Supporting Information

Synthesis of Cytochalasan Analogues with Aryl Substituents at Position 10

Žaneta Javorská,[a] Silvie Rimpelová,[b] Magdaléna Labíková,[a] and Pavla Perlíková*[a,c]

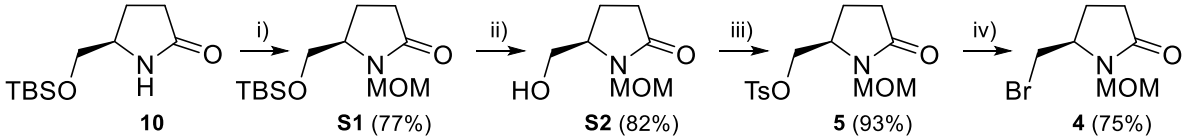
a) Department of Organic Chemistry, Faculty of Chemical Technology, University of Chemistry and Technology, Prague, Technická 5, 166 28 Prague, Czech Republic. E-mail: perlikop@vscht.cz

b) Department of Biochemistry and Microbiology, Faculty of Food and Biochemical Technology, University of Chemistry and Technology Prague, Technická 5, 166 28 Prague, Czech Republic.

c) Institute of Organic Chemistry and Biochemistry, Czech Academy of Sciences, Flemingovo namesti 2, 160 00 Prague, Czech Republic.

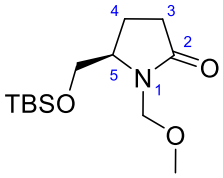
Contents:

Synthesis of compounds 4 and 5



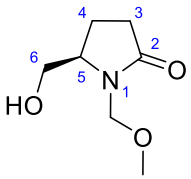
Scheme S1. Reagents and conditions: i) 1. $(MeO)_2CH_2$, AcCl, $ZnBr_2$, toluene, RT, 4 h, 2. BuLi, THF, RT, 16 h; ii) $(HF)_3.NEt_3$, DCM/THF, RT, 6 h; iii) TsCl, pyridine, RT, 24 h; iv) LiBr, acetone, 40 °C, 24 h.

(*R*)-5-{[(*tert*-butyldimethylsilyl)oxy]methyl}-1-(methoxymethyl)pyrrolidin-2-one (S1)



Preparation of MOMCl: First, zinc bromide (15 mg, 65.4 µmol) was dried under high vacuum (heatgun 150-200 °C). Then, dry toluene (5 mL) and dimethoxymethane (1.16 mL, 13.1 mmol) were added at RT under argon atmosphere and the resulting mixture was stirred while acetyl chloride (930 µL, 13.1 mmol) was slowly added dropwise (exothermic reaction). The mixture was then stirred for an additional 4 h at RT under argon atmosphere. **Preparation of pyrrolidin-2-one salt:** To a solution of (*R*)-5-{[(*tert*-butyldimethylsilyl)oxy]methyl}pyrrolidin-2-one (**10**) (1.5 g, 6.54 mmol) in dry toluene (8 mL) and dry THF (2 mL), *n*-BuLi (3.9 mL, 2.5 M in hexanes, 9.81 mmol) was added at -78 °C under argon atmosphere and stirred at 0 °C for 1 h. **Preparation of product:** The mixture containing pyrrolidin-2-one salt was slowly added to the mixture containing MOMCl at 0 °C under argon atmosphere and stirred at RT for 16 h. Then, EtOAc (20 mL) and a solution of NH_4Cl (20 mL) were added and resulting mixture was vigorously stirred for an additional 2 h. The layers were separated and aqueous phase was extracted with EtOAc (2 × 20 mL) and the combined organic layers were washed with a solution of $NaHCO_3$ (25 mL), brine (25 mL), dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (eluent: EtOAc in hexane 0% to 100%, product elutes at 50%) to give **S1** (1.37 mg, 77%) as a yellowish oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.80 (d, J_{gem} = 10.5 Hz, 1H, NCH_2a), 4.64 (d, J_{gem} = 10.5 Hz, 1H, NCH_2b), 3.78 – 3.71 (m, 2H, OCH_2a, H-5), 3.62 (m, Σ*J* = 16.5 Hz, 1H, OCH_2b), 3.27 (s, 3H, OCH_3), 2.51 (m, Σ*J* = 35.3 Hz, 1H, H-3a), 2.33 (ddd, J_{gem} = 17.1, $J_{3b,4b}$ = 10.0, $J_{3b,4a}$ = 4.6 Hz, 1H, H-3b), 2.15 – 2.01 (m, Σ*J* = 48.3 Hz, 1H, H-4a), 1.91 (dddd, J_{gem} = 13.4, $J_{4b,3b}$ = 10.0, $J_{4b,3a}$ = 4.7, $J_{4b,5}$ = 3.6 Hz, 1H, H-4b), 0.85 (s, 9H, $C(CH_3)_3$), 0.03 (s, 3H, $SiCH_3$), 0.02 (s, 3H, $SiCH_3$) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.91 (C-2), 72.58 (NCH_2), 63.74 (OCH_2), 58.46 (CH-5), 56.03 (OCH_3), 30.47 (CH_2-3), 25.71 (Si*C*CH_3), 21.48 (CH_2-4), 18.08 (Si*C*CH_3), -5.63 (2x$SiCH_3$) ppm. **HRMS** (ESI) *m/z* calcd for $C_{13}H_{27}O_3NNaSi$ $[M+Na]^+$ 296.1652; found 296.1653.

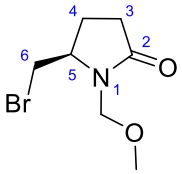
(*R*)-5-(hydroxymethyl)-1-(methoxymethyl)pyrrolidin-2-one (S2)



This compound was synthesized following the procedure for the preparation of compound **19**. Triethylamine trihydrofluoride (4.10 mL, 25.2 mmol) was added to a solution of **S1** (1.15 g, 4.19 mmol) in dry DCM (10 mL) and dry THF (10 mL) at RT under argon atmosphere and the resulting mixture was stirred until full conversion (18 h, TLC, EtOAc/MeOH : 20/1). A solution of $NaHCO_3$ (30 mL) was slowly added (release of gas) and the resulting mixture was extracted with DCM (5 × 50 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (eluent: MeOH in EtOAc 0% to 5%, product elutes at 5%) to give **S2** (550 mg, 82%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.05 (d, J_{gem} = 10.3 Hz, 1H, NCH_2a), 4.40 (d, J_{gem} = 10.4 Hz, 1H, NCH_2b), 3.76 – 3.67 (m, 2H, H-5,6a), 3.52 (m, Σ*J* = 26.7 Hz, 1H, H-6b), 3.40 (dd, $J_{OH,6a}$ = 8.1, $J_{OH,6b}$ = 5.7 Hz, 1H, OH), 3.38 (s, 3H, OCH_3), 2.49 (ddd, J_{gem} = 17.5, $J_{3a,4b}$ = 10.0, $J_{3a,4a}$ = 6.6 Hz, 1H, H-3a), 2.38 (ddd, J_{gem} = 17.4, $J_{3b,4a}$ = 10.1, $J_{3b,4b}$ = 6.6 Hz, 1H, H-3b), 2.12 (dddd, J_{gem} = 13.2, $J_{4a,3b}$ = 10.1, $J_{4a,5}$ = 8.2, $J_{4a,3a}$ = 6.6 Hz, 1H, H-4a), 1.80 (m, Σ*J* = 36.5 Hz, 1H, H-4b) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.70 (C-2), 73.56 (NCH_2), 65.01 (CH_2-6), 61.30 (CH-5), 56.37

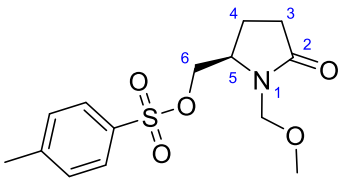
(OCH_3), 30.18 (CH_2-3), 20.55 (CH_2-4) ppm. **HRMS** (ESI) *m/z* calcd for $C_7H_{13}O_3NNa$ $[M+Na]^+$ 182.0788; found 182.0787.

(*R*)-5-(bromomethyl)-1-(methoxymethyl)pyrrolidin-2-one (4)



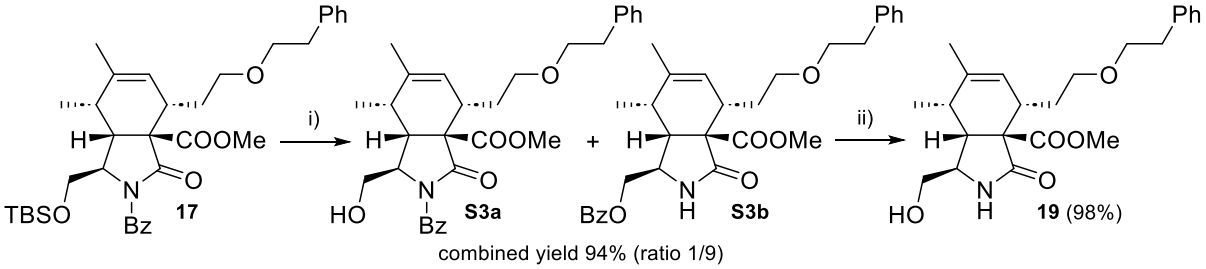
First, lithium bromide (108 mg, 1.25 mmol) was dried under high vacuum (heatgun 150-200 °C). Then, dry acetone (5 mL) and **5** (80 mg, 0.26 mmol) were added at RT under argon atmosphere and the resulting mixture was stirred at 40 °C until full conversion (24 h, TLC, EtOAc). After cooling reaction mixture to RT, H_2O (5 ml) was added. The resulting mixture was extracted with Et_2O (1 × 10 mL) and EtOAc (2 x 10 mL). The combined organic layers were washed with brine (15 mL), dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (eluent: EtOAc in hexane 0% to 100%, product elutes at 100%) to give **4** (43 mg, 75%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.76 (d, J_{gem} = 10.9 Hz, 1H, NCH_2a), 4.67 (d, J_{gem} = 10.8 Hz, 1H, NCH_2b), 3.98 (dtd, $J_{5,4a}$ = 8.4, $J_{5,4b}$ = $J_{5,6a}$ = 4.8, $J_{5,6b}$ = 3.8 Hz, 1H, H-5), 3.57 (m, ΣJ = 28.1 Hz, 2H, H-6a,b), 3.30 (s, 3H, OCH_3), 2.58 (ddd, J_{gem} = 17.3, $J_{3a,4b}$ = 10.1, $J_{3a,4a}$ = 7.0 Hz, 1H, H-3a), 2.39 (ddd, J_{gem} = 17.3, $J_{3b,4a}$ = 10.3, $J_{3b,4b}$ = 5.6 Hz, 1H, H-3b), 2.22 (dddd, J_{gem} = 13.2, $J_{4a,\,3b}$ = 10.2, $J_{4a,5}$ = 8.3, $J_{4a,3a}$ = 7.0 Hz, 1H, H-4a), 1.98 (dddd, J_{gem} = 13.3, $J_{4b,3a}$ = 10.1, $J_{4b,3b}$ = 5.6, $J_{4b,5}$ = 4.4 Hz, 1H, H-4b) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.17 (C-2), 72.74 (NCH_2), 57.22 (CH_2-5), 56.43 (OCH_3), 35.52 (CH_2-6), 29.84 (CH_2-3), 23.03 (CH_2-4) ppm. **HRMS** (ESI) *m/z* calcd for $C_7H_{12}O_2N^{79}BrNa$ $[M+Na]^+$ 243.9944; found 243.9944.

(*R*)-(1-(methoxymethyl)-5-oxopyrrolidin-2-yl)methyl 4-methylbenzenesulfonate (5)



A solution of **S2** (522 mg, 3.28 mmol) in dry pyridine (5 mL) was treated with TsCl (988 mg, 5.18 mmol) at RT under argon atmosphere and the resulting mixture was stirred until full conversion (24 h, TLC, EtOAc). Next, H_2O (45 ml) was added and the solution was stirred for an additional 5 min. Then, DCM (50 mL) was added, the resulting phases were separated and the aqueous phase was extracted with DCM (2 × 25 mL). The combined organic layers were washed with 10% citric acid (30 mL), 8% $NaHCO_3$ (45 mL), dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. The FC of the residue on silica gel (eluent: EtOAc in hexane 0% to 100%, product elutes at 100%) furnished compound **5** (957 mg, 93%) as a yellowish oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, $J_{H\text{-}o\text{-}Ts,H\text{-}m\text{-}Ts}$ = 8.2 Hz, 2H, 2xH-*o*-Ts), 7.35 (d, $J_{H\text{-}m\text{-}Ts,H\text{-}o\text{-}Ts}$ = 7.9 Hz, 2H, 2xH-*m*-Ts), 4.63 (d, J_{gem} = 10.8 Hz, 1H, NCH_2a), 4.51 (d, J_{gem} = 10.7 Hz, 1H, NCH_2b), 4.12 (m, ΣJ = 29.8 Hz, 2H, H-6a,b), 3.88 (dq, $J_{5,4a}$ = 8.3, $J_{5,4b}$ = $J_{5,6a}$ = $J_{5,6b}$ = 4.1 Hz, 1H, H-5), 3.18 (s, 3H, OCH_3), 2.55 – 2.43 (m, 4H, OTs-CH_3, H-3a), 2.34 (ddd, J_{gem} = 17.3, $J_{3b,4a}$ = 10.0, $J_{3b,4b}$ = 5.0 Hz, 1H, H-3b), 2.16 (dddd, J_{gem} = 13.2, $J_{4a,\,3b}$ = 10.0, $J_{4a,5}$ = 8.6, $J_{4a,3a}$ = 7.9 Hz, 1H, H-4a), 1.91 (dddd, J_{gem} = 13.3, $J_{4b,3a}$ = 9.9, $J_{4b,3b}$ = 4.9, $J_{4b,5}$ = 4.1 Hz, 1H, H-4b) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.08 (C-2), 145.26 (C-*p*-OTs), 132.32 (C-*i*-OTs), 129.96 (C-*m*-OTs), 127.85 (C-*o*-OTs), 72.62 (NCH_2), 69.46 (CH_2-6), 56.04 (OCH_3), 55.82 (CH_2-5), 29.77 (CH_2-3), 21.63 (OTs-*C*H_3), 21.16 (CH_2-4) ppm. **HRMS** (ESI) *m/z* calcd for $C_{14}H_{19}O_5NNaS$ $[M+Na]^+$ 336.0876; found 336.0875.

Synthesis of compound 16 using an alternative approach

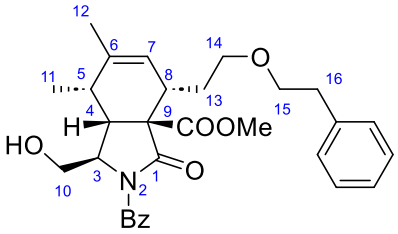


Scheme S2. Reagents and conditions: i) $(HF)_3.NEt_3$, CH_3CN, RT, 24 h ii) Na, MeOH, RT, 30 min.

Mixture of methyl (1*R*,3a*R*,4*S*,7*S*,7a*R*)-2-benzoyl-1-(hydroxymethyl)-6,7-dimethyl-3-oxo-4-(2-phenethoxyethyl)-1,2,3,4,7,7a-hexahydro-3a*H*-isoindole-3a-carboxylate (S3a) and methyl (1*R*,3a*R*,4*S*,7*S*,7a*R*)-1-[(benzoyloxy)methyl]-6,7-dimethyl-3-oxo-4-(2-phenethoxyethyl)-1,2,3,4,7,7a-hexahydro-3a*H*-isoindole-3a-carboxylate (S3b)

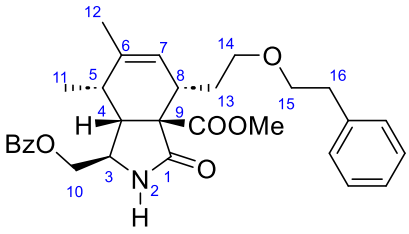
Triethylamine trihydrofluoride (284 µL, 1.74 mmol) was added to a solution of **17** (157 mg, 0.25 mmol) in dry acetonitrile (3 mL) at RT under argon atmosphere and the resulting mixture was stirred until full conversion (24 h, TLC, hexanes/EtOAc : 1/1). A solution of $NaHCO_3$ (5 mL) was slowly added (release of gas) and the resulting mixture was extracted with DCM (3 × 15 mL) and EtOAc (1 × 15 mL). The combined organic layers were washed with brine (5 mL), dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. The crude products were purified by flash chromatography on silica gel (eluent: EtOAc in hexane 0% to 100%, product elutes at 40%) to give inseparable mixture (120 mg, 94%) of two products **S3b** and unstable **S3a** in ratio 9/1 as a colorless dense oil. Product **S3a** undergoes spontaneous isomerization to product **S3b**. Due to the instability of **S3a**, it is not possible to obtain clean ^{1}H and ^{13}C NMR spectra. Therefore, only the ^{1}H NMR of the compound **S3a** in the mixture is presented. **HRMS** (ESI) (mixture) *m/z* calcd for $C_{30}H_{35}O_6NNa$ $[M+Na]^+$ 528.2357; found 528.2349.

Methyl (1*R*,3a*R*,4*S*,7*S*,7a*R*)-2-benzoyl-1-(hydroxymethyl)-6,7-dimethyl-3-oxo-4-(2-phenethoxyethyl)-1,2,3,4,7,7a-hexahydro-3a*H*-isoindole-3a-carboxylate (S3a)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (m, Σ*J* = 12.0 Hz, 2H, H-*o*-Bz), 7.51 (m, Σ*J* = 20.0 Hz, 1H, H-*p*-Bz), 7.44 – 7.37 (m, 2H *overlapped*, H-*m*-Bz), 7.30 – 7.15 (m, 5H *overlapped*, H-*o*,*m*,*p*-Ph), 5.52 (m, Σ*J* = 12.0 Hz, 1H, H-7), 4.15 – 4.09 (m, 1H *overlapped*, H-10a), 3.90 (dd, J_{gem} = 11.7, $J_{10b,3}$ = 3.2 Hz, 1H, H-10b), 3.81 (s, 3H, OCH_3), 3.72 – 3.44 (m, 5H *overlapped*, H-3,14,15), 2.90 – 2.82 (m, 2H *overlapped*, H-16), 2.76 – 2.70 (m, 2H *overlapped*, H-4,8), 2.57 (m, Σ*J* = 20.0 Hz, 1H, H-5), 2.20 – 2.11 (m, 3H *overlapped*, H-13a), 1.96 – 1.84 ((m, 3H *overlapped*, H-13b), 1.79 – 1.76 (m, 3H *overlapped*, H-12), 1.28 (d, $J_{11,5}$ = 7.3 Hz, 3H) ppm.

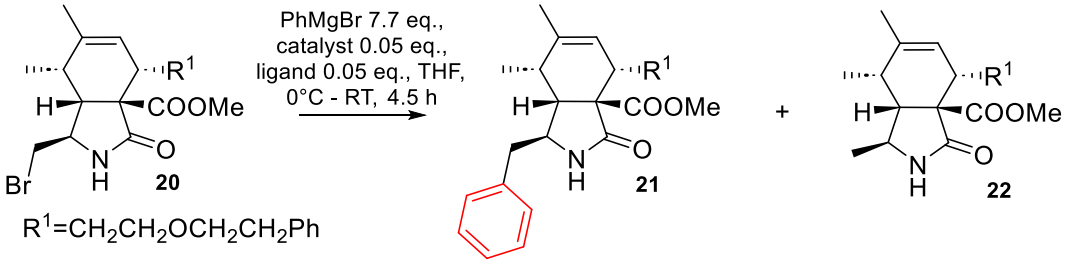
Methyl (1*R*,3a*R*,4*S*,7*S*,7a*R*)-1-[(benzoyloxy)methyl]-6,7-dimethyl-3-oxo-4-(2-phenethoxyethyl)-1,2,3,4,7,7a-hexahydro-3a*H*-isoindole-3a-carboxylate (S3b)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (m, Σ*J* = 11.6 Hz, 2H, H-*o*-Bz), 7.56 (ddt, $J_{p,m}$ = 7.9, $J_{p,m}$ = 6.9, $J_{p,o}$ = 1.4 Hz, 1H, H-*p*-Bz), 7.44 (m, Σ*J* = 18.5 Hz, 2H, H-*m*-Bz), 7.30 – 7.15 (m, 5H, H-*o*,*m*,*p*-Ph), 6.83 (s, 1H, NH), 5.55 (m, Σ*J* = 7.8 Hz, 1H, H-7), 4.44 (dd, J_{gem} = 11.1, $J_{10a,3}$ = 3.5 Hz, 1H, H-10a), 4.05 (dd, J_{gem} = 11.1, $J_{10b,3}$ = 8.8 Hz, 1H, H-10b), 3.72 – 3.50 (m, 7H, OCH_3, H-14,15), 3.42 (m, Σ*J* = 20.8 Hz, 1H, H-3), 2.88 (t, $J_{16,15}$ = 7.2 Hz, 2H, H-16), 2.74 (m, Σ*J* = 13.8 Hz, 1H, H-8), 2.53 – 2.46 (m, 2H, H-4,5), 2.16 (m, Σ*J* = 32.0 Hz, 1H, H-13b), 1.90 (ddt, J_{gem} = 13.9, $J_{13b,14a}$ =11.2, $J_{13b,14b}$ = $J_{13b,8}$ = 5.5 Hz, 1H, H-13b), 1.77 (s, 3H, H-12), 1.22 (d, $J_{11,5}$ = 7.0 Hz, 3H, H-11) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.25 (C-1), 172.70 (*C*$OOCH_3$), 166.27 (C=O-Bz), 139.25 (C-*i*-Ph), 138.92 (C-6), 133.39 (C-*p*-Bz), 129.74 (C-*o*-Bz), 129.34 (C-*i*-Bz), 128.95 (C-*o*-Ph), 128.48 (C-*m*-Bz), 128.20 (C-*m*-Ph), 126.88 (C-7), 125.98 (C-*p*-

Ph), 71.38 (C-15), 69.86 (C-14), 68.43 (C-10), 59.80 (C-9), 53.21 (C-3), 52.70 (COO*C*H_3), 50.64 (C-4), 36.43 (C-8), 36.33 (C-16), 33.90 (C-5), 29.99 (C-13), 20.27 (C-12), 14.03 (C-11) ppm. **HRMS** (ESI) *m/z* calcd for $C_{30}H_{35}O_6NNa$ $[M+Na]^+$ 528.2357; found 528.2354.

Screening of alternative ligands



Scheme S3. Optimization of the cross-coupling reaction using cytochalasan bromide **20**

Table 1. Optimization of the cross-coupling reaction using cytochalasan bromide **20**

Entry	Catalyst	Ligand	NMR ratio 20:21:22
S1	-	TMEDA	86:**14**:0
S2	$Fe(acac)_3$	-	18:**36**:46
S3	$Fe(acac)_3$	Ipr	12:**41**:47
S4	$Fe(acac)_3$	IMes	21:**30**:49
S5	$Fe(acac)_3$	Bipy	15:**35**:50

HPLC purity of final cytochalasan analogues

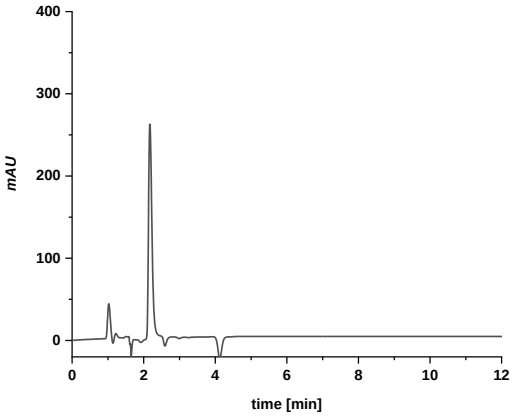
Separation conditions:

A: Galo-RP (3 μm, 120 Å, 3.0 × 150 mm i.d.), mobile phase: MeCN/H_2O (7/3), flow rate: 0.6 mL/min.

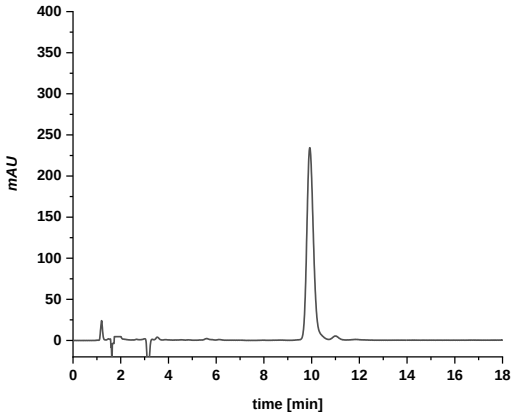
B: XBridge C18 (5 μm, 130 Å, 4.0 × 100 mm i.d.), mobile phase: MeCN/H_2O (7/3), flow rate: 0.75 mL/min.

Sample	Purity (%)	Separation conditions	Retention time (min)
22	98.1	A	2.18
23	98.0	B	9.83
24	96.5	B	9.80
25	99.9	A	3.18
26	95.2	B	11.95
27	96.8	B	7.96
28	98.7	A	2.53

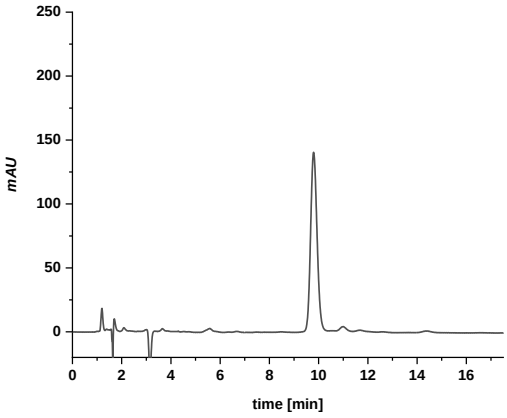
22 – purity 98.1, T_R = 2.18 min



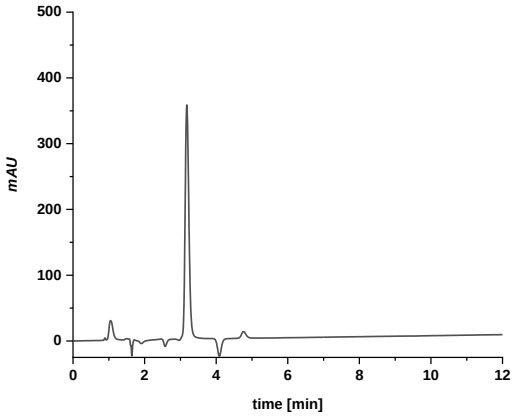
23 – purity 98.0, T_R = 9.83 min



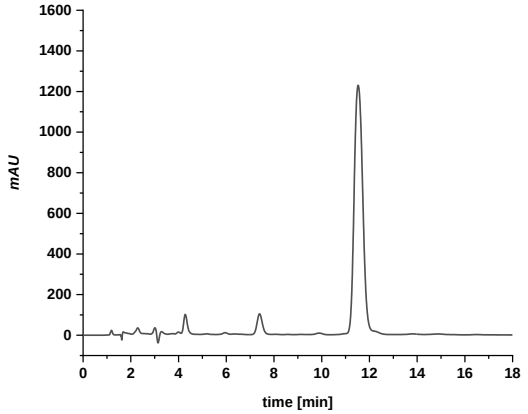
24 – purity 96.5, T_R = 9.80 min



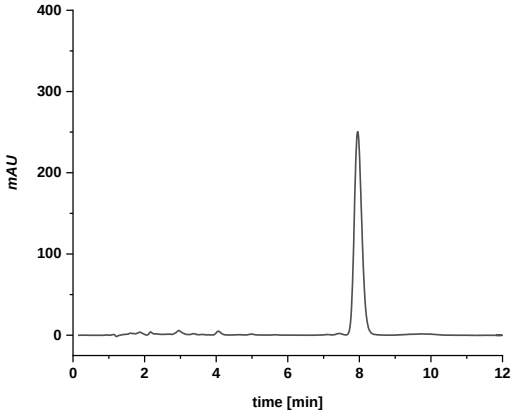
25 – purity 99.9, T_R = 3.18 min



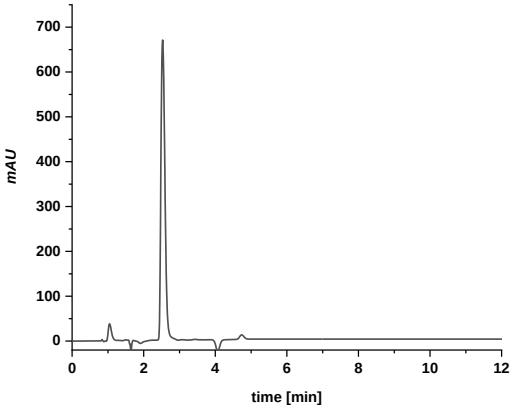
26 – purity 95.2, T_R = 11.95 min



27 – purity 96.8, T_R = 7.96 min

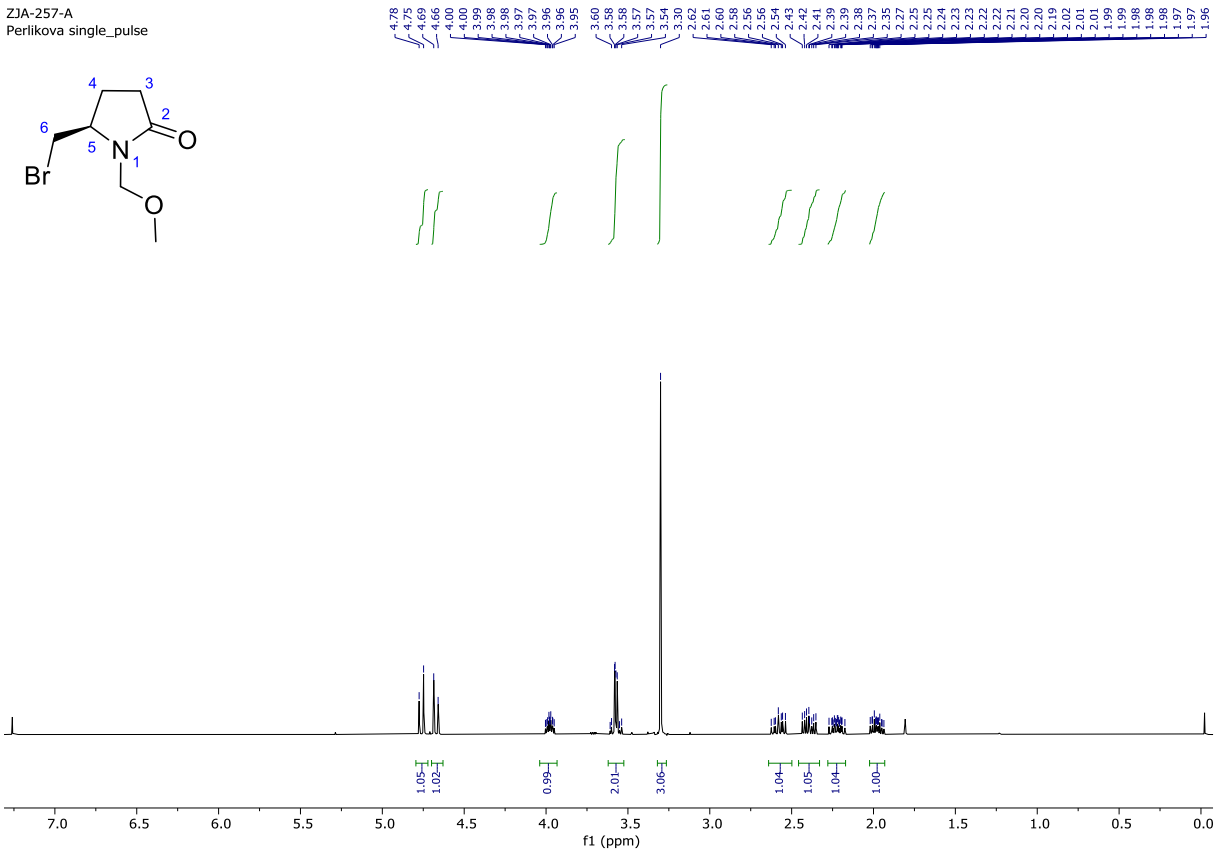


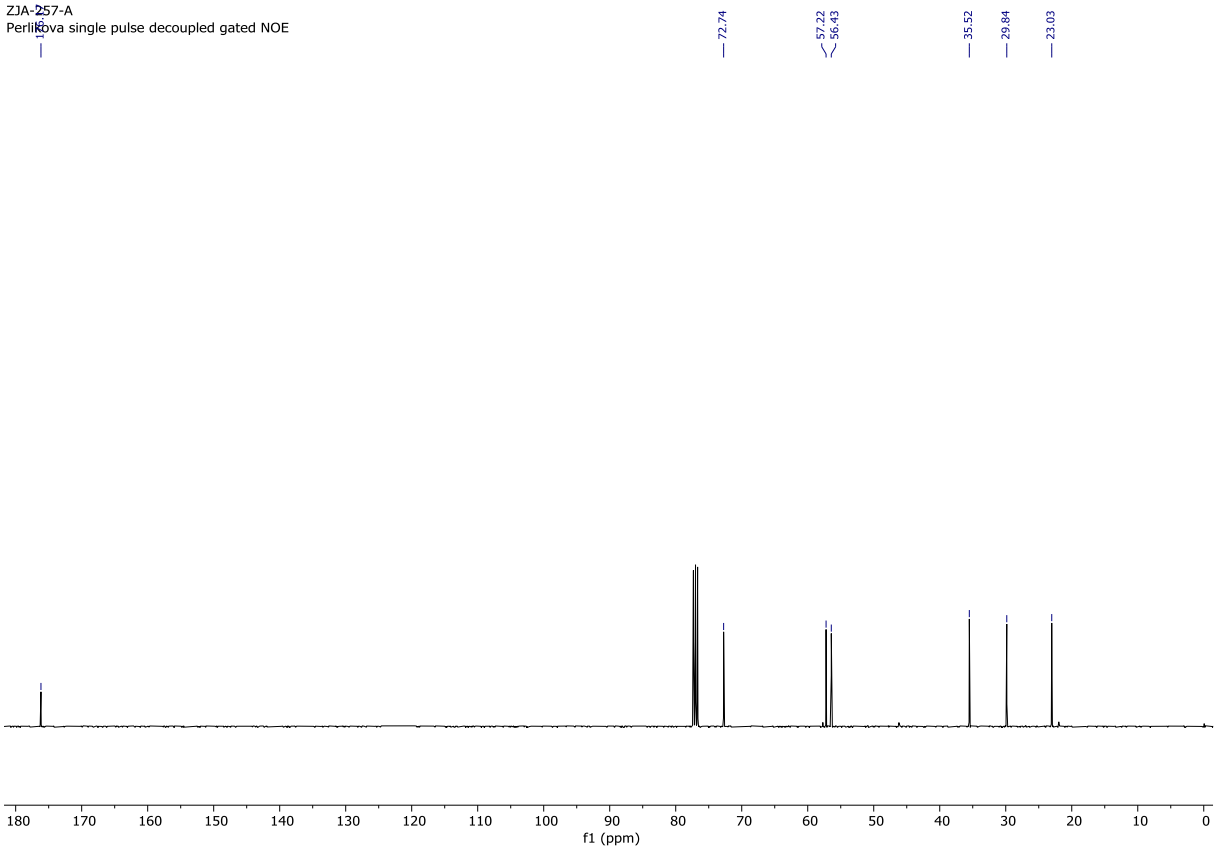
28 – purity 98.7, T_R = 2.53 min



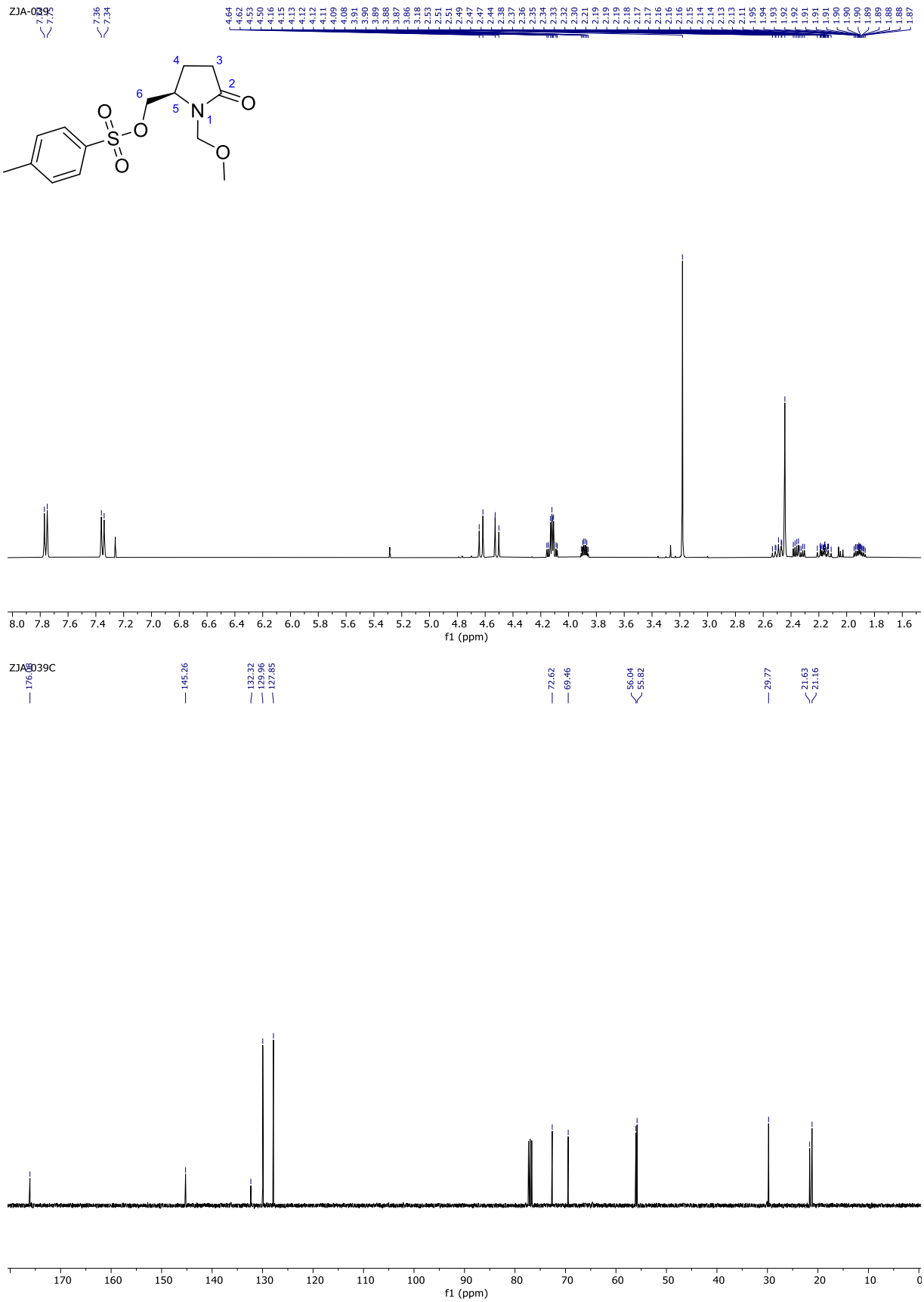
Copies of NMR spectra

4

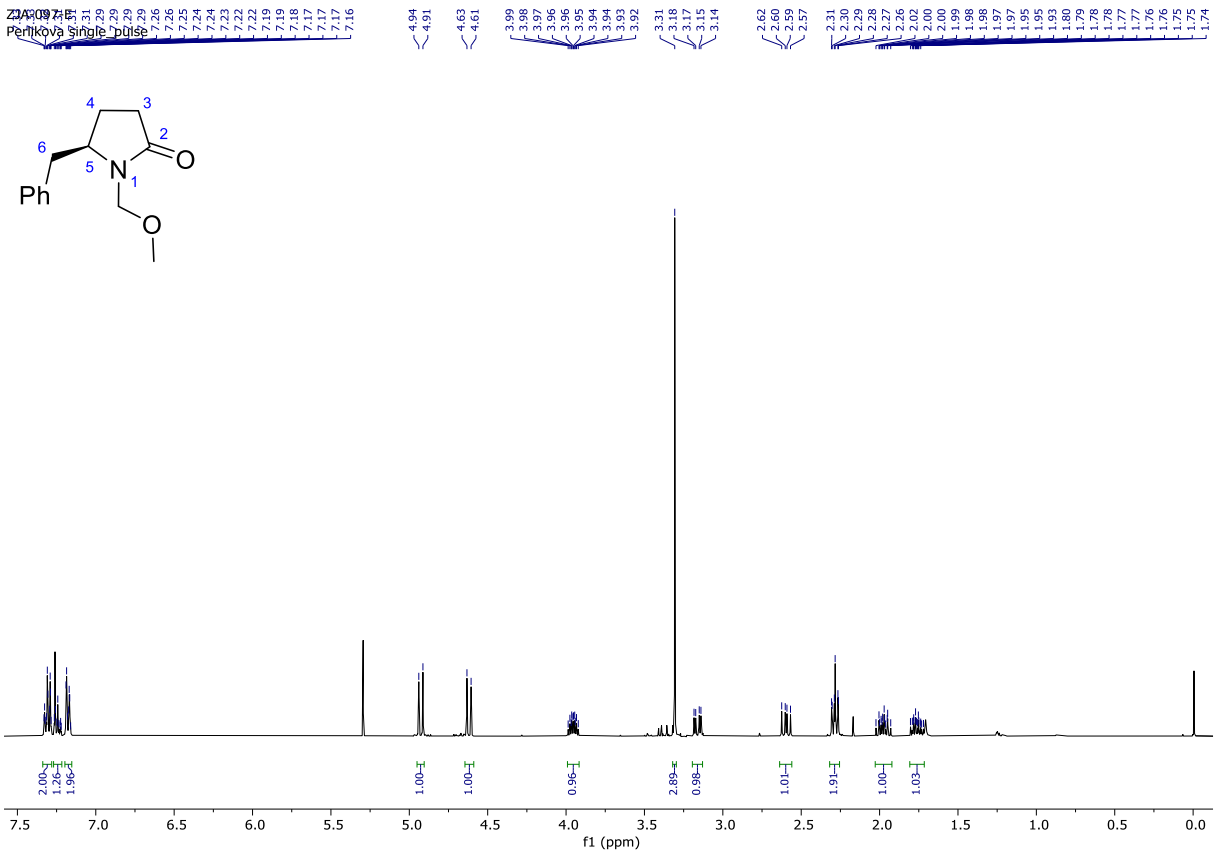


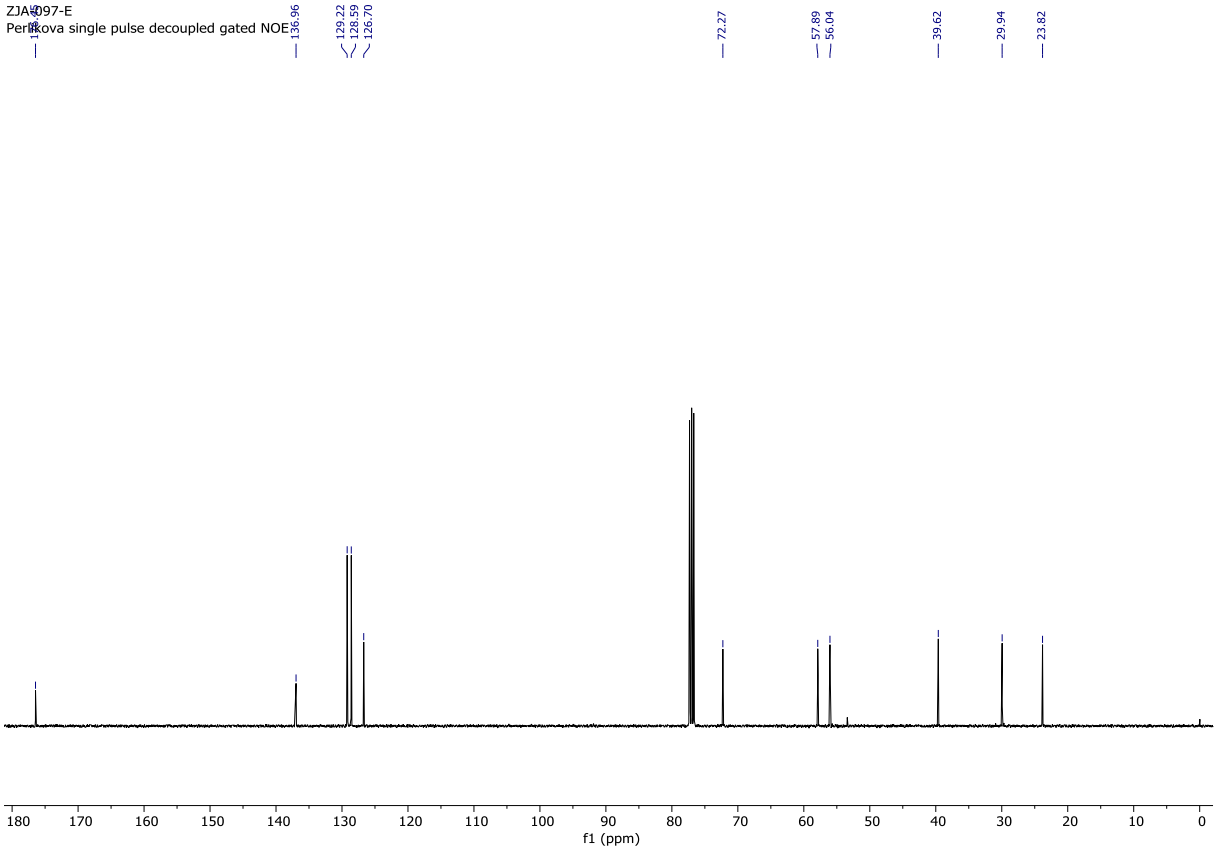


5

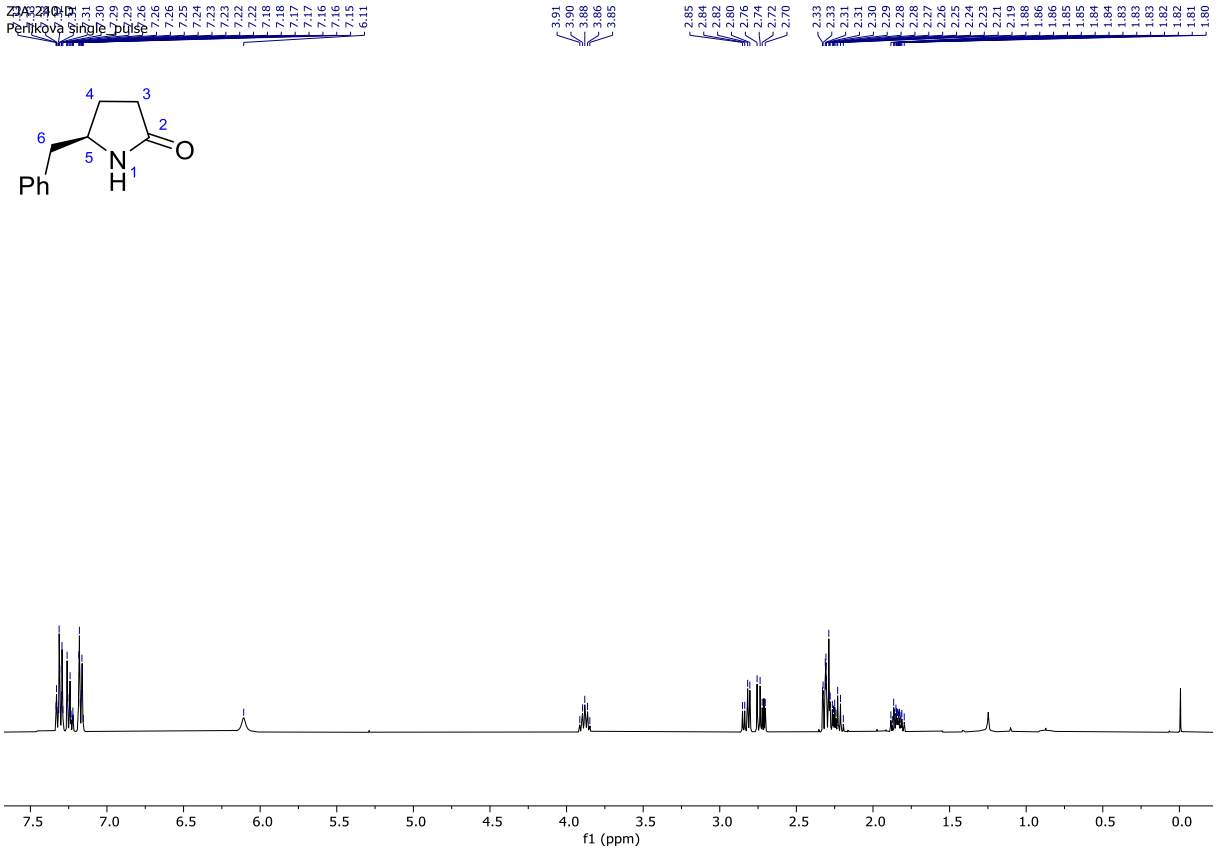

ZJA-039
7.75
7.73
7.36
7.34
4.64
4.62
4.53
4.50
4.16
4.15
4.13
4.12
4.12
4.11
4.09
4.08
3.91
3.90
3.89
3.88
3.87
3.86
3.18
2.53
2.51
2.51
2.49
2.47
2.47
2.44
2.38
2.37
2.36
2.35
2.34
2.33
2.32
2.30
2.21
2.19
2.19
2.19
2.18
2.17
2.17
2.16
2.16
2.16
2.15
2.14
2.14
2.13
2.13
2.11
1.95
1.94
1.93
1.92
1.92
1.91
1.91
1.91
1.90
1.90
1.90
1.89
1.89
1.88
1.88
1.87
4
3
2
6
5
N
1
O
O
O
O
O
O
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6
f1 (ppm)
ZJA-039C
176.88
145.26
132.32
129.96
127.85
72.62
69.46
56.04
55.82
29.77
21.63
21.16
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

6

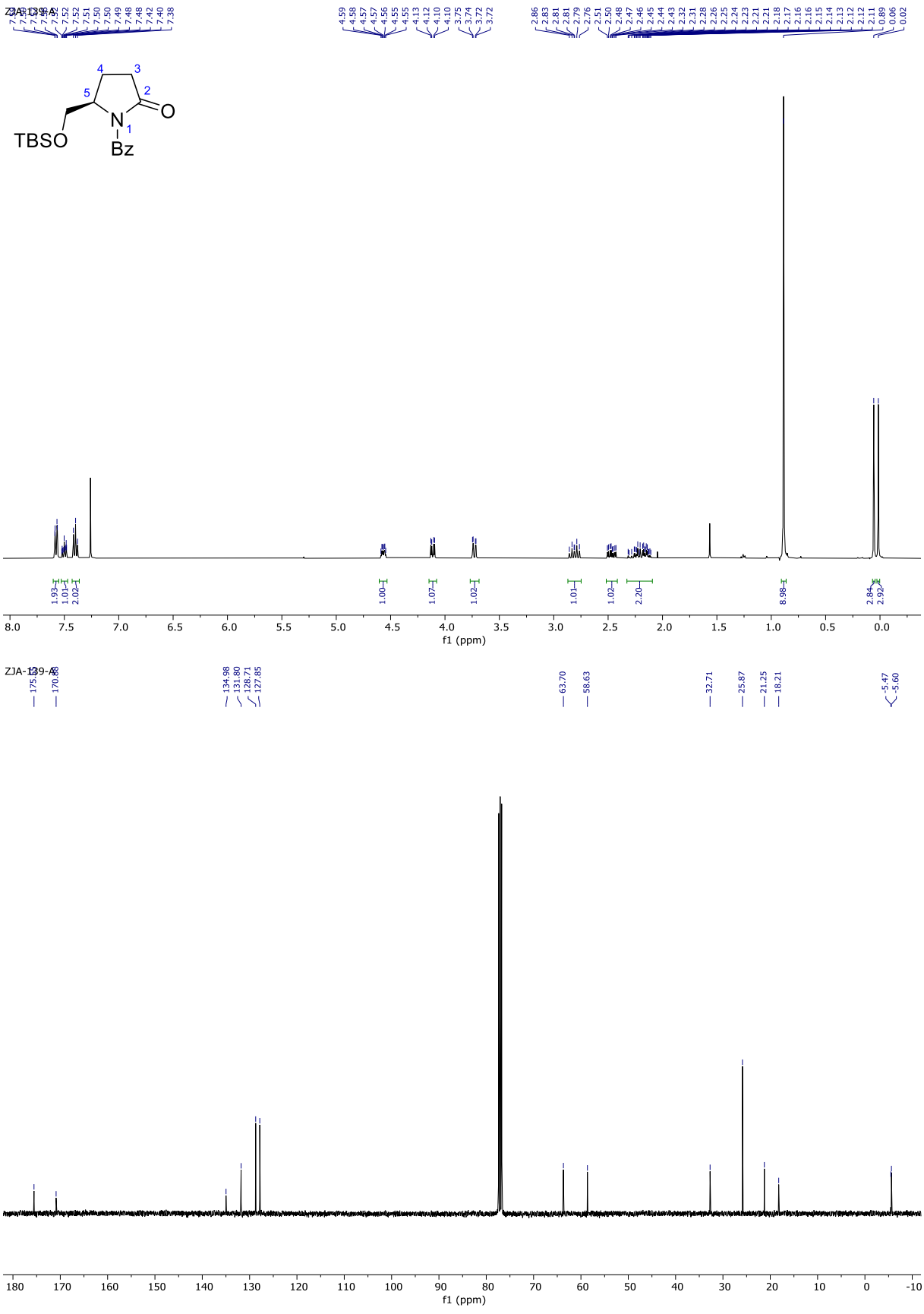

ZJA097-H
Perlikova single pulse
4
3
2
O
6
5
N
1
Ph
O
f1 (ppm)


ZJA097-E
Perlikova single pulse decoupled gated NOE
f1 (ppm)

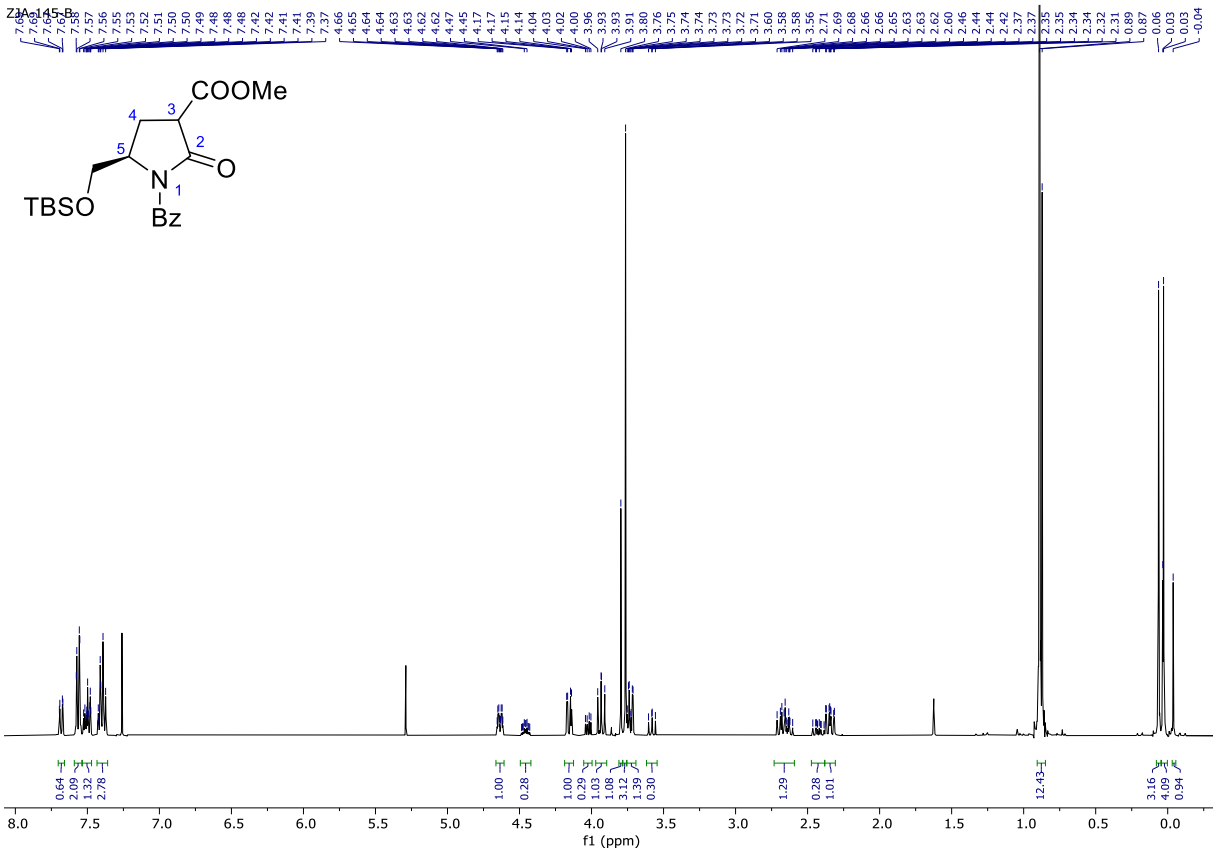
8

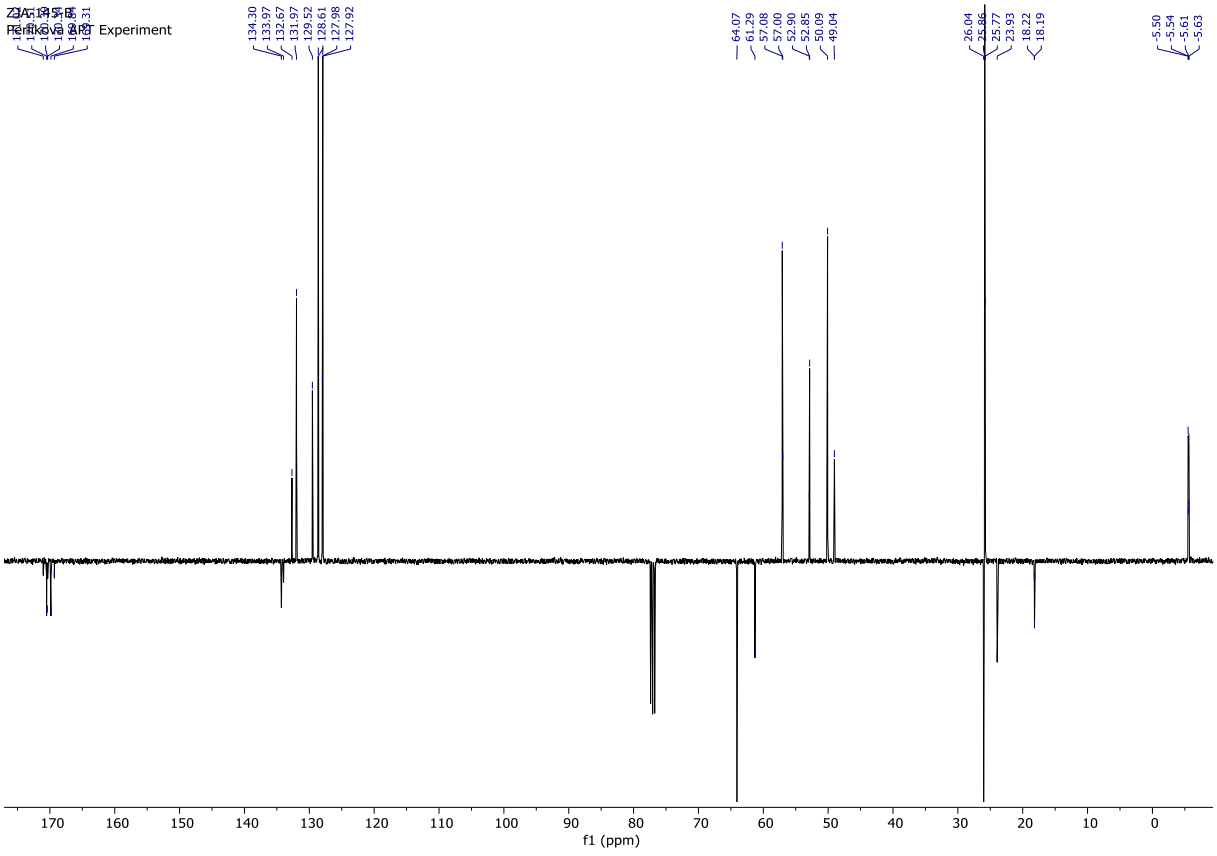

Perlikova single pulse
4
3
2
6
5
N
H
1
O
Ph
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

11

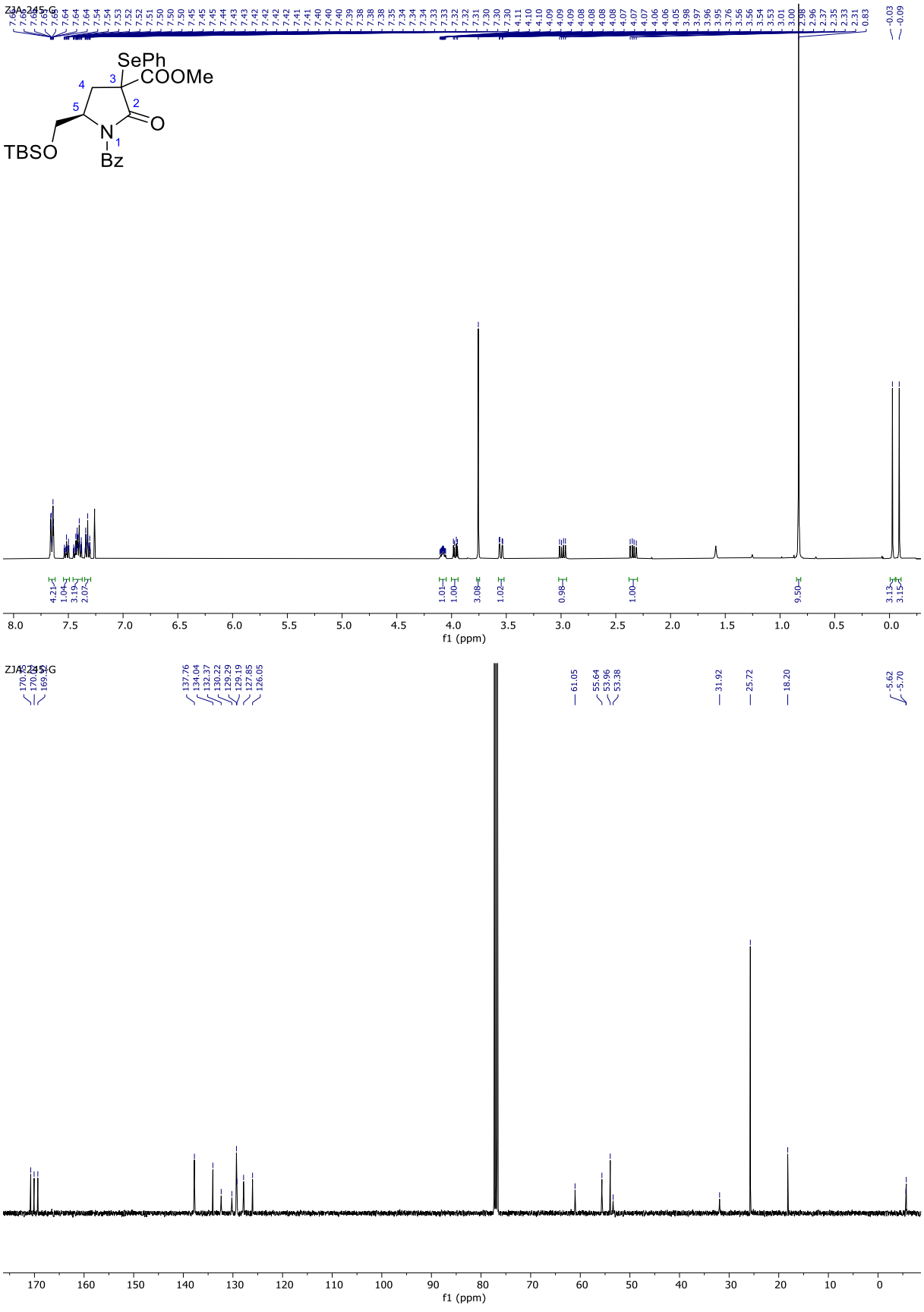


12

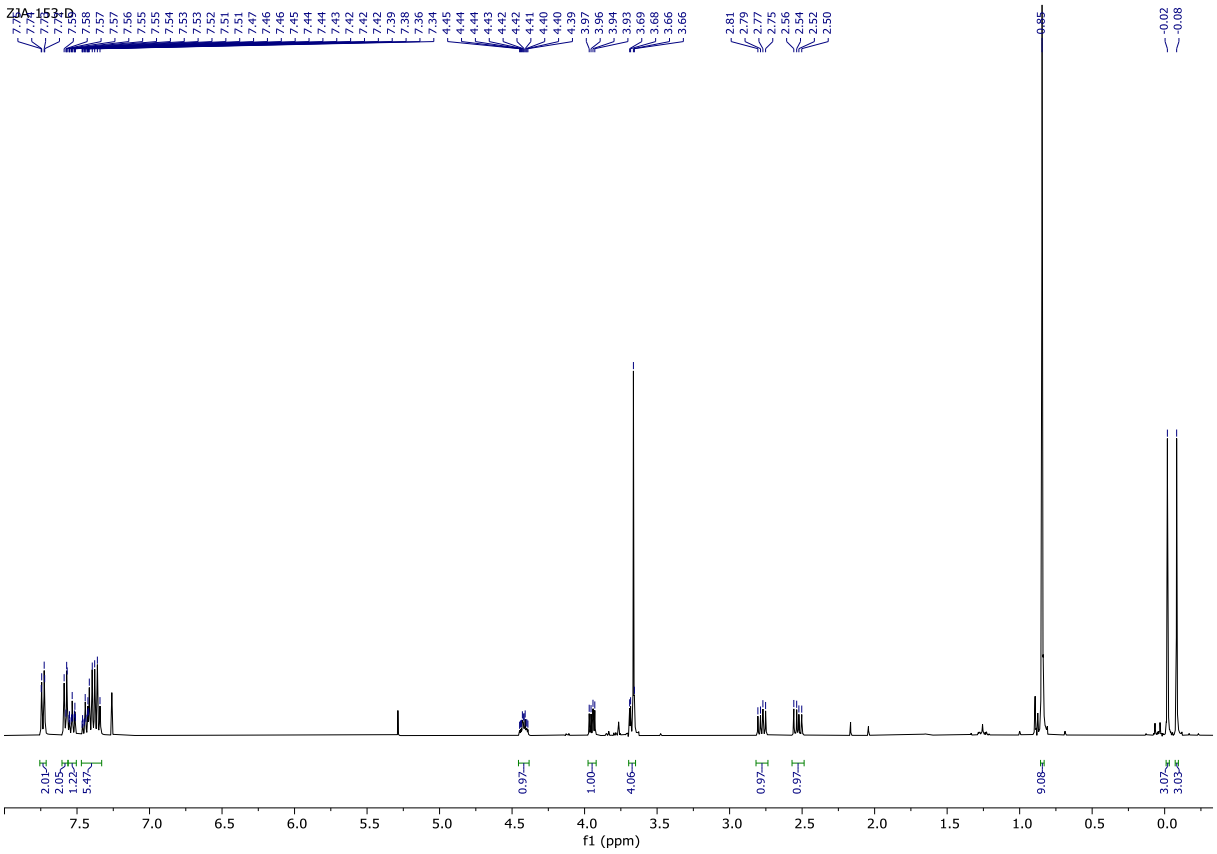

ZJA-145-B
COOMe
TBSO
Bz
f1 (ppm)

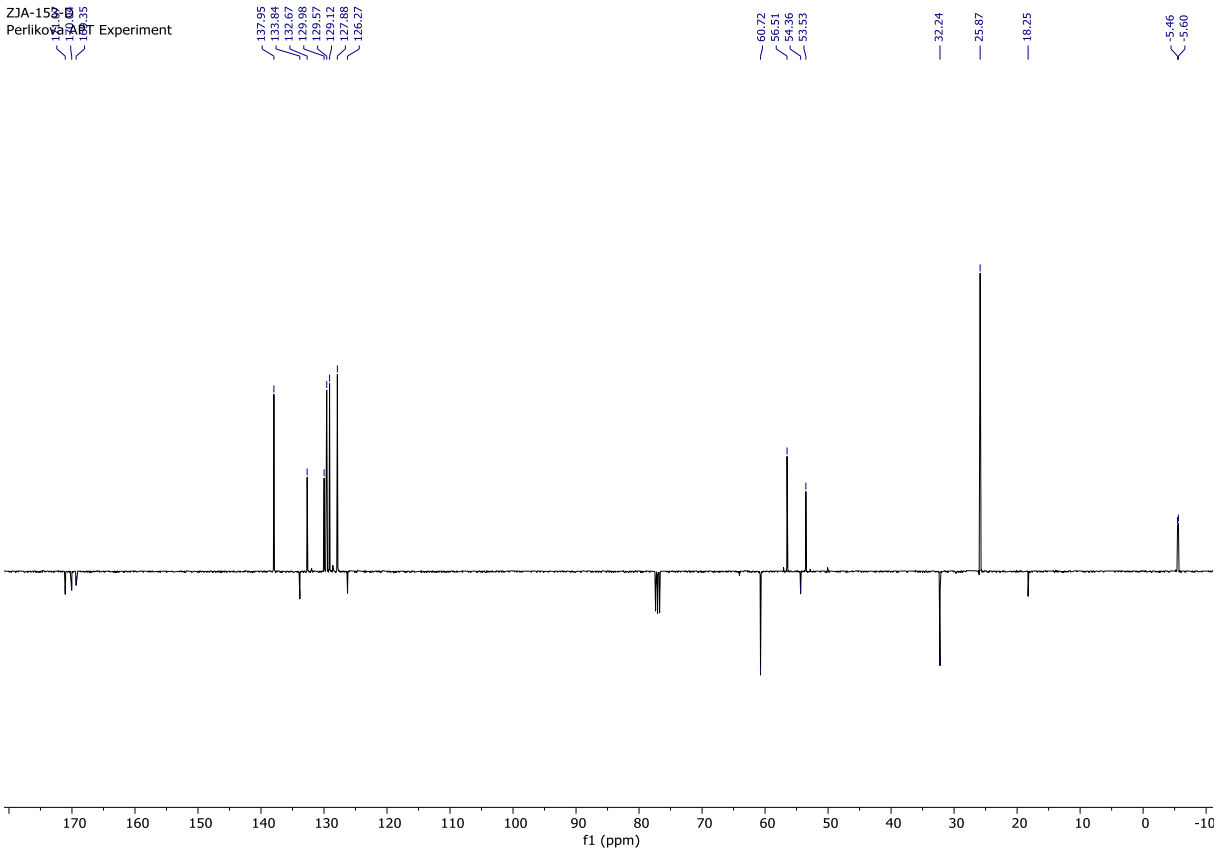

ZJA-145-B
Perkin Elmer 300 MHz FT Experiment
f1 (ppm)

13-major

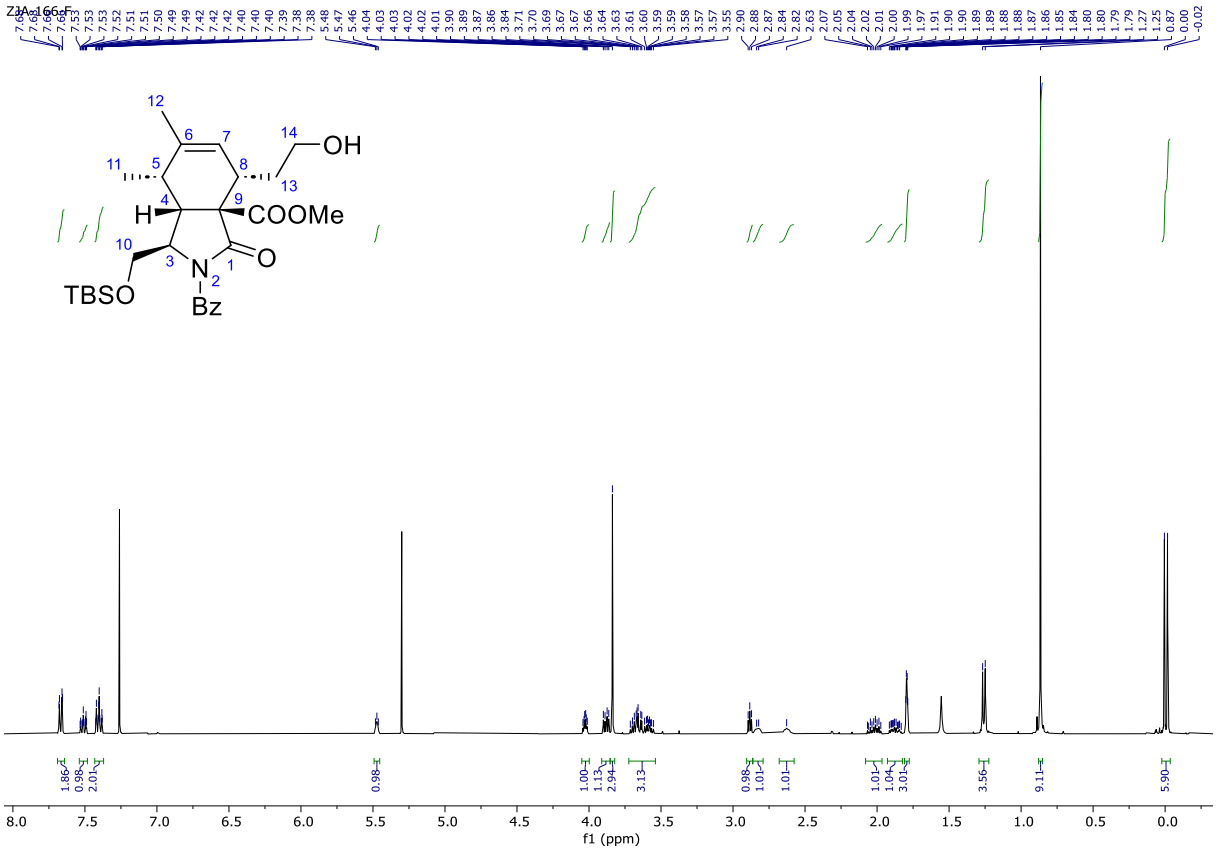


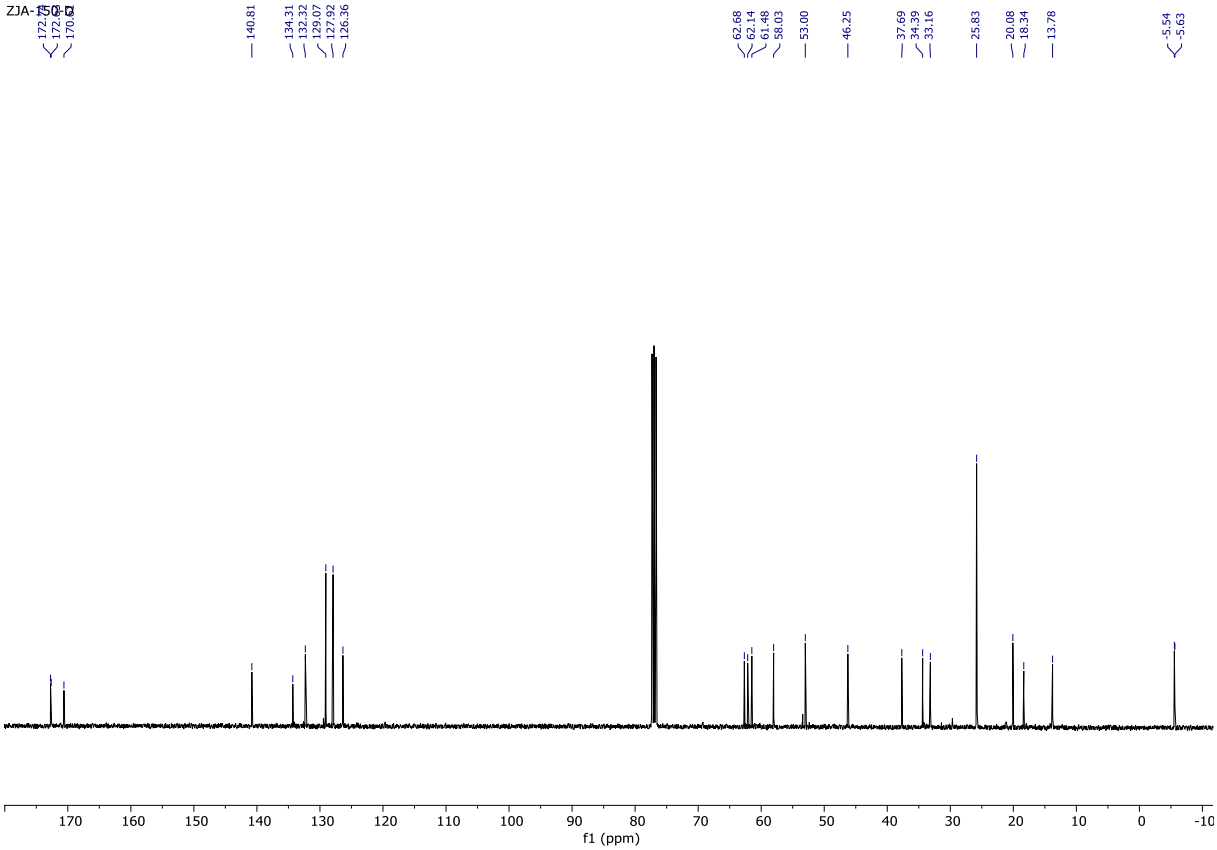
13-minor



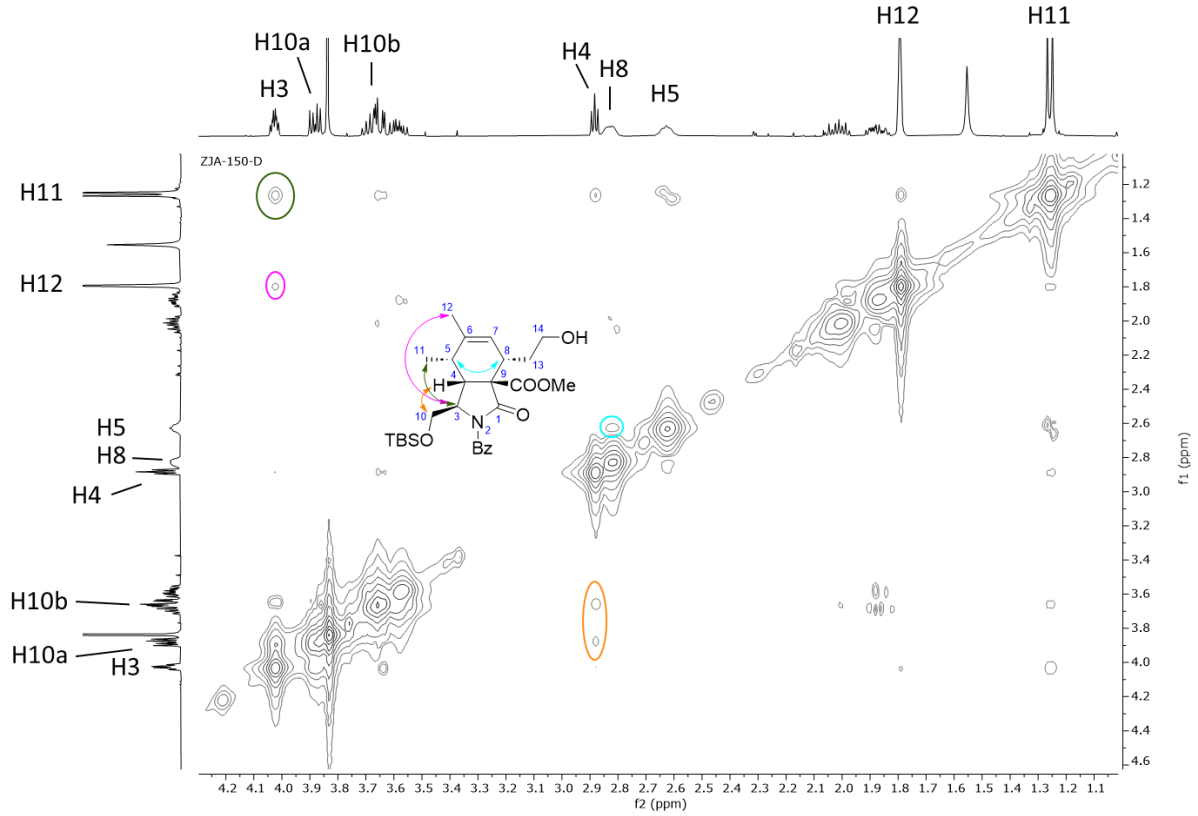


16

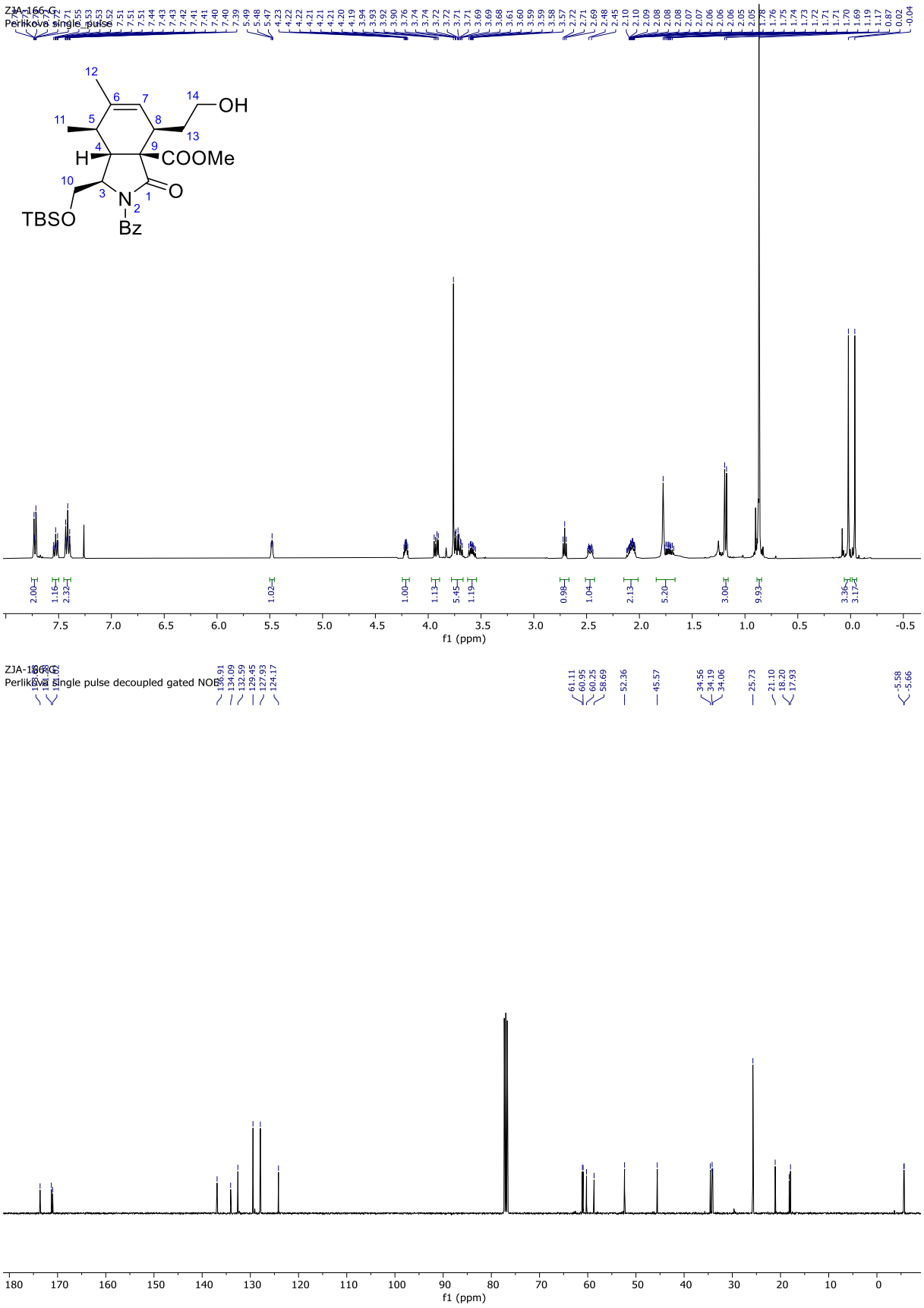

ZJA-166-F
12
6
7
14
OH
11
5
8
13
4
9
H
COOMe
10
3
N
2
1
O
TBSO
Bz
f1 (ppm)


ZJA-150-C
f1 (ppm)

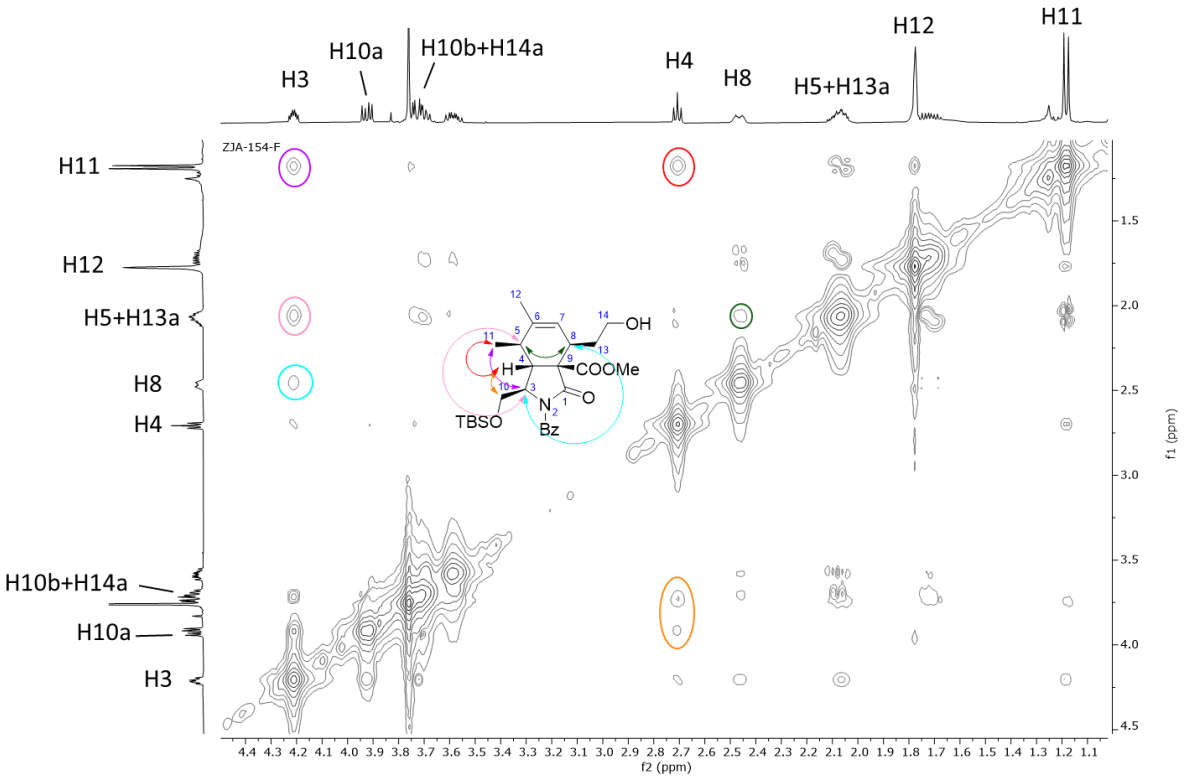
ROESY


H10a
H10b
H3
H4
H8
H5
H12
H11
ZJA-150-D
H11
H12
H5
H8
H4
H10b
H10a
H3
OH
COOMe
TBSO
Bz
f1 (ppm)
f2 (ppm)

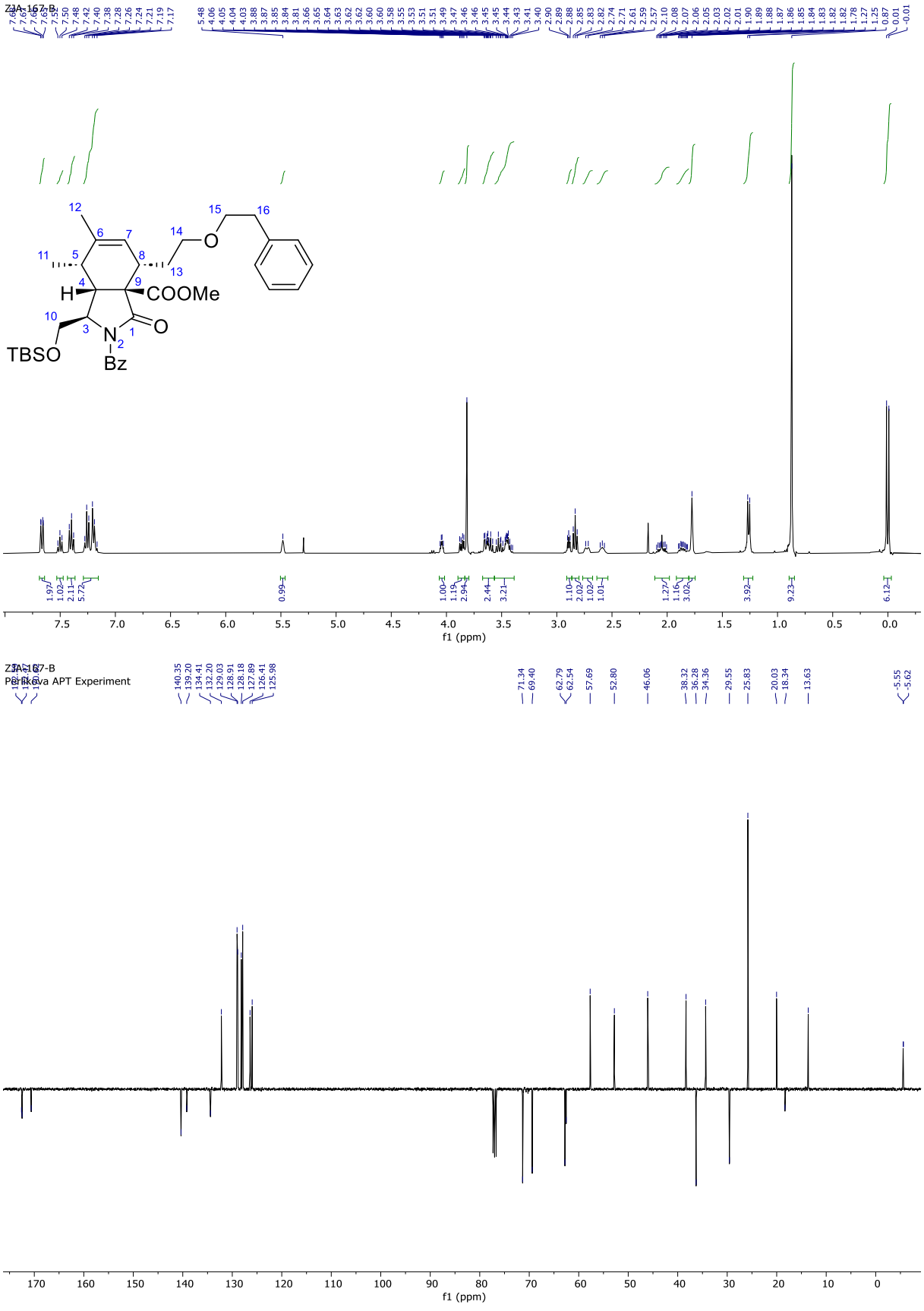
16’


ZJA-166-G
Perlikova single pulse
12
6
7
14
OH
11
5
8
13
4
9
H
COOMe
10
3
N
2
1
O
TBSO
Bz
2.00
1.16
2.32
1.02
1.00
1.13
5.45
1.19
0.98
1.04
2.13
5.20
3.00
9.93
3.36
3.17
f1 (ppm)
ZJA-166-G
Perlikova single pulse decoupled gated NOE
135.91
134.09
132.59
129.45
127.93
124.17
61.11
60.95
60.25
58.69
52.36
45.57
34.56
34.19
34.06
25.73
21.10
18.20
17.93
-5.58
-5.66
f1 (ppm)

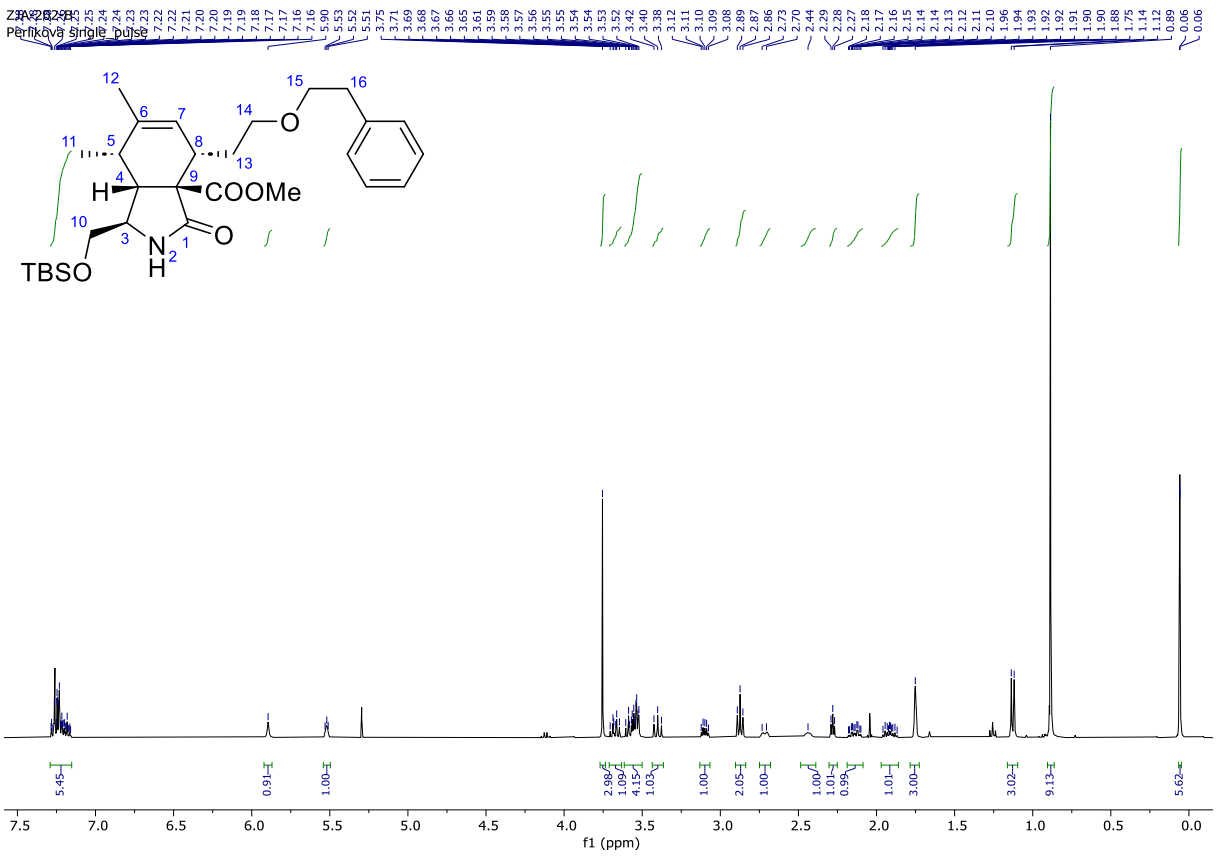
ROESY

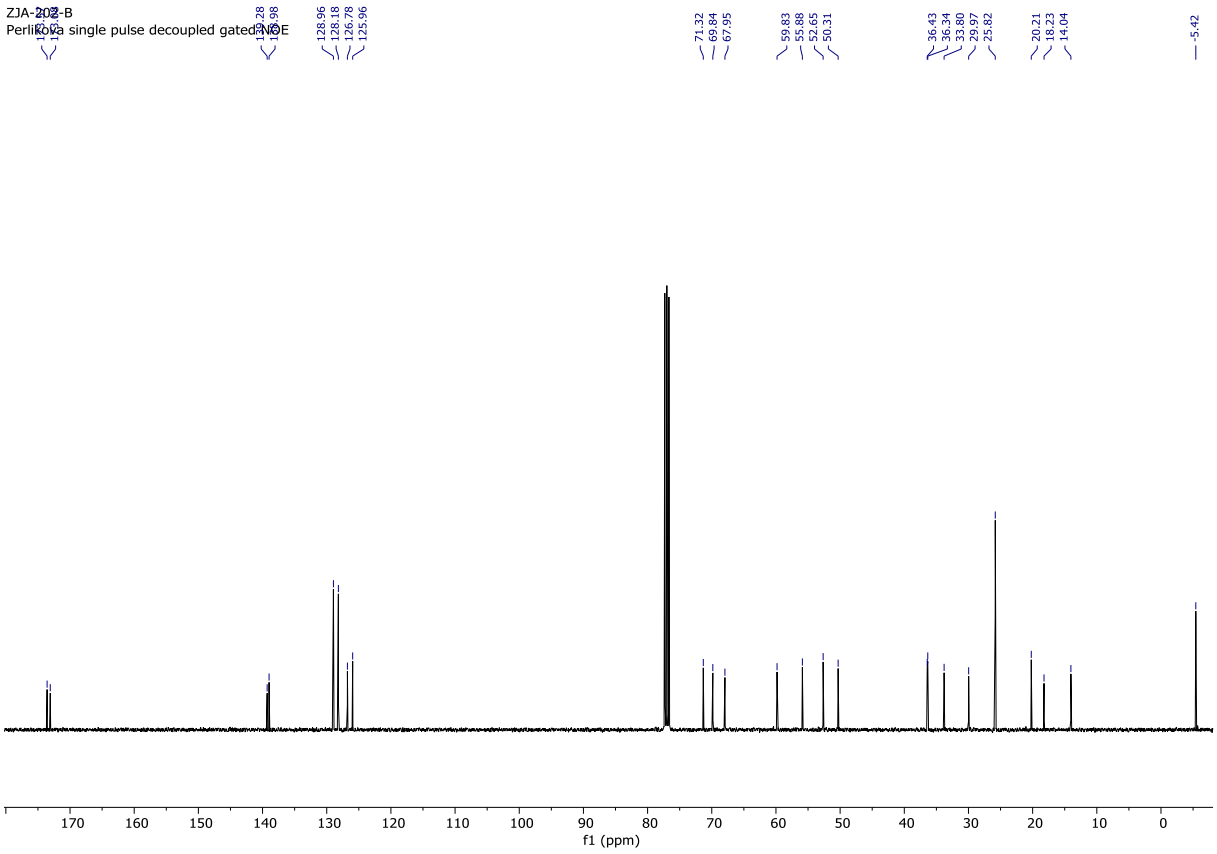

H3
H10a
H10b+H14a
H4
H8
H5+H13a
H12
H11
ZJA-154-F
OH
COOMe
TBSO
Bz
f2 (ppm)
f1 (ppm)

17

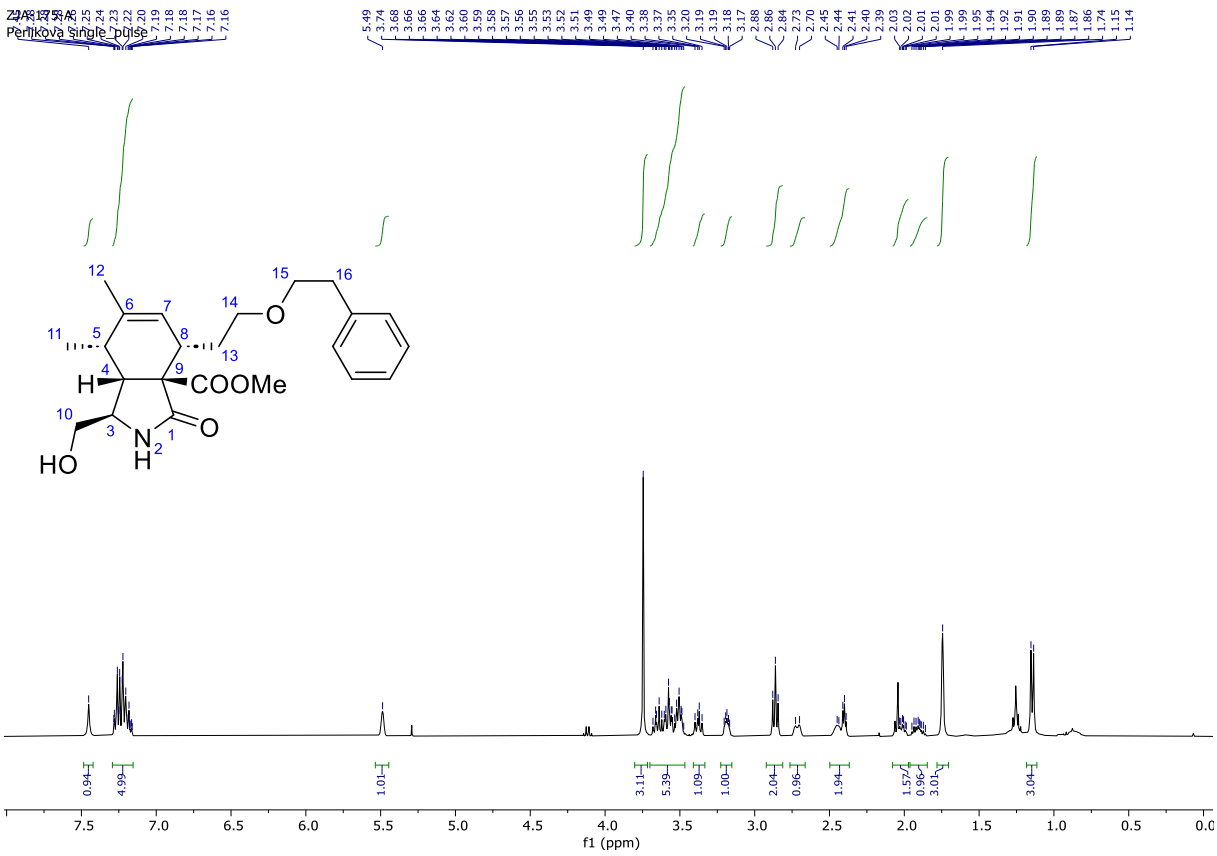

ZJA-167-B
TBSO
Bz
COOMe
f1 (ppm)
ZJA-167-B
Perkova APT Experiment
f1 (ppm)

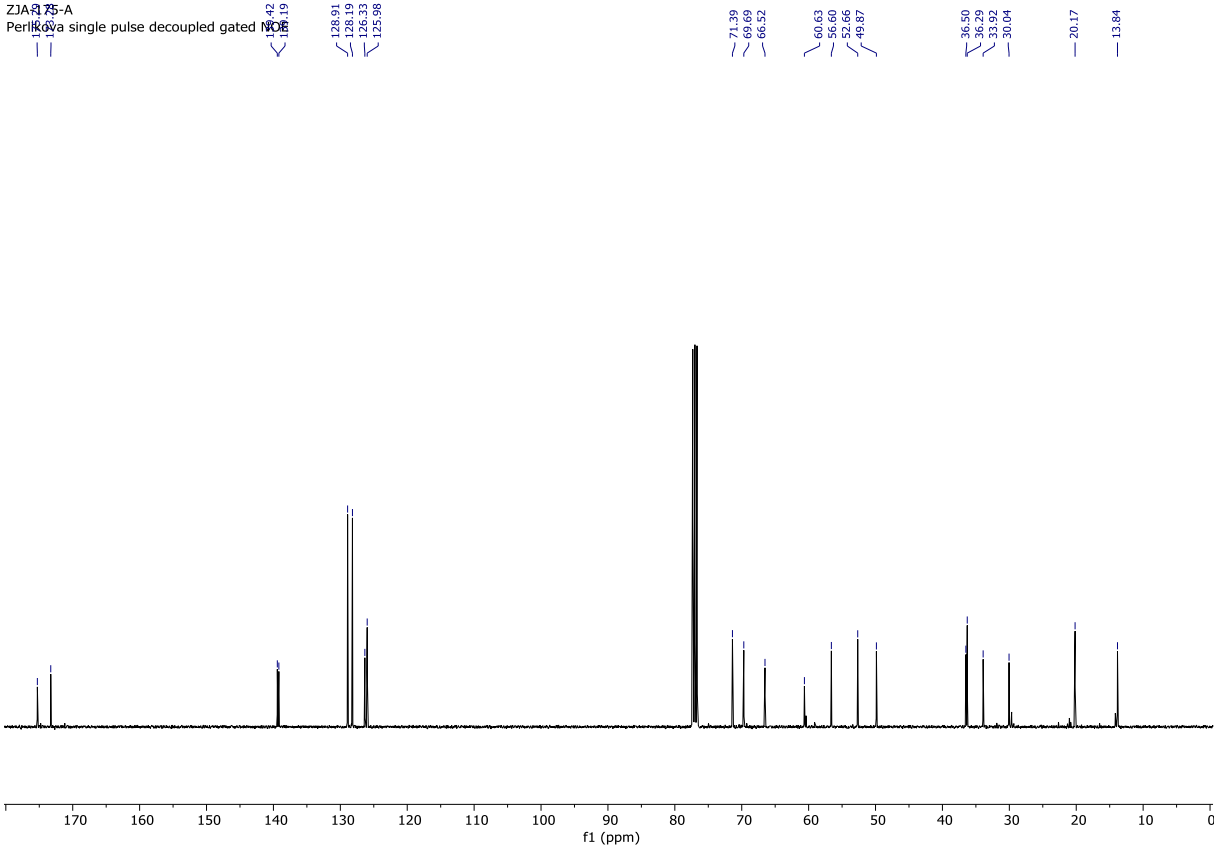
18


ZJA-202-B
Perlikova single pulse
12
6
7
14
O
15
16
11
5
8
13
4
9
H
COOMe
10
3
N
H
2
1
O
TBSO
5.45
0.91
1.00
2.98
1.09
4.15
1.03
1.00
2.05
1.00
1.00
1.01
0.99
1.01
3.00
3.02
9.13
5.62
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
f1 (ppm)

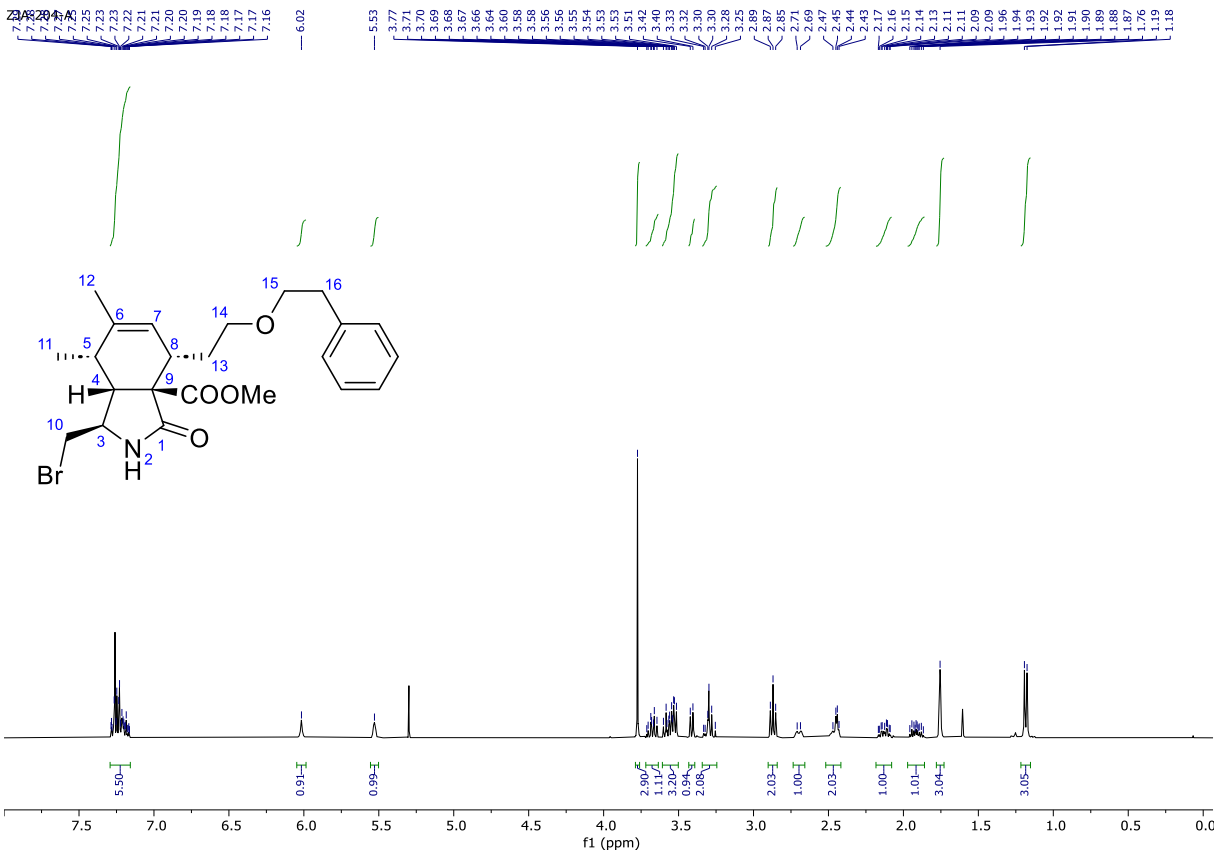

ZJA-202-B
Perlikova single pulse decoupled gated NOE
139.28
129.98
128.96
128.18
126.78
125.96
71.32
69.84
67.95
59.83
55.88
52.65
50.31
36.43
36.34
33.80
29.97
25.82
20.21
18.23
14.04
-5.42
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

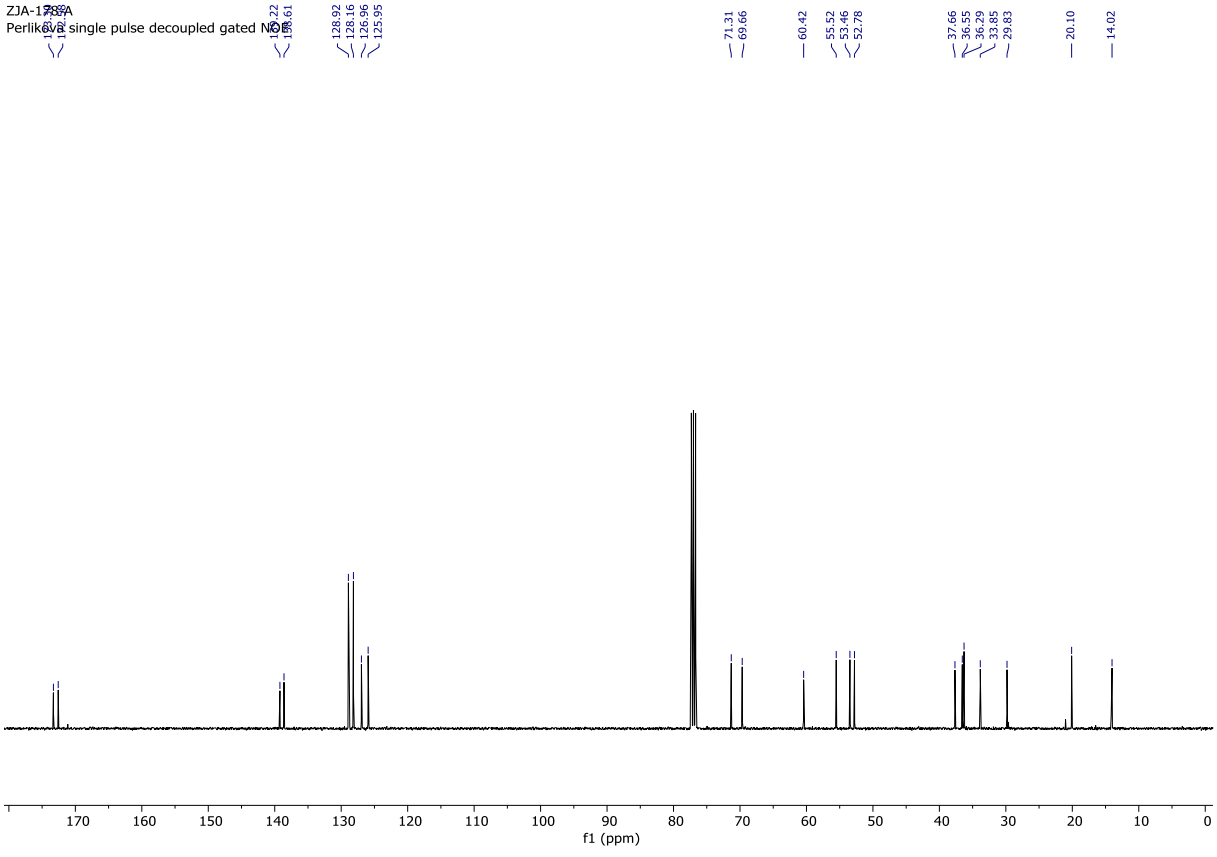
19


ZJA-175-A
Perlikova single pulse
COOMe
HO
f1 (ppm)

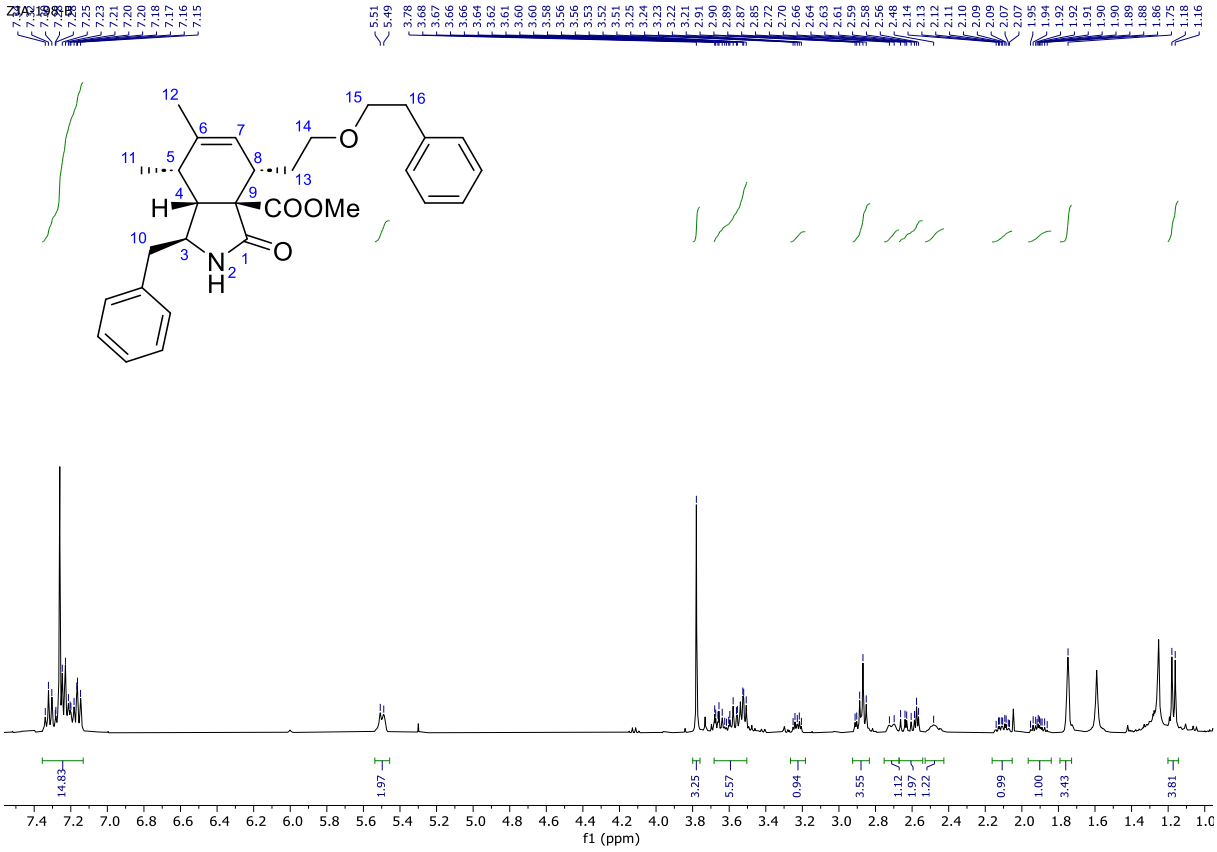

ZJA-175-A
Perlikova single pulse decoupled gated NOE
f1 (ppm)

20

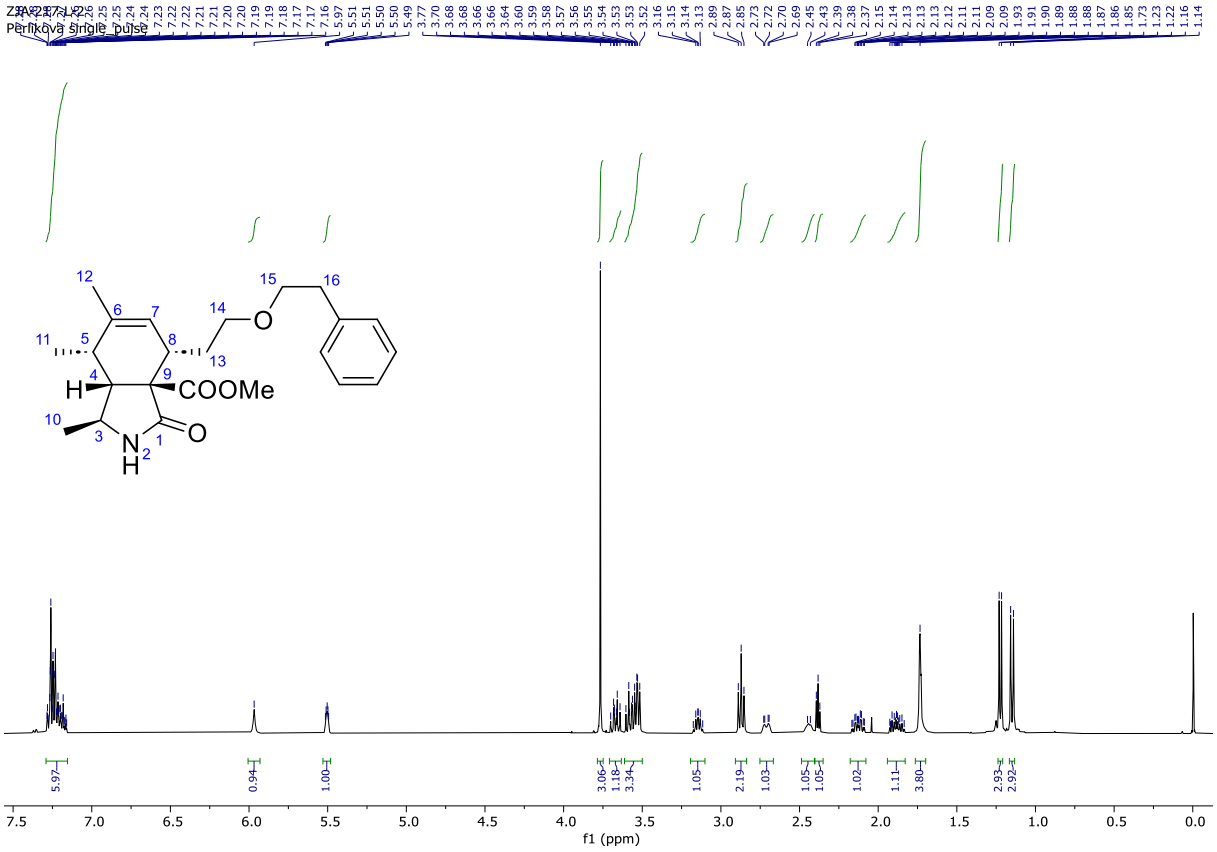


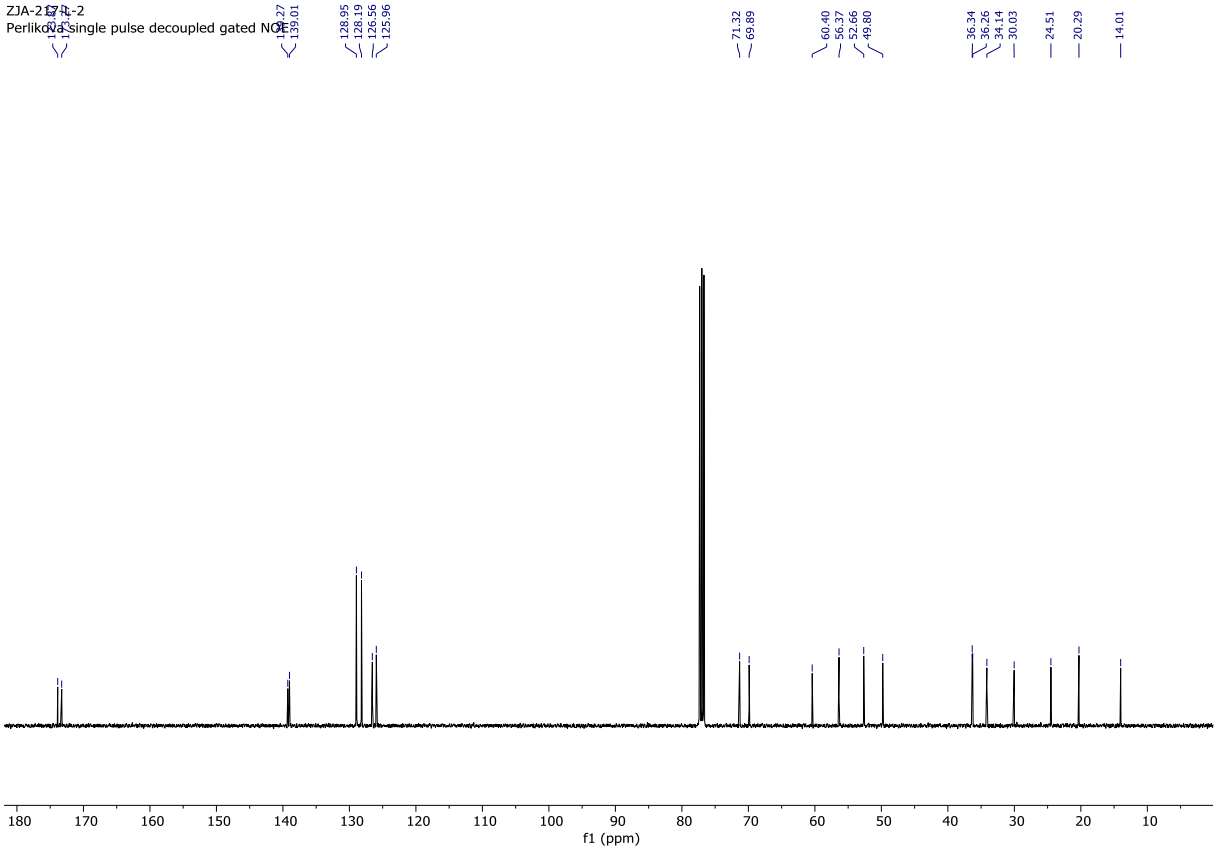


21

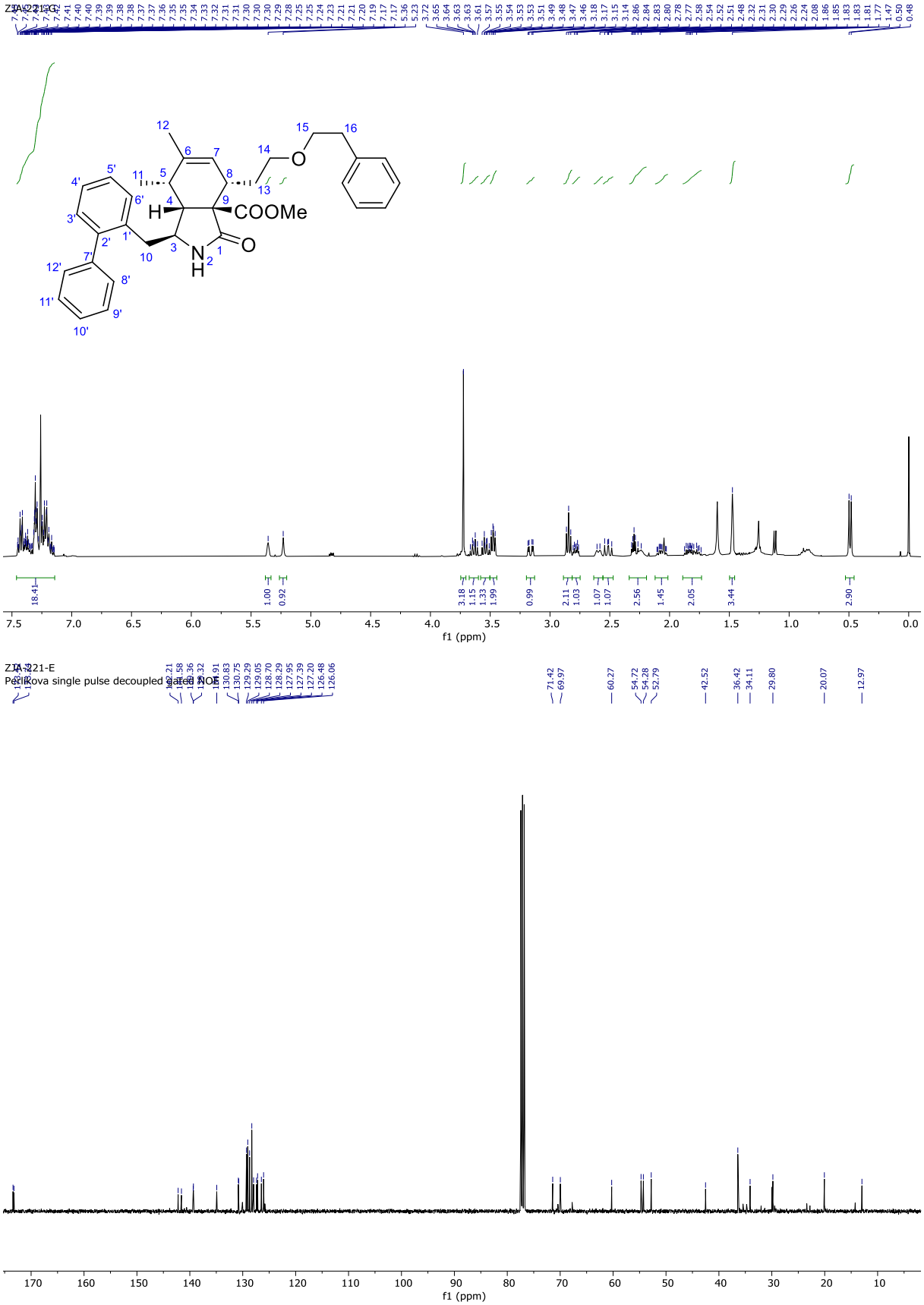

12
6
7
14
O
15
16
11
5
8
13
4
9
H
COOMe
10
3
N
1
2
H
O
14.83
1.97
3.25
5.57
0.94
3.55
1.12
1.97
1.22
0.99
1.00
3.43
3.81
7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0
f1 (ppm)

22

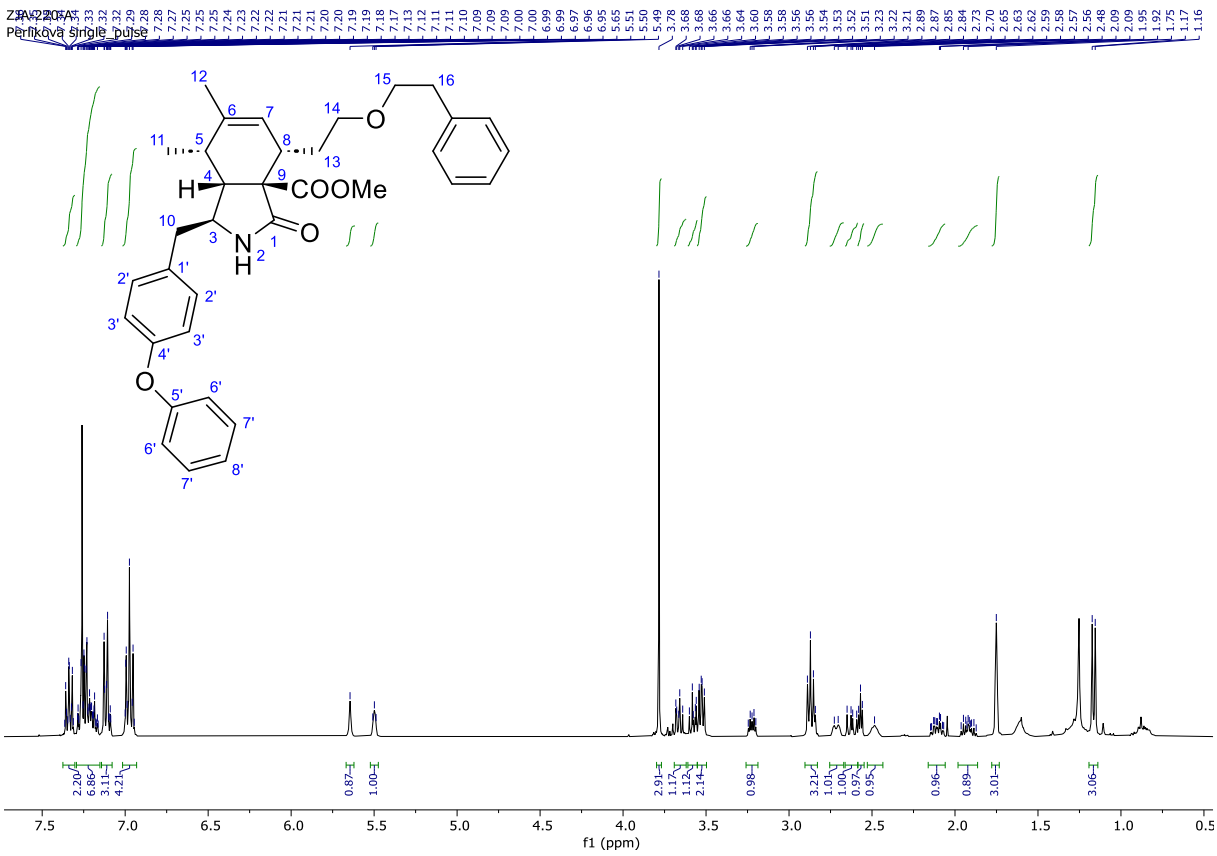

ZJA-217-1-2
Perlikova single pulse
COOMe
f1 (ppm)

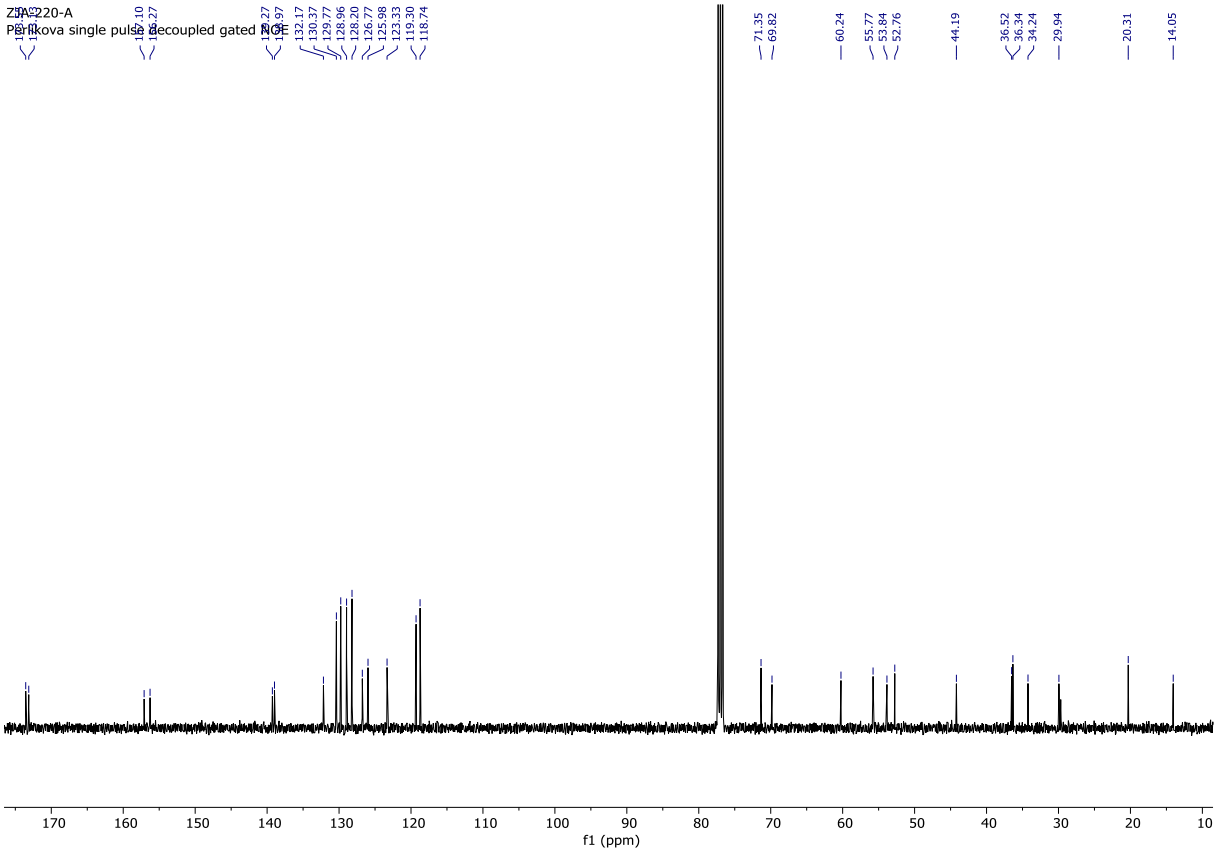

ZJA-217-1-2
Perlikova single pulse decoupled gated NOE
f1 (ppm)

23

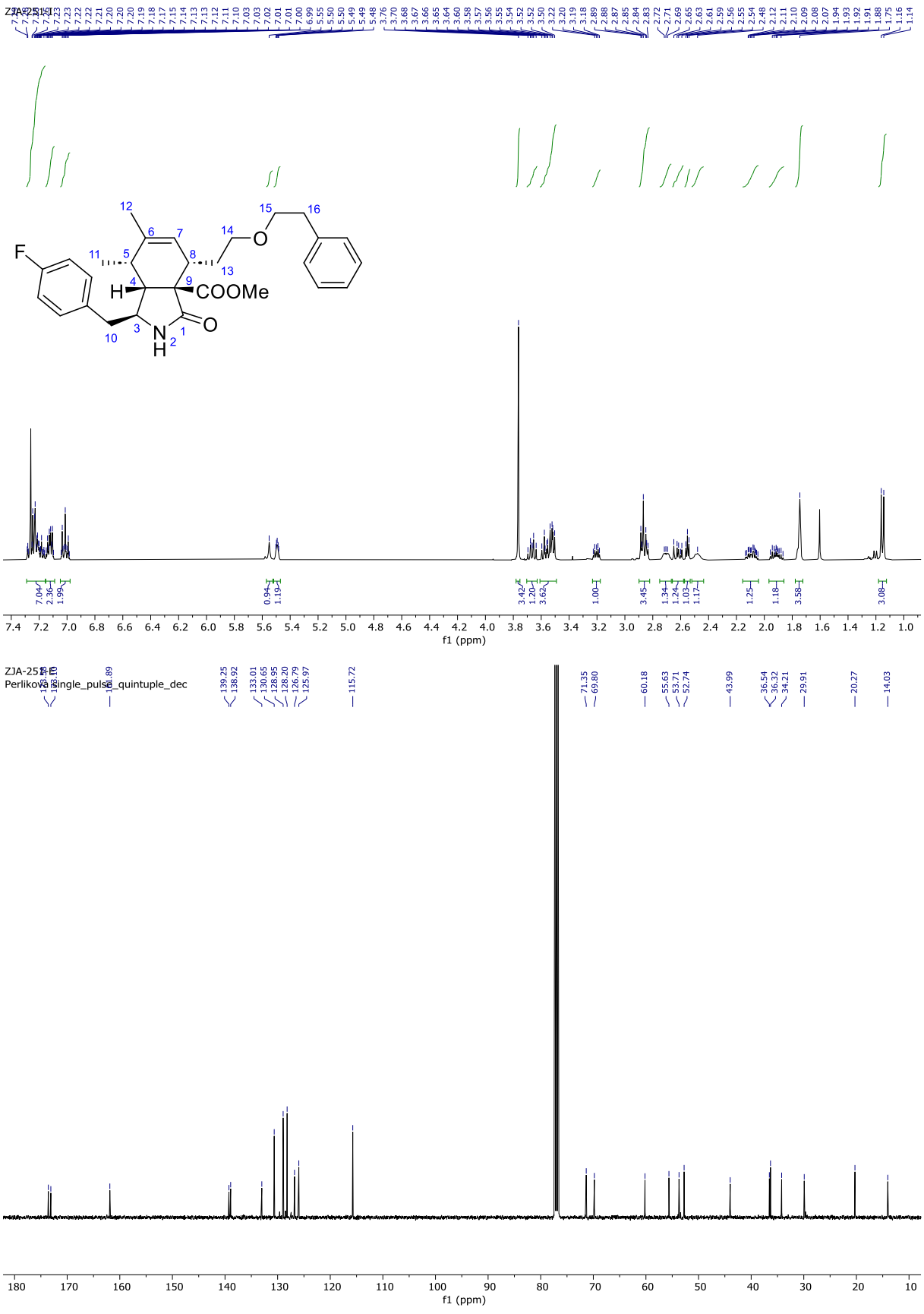


24

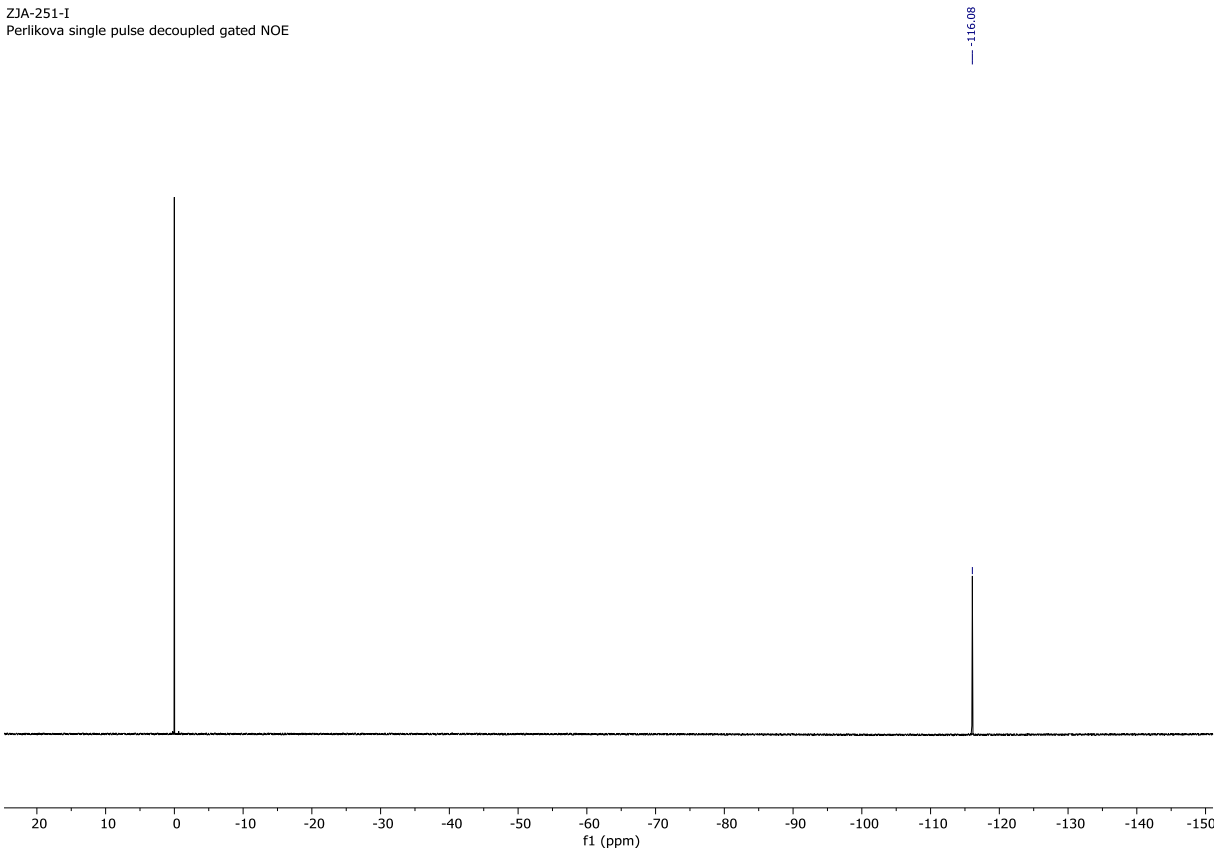

ZIA-220-A
Perlikova single_pulse
COOMe
f1 (ppm)


ZIA-220-A
Perlikova single pulse decoupled gated NOE
f1 (ppm)

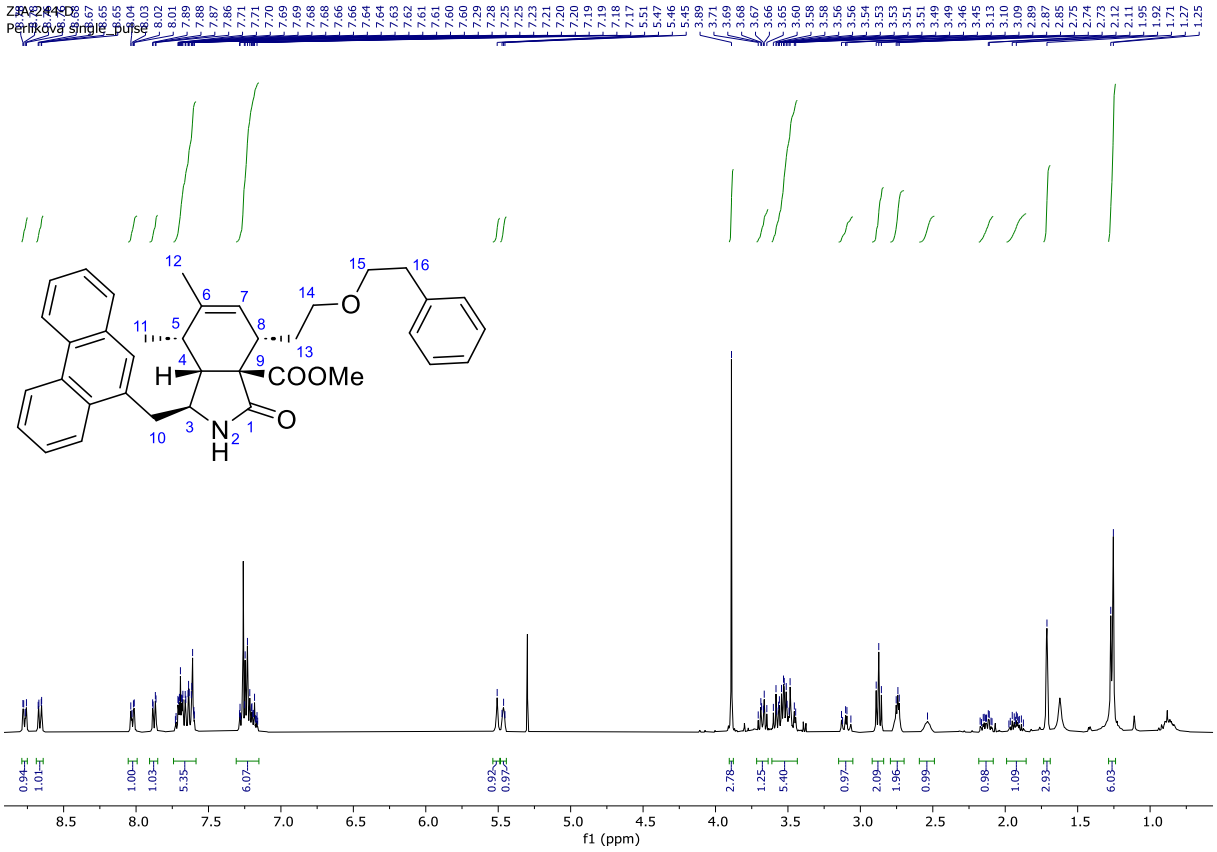
25

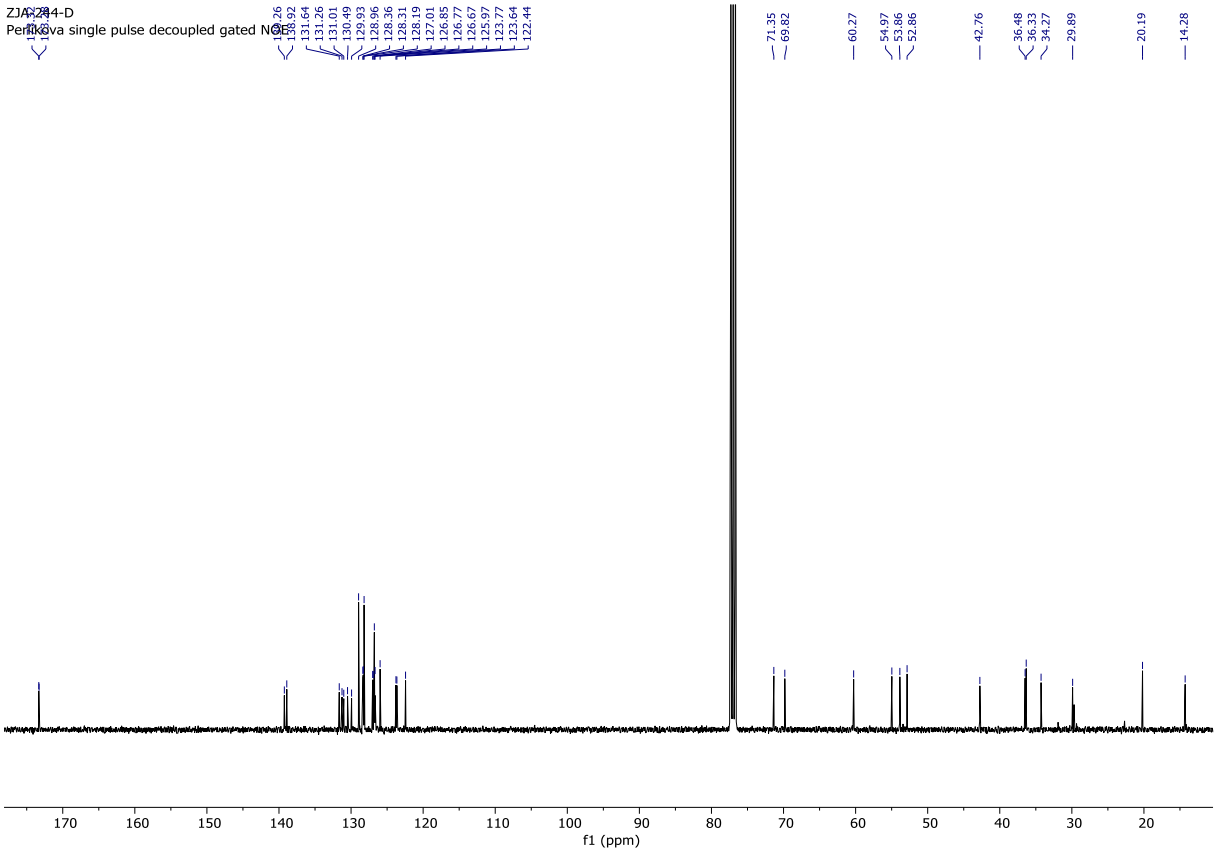


ZJA-251-I
Perlikova single pulse decoupled gated NOE

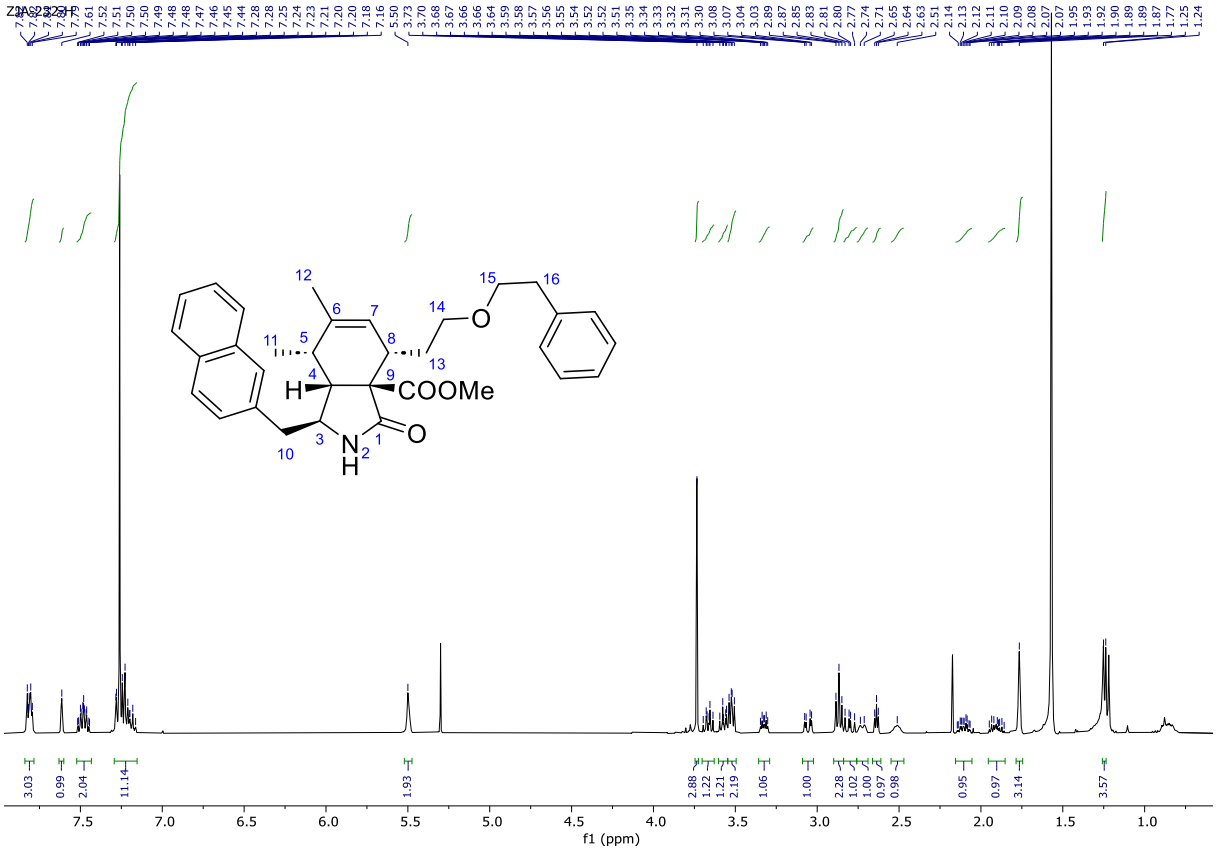


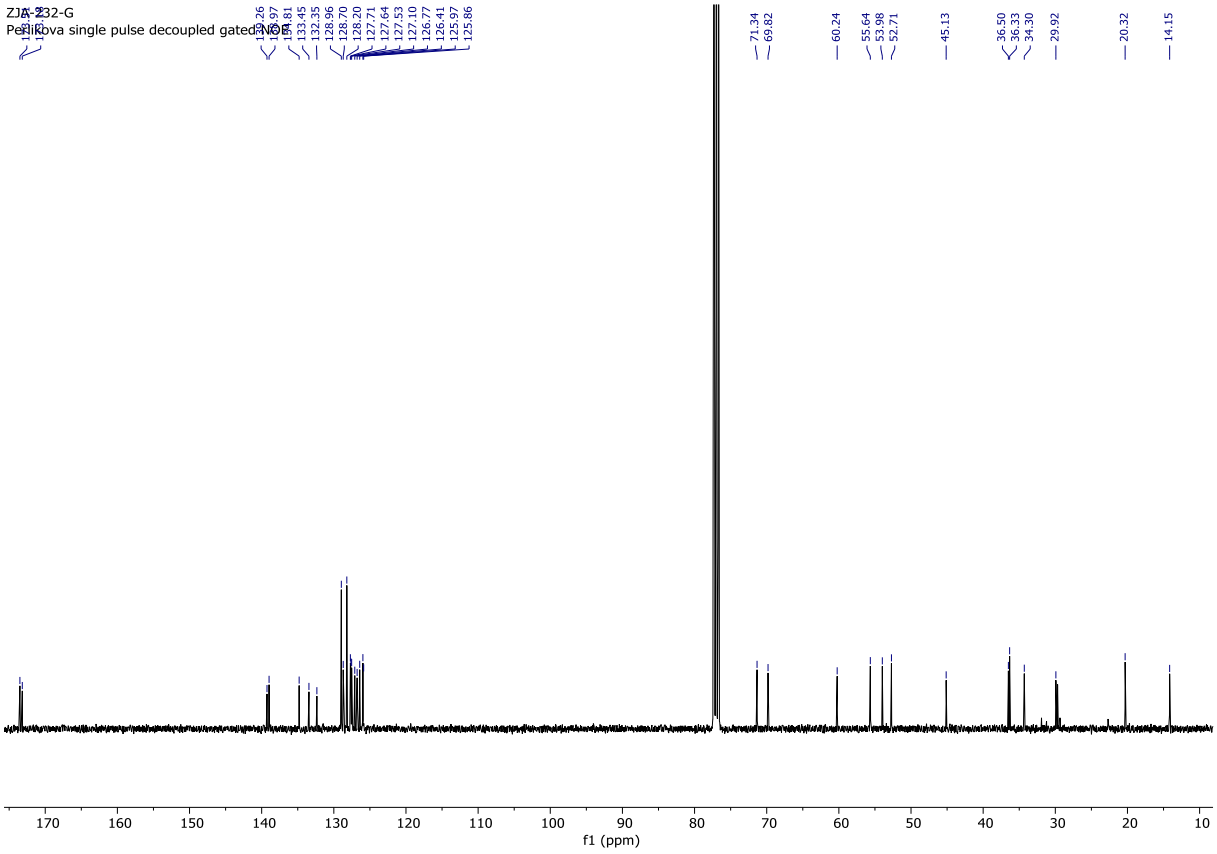
26


ZJA-244-D
Perfilova single pulse
12
6
7
14
O
15
16
11
5
8
13
4
9
H
COOMe
10
3
N
2
1
O
H
f1 (ppm)

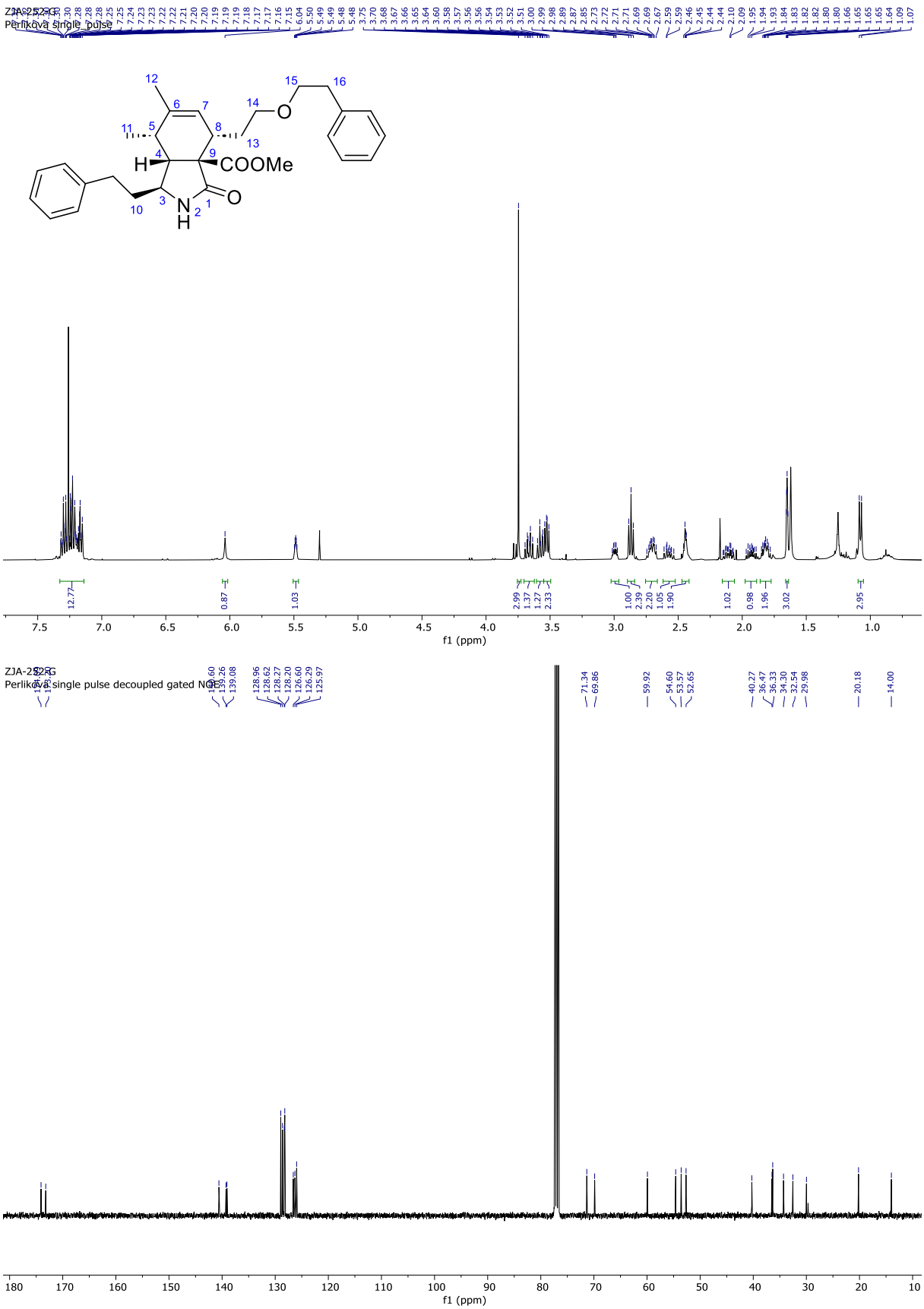

ZJA-244-D
Perfilova single pulse decoupled gated NOE
71.35
69.82
60.27
54.97
53.86
52.86
42.76
36.48
36.33
34.27
29.89
20.19
14.28
f1 (ppm)

27

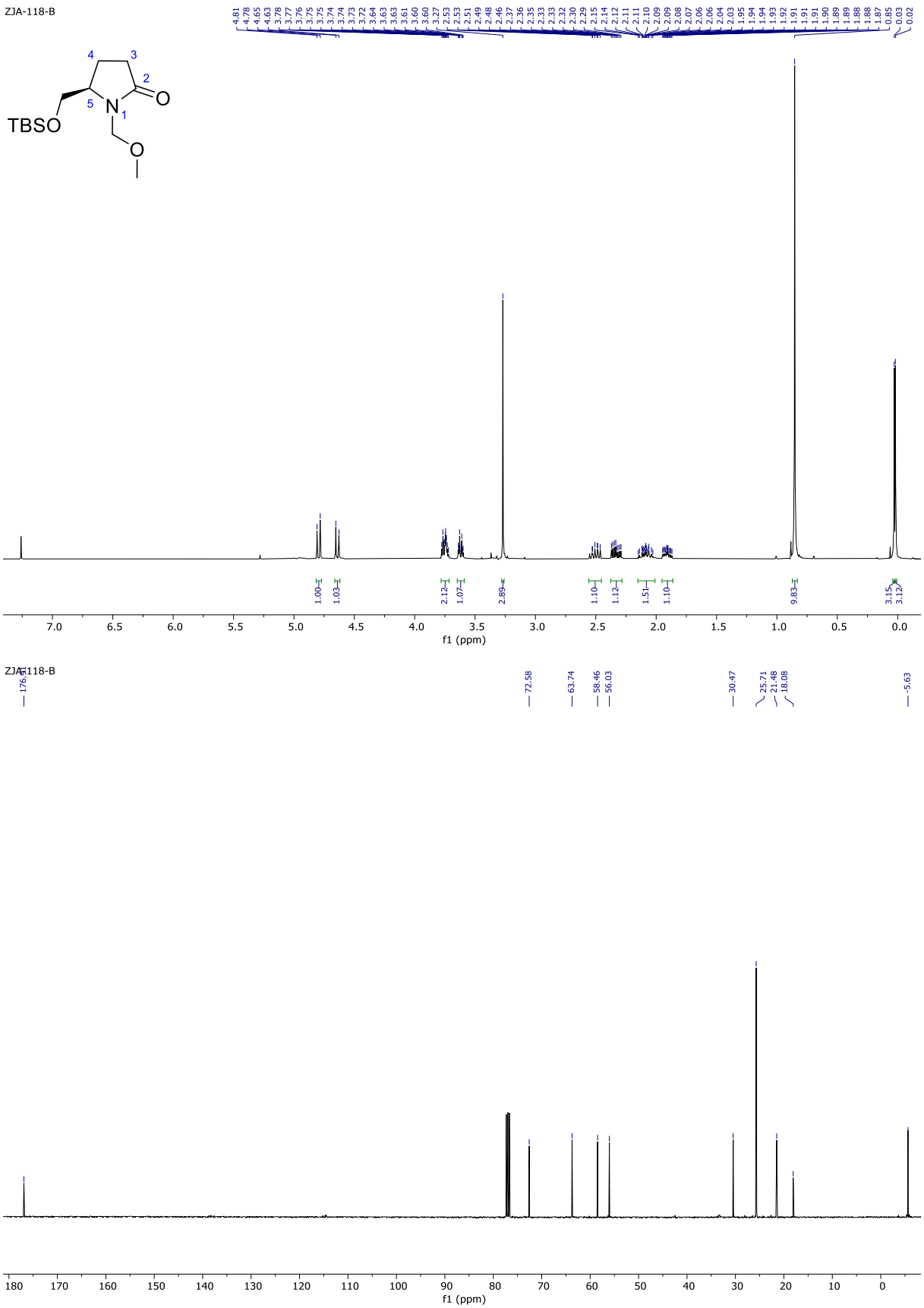

12
15
16
6
7
14
O
11
5
8
13
4
9
H
COOMe
10
3
N
2
1
O
H
3.03
0.99
2.04
11.14
1.93
2.88
1.22
1.21
2.19
1.06
1.00
2.28
1.02
1.00
0.97
0.98
0.95
0.97
3.14
3.57
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


ZJA-232-G
Pelikova single pulse decoupled gated NOE
71.34
69.82
60.24
55.64
53.98
52.71
45.13
36.50
36.33
34.30
29.92
20.32
14.15
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

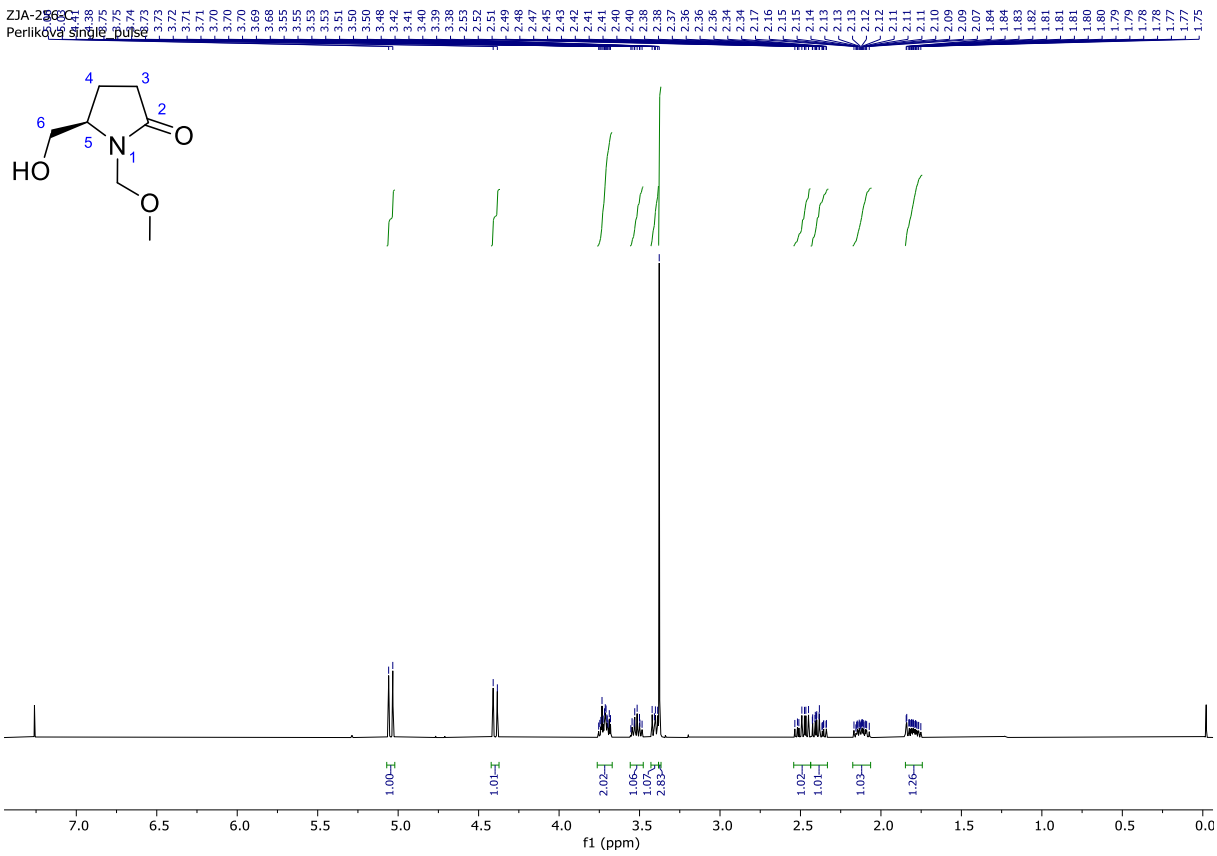
28

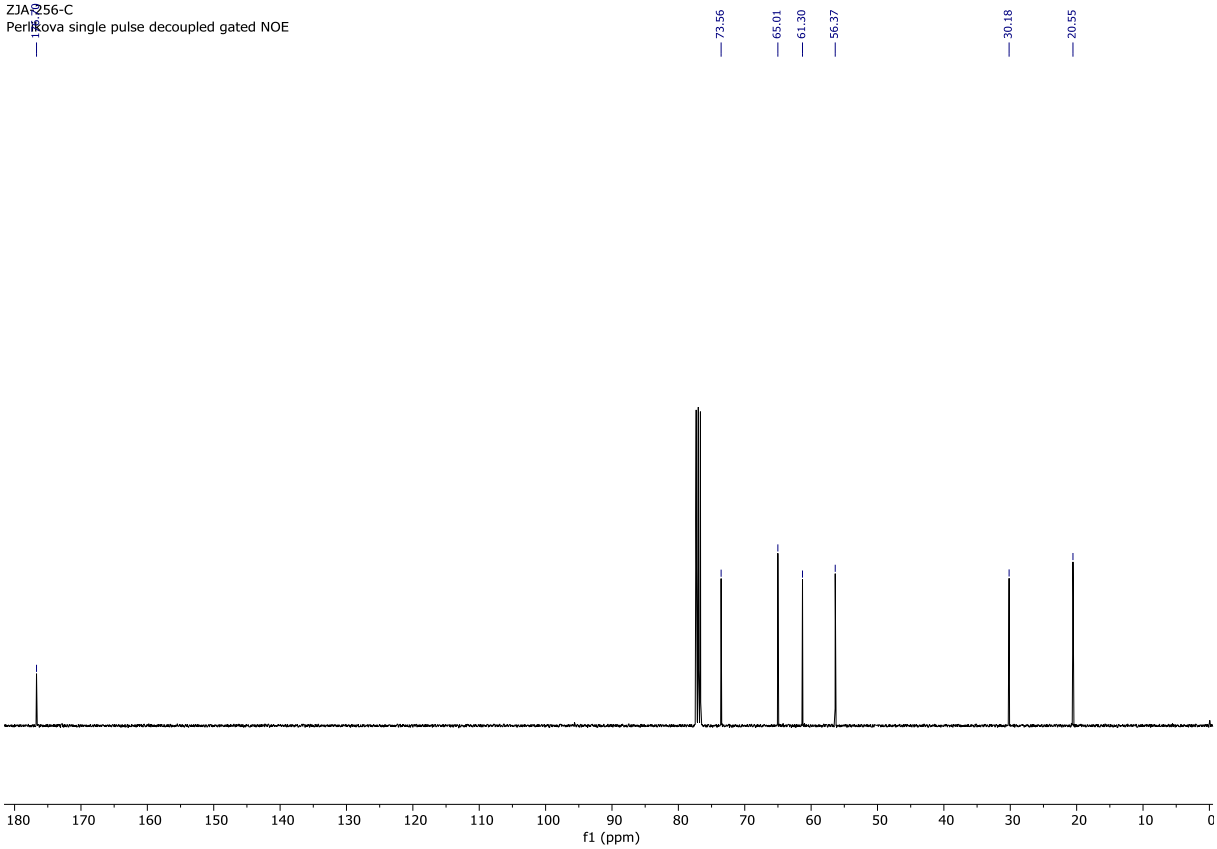

ZJA-252-G
Perlikova single pulse
12
6
7
14
O
15
16
11
5
8
13
4
9
H
COOMe
3
10
N
2
1
H
O
12.77
0.87
1.03
2.99
1.37
1.27
2.33
1.00
2.39
2.20
1.05
1.90
1.02
0.98
1.96
3.02
2.95
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)
ZJA-252-G
Perlikova single pulse decoupled gated NOE
171.60
139.26
139.08
128.96
128.62
128.27
128.20
126.60
126.29
125.97
71.34
69.86
59.92
54.60
53.57
52.65
40.27
36.47
36.33
34.30
32.54
29.98
20.18
14.00
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

S1

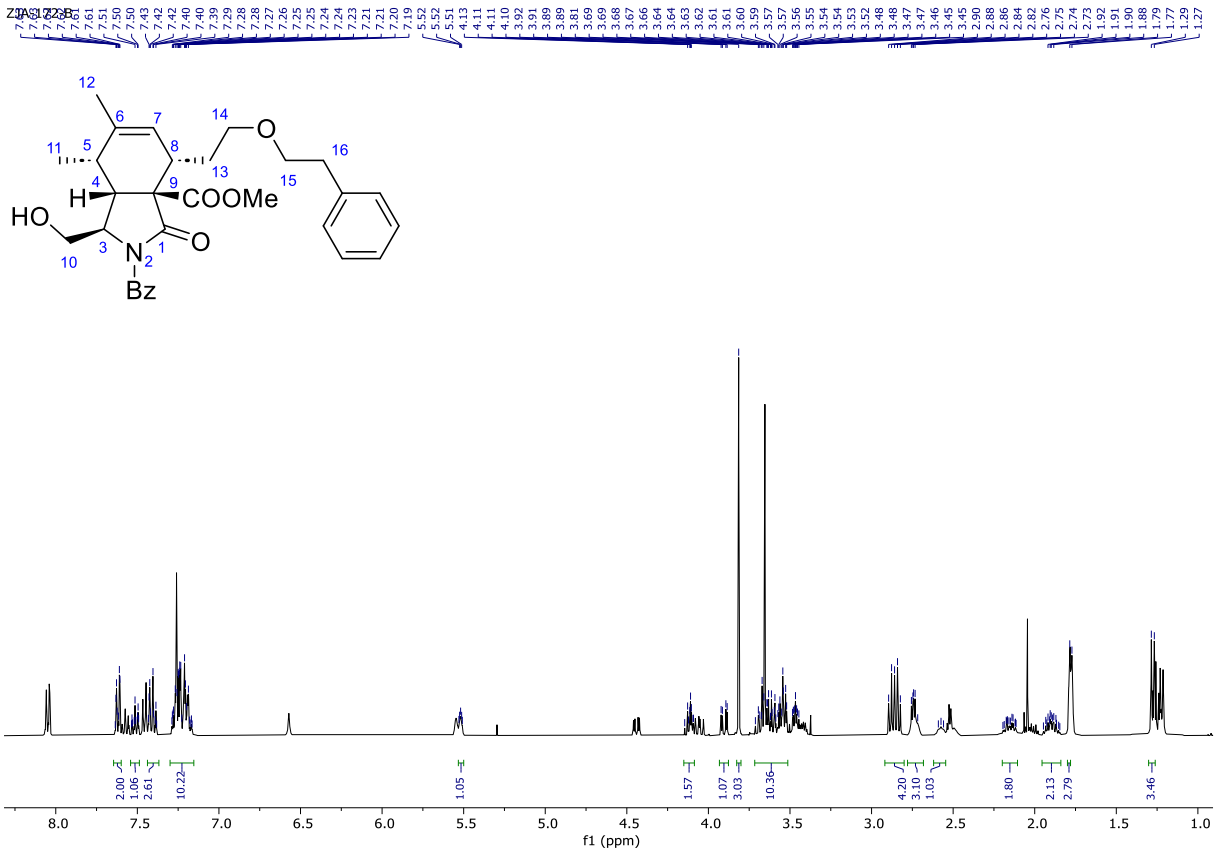


S2

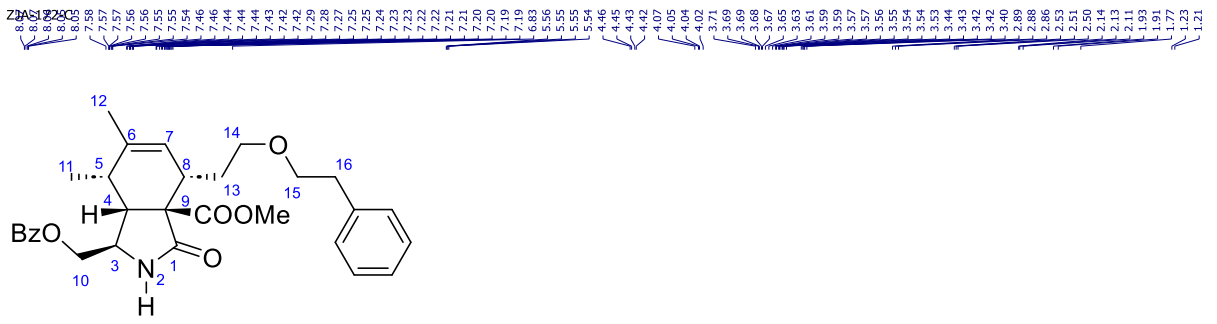

ZJA-256-C
Perlikova single pulse
HO
O
N
O
1.00
1.01
2.02
1.06
1.07
2.83
1.02
1.01
1.03
1.26
f1 (ppm)


ZJA-256-C
Perlikova single pulse decoupled gated NOE
73.56
65.01
61.30
56.37
30.18
20.55
f1 (ppm)

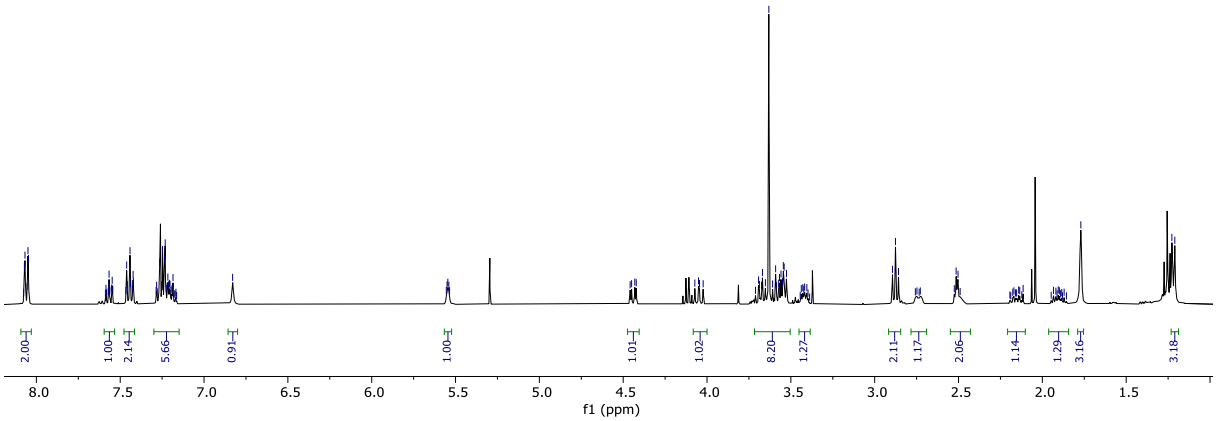
S3a

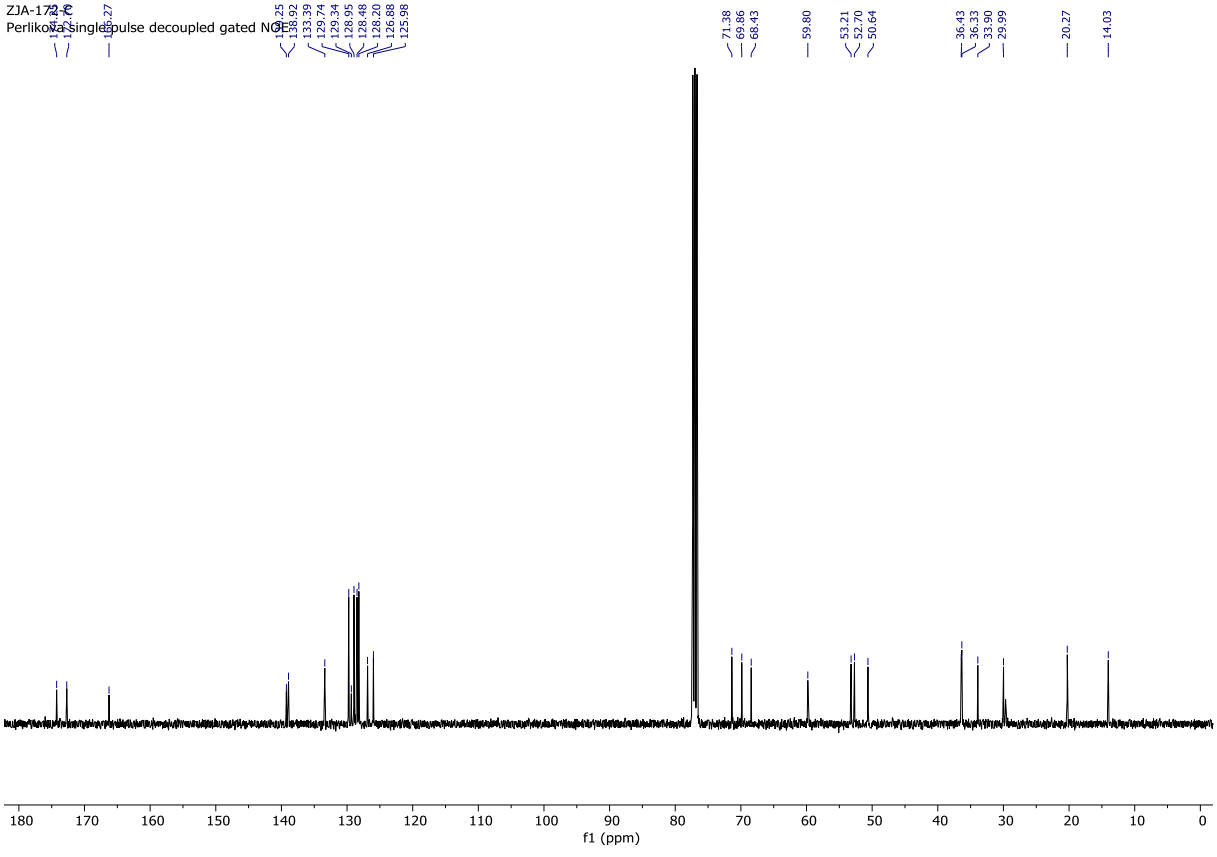

ZJAS1228
12
6
7
14
O
11
5
8
16
13
4
9
15
H
COOMe
HO
3
1
O
10
N
2
Bz
2.00
1.06
2.61
10.22
1.05
1.57
1.07
3.03
10.36
4.20
3.10
1.03
1.80
2.13
2.79
3.46
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

S3b



12
6
7
14
O
11
5
8
16
13
15
4
9
H
COOMe
BzO
3
N
1
O
10
2
H


2.00
1.00
2.14
5.66
0.91
1.00
1.01
1.02
8.20
1.27
2.11
1.17
2.06
1.14
1.29
3.16
3.18
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
f1 (ppm)


ZJA-172-C
Perlikowa,Esingle pulse decoupled gated NOE
138.92
133.39
129.74
129.34
128.95
128.48
128.20
126.88
125.98
71.38
69.86
68.43
59.80
53.21
52.70
50.64
36.43
36.33
33.90
29.99
20.27
14.03
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)