Supporting Information

Title. **Multifunctional Phosphoramide-(*S*)-Prolinamide Derivatives as Efficient Organocatalysts in Asymmetric Aldol and Michael Reactions**

Carlos Crúz-Hernández,[a] José M. Landeros,[a] Eusebio Juaristi*[a,b]

[a]Departamento de Química, Centro de Investigación y de Estudios Avanzados, Instituto Politécnico Nacional, Apartado Postal 14-740, 07000 Ciudad de México, Mexico.

[b]El Colegio Nacional, Luis González Obregón 23, Centro Histórico, 06020 Ciudad de México, Mexico.

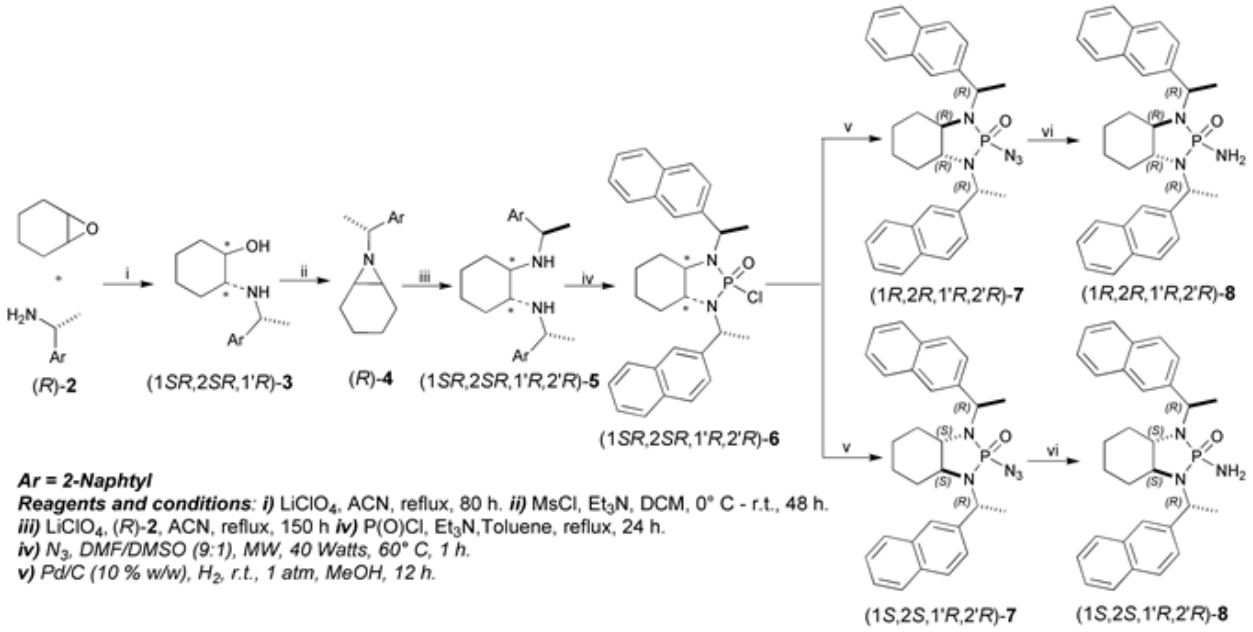
Index page

1. General experimental and characterization

Materials and apparatus. All reagents were purchased from Sigma-Aldrich and used as received unless otherwise indicated. Solvents were dried by conventional methods. For reactions under microwave radiation were run in a single-mode Discover System reactor (CEM corp.). Column Chromatography were performed with Merck Silica Gel (0.040-0.063 mm). TLC were run on Merck DC-F254 plates using UV light or iodine vapors as revelator. **Samples Characterization**. NMR spectra were performed on a JEOL eclipse 400 and JEOL ECA-500 spectrometers, and the chemical shifts were referenced to the deuterate solvent peak. Melting points data were determined on a Büchi B-540 apparatus and are uncorrected. Optical rotations were determined in an Anton Paar MCP-100 Polarimeter using reagent grade solvents. FTIR spectra were recorded on a Varian 640-IR Spectrometer. Crystallographic data were determined on an Enraf-Nonius Kappa CCD and Enraf-Nonius CAD-4. High resolution mass spectra (HRMS) were measured on a HPLC 1100 coupled to an MSD-TOF Agilent Technologies HR-MSTOF 1069A. Determination of diastereomeric and enantiomeric excess were carried out on a Dionex HPLC ultimate 3000 with UV/Visible detector, diode array, at 210 and 254 nm, using a suitable chiral column.

Complete Synthesis of *bis*-amidophosphoryl amine fragment incorporating the naphthylethyl moiety.

To synthesize the desired catalysts we first prepared the required chiral phosphoramides **8** according to a general procedure reported previously[1] (See Scheme S1). The synthetic strategy began with the opening of cyclohexene oxide (**1**) with (*R*)-1-(2-naphthyl)ethylamine [(*R*)-**2**], promoted by lithium perchlorate in refluxing acetonitrile, to afford diastereomeric aminoalcohols (1*SR,*2*SR,*1'*R*)-**3** (99% yield, 1:1 dr). The mixture of β-aminoalcohols **3** was employed in the formation of aziridine (*R*)-**4**, in 98 yield), via a reaction sequence that involved the initial activation of the hydroxyl group as the corresponding *p*-toluenesulfonate and subsequent internal nucleophilic substitution (S_Ni) by the amino group. Aziridine (*R*)-**4** was treated with chiral amine (*R*)-**2** to afford the anticipated mixture of diastereomeric *trans* diamines (*1SR,2SR,1'R,2'R*)-**5** in 85% yield. This diastereomeric mixture could not be separated under standard procedures (chromatographic column, fractional precipitation or recrystallization) and was used as such in the subsequent condensation with phosphorus oxychloride, obtaining a mixture of *P*-chloro-*bis*-phosphoramides (*1R,2R,1'R,2'R*)-**6** and (*1S,2S,1'R,2'R*)-**6** in good yield (80 %) and 2:1 diastereomeric ratio (verified by ^{1}H and ^{31}P NMR, see SI). Following steps to get compound (*1R,2R,1'R,2'R*)-**8** are described in the paper.



Scheme S1. Full Synthesis of phosphoramides (*1R,2R,1'R,2'R*)-**8** and (*1S,2S,1'R,2'R*)-**8** incorporating (2-naphthyl)ethyl moieties.

2. NMR spectra comparing compounds with (2-naphthyl)ethyl-moieties and phenyl-moieties

In order to determine the configuration of compounds (1*R,*2*R,*1'*R,*2'*R*)-**6** and (1*S,*2*S,*1'*R,*2'*R*)-**6** [as well as (1*R,*2*R,*1'*R,*2'*R*)-**7**, (1*S,*2*S,*1'*R,*2'*R*)-**7**, (1*R,*2*R,*1'*R,*2'*R*)-**8** and (1*S,*2*S,*1'*R,*2'*R*)-**8**] a carefully analysis of their ^{1}H-NMR spectra (Figure S1 – S9) was conducted. As it turns out, the ^{1}H NMR spectra of diastereomeric (1*R,*2*R,*1'*R,*2'*R*)-**6**-**8** and (1*S,*2*S,*1'*R,*2'*R*)-**6**-**8** show a distinctive pattern for the methyl groups (marked in red), the endocyclic methines (marked in blue) and the exocyclic methines (marked in green). It can be appreciated in Figure S1 that the difference in chemical shifts for the exocyclic methine protons (marked in green) are larger in the all-(*R*) diastereomer relative to the difference in chemical shift observed in the (1*S,*2*S,*1'*R,*2'*R*) diastereomers. By contrast, the chemical shifts recorded for the corresponding methyl groups (marked in red) exhibit an opposite trend, i.e. larger chemical shift difference observed in the (1*S,*2*S,*1'*R,*2'*R*) diastereomers. These observations are in line with assignments made on ^{1}H-NMR spectra of previously reported analogous compounds[1] (Figure S2) which were secured with support from X-ray crystallographic structures and allowed the determination of the configuration of the major *P*-chloride diastereomer as (1*R,*2*R,*1'*R,*2'*R*)-**6**. To enforce this assumption, similar analysis was conducted for the diastereomeric pairs (1*R,*2*R,*1'*R,*2'*R*)-**7** and (1*S,*2*S,*1'*R,*2'*R*)-**7** (Figure S4 and S5), and (1*R*,2*R*,1'*R*,2'*R*)-**8** and (1*S*,2*S*,1'*R*,2'*R*)-**8** (Figure S7 and S8). As expected, the corresponding ^{1}H-NMR spectra exhibit similar patterns, to those observed in the reference compounds (Figure S3, S6 and S9).[1]

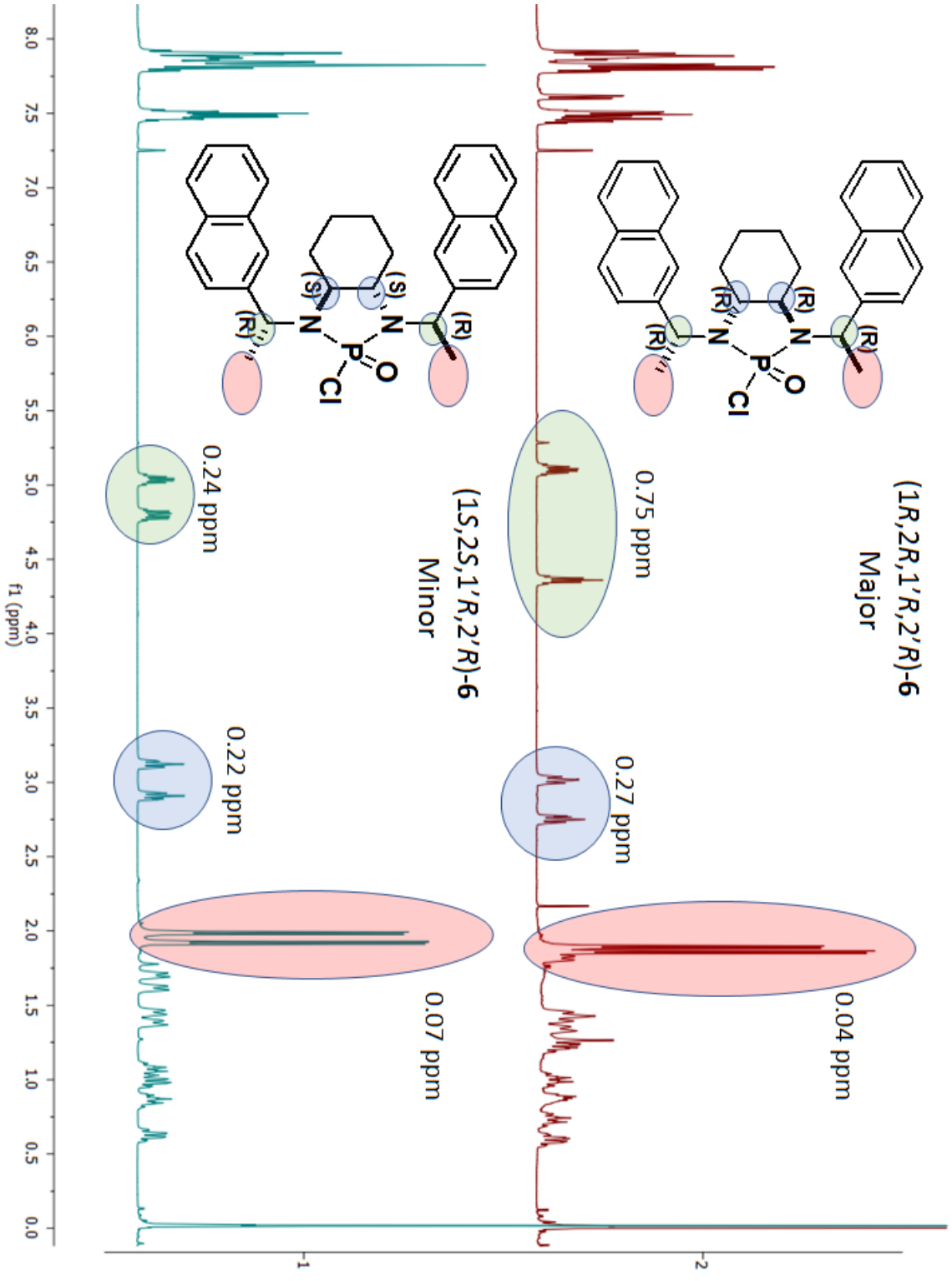


Figure S1 Comparison of ^{1}H-NMR spectra of diastereomeric pairs (1*R*,2*R*,1'*R*,2'*R*)-**6** and (1*S*,2*S*,1'*R*,2'*R*)-**6**.

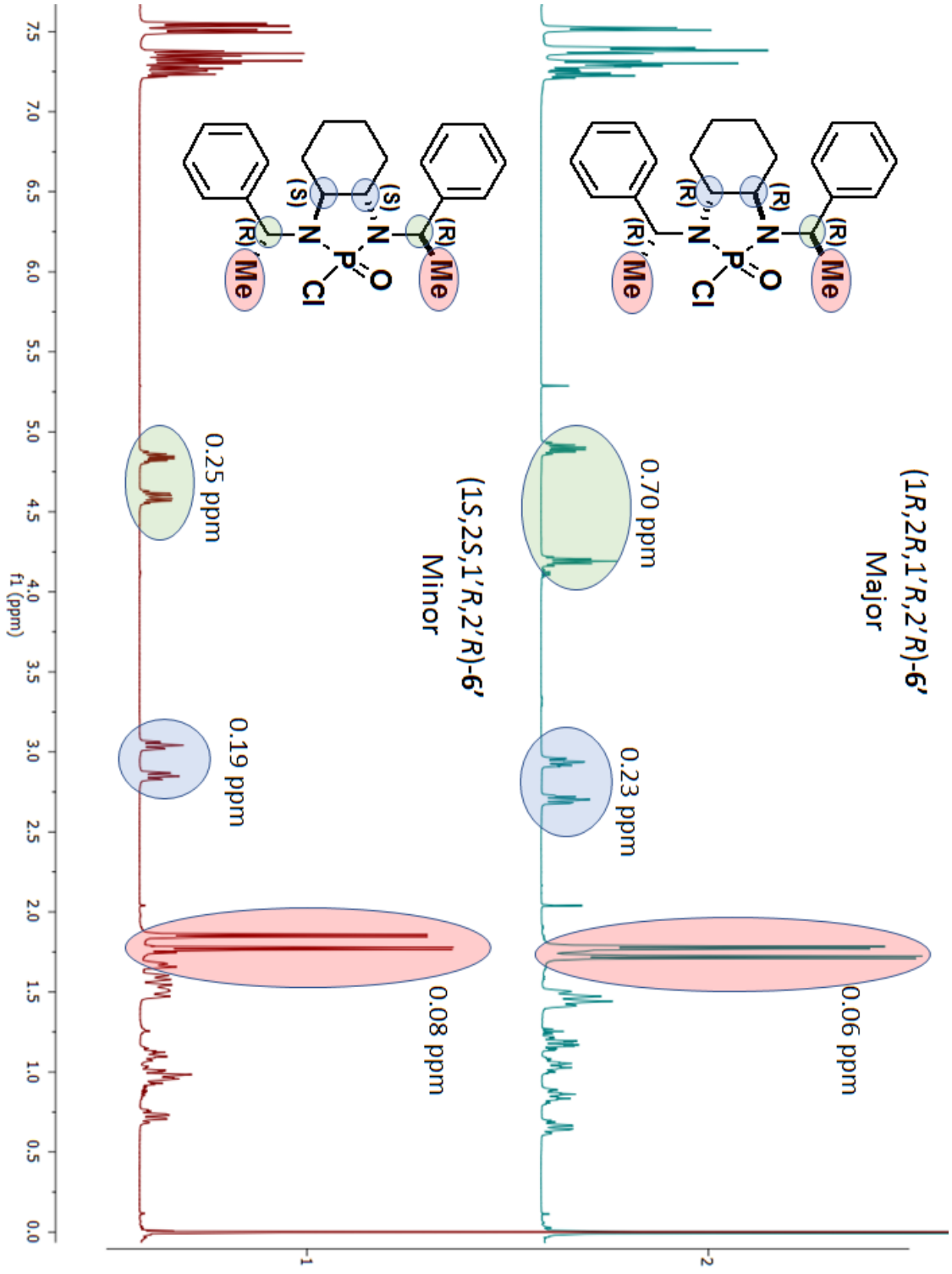


Figure S2 NMR spectra of diastereomers *(1R,2R,1'R,2'R)*-**6'** and (1R,2R,1'R,2'R)-**6'.**[1]

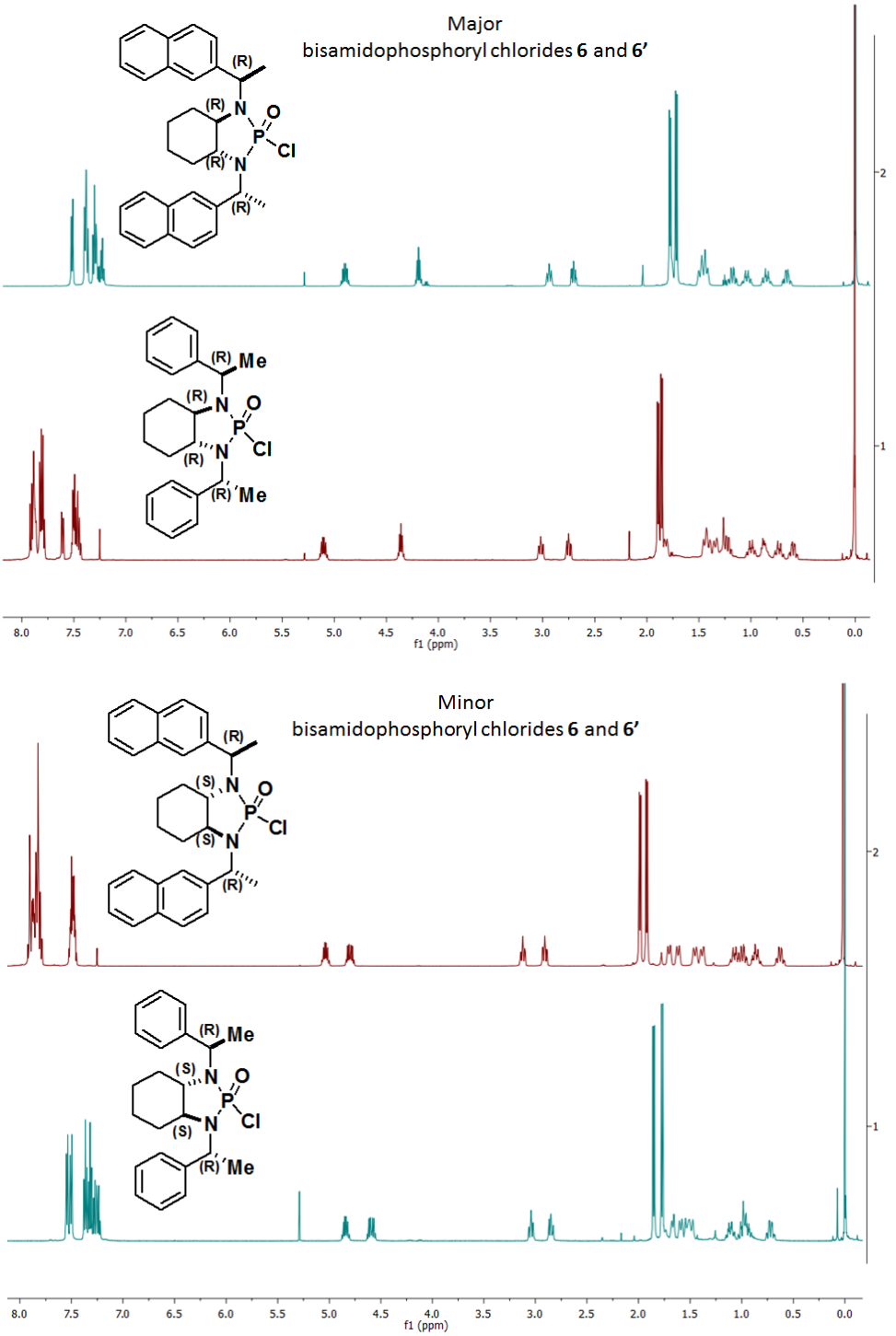


Figure S3 NMR spectra of diastereomers *(1R,2R,1'R,2'R)*-**6'** and (1S,2S,1'R,2'R)-**6'** (previous work)[1] versus diastereomers *(1R,2R,1'R,2'R)*-**6** and (1S,2S,1'R,2'R)-**6** (this work).[1]

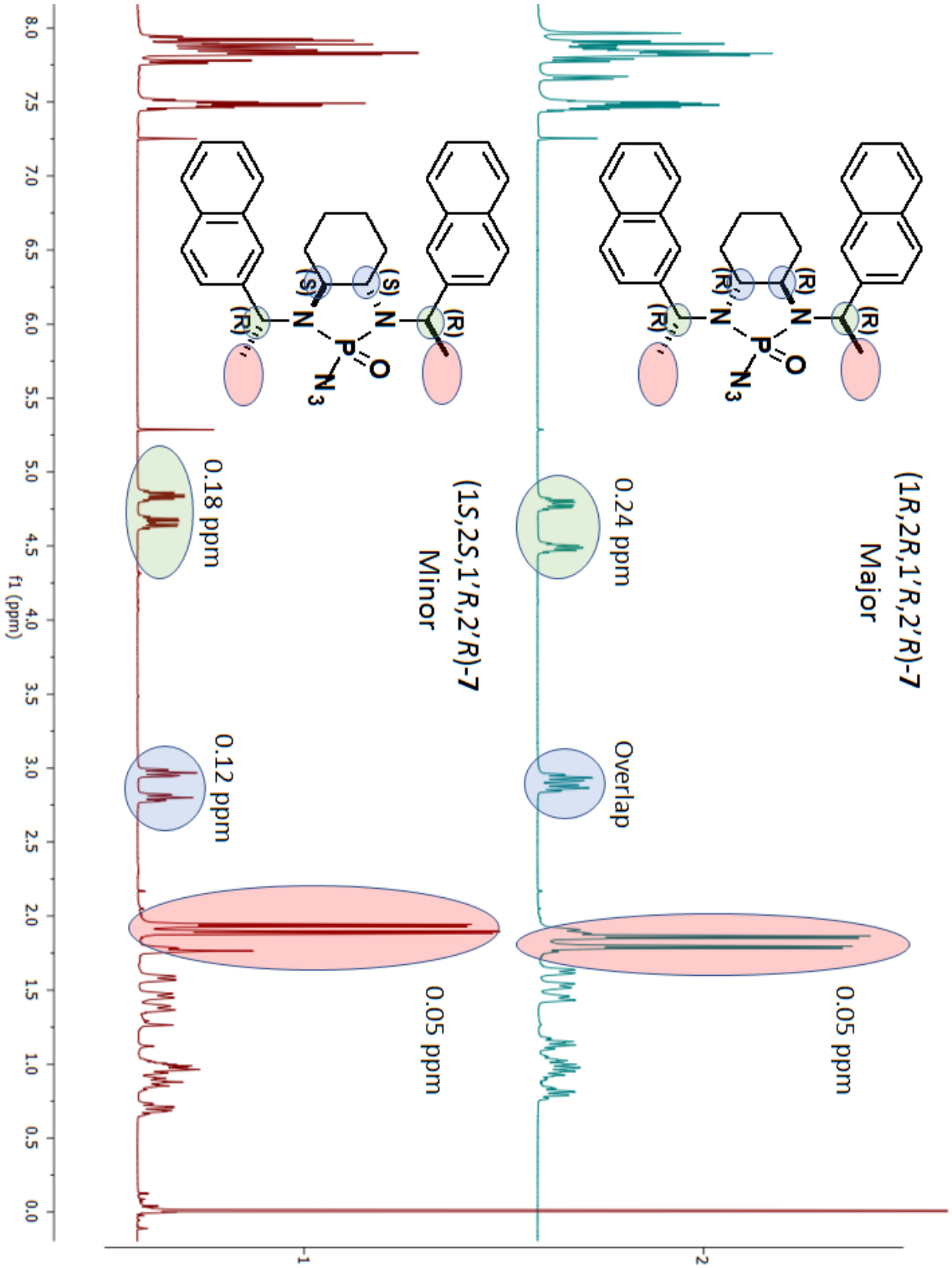


Figure S4 Comparison of ^{1}H-NMR spectra of diastereomeric pairs (1*R*,2*R*,1'*R*,2'*R*)-**7** and (1*S*,2*S*,1'*R*,2'*R*)-**7**

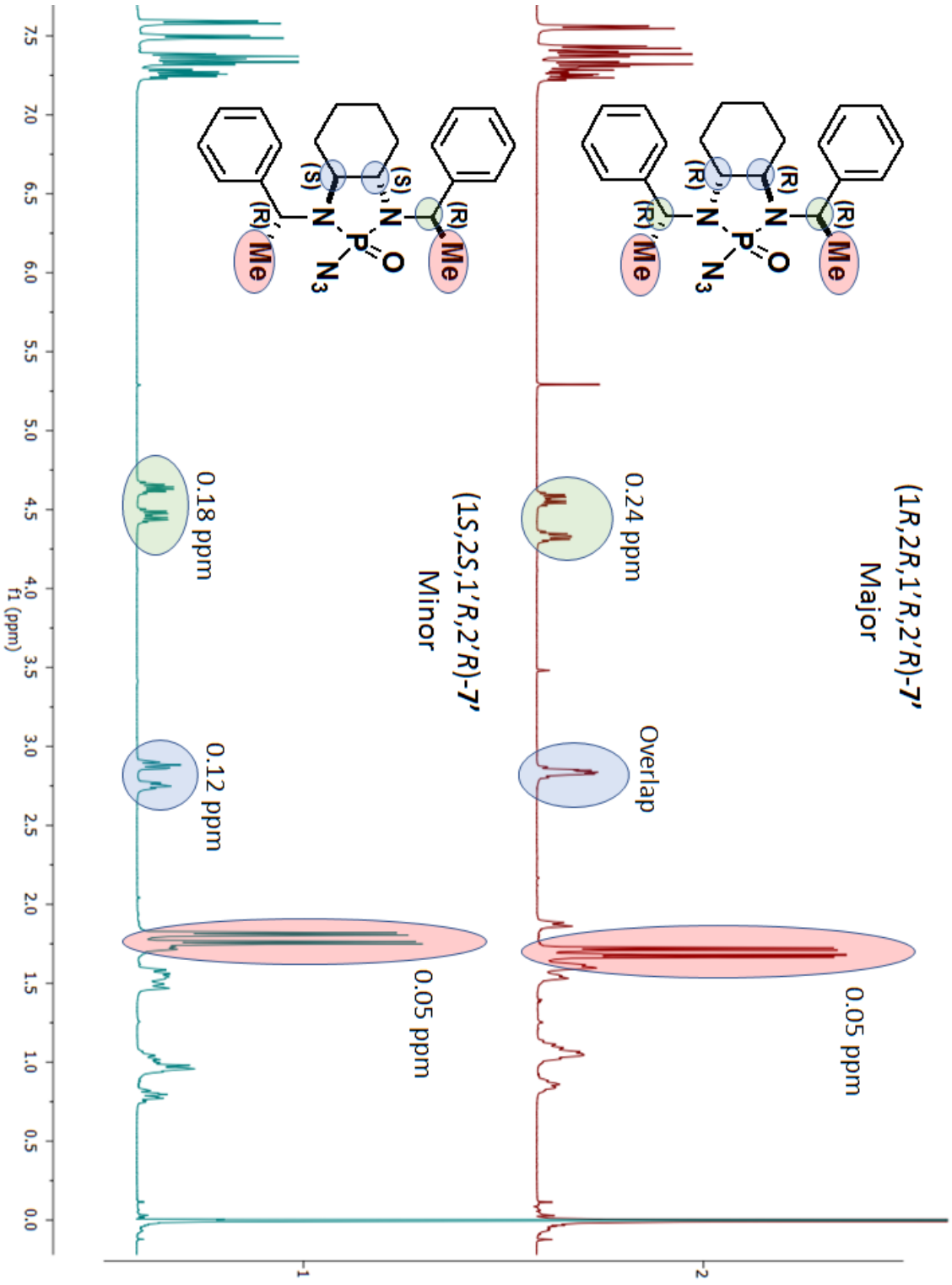


Figure S5 NMR spectra of diastereomers *(1R,2R,1'R,2'R)*-**7'** and (1R,2R,1'R,2'R)-**7'.**[1]

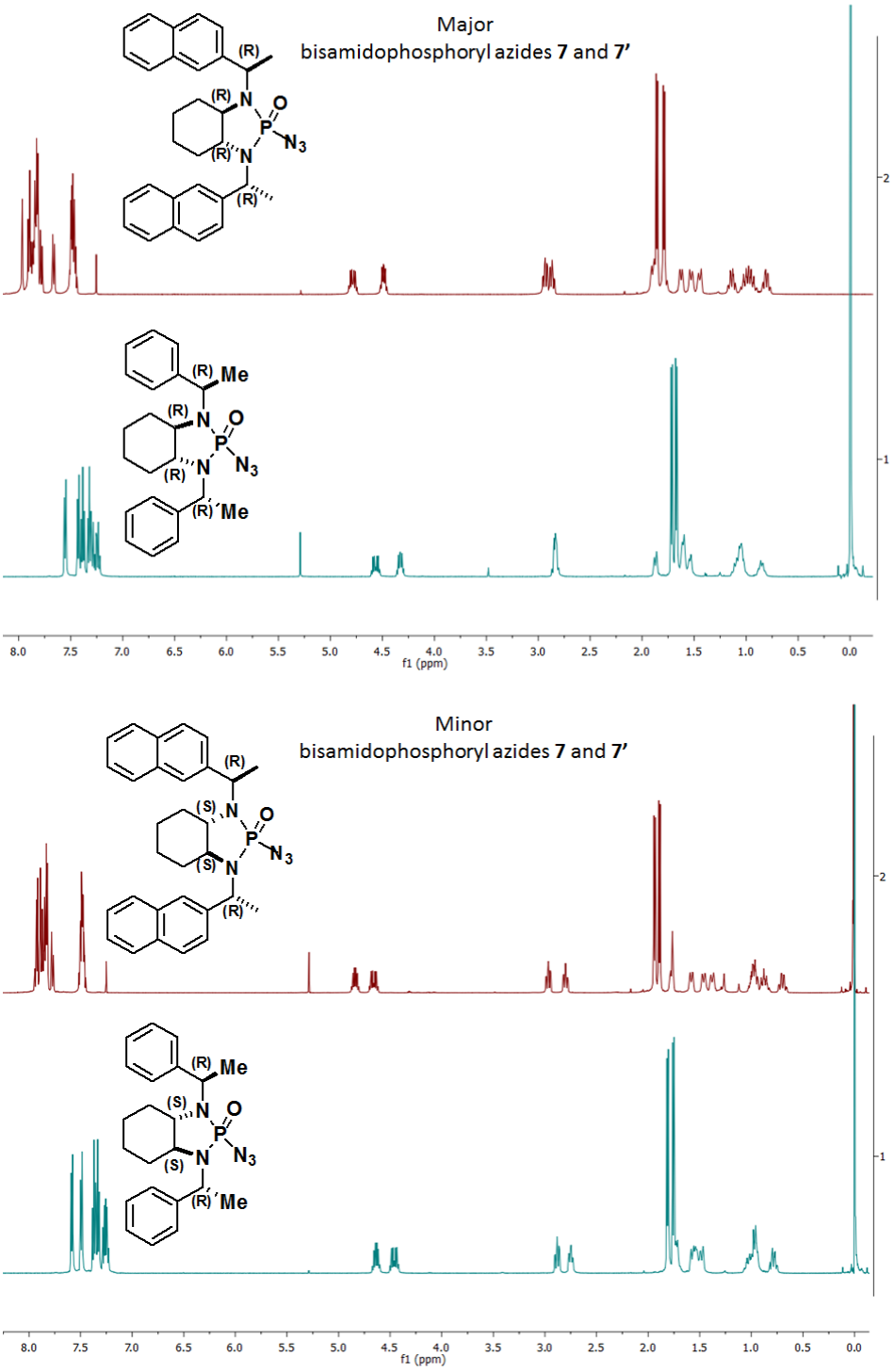


Figure S6 NMR spectra of diastereomers *(1R,2R,1'R,2'R)*-**7'** and (1S,2S,1'R,2'R)-**7'** (previous work)[1] versus diastereomers *(1R,2R,1'R,2'R)*-**7** and (1S,2S,1'R,2'R)-**7** (this work).[1]

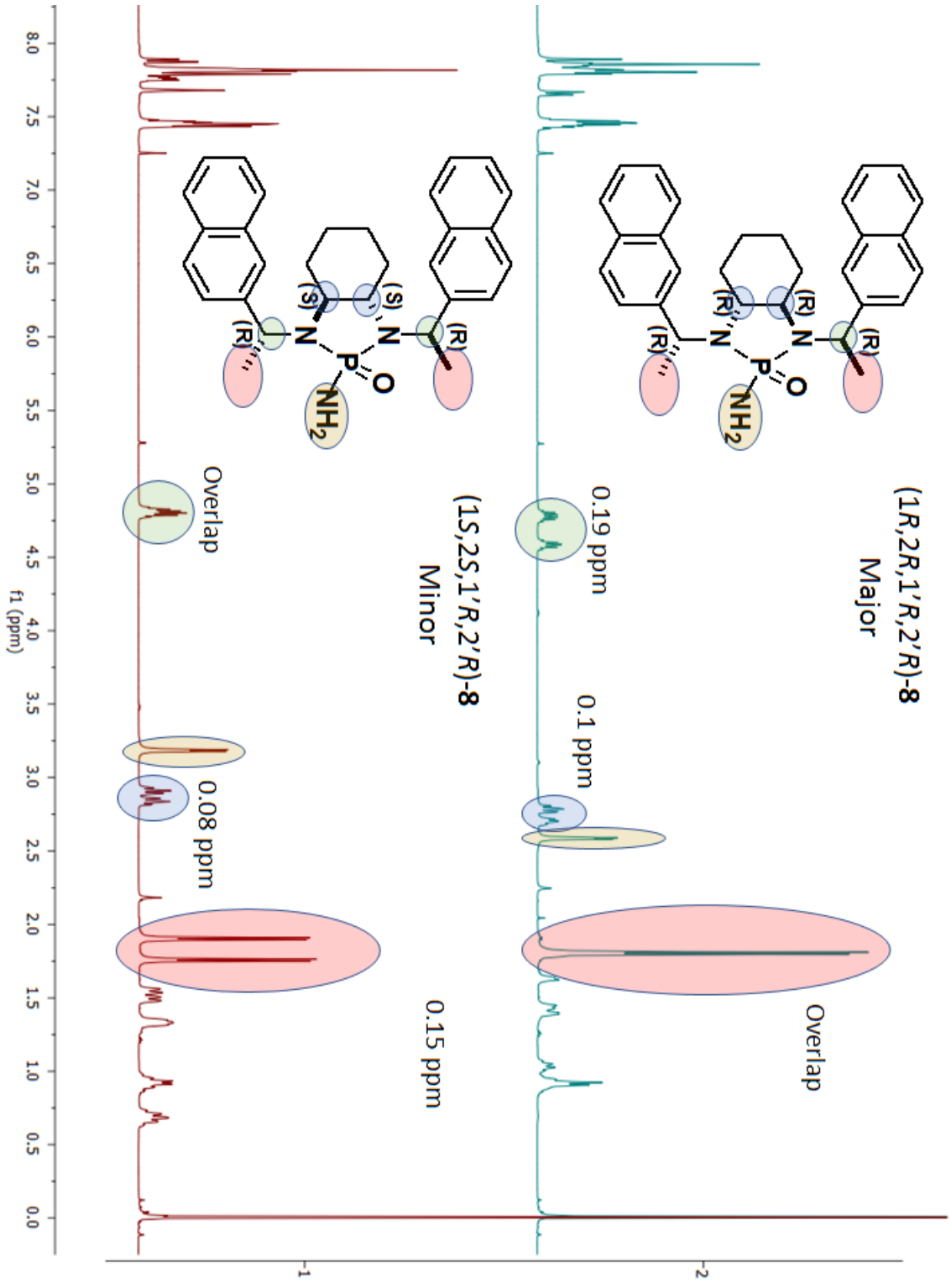


Figure S7 Comparison of ^{1}H-NMR spectra of diastereomeric pairs (1*R*,2*R*,1'*R*,2'*R*)-**8** and (1*S*,2*S*,1'*R*,2'*R*)-**8**

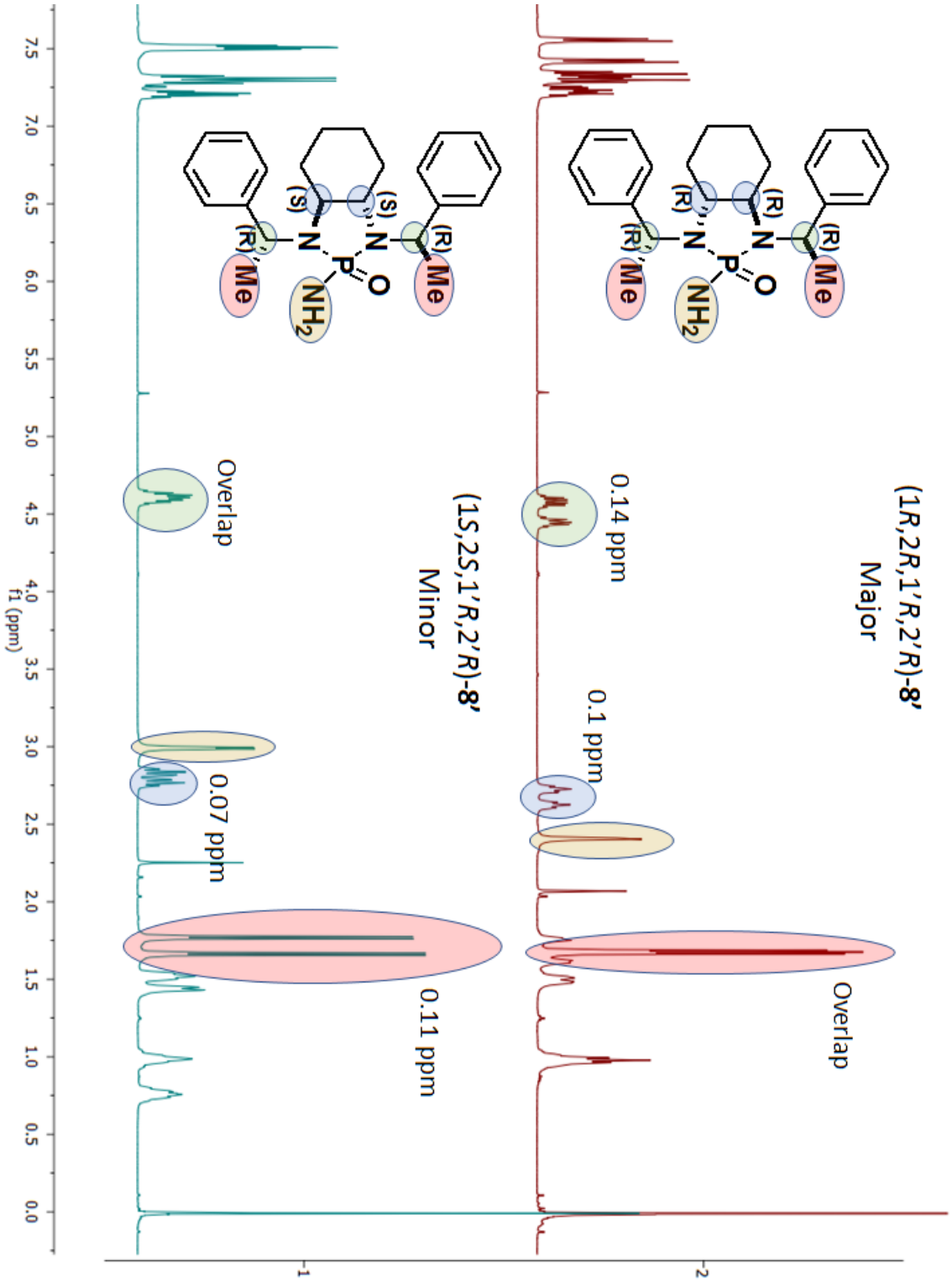


Figure S8 NMR spectra of diastereomers *(1R,2R,1'R,2'R)*-**8'** and (1R,2R,1'R,2'R)-**8'**.[1]

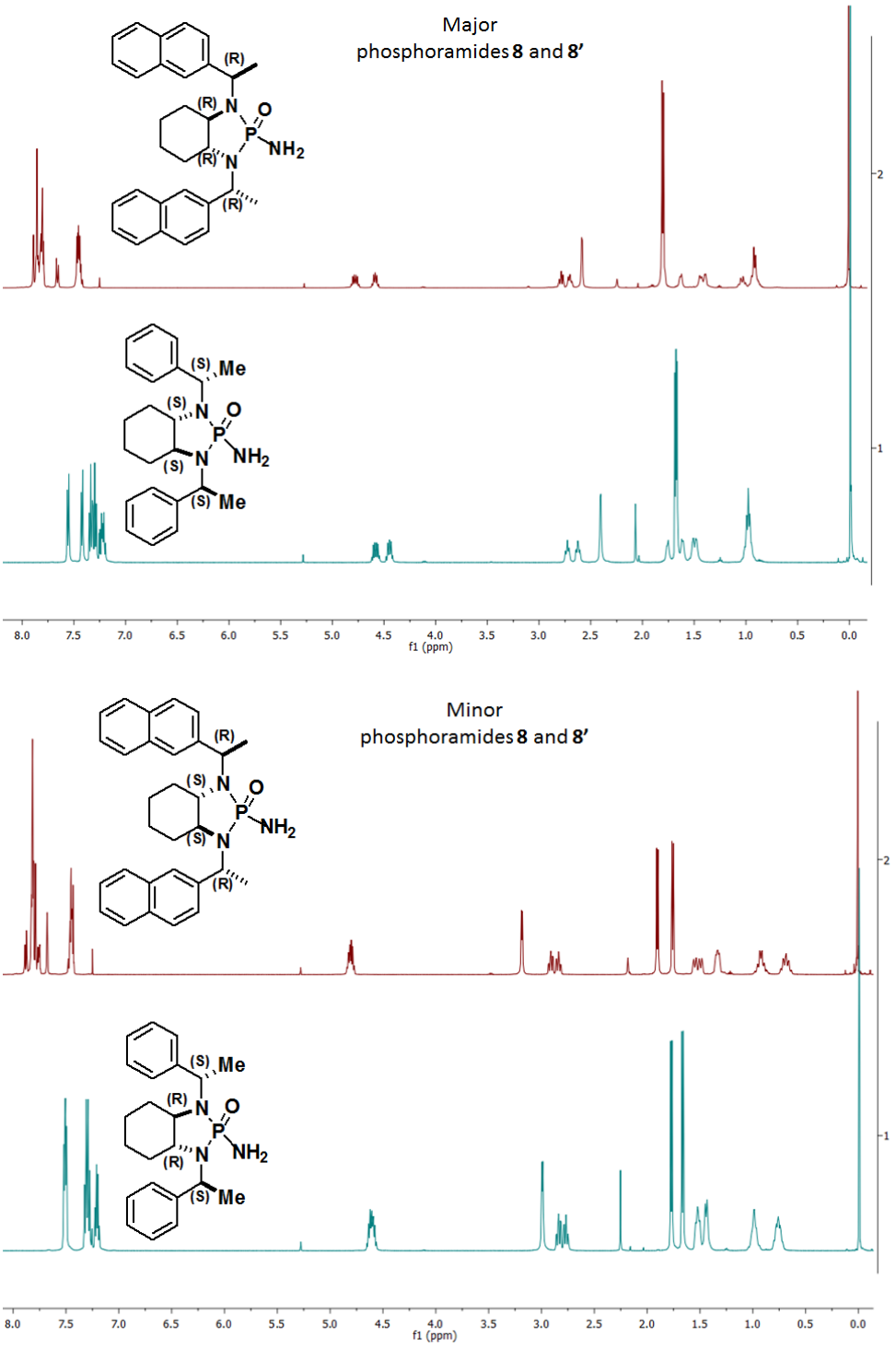
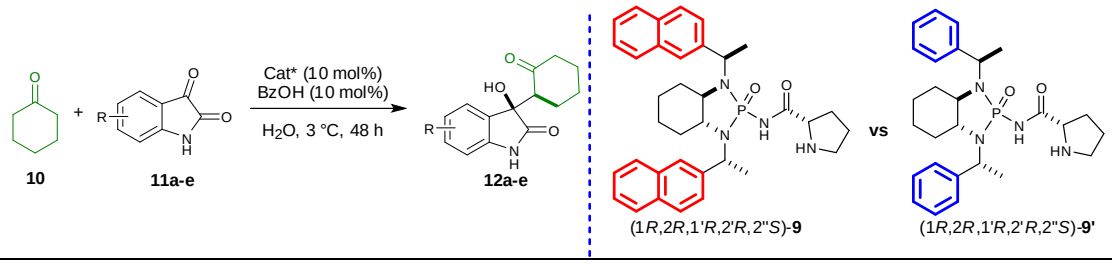


Figure S9 NMR spectra of diastereomers *(1R,2R,1'R,2'R)*-**8'** and (1S,2S,1'R,2'R)-**8'** (previous work)[1] versus diastereomers *(1R,2R,1'R,2'R)*-**8** and (1S,2S,1'R,2'R)-**8** (this work).[1]

3. Comparison of organocatalysts with (2-naphtly)ethyl- versus phenyl-moieties

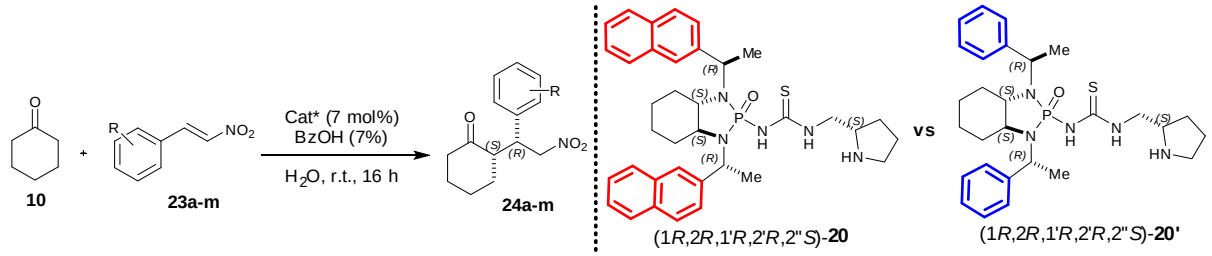
Table S1 Comparison between (*1R,2R,1'R,2'R,2''S*)-**9** and (*1R,2R,1'R,2'R,2''S*)-**9'** organocatlyst in aldol addition reaction of cyclohexanone to aryl-substituted isatins.[1]



Entry	Cat*[a]	R	Yield[b]	rd[b] (*l*/*ul*)	er[c]
1	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**9'**	5-NO_2	94	90:10	92:8
2	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**9**	5-NO_2	92	90:10	90:10
3	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**9'**	5-Br	85	90:10	76:24
4	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**9**	5-Br	84	91:9	73:27
5	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**9'**	7-Cl	84	80:20	86:14
6	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**9**	7-Cl	79	84:16	66:34

[a]Reaction conditions: Aryl-substituted isatin (1.0 mmol, 1.0 equiv.), cyclohexanone (7.0 equiv.), benzoic acid (0.1 equiv.), Cat* (10 mol%) and water (1 mL), 48 h at 3 °C. [b]Determined of isolated products after chromatographic purification based on isatin. [c]Determined by ^{1}H NMR. [d]Determined by chiral HPLC.

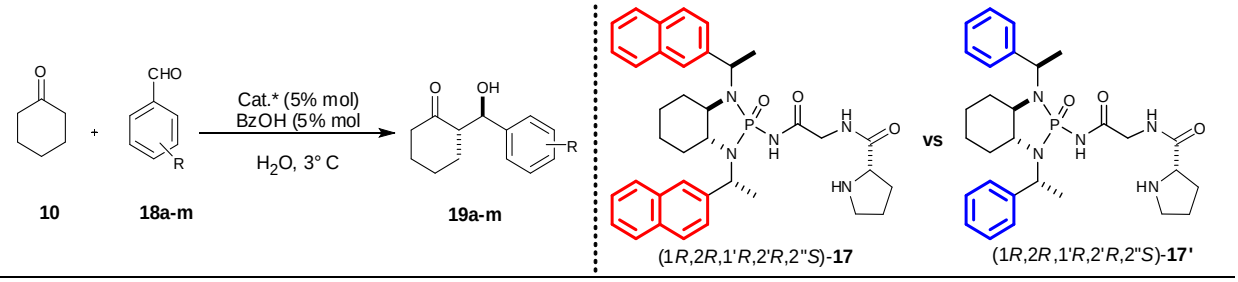
Table S2 Comparison of (1*S*,2*S*,1'*R*,2'*R*,2''*S*)-**20** and (1*S*,2*S*,1'*R*,2'*R*,2''*S*)-**20'** organocatalysts in Michael addition reaction of cyclohexanone to various substituted β-nitroolefins.[3]



Entry	R	Cat*[a]	Yield (%)[b]	dr (*syn*/*anti*)[c]	er[d]
1	2-Cl	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**20'**	99	94:6	98:2
2	2-Cl	(1S,2S,1'*R*,2'*R*,2''*S*)-**20**	99	95:5	97:3
3	3-Cl	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**20'**	37	97:3	96:4
4	3-Cl	(1S,2S,1'*R*,2'*R*,2''*S*)-**20**	32	92:8	97:3
5	4-Cl	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**20'**	52	97:3	98:2
6	4-Cl	(1S,2S,1'*R*,2'*R*,2''*S*)-**20**	46	94:6	97:3
7	2-Br	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**20'**	99	94:6	97:3
8	2-Br	(1S,2S,1'*R*,2'*R*,2''*S*)-**20**	99	96:4	93:7
9	3-Br	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**20'**	31	97:3	98:2
10	3-Br	(1S,2S,1'*R*,2'*R*,2''*S*)-**20**	33	92:8	97:3
11	4-Br	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**20'**	99	97:3	96:4
12	4-Br	(1S,2S,1'*R*,2'*R*,2''*S*)-**20**	95	95:5	98:2
13	4-NO_2	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**20'**	94	96:4	97:3
14	4-NO_2	(1S,2S,1'*R*,2'*R*,2''*S*)-**20**	99	90:10	97:3
15	4-Me	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**20'**	86	96:4	96:4
16	4-Me	(1S,2S,1'*R*,2'*R*,2''*S*)-**20**	77	96:4	96:4

[a]Reaction conditions: Substituted β-nitroolefins (1.0 mmol, 1.0 equiv.), cyclohexanone (7.0 equiv.), benzoic acid (0.07 equiv.), Cat.* (7 mol%) and water (1 mL), at room temperature for 16 h. [b]Determined of isolated products after chromatographic purification based on β-nitroolefin. [c]Determined by ^{1}H NMR of crude product. [d]Determined by chiral HPLC.

Table S3 Comparison between (*1R,2R,1'R,2'R,2''S*)-**17** and (*1R,2R,1'R,2'R,2''S*)-**17'** organocatalyst in Aldol addition reaction of cyclohexanone to substituted arylcarbaldehyde.[2]

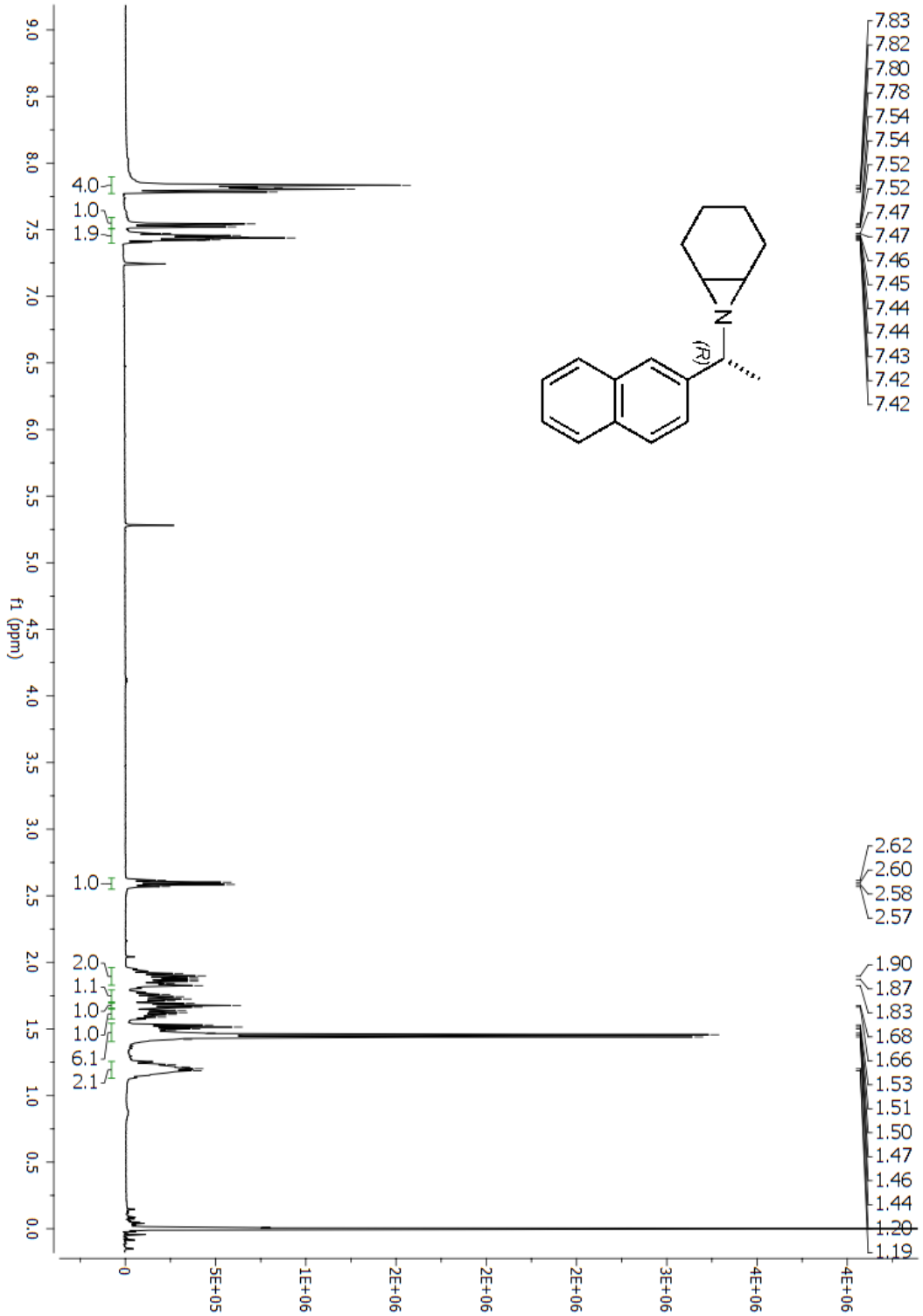


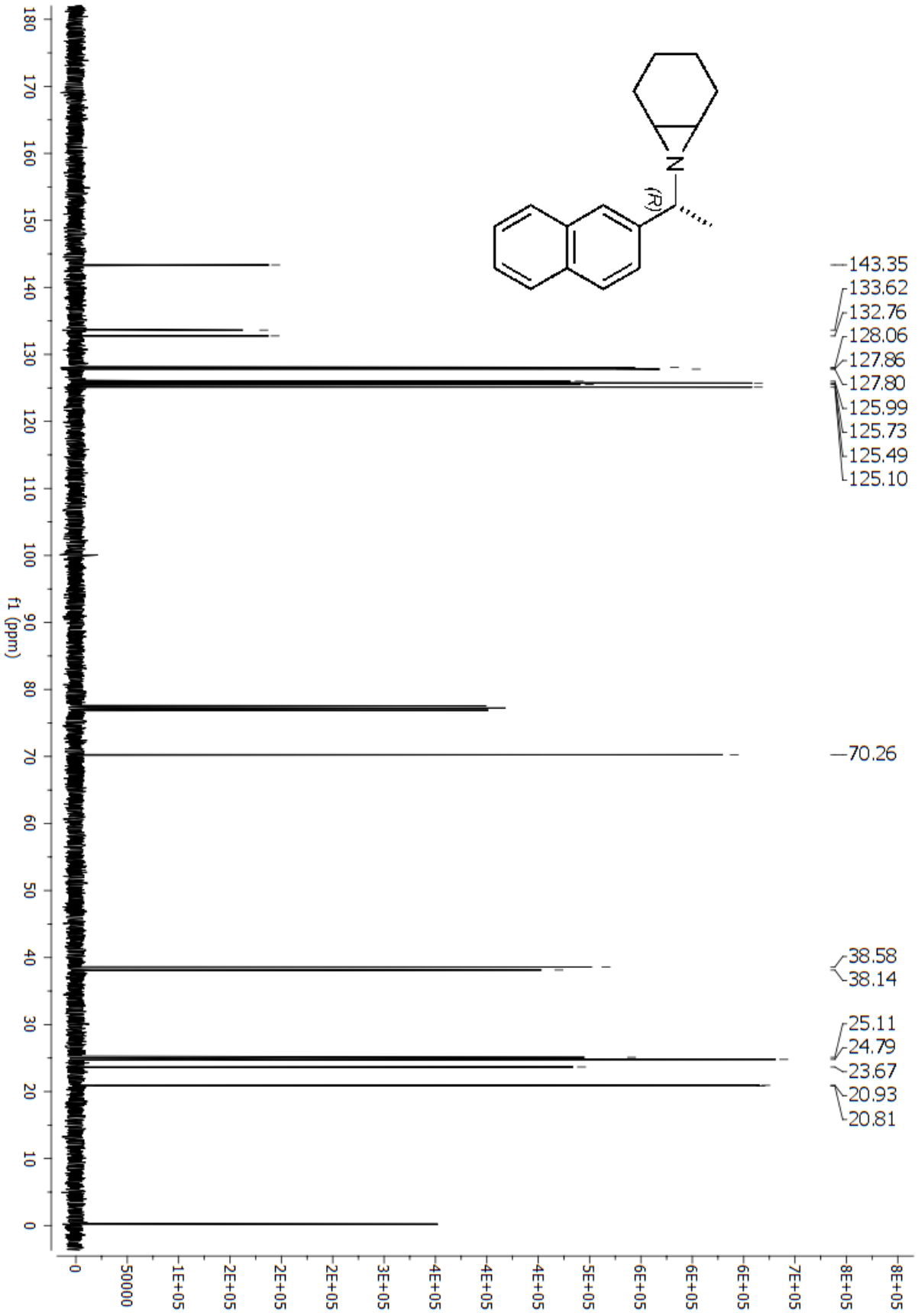
Entry	Cat.*[a]	R	T (h)	Yield (%)[b]	dr (anti/syn)[c]	er[d]
1	(1*S*,2*S*,1'*R*,2'*R*,2''*S*)-**17'**	2-Cl	96	96	89:11	91:9
2	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**17**	2-Cl	96	99	92:8	93:7
3	(1*S*,2*S*,1'*R*,2'*R*,2''*S*)-**17'**	3-Cl	96	96	93:7	92:8
4	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**17**	3-Cl	96	99	93:7	94:6
5	(1*S*,2*S*,1'*R*,2'*R*,2''*S*)-**17'**	4-Cl	96	83	91:9	89:11
6	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**17**	4-Cl	96	80	93:7	96:4
7	(1*S*,2*S*,1'*R*,2'*R*,2''*S*)- **11'**	4-Br	96	87	92:8	90:10
8	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**17**	4-Br	96	85	92:8	93:7
9	(1*S*,2*S*,1'*R*,2'*R*,2''*S*)-**17'**	4-NO_2	30	98	92:8	93:7
10	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**17**	4-NO_2	30	99	93:7	94:6
11	(1*S*,2*S*,1'*R*,2'*R*,2''*S*)-**17'**	2-CF_3	96	72	91:9	87:13
12	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**17**	2-CF_3	96	99	92:8	92:8
13	(1*S*,2*S*,1'*R*,2'*R*,2''*S*)-**17'**	4-CF_3	24	99	93:7	93:7
14	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**17**	4-CF_3	24	99	94:6	93:7
15	(1*S*,2*S*,1'*R*,2'*R*,2''*S*)-**17'**	H	168	80	90:10	90:10
16	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**17**	H	168	83	88:12	92:8
17	(1*S*,2*S*,1'*R*,2'*R*,2''*S*)-**17'**	4-CH_3	168	44	88:12	86:14
18	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**17**	4-CH_3	168	56	90:10	93:7
19	(1*S*,2*S*,1'*R*,2'*R*,2''*S*)-**17'**	4-C_6H_5	168	46	89:11	87:13
20	(1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**17**	4-C_6H_5	168	54	91:9	91:9

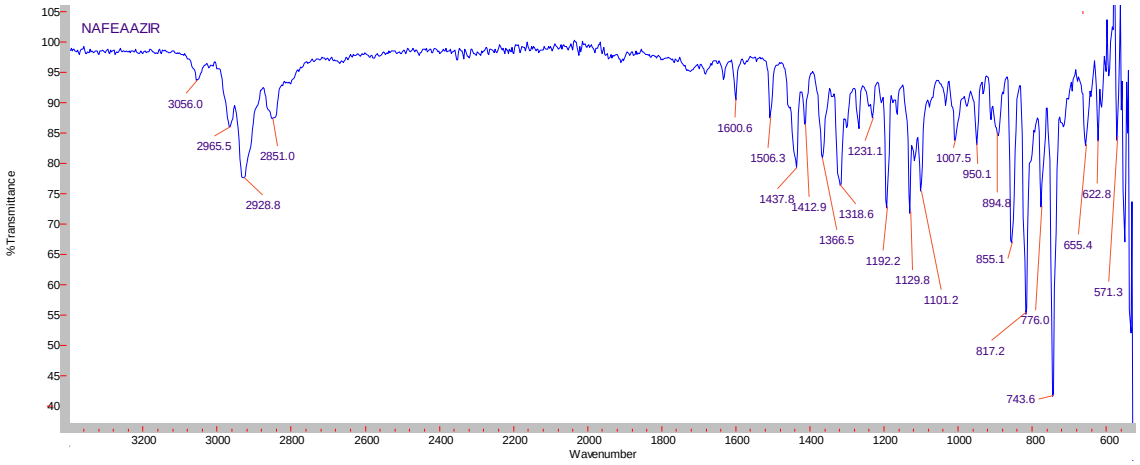
[a]Reaction conditions: Substituted arylcarbaldehyde (1.0 mmol, 1.0 equiv.), cyclohexanone (5.0 equiv.), benzoic acid (0.05 equiv.), Cat* = (1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**17** or (1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**17'** (0.05 equiv.) and water (1 mL) at 3 °C. [b]Determined of isolated products after chromatographic purification based on arylcarbaldehyde. [c]Determined by ^{1}H NMR of crude product. [d]Determined by chiral HPLC.

4. NMR spectra of synthetized compound

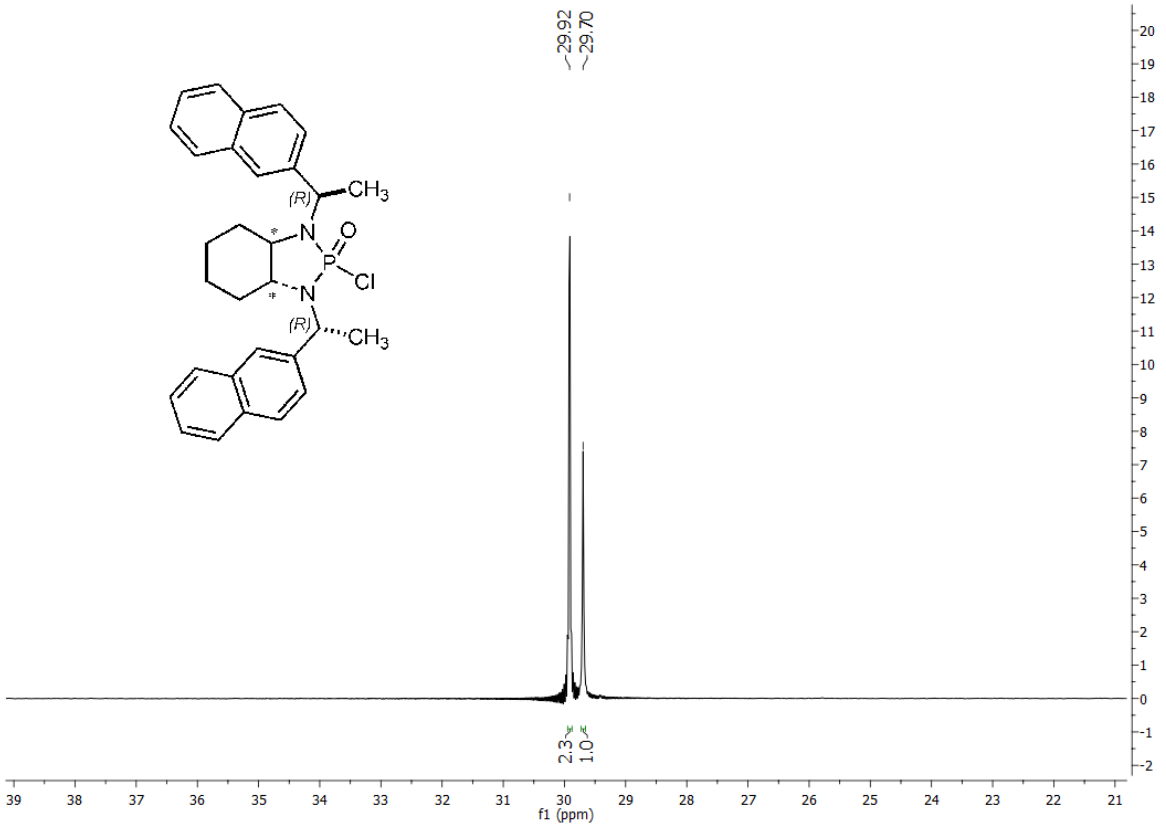
7-[(*R*)-1-(2-naphthyl)ethyl]-7-azabicyclo[4.1.0]heptane (*R*)-**3**

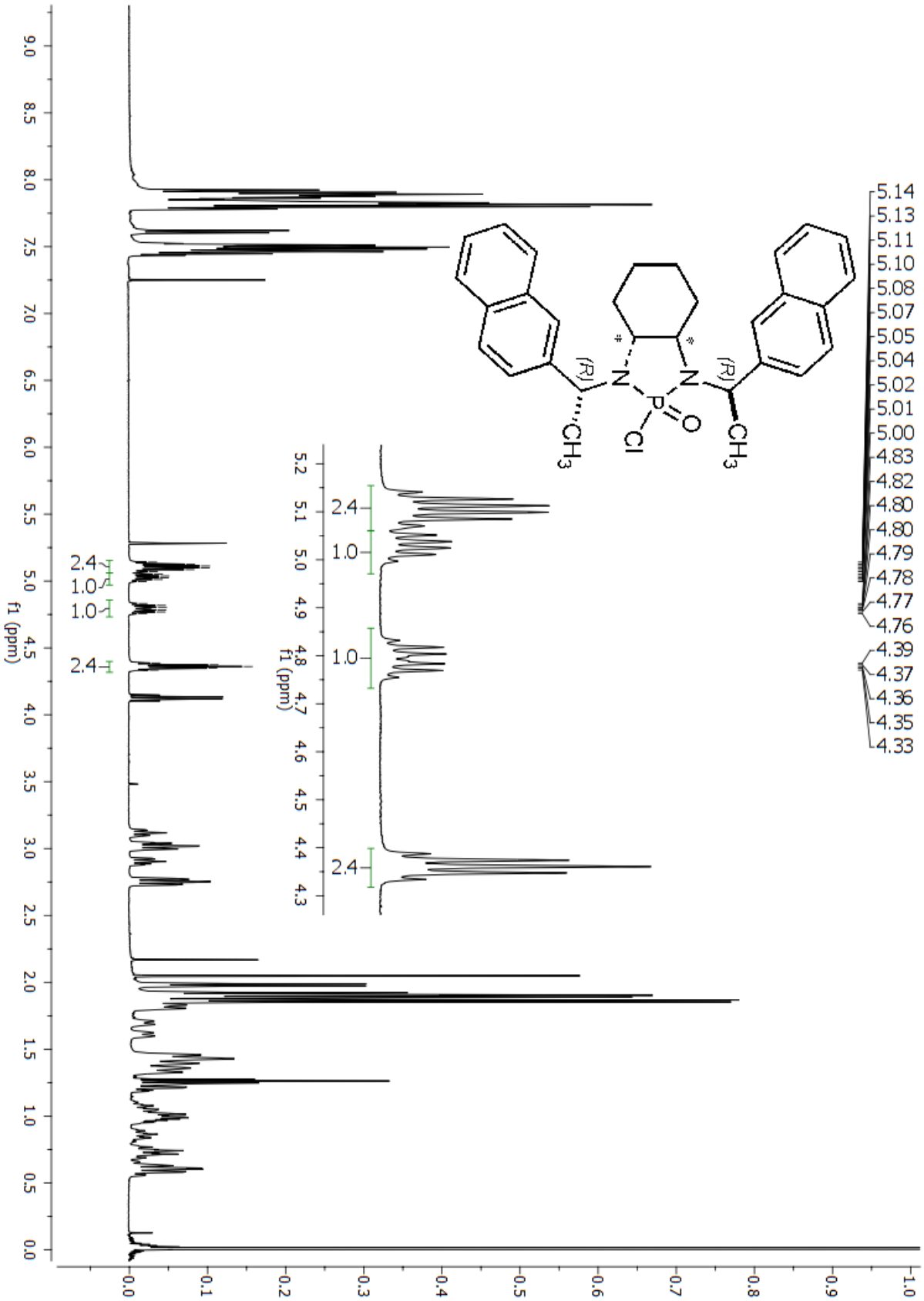



143.35
133.62
132.76
128.06
127.86
127.80
125.99
125.73
125.49
125.10
70.26
38.58
38.14
25.11
24.79
23.67
20.93
20.81
f1 (ppm)

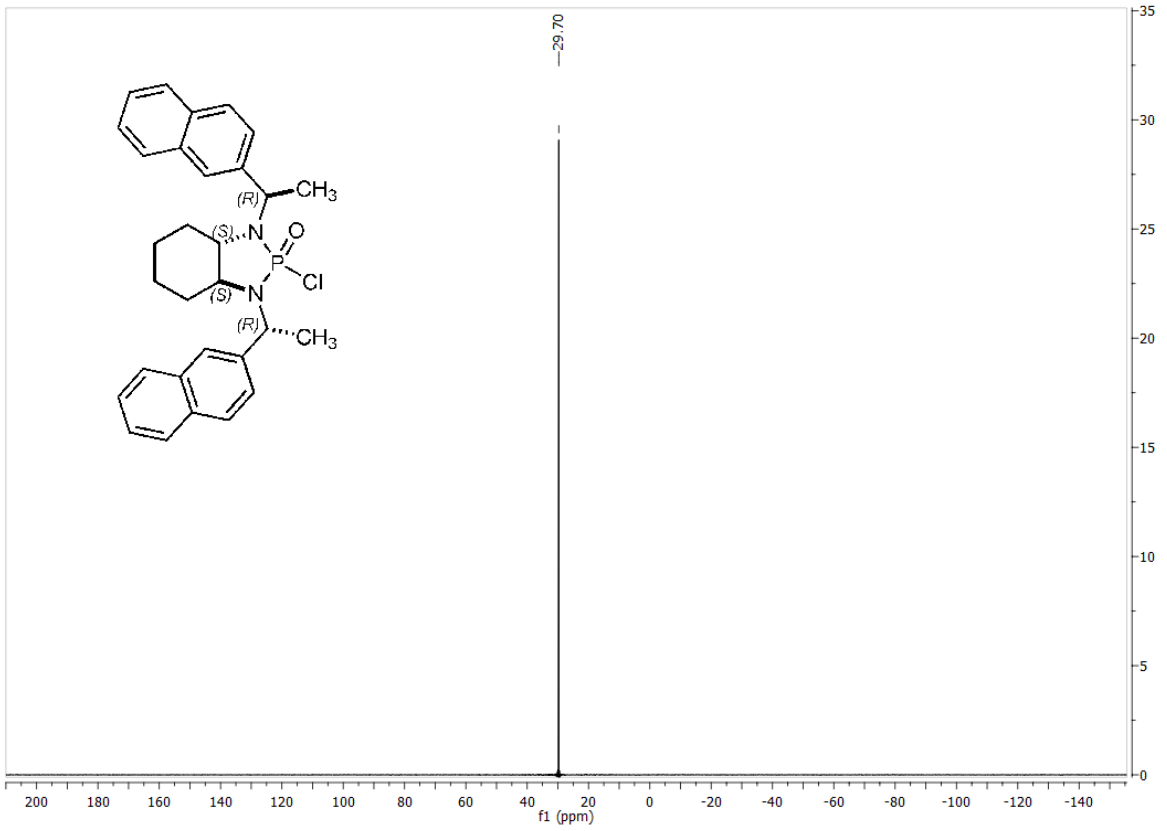


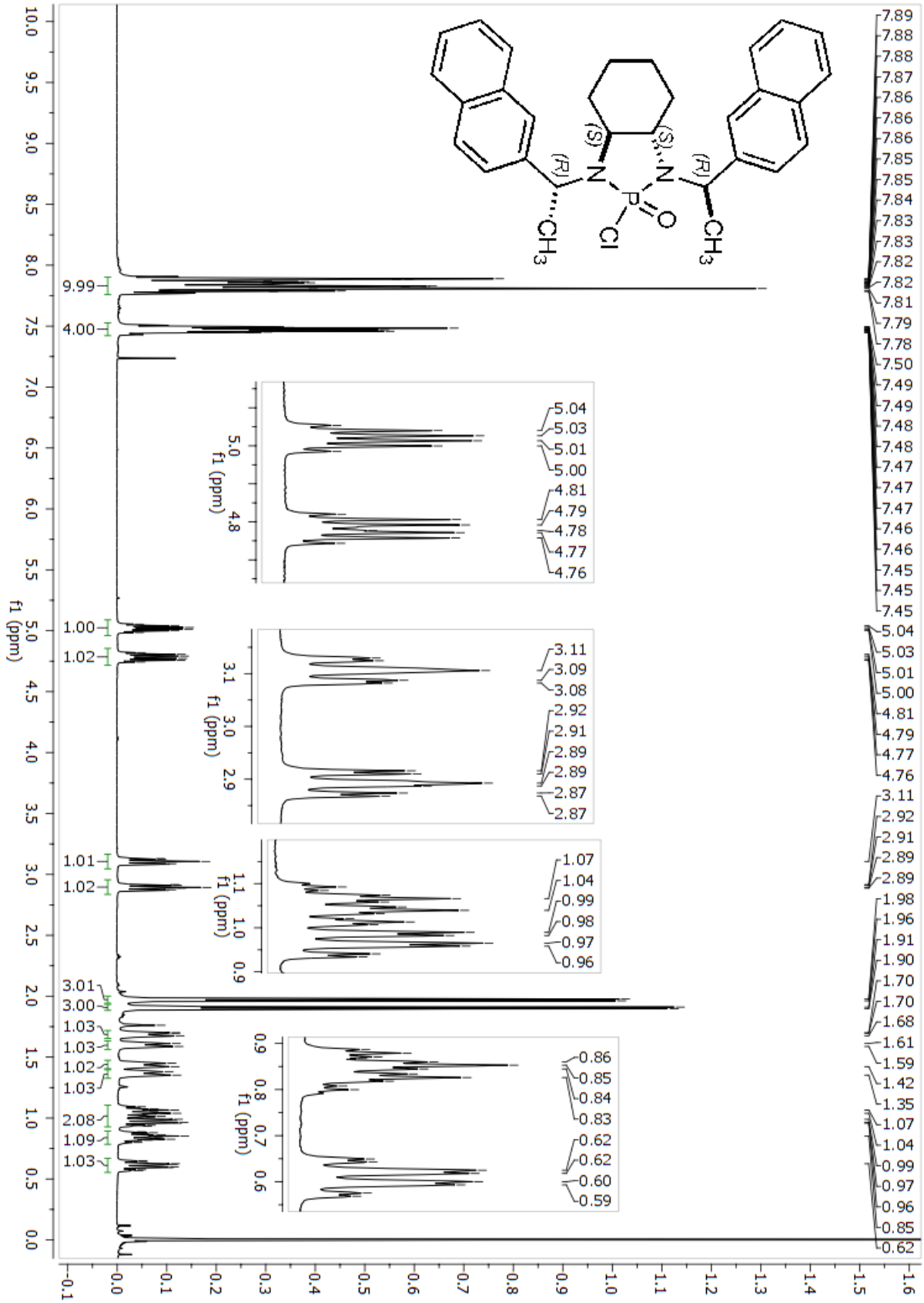
Diastereomeric mixture of (3a*RS*,7a*RS*)-2-Oxide-2-chlorooctahydro-1,3-bis[(1*R*)-1-(2-naphthyl)ethyl]-1*H*-1,3,2-benzodiazaphosphole, *(1RS,2RS,1'R,2'R)*-**6**

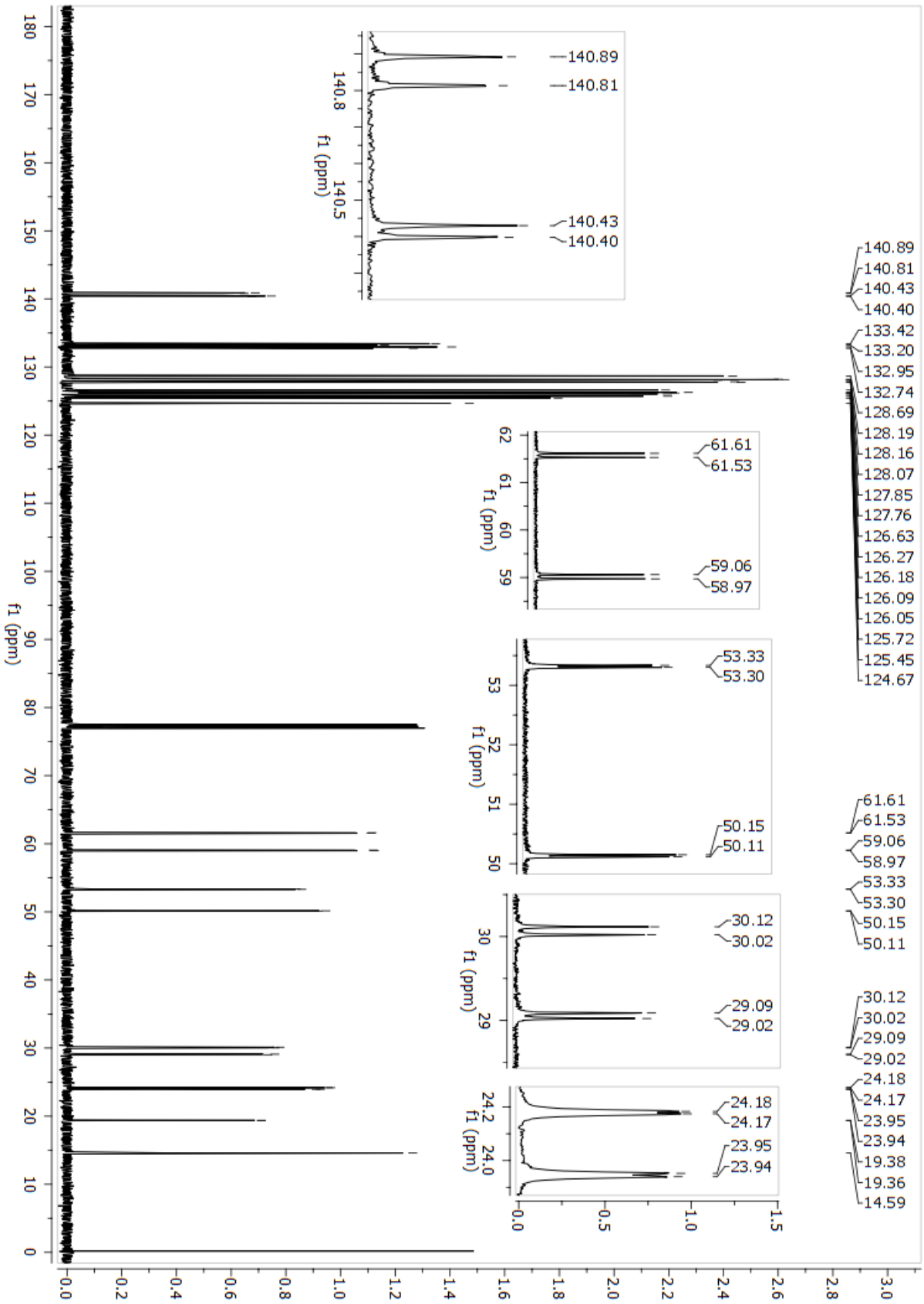


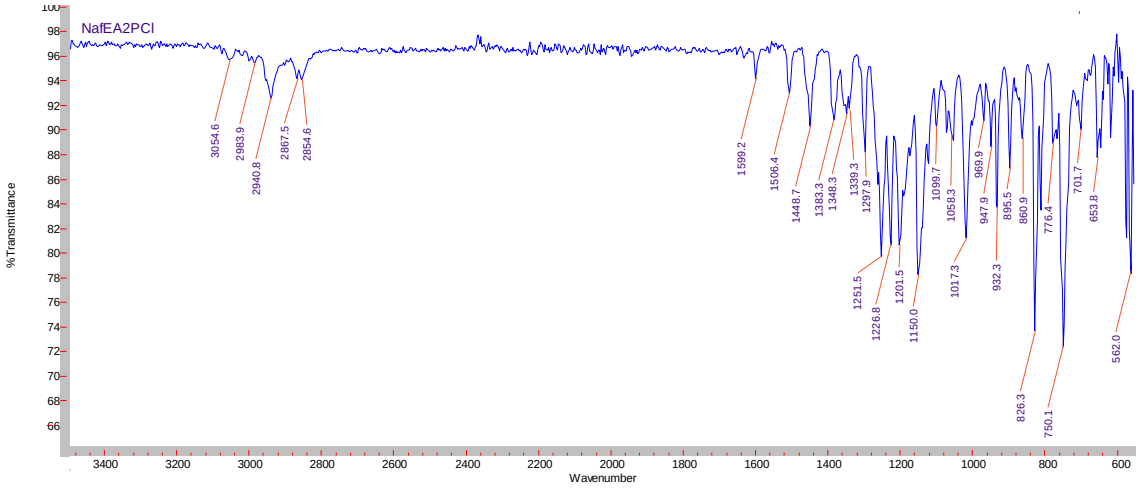

f1 (ppm)
2.4
1.0
1.0
2.4
5.14
5.13
5.11
5.10
5.08
5.07
5.05
5.04
5.02
5.01
5.00
4.83
4.82
4.80
4.80
4.79
4.78
4.77
4.76
4.39
4.37
4.36
4.35
4.33
(R)
(R)
CH3
CH3
N
N
P
O
Cl

(3a*S*,7a*S*)-2-Oxide-2-chlorooctahydro-1,3-bis[(1*R*)-1-(2-naphthyl)ethyl]-1*H*-1,3,2-benzodiazaphosphol, *(1S,2S,1'R,2'R)*-**6** (minor diastereoisomer)

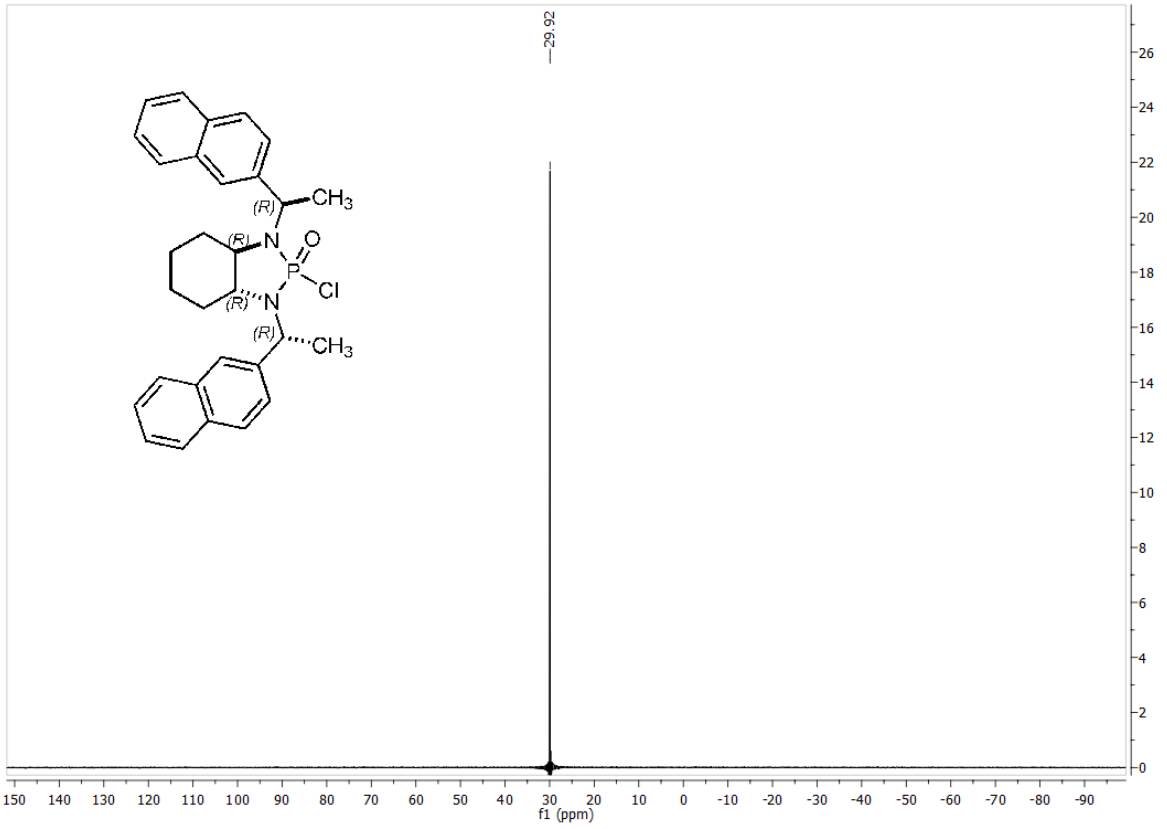


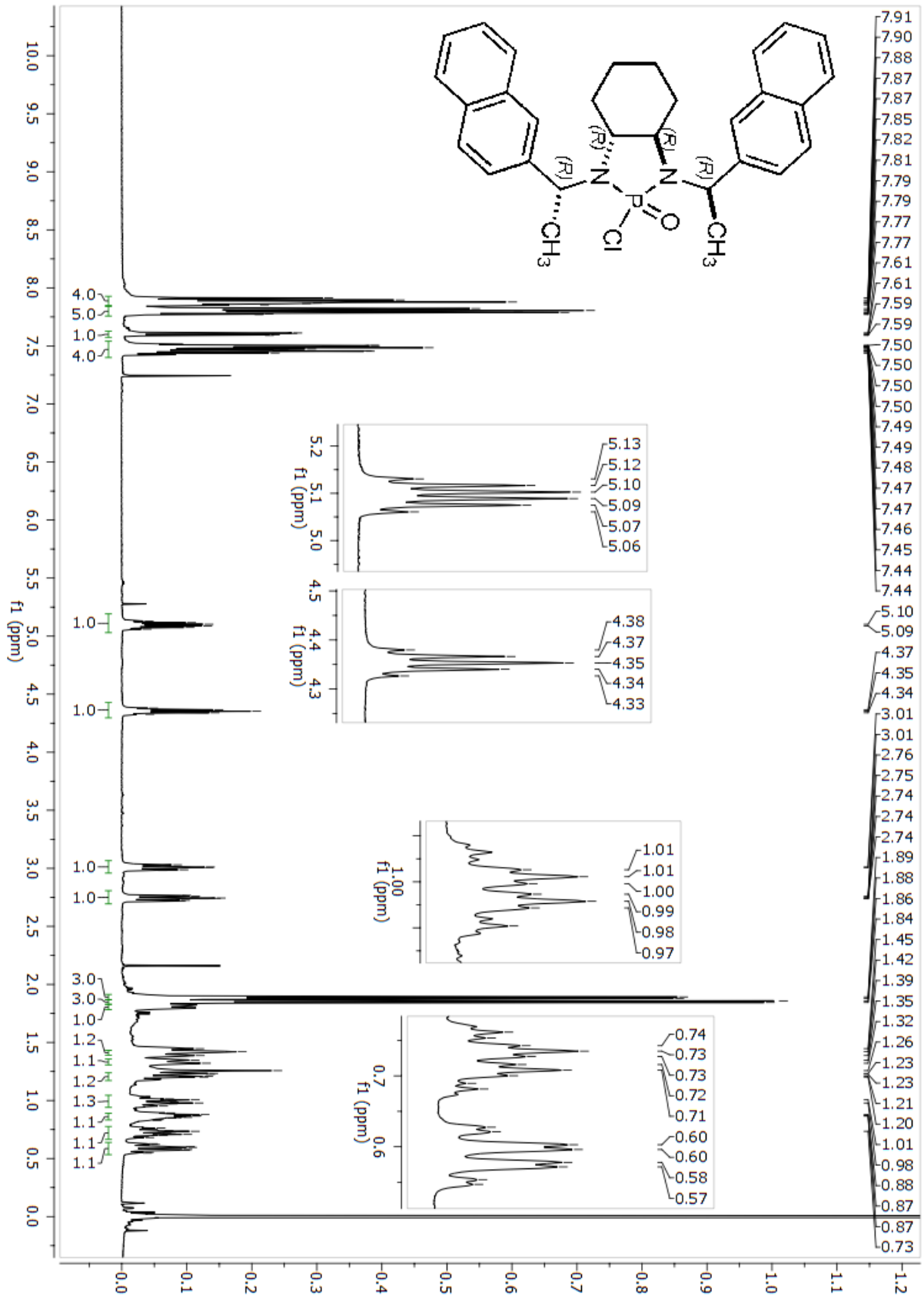

(S)
(S)
(R)
(R)
CH3
CH3
N
N
P
O
Cl
9.99
4.00
1.00
1.02
1.01
1.02
3.01
3.00
1.03
1.03
1.02
1.03
2.08
1.09
1.03
f1 (ppm)

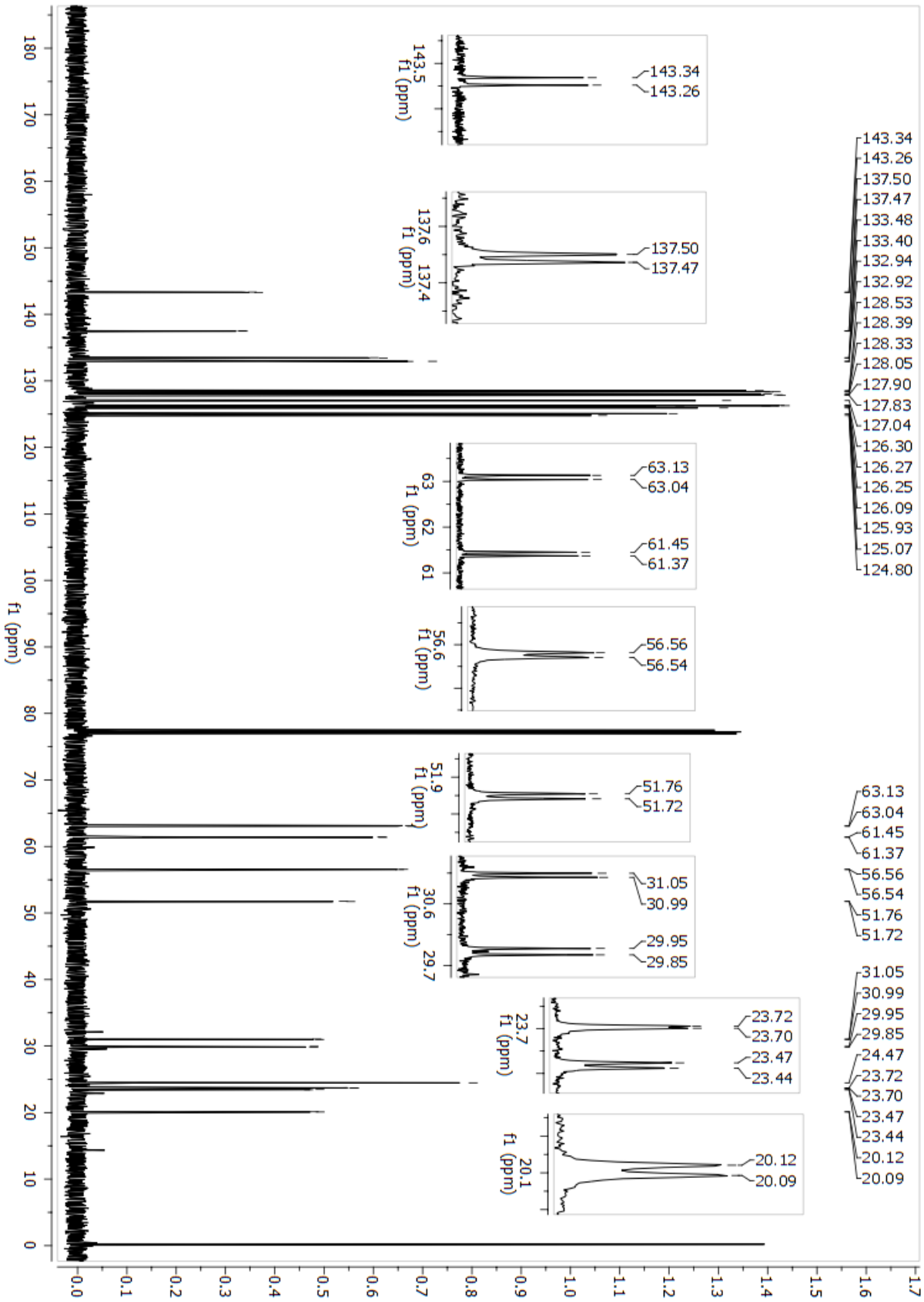

f1 (ppm)
140.89
140.81
140.43
140.40
133.42
133.20
132.95
132.74
128.69
128.19
128.16
128.07
127.85
127.76
126.63
126.27
126.18
126.09
126.05
125.72
125.45
124.67
61.61
61.53
59.06
58.97
53.33
53.30
50.15
50.11
30.12
30.02
29.09
29.02
24.18
24.17
23.95
23.94
19.38
19.36
14.59

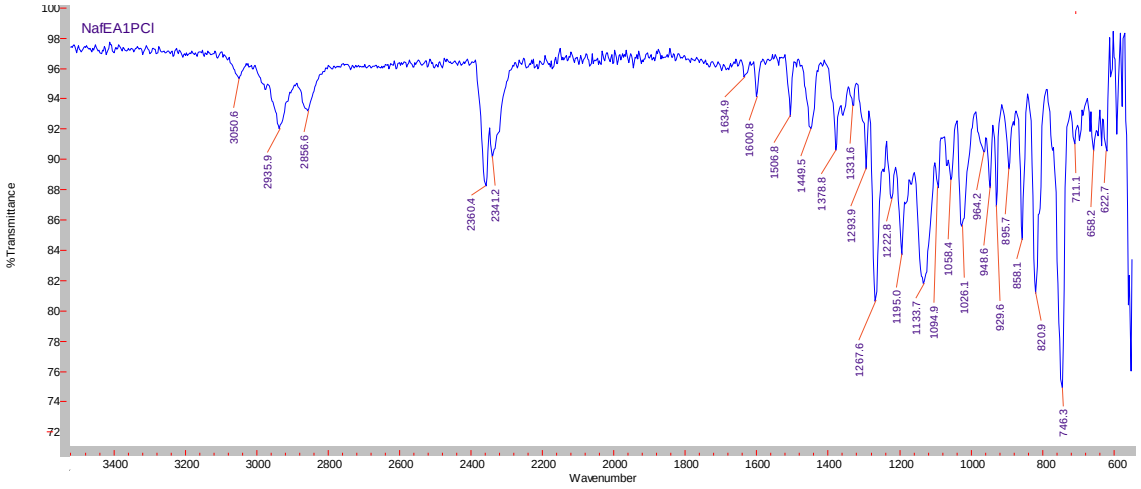


(3a*R*,7a*R*)-2-Oxide-2-chlorooctahydro-1,3-bis[(1*R*)-1-(2-naphthyl)ethyl]-1*H*-1,3,2-benzodiazaphosphol, *(1S,2S,1'R,2'R)*-**6** (major diastereoisomer)

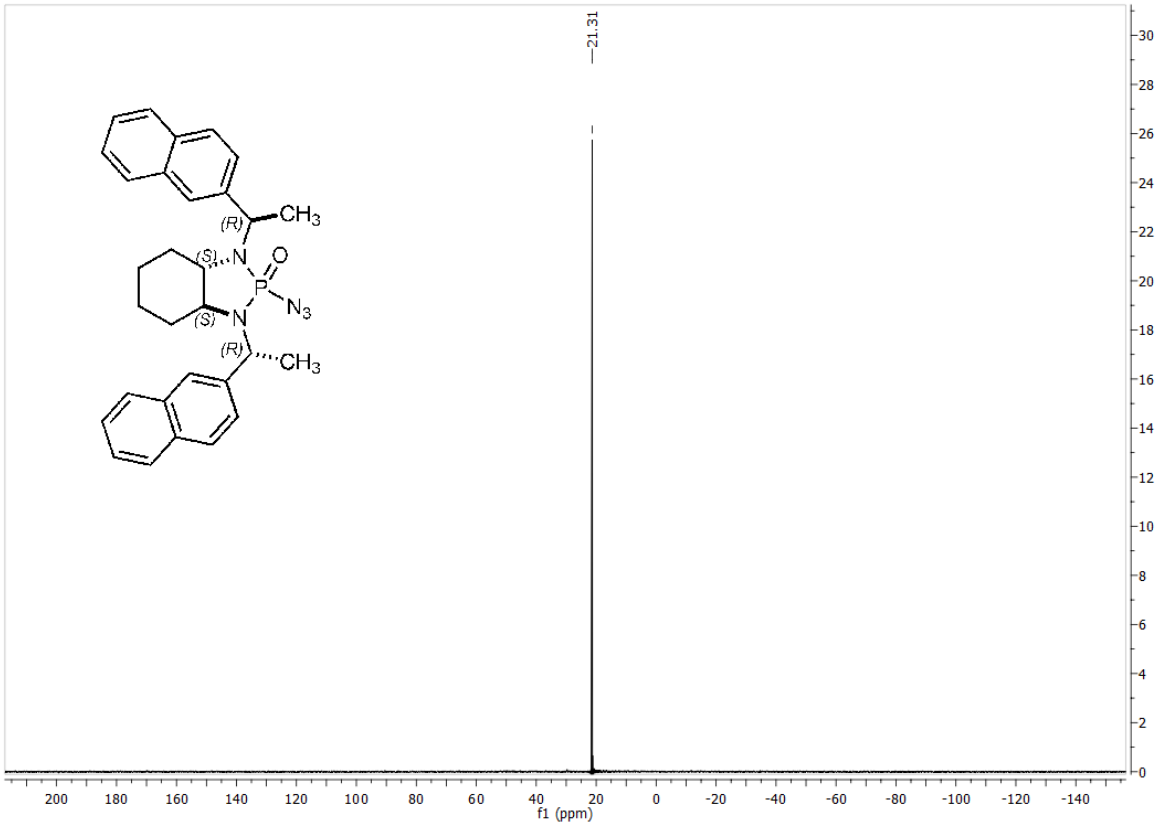


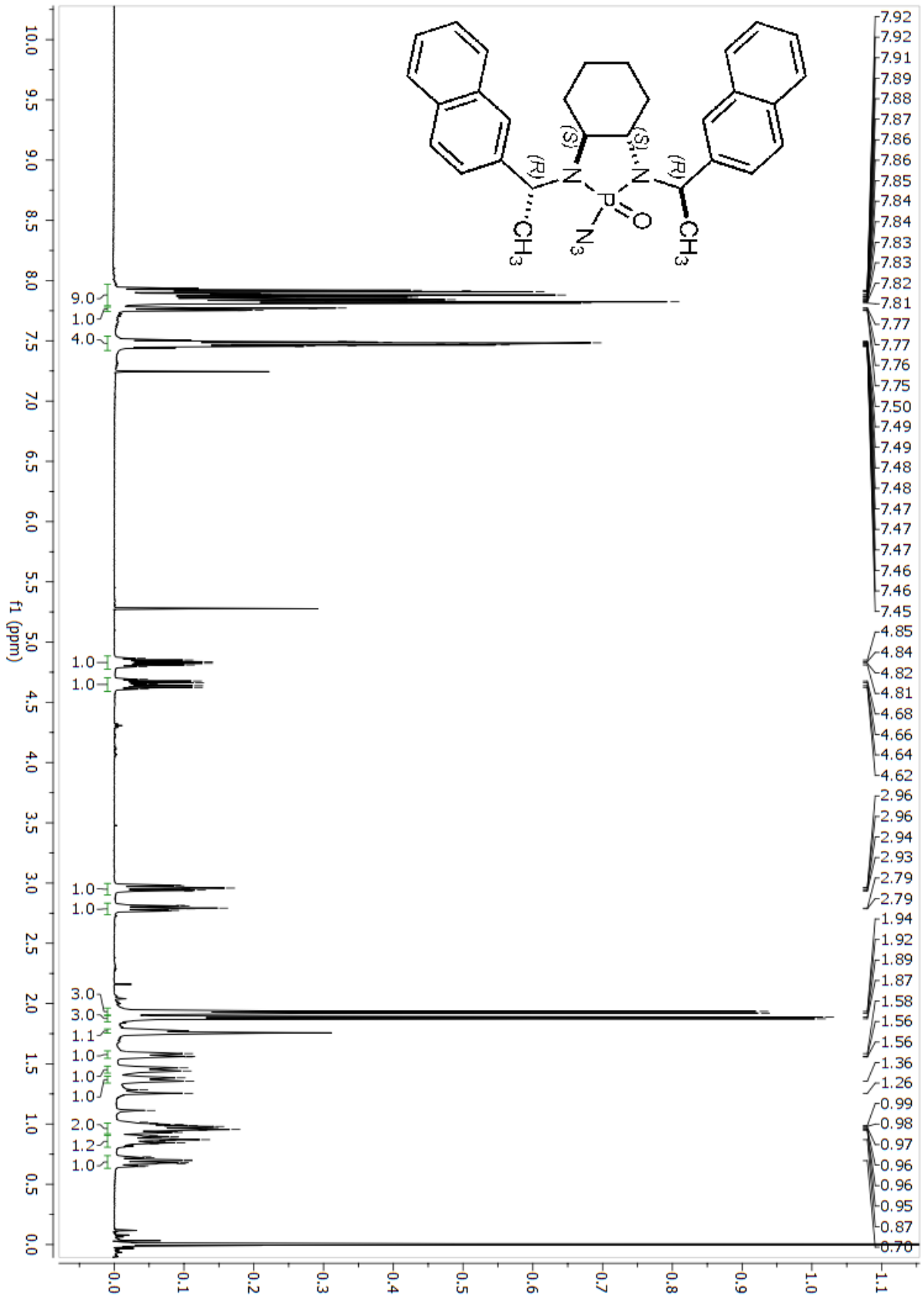


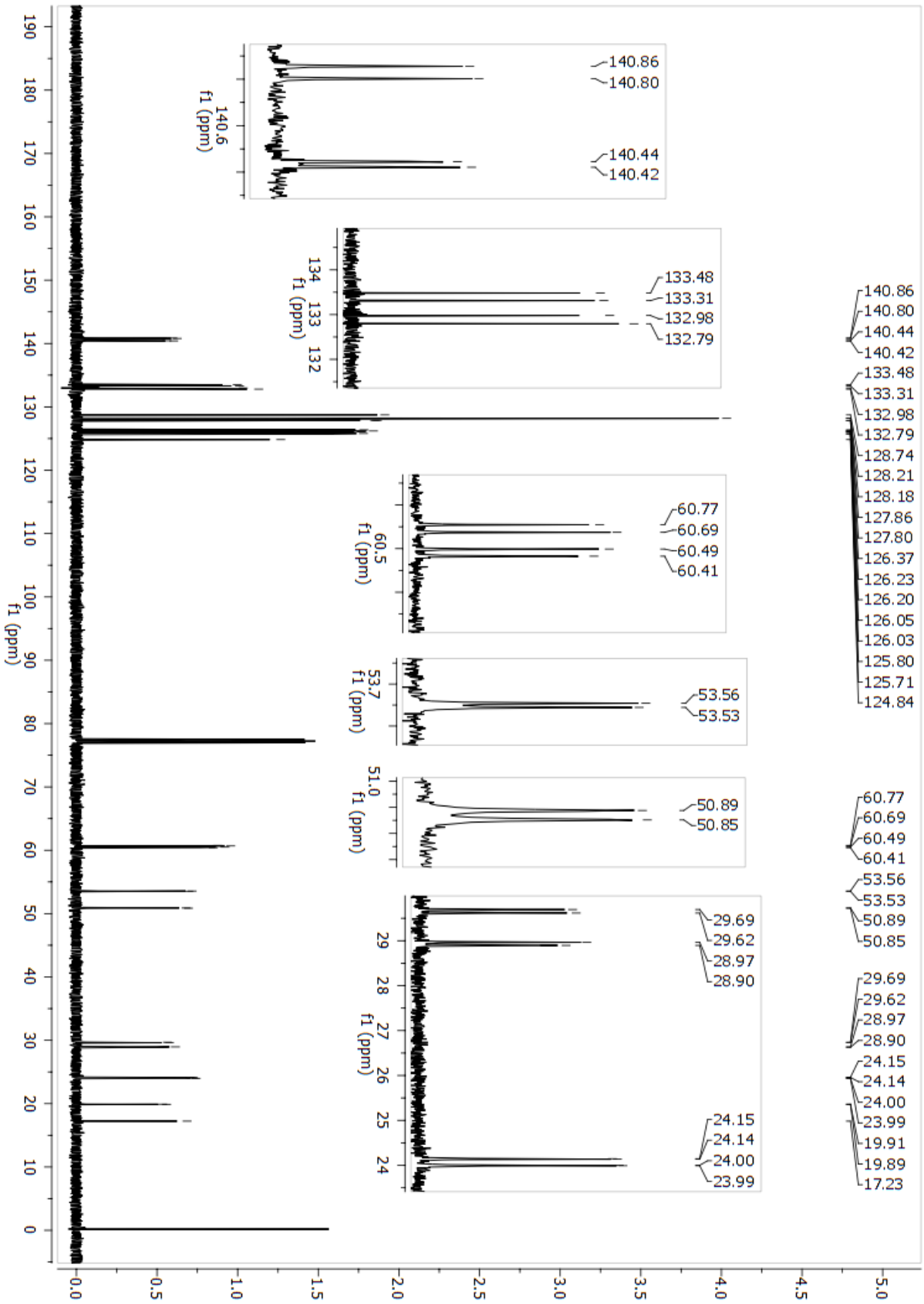

143.34
143.26
137.50
137.47
133.48
133.40
132.94
132.92
128.53
128.39
128.33
128.05
127.90
127.83
127.04
126.30
126.27
126.25
126.09
125.93
125.07
124.80
63.13
63.04
61.45
61.37
56.56
56.54
51.76
51.72
31.05
30.99
29.95
29.85
24.47
23.72
23.70
23.47
23.44
20.12
20.09
f1 (ppm)

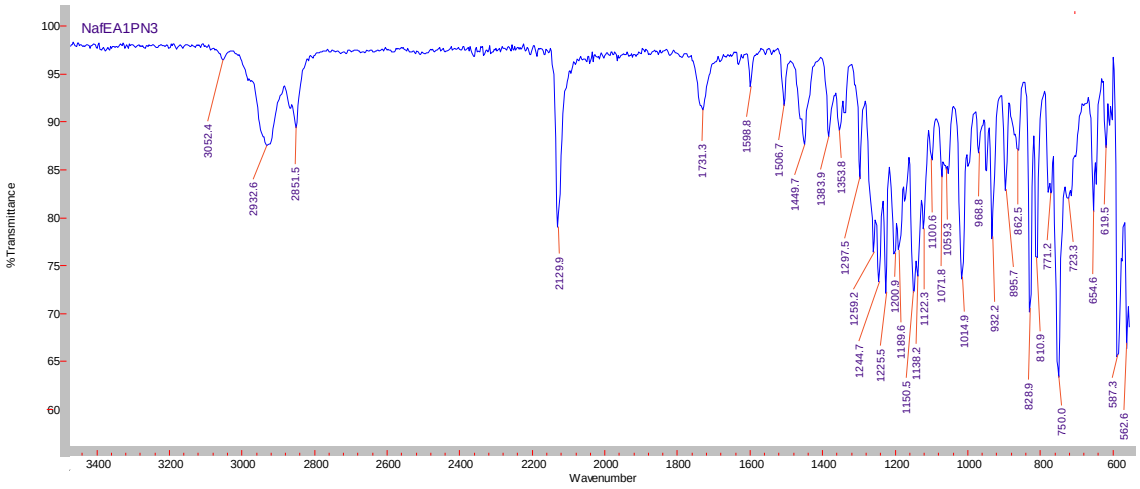


(3a*S*,7a*S*)-2-Oxide-2-azidooctahydro-1,3-bis[(1*R*)-1-(2-naphthyl)ethyl]-1*H*-1,3,2-benzodiazaphosphol, *(1S,2S,1'R,2'R)*-**7** (minor diastereoisomer)

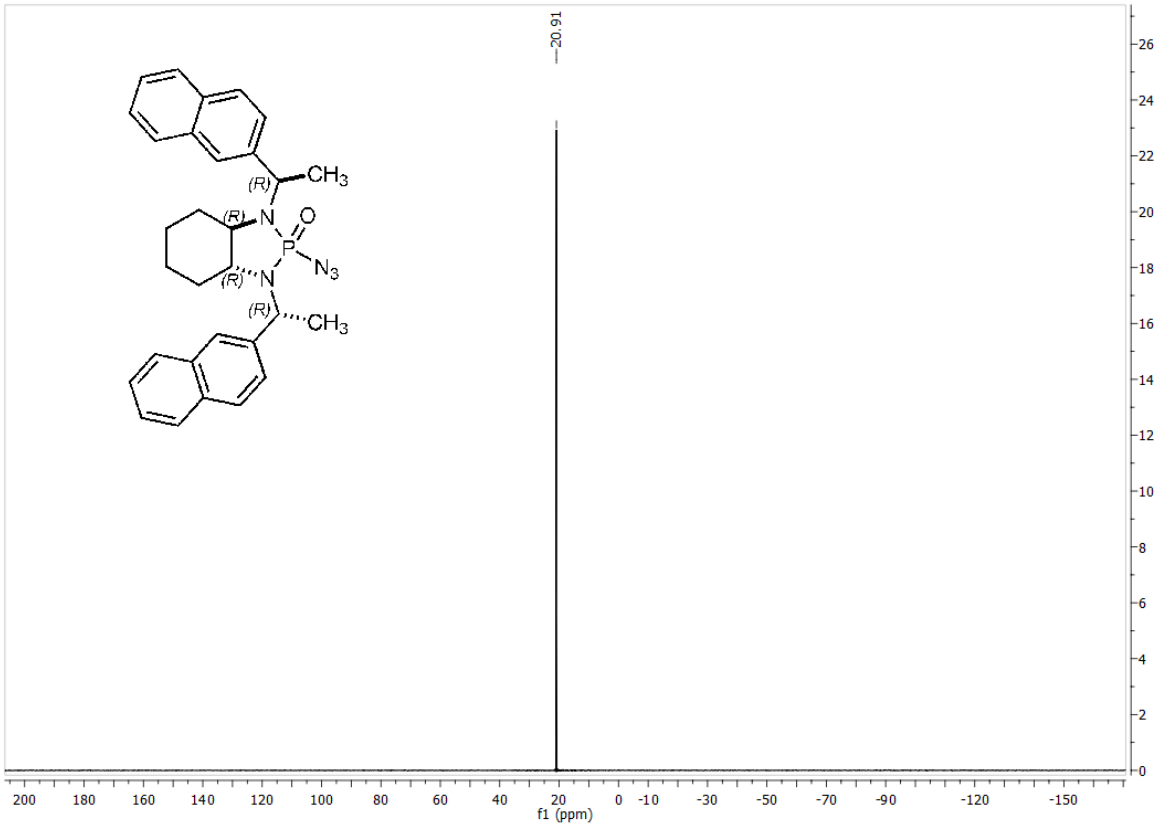


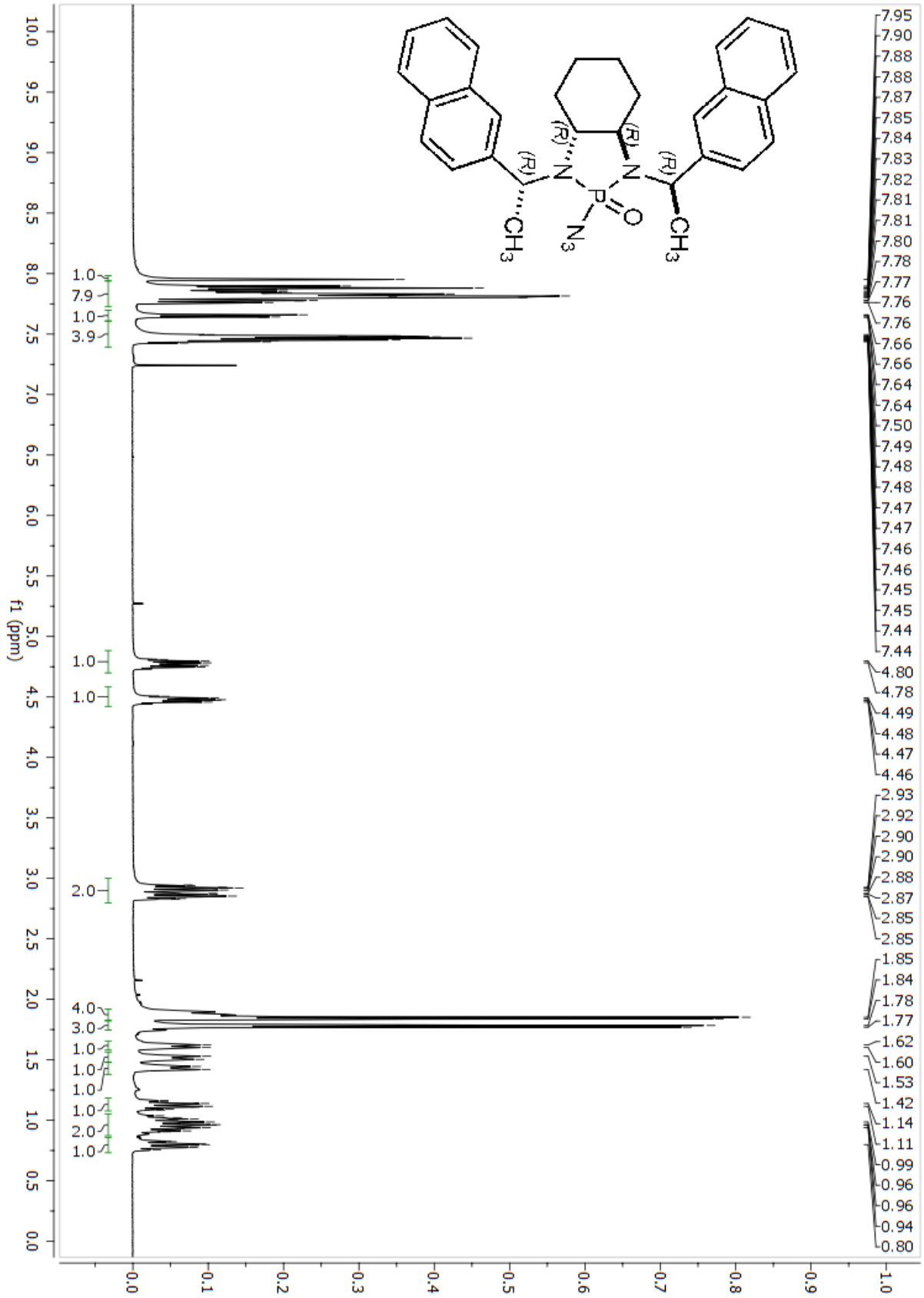

f1 (ppm)
9.0
1.0
4.0
1.0
1.0
1.0
1.0
3.0
3.0
1.1
1.0
1.0
1.0
2.0
1.2
1.0
7.92
7.92
7.91
7.89
7.88
7.87
7.86
7.86
7.85
7.84
7.84
7.83
7.83
7.82
7.81
7.77
7.77
7.76
7.75
7.50
7.49
7.49
7.48
7.48
7.47
7.47
7.47
7.46
7.46
7.45
4.85
4.84
4.82
4.81
4.68
4.66
4.64
4.62
2.96
2.96
2.94
2.93
2.79
2.79
1.94
1.92
1.89
1.87
1.58
1.56
1.56
1.36
1.26
0.99
0.98
0.97
0.96
0.96
0.95
0.87
0.70
(R)
(S)
(S)
(R)
CH3
CH3
N3
P
O
N
N

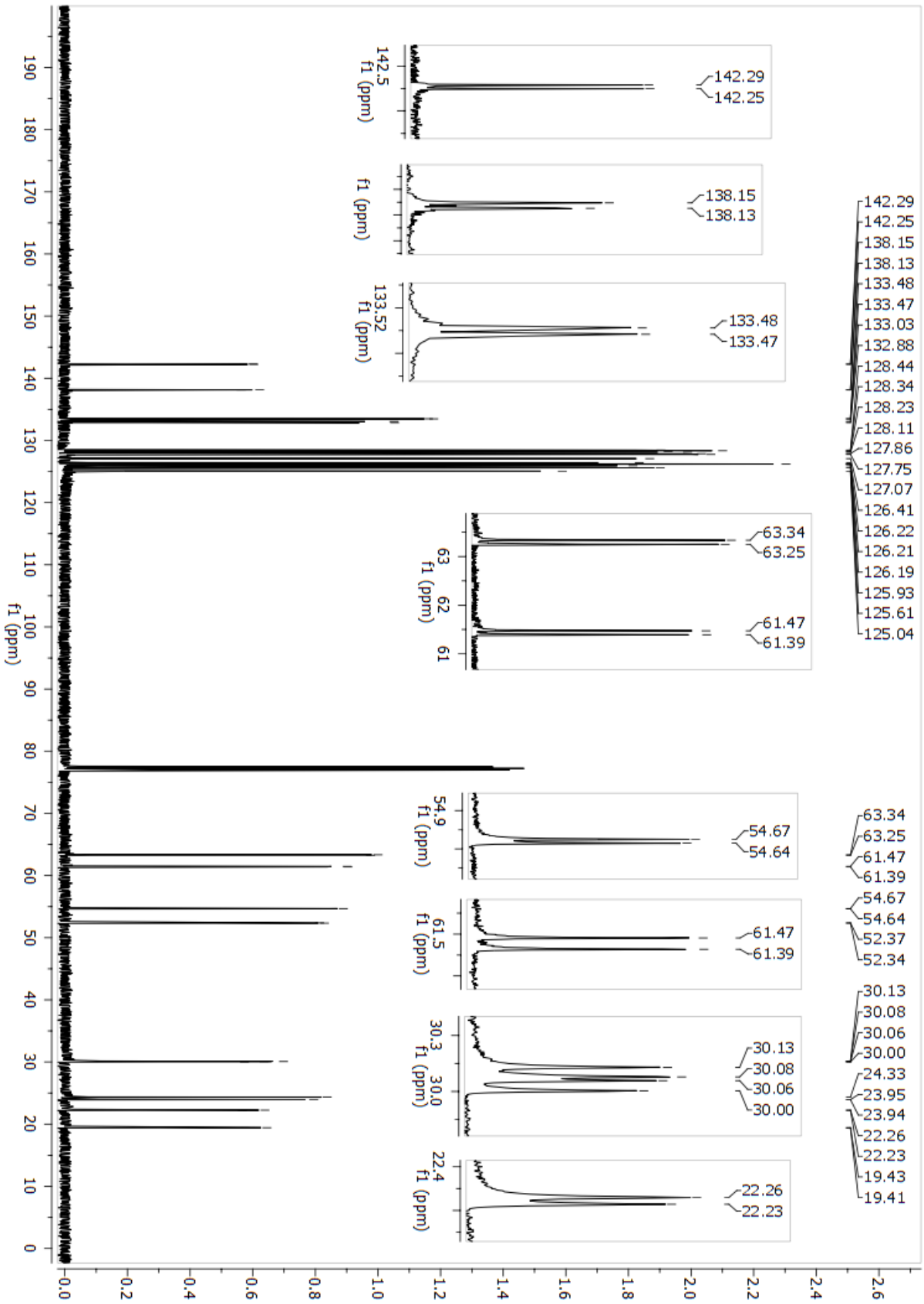

f1 (ppm)
140.6
140.86
140.80
140.44
140.42
134
133
132
133.48
133.31
132.98
132.79
60.5
60.77
60.69
60.49
60.41
53.7
53.56
53.53
51.0
50.89
50.85
29
28
27
26
25
24
29.69
29.62
28.97
28.90
24.15
24.14
24.00
23.99
140.86
140.80
140.44
140.42
133.48
133.31
132.98
132.79
128.74
128.21
128.18
127.86
127.80
126.37
126.23
126.20
126.05
126.03
125.80
125.71
124.84
60.77
60.69
60.49
60.41
53.56
53.53
50.89
50.85
29.69
29.62
28.97
28.90
24.15
24.14
24.00
23.99
19.91
19.89
17.23

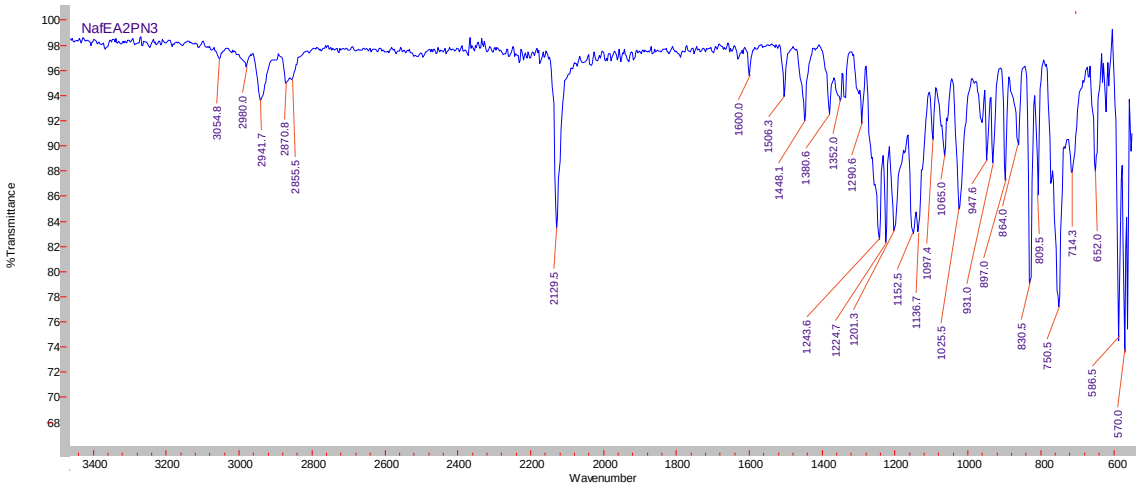


(3a*R*,7a*R*)-2-Oxide-2-clorooctahydro-1,3-bis[(1*R*)-1-(2-naphthyl)ethyl]-1*H*-1,3,2-benzodiazaphosphol, *(1R,2R,1'R,2'R)*-**7** (major diastereoisomer)

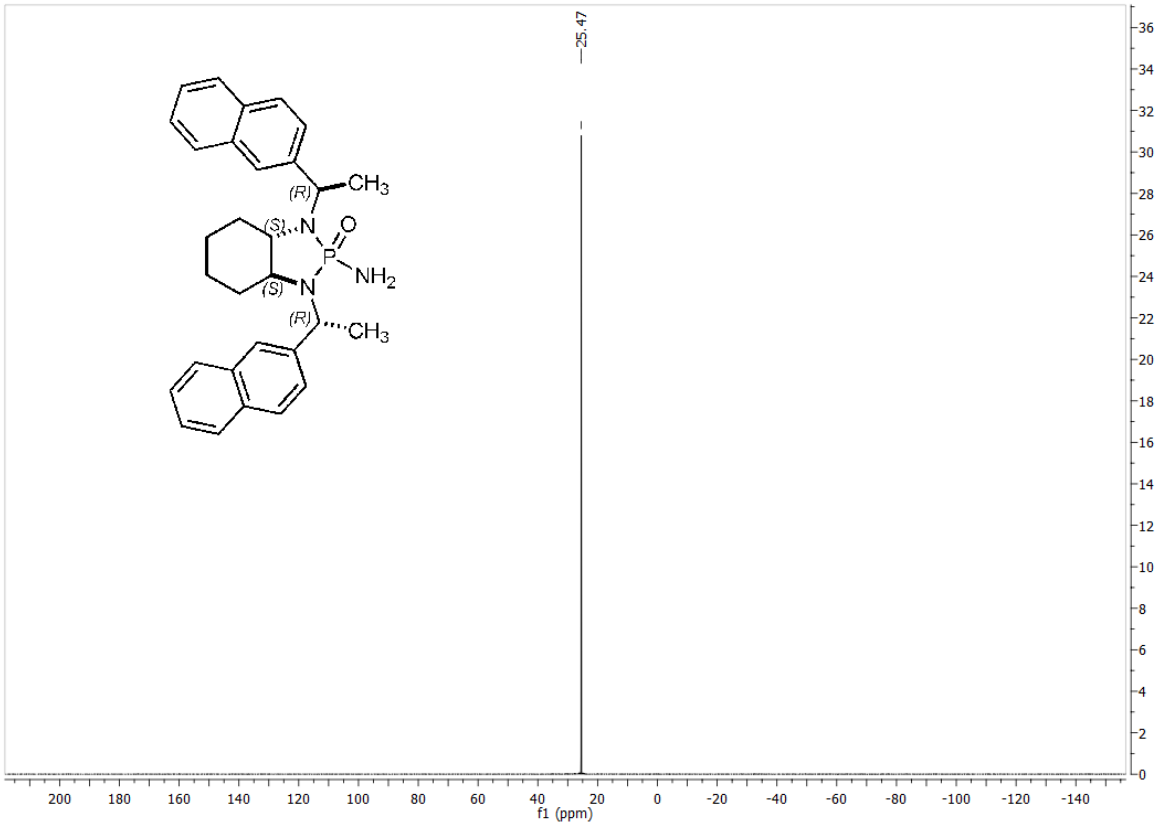


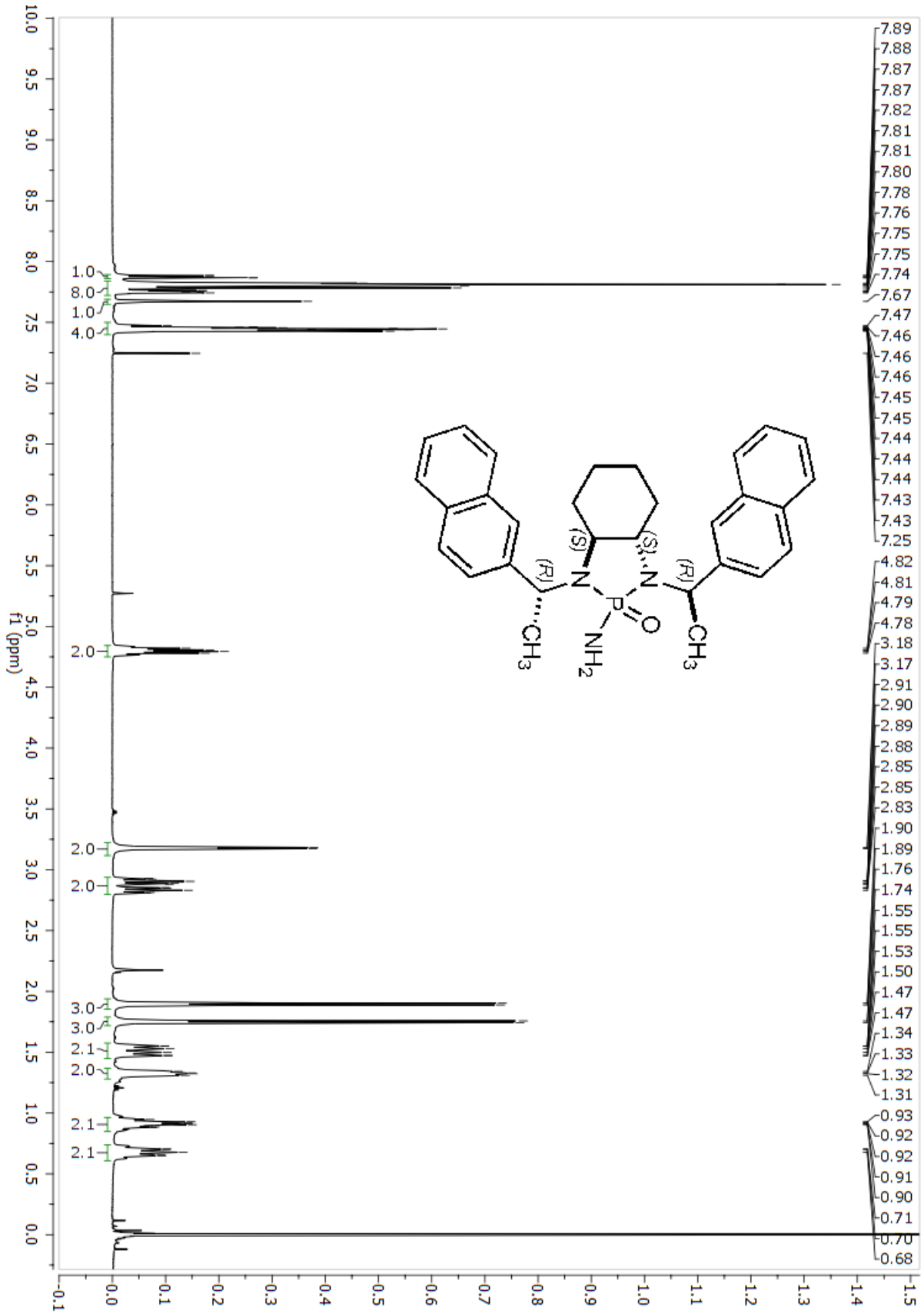

f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.0
7.9
1.0
3.9
1.0
1.0
2.0
4.0
3.0
1.0
1.0
1.0
1.0
2.0
1.0
7.95
7.90
7.88
7.88
7.87
7.85
7.84
7.83
7.82
7.81
7.81
7.80
7.78
7.77
7.76
7.76
7.66
7.66
7.64
7.64
7.50
7.49
7.48
7.48
7.47
7.47
7.46
7.46
7.45
7.45
7.44
7.44
4.80
4.78
4.49
4.48
4.47
4.46
2.93
2.92
2.90
2.90
2.88
2.87
2.85
2.85
1.85
1.84
1.78
1.77
1.62
1.60
1.53
1.42
1.14
1.11
0.99
0.96
0.96
0.94
0.80
(R)
(R)
(R)
(R)
CH3
CH3
N
N
P
O
N3

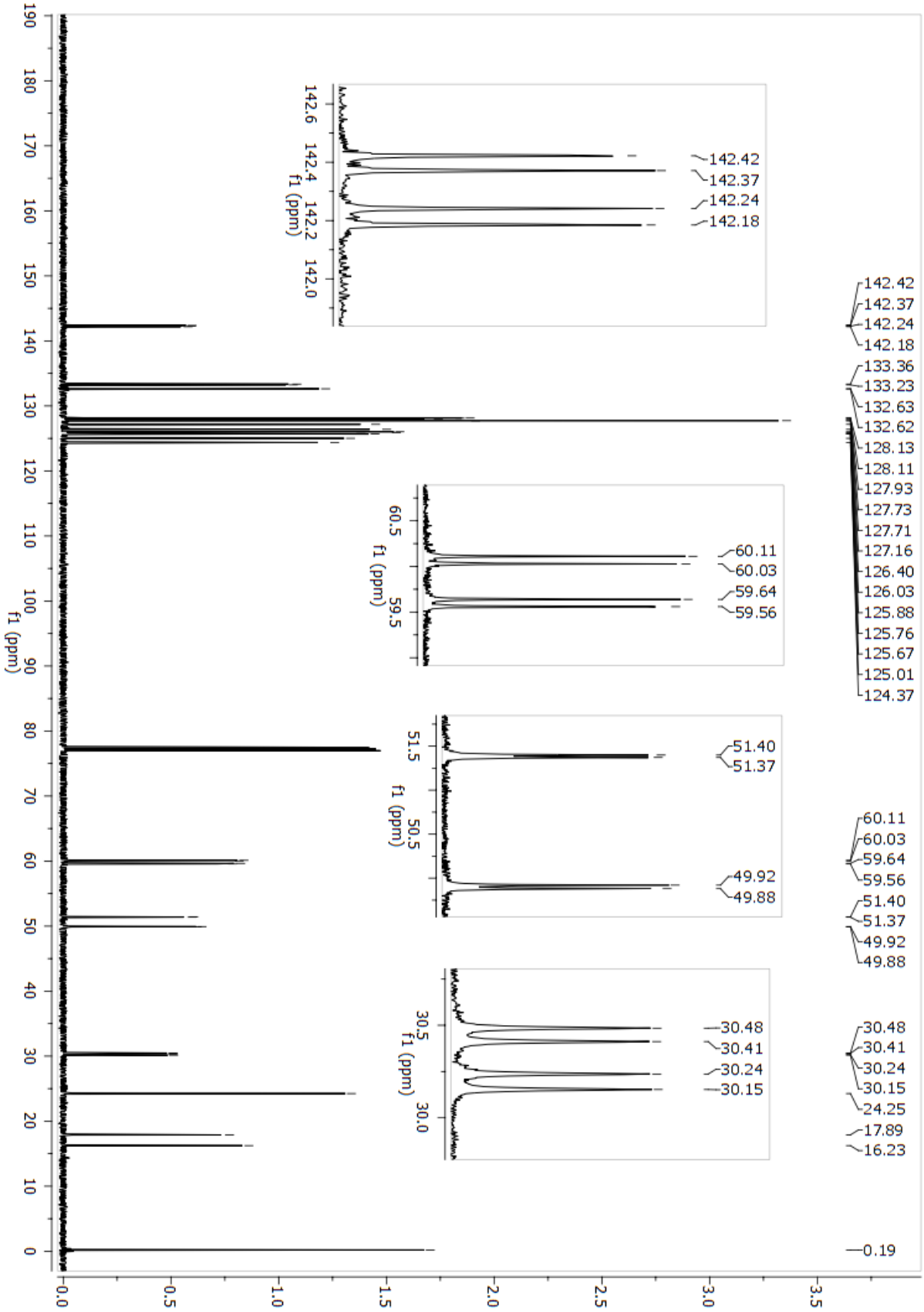

142.29
142.25
138.15
138.13
133.48
133.47
133.03
132.88
128.44
128.34
128.23
128.11
127.86
127.75
127.07
126.41
126.22
126.21
126.19
125.93
125.61
125.04
63.34
63.25
61.47
61.39
54.67
54.64
52.37
52.34
30.13
30.08
30.06
30.00
24.33
23.95
23.94
22.26
22.23
19.43
19.41
f1 (ppm)

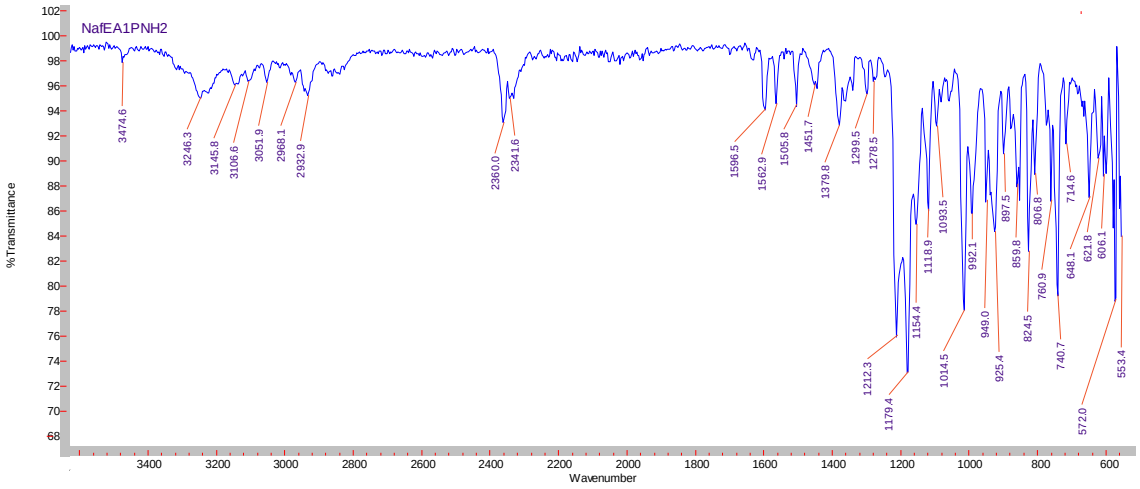


(3a*S*,7a*S*)-2-Oxide-2-aminooctahydro-1,3-bis[(1*R*)-1-(2-naphthyl)ethyl]-1*H*-1,3,2-benzodiazaphosphol, *(1S,2S,1'R,2'R)*-**8** (minor diastereoisomer)

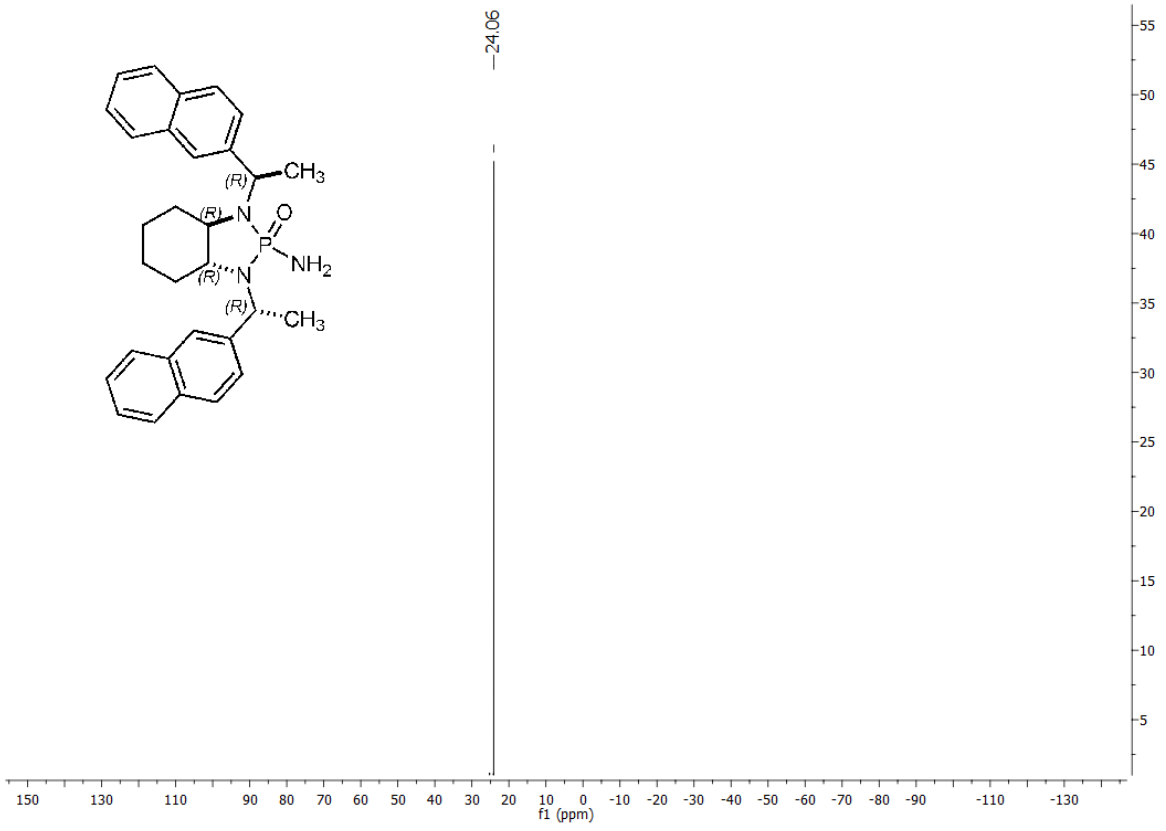


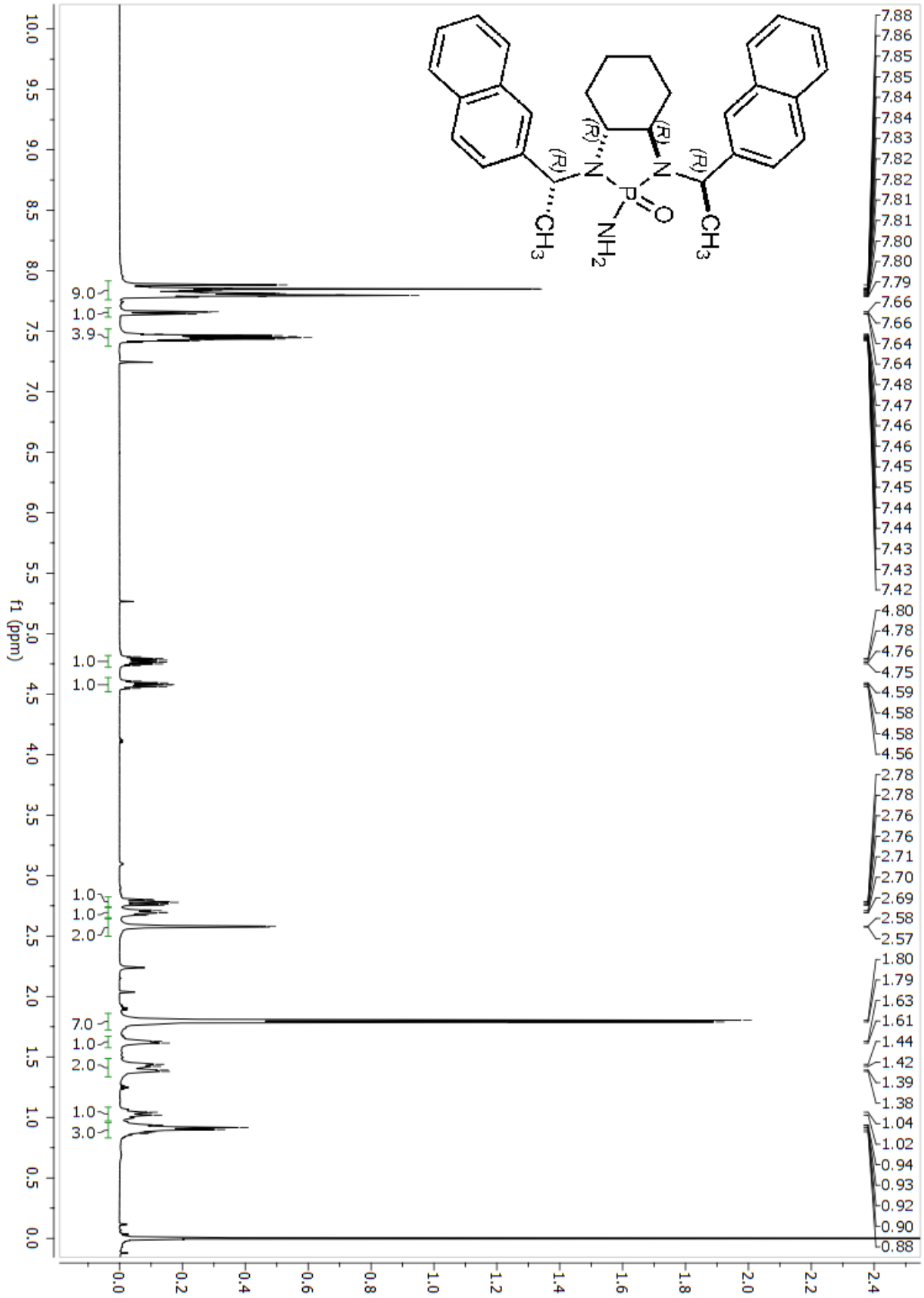

f1 (ppm)
1.0
8.0
1.0
4.0
2.0
2.0
2.0
3.0
3.0
2.1
2.0
2.1
2.1
7.89
7.88
7.87
7.87
7.82
7.81
7.81
7.80
7.78
7.76
7.75
7.75
7.74
7.67
7.47
7.46
7.46
7.46
7.45
7.45
7.44
7.44
7.44
7.43
7.43
7.25
4.82
4.81
4.79
4.78
3.18
3.17
2.91
2.90
2.89
2.88
2.85
2.85
2.83
1.90
1.89
1.76
1.74
1.55
1.55
1.53
1.50
1.47
1.47
1.34
1.33
1.32
1.31
0.93
0.92
0.92
0.91
0.90
0.71
0.70
0.68
(S)
(S)
(R)
(R)
CH3
CH3
NH2
P
O
N
N

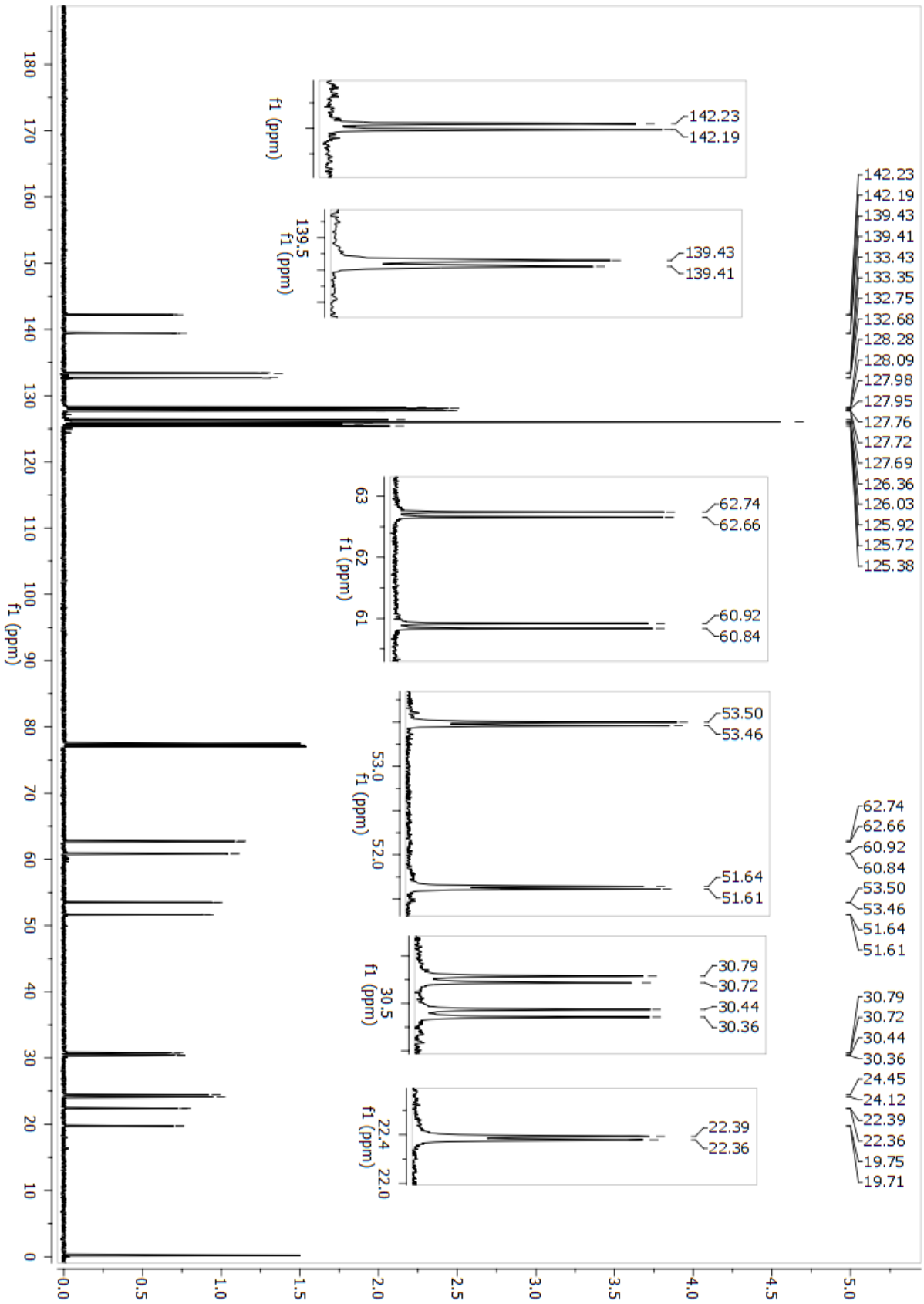

142.42
142.37
142.24
142.18
133.36
133.23
132.63
132.62
128.13
128.11
127.93
127.73
127.71
127.16
126.40
126.03
125.88
125.76
125.67
125.01
124.37
60.11
60.03
59.64
59.56
51.40
51.37
49.92
49.88
30.48
30.41
30.24
30.15
24.25
17.89
16.23
0.19
f1 (ppm)

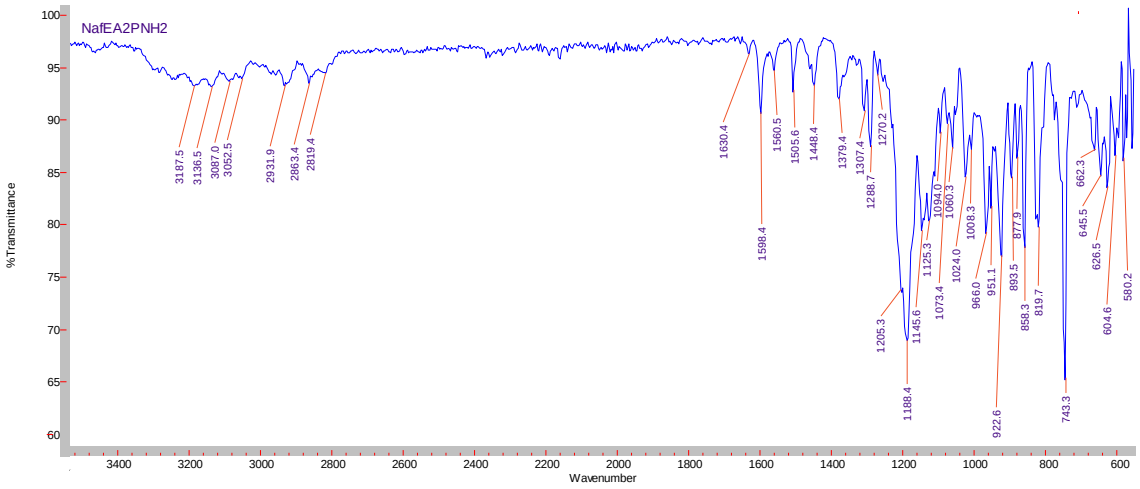


(3a*R*,7a*R*)-2-Oxide-2-aminooctahydro-1,3-bis[(1*R*)-1-(2-naphthyl)ethyl]-1*H*-1,3,2-benzodiazaphosphol, *(1R,2R,1'R,2'R)*-**8** (major diastereoisomer)

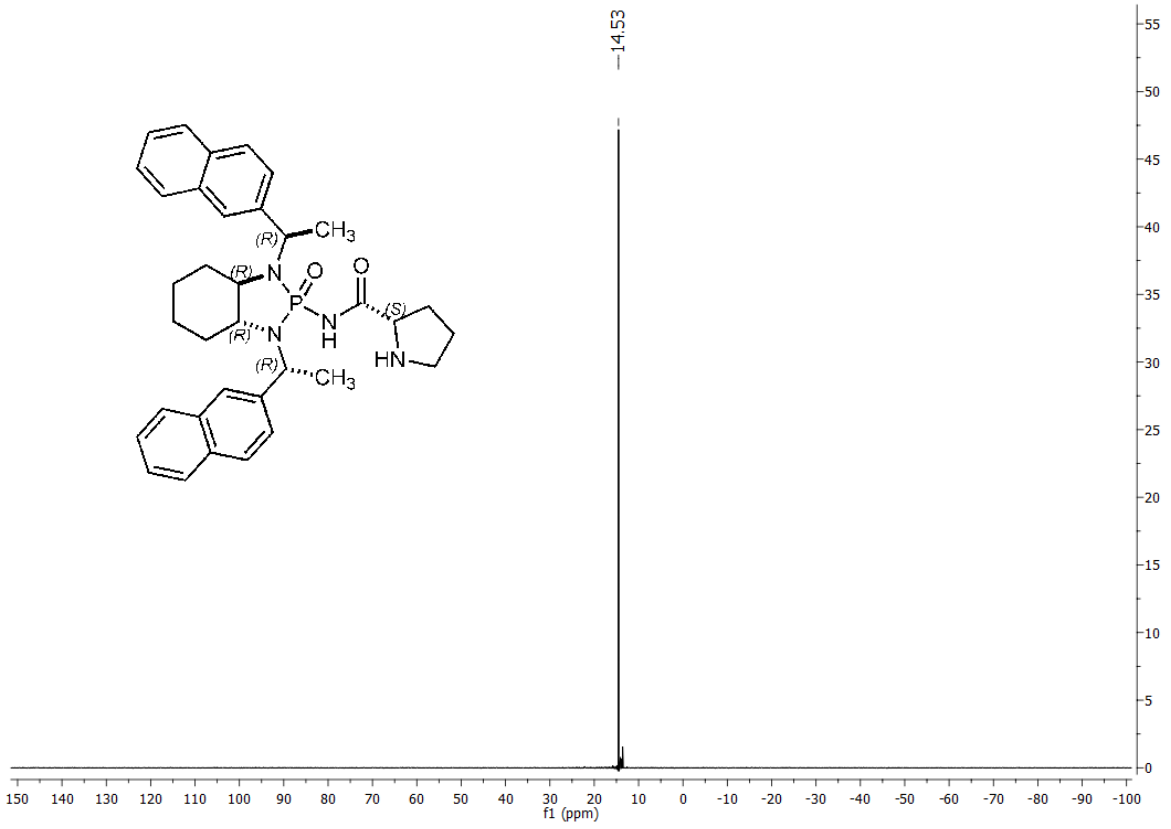


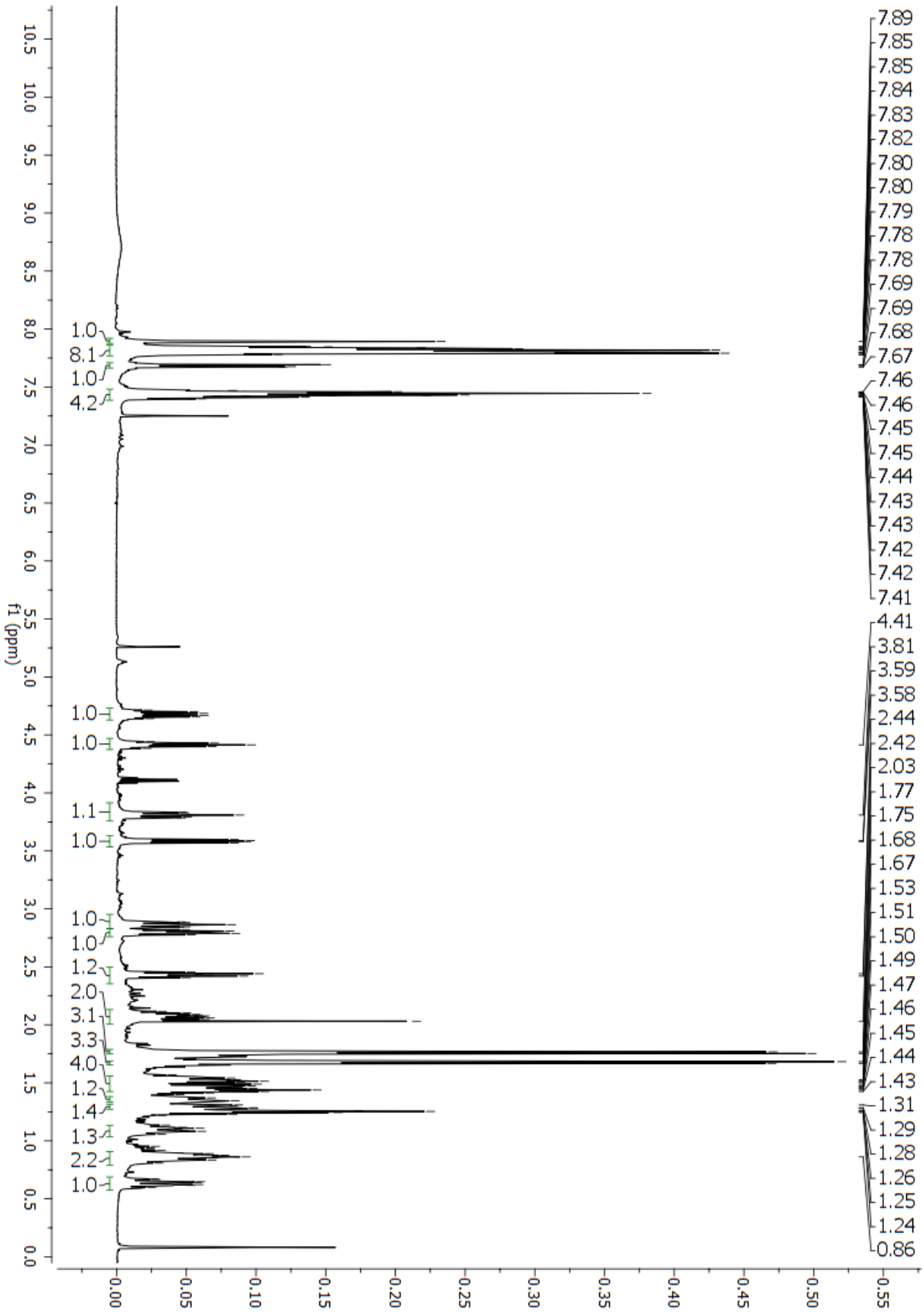

f1 (ppm)
9.0
1.0
3.9
1.0
1.0
1.0
1.0
2.0
7.0
1.0
2.0
1.0
3.0
7.88
7.86
7.85
7.85
7.84
7.84
7.83
7.82
7.82
7.81
7.81
7.80
7.80
7.79
7.66
7.66
7.64
7.64
7.48
7.47
7.46
7.46
7.45
7.45
7.44
7.44
7.43
7.43
7.42
4.80
4.78
4.76
4.75
4.59
4.58
4.58
4.56
2.78
2.78
2.76
2.76
2.71
2.70
2.69
2.58
2.57
1.80
1.79
1.63
1.61
1.44
1.42
1.39
1.38
1.04
1.02
0.94
0.93
0.92
0.90
0.88
NH2
CH3
CH3

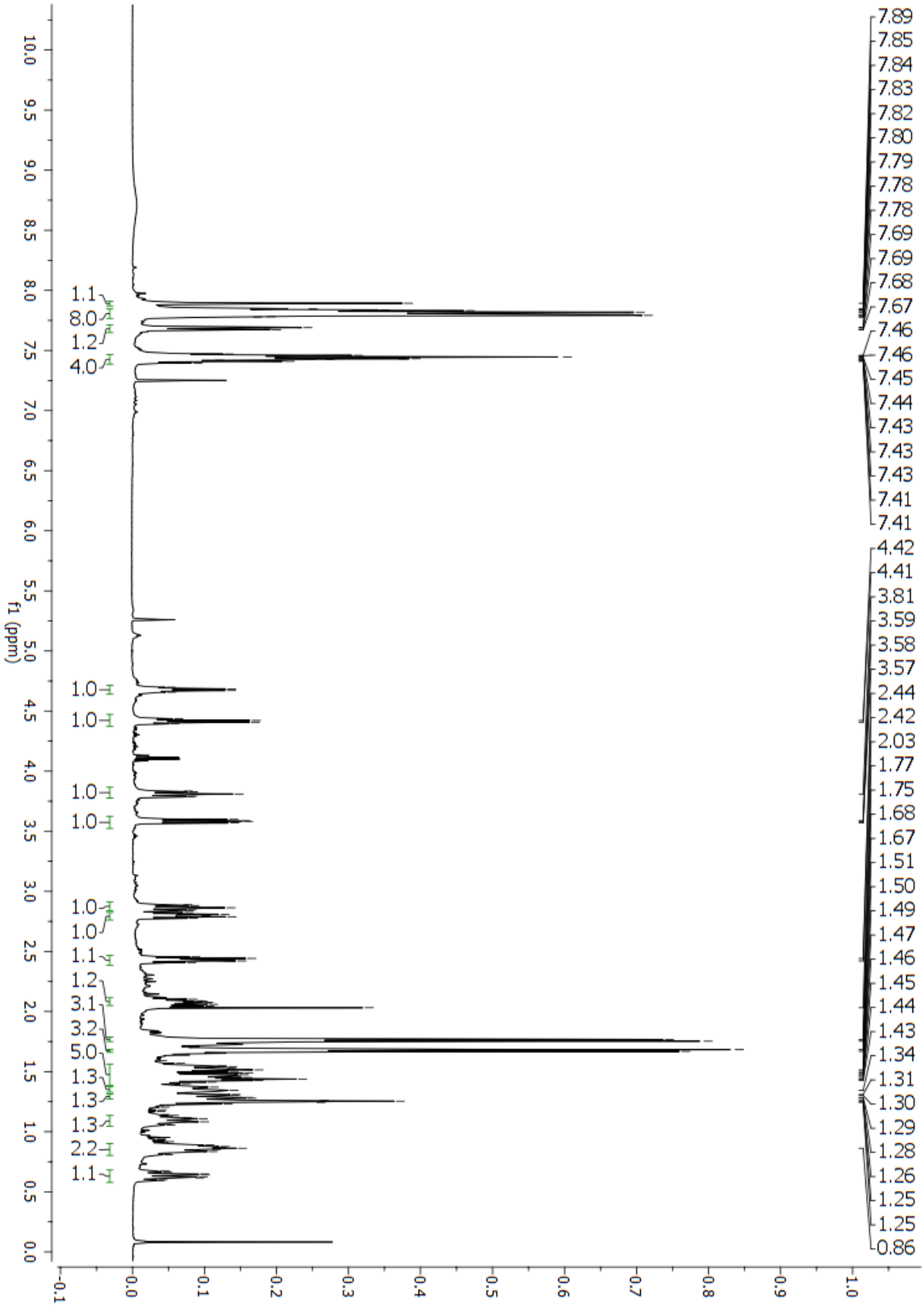

f1 (ppm)
142.23
142.19
139.43
139.41
133.43
133.35
132.75
132.68
128.28
128.09
127.98
127.95
127.76
127.72
127.69
126.36
126.03
125.92
125.72
125.38
62.74
62.66
60.92
60.84
53.50
53.46
51.64
51.61
30.79
30.72
30.44
30.36
24.45
24.12
22.39
22.36
19.75
19.71

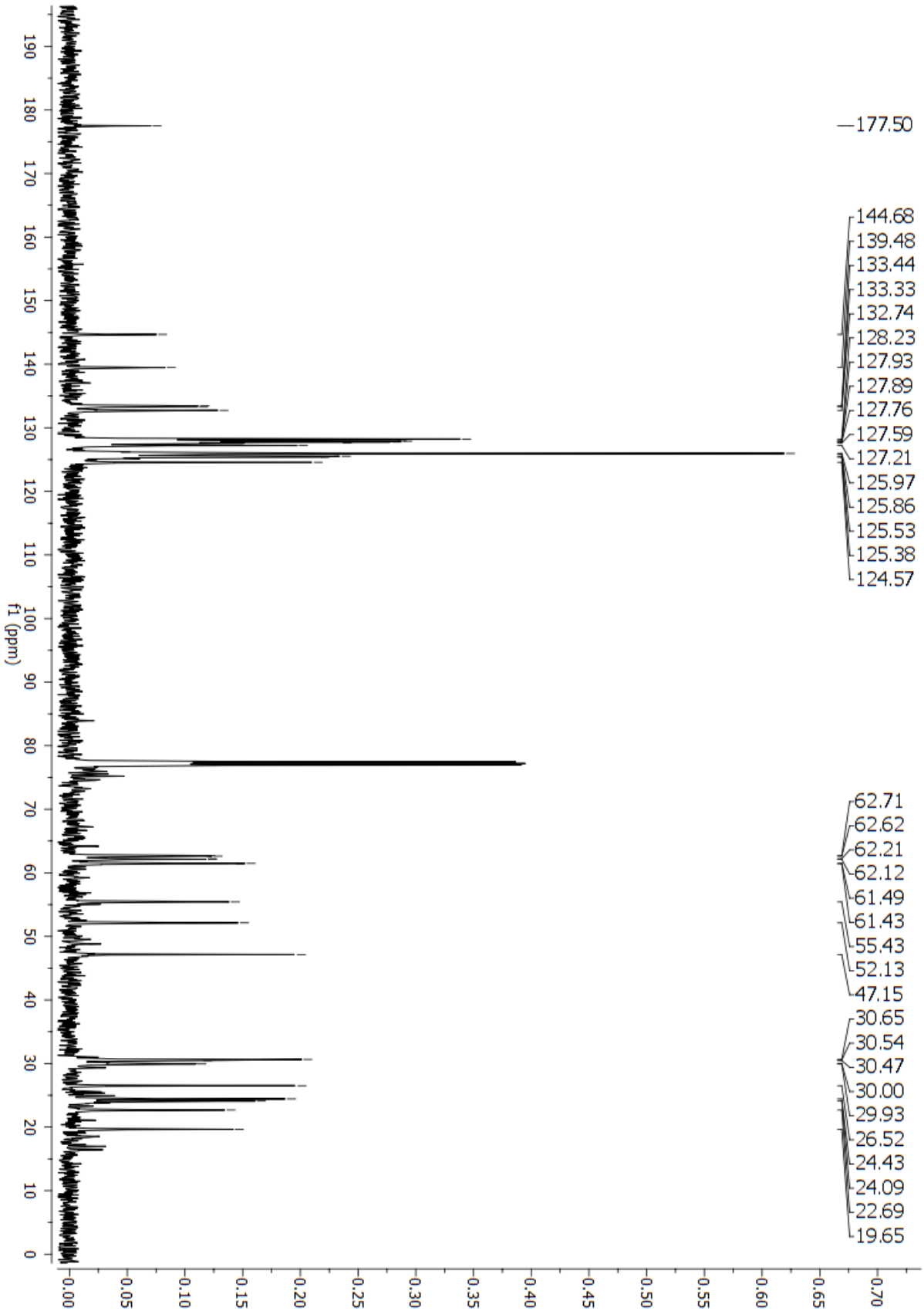


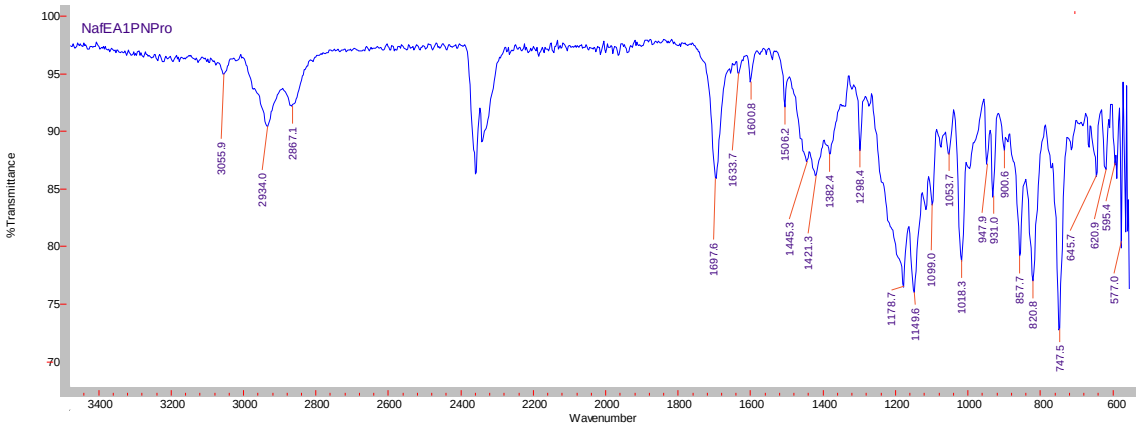
Catalyst (1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**9**



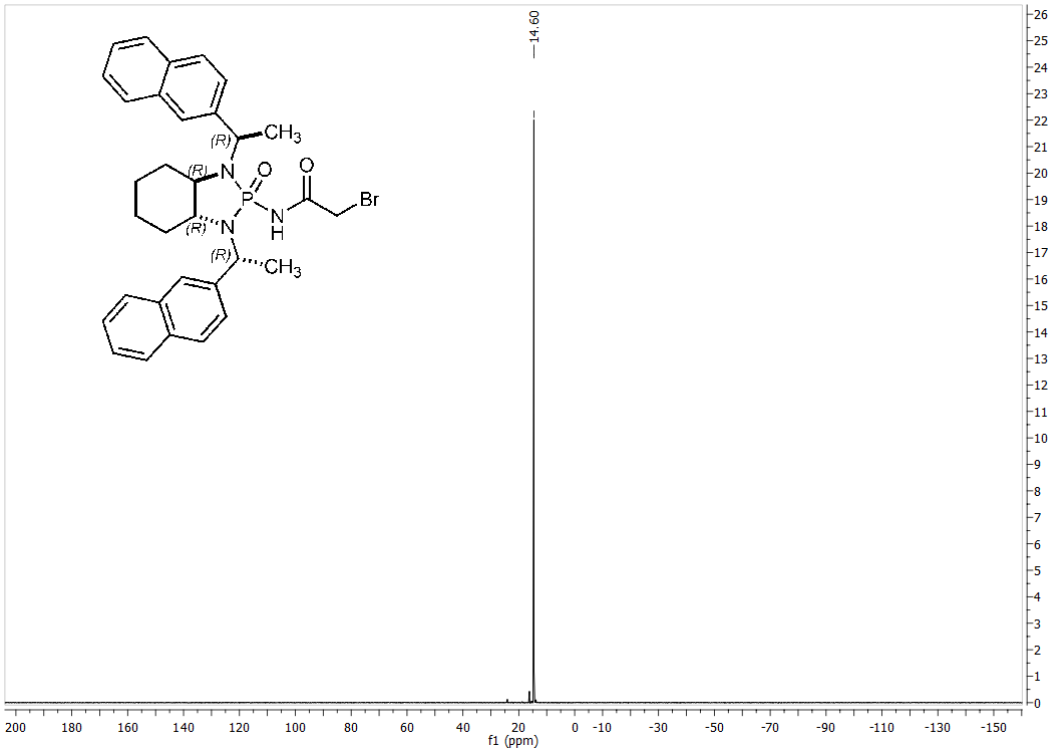

f1 (ppm)
1.0
8.1
1.0
4.2
1.0
1.0
1.1
1.0
1.0
1.0
1.2
2.0
3.1
3.3
4.0
1.2
1.4
1.3
2.2
1.0
7.89
7.85
7.85
7.84
7.83
7.82
7.80
7.80
7.79
7.78
7.78
7.69
7.69
7.68
7.67
7.46
7.46
7.45
7.45
7.44
7.43
7.43
7.42
7.42
7.41
4.41
3.81
3.59
3.58
2.44
2.42
2.03
1.77
1.75
1.68
1.67
1.53
1.51
1.50
1.49
1.47
1.46
1.45
1.44
1.43
1.31
1.29
1.28
1.26
1.25
1.24
0.86

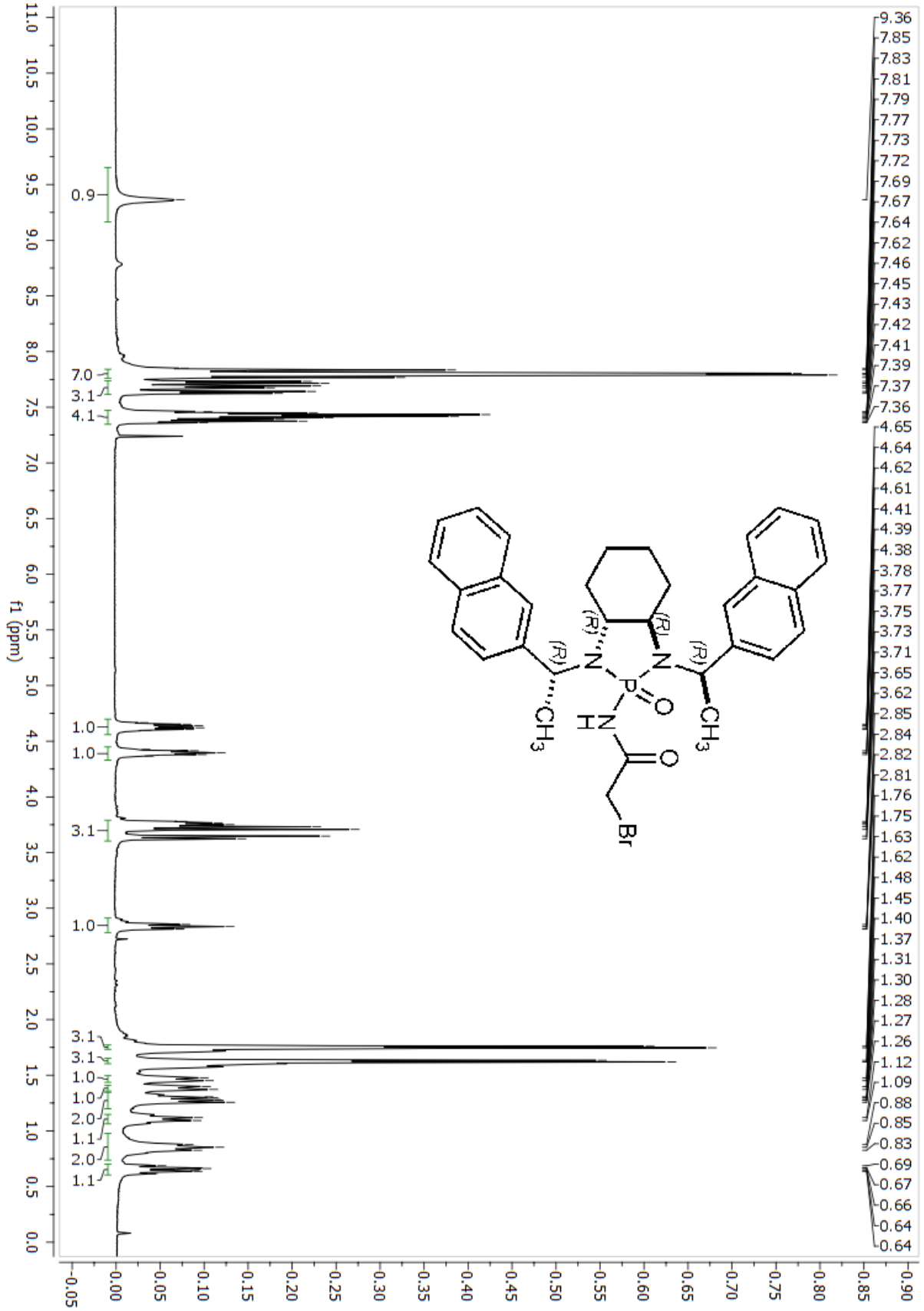

f1 (ppm)
1.1
8.0
1.2
4.0
1.0
1.0
1.0
1.0
1.0
1.0
1.1
1.2
3.1
3.2
5.0
1.3
1.3
1.3
2.2
1.1
7.89
7.85
7.84
7.83
7.82
7.80
7.79
7.78
7.78
7.69
7.69
7.68
7.67
7.46
7.46
7.45
7.44
7.43
7.43
7.43
7.41
7.41
4.42
4.41
3.81
3.59
3.58
3.57
2.44
2.42
2.03
1.77
1.75
1.68
1.67
1.51
1.50
1.49
1.47
1.46
1.45
1.44
1.43
1.34
1.31
1.30
1.29
1.28
1.26
1.25
1.25
0.86

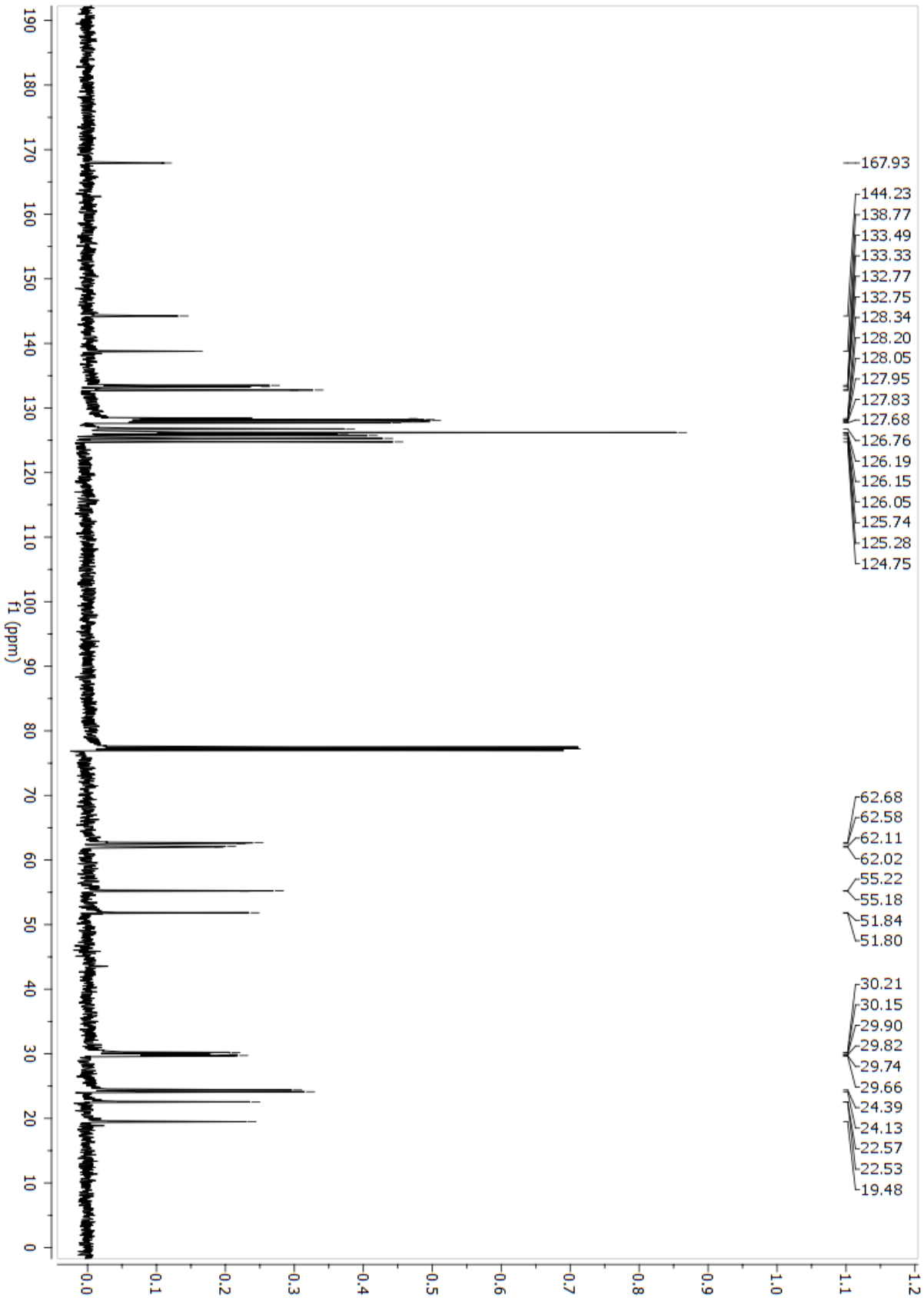

177.50
144.68
139.48
133.44
133.33
132.74
128.23
127.93
127.89
127.76
127.59
127.21
125.97
125.86
125.53
125.38
124.57
62.71
62.62
62.21
62.12
61.49
61.43
55.43
52.13
47.15
30.65
30.54
30.47
30.00
29.93
26.52
24.43
24.09
22.69
19.65
f1 (ppm)

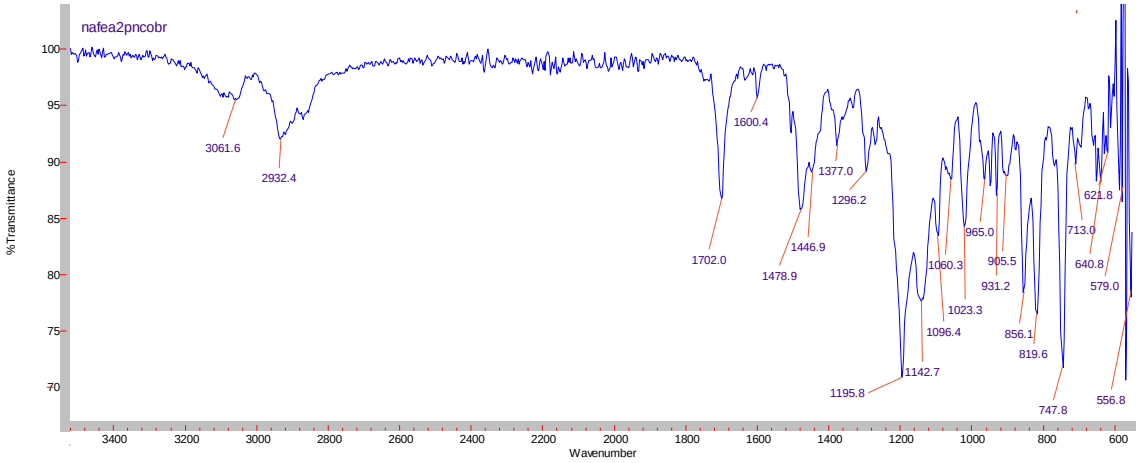


(3a*R*,7a*R*)-2-oxide-*N*-(2-bromoacethyl)-octahydro-1,3-bis[(1*R*)-1-(2-naphthyl)ethyl]-2*H*-1,3,2-benzodiazaphosphol-2-amine, (*1R,2R,1'R,2'R*)-**13**

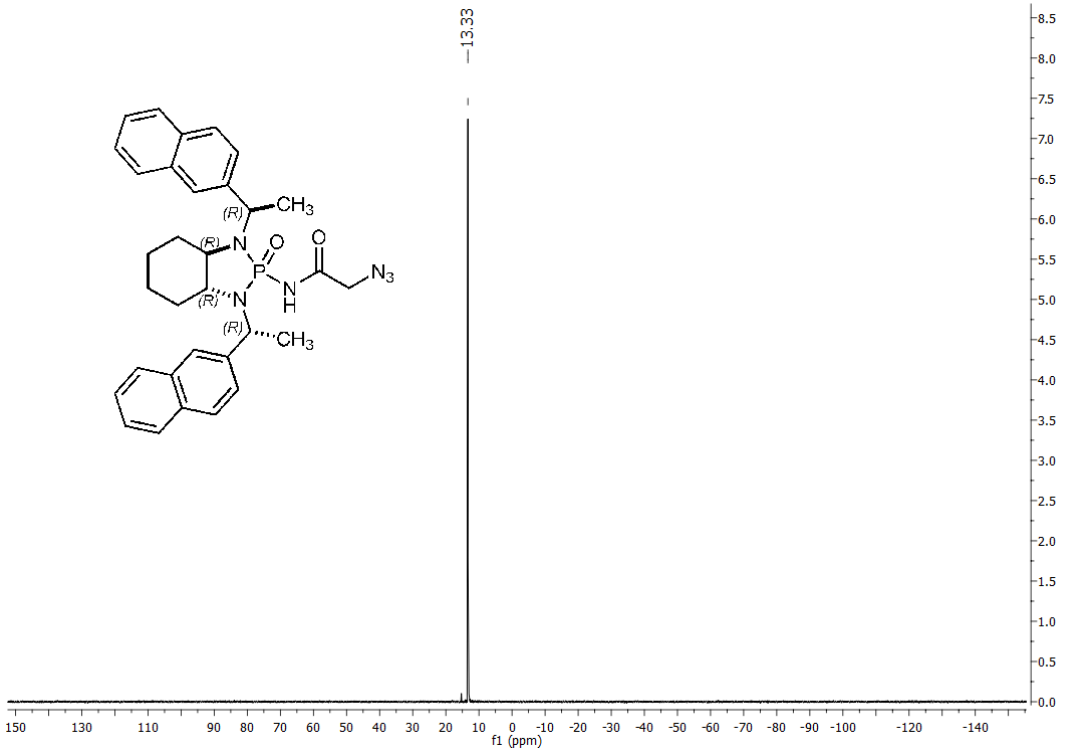


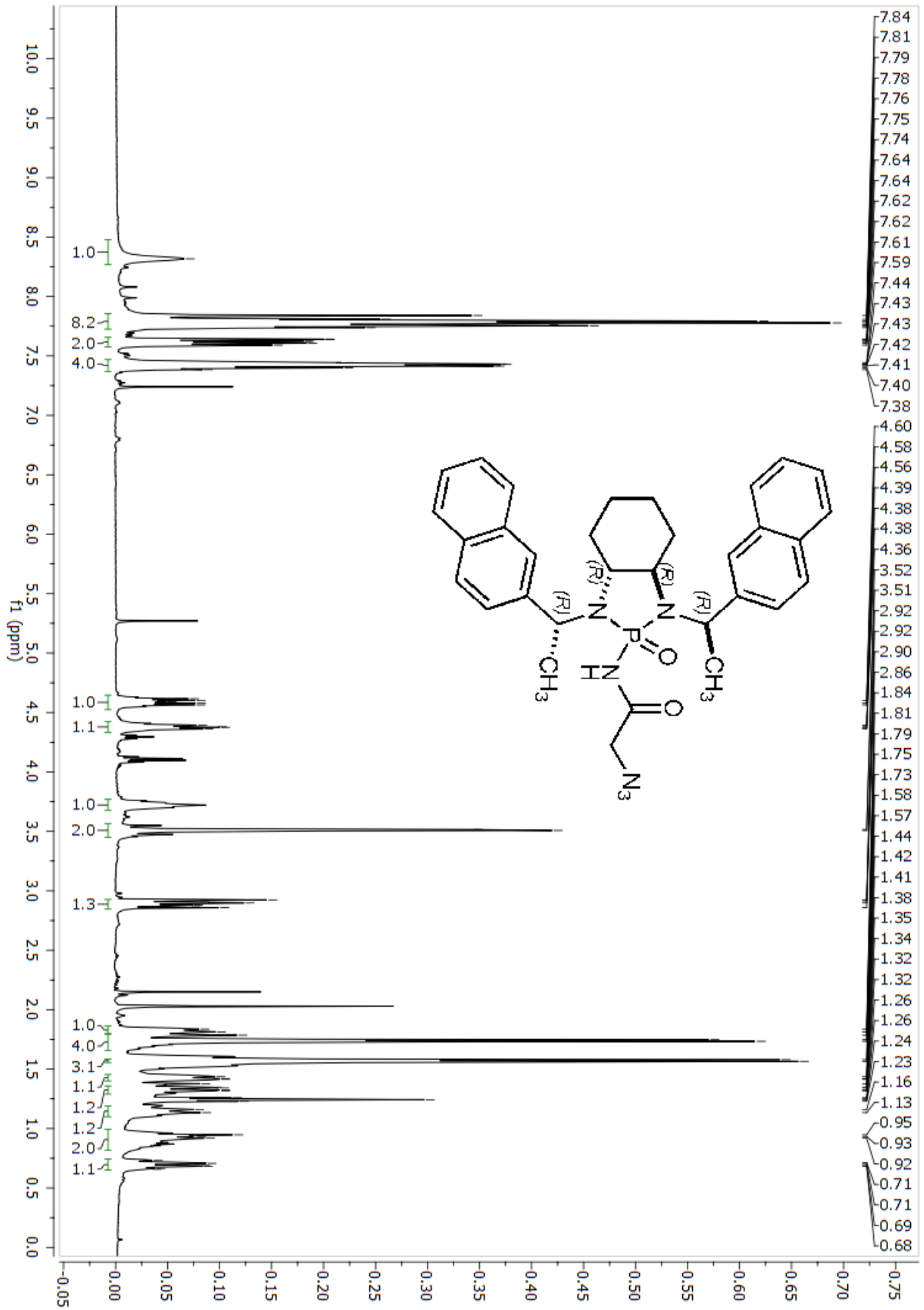

f1 (ppm)
0.9
7.0
3.1
4.1
1.0
1.0
3.1
1.0
3.1
3.1
1.0
1.0
2.0
1.1
2.0
1.1
9.36
7.85
7.83
7.81
7.79
7.77
7.73
7.72
7.69
7.67
7.64
7.62
7.46
7.45
7.43
7.42
7.41
7.39
7.37
7.36
4.65
4.64
4.62
4.61
4.41
4.39
4.38
3.78
3.77
3.75
3.73
3.71
3.65
3.62
2.85
2.84
2.82
2.81
1.76
1.75
1.63
1.62
1.48
1.45
1.40
1.37
1.31
1.30
1.28
1.27
1.26
1.12
1.09
0.88
0.85
0.83
0.69
0.67
0.66
0.64
0.64
(R)
(R)
(R)
(R)
(R)
CH3
CH3
N
N
P
O
N
H
O
Br

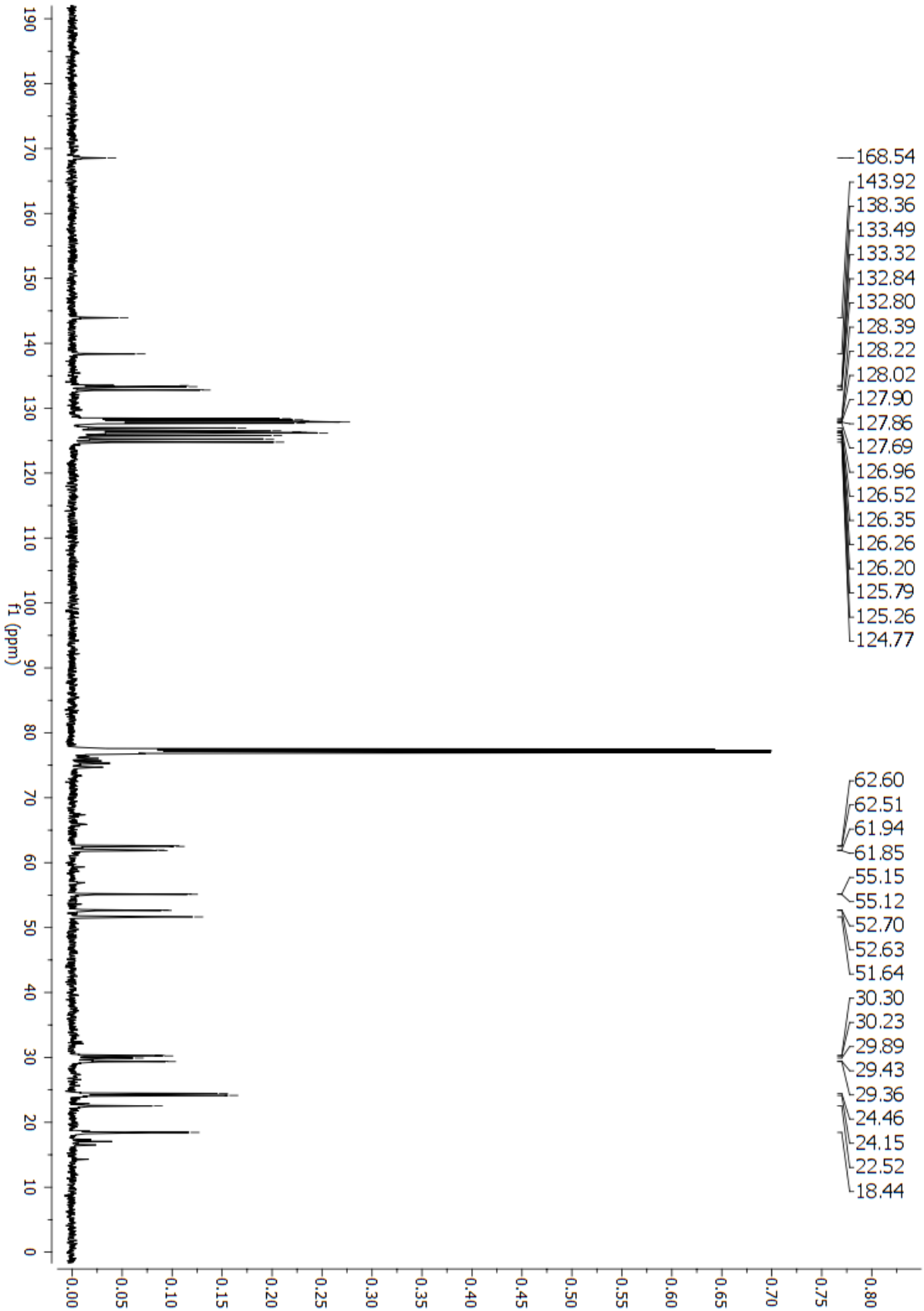

167.93
144.23
138.77
133.49
133.33
132.77
132.75
128.34
128.20
128.05
127.95
127.83
127.68
126.76
126.19
126.15
126.05
125.74
125.28
124.75
62.68
62.58
62.11
62.02
55.22
55.18
51.84
51.80
30.21
30.15
29.90
29.82
29.74
29.66
24.39
24.13
22.57
22.53
19.48
f1 (ppm)

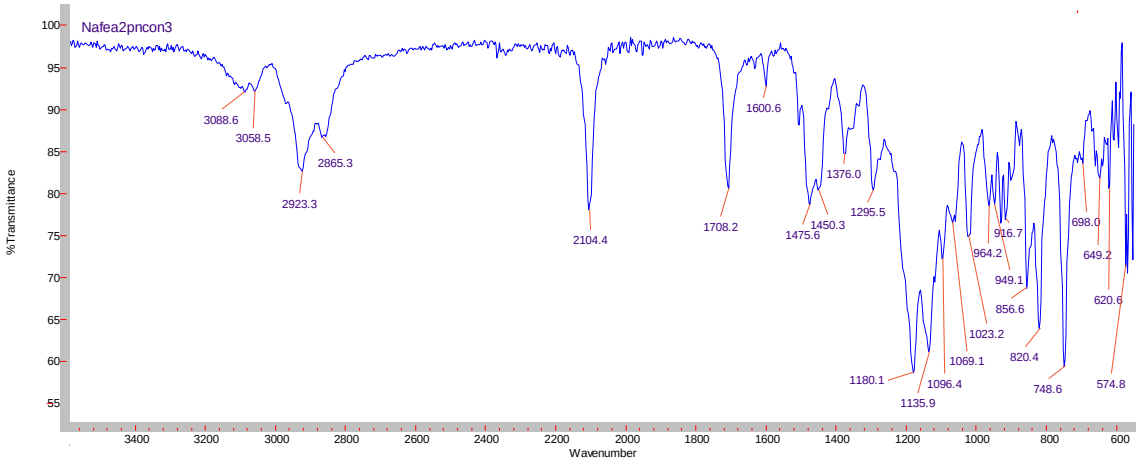


(3a*R*,7a*R*)-2-oxide-*N*-(2-azidoacethyl)-octahydro-1,3-bis[(1*R*)-1-(2-naphthyl)ethyl]-2*H*-1,3,2-benzodiazaphosphol-2-amine, (*1S,2S,1'R,2'R*)-**14**

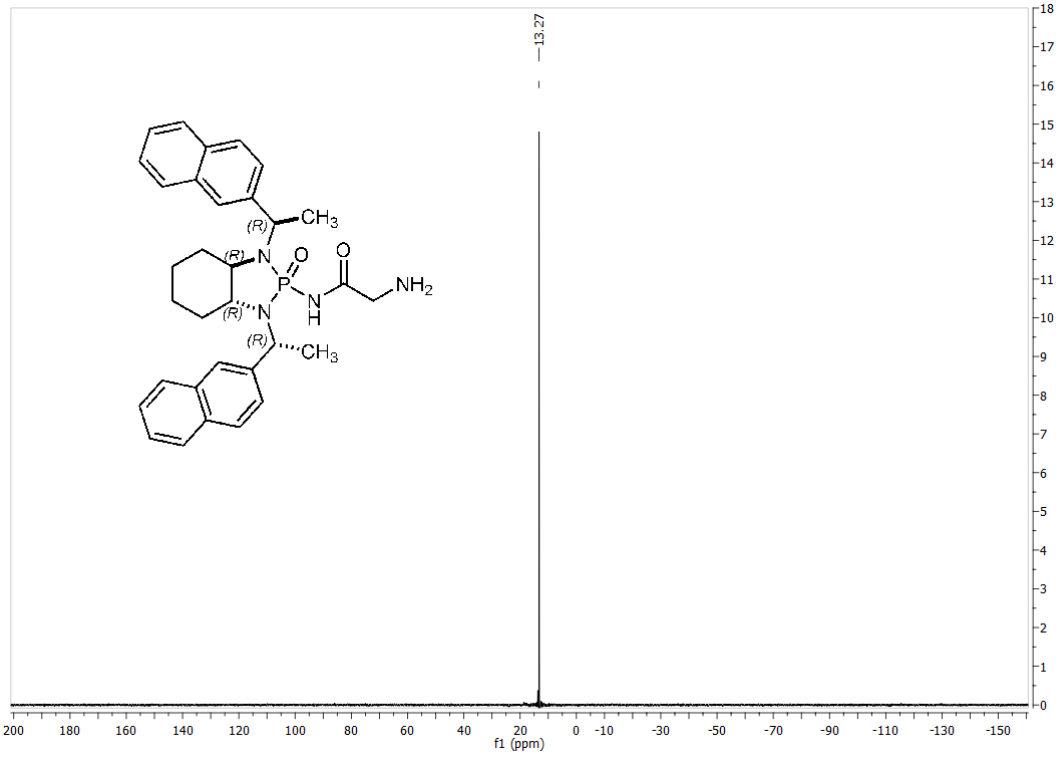


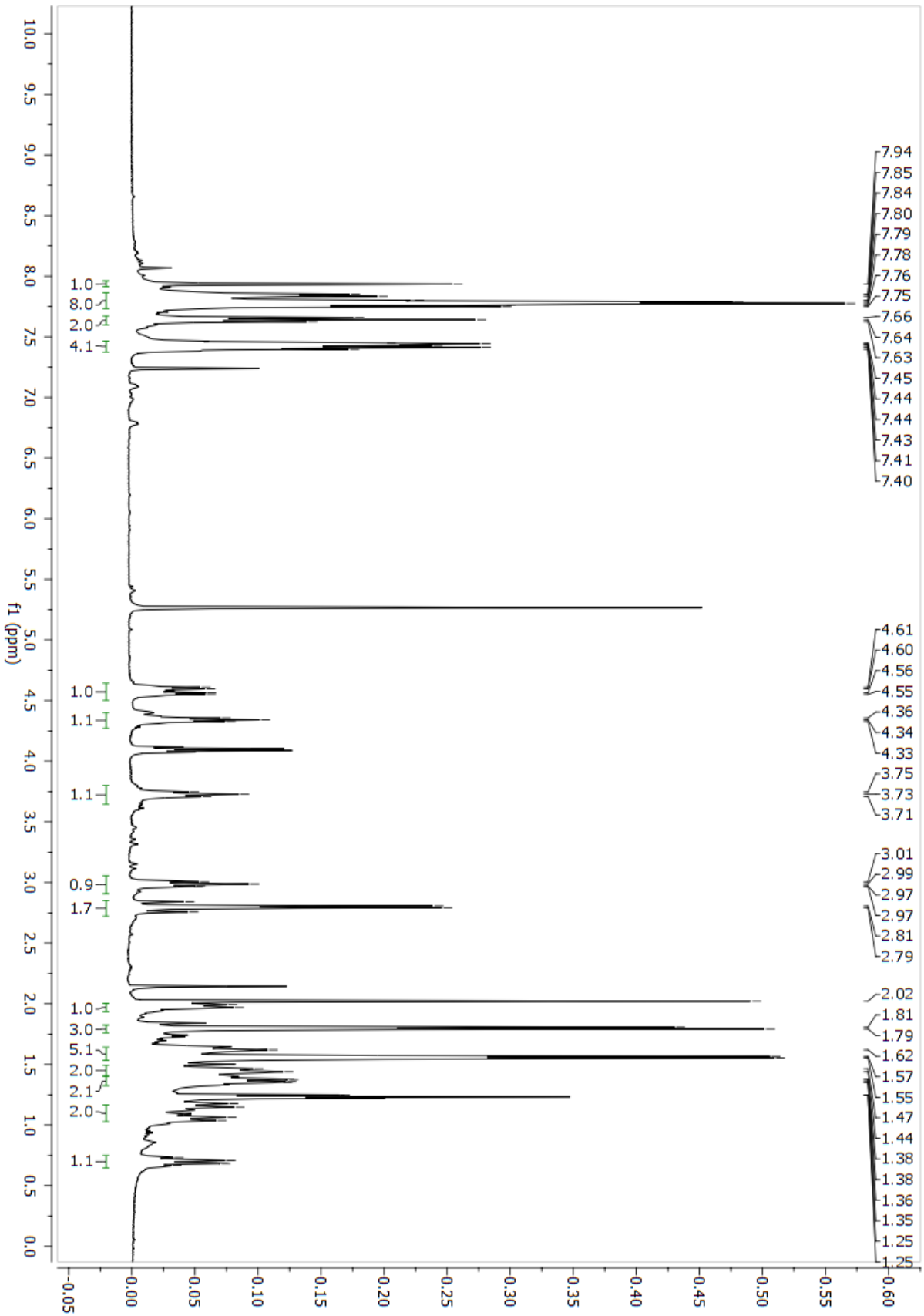

f1 (ppm)
1.0
8.2
2.0
4.0
1.0
1.1
1.0
2.0
1.3
1.0
4.0
3.1
1.1
1.2
1.2
2.0
1.1
7.84
7.81
7.79
7.78
7.76
7.75
7.74
7.64
7.64
7.62
7.62
7.61
7.59
7.44
7.43
7.43
7.42
7.41
7.40
7.38
4.60
4.58
4.56
4.39
4.38
4.38
4.36
3.52
3.51
2.92
2.92
2.90
2.86
1.84
1.81
1.79
1.75
1.73
1.58
1.57
1.44
1.42
1.41
1.38
1.35
1.34
1.32
1.32
1.26
1.26
1.24
1.23
1.16
1.13
0.95
0.93
0.92
0.71
0.71
0.69
0.68
(R)
(R)
(R)
(R)
CH3
CH3
P
O
N
H
O
N3

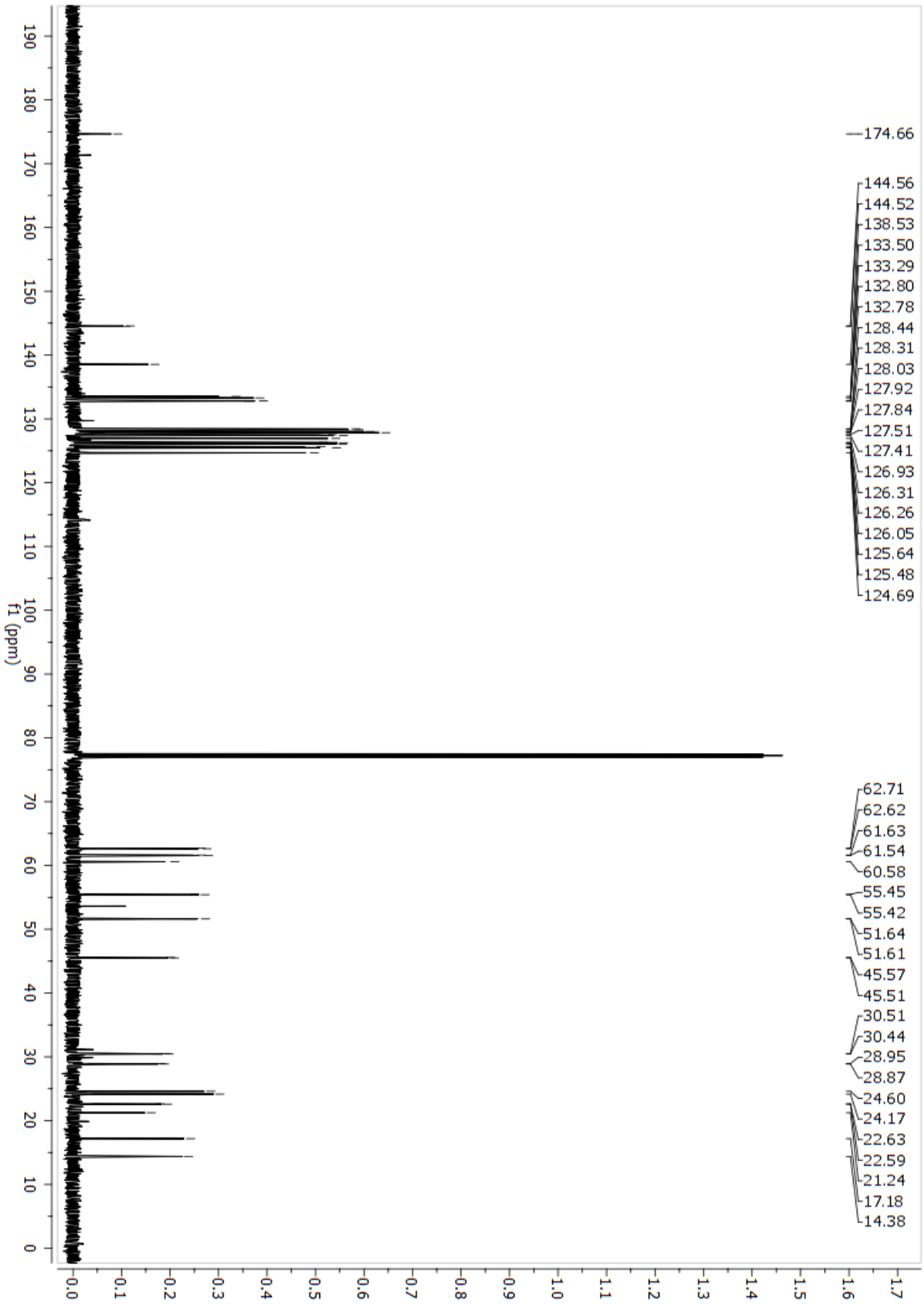

168.54
143.92
138.36
133.49
133.32
132.84
132.80
128.39
128.22
128.02
127.90
127.86
127.69
126.96
126.52
126.35
126.26
126.20
125.79
125.26
124.77
62.60
62.51
61.94
61.85
55.15
55.12
52.70
52.63
51.64
30.30
30.23
29.89
29.43
29.36
24.46
24.15
22.52
18.44
f1 (ppm)

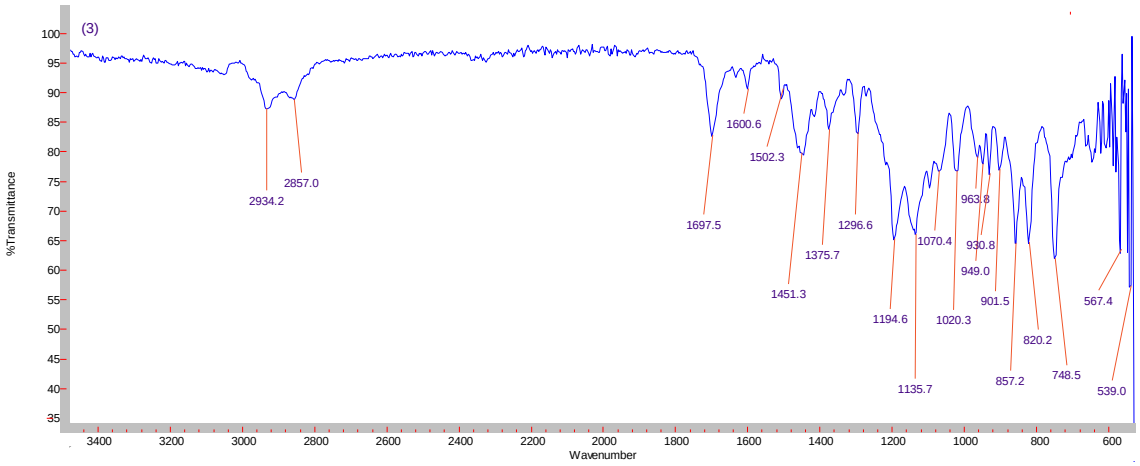


(3a*R*,7a*R*)-2-oxide-*N*-(2-aminoacethyl)-octahydro-1,3-bis[(1*R*)-1-(2-naphthyl)ethyl]-2*H*-1,3,2-benzodiazaphosphol-2-amine, (*1S,2S,1'R,2'R*)-**15**

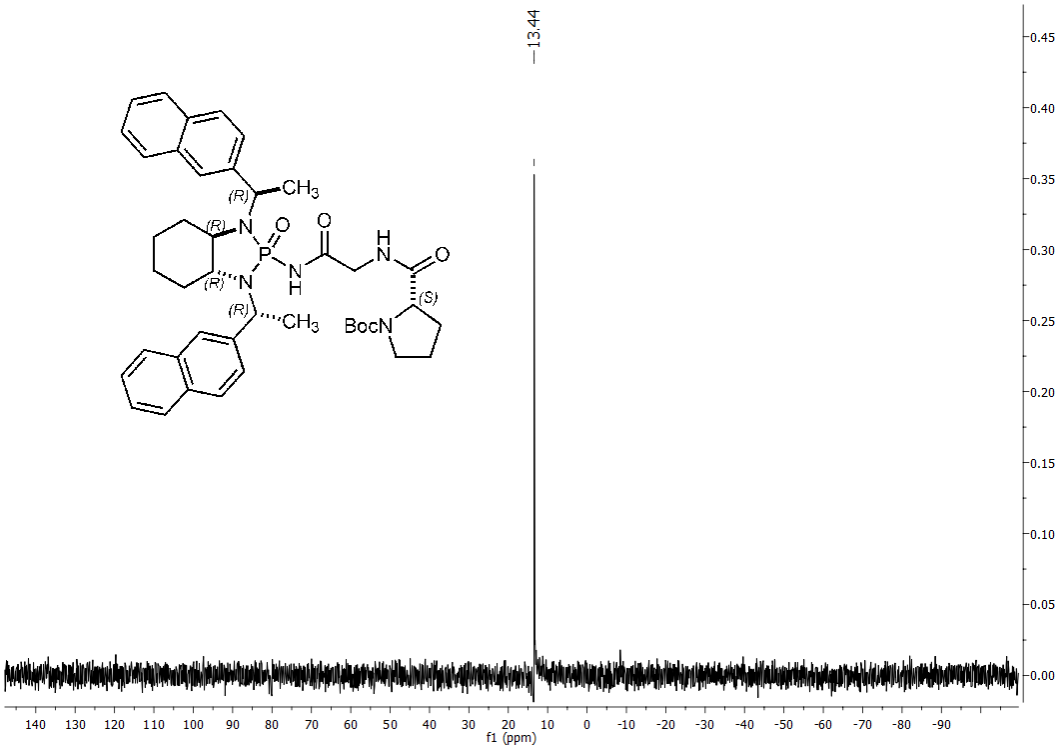


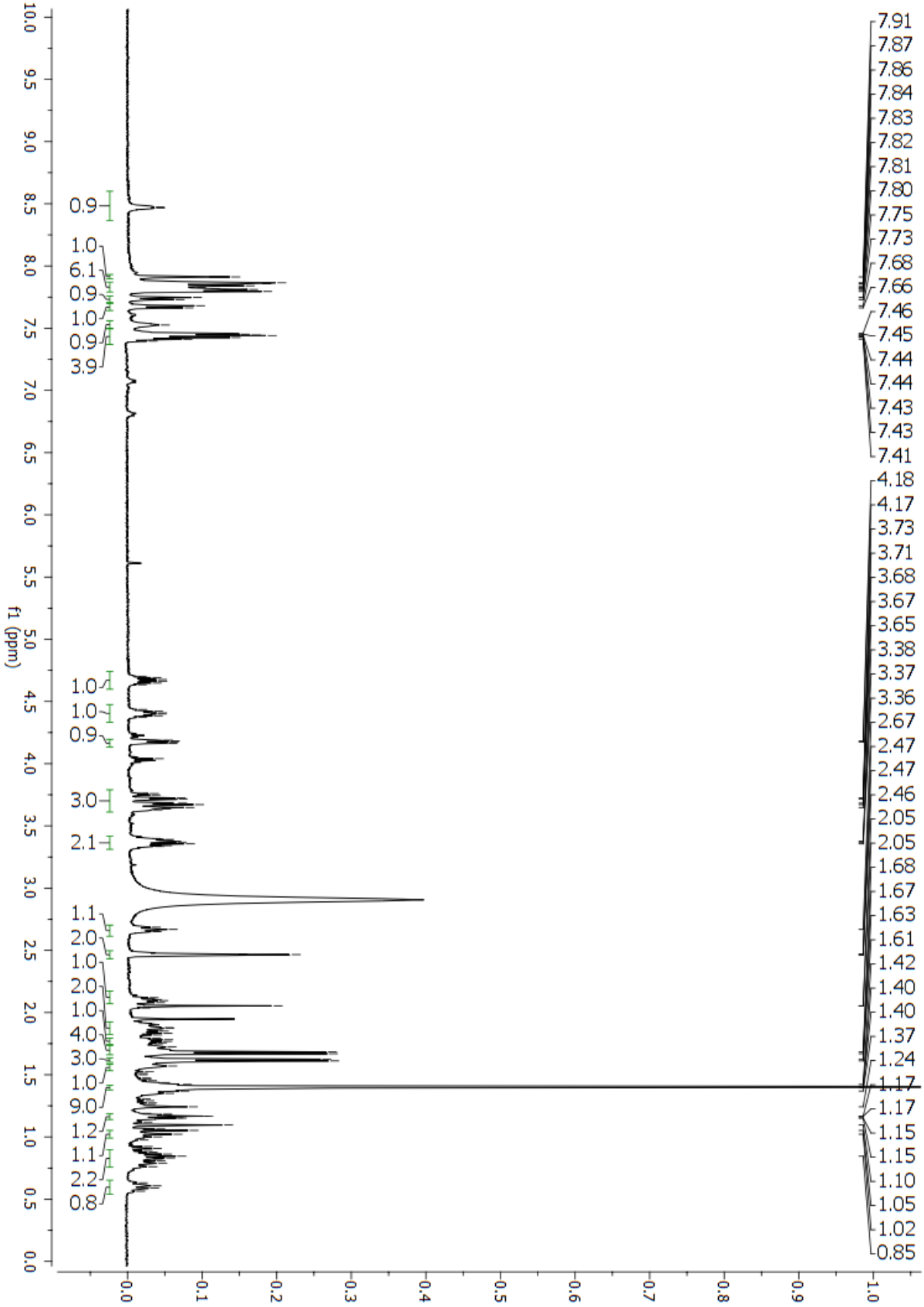

f1 (ppm)
7.94
7.85
7.84
7.80
7.79
7.78
7.76
7.75
7.66
7.64
7.63
7.45
7.44
7.44
7.43
7.41
7.40
4.61
4.60
4.56
4.55
4.36
4.34
4.33
3.75
3.73
3.71
3.01
2.99
2.97
2.97
2.81
2.79
2.02
1.81
1.79
1.62
1.57
1.55
1.47
1.44
1.38
1.38
1.36
1.35
1.25
1.25
1.0
8.0
2.0
4.1
1.0
1.1
1.1
0.9
1.7
1.0
3.0
5.1
2.0
2.1
2.0
1.1

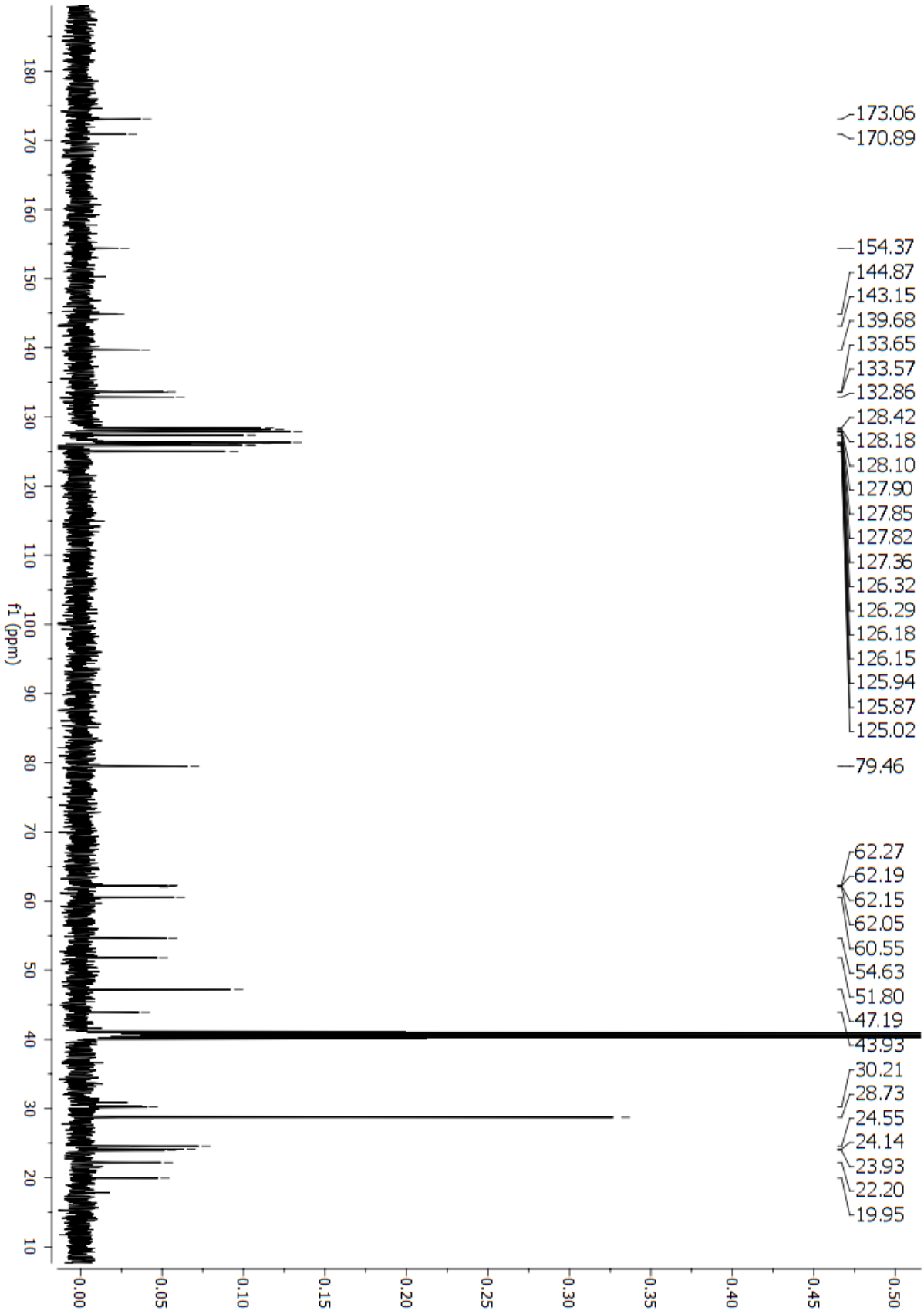

174.66
144.56
144.52
138.53
133.50
133.29
132.80
132.78
128.44
128.31
128.03
127.92
127.84
127.51
127.41
126.93
126.31
126.26
126.05
125.64
125.48
124.69
62.71
62.62
61.63
61.54
60.58
55.45
55.42
51.64
51.61
45.57
45.51
30.51
30.44
28.95
28.87
24.60
24.17
22.63
22.59
21.24
17.18
14.38
f1 (ppm)

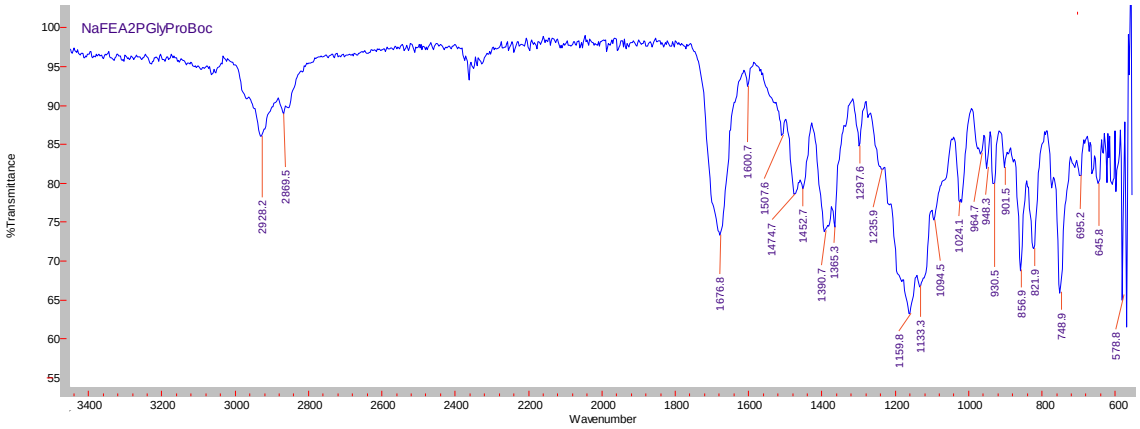


Pre-catalyst (1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**16**

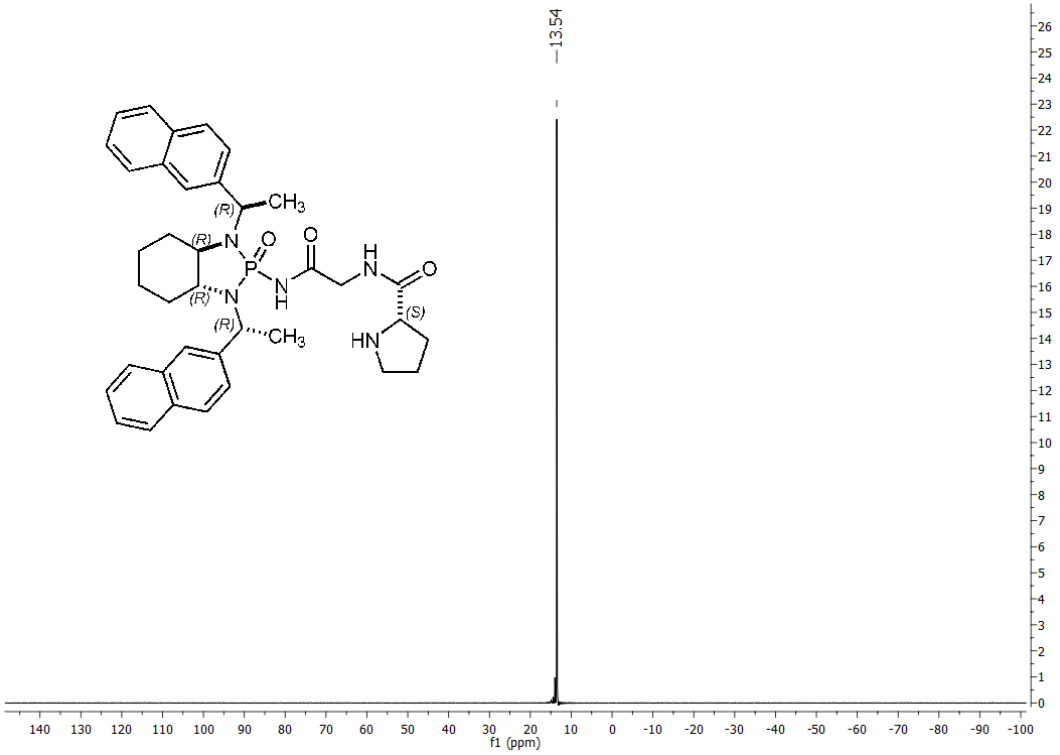


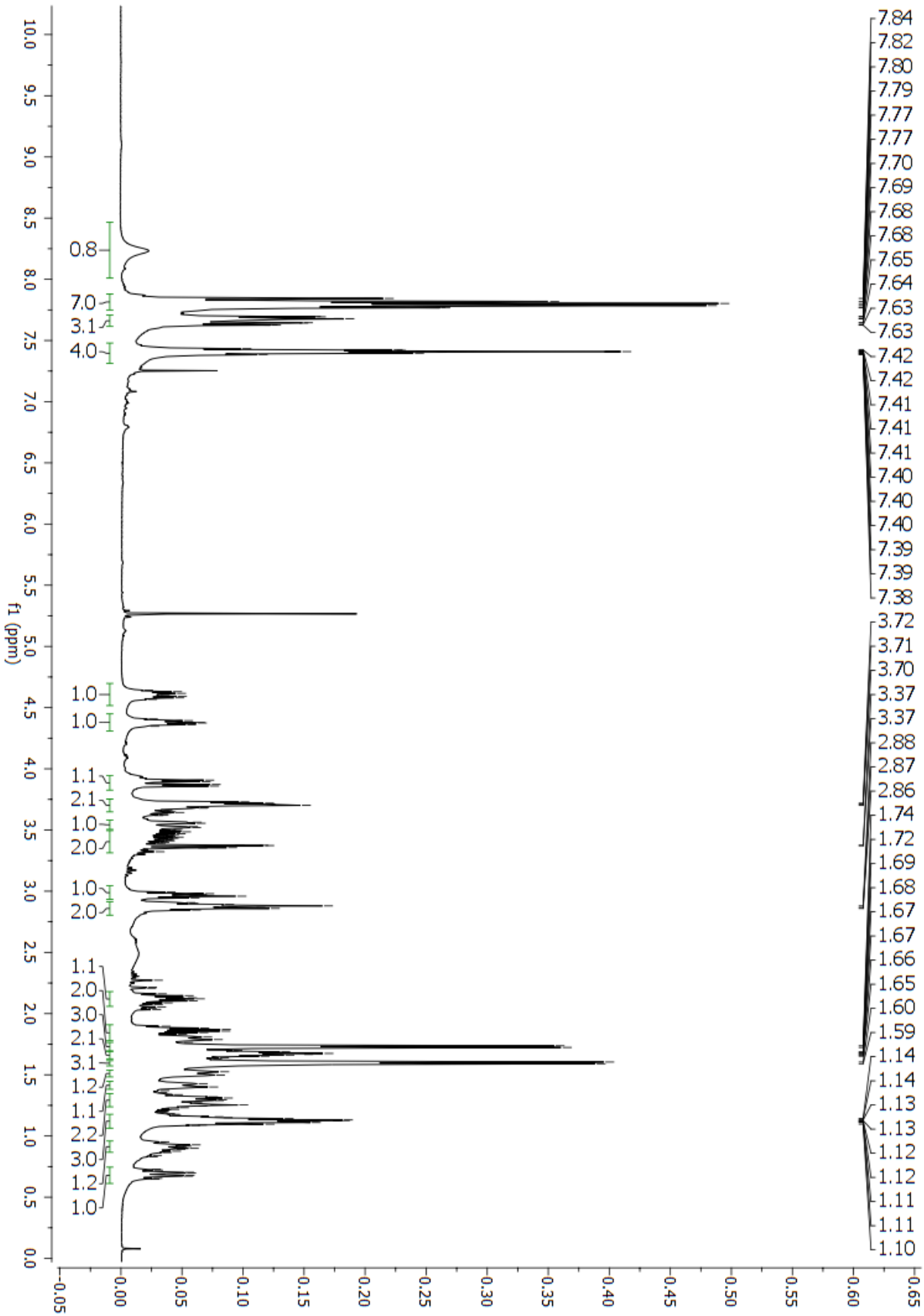

f1 (ppm)
0.9
1.0
6.1
0.9
1.0
0.9
3.9
1.0
1.0
0.9
3.0
2.1
1.1
2.0
1.0
2.0
1.0
4.0
3.0
1.0
9.0
1.2
1.1
2.2
0.8
7.91
7.87
7.86
7.84
7.83
7.82
7.81
7.80
7.75
7.73
7.68
7.66
7.46
7.45
7.44
7.44
7.43
7.43
7.41
4.18
4.17
3.73
3.71
3.68
3.67
3.65
3.38
3.37
3.36
2.67
2.47
2.47
2.46
2.05
2.05
1.68
1.67
1.63
1.61
1.42
1.40
1.40
1.37
1.24
1.17
1.17
1.15
1.15
1.10
1.05
1.02
0.85

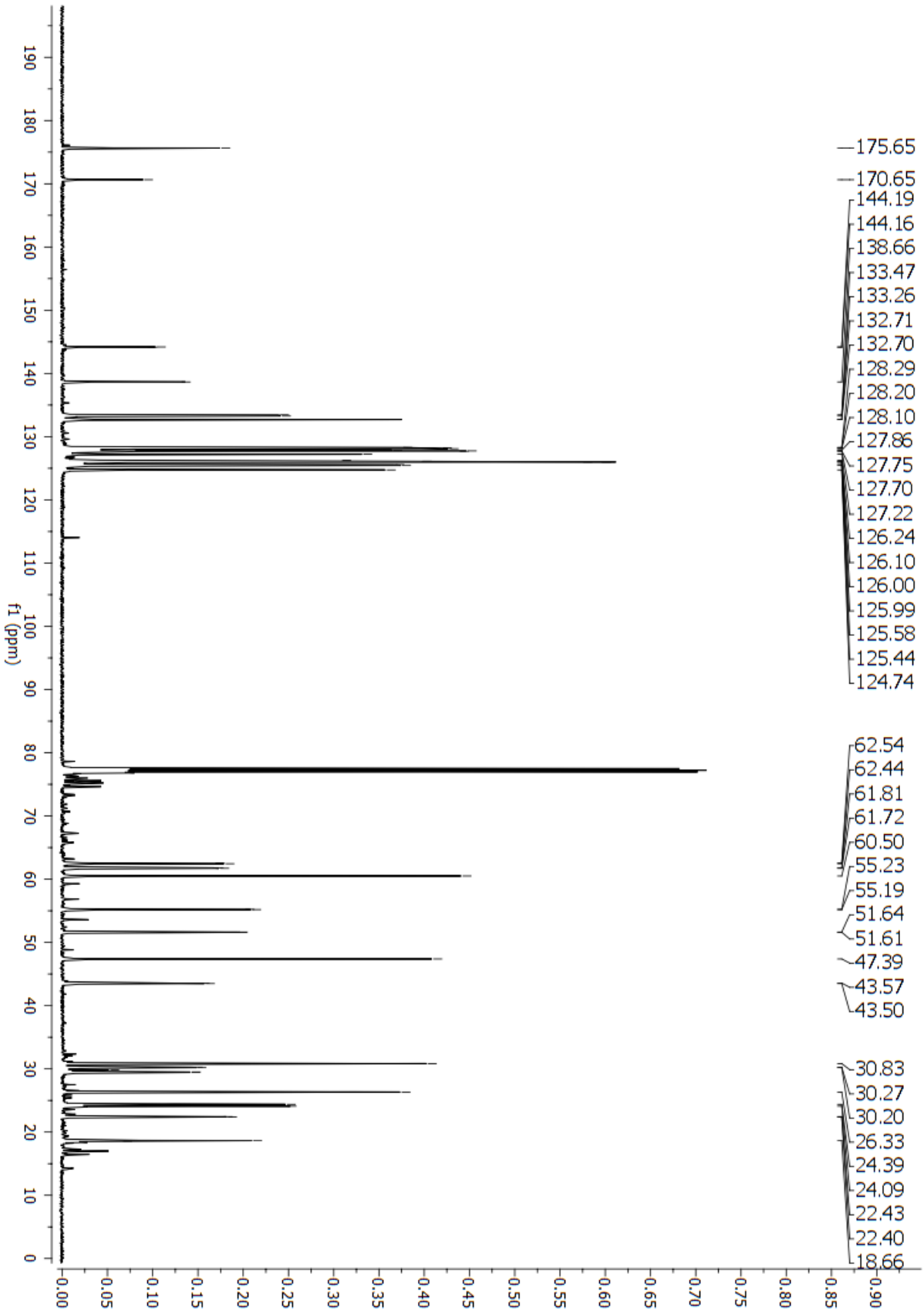

173.06
170.89
154.37
144.87
143.15
139.68
133.65
133.57
132.86
128.42
128.18
128.10
127.90
127.85
127.82
127.36
126.32
126.29
126.18
126.15
125.94
125.87
125.02
79.46
62.27
62.19
62.15
62.05
60.55
54.63
51.80
47.19
43.93
30.21
28.73
24.55
24.14
23.93
22.20
19.95
f1 (ppm)

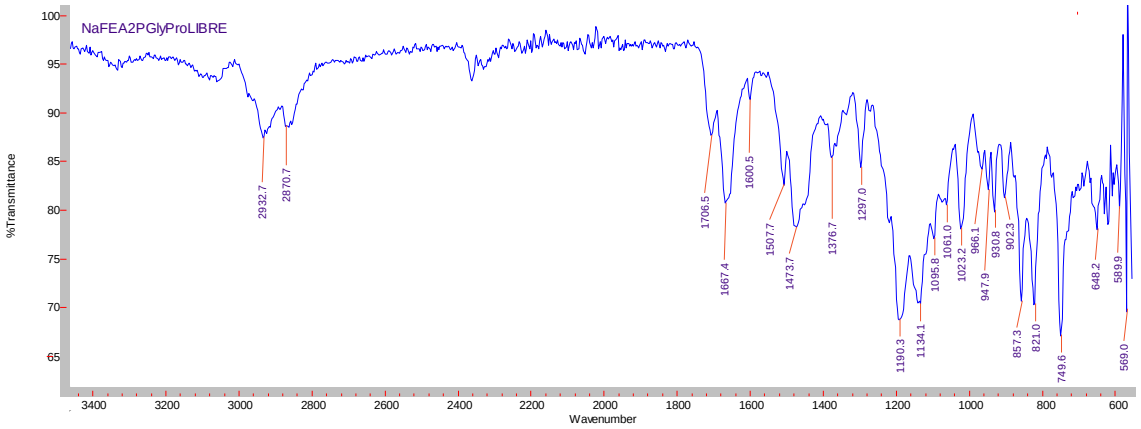


Catalyst (1*R*,2*R*,1'*R*,2'*R*,2''*S*)-**17**

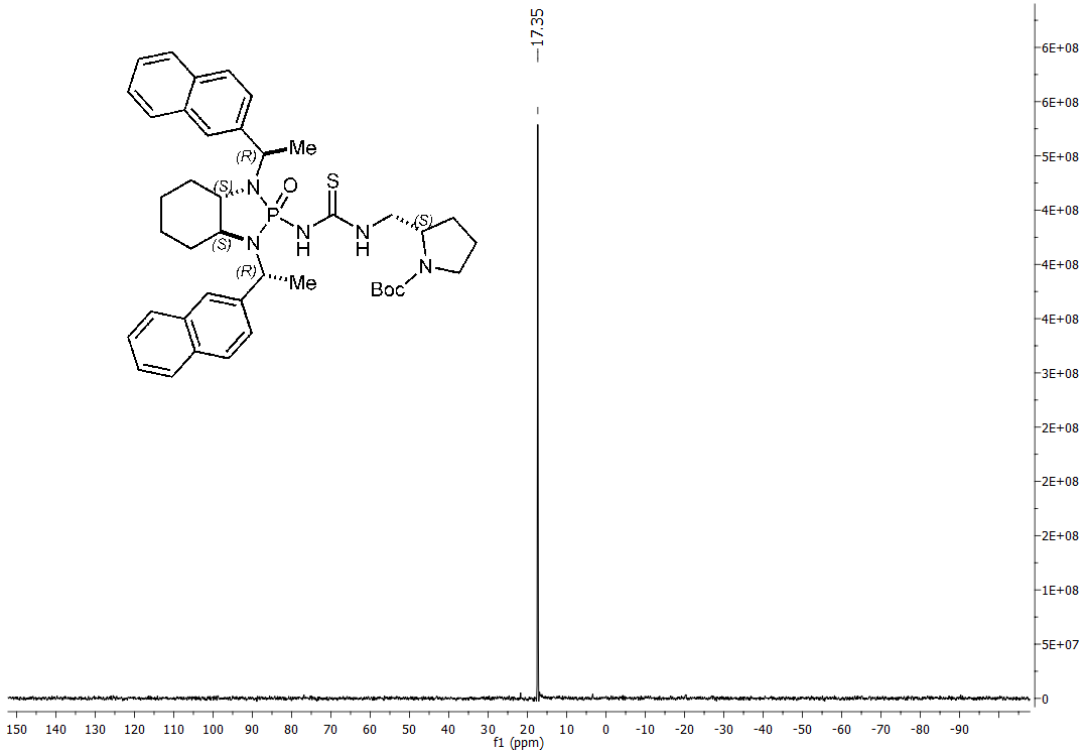


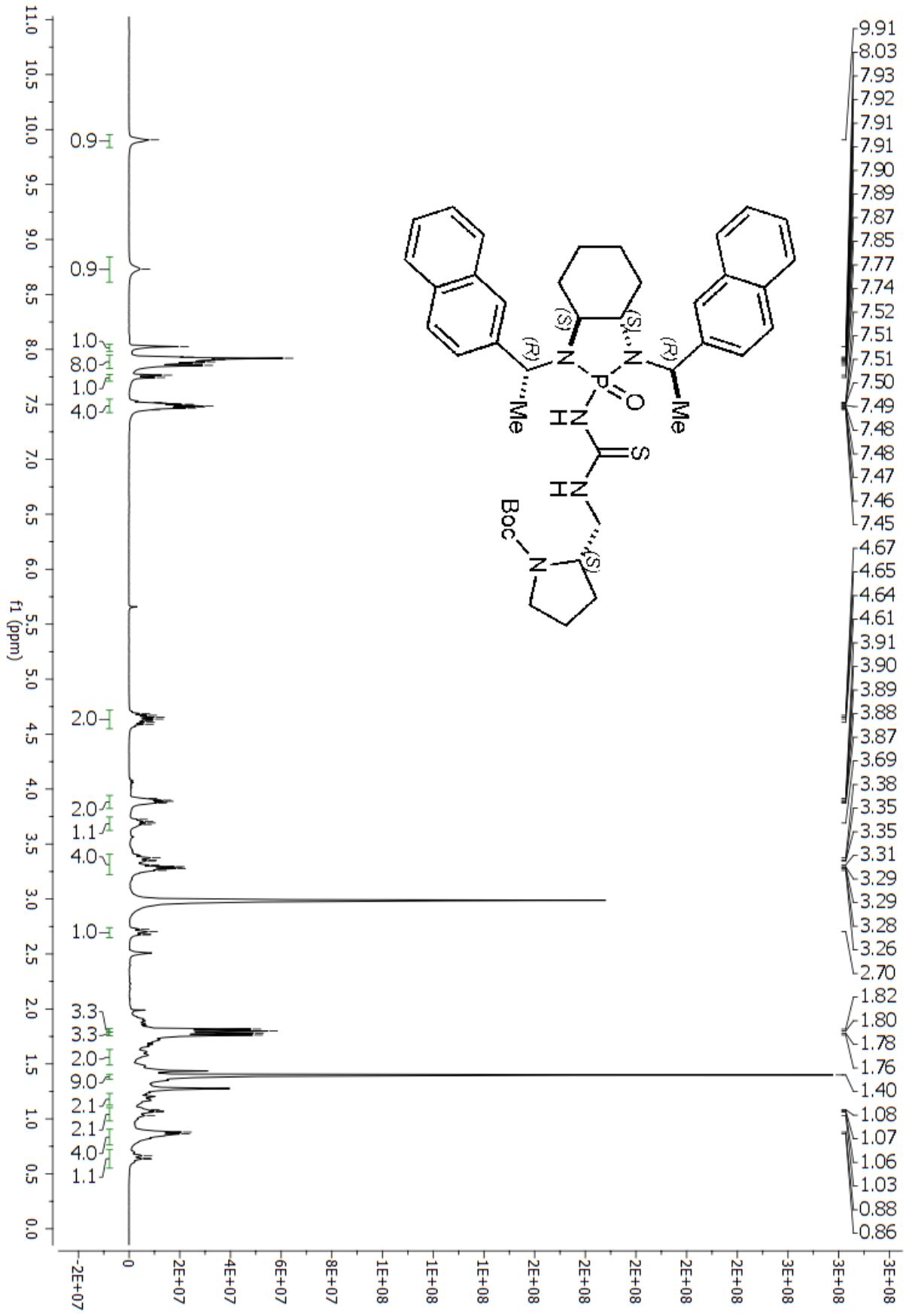

f1 (ppm)
0.8
7.0
3.1
4.0
1.0
1.0
1.1
2.1
1.0
2.0
1.0
2.0
1.1
2.0
3.0
2.1
3.1
1.2
1.1
2.2
3.0
1.2
1.0
7.84
7.82
7.80
7.79
7.77
7.77
7.70
7.69
7.68
7.68
7.65
7.64
7.63
7.63
7.42
7.42
7.41
7.41
7.41
7.40
7.40
7.40
7.39
7.39
7.38
3.72
3.71
3.70
3.37
3.37
2.88
2.87
2.86
1.74
1.72
1.69
1.68
1.67
1.67
1.66
1.65
1.60
1.59
1.14
1.14
1.13
1.13
1.12
1.12
1.11
1.11
1.10

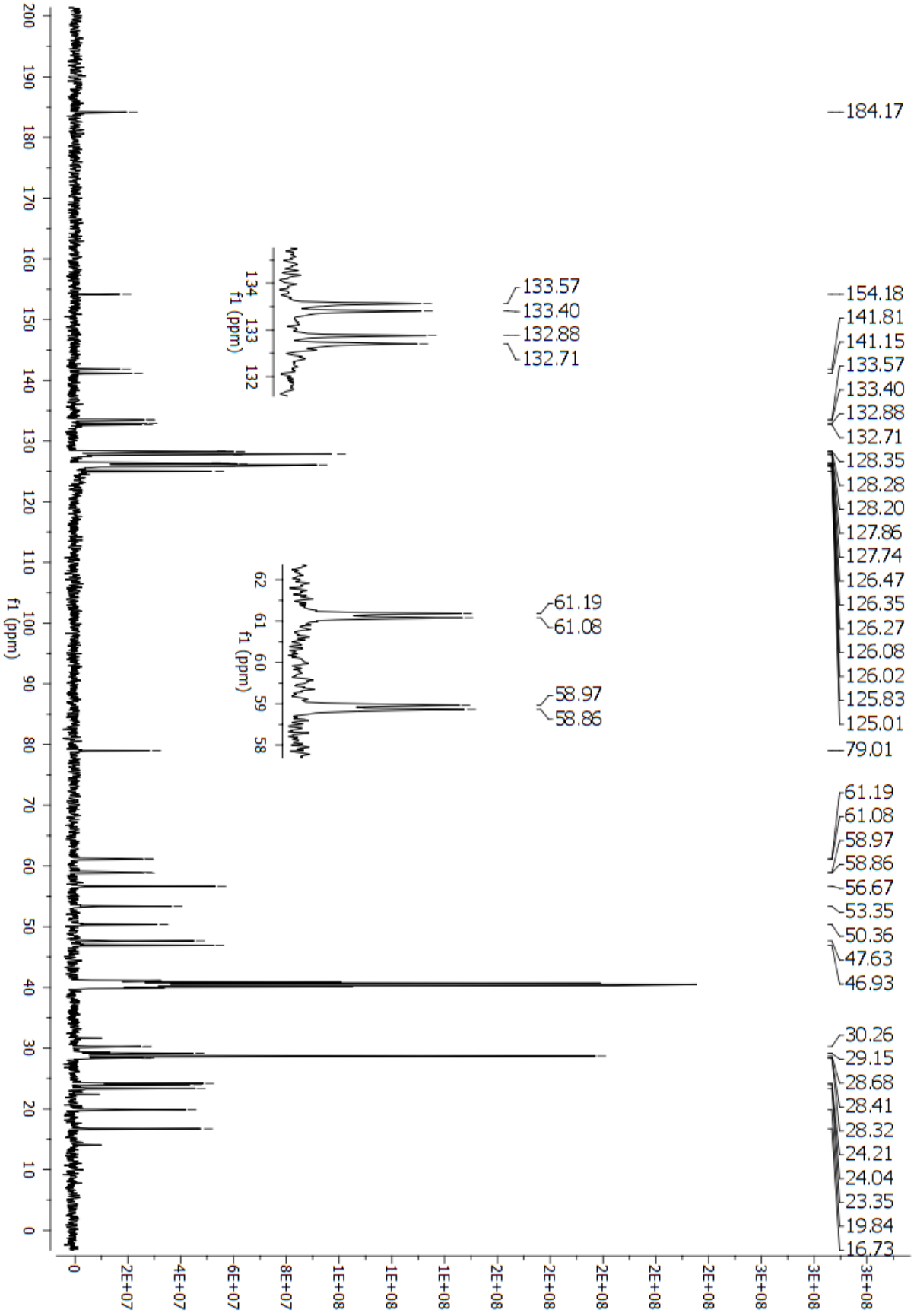

f1 (ppm)
175.65
170.65
144.19
144.16
138.66
133.47
133.26
132.71
132.70
128.29
128.20
128.10
127.86
127.75
127.70
127.22
126.24
126.10
126.00
125.99
125.58
125.44
124.74
62.54
62.44
61.81
61.72
60.50
55.23
55.19
51.64
51.61
47.39
43.57
43.50
30.83
30.27
30.20
26.33
24.39
24.09
22.43
22.40
18.66

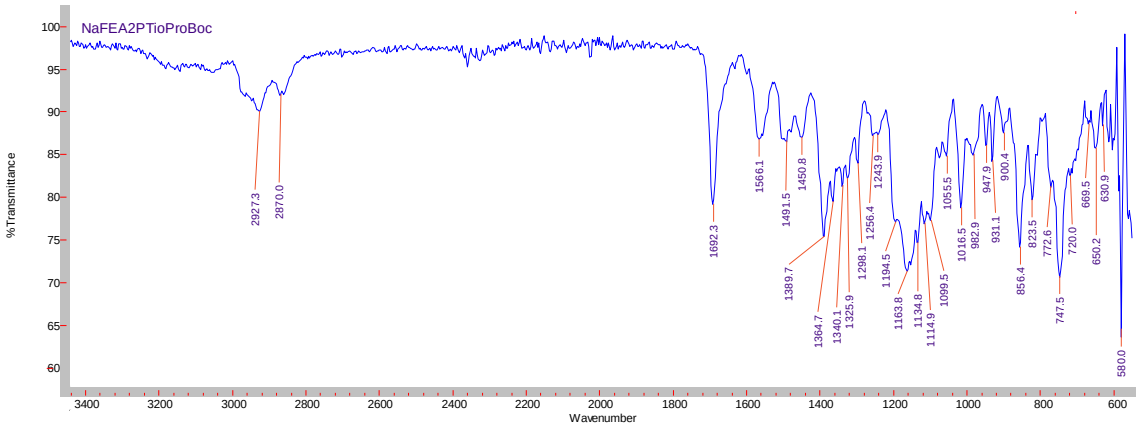


Pre-catalyst (1*S*,2*S*,1'*R*,2'*R*,2''*S*)-**22**

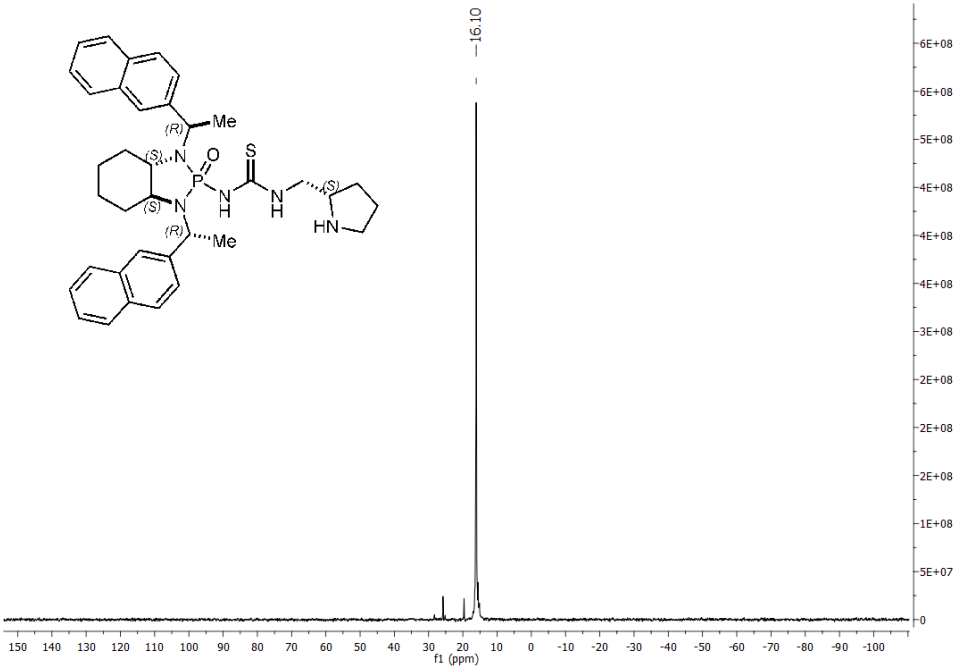


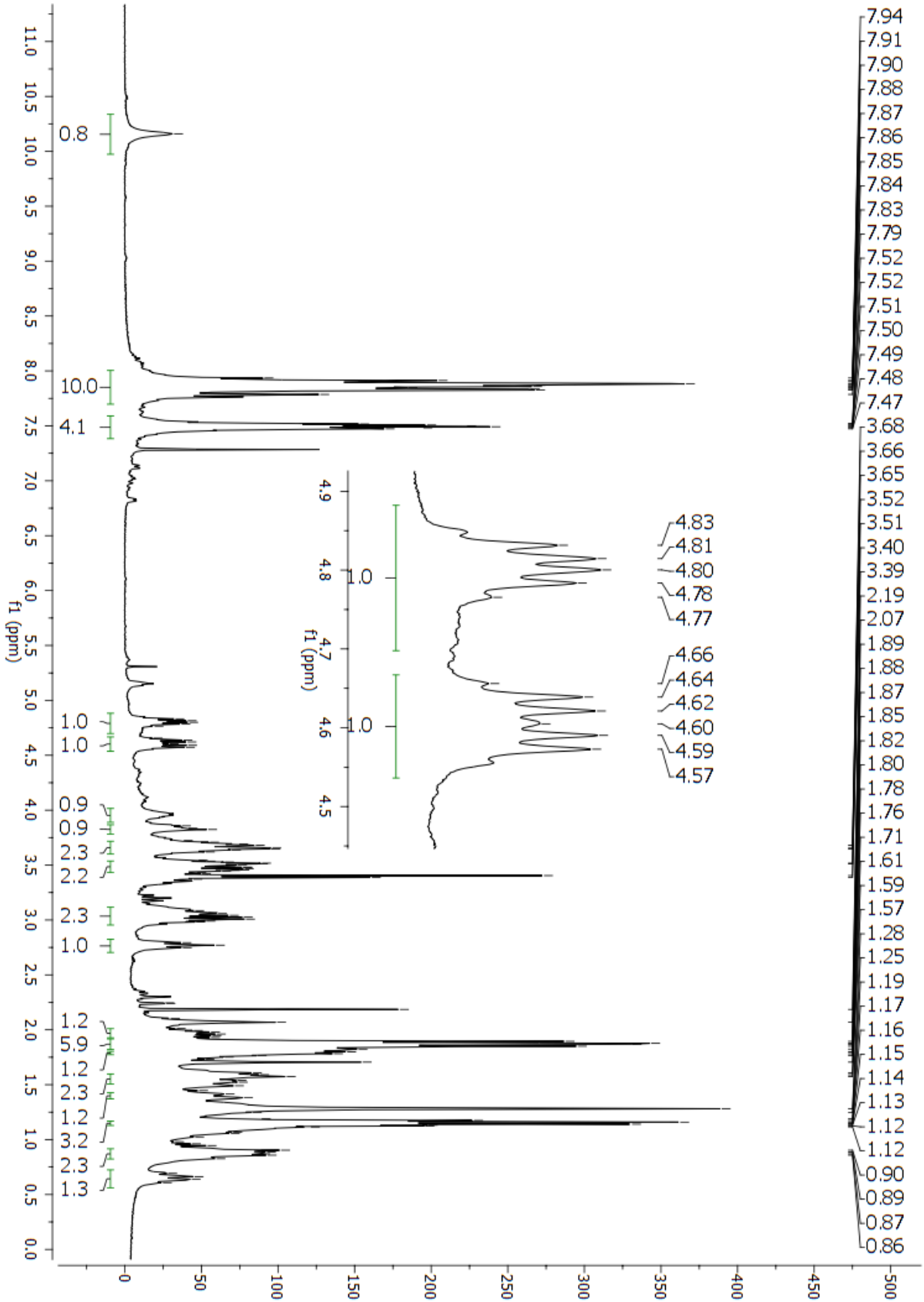

f1 (ppm)
Me
Me
Boc

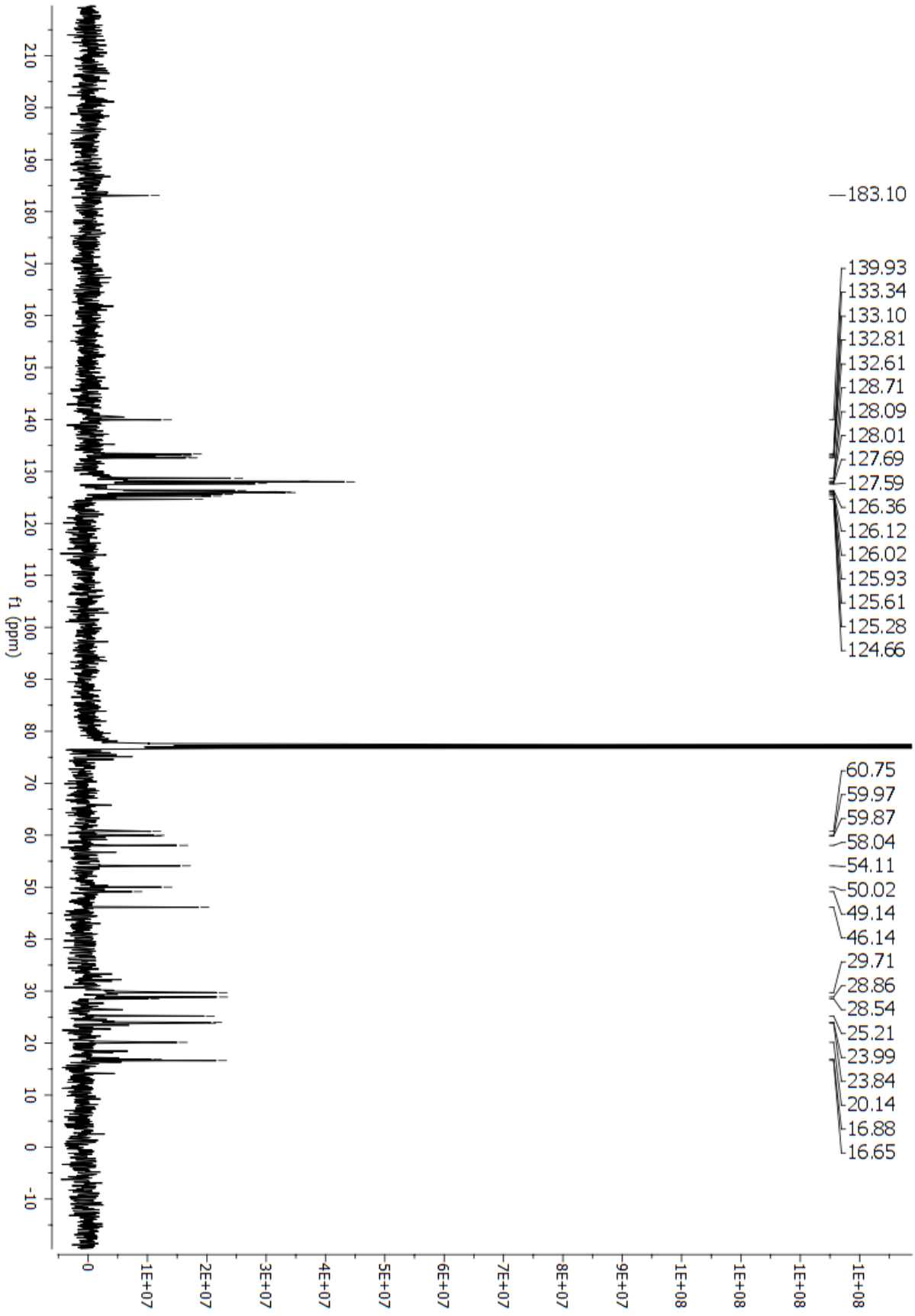

f1 (ppm)
184.17
154.18
141.81
141.15
133.57
133.40
132.88
132.71
128.35
128.28
128.20
127.86
127.74
126.47
126.35
126.27
126.08
126.02
125.83
125.01
79.01
61.19
61.08
58.97
58.86
56.67
53.35
50.36
47.63
46.93
30.26
29.15
28.68
28.41
28.32
24.21
24.04
23.35
19.84
16.73



Catalyst (1*S*,2*S*,1'*R*,2'*R*,2''*S*)-**20**



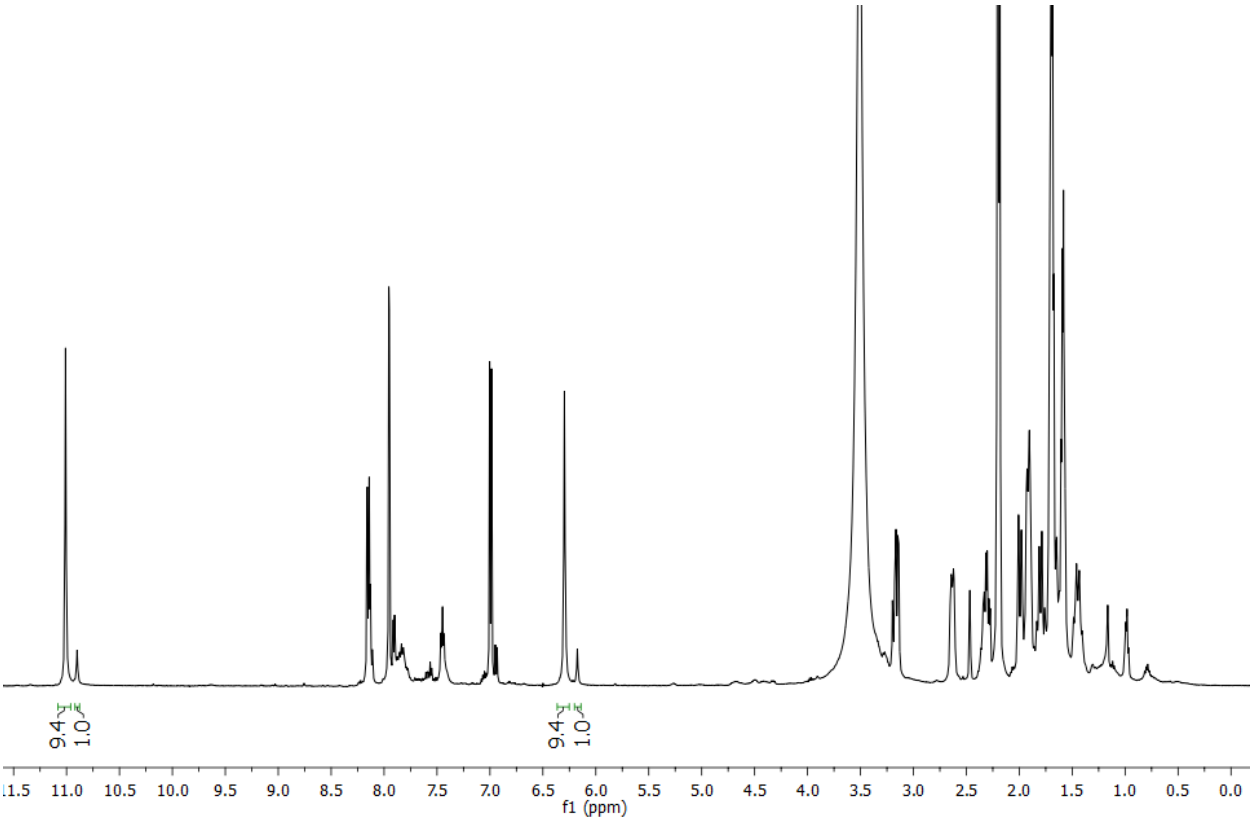

f1 (ppm)
0.8
10.0
4.1
1.0
1.0
0.9
0.9
2.3
2.2
2.3
1.0
1.2
5.9
1.2
2.3
1.2
3.2
2.3
1.3
1.0
1.0
4.83
4.81
4.80
4.78
4.77
4.66
4.64
4.62
4.60
4.59
4.57
7.94
7.91
7.90
7.88
7.87
7.86
7.85
7.84
7.83
7.79
7.52
7.52
7.51
7.50
7.49
7.48
7.47
3.68
3.66
3.65
3.52
3.51
3.40
3.39
2.19
2.07
1.89
1.88
1.87
1.85
1.82
1.80
1.78
1.76
1.71
1.61
1.59
1.57
1.28
1.25
1.19
1.17
1.16
1.15
1.14
1.13
1.12
1.12
0.90
0.89
0.87
0.86


183.10
139.93
133.34
133.10
132.81
132.61
128.71
128.09
128.01
127.69
127.59
126.36
126.12
126.02
125.93
125.61
125.28
124.66
60.75
59.97
59.87
58.04
54.11
50.02
49.14
46.14
29.71
28.86
28.54
25.21
23.99
23.84
20.14
16.88
16.65
f1 (ppm)

5. Aldolic and Michael adducts (NMR, HPLC-chromatograms)

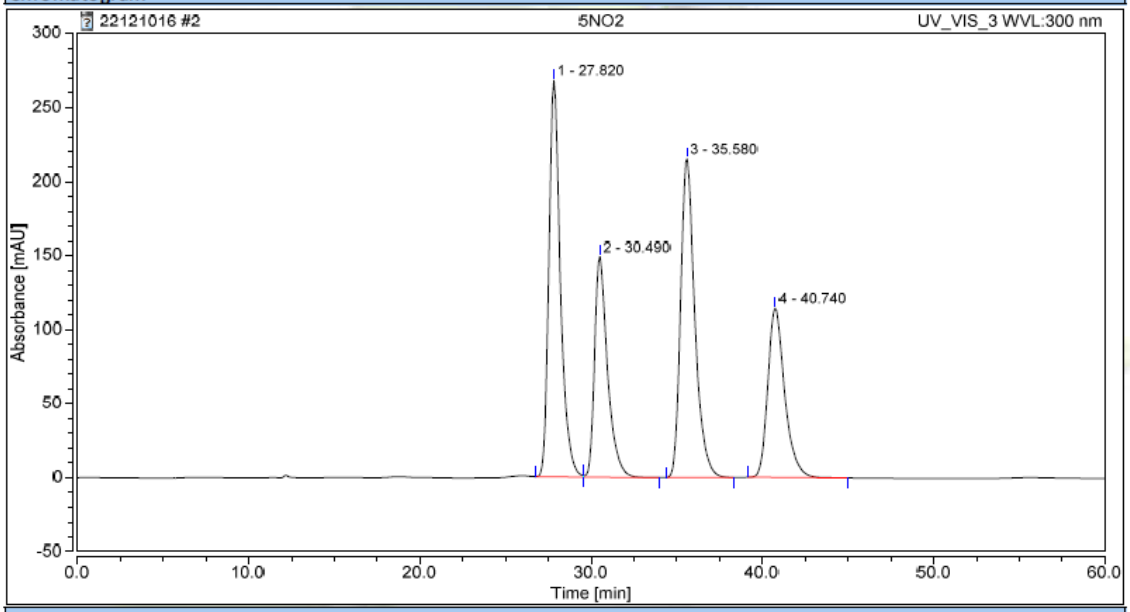
^{1}H-RMN and chiral HPLC-chromatograms for the dr and er for the aldol addition of cyclohexanone to isatins catalyzed by (1*R*,2*R*,1'*R*,2'*R*,2''*S*)-9.

(*R*)-3-hydroxy-5-nitro-3-((*S*)-2-oxocyclohexyl)indolin-2-one, (3*R*,2'*S*)-**12a**



Conditions: Chiralpack AD-H, Hex-IPA (80:20), 0.5 mL/min, 70 minutes.

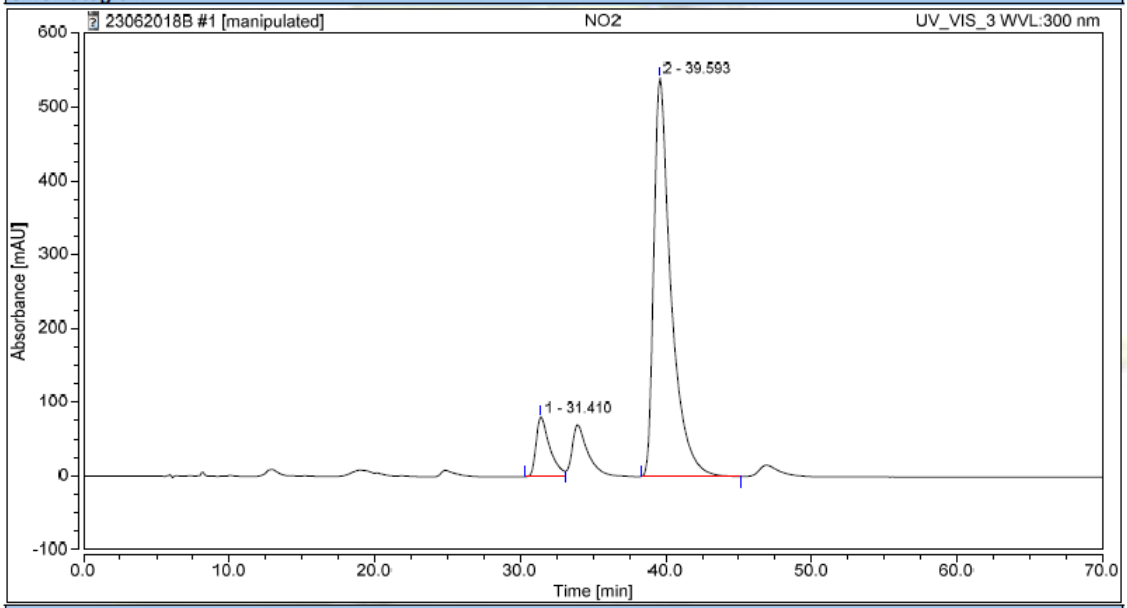
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		27.820	207.256	267.722	30.70	35.87	n.a.
2		30.490	130.310	148.977	19.30	19.96	n.a.
3		35.580	207.209	215.342	30.69	28.85	n.a.
4		40.740	130.351	114.322	19.31	15.32	n.a.
Total:			675.125	746.362	100.00	100.00	

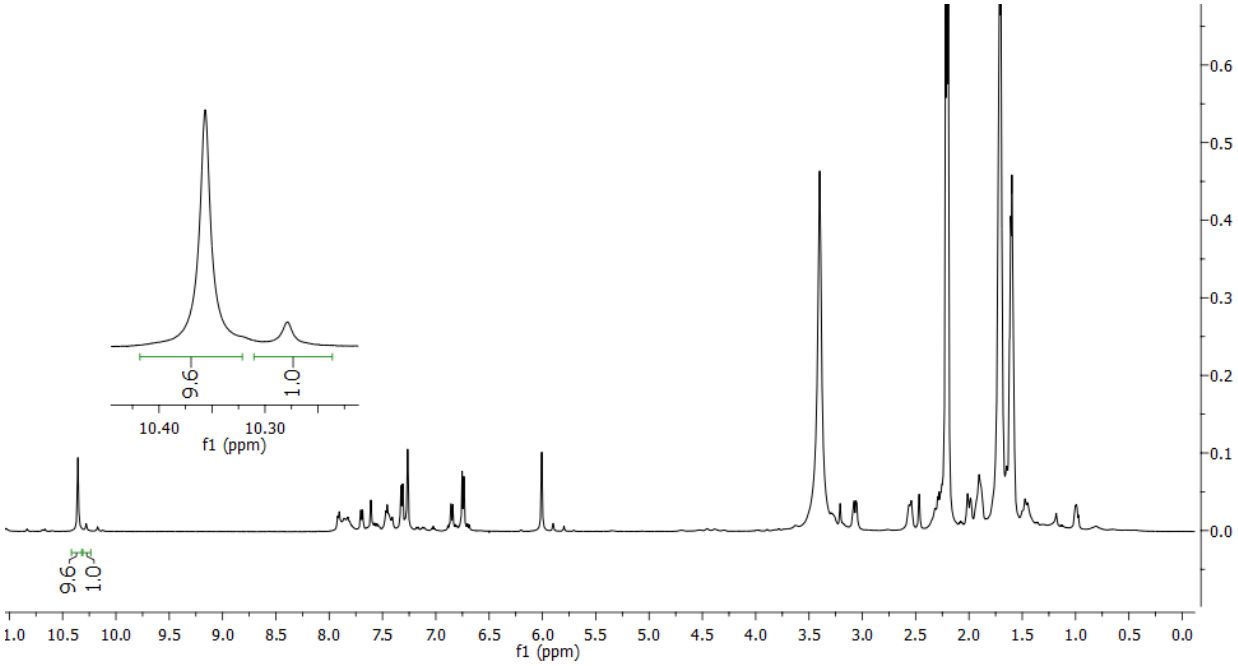
Chromatogram



Integration Results

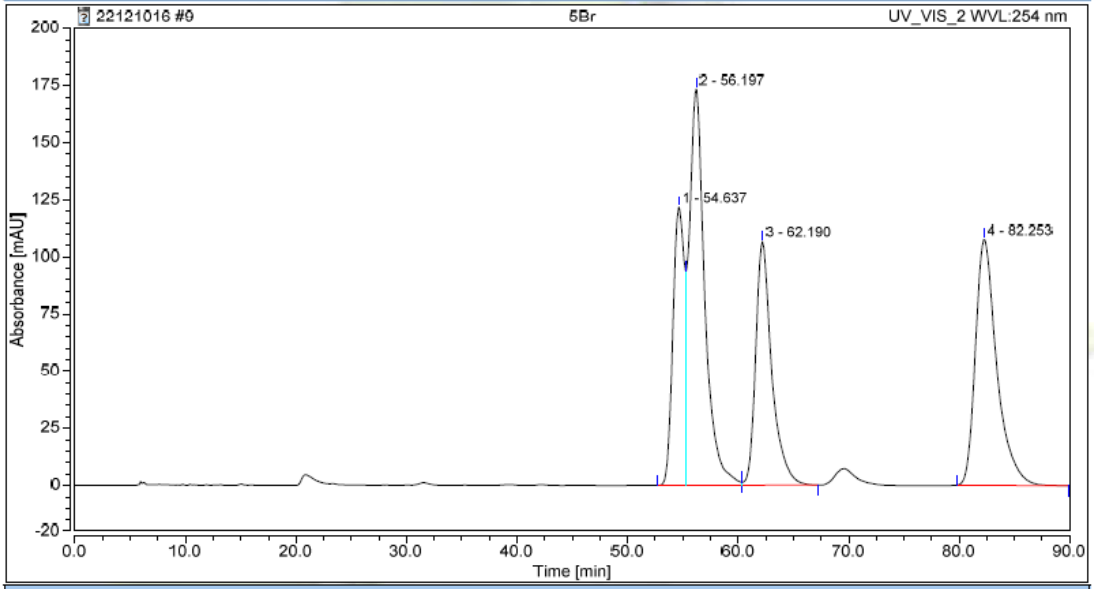
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		31.410	87.870	81.080	10.64	13.05	n.a.
2		39.593	738.226	540.109	89.36	86.95	n.a.
Total:			826.096	621.189	100.00	100.00	

(*R*)-5-bromo-3-hydroxy-3-((*S*)-2-oxocyclohexyl)indolin-2-one, (3*R*,2'*S*)-**12b**



Conditions: Chiralpack AD-H, Hex-IPA (90:10), 0.5 mL/min, 110 minutes.

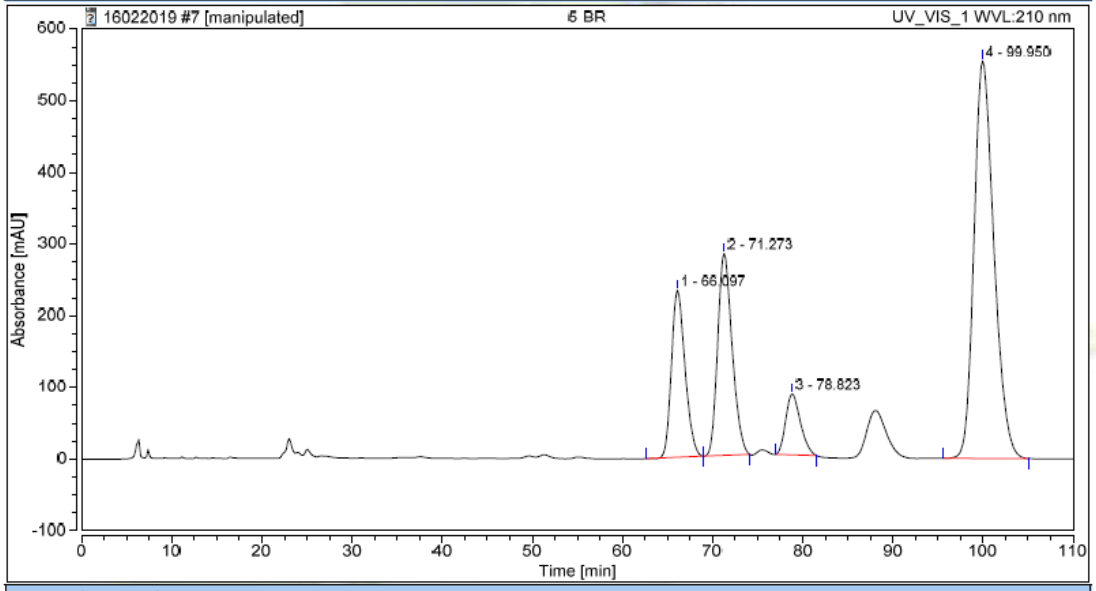
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		54.637	144.641	121.757	17.02	23.90	n.a.
2		56.197	284.549	173.412	33.48	34.04	n.a.
3		62.190	180.019	106.628	21.18	20.93	n.a.
4		82.253	240.609	107.677	28.31	21.13	n.a.
Total:			849.818	509.474	100.00	100.00	

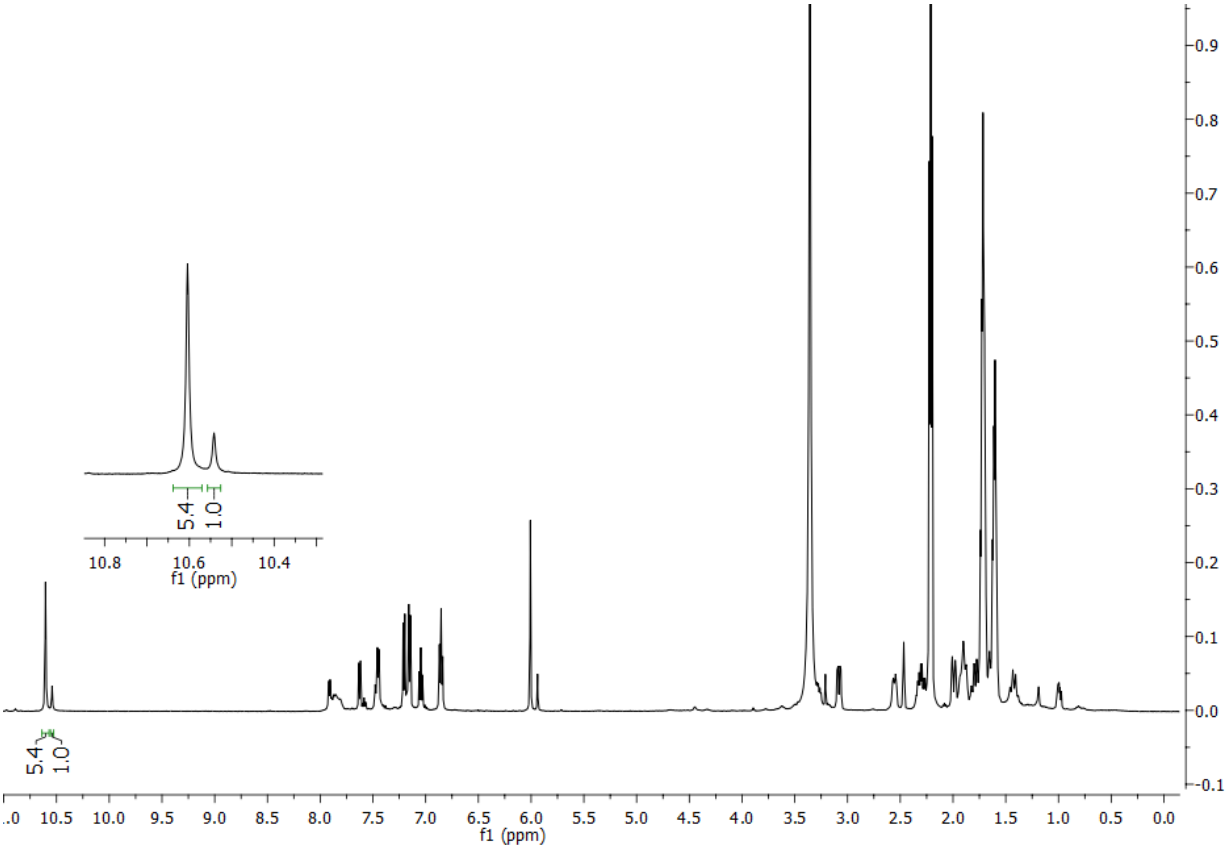
Chromatogram



Integration Results

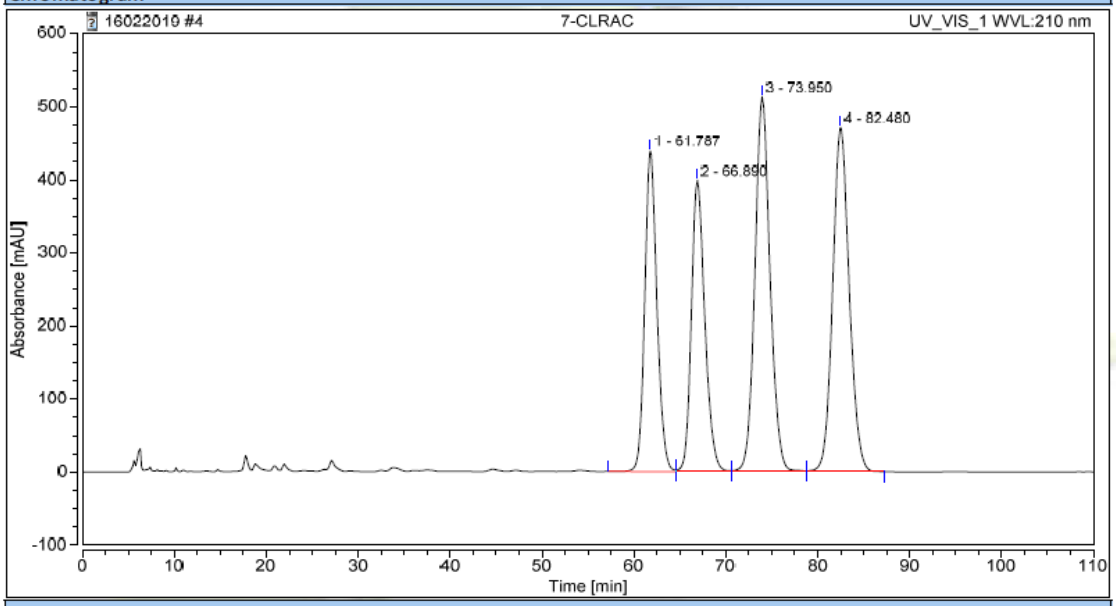
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		66.097	405.873	233.304	16.19	20.21	n.a.
2		71.273	521.788	281.669	20.81	24.40	n.a.
3		78.823	160.887	84.992	6.42	7.36	n.a.
4		99.950	1418.289	554.362	56.58	48.02	n.a.
Total:			2506.837	1154.327	100.00	100.00	

(*R*)-7-chloro-3-hydroxy-((*S*)-2-oxocyclohexyl)indolin-2-one, (3*R*,2'*S*)-**12c**



Conditions: Chiralpack AD-H, Hex-IPA (90:10), 0.5 mL/min, 110 minutes.

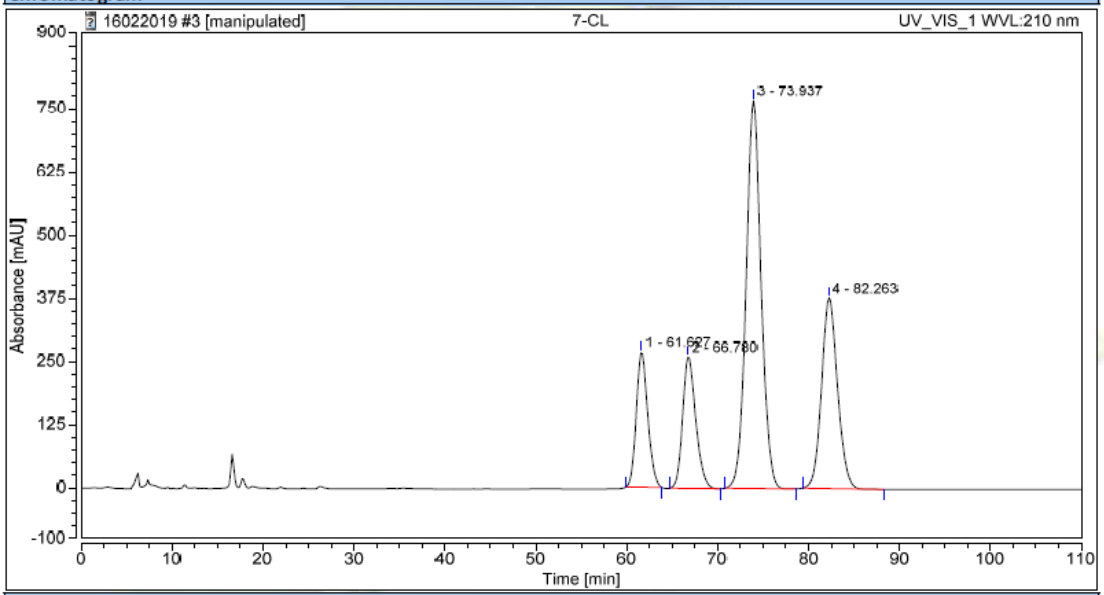
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		61.787	671.360	438.676	20.29	24.09	n.a.
2		66.890	673.743	398.517	20.36	21.88	n.a.
3		73.950	983.783	512.825	29.73	28.16	n.a.
4		82.480	980.448	471.003	29.63	25.86	n.a.
Total:			**3309.334**	**1821.021**	**100.00**	**100.00**	

Chromatogram

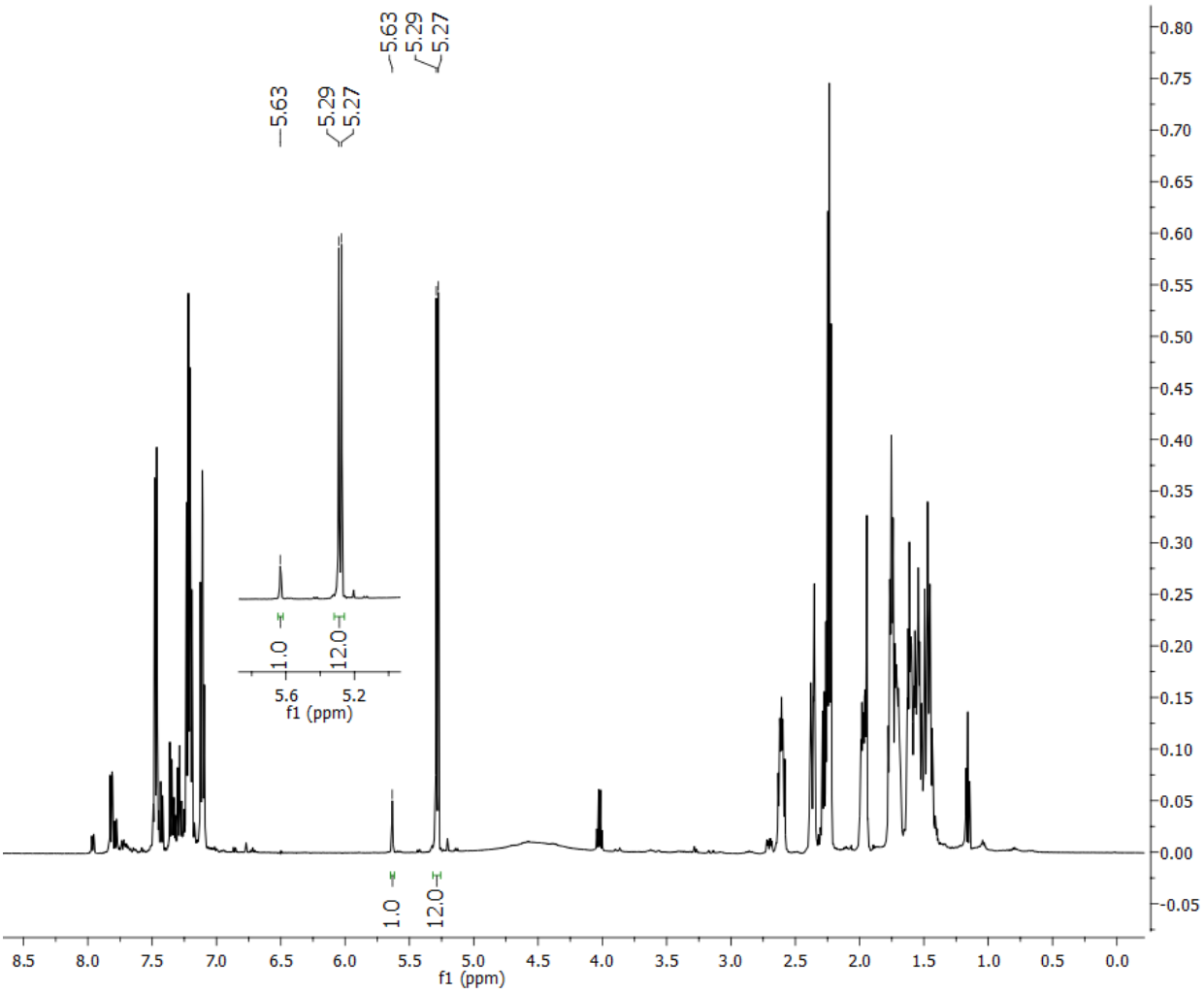


Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		61.627	389.613	267.506	12.75	16.00	n.a.
2		66.780	433.857	260.497	14.19	15.58	n.a.
3		73.937	1468.560	766.838	48.05	45.86	n.a.
4		82.263	764.429	377.387	25.01	22.57	n.a.
Total:			**3056.459**	**1672.228**	**100.00**	**100.00**	

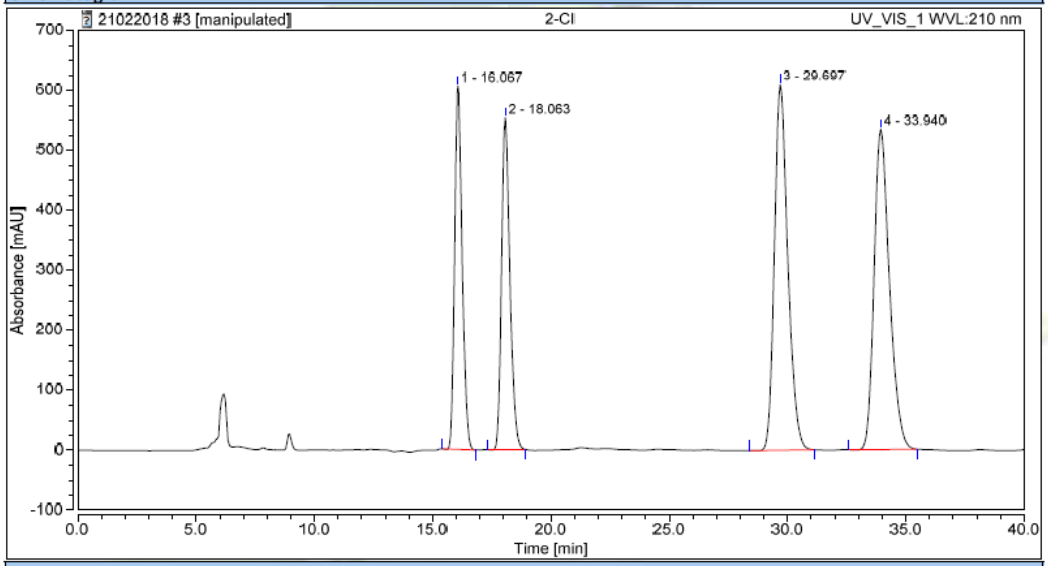
[1]H-RMN and chiral HPLC-chromatograms for the dr and er for the aldol addition of cyclohexanone to aryl carbaldehydes catalyzed by (1*R*,2*R*,1'*R*,2'*R*,2''*S*)-17.

(*S*)-2-[(*R*)-(2-chlorophenyl)(hydroxy)methyl]cyclohexanone **19a**



Conditions: Chiralpack AD-H, Hex-IPA (95:5), 0.5 mL/min, 40 minutes.

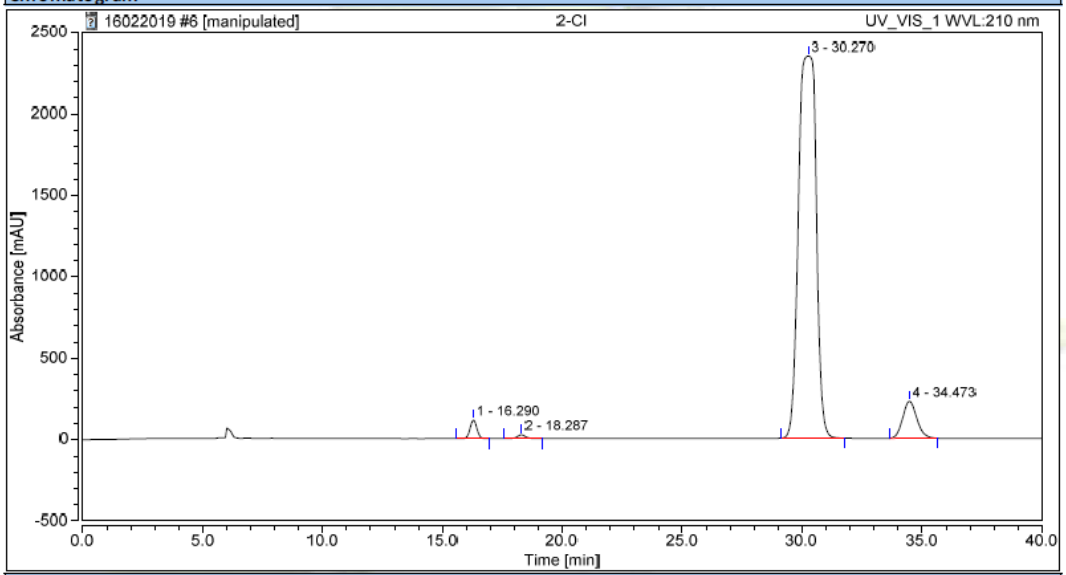
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.067	222.475	606.127	17.78	26.30	n.a.
2		18.063	226.674	553.636	18.12	24.03	n.a.
3		29.697	400.960	610.175	32.05	26.48	n.a.
4		33.940	401.030	534.338	32.05	23.19	n.a.
Total:			**1251.139**	**2304.277**	**100.00**	**100.00**	

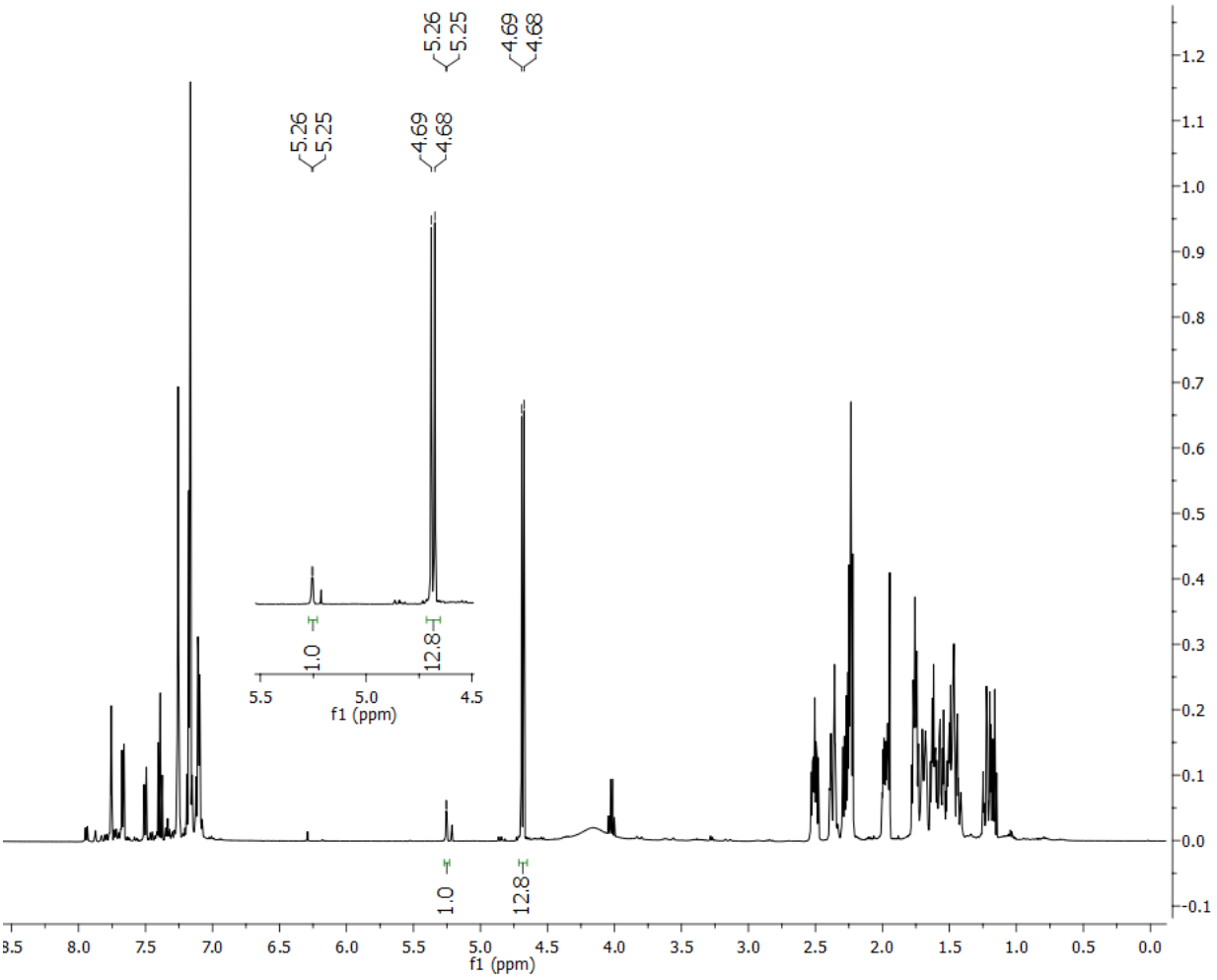
Chromatogram



Integration Results

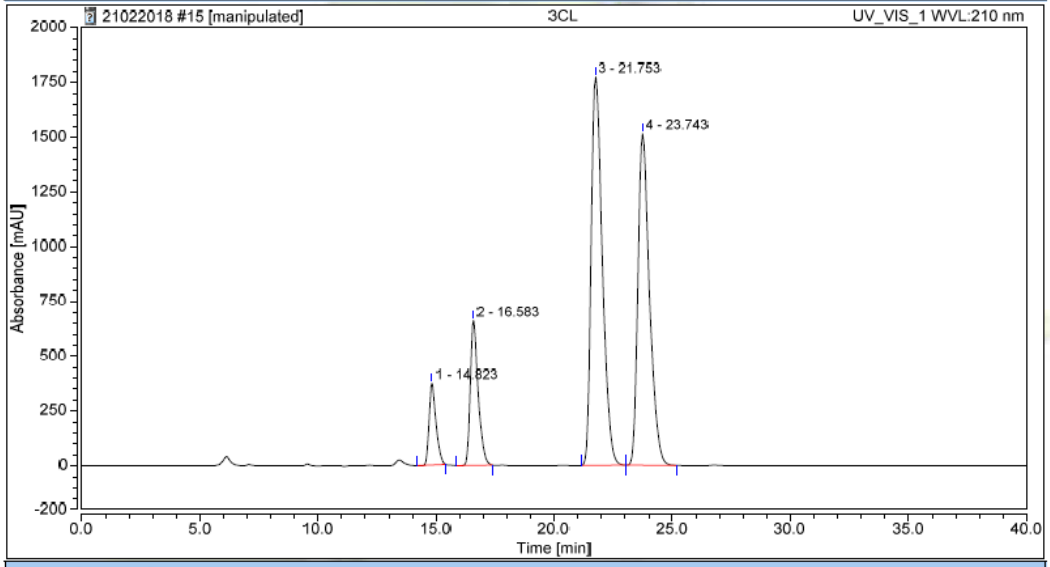
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.290	36.768	114.643	1.66	4.23	n.a.
2		18.287	8.347	22.407	0.38	0.83	n.a.
3		30.270	2019.770	2346.593	90.99	86.54	n.a.
4		34.473	154.957	227.862	6.98	8.40	n.a.
Total:			**2219.841**	**2711.505**	**100.00**	**100.00**	

(*S*)-2-[(*R*)-(3-chlorophenyl)(hydroxy)methyl]cyclohexanone **19b**



Conditions: Chiralpack AD-H, Hex-IPA (90:10), 0.5 mL/min., 40 minutes.

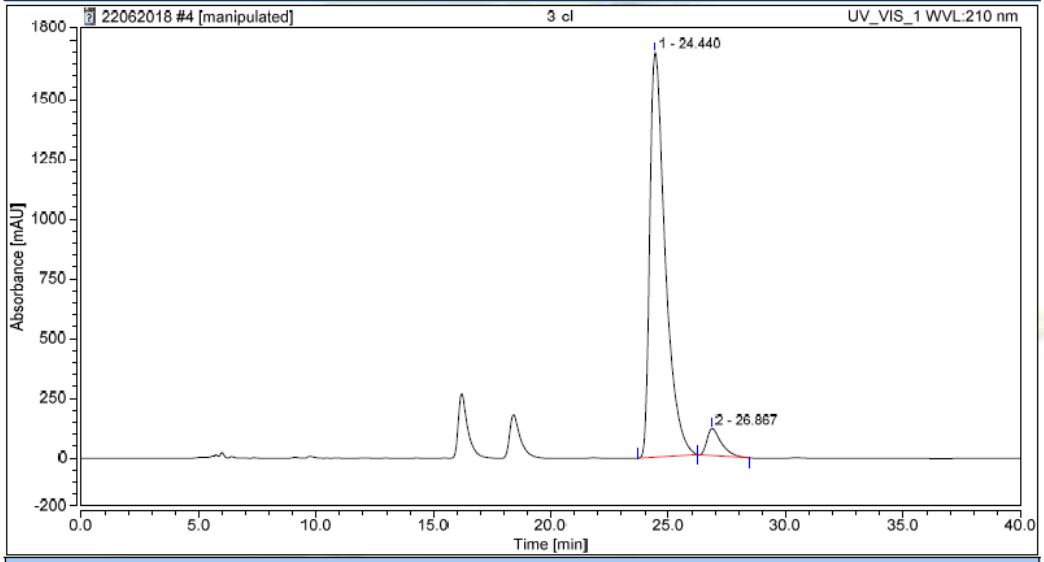
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		14.823	124.608	372.583	5.64	8.62	n.a.
2		16.583	253.736	660.985	11.49	15.30	n.a.
3		21.753	971.892	1773.912	44.00	41.05	n.a.
4		23.743	858.523	1513.889	38.87	35.03	n.a.
Total:			**2208.759**	**4321.368**	**100.00**	**100.00**	

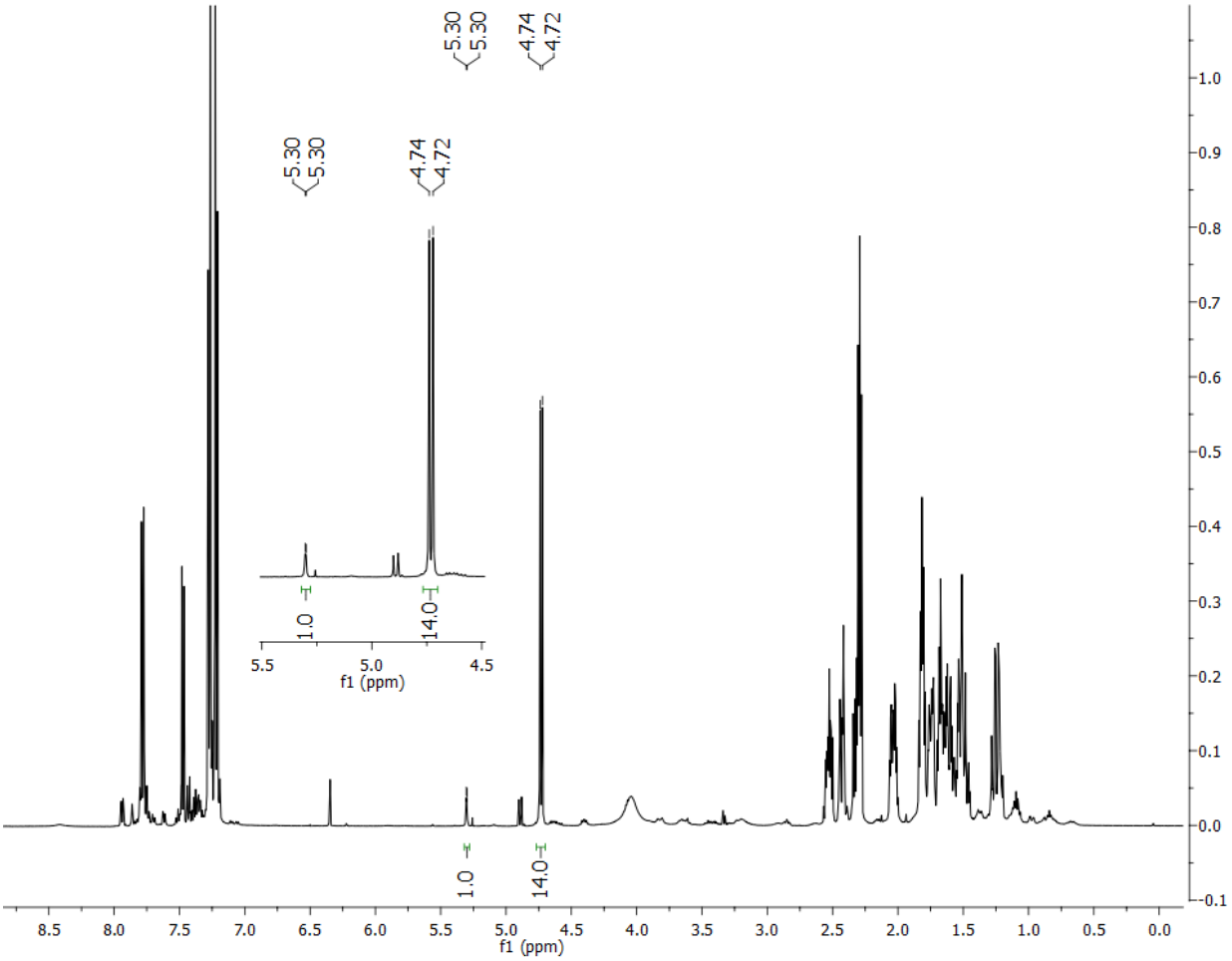
Chromatogram



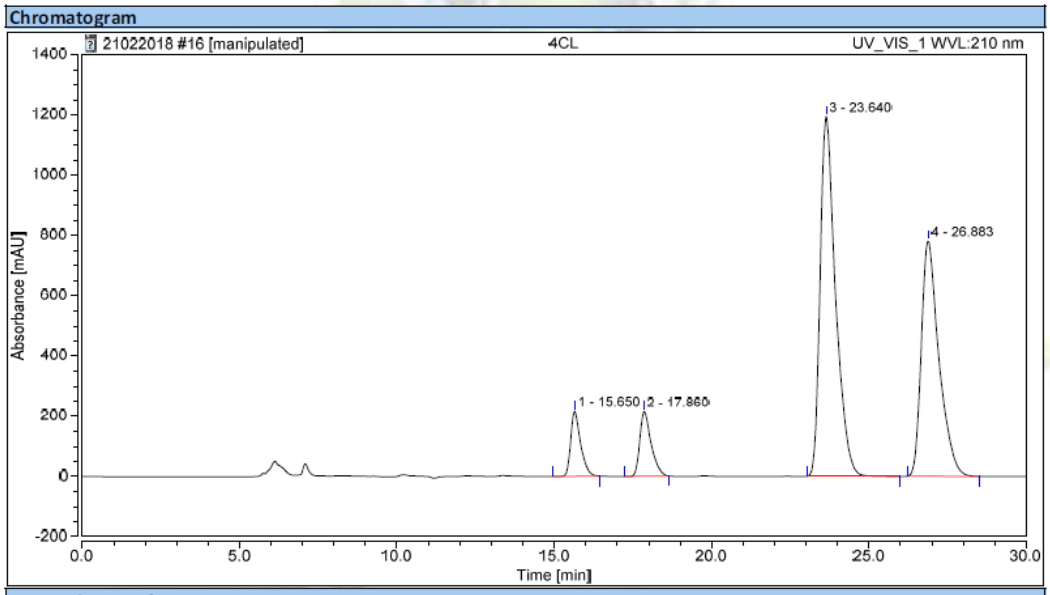
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		24.440	1291.824	1693.756	94.21	93.74	n.a.
2		26.867	79.381	113.053	5.79	6.26	n.a.
Total:			**1371.206**	**1806.809**	**100.00**	**100.00**	

(*S*)-2-[(*R*)-(4-chlorophenyl)(hydroxy)methyl]cyclohexanone **19c**

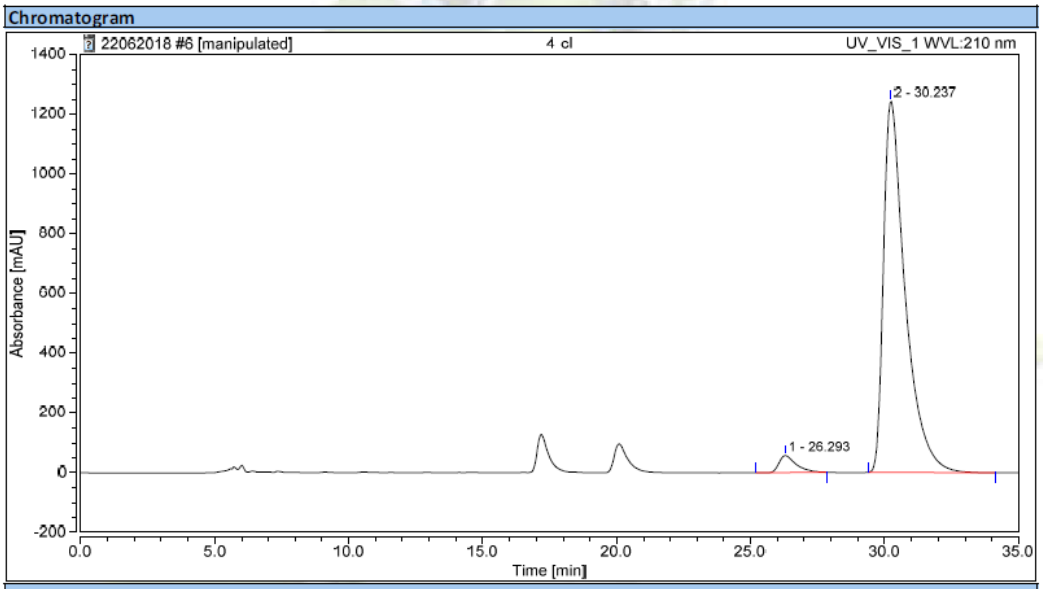


Conditions: Chiralpack AD-H, Hex-IPA (90:10), 0.5 mL/min., 30 minutes.



Integration Results

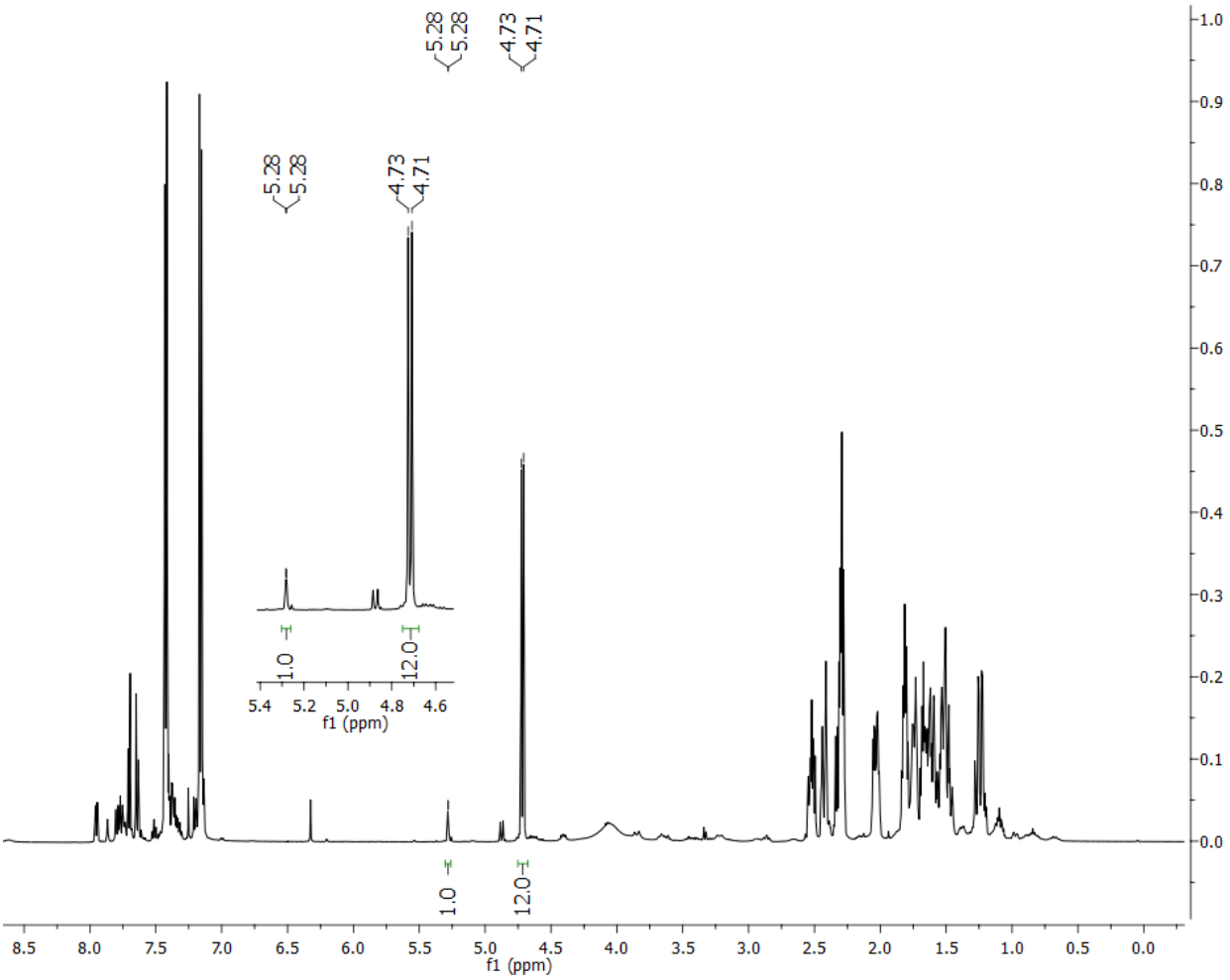
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		15.650	78.596	217.023	5.82	9.00	n.a.
2		17.860	89.313	215.612	6.61	8.94	n.a.
3		23.640	677.368	1195.207	50.12	49.58	n.a.
4		26.883	506.246	782.718	37.46	32.47	n.a.
Total:			**1351.522**	**2410.560**	**100.00**	**100.00**	



Integration Results

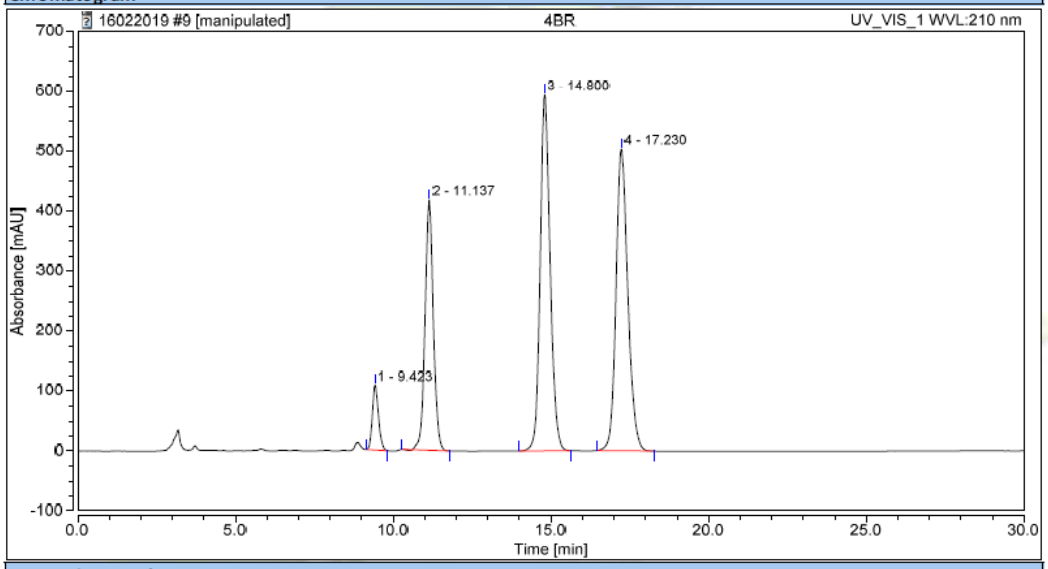
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		26.293	42.168	56.788	3.48	4.36	n.a.
2		30.237	1170.093	1245.029	96.52	95.64	n.a.
Total:			**1212.260**	**1301.817**	**100.00**	**100.00**	

(*S*)-2-[(*R*)-(4-bromophenyl)(hydroxy)methyl]cyclohexanone **19d**



Conditions: Chiralpack AD-H, Hex-IPA (90:10), 1.0 mL/min., 30 minutes

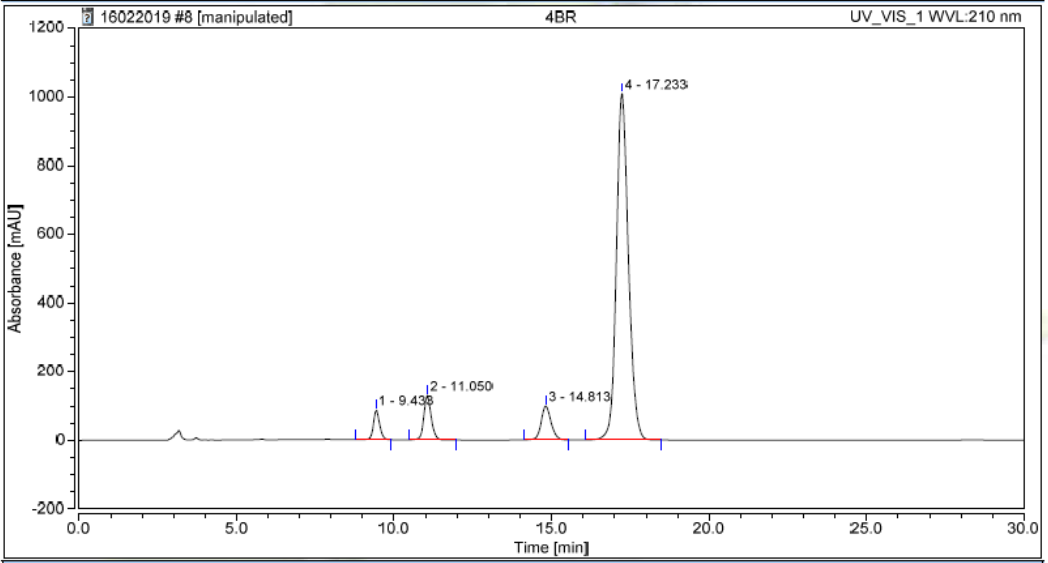
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		9.423	24.175	108.619	4.11	6.68	n.a.
2		11.137	126.957	418.134	21.60	25.73	n.a.
3		14.800	217.475	594.397	37.00	36.57	n.a.
4		17.230	219.133	504.054	37.28	31.01	n.a.
Total:			**587.740**	**1625.205**	**100.00**	**100.00**	

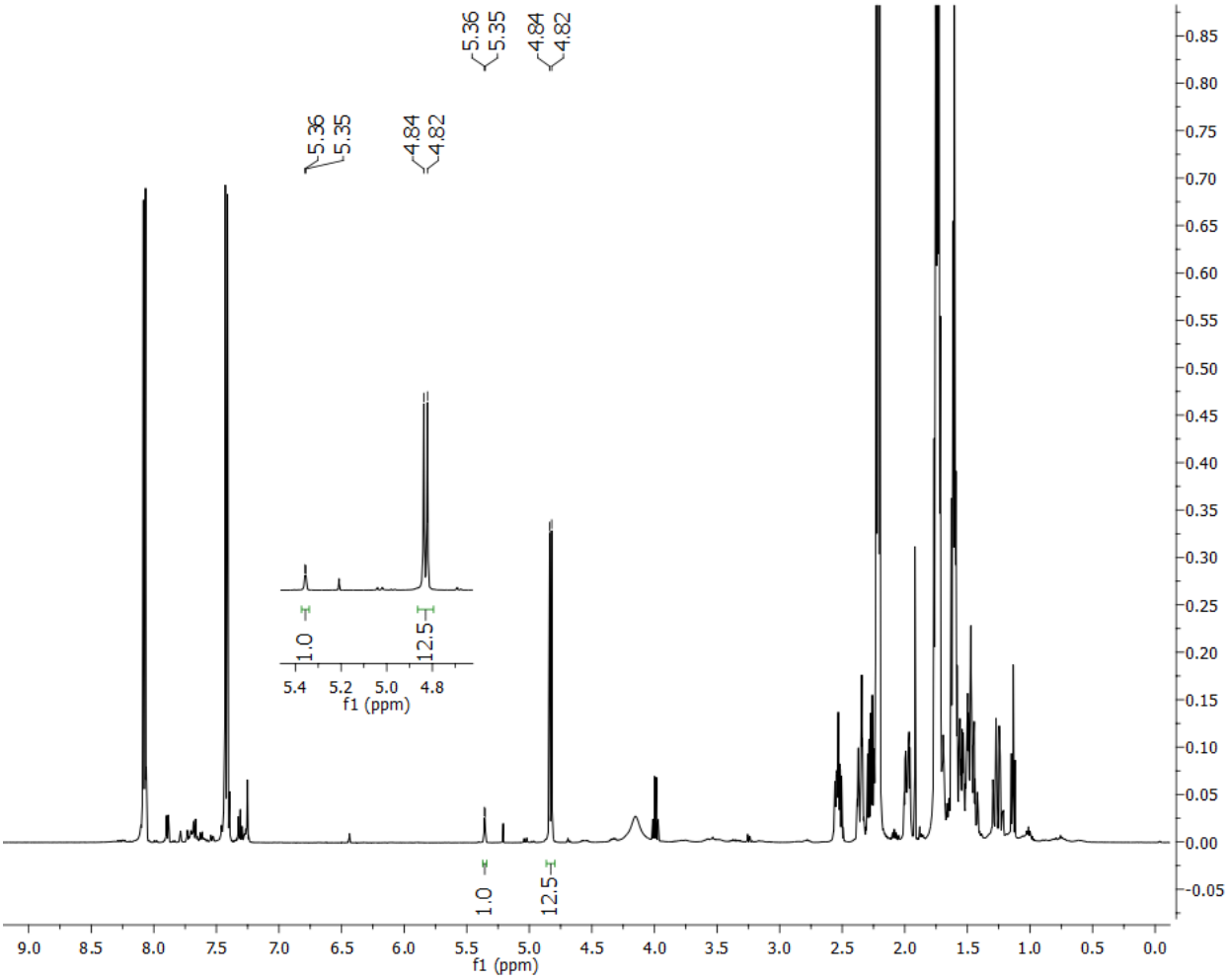
Chromatogram



Integration Results

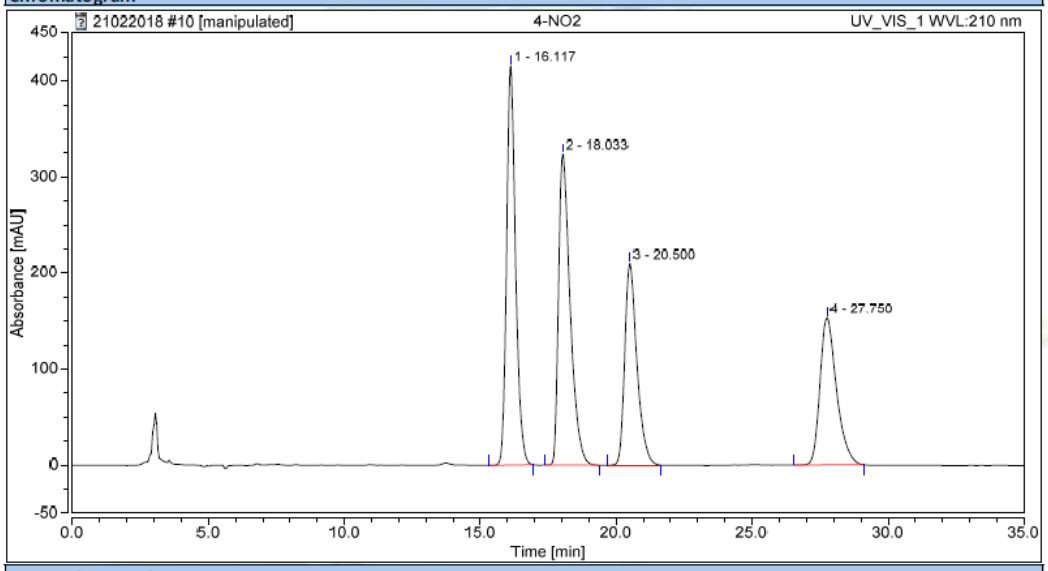
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		9.433	19.805	86.703	3.68	6.55	n.a.
2		11.050	34.876	129.418	6.48	9.77	n.a.
3		14.813	36.004	99.418	6.69	7.51	n.a.
4		17.233	447.536	1009.058	83.15	76.18	n.a.
Total:			**538.221**	**1324.598**	**100.00**	**100.00**	

(*S*)-2-[(*R*)-hydroxy(4-nitrophenyl)methyl)cyclohexanone **19g**



Conditions: Chiralpack AD-H, Hex-IPA (90:10), 1.0 mL/min., 35 minutes

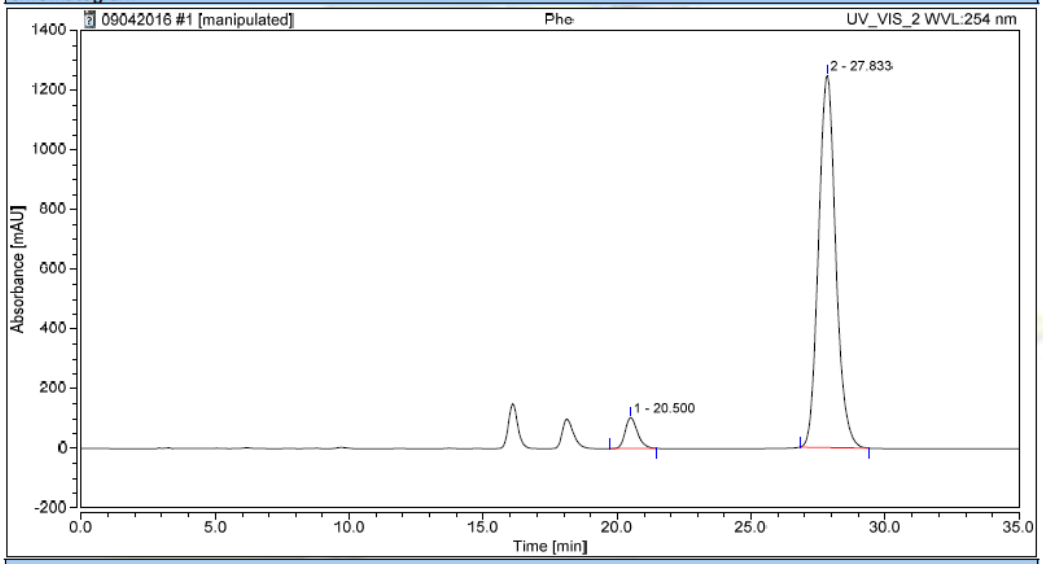
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.117	158.733	415.672	29.66	37.69	n.a.
2		18.033	159.928	323.777	29.88	29.35	n.a.
3		20.500	108.738	210.306	20.32	19.07	n.a.
4		27.750	107.747	153.217	20.13	13.89	n.a.
Total:			**535.146**	**1102.972**	**100.00**	**100.00**	

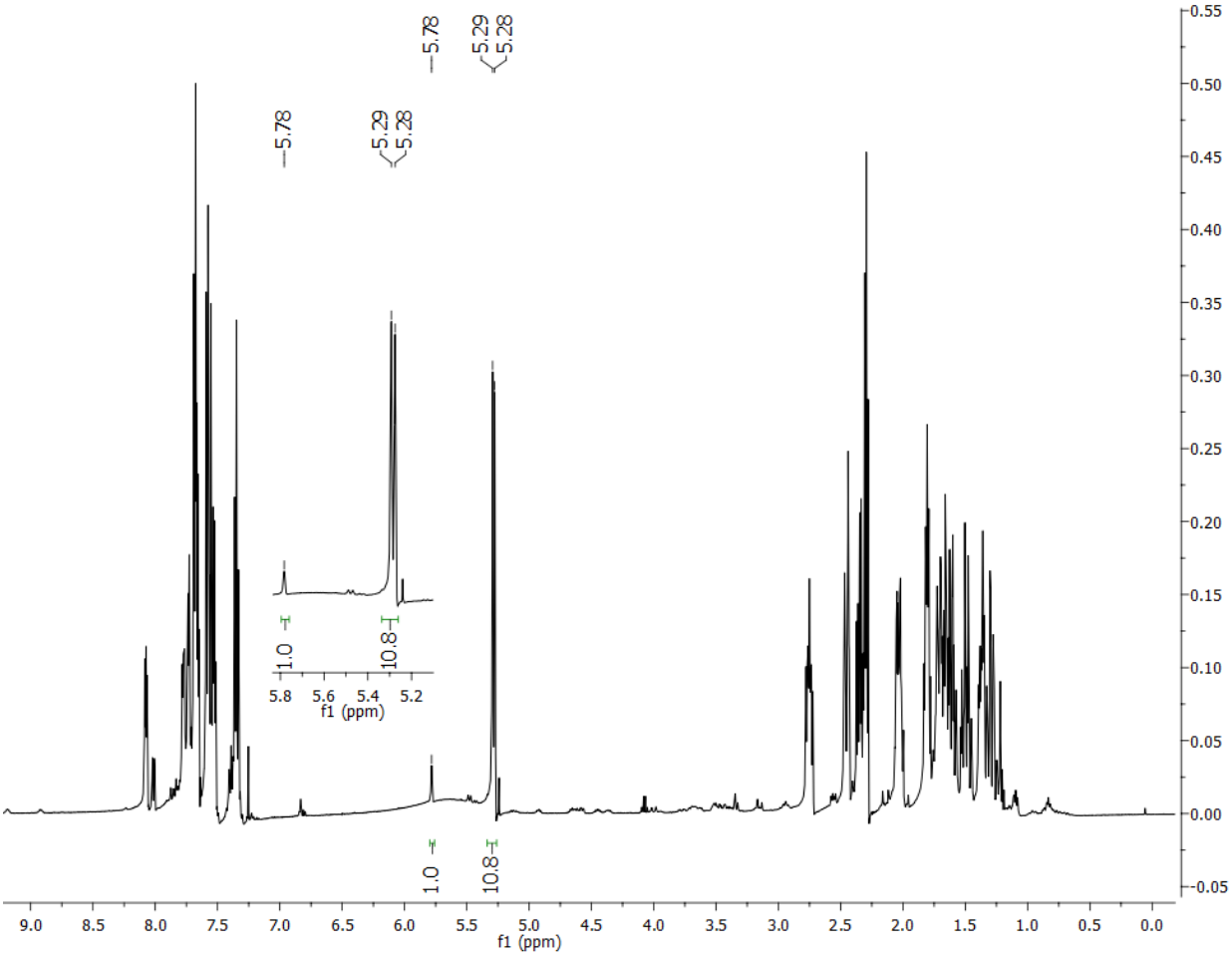
Chromatogram



Integration Results

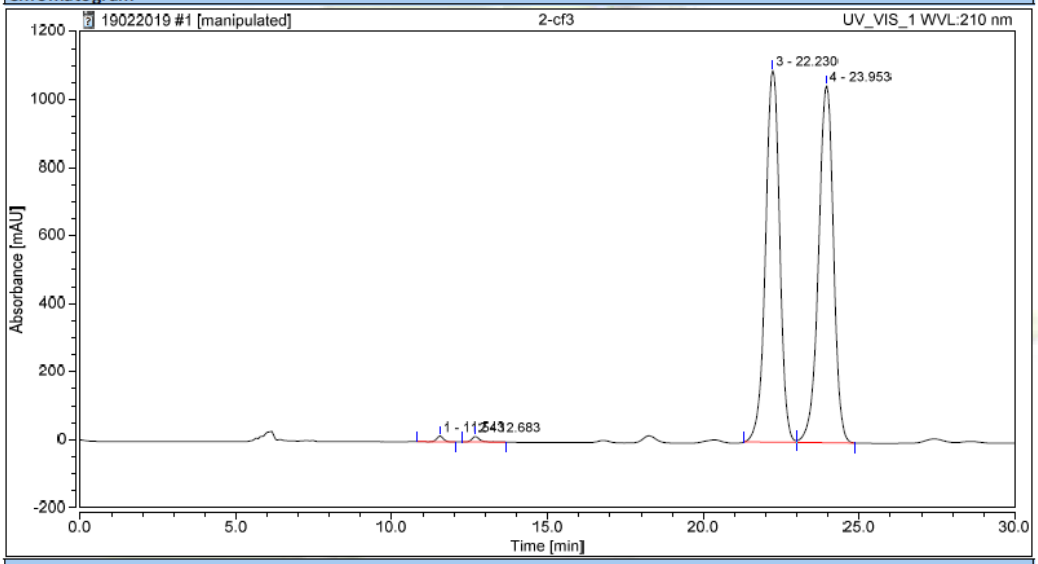
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		20.500	55.005	103.757	5.58	7.67	n.a.
2		27.833	930.876	1248.988	94.42	92.33	n.a.
Total:			**985.881**	**1352.746**	**100.00**	**100.00**	

(*S*)-2-[(*R*)-hydroxy(2-trifluoromethyl)(phenyl)methyl]cyclohexanone **19i**



Conditions: Columnd Chiralpack AD-H, Hex-IPA (90:10), 0.5 mL/min, 30 minutes

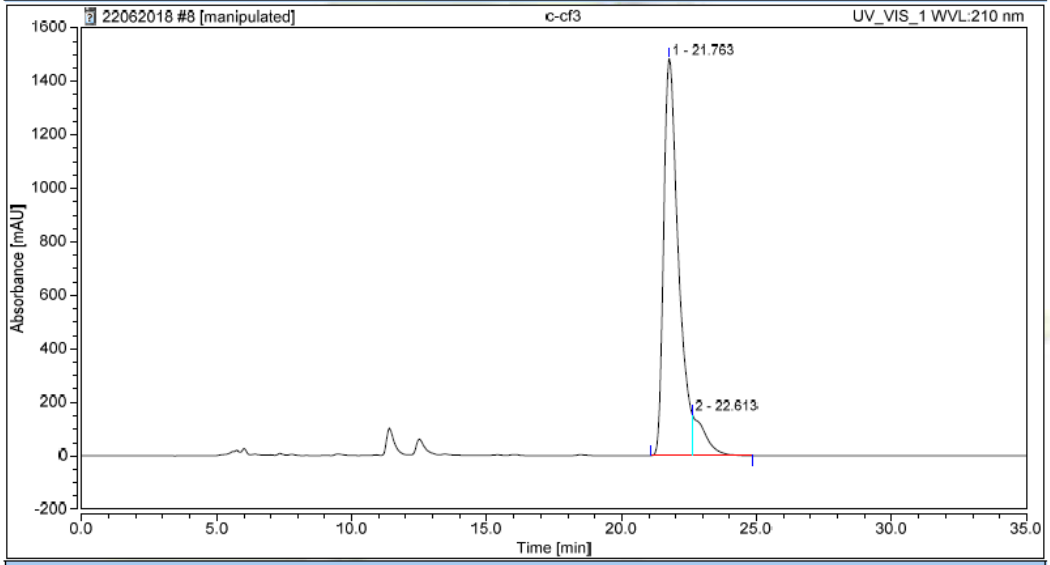
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		11.543	3.974	16.698	0.34	0.77	n.a.
2		12.683	4.633	16.010	0.40	0.74	n.a.
3		22.230	574.955	1092.861	49.22	50.25	n.a.
4		23.953	584.624	1049.200	50.05	48.24	n.a.
Total:			**1168.186**	**2174.769**	**100.00**	**100.00**	

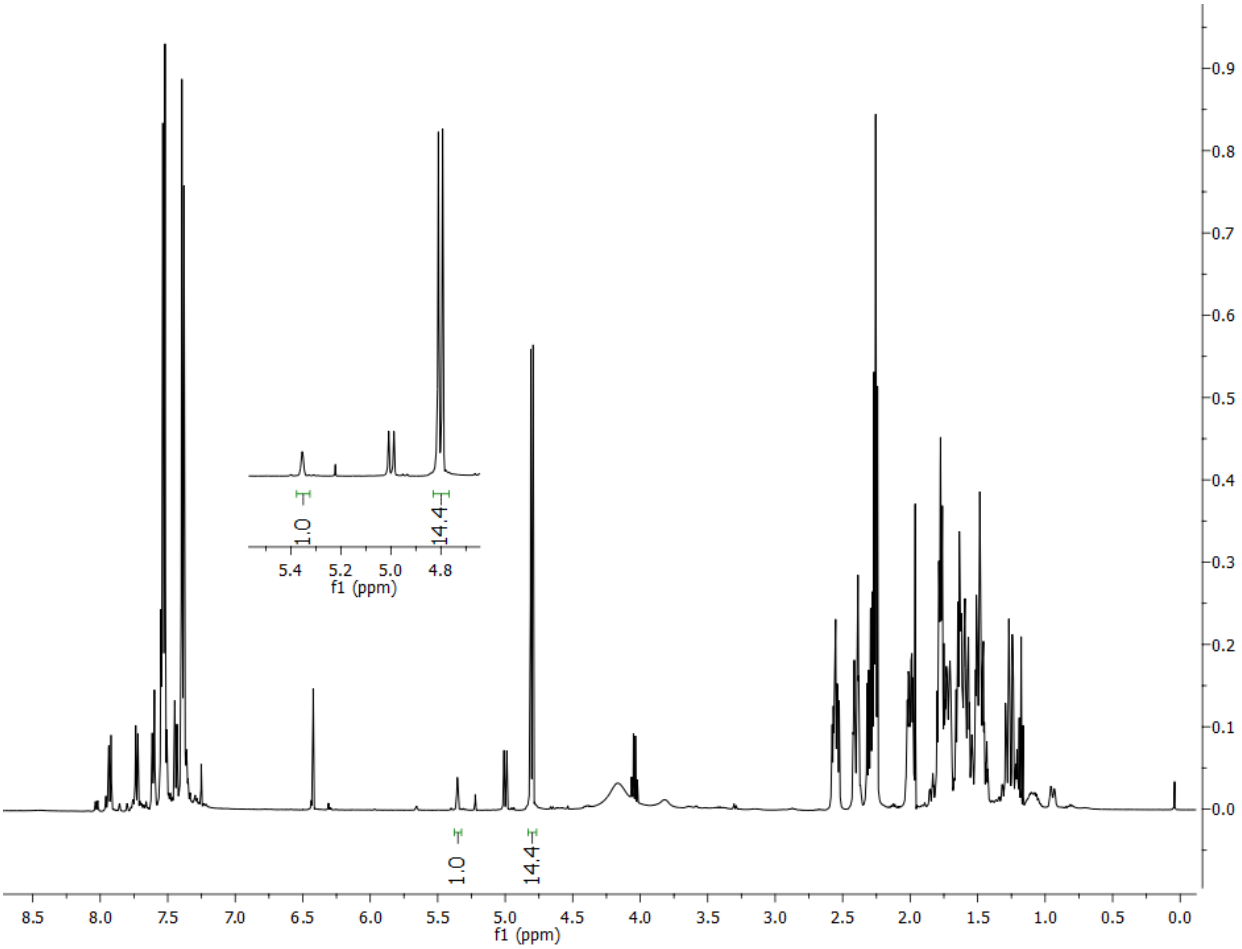
Chromatogram



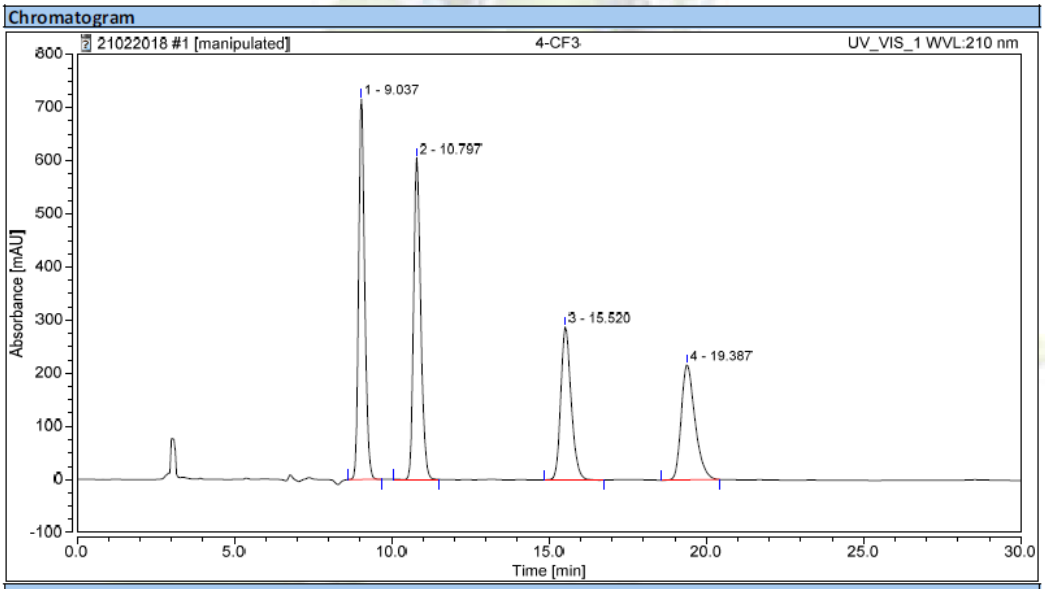
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		21.763	929.582	1484.048	91.74	90.56	n.a.
2		22.613	83.682	154.781	8.26	9.44	n.a.
Total:			**1013.264**	**1638.829**	**100.00**	**100.00**	

(*S*)-2-[(*R*)-hydroxy(4-trifluoromethyl)(phenhyl)methyl]cyclohexanone **19j**

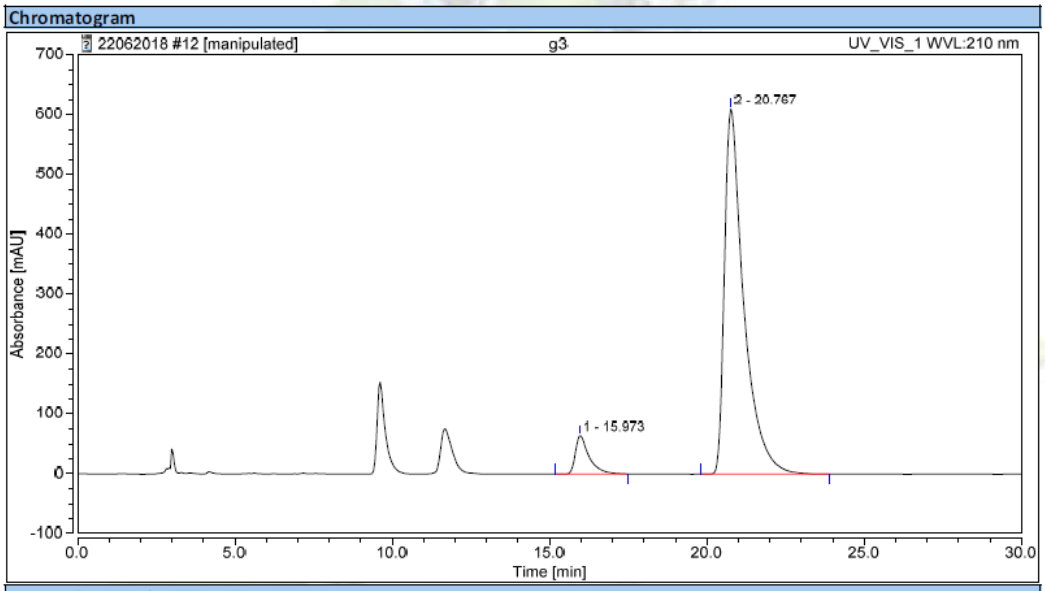


Conditions: Columnd Chiralpack AD-H, Hex-IPA (95:5), 1.0 mL/min, 30 minutes



Integration Results

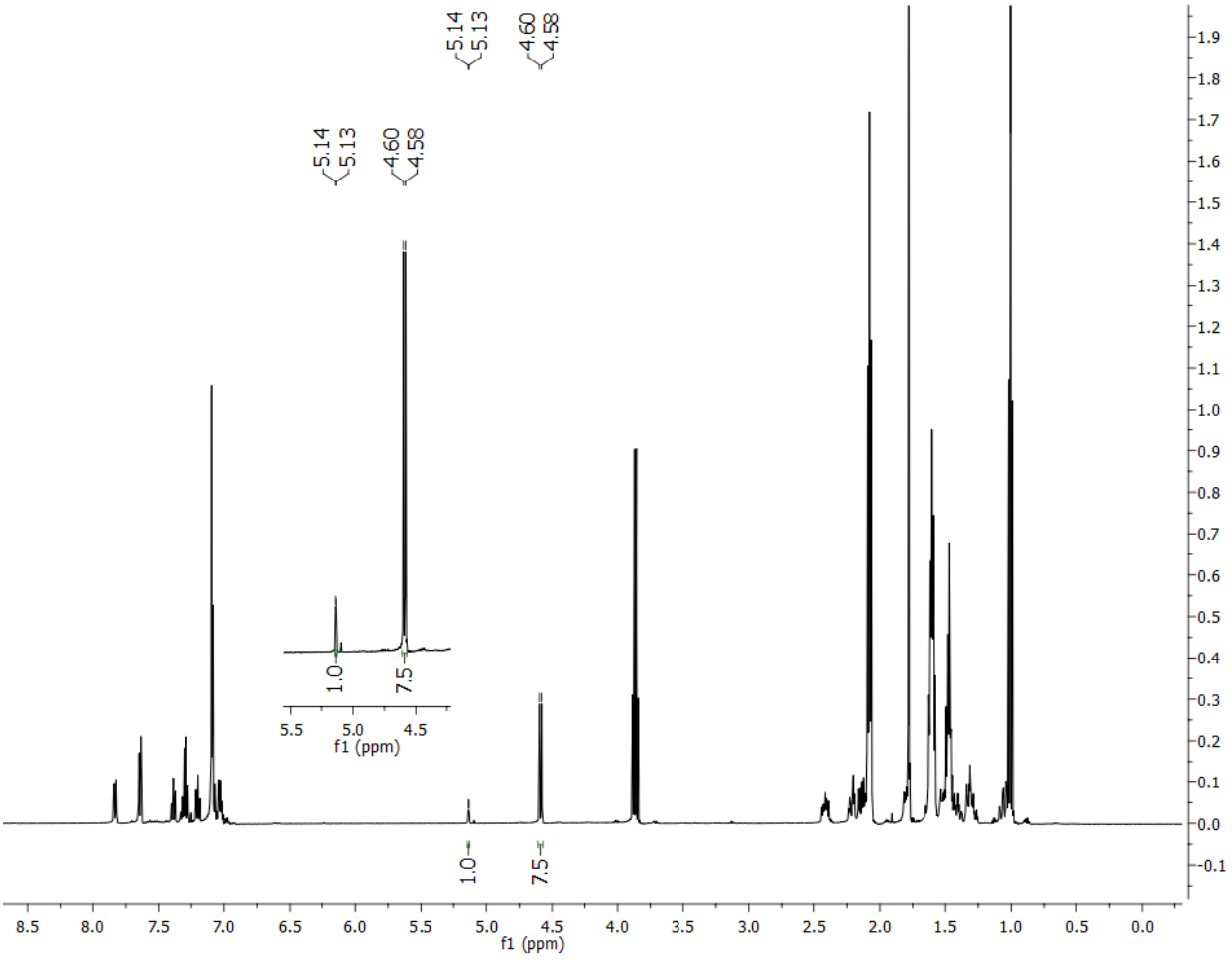
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		9.037	157.994	716.086	29.46	39.19	n.a.
2		10.797	157.923	605.593	29.44	33.14	n.a.
3		15.520	110.397	288.498	20.58	15.79	n.a.
4		19.387	110.033	216.953	20.52	11.87	n.a.
Total:			**536.348**	**1827.130**	**100.00**	**100.00**	



Integration Results

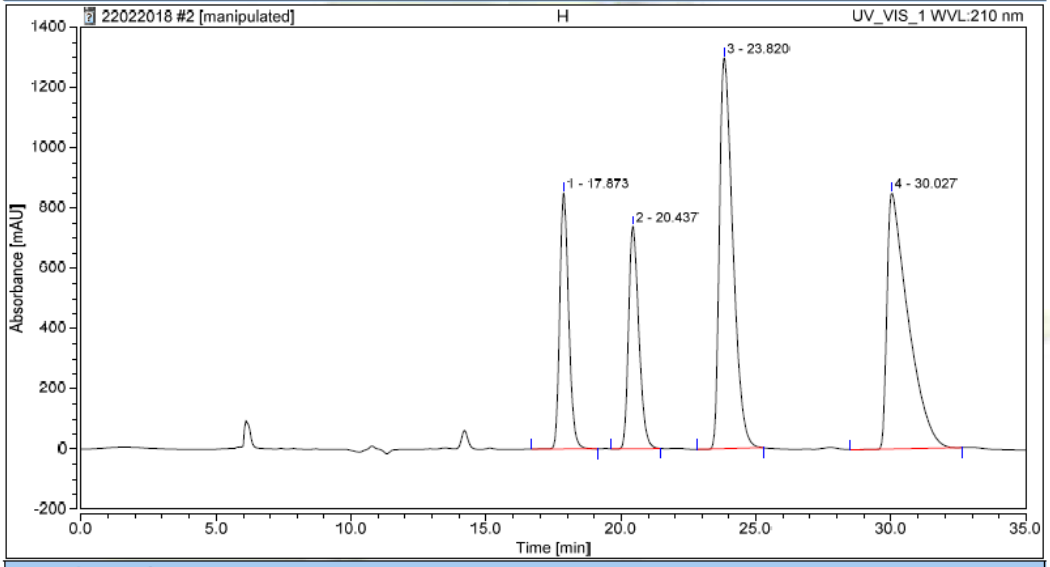
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		15.973	32.245	64.519	6.92	9.56	n.a.
2		20.767	433.878	610.386	93.08	90.44	n.a.
Total:			**466.123**	**674.905**	**100.00**	**100.00**	

(*S*)-2-[(*R*)-hydroxy(phenyl)methyl]cyclohexanone **19k**



Conditions: Columnd Chiralpack OD-H, Hex-IPA (95:5), 0.5 mL/min, 35 minutes

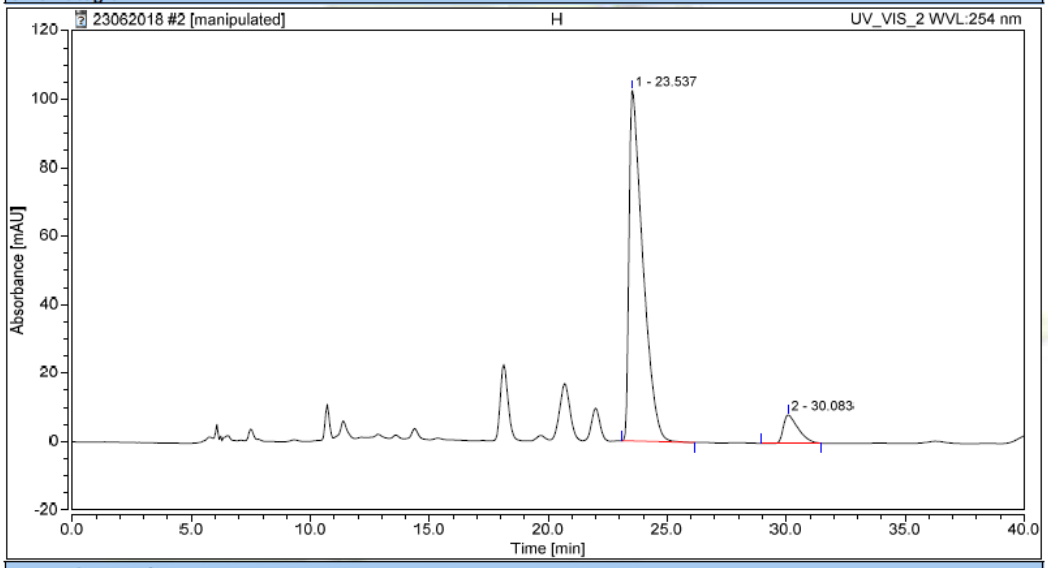
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.873	326.652	850.951	15.05	22.76	n.a.
2		20.437	324.152	738.521	14.93	19.75	n.a.
3		23.820	750.421	1298.534	34.57	34.73	n.a.
4		30.027	769.256	851.012	35.44	22.76	n.a.
Total:			**2170.480**	**3739.018**	**100.00**	**100.00**	

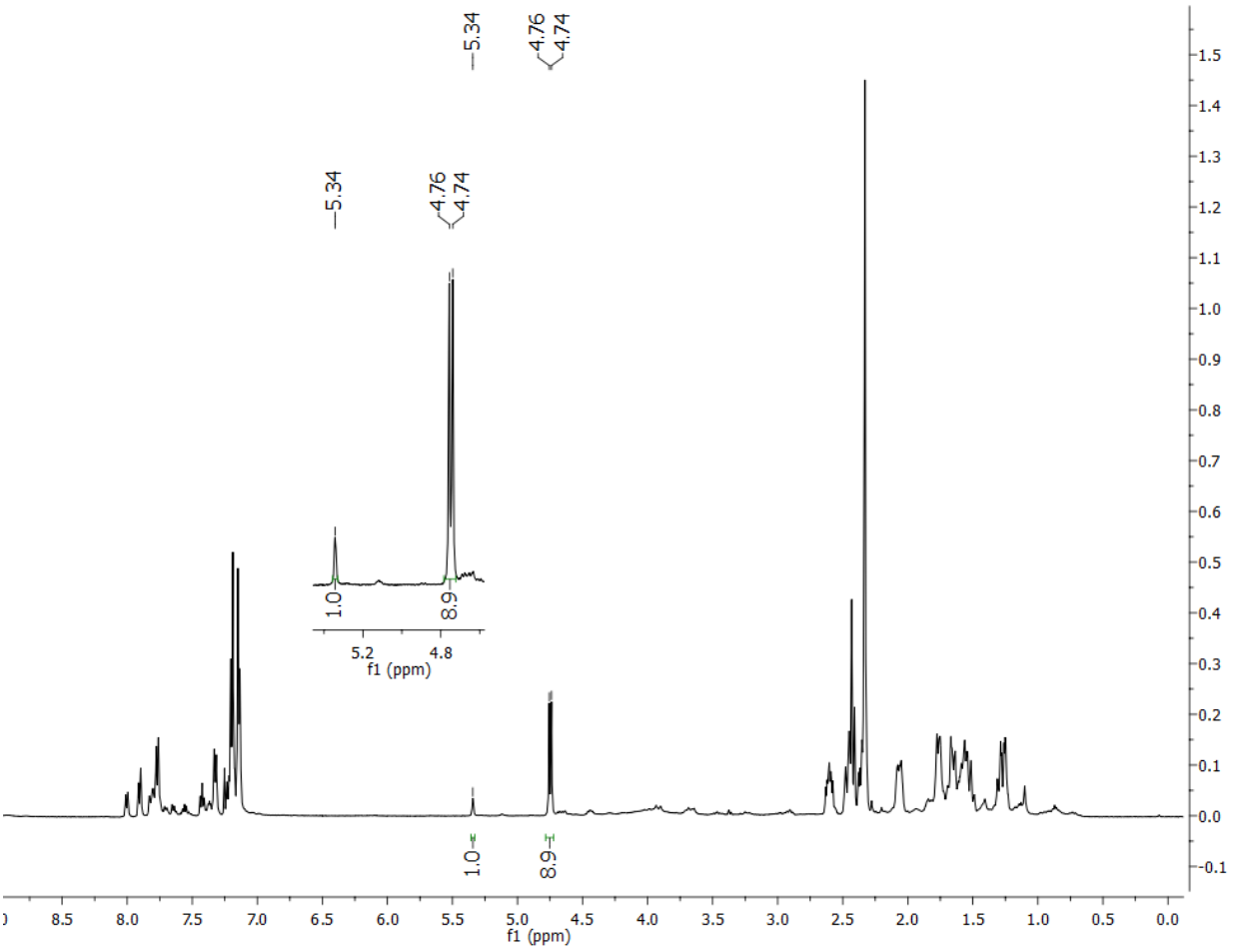
Chromatogram



Integration Results

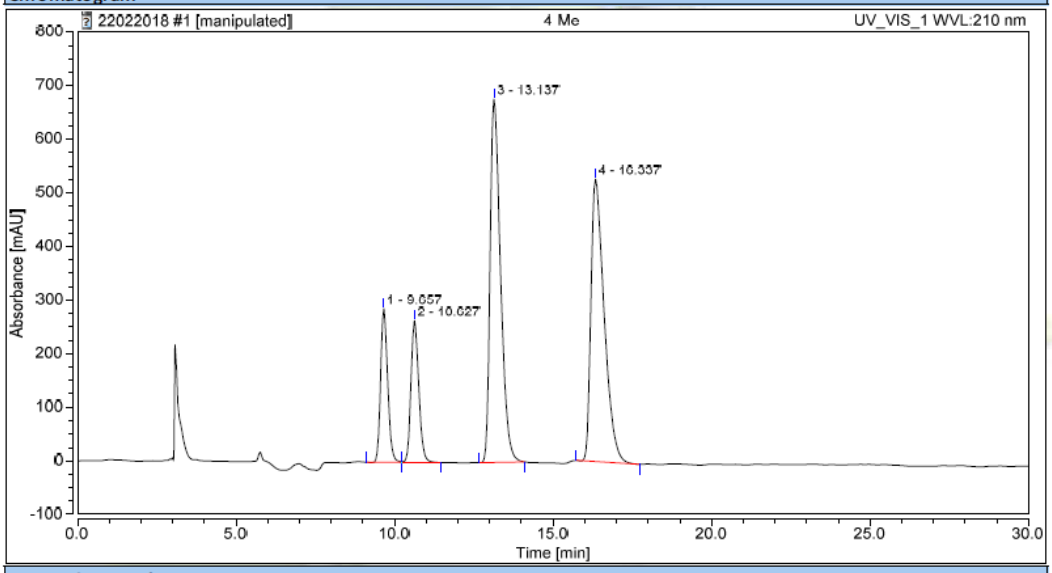
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		23.537	68.432	102.304	92.06	92.54	n.a.
2		30.083	5.902	8.242	7.94	7.46	n.a.
Total:			**74.335**	**110.545**	**100.00**	**100.00**	

(*S*)-2-[(*R*)-hydroxy(*p*-tolyl)methyl]cyclohexanone **19l**



Conditions: Chiralpack OD-H, Hex-IPA (97:3), 1.0 mL/min., 25 minutes

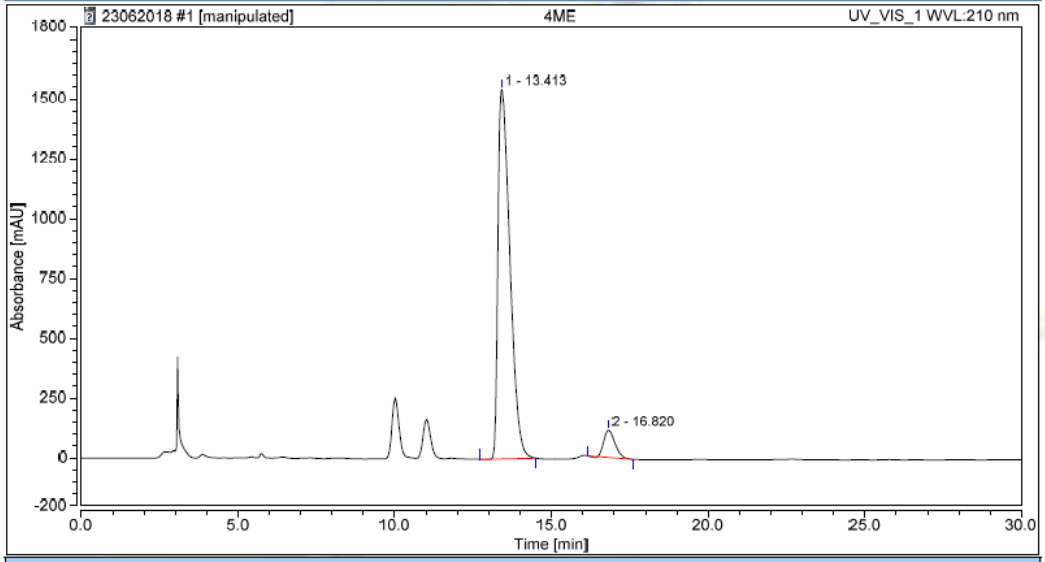
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		9.657	73.940	286.344	11.17	16.31	n.a.
2		10.627	75.367	264.441	11.38	15.06	n.a.
3		13.137	257.748	677.896	38.93	38.61	n.a.
4		16.337	254.960	527.013	38.51	30.02	n.a.
Total:			**662.016**	**1755.695**	**100.00**	**100.00**	

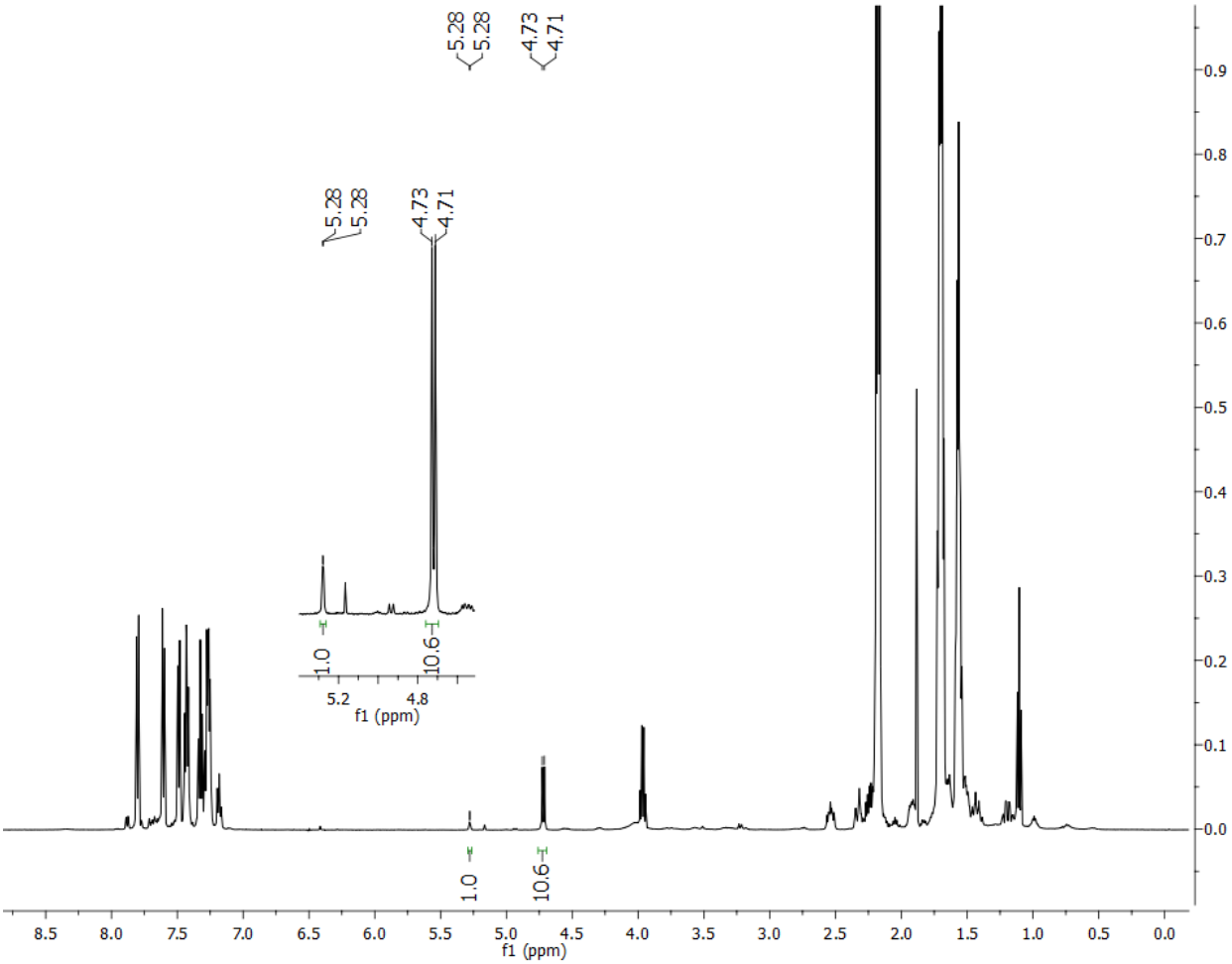
Chromatogram



Integration Results

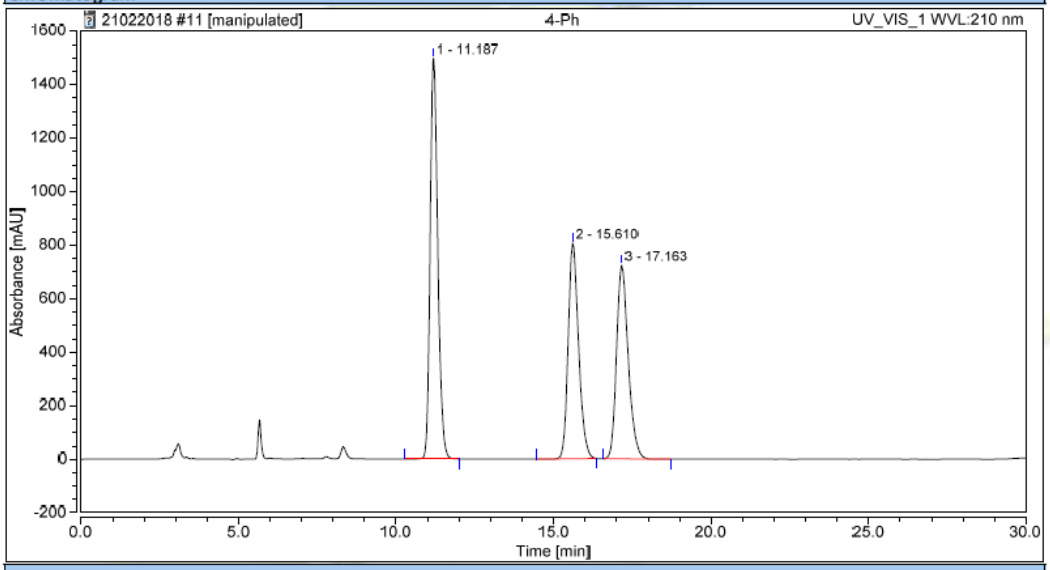
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.413	679.892	1544.220	93.65	93.13	n.a.
2		16.820	46.128	113.923	6.35	6.87	n.a.
Total:			**726.020**	**1658.143**	**100.00**	**100.00**	

(*S*)-2-[(*R*)-biphenyl-4-yl(hydroxy)methyl]cyclohexanone **19m**



Conditions: Chiralpack AD-H, Hex-IPA (90:10), 1.0 mL/min., 30 minutes

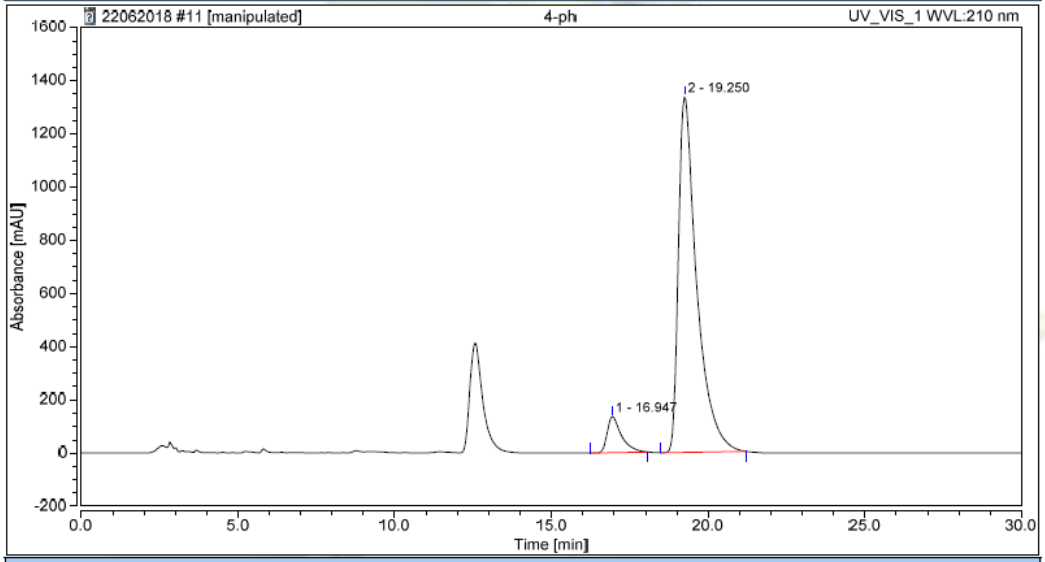
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		11.187	420.460	1498.138	40.44	49.48	n.a.
2		15.610	308.531	805.948	29.68	26.62	n.a.
3		17.163	310.681	723.376	29.88	23.89	n.a.
Total:			**1039.672**	**3027.462**	**100.00**	**100.00**	

Chromatogram

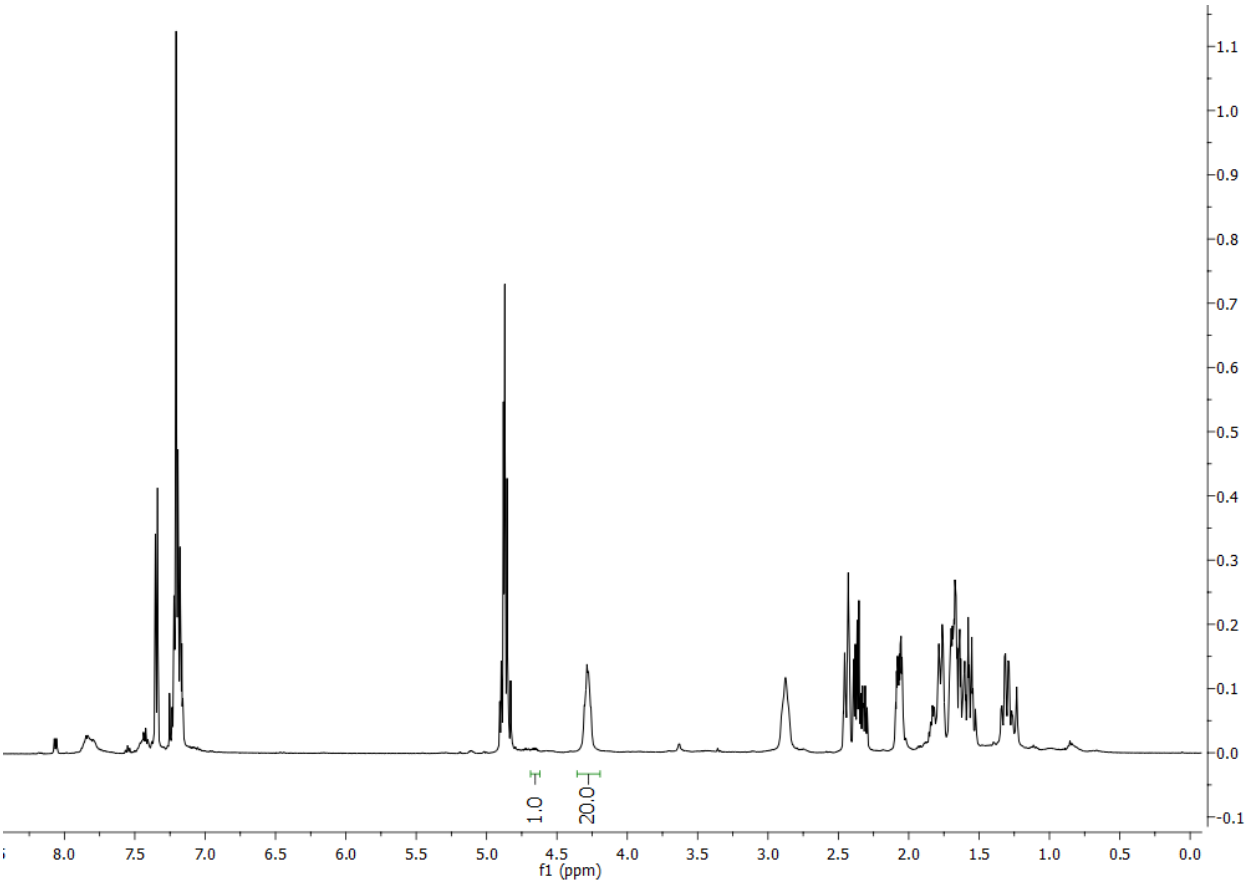


Integration Results

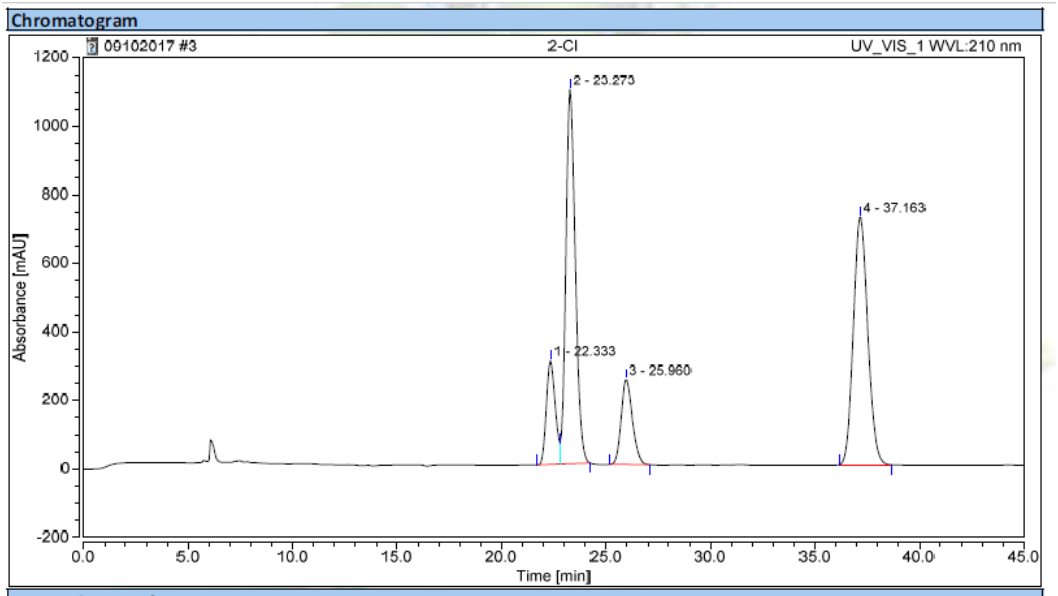
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.947	70.775	135.875	7.26	9.22	n.a.
2		19.250	904.368	1338.184	92.74	90.78	n.a.
Total:			**975.142**	**1474.060**	**100.00**	**100.00**	

^{1}H-RMN and chiral HPLC-chromatograms for the dr and er for the Michael addition of cyclohexanone to nitrostyrenes catalyzed by (1*S*,2*S*,1'*R*,2'*R*,2''*S*)-20.

(*S*)-2-((*R*)-1-(2-chlorophenyl)-2-nitroethyl)cyclohexanone **24a**.

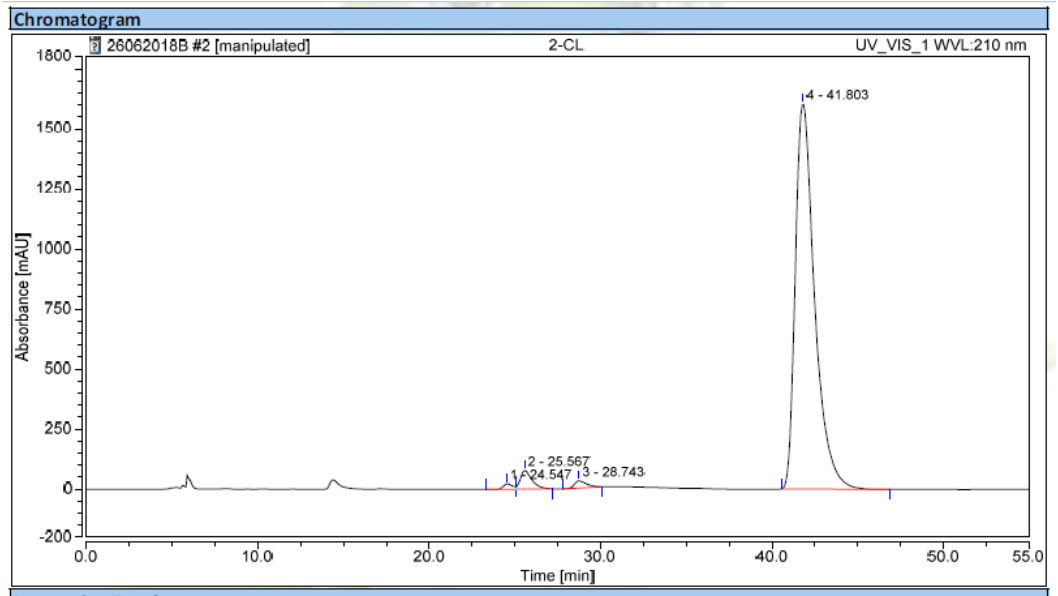


Conditions: Chiralpack AD-H, Hex-IPA (95:5), 0.5 mL/min, 45 minutes.



Integration Results

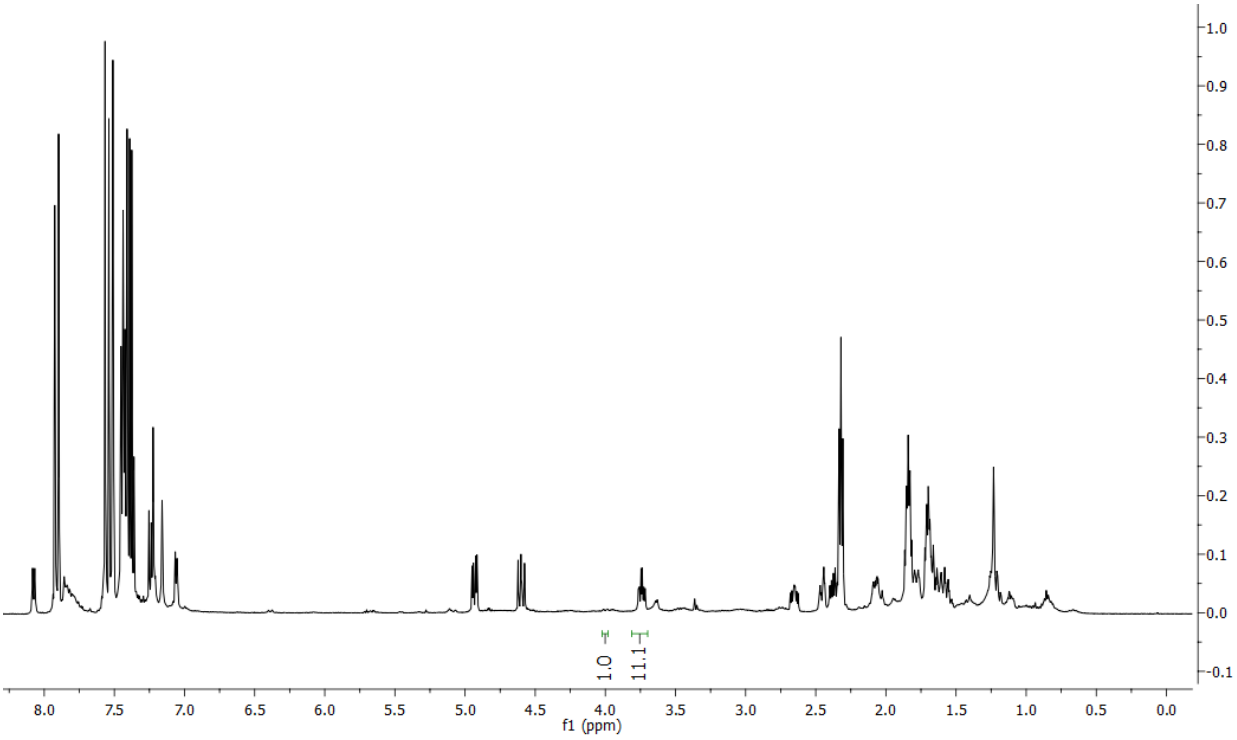
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		22.333	148.414	303.658	10.22	12.83	n.a.
2		23.273	572.947	1091.759	39.44	46.12	n.a.
3		25.960	154.213	248.589	10.62	10.50	n.a.
4		37.163	577.036	723.198	39.72	30.55	n.a.
Total:			1452.609	2367.204	100.00	100.00	



Integration Results

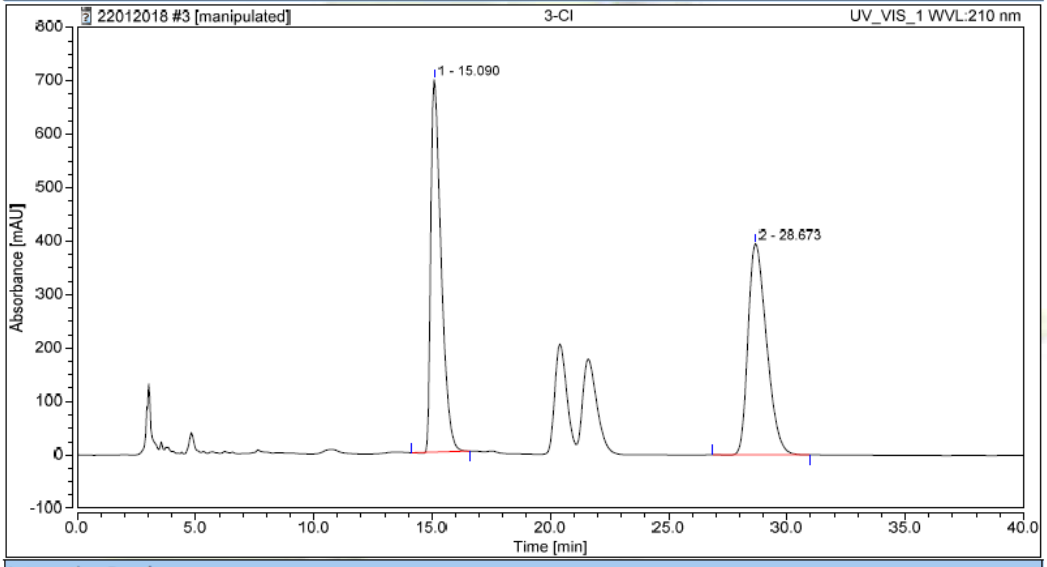
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		24.547	13.143	21.759	0.60	1.26	n.a.
2		25.567	60.095	77.459	2.74	4.47	n.a.
3		28.743	24.082	29.510	1.10	1.70	n.a.
4		41.803	2095.248	1604.344	95.56	92.57	n.a.
Total:			2192.568	1733.072	100.00	100.00	

(*S*)-2-((*R*)-1-(3-chlorophenyl)-2-nitroethyl)cyclohexanone **24b**.



Conditions: Chiralpack AS-H, Hex-IPA (90:10), 1.0 mL/min, 40 minutes.

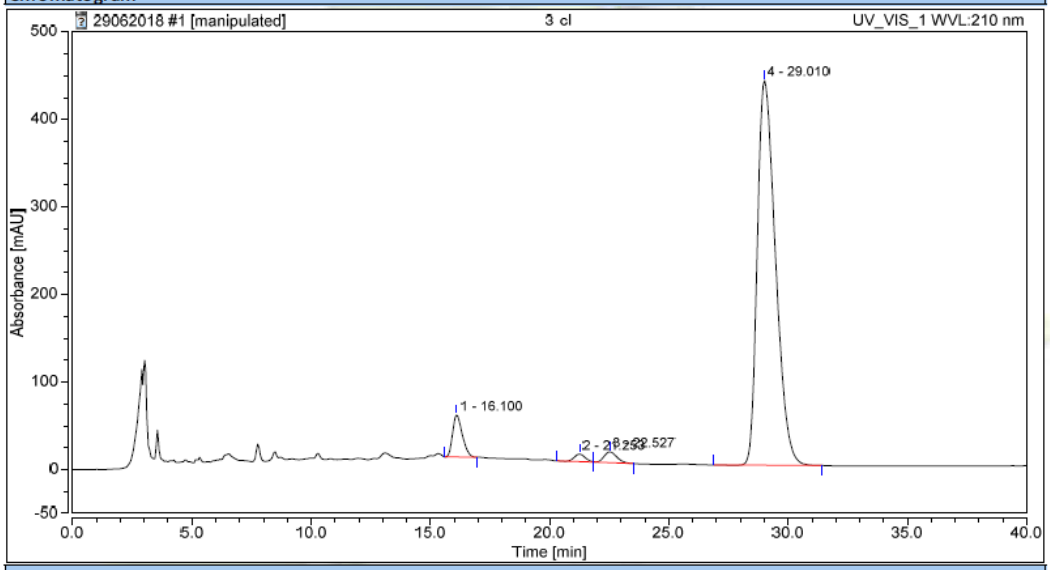
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		15.090	352.861	696.869	49.67	63.81	n.a.
2		28.673	357.569	395.146	50.33	36.19	n.a.
Total:			710.430	1092.014	100.00	100.00	

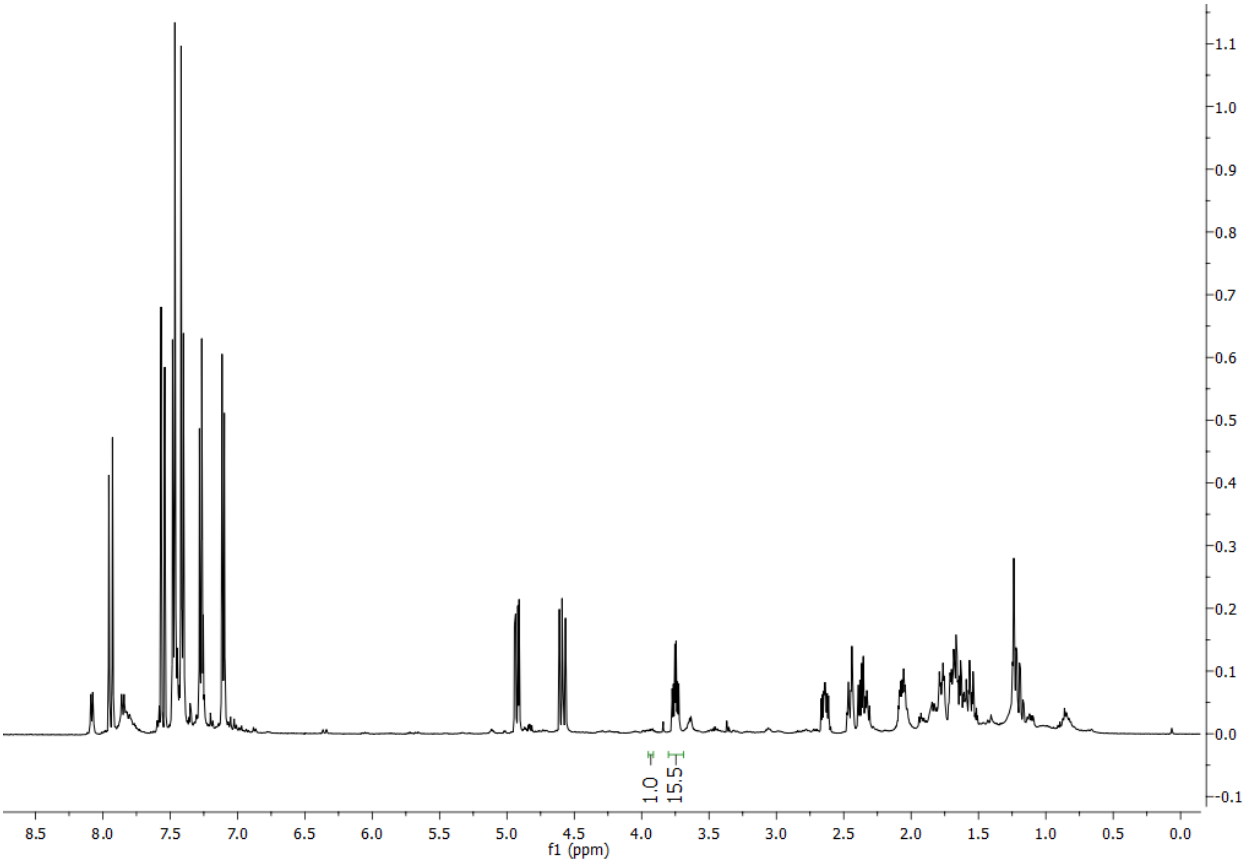
Chromatogram



Integration Results

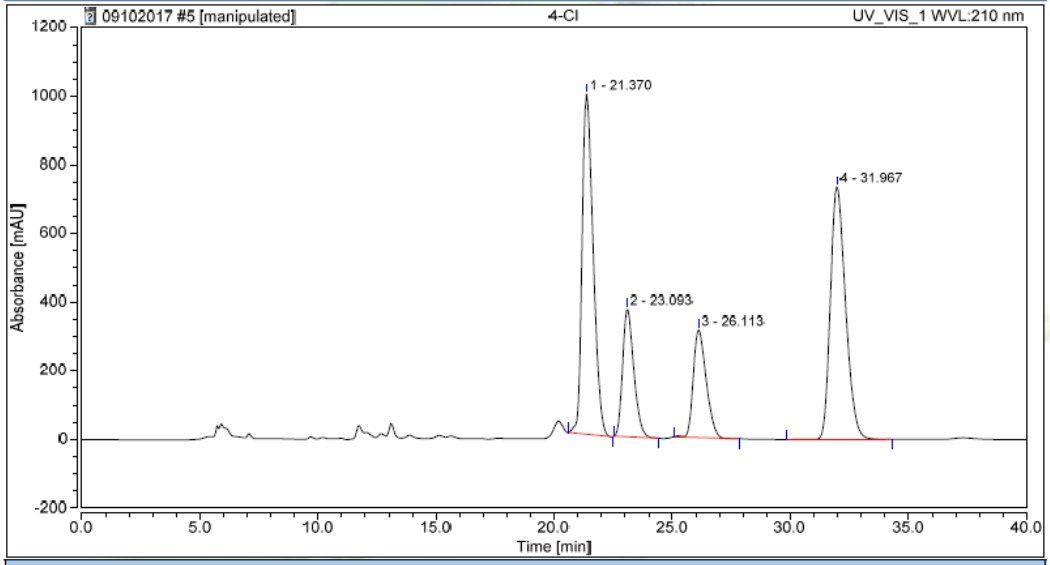
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.100	22.433	47.777	5.30	9.40	n.a.
2		21.253	4.511	8.553	1.07	1.68	n.a.
3		22.527	7.770	12.434	1.84	2.45	n.a.
4		29.010	388.179	439.549	91.79	86.47	n.a.
Total:			422.893	508.314	100.00	100.00	

(*S*)-2-((*R*)-1-(4-chlorophenyl)-2-nitroethyl)cyclohexanone **24c**.



Conditions: Chiralpack AD-H, Hex-IPA (90:10), 0.5 mL/min, 40 minutes.

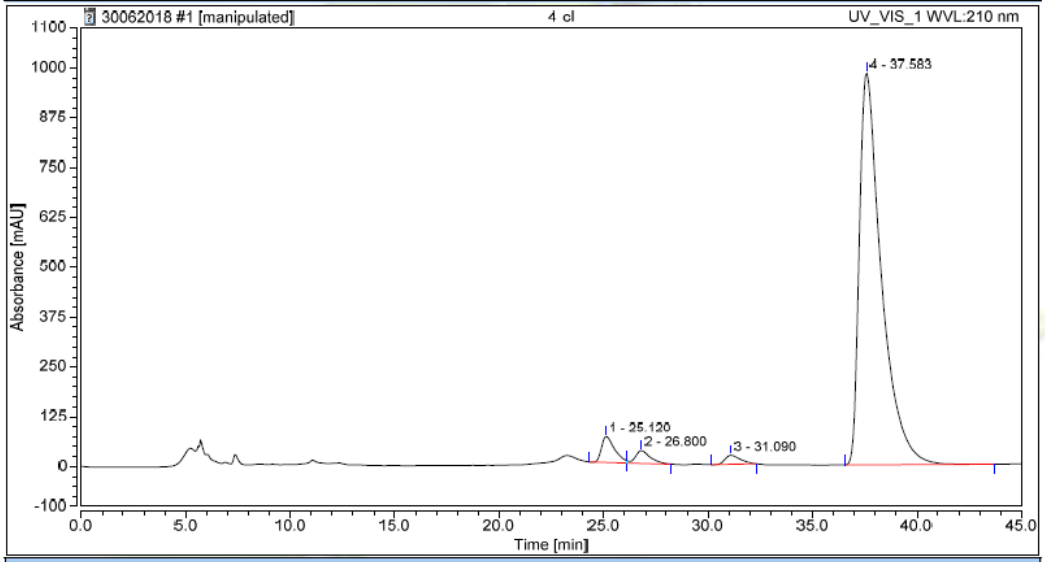
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		21.370	537.114	991.140	36.12	41.06	n.a.
2		23.093	204.082	372.398	13.72	15.43	n.a.
3		26.113	197.231	313.891	13.26	13.00	n.a.
4		31.967	548.576	736.494	36.89	30.51	n.a.
Total:			**1487.003**	**2413.923**	**100.00**	**100.00**	

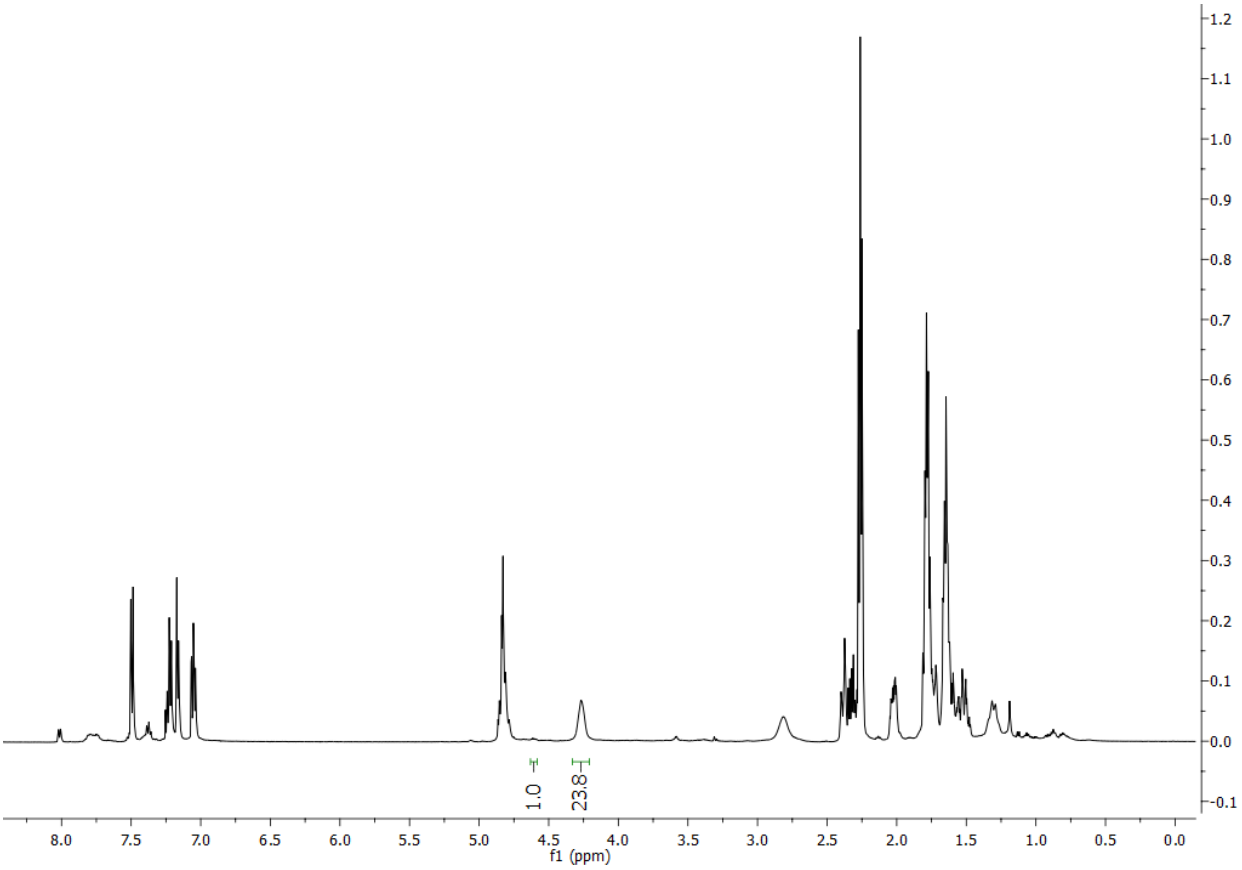
Chromatogram



Integration Results

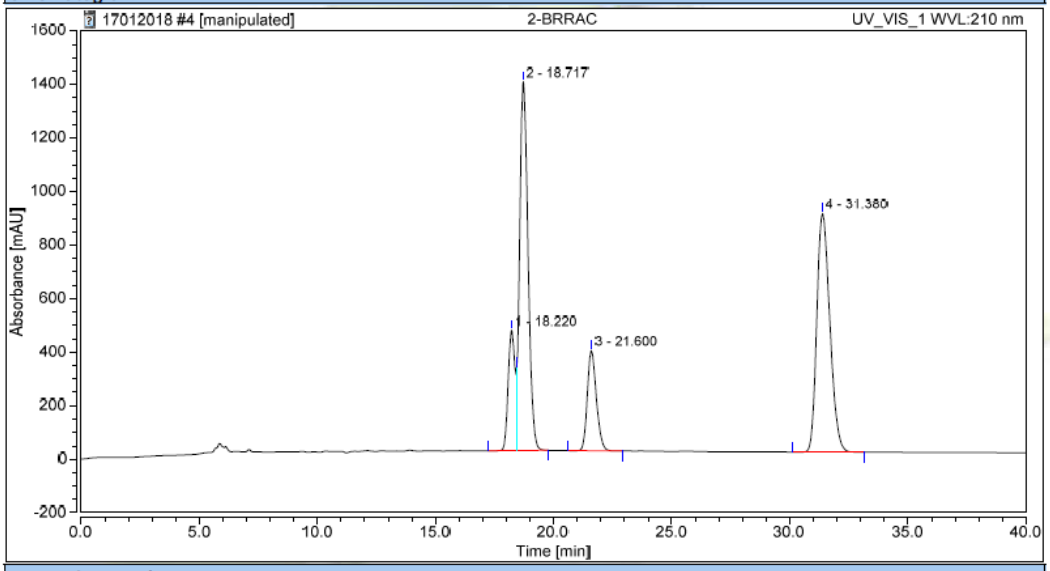
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		25.120	46.963	65.143	3.63	5.91	n.a.
2		26.800	26.192	31.943	2.02	2.90	n.a.
3		31.090	19.120	22.649	1.48	2.05	n.a.
4		37.583	1201.900	983.336	92.87	89.15	n.a.
Total:			**1294.176**	**1103.072**	**100.00**	**100.00**	

(*S*)-2-((*R*)-1-(2-bromophenyl)-2-nitroethyl)cyclohexanone **24e**.



Conditions: Chiralpack AD-H, Hex-IPA (90:10), 0.5 mL/min, 45 minutes.

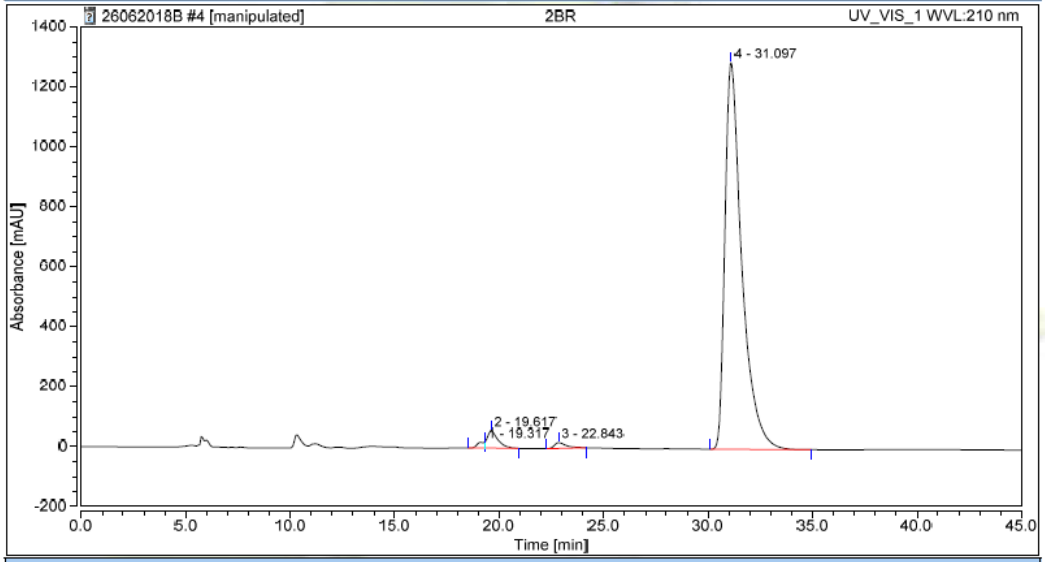
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		18.220	156.357	450.710	10.73	14.55	n.a.
2		18.717	564.021	1378.439	38.72	44.50	n.a.
3		21.600	165.868	375.173	11.39	12.11	n.a.
4		31.380	570.604	893.084	39.17	28.83	n.a.
Total:			**1456.851**	**3097.406**	**100.00**	**100.00**	

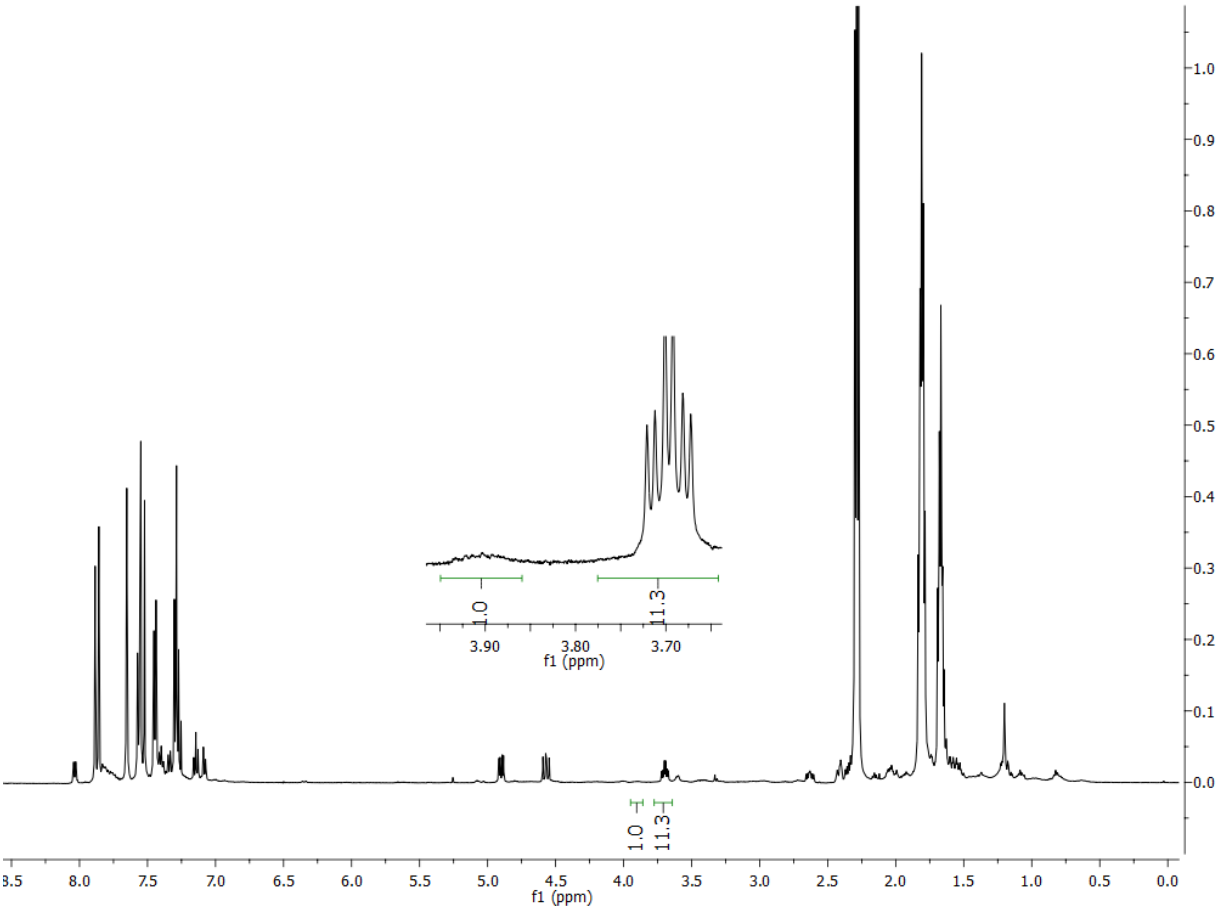
Chromatogram



Integration Results

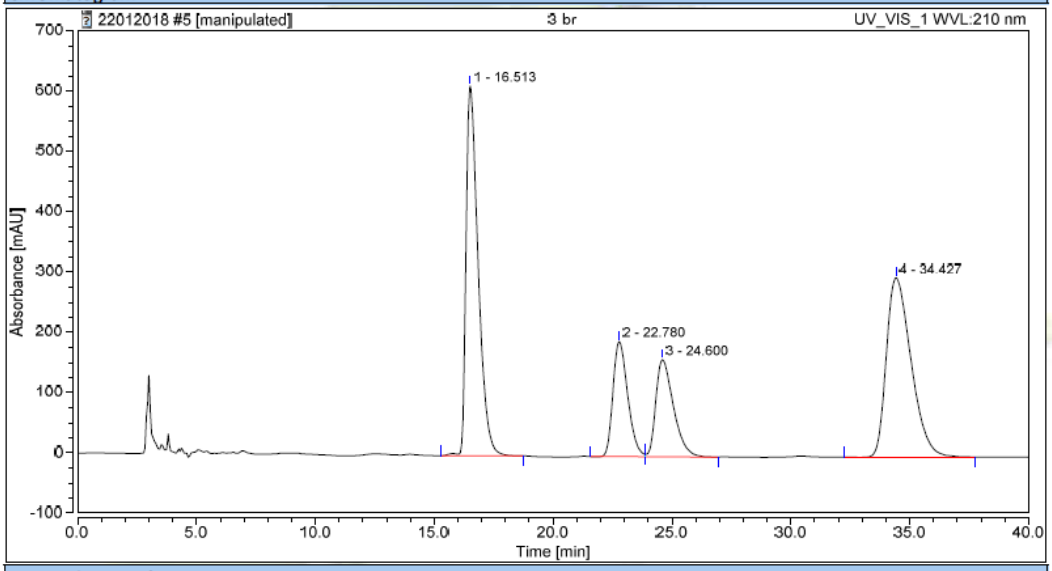
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		19.317	7.629	19.970	0.60	1.44	n.a.
2		19.617	33.847	57.001	2.67	4.11	n.a.
3		22.843	12.794	19.253	1.01	1.39	n.a.
4		31.097	1215.077	1291.069	95.72	93.06	n.a.
Total:			**1269.348**	**1387.293**	**100.00**	**100.00**	

(*S*)-2-((*R*)-1-(3-bromophenyl)-2-nitroethyl)cyclohexanone **24f**.



Conditions: Chiralpack AS-H, Hex-IPA (90:10), 1.0 mL/min, 40 minutes.

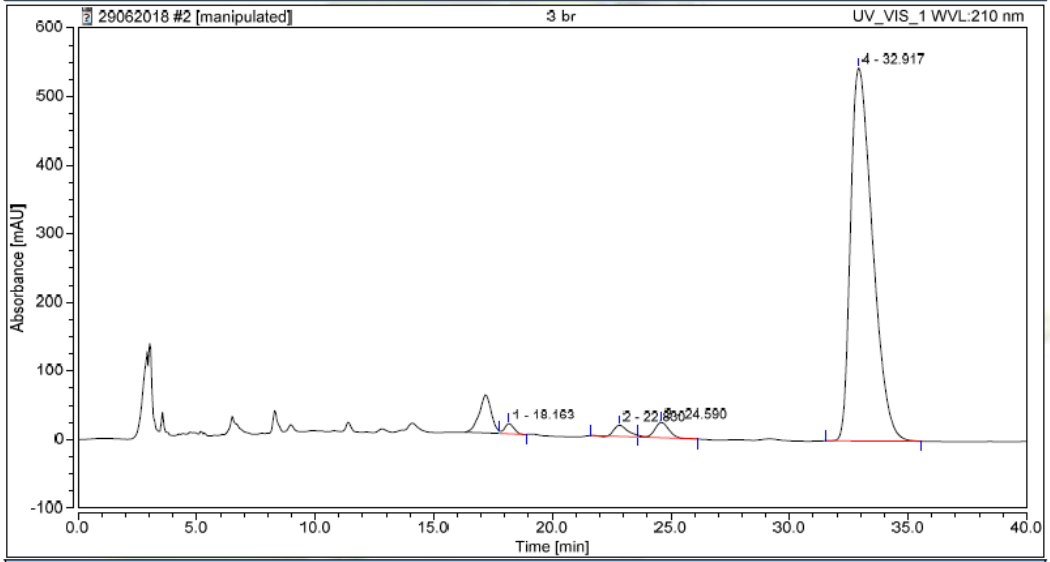
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.513	360.973	613.585	36.28	48.56	n.a.
2		22.780	136.965	191.179	13.76	15.13	n.a.
3		24.600	138.619	161.109	13.93	12.75	n.a.
4		34.427	358.468	297.626	36.03	23.56	n.a.
Total:			**995.025**	**1263.499**	**100.00**	**100.00**	

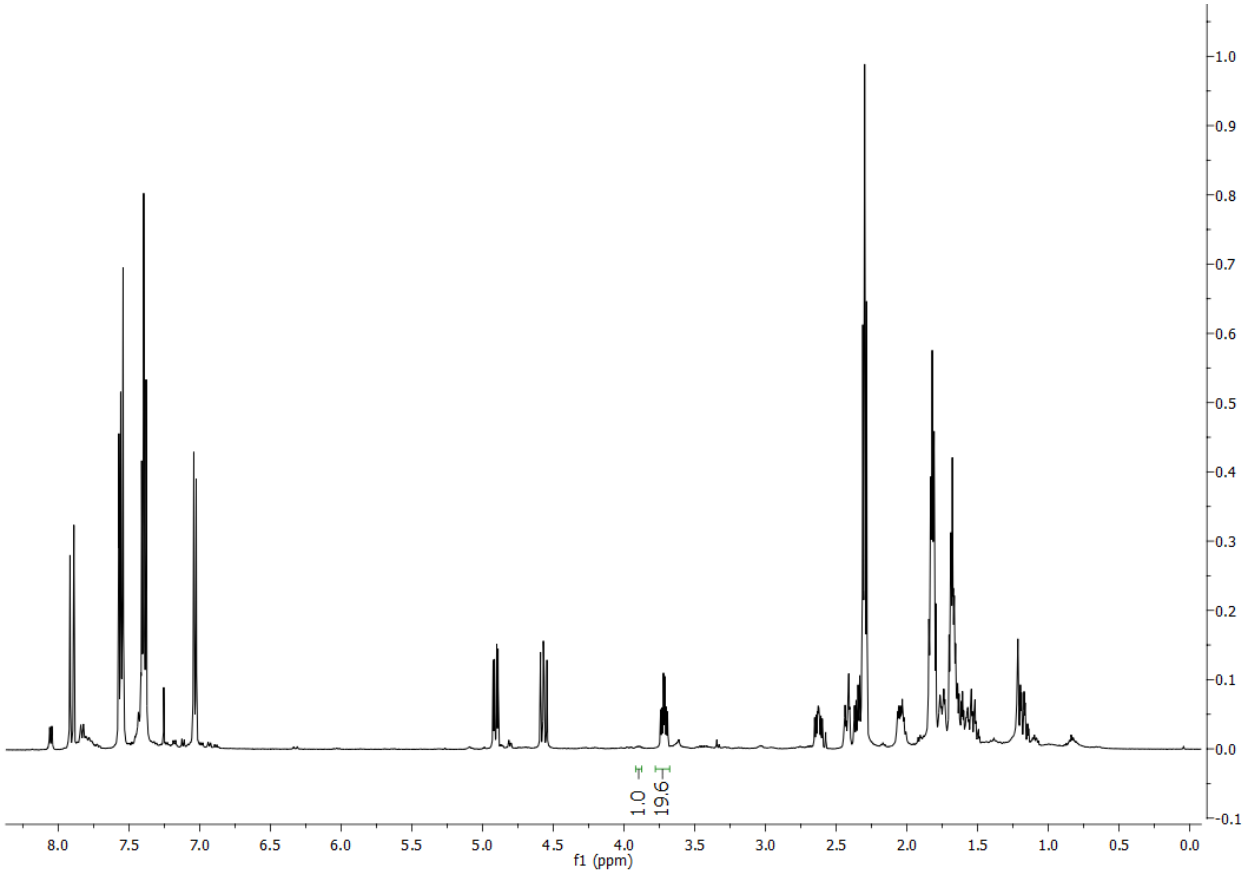
Chromatogram



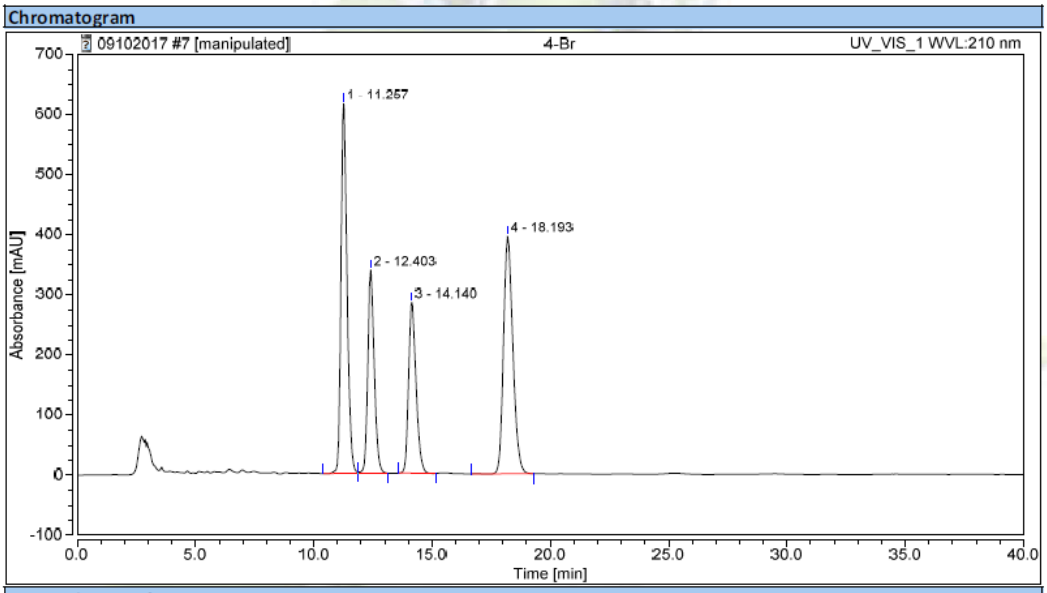
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		18.163	6.850	14.675	1.11	2.46	n.a.
2		22.830	10.675	16.370	1.73	2.74	n.a.
3		24.590	15.769	22.377	2.56	3.75	n.a.
4		32.917	583.252	543.713	94.60	91.05	n.a.
Total:			**616.545**	**597.134**	**100.00**	**100.00**	

(*S*)-2-((*R*)-1-(4-bromophenyl)-2-nitroethyl)cyclohexanone **24g**.

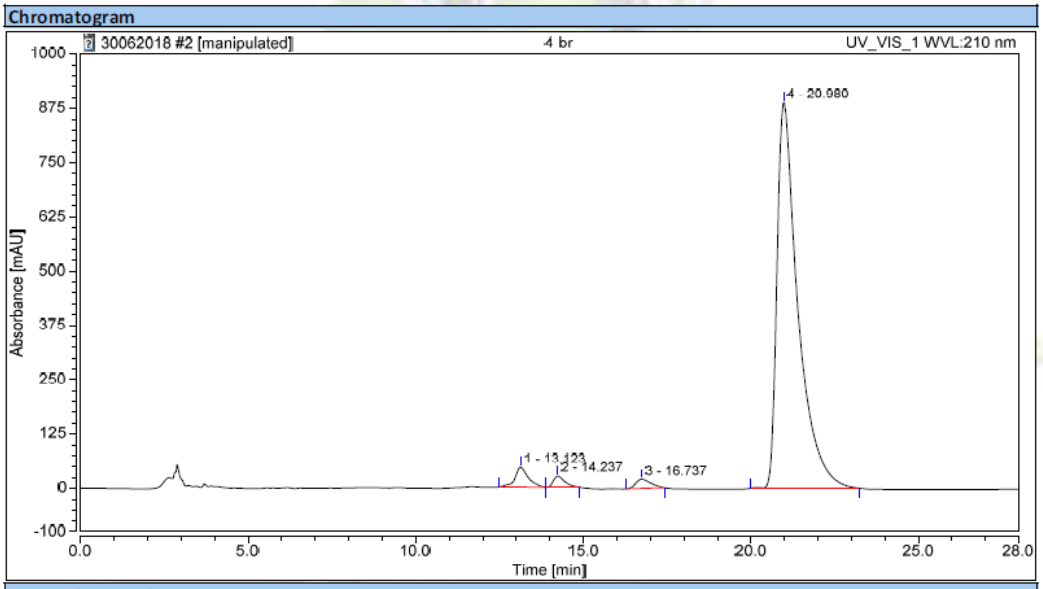


Conditions: Chiralpack AD-H, Hex-IPA (90:10), 1.0 mL/min, 30 minutes.



Integration Results

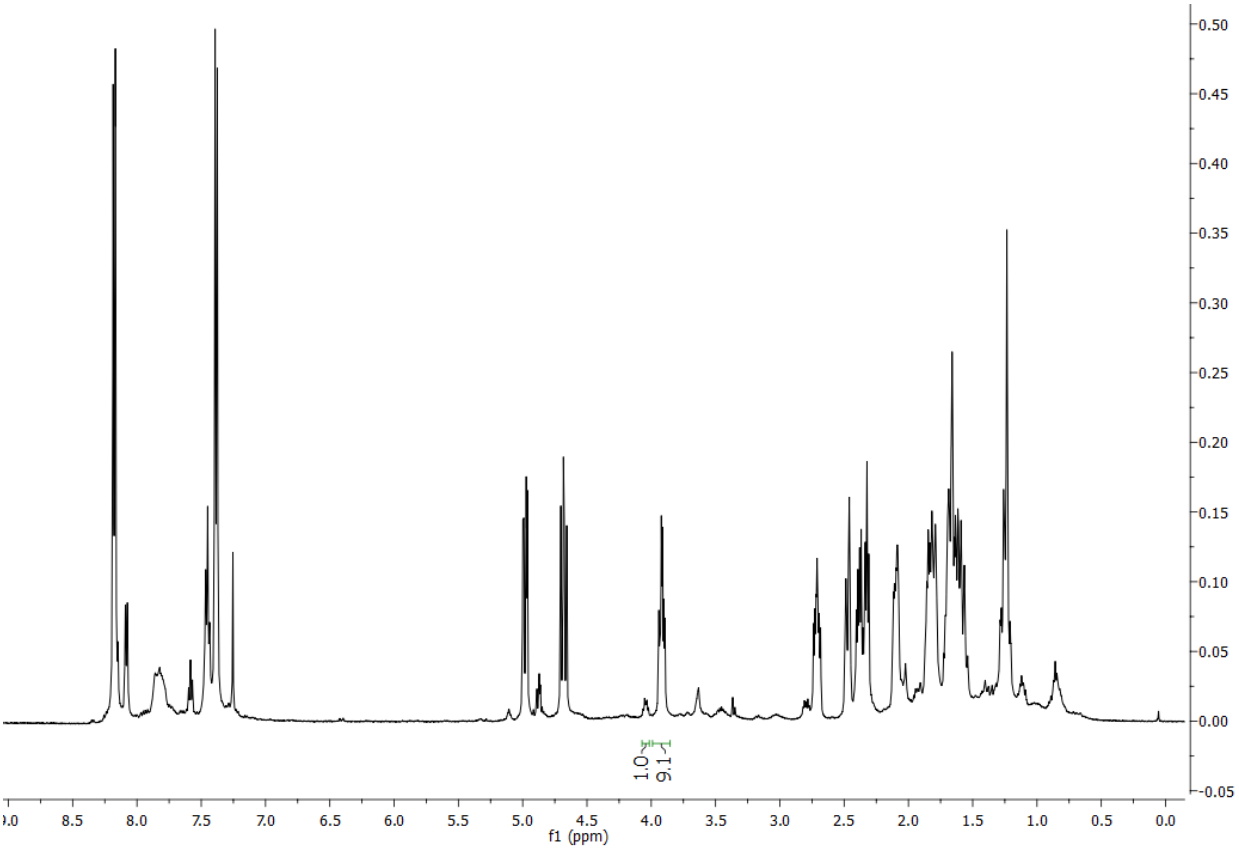
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		11.257	182.451	615.744	31.77	37.67	n.a.
2		12.403	106.718	338.648	18.58	20.72	n.a.
3		14.140	103.963	284.751	18.11	17.42	n.a.
4		18.193	181.085	395.508	31.54	24.20	n.a.
Total:			**574.217**	**1634.652**	**100.00**	**100.00**	



Integration Results

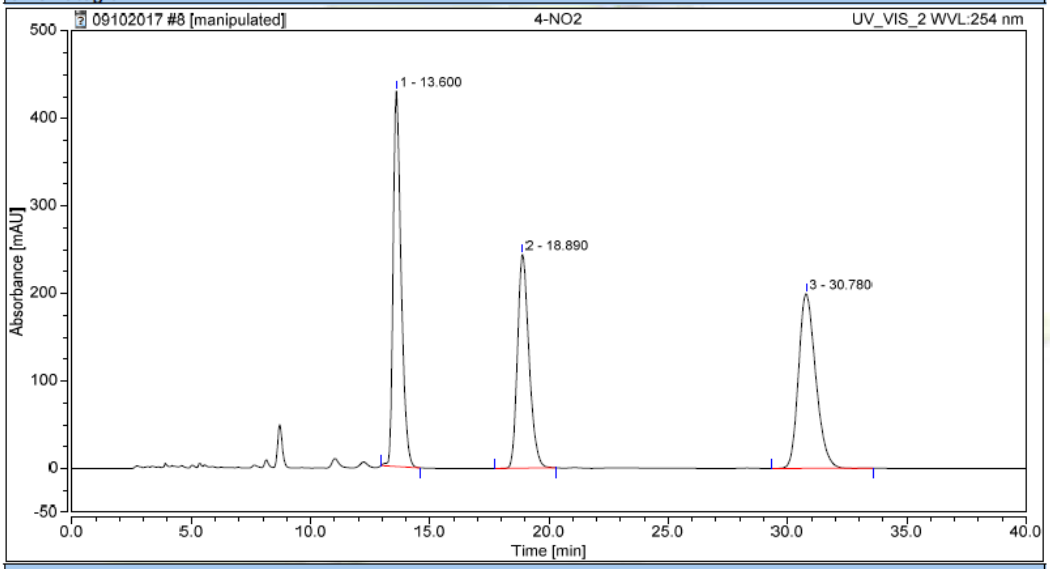
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.123	20.984	46.100	3.07	4.70	n.a.
2		14.237	9.809	25.494	1.44	2.60	n.a.
3		16.737	10.987	21.296	1.61	2.17	n.a.
4		20.980	641.140	888.099	93.88	90.53	n.a.
Total:			**682.920**	**980.989**	**100.00**	**100.00**	

(*S*)-2-((*R*)-2-nitro-1-(4-nitrophenyl)ethyl)cyclohexanone **24i**.



Conditions: Chiralpack AD-H, Hex-IPA (80:20), 1.0 mL/min, 40 minutes.

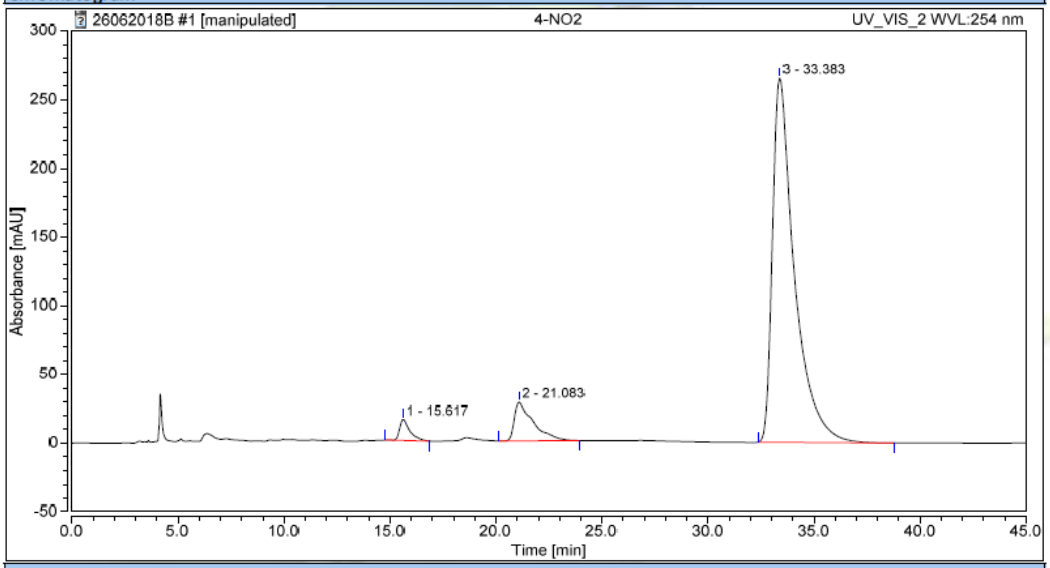
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.600	166.527	429.052	35.43	49.17	n.a.
2		18.890	136.900	244.001	29.13	27.96	n.a.
3		30.780	166.550	199.600	35.44	22.87	n.a.
Total:			469.977	872.652	100.00	100.00	

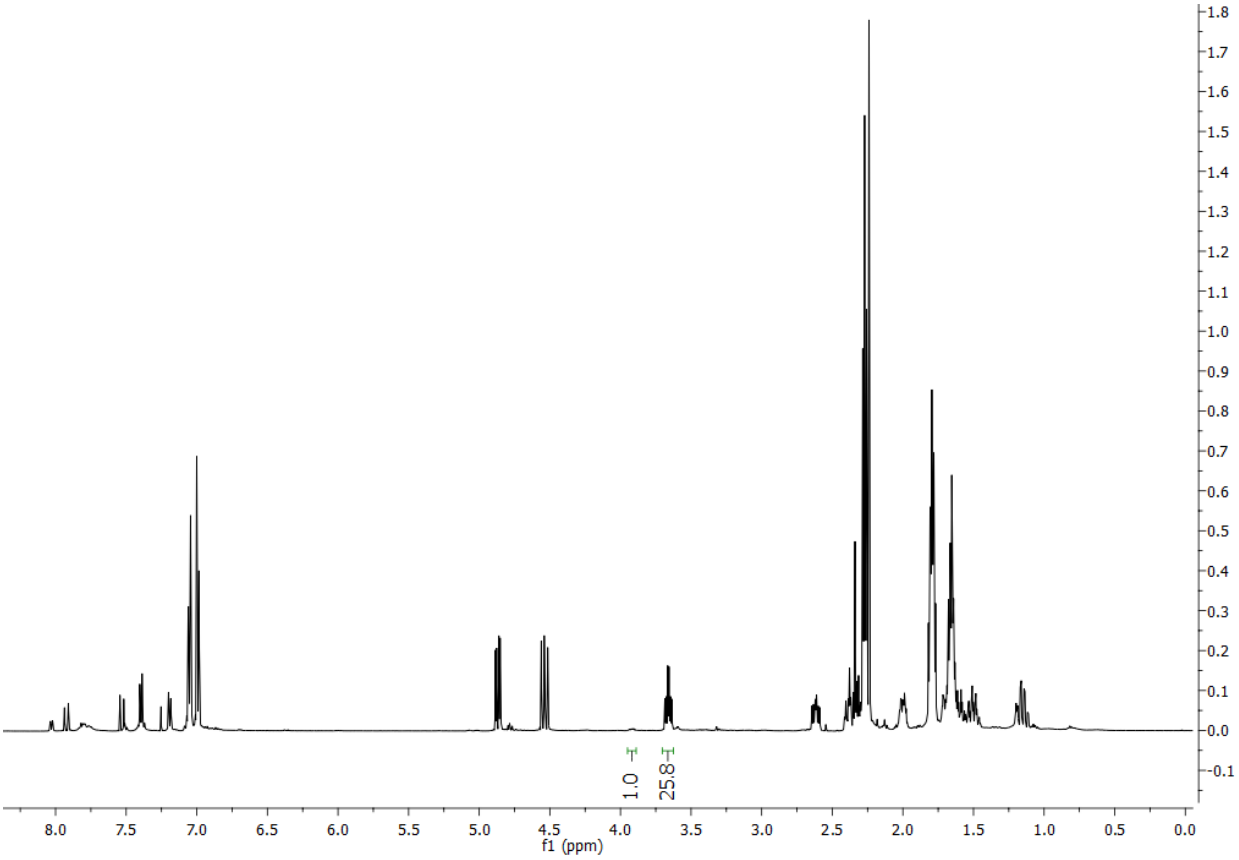
Chromatogram



Integration Results

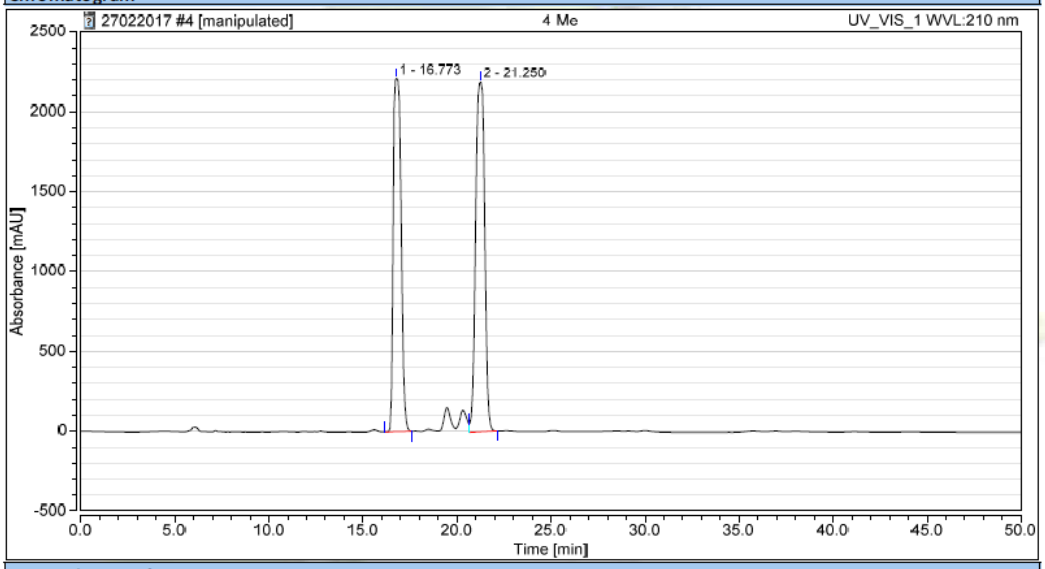
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		15.617	8.484	15.295	2.39	4.95	n.a.
2		21.083	28.873	28.361	8.13	9.19	n.a.
3		33.383	317.827	265.067	89.48	85.86	n.a.
Total:			355.184	308.723	100.00	100.00	

(*S*)-2-((*R*)-2-nitro-1-p-tolylethyl)cyclohexanone **24k**.



Conditions: Chiralpack AD-H, Hex-IPA (90:10), 0.5 mL/min, 35 minutes.

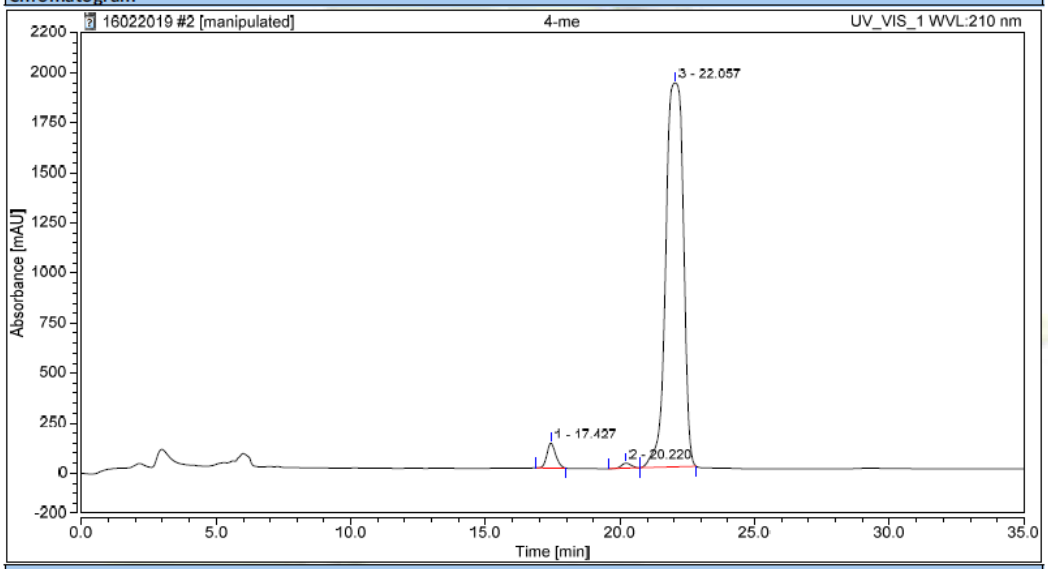
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.773	1073.099	2213.764	46.89	50.24	n.a.
2		21.250	1215.420	2192.762	53.11	49.76	n.a.
Total:			**2288.519**	**4406.525**	**100.00**	**100.00**	

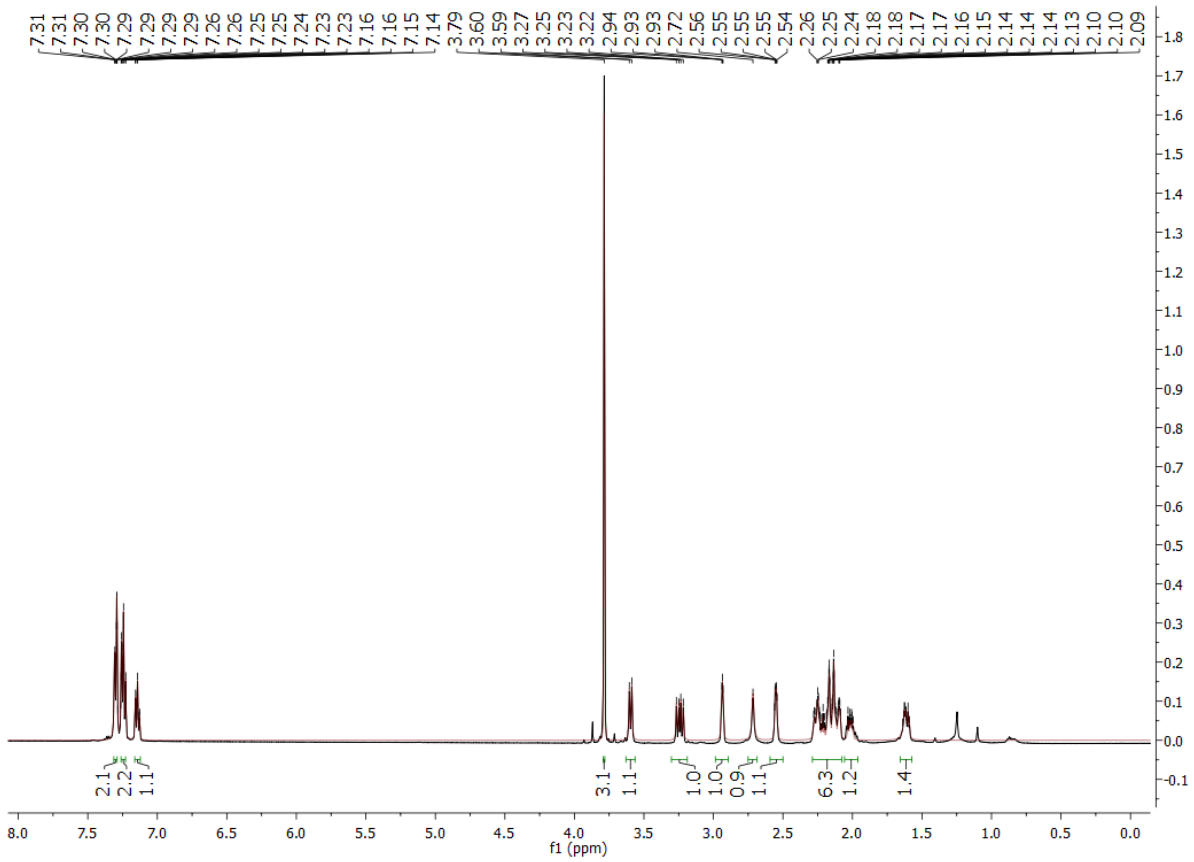
Chromatogram

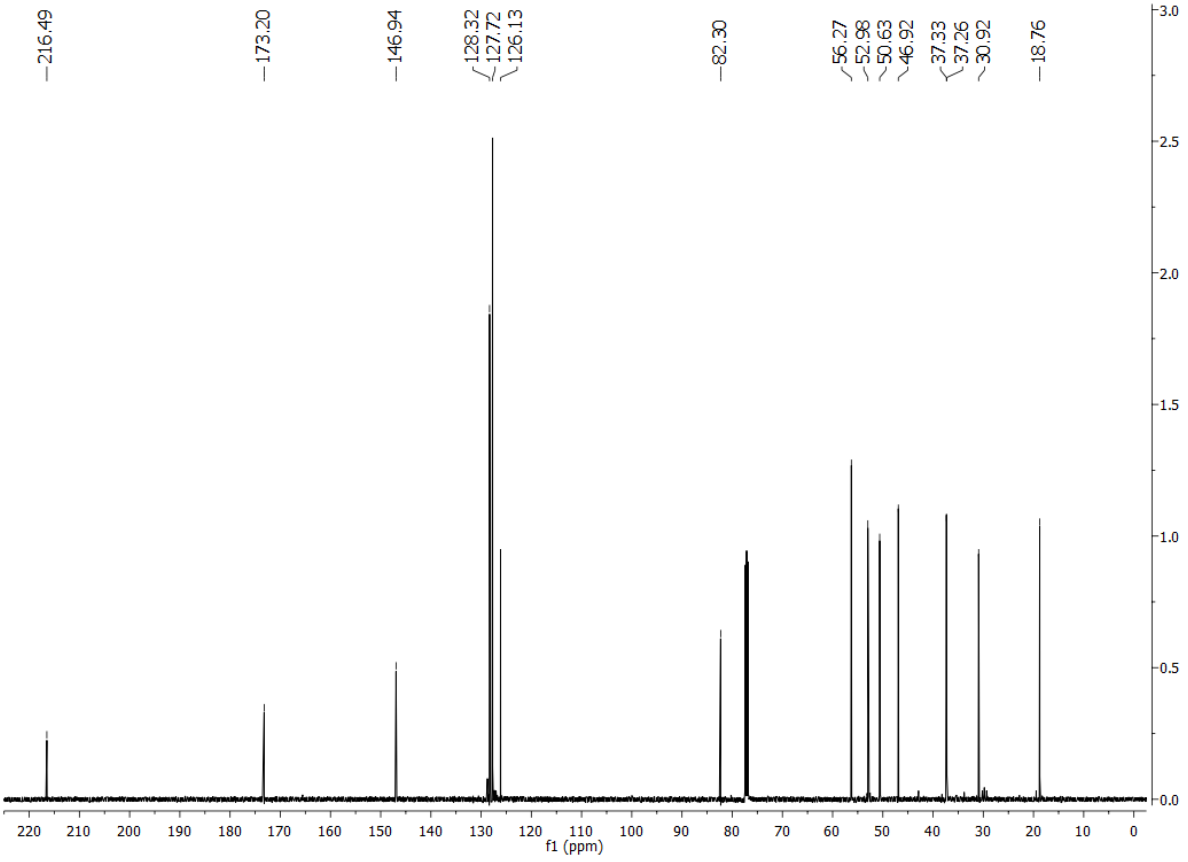


Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.427	47.582	125.364	3.15	6.06	n.a.
2		20.220	9.866	25.248	0.65	1.22	n.a.
3		22.057	1452.182	1918.404	96.19	92.72	n.a.
Total:			**1509.630**	**2069.016**	**100.00**	**100.00**	

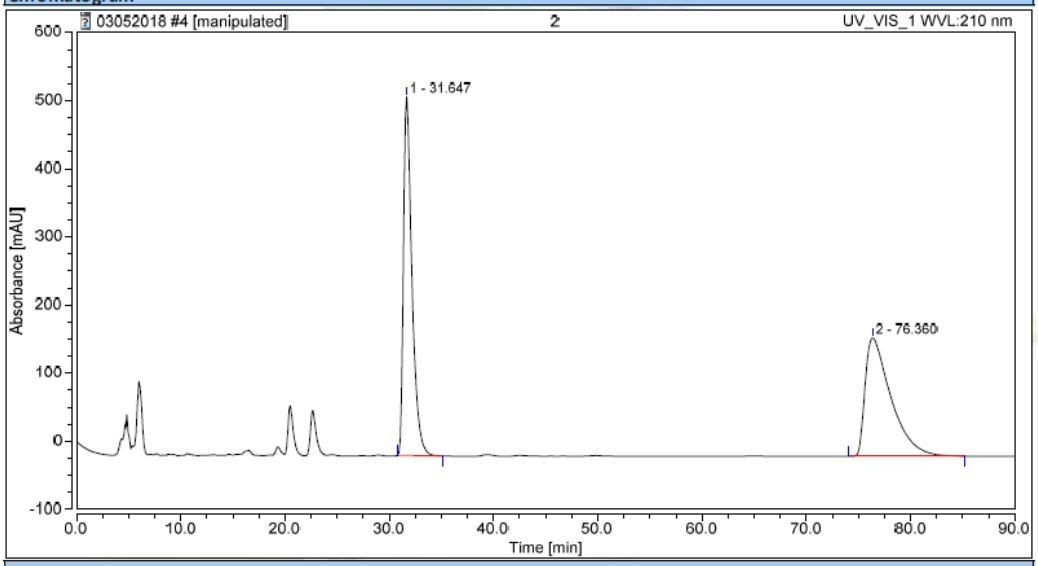
(1*R*,2*S*,4*R*,5*S*)-methyl 2-hydroxy-9-oxo-4-phenylbicyclo[3.3.1]nonane-2-carboxylate **18a**.




216.49
173.20
146.94
128.32
127.72
126.13
82.30
56.27
52.98
50.63
46.92
37.33
37.26
30.92
18.76
f1 (ppm)

Conditions: Chiralpack AD-H, Hex-IPA (90:10), 0.6 mL/min, 90 minutes.

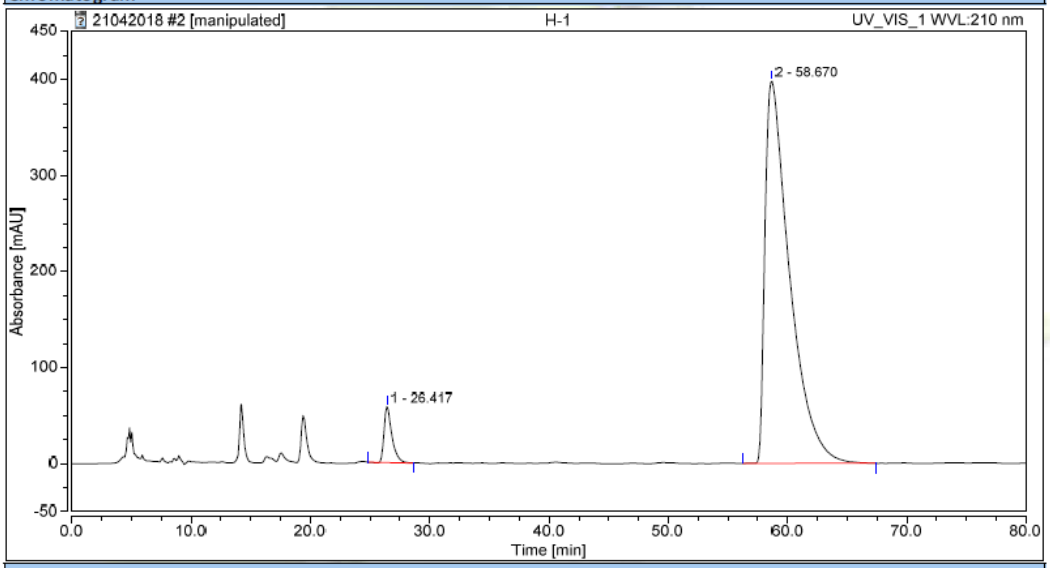
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		31.647	494.249	526.264	49.81	75.16	n.a.
2		76.360	497.950	173.890	50.19	24.84	n.a.
Total:			**992.199**	**700.154**	**100.00**	**100.00**	

Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		26.417	44.065	58.387	4.42	12.79	n.a.
2		58.670	951.953	398.177	95.58	87.21	n.a.
Total:			**996.018**	**456.565**	**100.00**	**100.00**	

6. References

1. C. Cruz-Hernández, P. E. Hernández-González, and E. Juaristi, *Synthesis*, **2018**, 50, 1827.
2. C. Cruz-Hernández, P. E. Hernández-González, and E. Juaristi, *Synthesis*, **2018**, 50, 3445.
3. C. Cruz-Hernández, E. Martinez-Martinez, P. E. Hernández-González, and E. Juaristi *Eur. J. Org. Chem*. **2018**, 6890-6900.