

Supplementary Information

Design and Synthesis of Amidine-type Peptide Bond Isostere: Application of Nitrile Oxide Derivatives as Active Ester Equivalents to Peptide and Peptidomimetics Synthesis

Eriko Inokuchi^a, Ai Yamada^a, Kentaro Hozumi^b, Kenji Tomita^a, Shinya Oishi^a, Hiroaki Ohno^a, Motoyoshi Nomizu^b, and Nobutaka Fujii^{a,*}

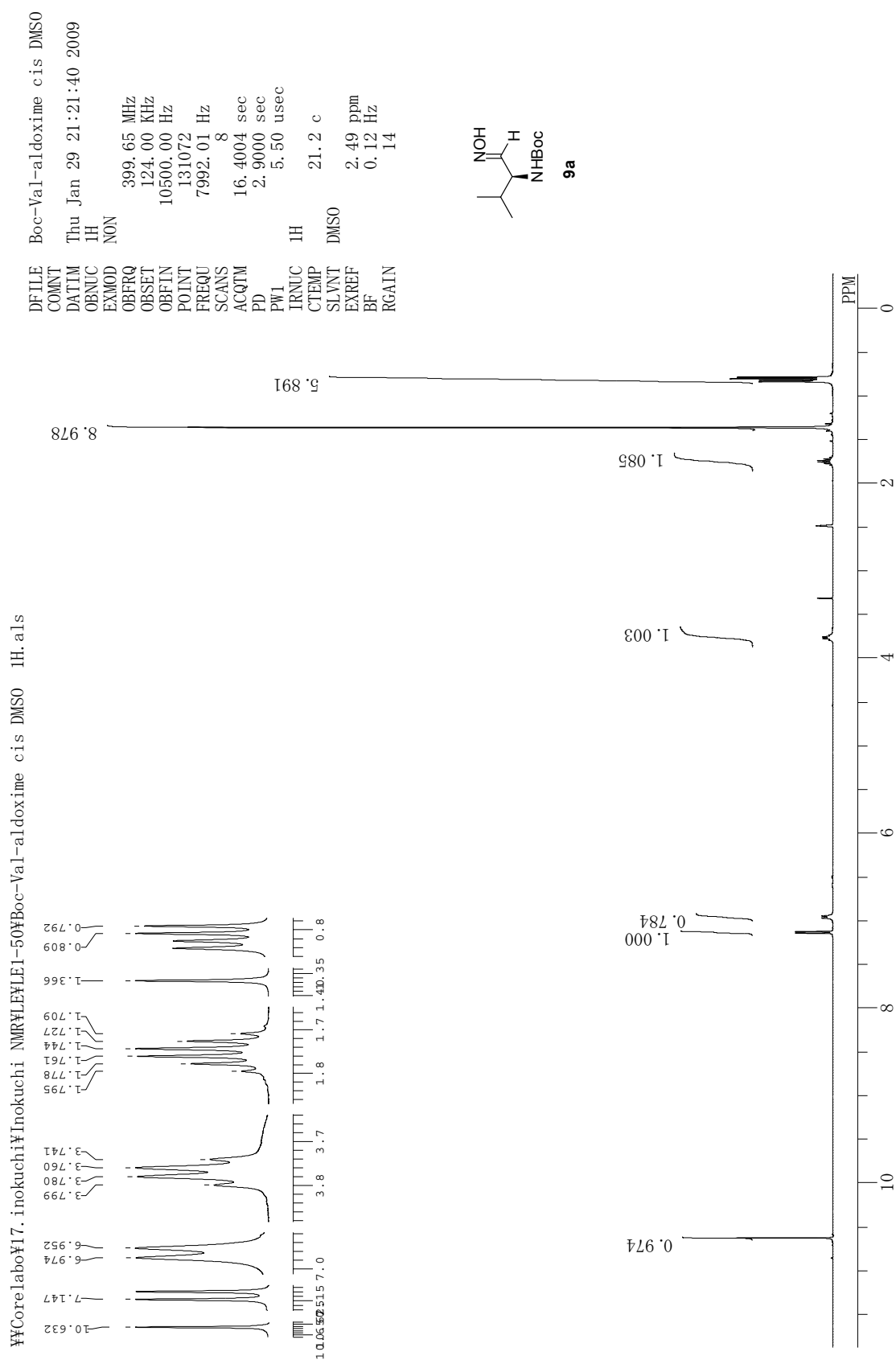
^a *Graduate School of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606-8501, Japan.*

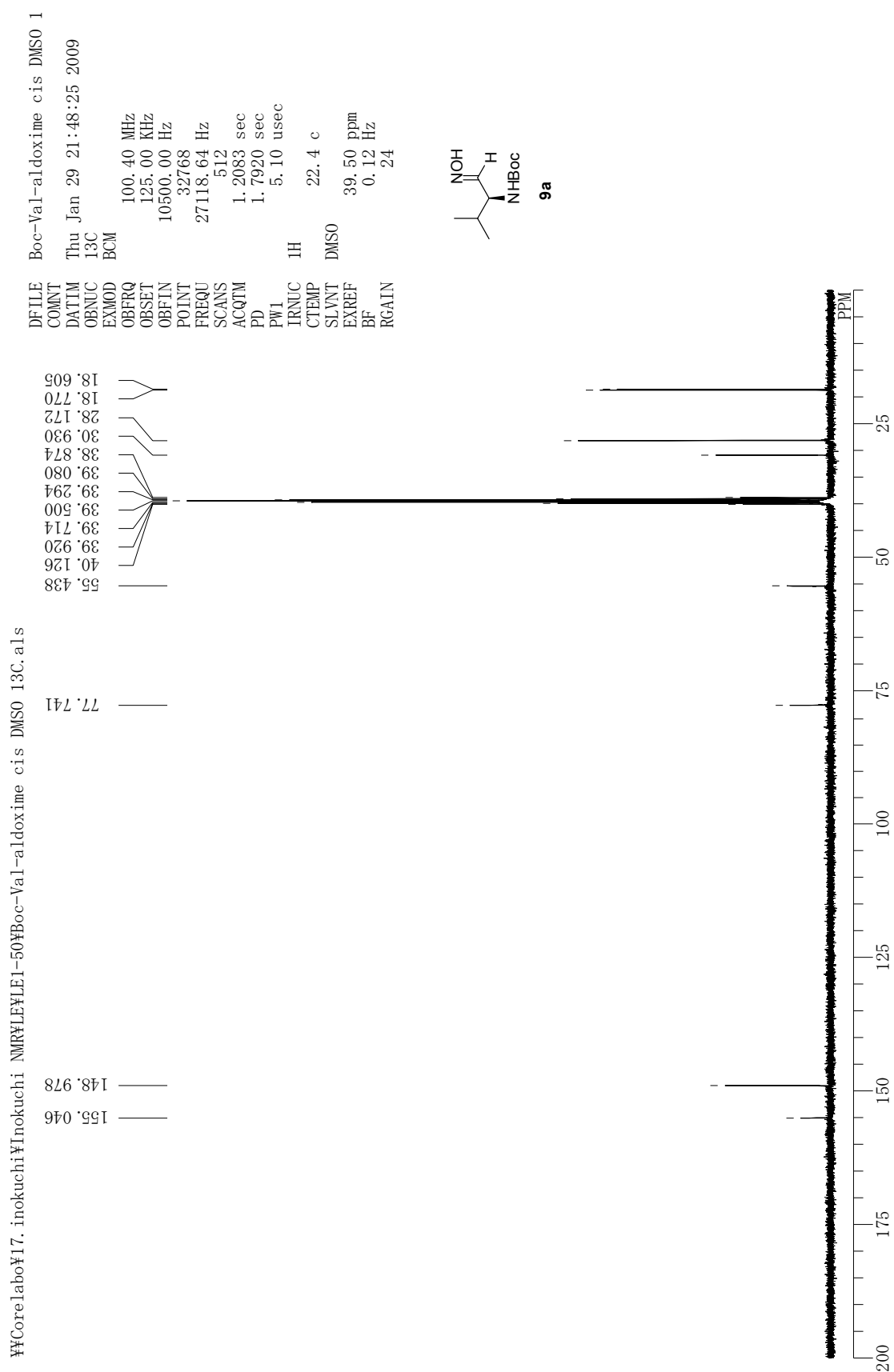
^b *School of Pharmacy, Tokyo University of Pharmacy and Life Sciences, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan*

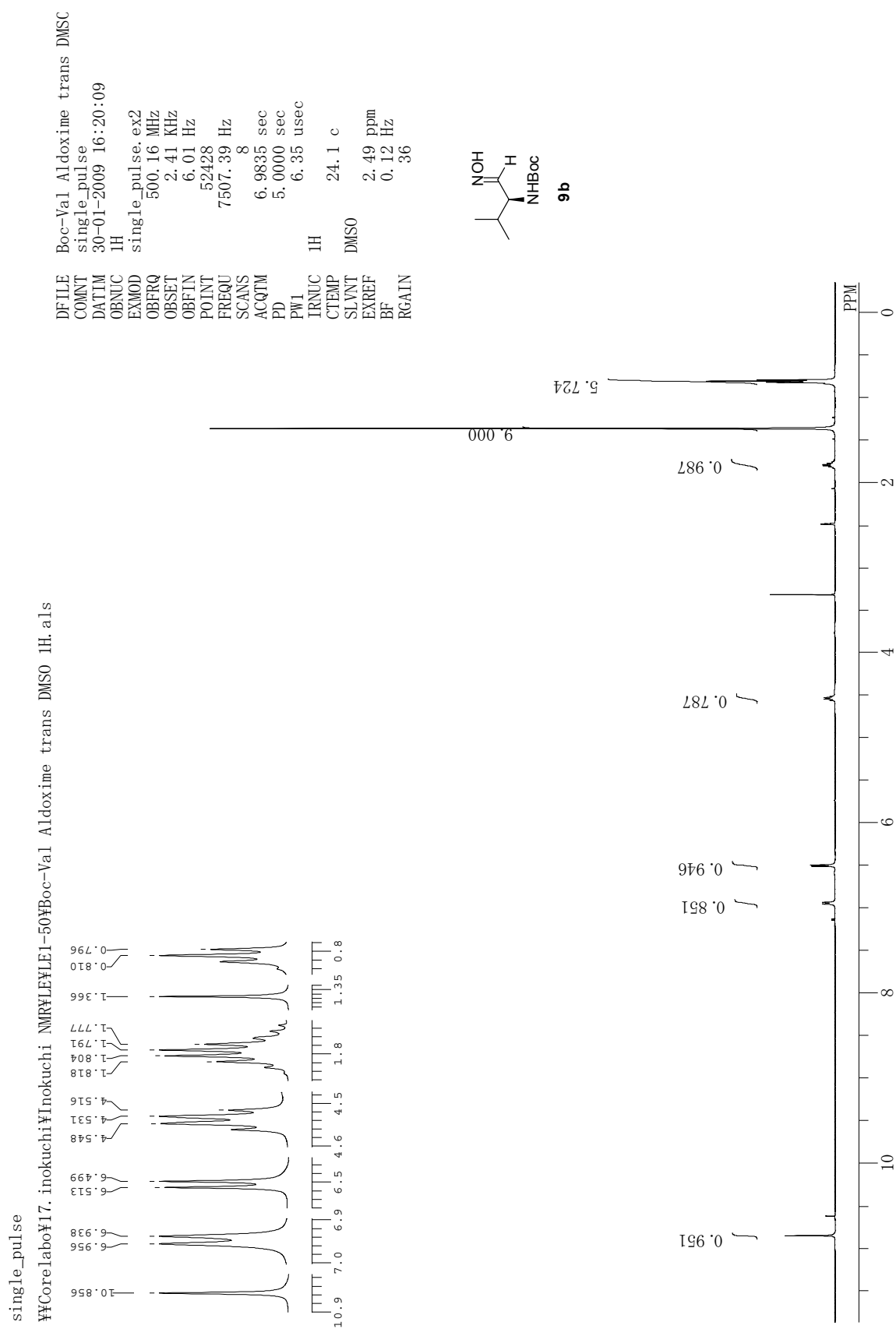
Table of Contents

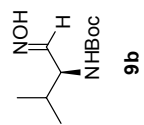
Experimental Section	S2
NMR spectra	S3
FAB-mass spectra.....	S25

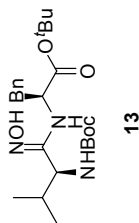
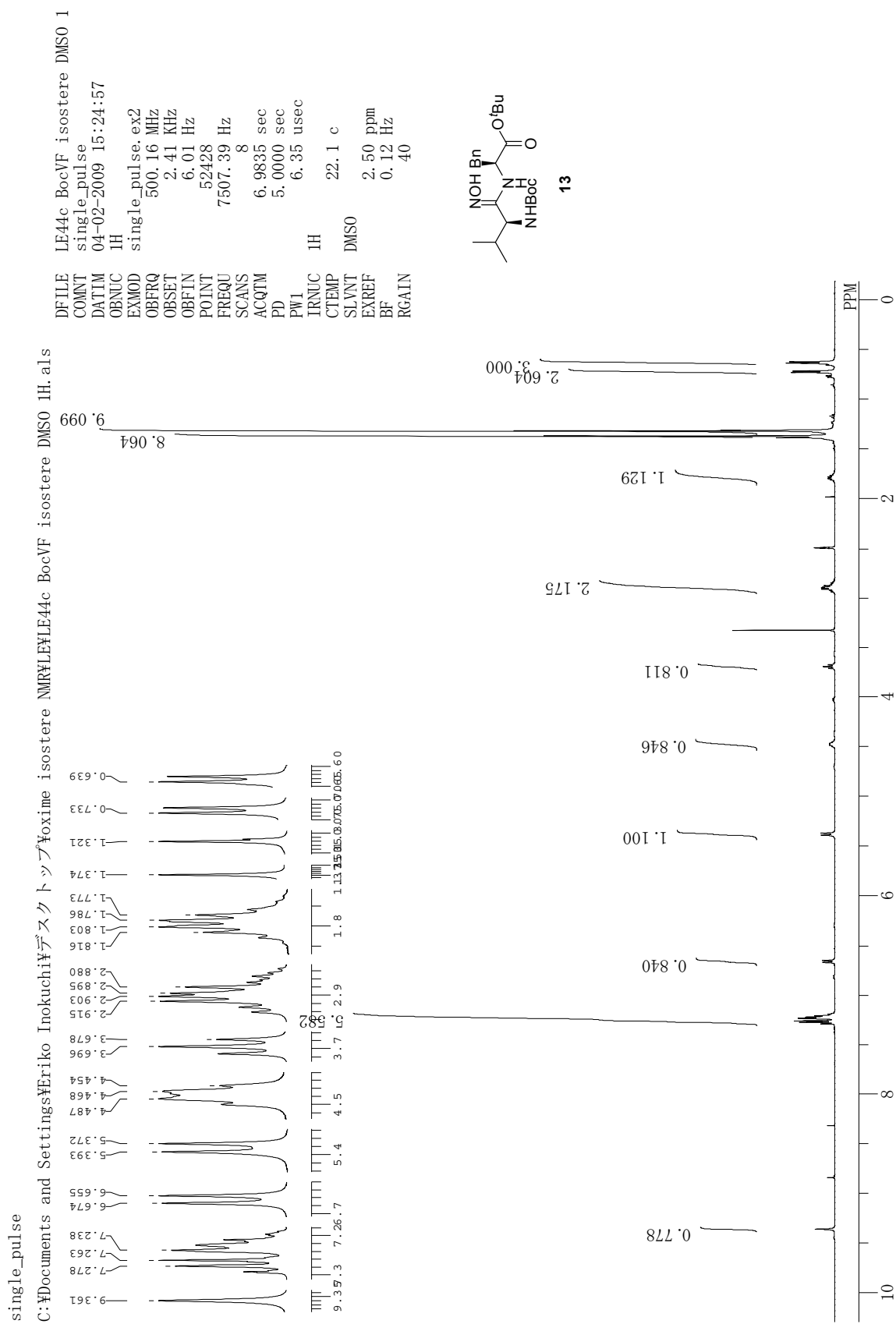
Synthesis of an epimer of compound 15: *tert*-Butyl (*S*)-2-[(*R*)-2-*tert*butoxy-carbonylamino-3-methylbutyrylamino]-3-phenylpropionate (*epi*-15). To a solution of *N*-Boc-D-valine (92 mg, 0.42 mmol) and H-Phe-O^tBu (100 mg, 0.42 mmol) in CH₂Cl₂ were added HOBt (79 mg, 0.59 mmol), HBTU (*O*-Benzotriazole-*N,N,N',N'*-tetramethyluroniumhexafluoro-phosphate) (142 mg, 0.44 mmol) and DIEA (293 mL, 1.68 mmol) and the mixture was stirred at room temperature overnight. The reaction mixture was washed with 5% citric acid, saturated NaHCO₃ and brine and dried over Na₂SO₄. Concentration under reduced pressure followed by flash chromatography over silica gel with CHCl₃/MeOH (95/5) gave the title compound *epi*-15 (95 mg, 54%) as a white solid: mp 125.0–126.0 °C; $[\alpha]_D^{24} +35.9$ (*c* 0.31, CHCl₃); δ_H (500 MHz, DMSO-*d*₆, Me₄Si) 0.82 (3H, d, *J* 6.8), 0.89 (3H, d, *J* 6.6), 1.39 (9H, s), 1.43 (9H, s), 2.04–2.16 (1H, m), 3.07 (2H, d, *J* 6.1), 3.97 (1H, br s), 4.76 (1H, dd, *J* 13.5 and 6.1), 4.96 (1H, br s), 6.36 (1H, d, *J* 7.6) and 7.10–7.31 (5H, m); δ_C (125 MHz, DMSO-*d*₆, Me₄Si) 17.2, 19.2, 27.9 (3C), 28.3 (3C), 30.8, 38.3, 53.4, 82.2 (2C), 127.0 (2C), 128.4 (3C), 129.4 (2C), 136.1, 170.4 and 171.0; HRMS (FAB) *m/z* calcd for C₂₃H₃₇N₂O₅ ([M+H]⁺) 421.2702, found 421.2705.

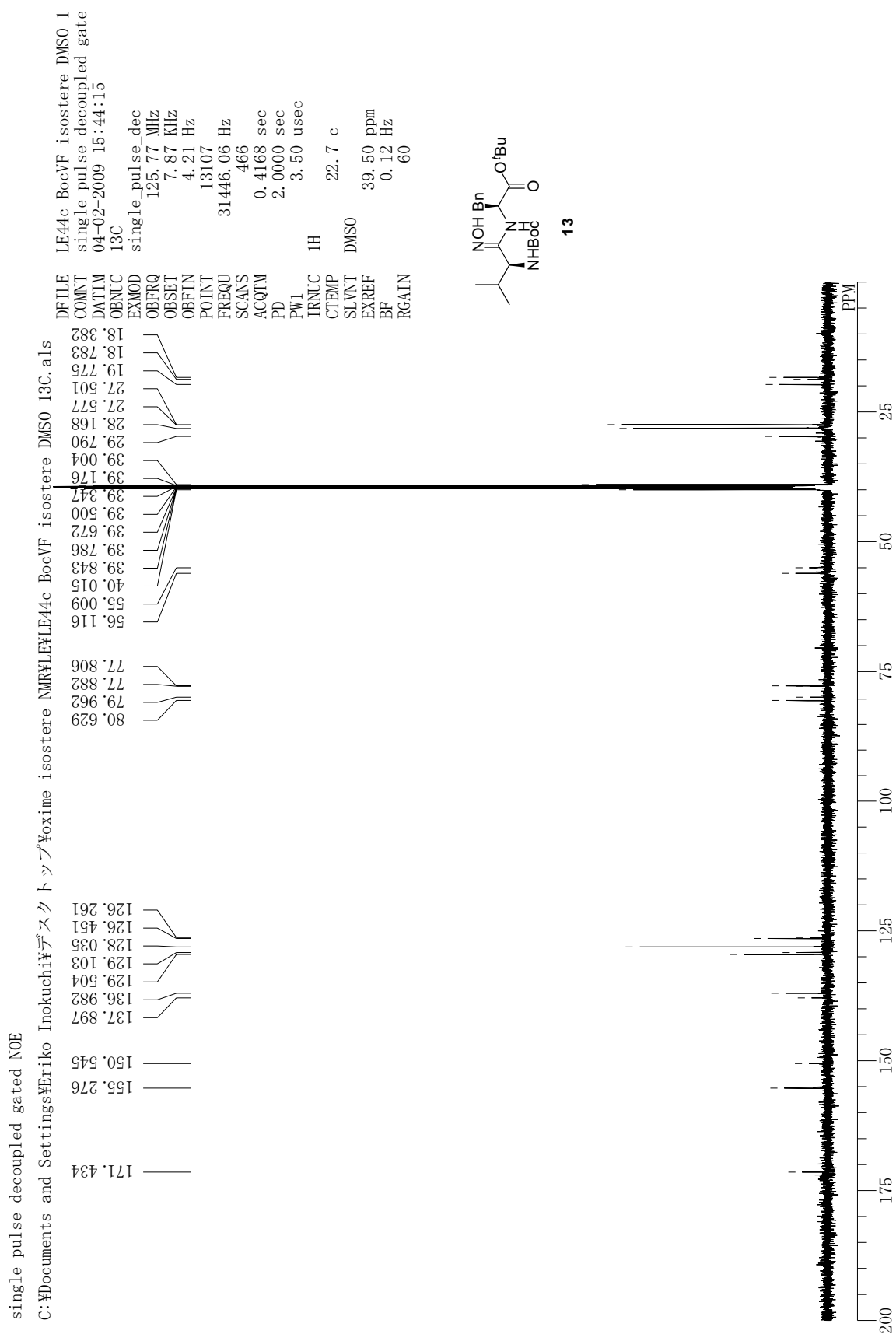


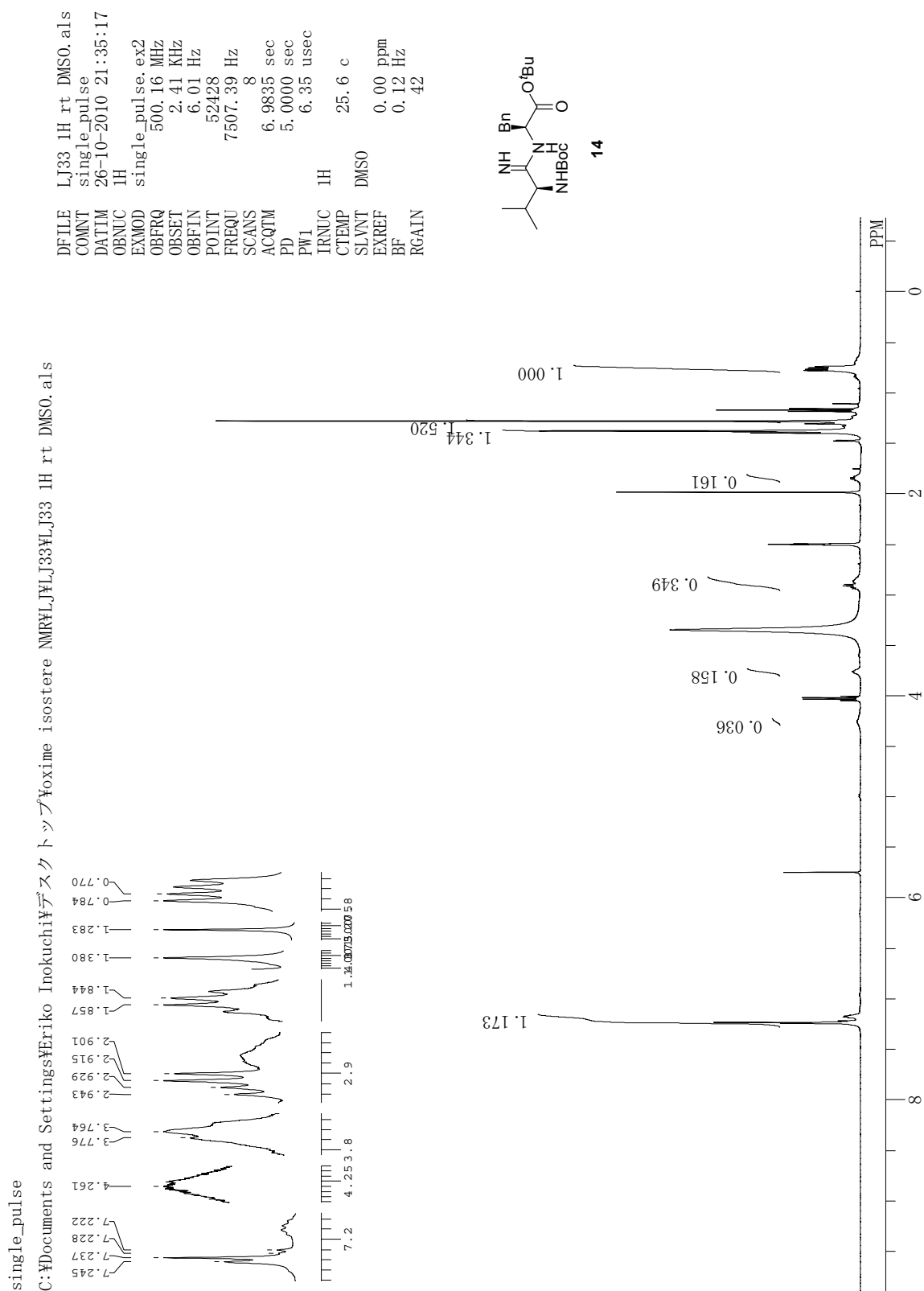


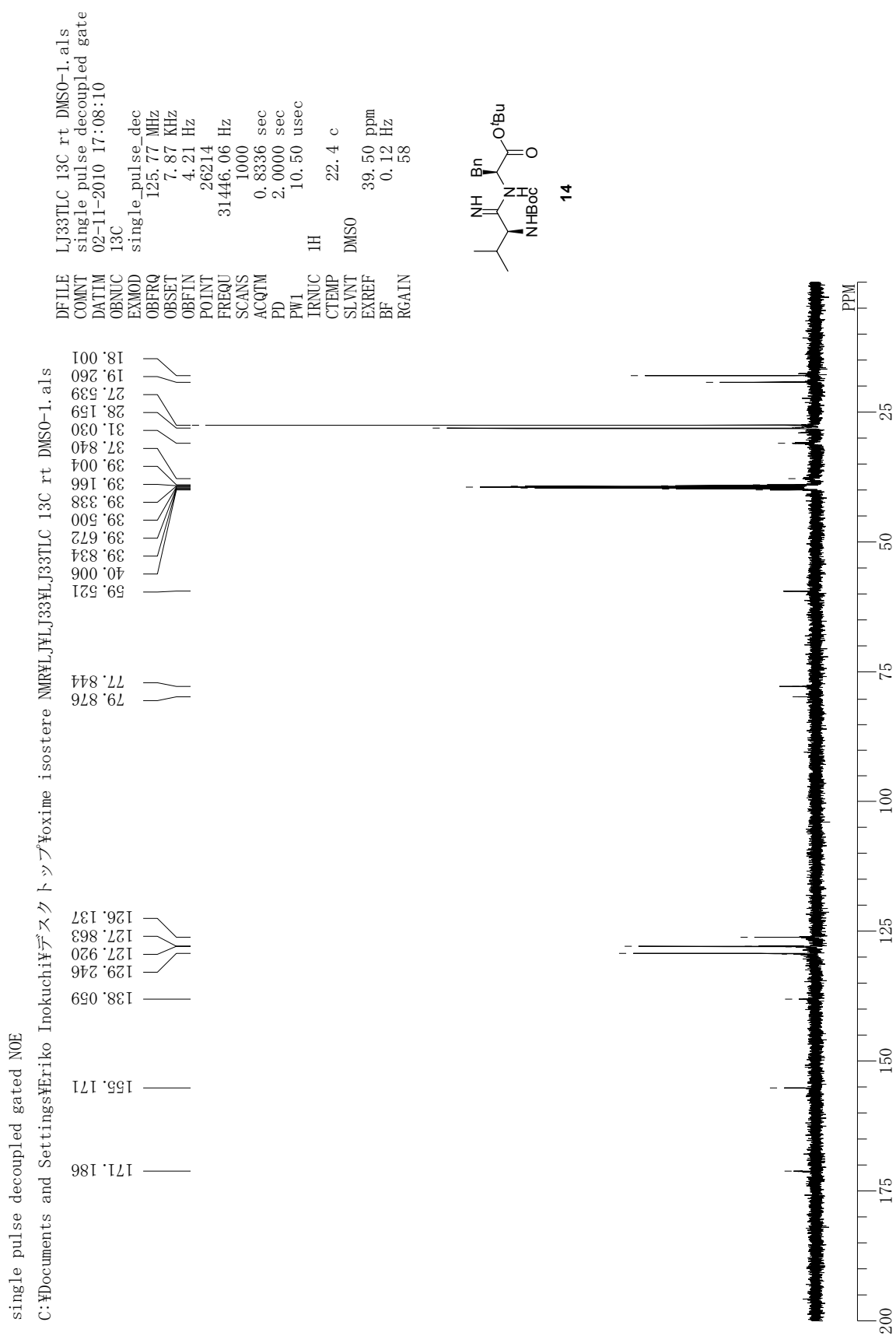


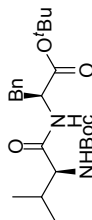
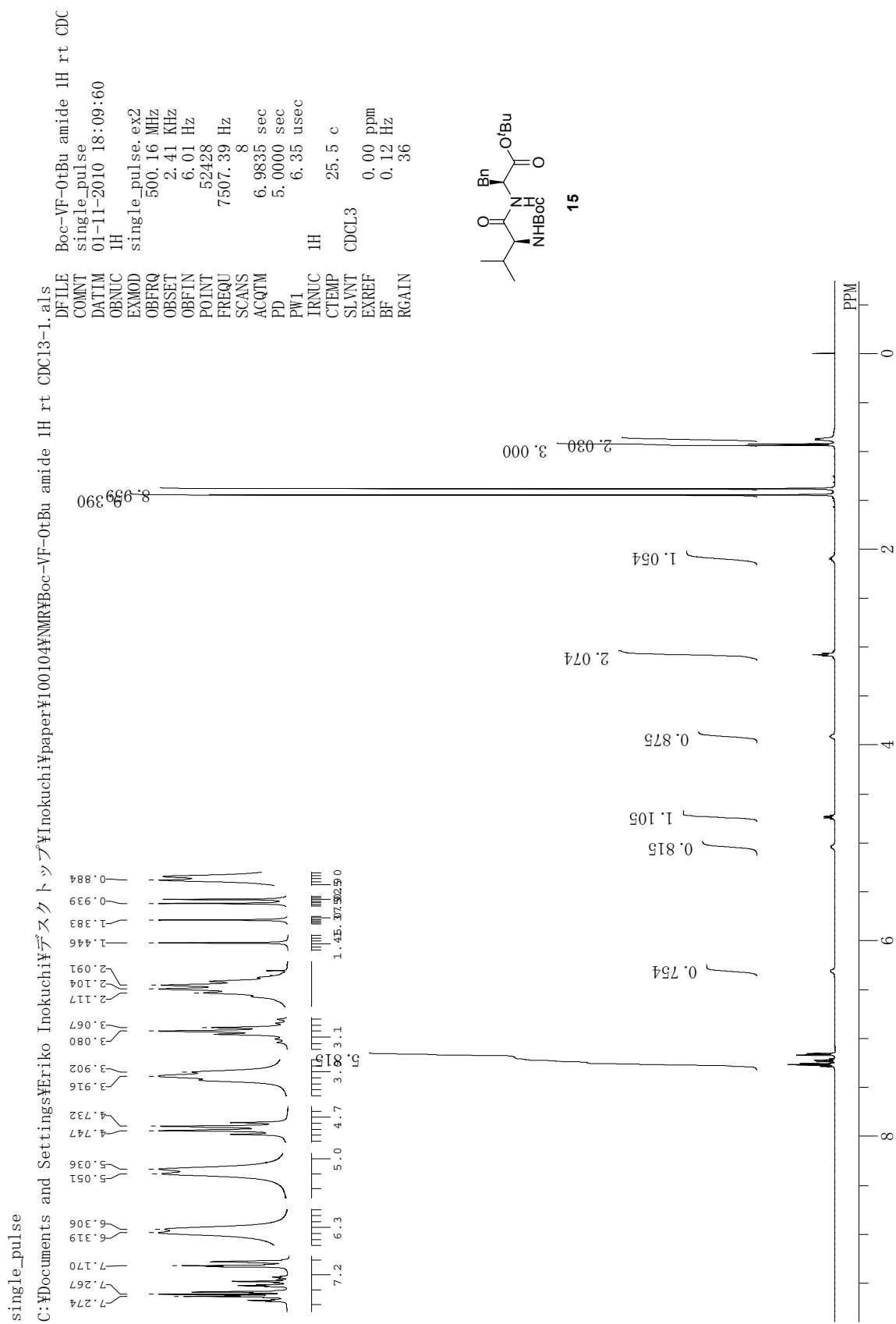


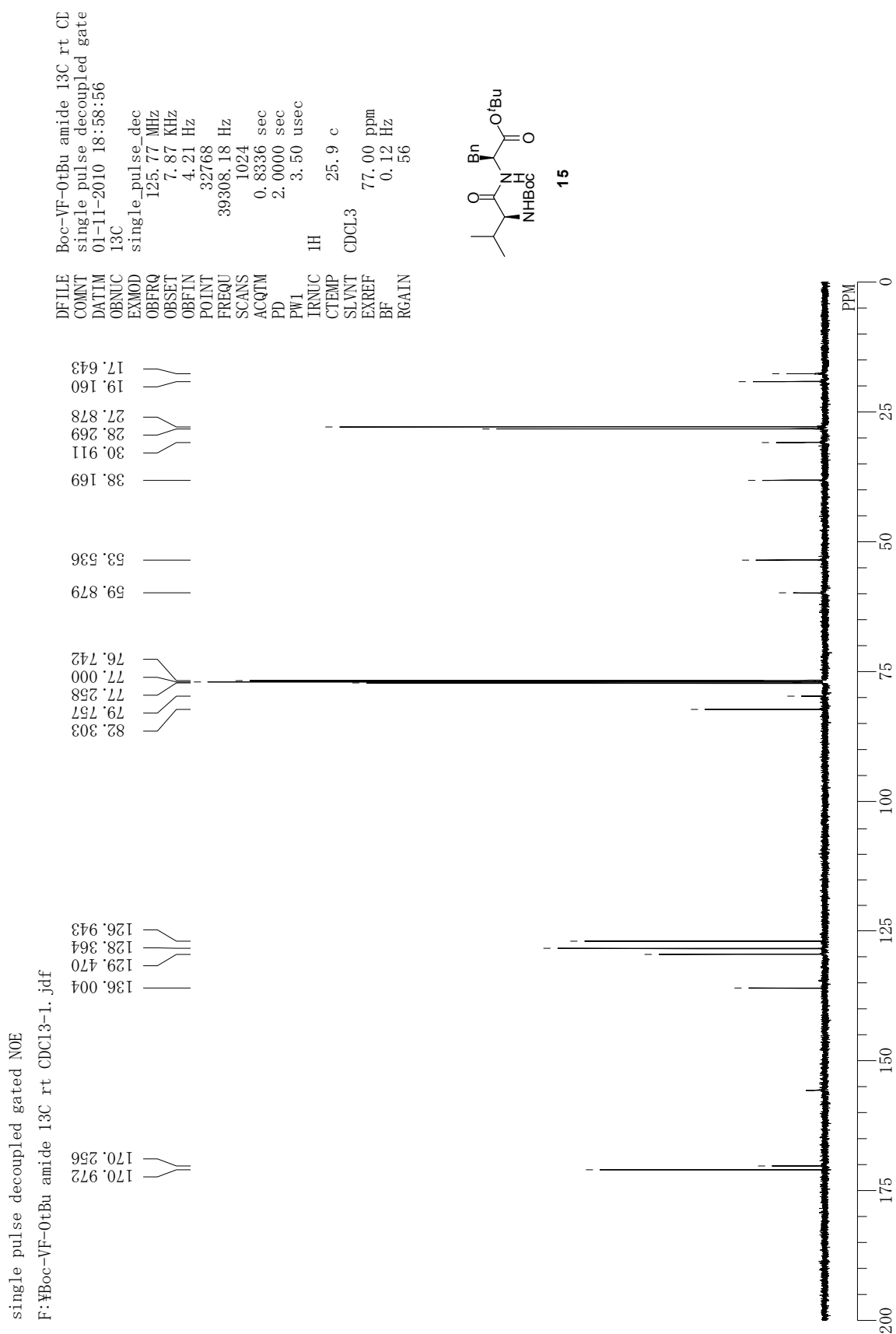


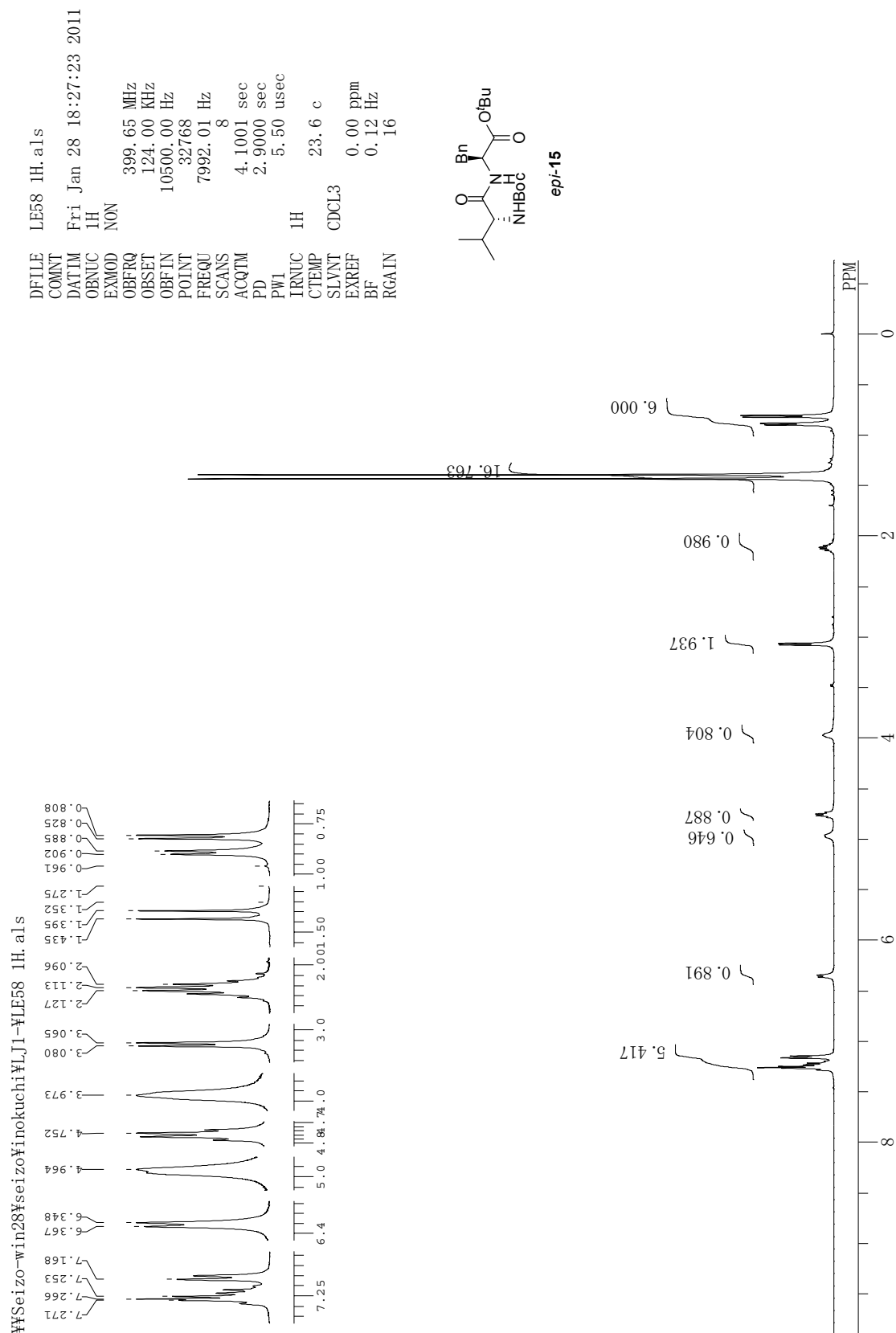


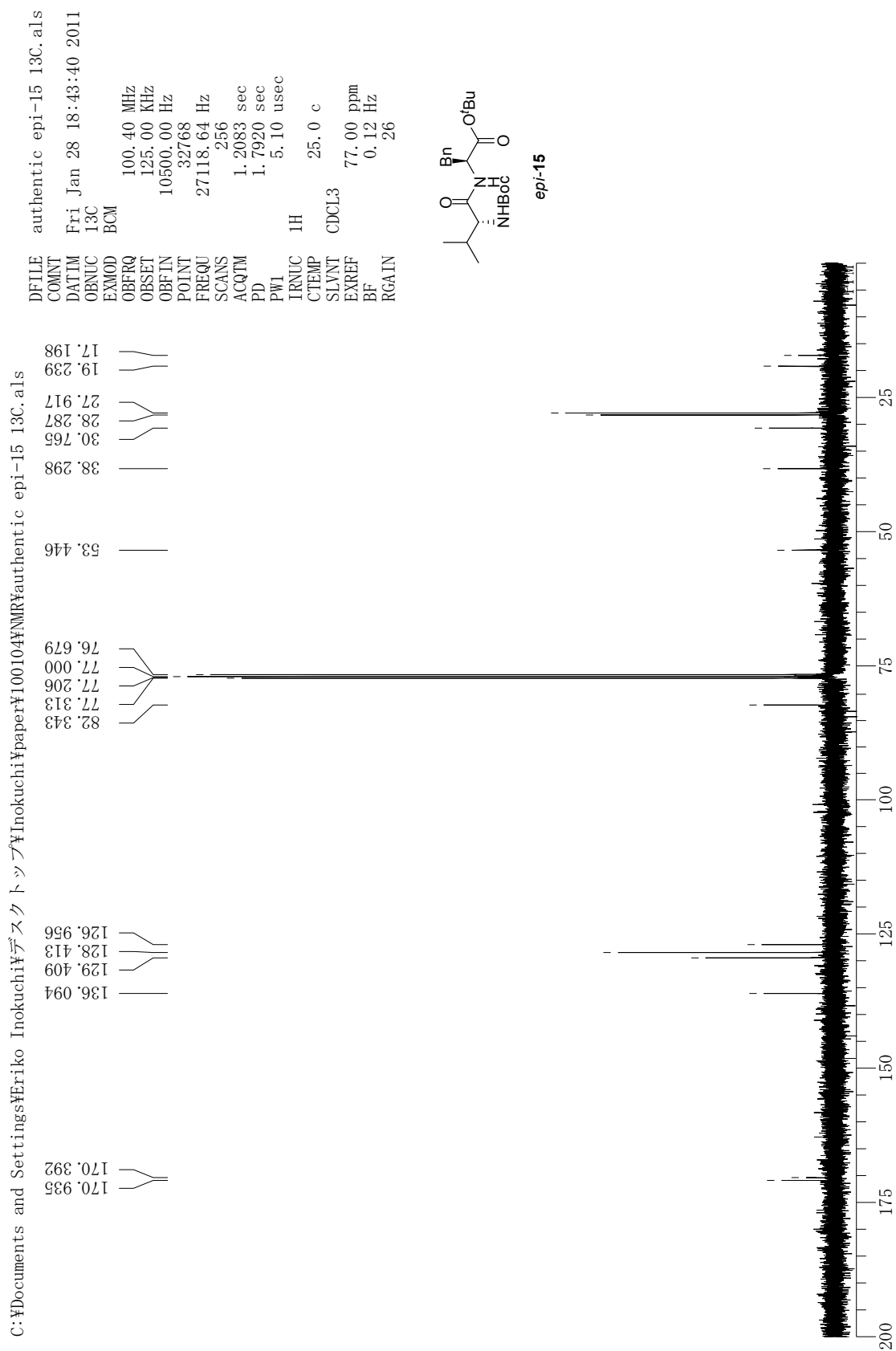


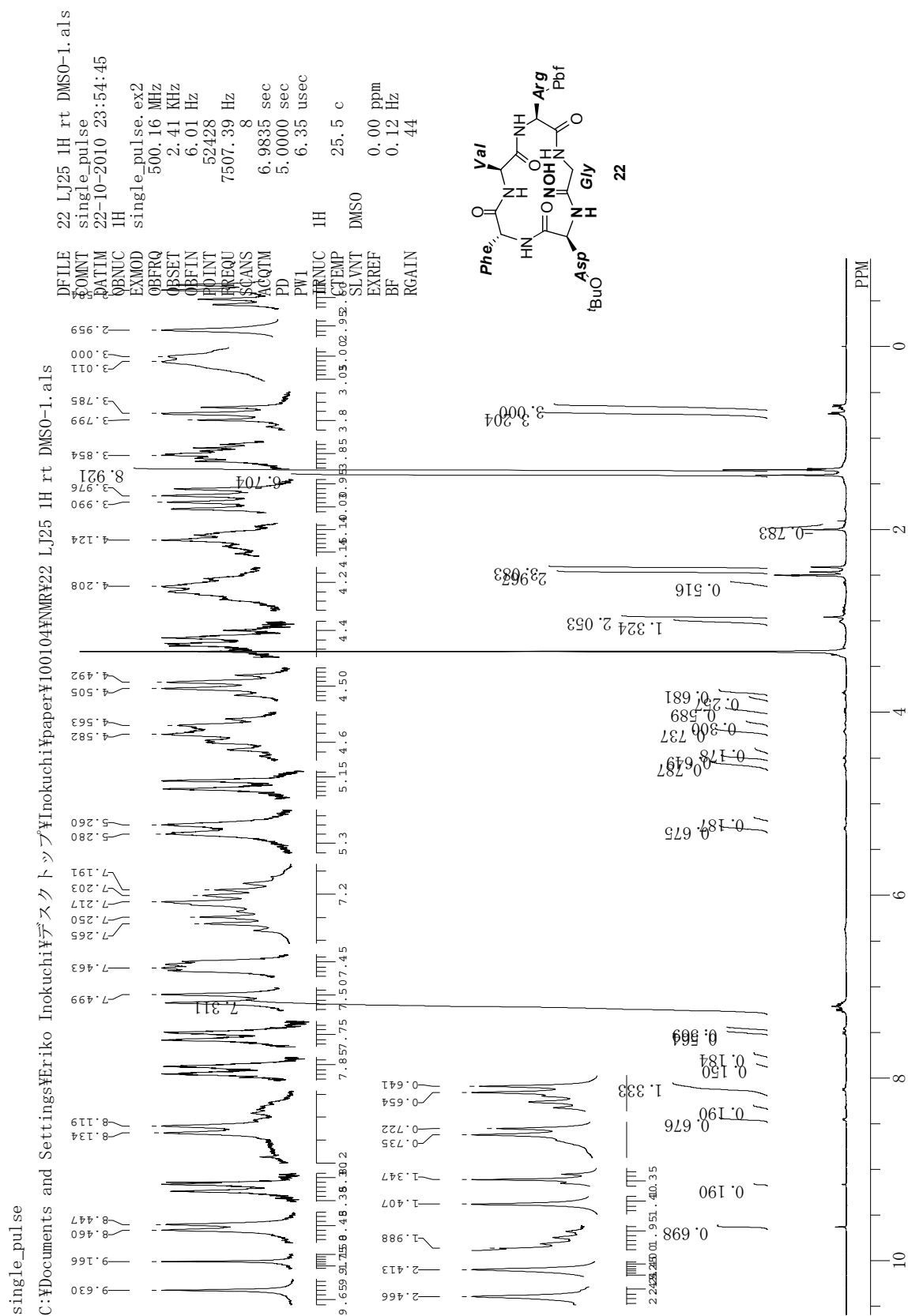












single pulse decoupled gated NOE

C:\Documents and Settings\Eriko Inokuchi\Desktop\トップ\Inokuchi\paper¥100104¥NMR¥22 LJ25 13C rt DMSO 101026-1.xls

22 LJ25 13C rt DMSO 101026-
single pulse decoupled gate
26-10-2010 08:25:19
13C
single_pulse_dec

single_pulse_dec

125.77 MHz

7.87 KHz

4.21 Hz

26214

31446.06 Hz

12288

0.8336 sec

2.000 sec

3.50 usec

HT
255
5
c

DMSO
0.07

DM30
39.50 ppm

0.12 Hz

85

22

