Supporting Information for

SYNTHESIS OF *TRANS*-2,6-PIPERIDINEDICARBOXAMIDE USING THE UGI REACTION. A PLAUSIBLE MODEL FOR THE BIOSYNTHESIS OF HALICHONADIN P

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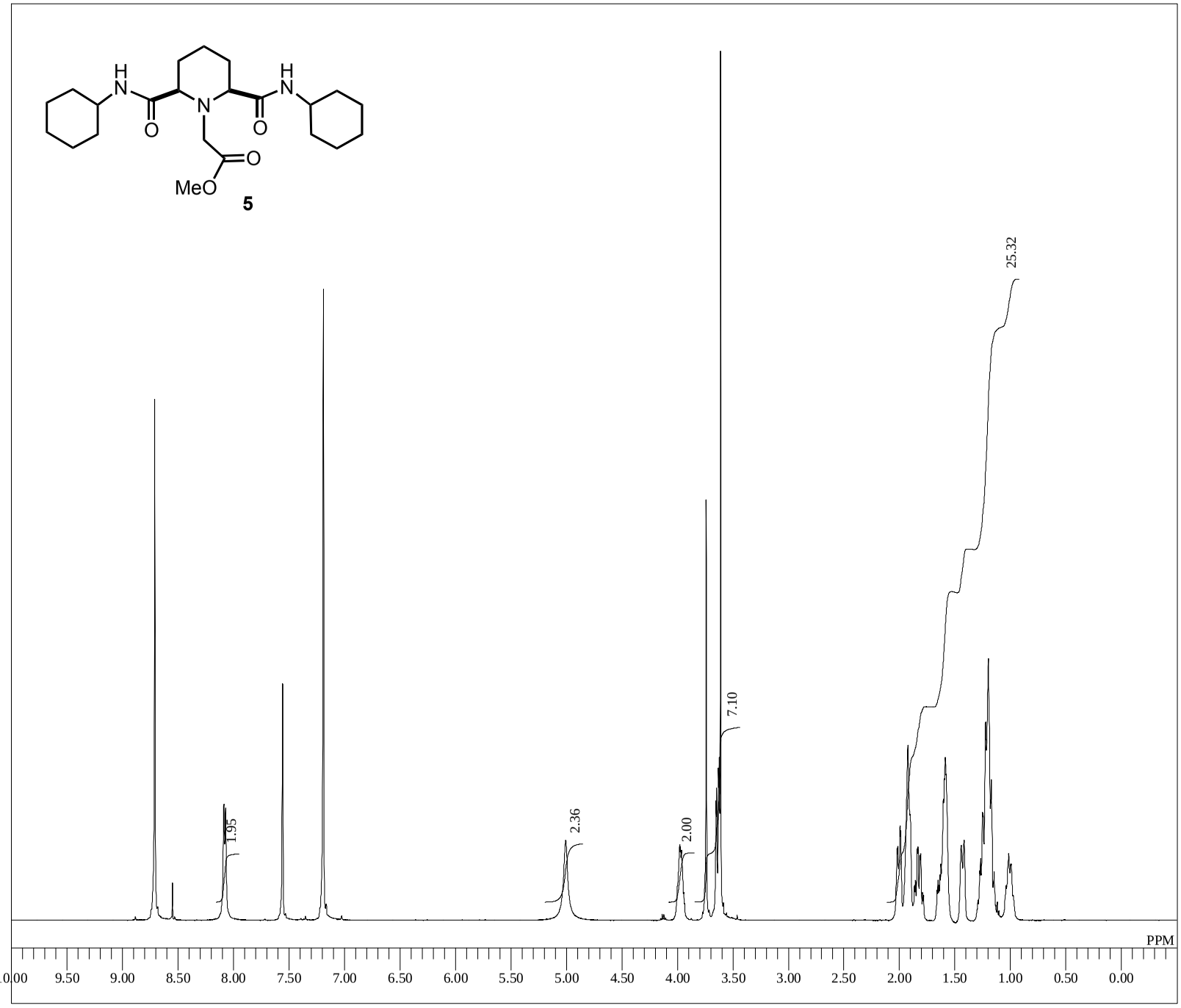

DFILE	AKI 2139 pyr_proton.als
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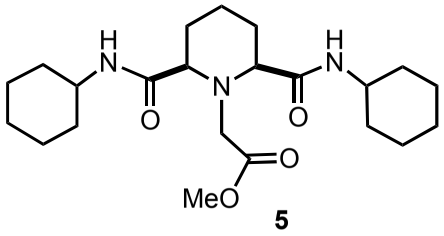
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	13107
FREQU	7507.51 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	20.3 c
SLVNT	C5D5N
EXREF	7.19 ppm
BF	0.12 Hz
RGAIN	40



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DFILE	halicho K -OMe proton.als
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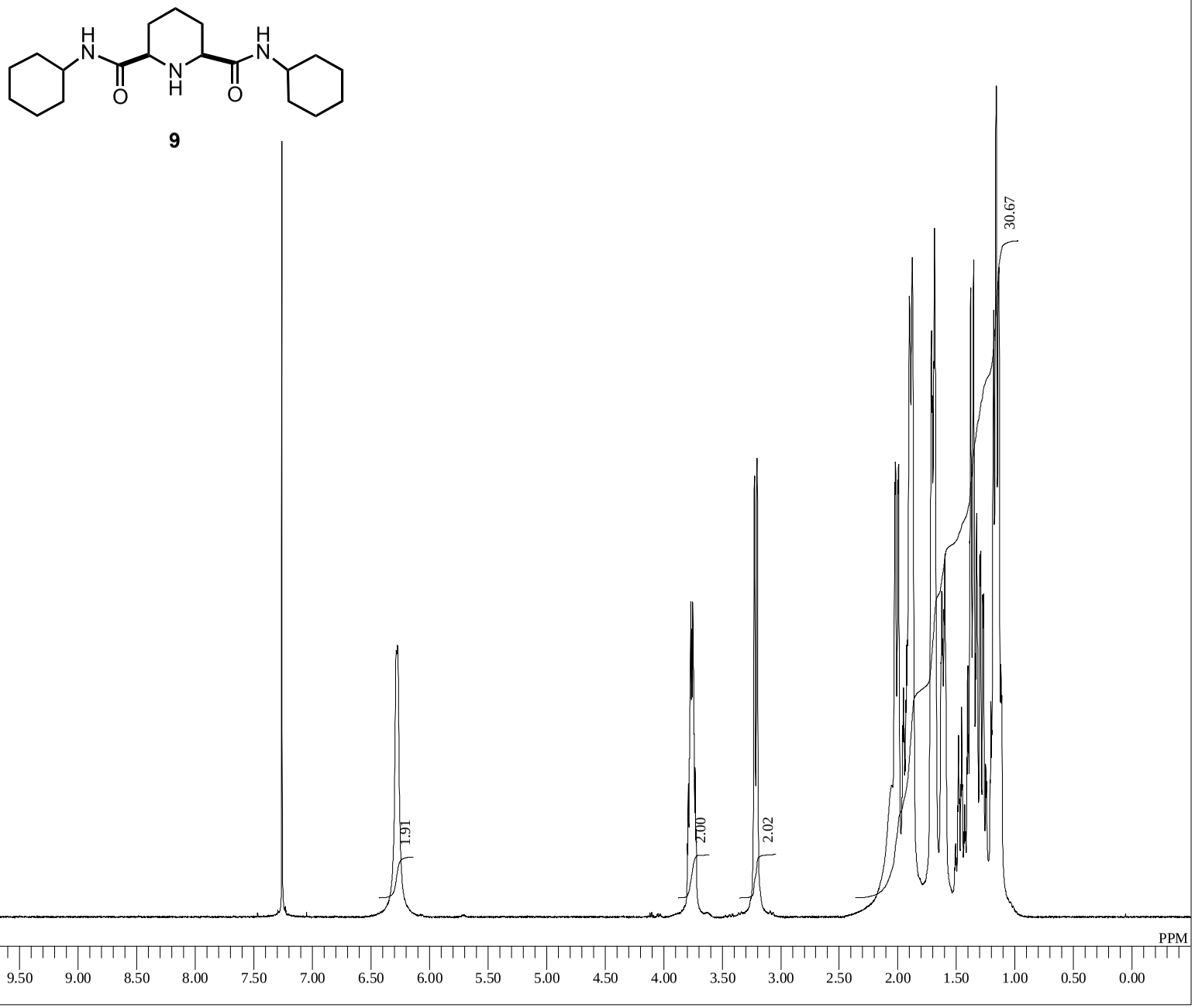
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16384
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	20.1 c
SLVNT	CDCL3
EXREF	7.26 ppm
BF	0.12 Hz
RGAIN	40



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COMNT	single_pulse
DATIM	2015-11-10 16:15:56
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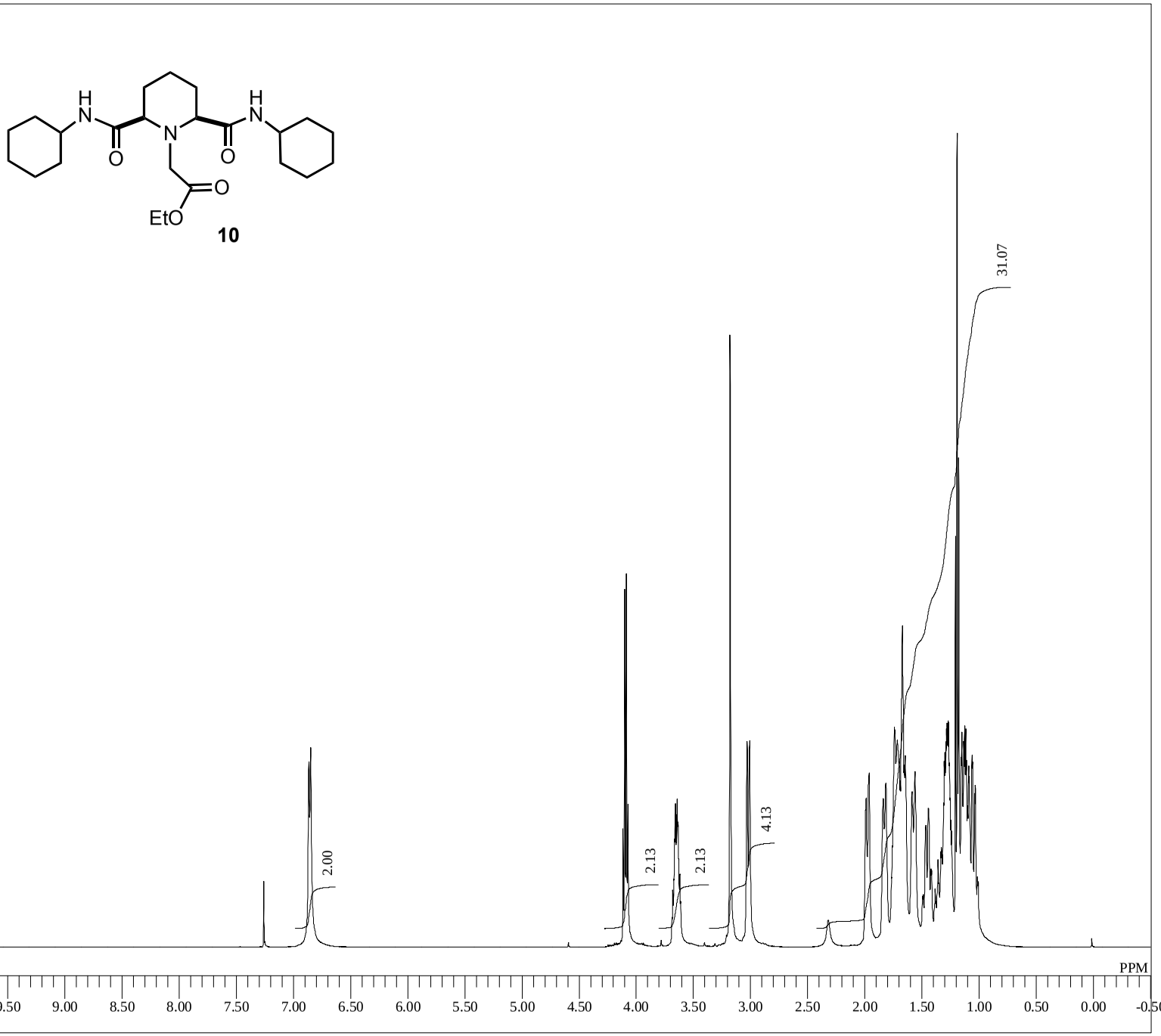
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	13107
FREQU	7507.51 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	19.8 c
SLVNT	CDCL3
EXREF	7.26 ppm
BF	0.12 Hz
RGAIN	50



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COMNT	single_pulse
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EXMOD	proton.jxp
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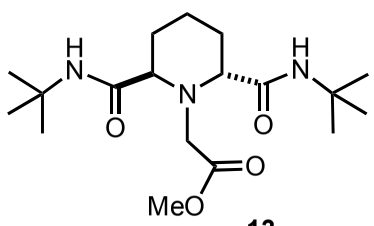
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16384
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	19.9 c
SLVNT	CDCL3
EXREF	7.26 ppm
BF	0.12 Hz
RGAIN	26



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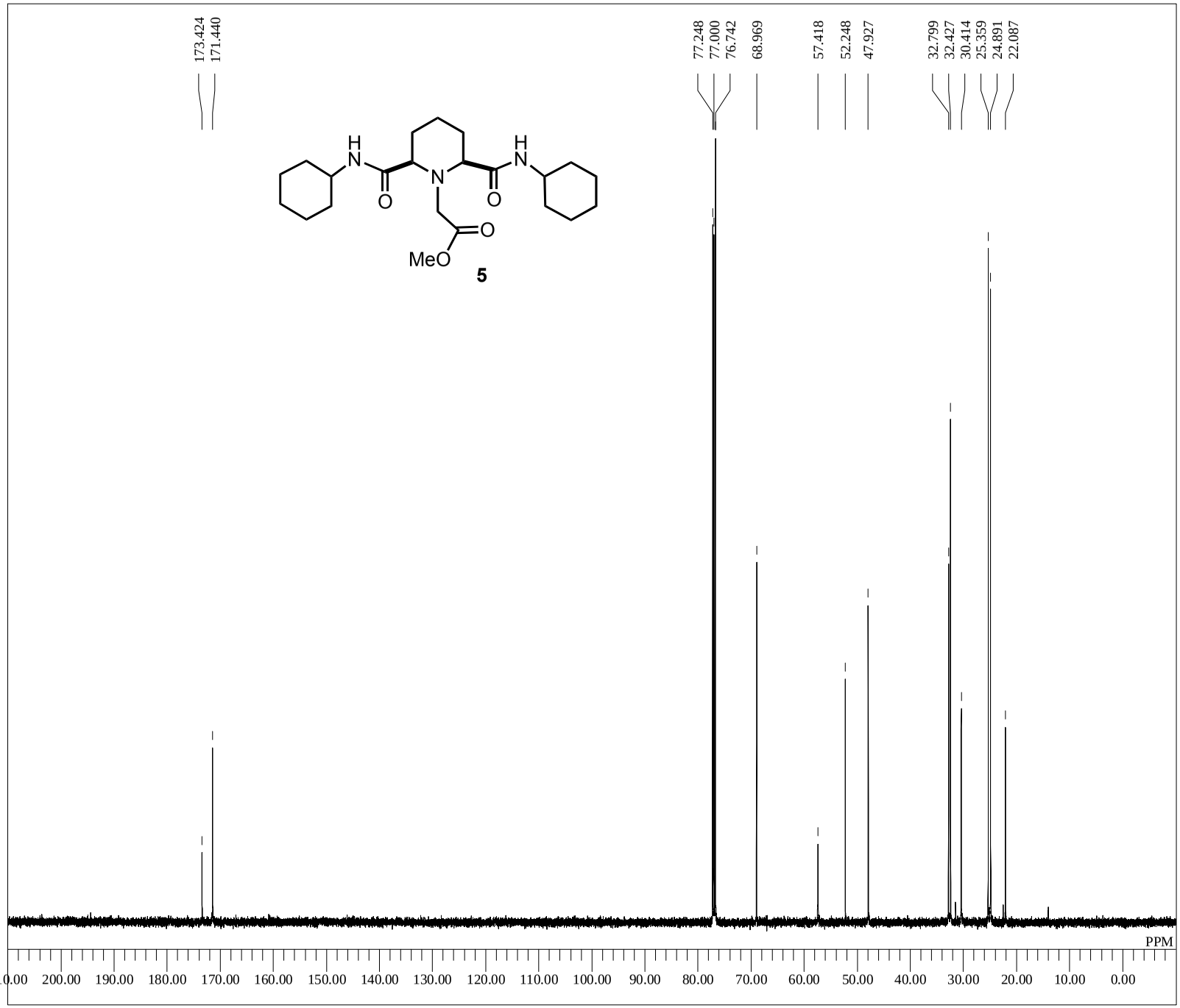
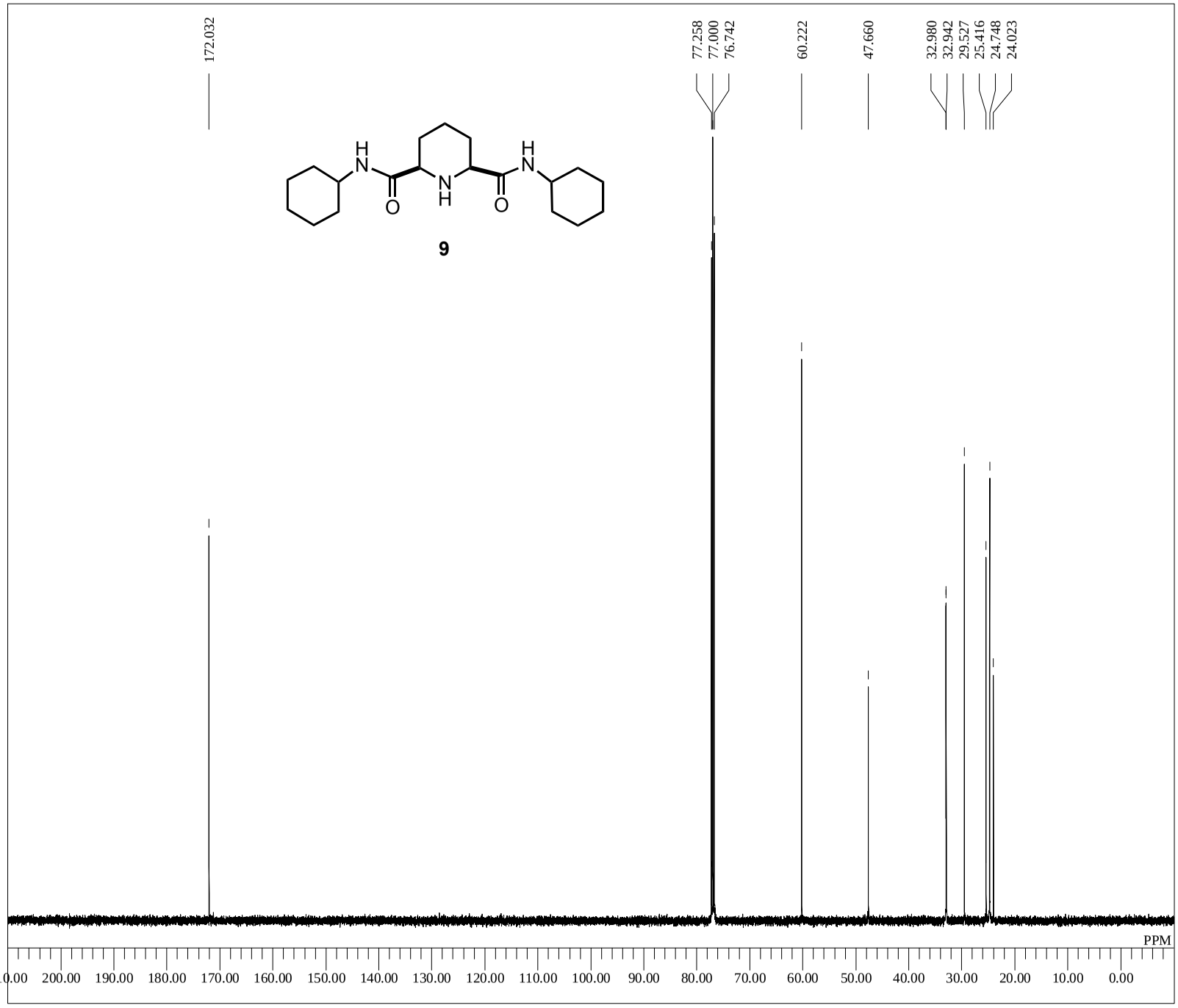
DFILE	MIM2139-recrystallization_proton-1-1.als
COMNT	single_pulse
DATIM	2015-11-07 14:52:38
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	13107
FREQU	7507.51 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	20.1 c
SLVNT	CDCL3
EXREF	7.26 ppm
BF	0.12 Hz
RGAIN	50

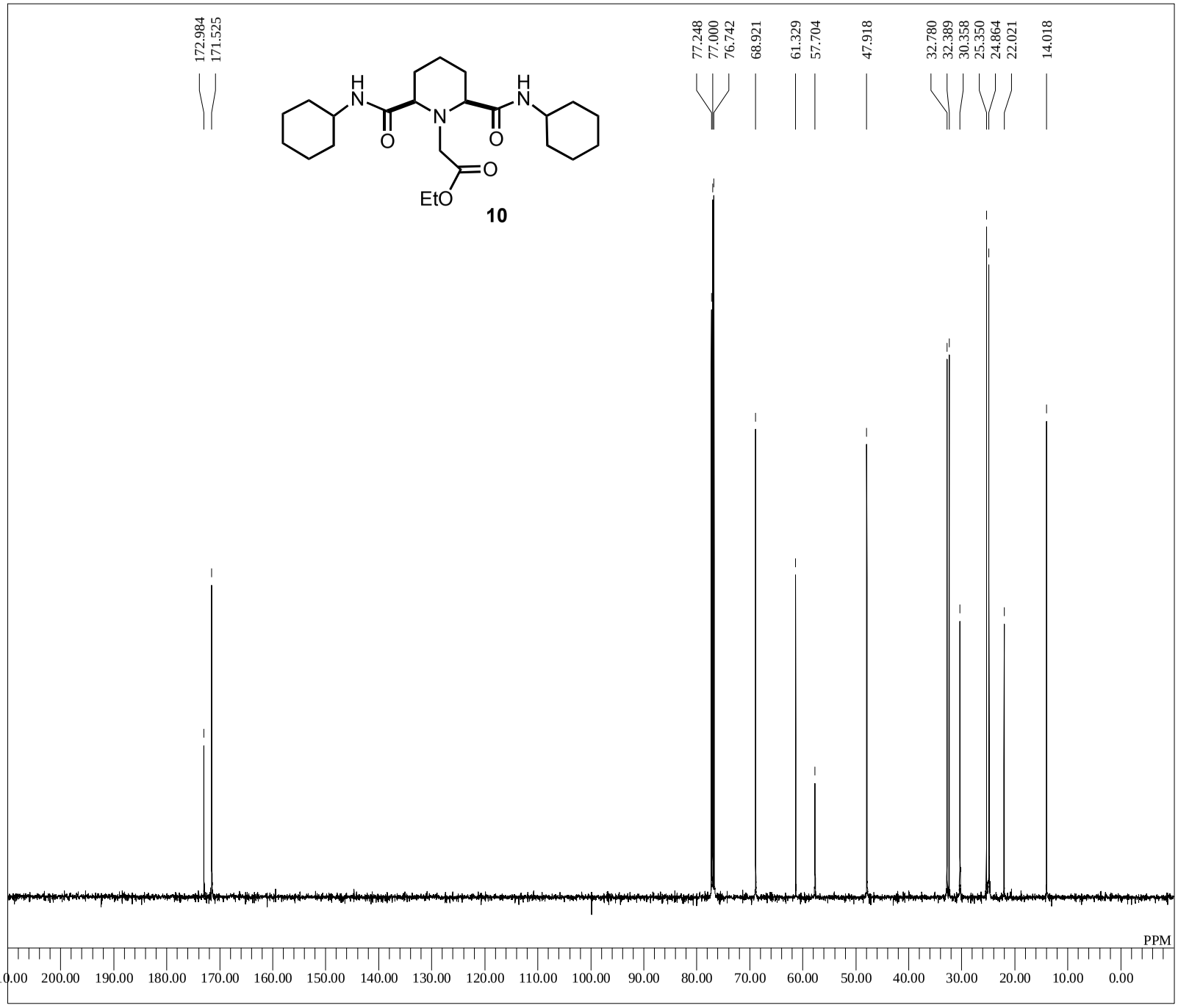
DFILE	AKI 2139 pyr_carbon.als
COMNT	single pulse decoupled gated NOE
DATIM	2015-11-17 21:54:40
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	26214
FREQU	31446.54 Hz
SCANS	943
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	20.7 c
SLVNT	C5D5N
EXREF	128.00 ppm
BF	0.12 Hz
RGAIN	50



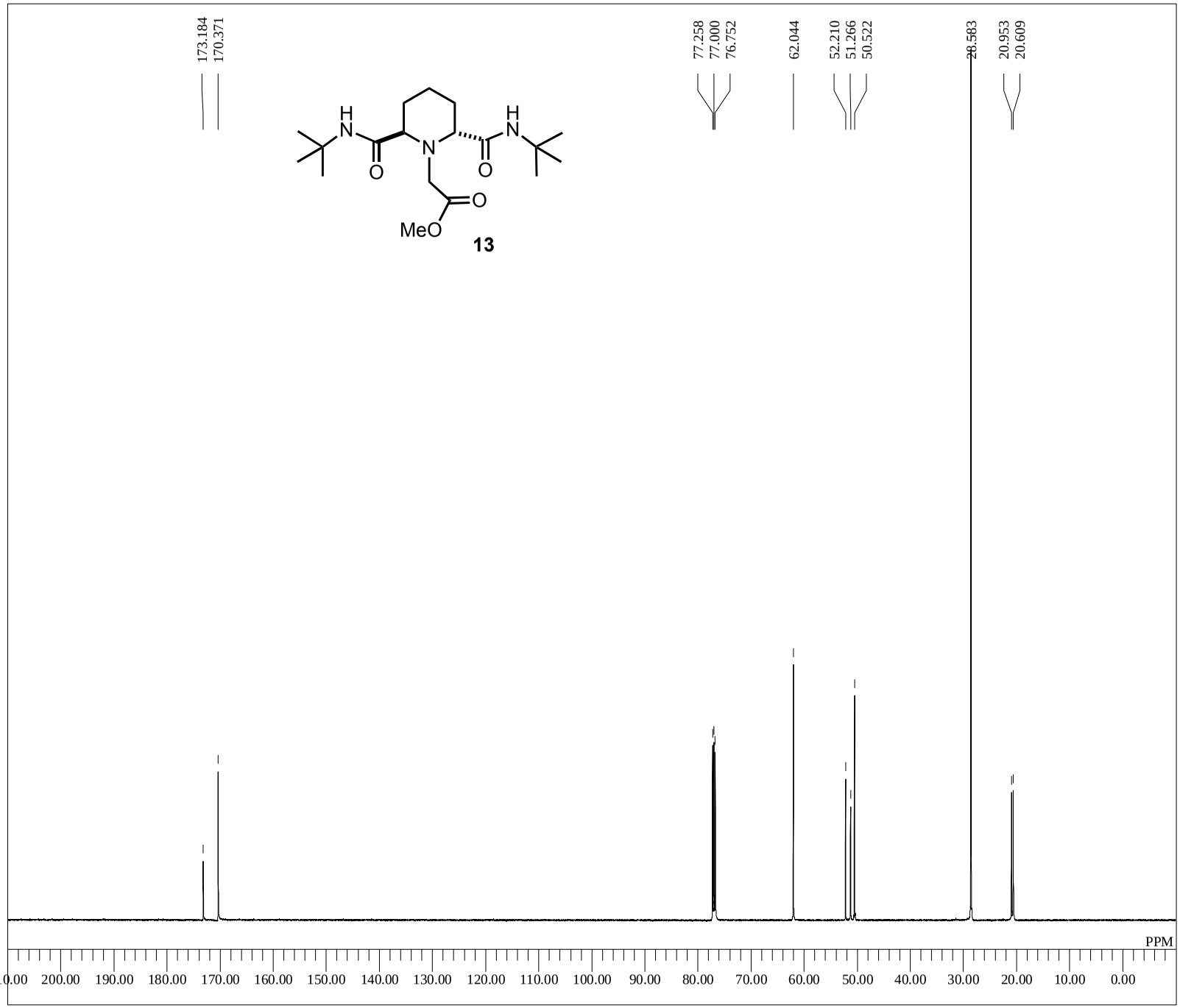
DFILE	halicho K -OMe carbon.als
COMNT	single pulse decoupled gated NOE
DATIM	2015-11-10 20:14:43
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	26214
FREQU	31446.54 Hz
SCANS	604
ACQTM	0.0000 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	20.2 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	58



DFILE	halicho K N-H carbon.als
COMNT	single pulse decoupled gated NOE
DATIM	2015-11-10 20:50:25
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	26214
FREQU	31446.54 Hz
SCANS	602
ACQTM	0.0000 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	20.1 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	58

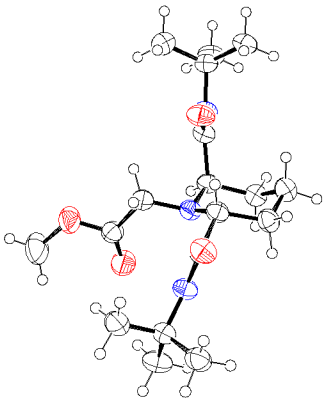


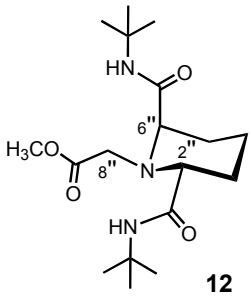
DFILE	halicho K -OEt carbon.als
COMNT	single pulse decoupled gated NOE
DATIM	2015-11-10 16:24:39
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32767
FREQU	39308.18 Hz
SCANS	234
ACQTM	0.0000 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	20.4 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	58



DFILE	MIM2139-recrystallization_carbon-1-2.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2015-11-07 15:06:31
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	40960
FREQU	49135.22 Hz
SCANS	1024
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	20.7 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

Fig. 5 X-ray crystallograpphic structure of the Ugi product **12**





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CCDC 1436736

Empirical Formula	$C_{18}H_{33}N_3O_4$
Formula Weight	355.48
Crystal Color, Habit	colorless, platelet
Crystal Dimensions	0.510 X 0.300 X 0.200 mm
Crystal System	orthorhombic
Lattice Type	Primitive
Lattice Parameters	a = 13.2392(6) Å b = 15.3139(7) Å c = 20.6773(9) Å V = 4192.2(3) Å^3
Space Group	Pbca (#61)
Z value	8
D_{calc}	1.126 g/cm^3
F_{000}	1552.00
μ(MoKα)	0.794 cm^{-1}

B. Intensity Measurements

Diffractometer	R-AXIS RAPID II
Radiation	MoKa (λ = 0.71075 Å)
	graphite monochromated
Voltage, Current	50kV, 80mA
Temperature	–100.0°C
Detector Aperture	460.0 x 256.0 mm
Data Images	74 exposures
ω oscillation Range (χ=45.0, ϕ=0.0)	130.0 - 190.0°
Exposure Rate	80.0 sec./°
ω oscillation Range (χ=45.0, ϕ=180.0)	0.0 - 162.0°
Exposure Rate	80.0 sec./°
Detector Position	127.40 mm
Pixel Size	0.100 mm
2θmax	55.0°
No. of Reflections Measured	Total: 38827
	Unique: 4796 (R_{int} = 0.0589)
Corrections	Lorentz-polarization
	Absorption
	(trans. factors: 0.277 - 0.984)

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR2011)
Refinement	Full-matrix least-squares on F^2
Function Minimized	Σ w $(Fo^2 - Fc^2)^2$
Least Squares Weights	$1/[0.0022Fo^2+1.0000s(Fo^2)]/(4Fo^2)$
2θmax cutoff	55.0^o
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	4796
No. Variables	358
Reflection/Parameter Ratio	13.40
Residuals: R_1 ($I > 2.00\sigma(I)$)	0.0564
Residuals: R (All reflections)	0.0761
Residuals: wR_2 (All reflections)	0.1622
Goodness of Fit Indicator	1.020
Max Shift/Error in Final Cycle	0.002
Maximum peak in Final Diff. Map	0.39 $e^-/Å^3$
Minimum peak in Final Diff. Map	–0.22 $e^-/Å^3$

X-Ray crystallographic analysis. Recrystallization of **13** from CH_2Cl_2/hexane gave a single crystal. A single crystal was mounted on a glass fiber and fixed by a bond. An X-ray diffraction measurement was made on a Rigaku R-AXIS RAPID II diffractometer using graphite monochromated Mo-*K*α radiation, operating at 50 kV and 80 mA at -100 ºC. Data were collected and processed on a PC using RAPID AUTO software (Rigaku) and was corrected for Lorentz and polarization effects. All calculations were performed using the CrystalStructure[1] (Ver. 4.1) crystallographic software package. The structure was solved by direct methods using SIR2011[2] and refined with program CRYSTALS[3] (Issue 11). The non-hydrogen atoms were refined anisotropically. The hydrogen atoms were placed from the difference map and refined with geometrical and isotropic displacement parameters. Molecular plot was obtained with the program ORTEP3 for windows[4] (Ver. 2.0).

References

[1] Crystal Structure Analysis Package, Rigaku Corporation (2000-2014). Tokyo 196-8666, Japan.

[2] Burla, M. C., Caliandro, R., Camalli, M., Carrozzini, B., Cascarano, G. L., Giacovazzo, C., Mallamo, M., Mazzone, A., Polidori, G. and Spagna, R. (2012). *J. Appl. Cryst*. 45, 357-361.

[3] Carruthers, J.R., Rollett,J.S., Betteridge, P.W., Kinna, D., Pearce, L., Larsen, A., and Gabe, E. Chemical Crystallography Laboratory, Oxford, UK. (1999).

[4] L. J. Farrugia, *J. Appl. Cryst.* (2012), **45**, 849-854.