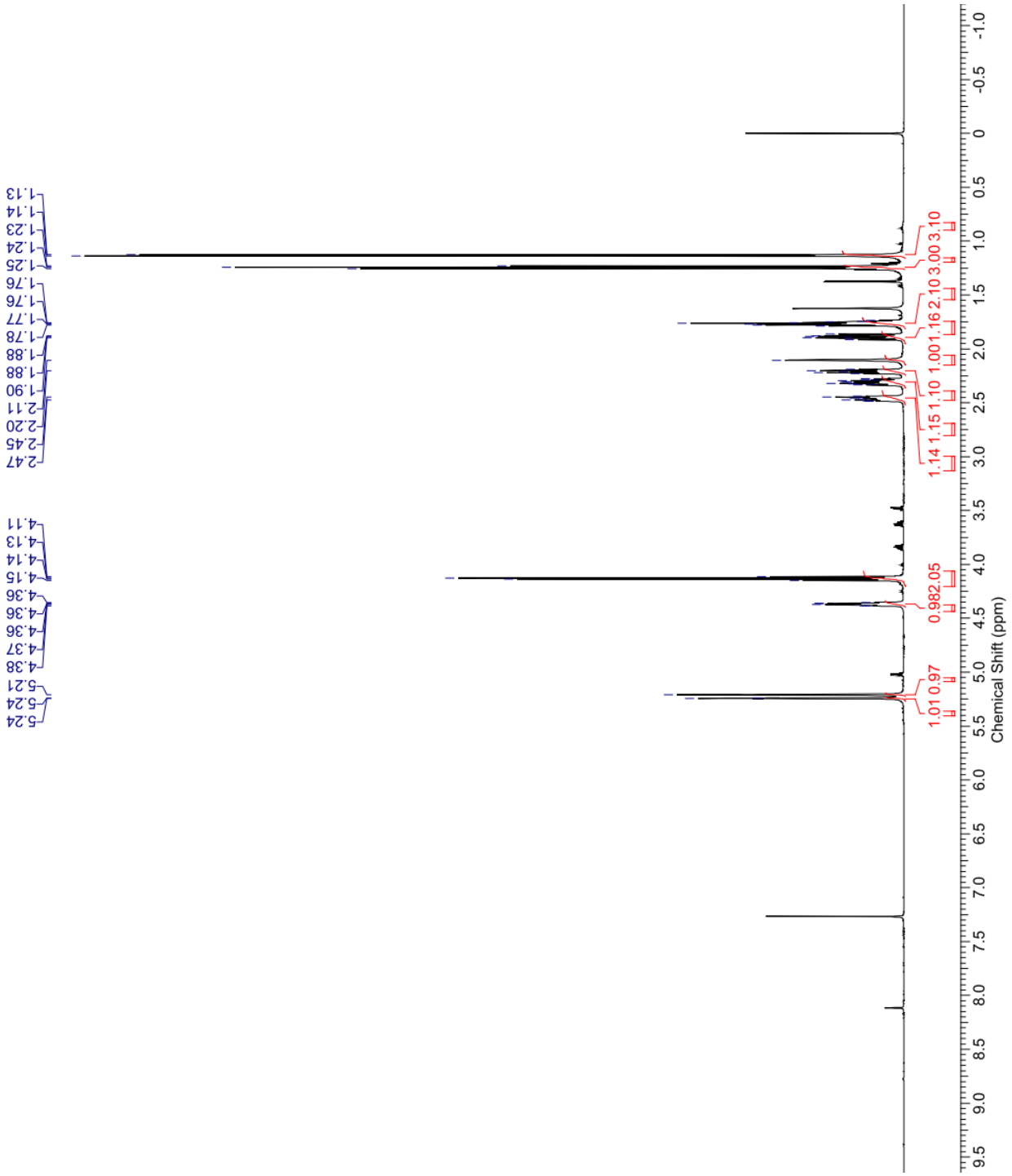

O
O
Me
OEt
O

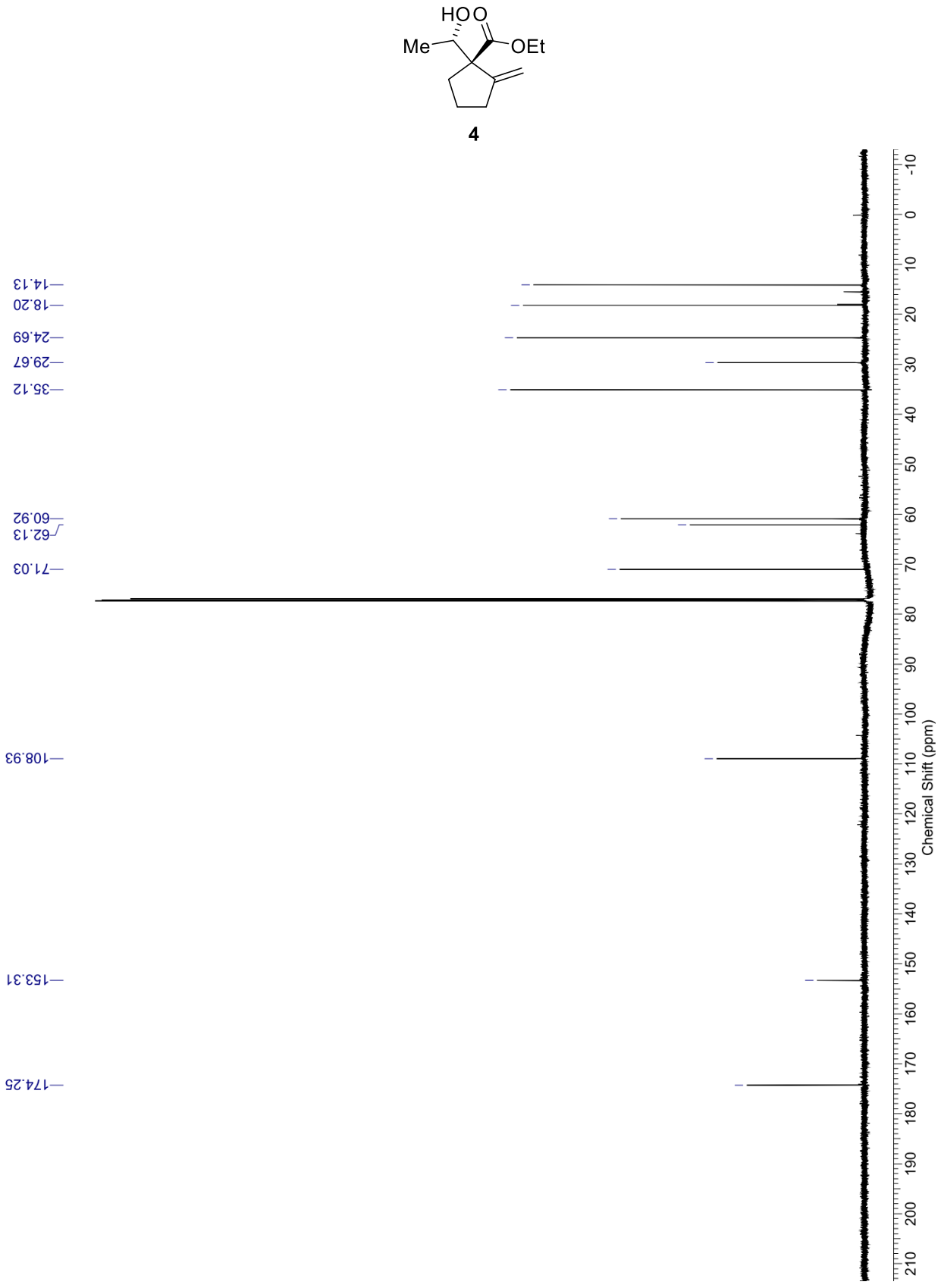
3

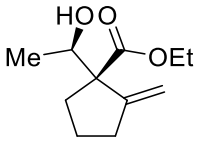

14.17
22.58
26.81
33.16
34.62
50.31
61.79
65.73
69.26
167.99
201.69
Chemical Shift (ppm)


HO
O
Me
OEt

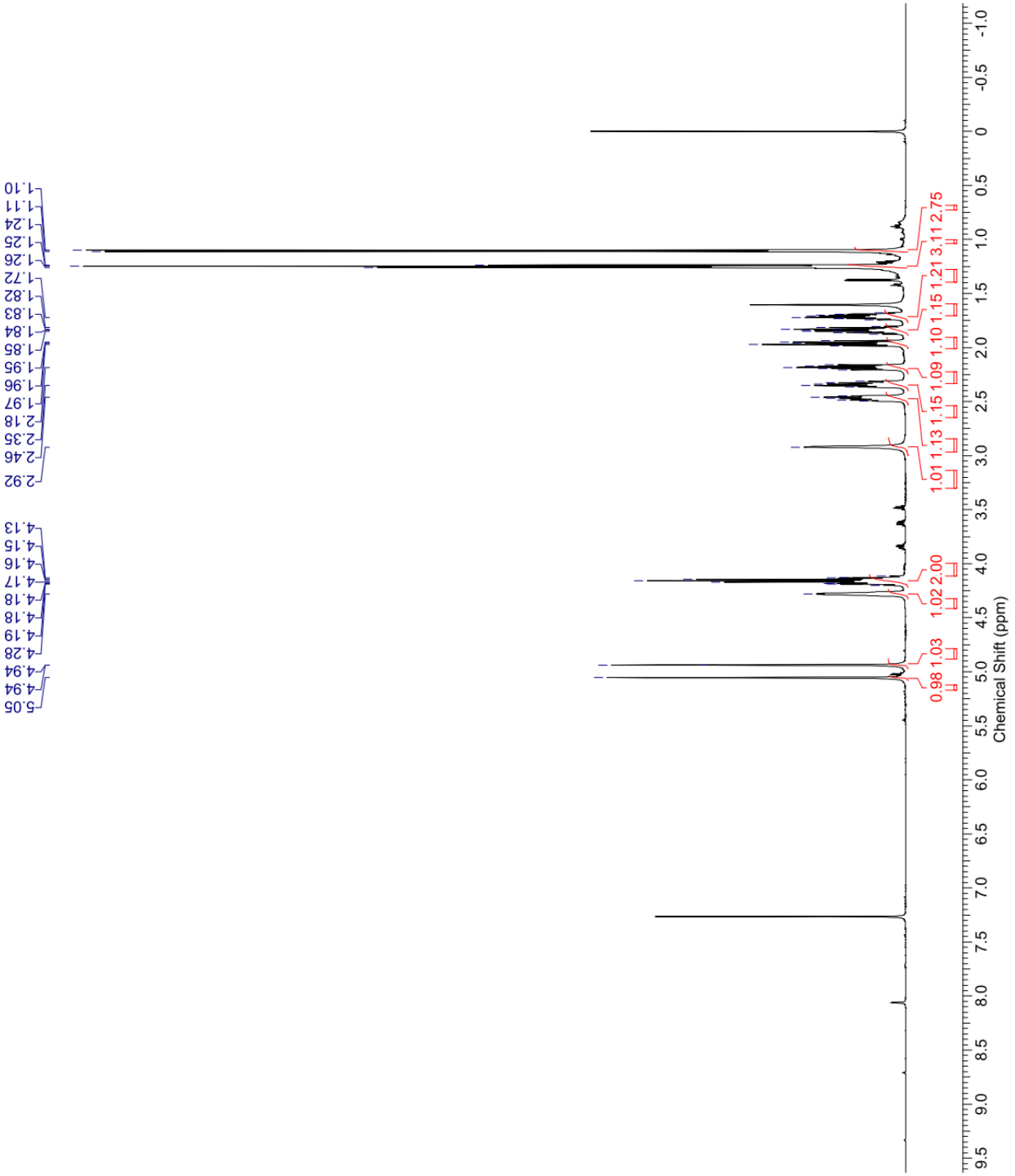
4

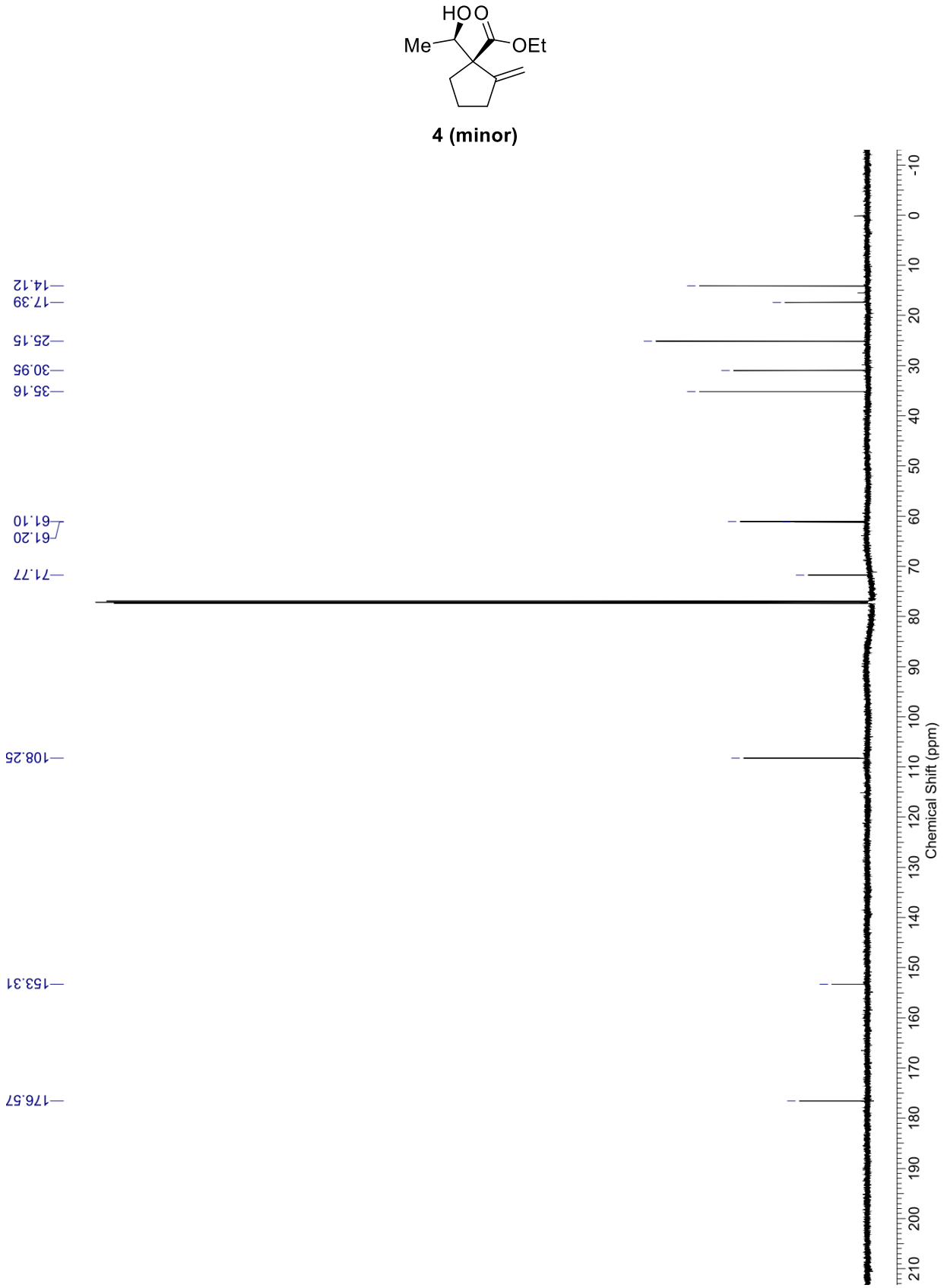

1.13
1.14
1.23
1.24
1.25
1.76
1.76
1.77
1.78
1.88
1.88
1.90
2.11
2.20
2.45
2.47
4.11
4.13
4.14
4.15
4.36
4.36
4.36
4.37
4.38
5.21
5.24
5.24
1.14
1.15
1.10
1.00
1.16
2.10
3.00
3.10
0.98
2.05
1.01
0.97
Chemical Shift (ppm)

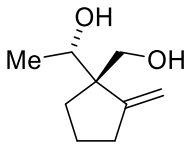

HO
O
Me
OEt
4
14.13
18.20
24.69
29.67
35.12
60.92
62.13
71.03
108.93
153.31
174.25
Chemical Shift (ppm)


HO
O
Me
OEt

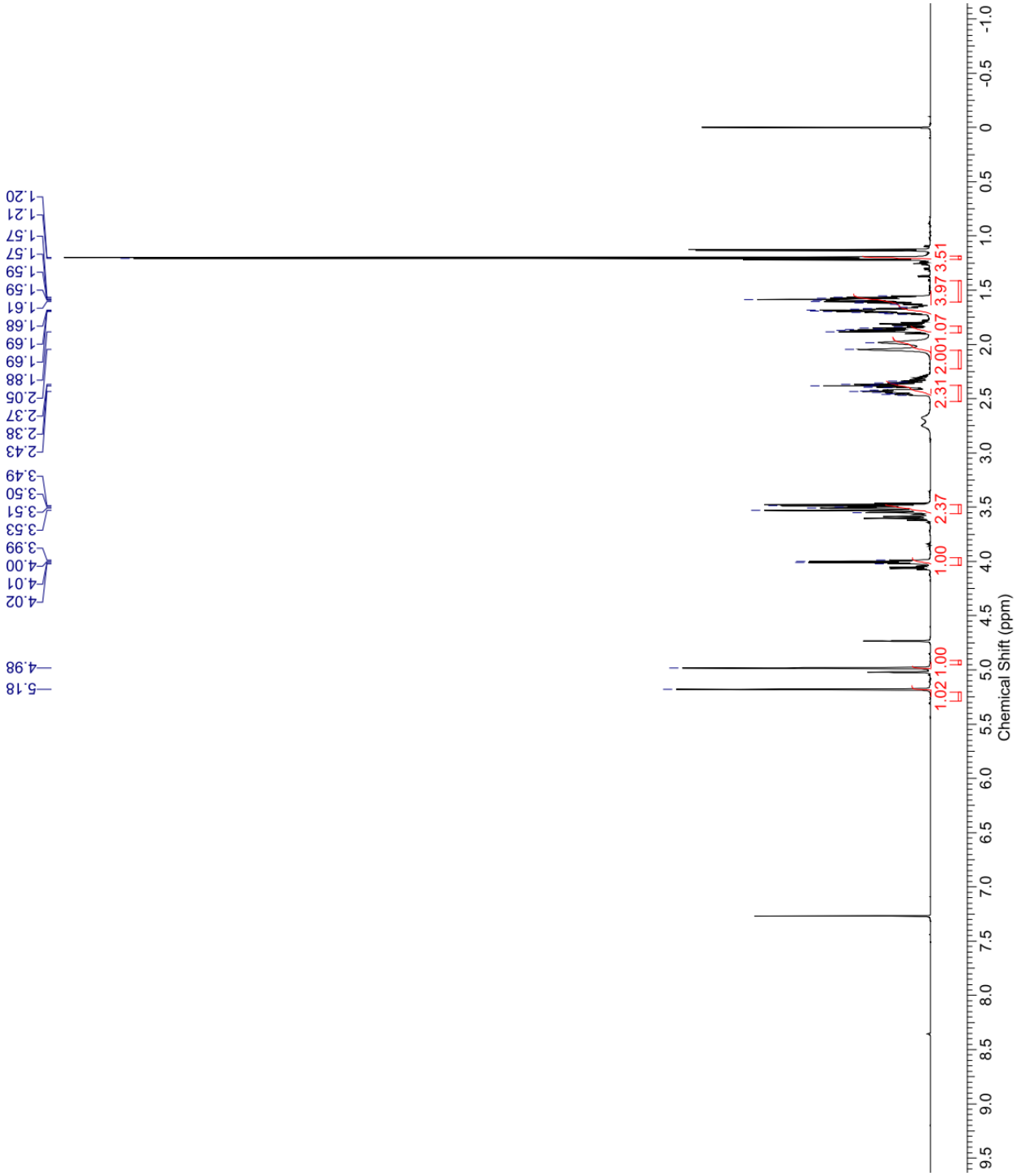
4 (minor)

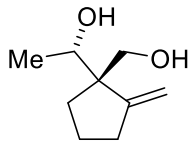

1.10
1.11
1.24
1.25
1.26
1.72
1.82
1.83
1.84
1.85
1.95
1.96
1.97
2.18
2.35
2.46
2.92
4.13
4.15
4.16
4.17
4.18
4.18
4.19
4.28
4.94
4.94
5.05
1.01 1.13 1.15 1.09 1.10 1.15 1.21 3.11 2.75
0.98 1.03 1.02 2.00
Chemical Shift (ppm)


HO
O
Me
OEt
4 (minor)
14.12
17.39
25.15
30.95
35.16
61.10
61.20
71.77
108.25
153.31
176.57
Chemical Shift (ppm)

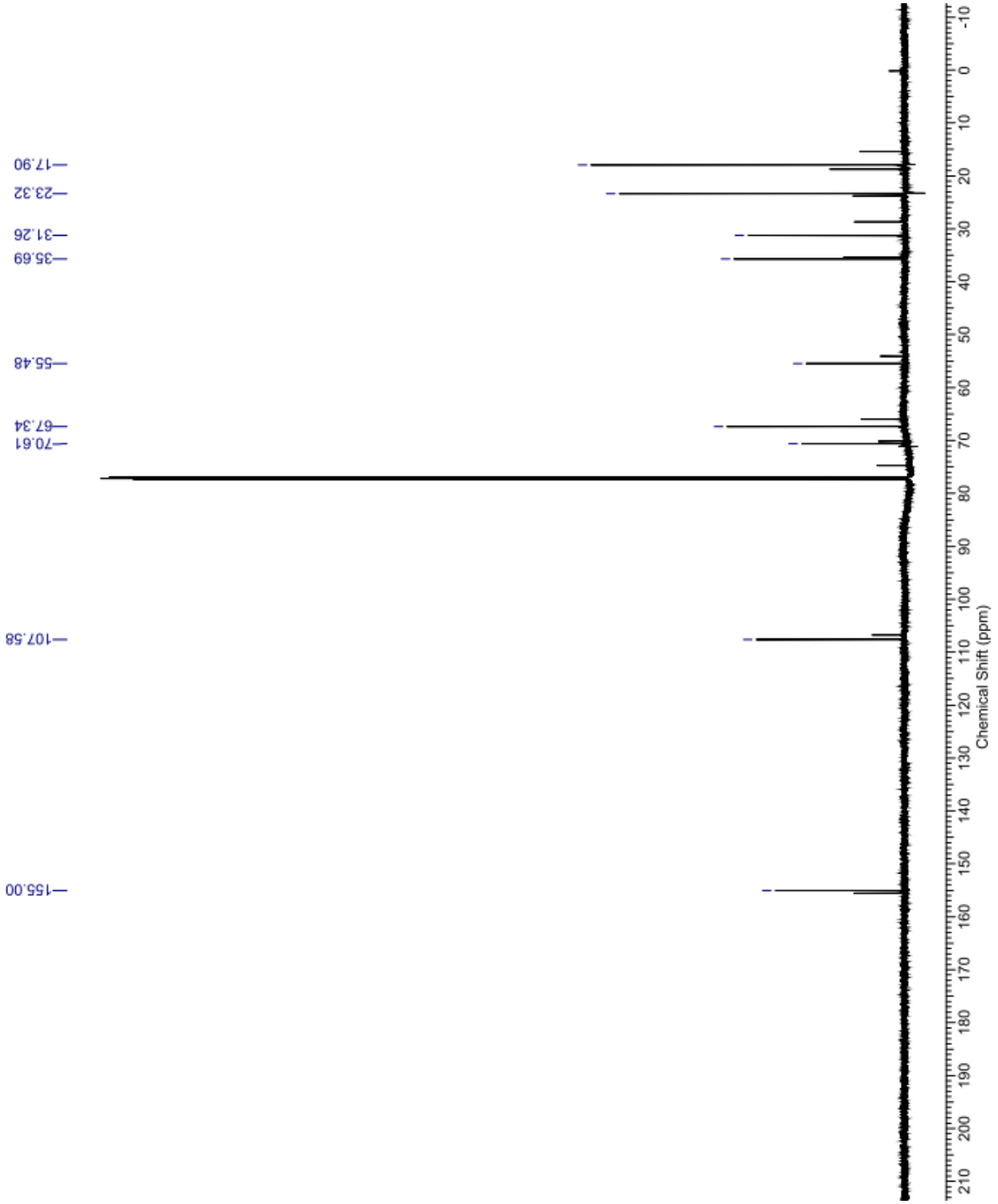

OH
Me
OH

5


1.20
1.21
1.57
1.57
1.59
1.59
1.61
1.68
1.69
1.69
1.88
2.05
2.37
2.38
2.43
3.49
3.50
3.51
3.53
3.99
4.00
4.01
4.02
4.98
5.18
1.02
1.00
1.00
2.37
2.31
2.00
1.07
3.97
3.51
Chemical Shift (ppm)


OH
Me
OH

5


17.90
23.32
31.26
35.69
55.48
67.34
70.61
107.58
155.00
Chemical Shift (ppm)