

Supporting Informations

Study of the Total Synthesis of (-)-Exiguolide

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^1H and ^{13}C NMR spectra for compound:

6	S4
11	S5
12	S7
13	S8
14	S9
15	S10
16	S12
17	S13
2	S14
23 and 24	S15
(-)-28	S16
7	S17
32	S18
8	S19
33	S20
34a	S22
34b	S23
35	S24
36	S25
37	S26
39	S28
40	S29
41	S30
42	S31
43	S32
44	S33
45	S34
46	S35
38	S36
47	S37

General Methods and Standard Procedures

Solvents: THF, Et₂O and toluene were refluxed on sodium-benzophenone and then distilled under argon. CH₂Cl₂ and NMP were dried by refluxing on CaH₂ and then distilled under argon. Acetone, CH₃CN, DMF, DMSO and EtOH were stored over 4 Å MS and MeOH over 3 Å MS. When required, solvent degassing was achieved by repeated freeze-vacuum cycles. Solvents used for extractions and purifications were used as received, except heptane and pentane, which were distilled using a rotational evaporator prior to use in chromatography, to remove non-volatile impurities.

Reagents and reactants: Unless otherwise noted, all reagents were obtained from commercial suppliers and were used as received. However, some of them were specifically purified prior to use:

- Et₃N was dried by refluxing on CaH₂ and distilled under argon.
- Acrolein was refluxed on CaSO₄ and distilled under argon prior to use.
- Commercial solution of organometallic reagents (*n*-BuLi, *t*-BuLi, MeMgBr, vinylmagnesium bromide, ethynylmagnesium bromide, KHMDS) were used as received, based on their theoretical concentrations. However, when needed, their actual concentration was assessed using the *s*-BuOH-1,10-phenanthroline titration method.¹
- LDA and LiHMDS were prepared prior to use by slow addition of the amine into a solution of *n*-BuLi in heptanes at 0 °C and stirred for 30 min. The concentration of these solutions might then be adjusted by addition of distilled THF.

Reaction conditions: Unless otherwise noted, all reactions were performed using oven dried glassware under an atmosphere of dry argon.

Purification methods: Classic **flash chromatography** was performed using silica gel 60 (35-70 µm). **Preparative HPLC** purifications were carried out normal phase silica gel columns and a differential refractometer as the detector. Several products were purified by **short-path and bulb-to-bulb distillation** apparatus. In this case, the given temperature (*T*_{set}) is not the actual temperature of distillation of the product but just an indicative setting temperature.

Analytical methods: **Thin-layer chromatography (TLC)** plates (F₂₅₄ aluminium sheets) were analyzed by ultraviolet (254 nm and/or 365 nm) and spraying with various stains, followed by heating:

- Vanillin: vanillin (1 g) and H₂SO₄ (2 mL) in EtOH (100 mL).

¹ S. C. Watson, J. F. Eastham, *J. Organomet. Chem.* **1967**, 9, 165-168.

- Phosphomolybdic acid: Phosphomolybdic acid (10 g) in EtOH (100 mL).
- FeCl₃: FeCl₃ (1 g) in EtOH (100 mL). Used for specific staining of phenols.
- Retention factors (**R_f**) are defined as the distance traveled by the compound divided by the distance traveled by the solvent.

Infrared spectra (IR) were recorded neat. Wavenumbers (ν) are reported in reciprocal centimeters (cm⁻¹).

For **¹H NMR-spectra** (300 or 500 MHz) and **¹³C NMR-spectra** (75,5 or 125.8 MHz), chemical shifts (δ) are given in ppm and were referenced to the internal solvent signal² or to TMS as an internal standard. Multiplicities are declared as follow: s (singlet), d (doublet), t (triplet), q (quadruplet), dd (doublet of doublet), ddd (doublet of doublet of doublet), ddt (doublet of doublet of triplet), ddq (doublet of doublet of quadruplet), td (triplet of doublet), m (multiplet) and br s (broad signal). Coupling constant (*J*) are given in Hz. Assignments of proton resonances were confirmed, when possible, by correlated spectroscopy (COSY ¹H-¹H, HMQC, HMBC).

Low- and high-resolution mass spectra methods (**LRMS** TOF and **HRMS** TOF) used are electrospray (ESI), electronic impact (EI) and chemical ionization (CI).

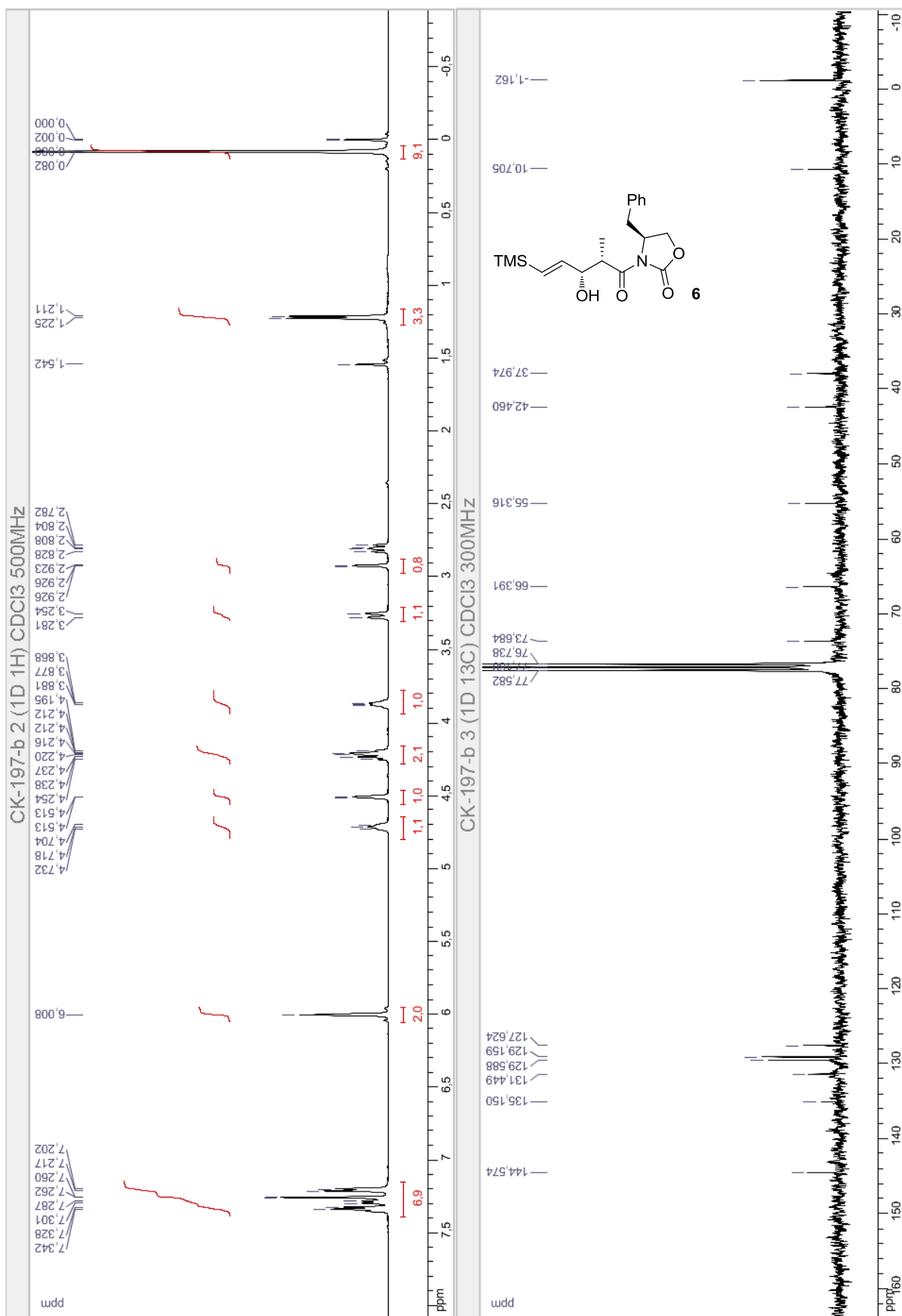
Elemental analyses (Anal.) results are given as the average values of at least two determinations.

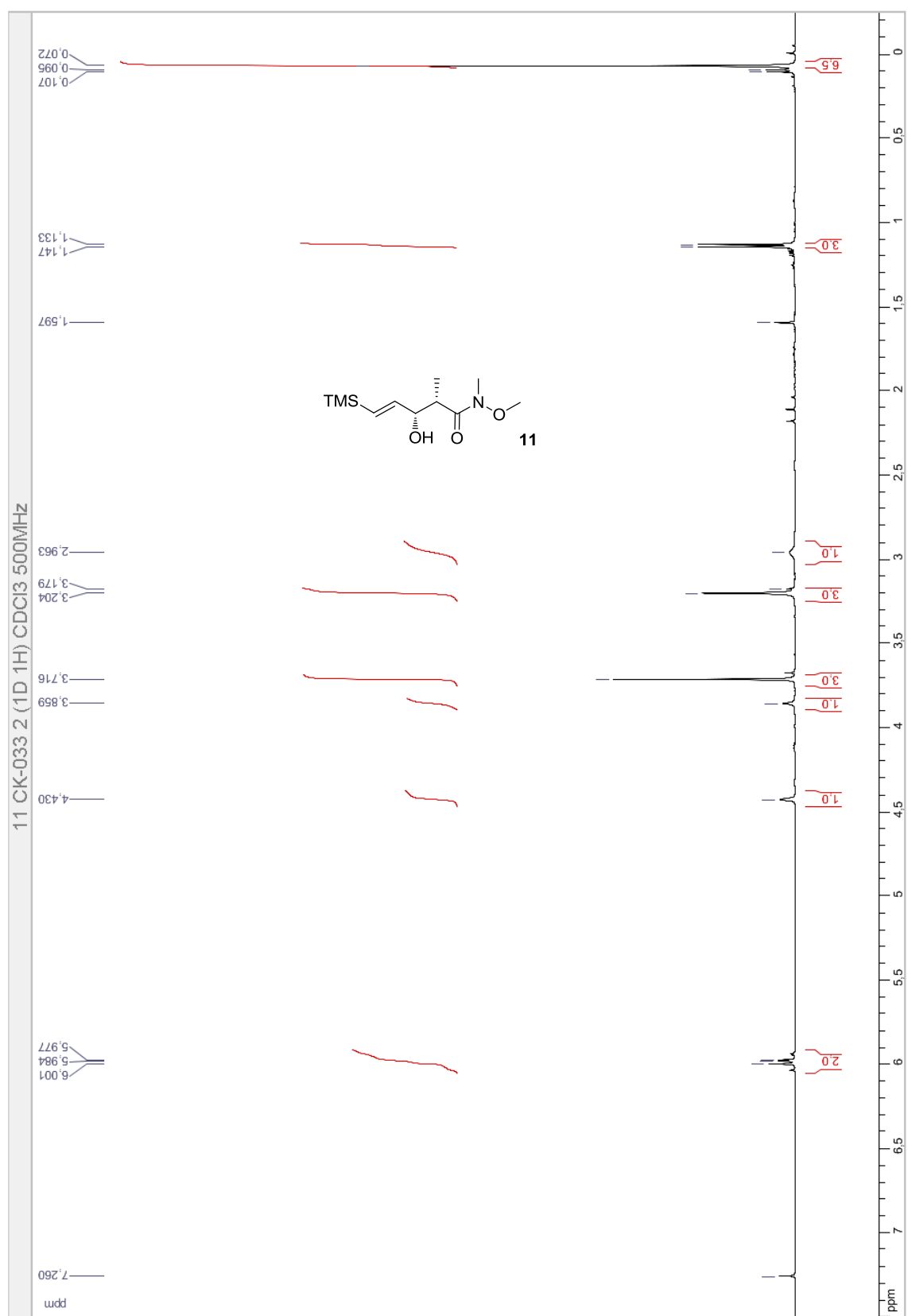
Melting points (MP) were determined after crystallization or precipitation from the solvents indicated between brackets.

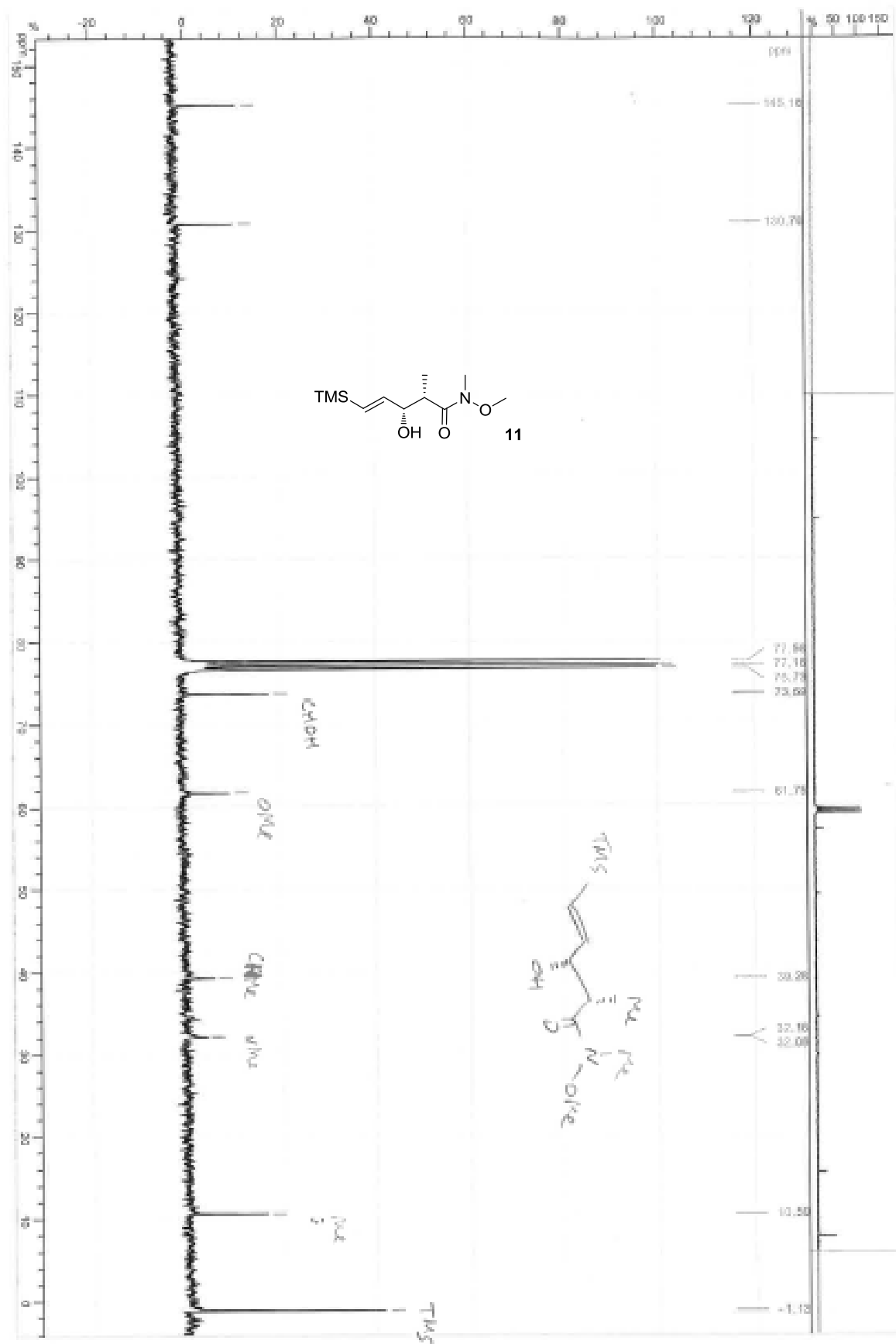
Special instructions for acid-sensitive compounds: Many compounds described in this work are acid-sensitive. In order to avoid their degradation, the following preventive measures were taken:

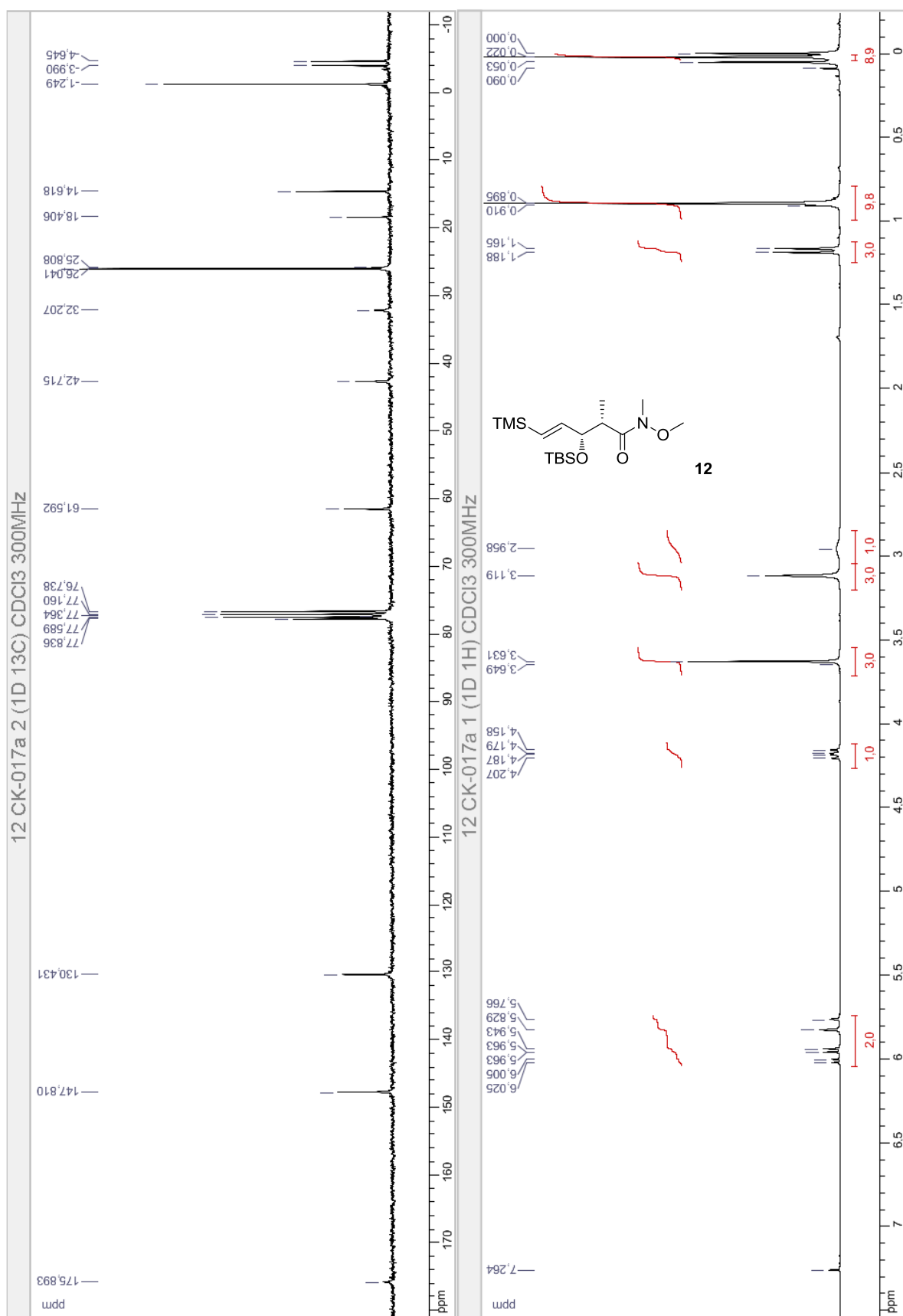
- washing with a saturated aqueous solution of NaHCO₃ at the end of the extraction;
- drying on a Na₂SO₄/K₂CO₃ mixture before filtration and removal of the solvents;
- purification on neutralized silica gel, prepared by treatment with Et₃N (25 mL per kg of silica gel) in EtOAc, followed by concentration and drying under vacuum;
- NMR experiments carried out in C₆D₆ instead of CDCl₃.

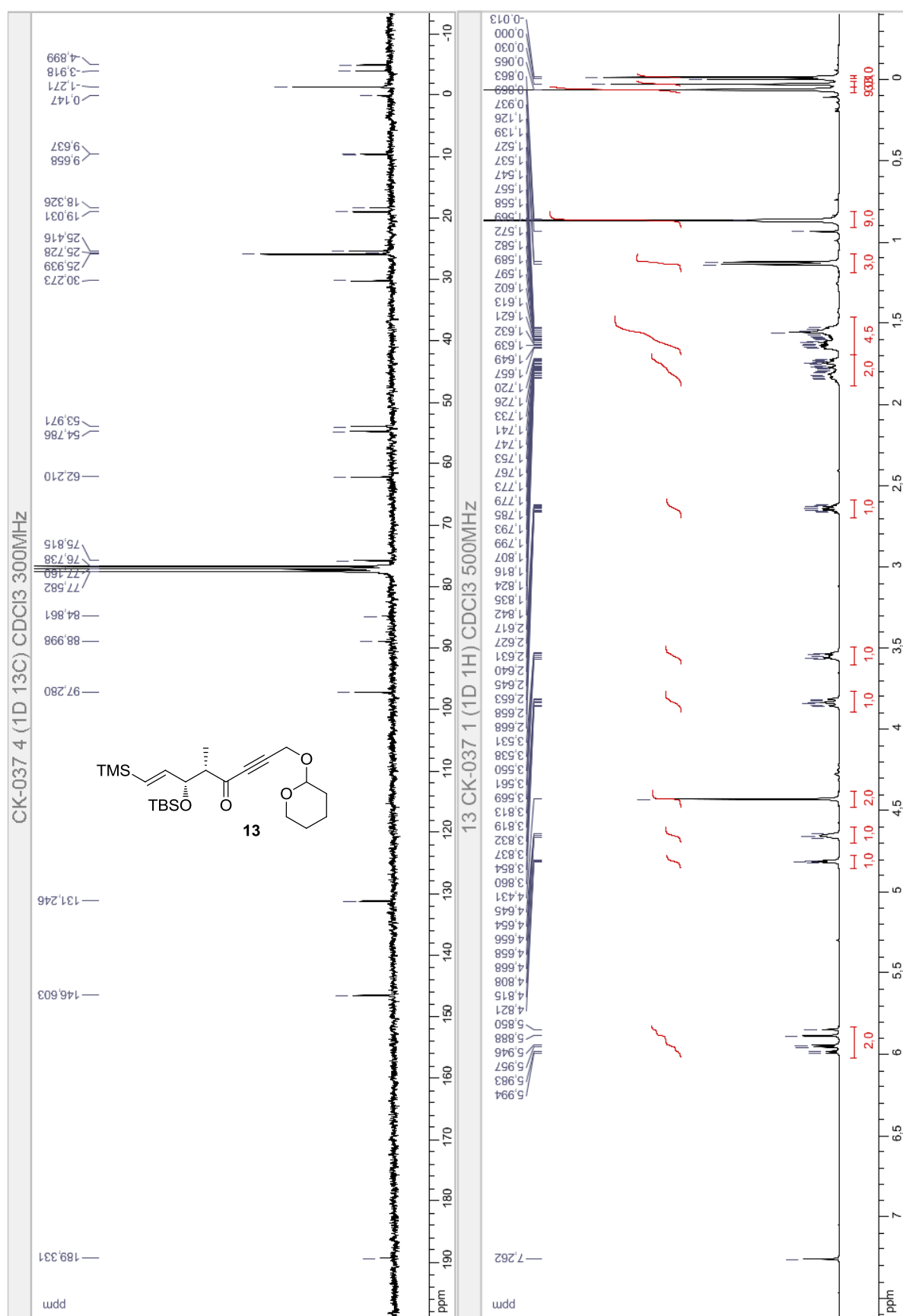
² H. E. Gottlieb, V. Kotlyar, A. Nudelman, *J. Org. Chem.* **1997**, 62, 7512-7515.

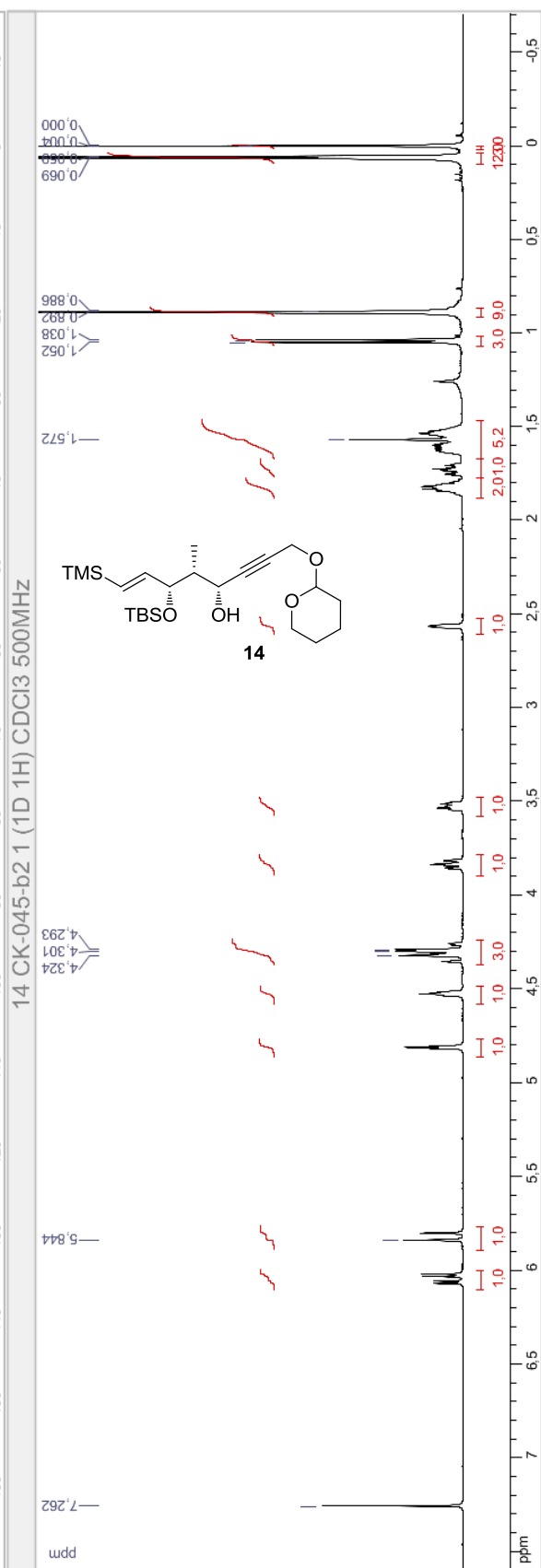
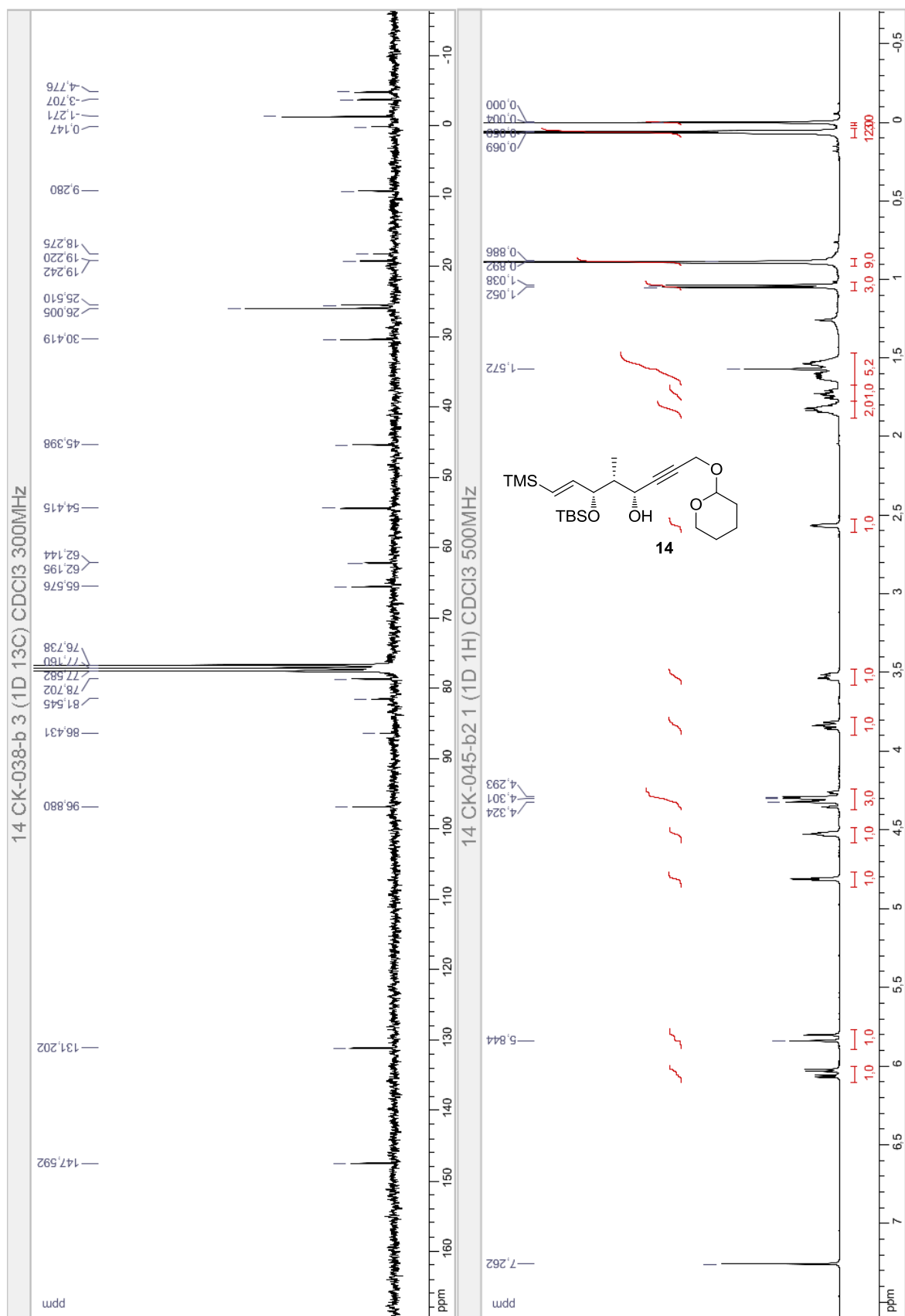


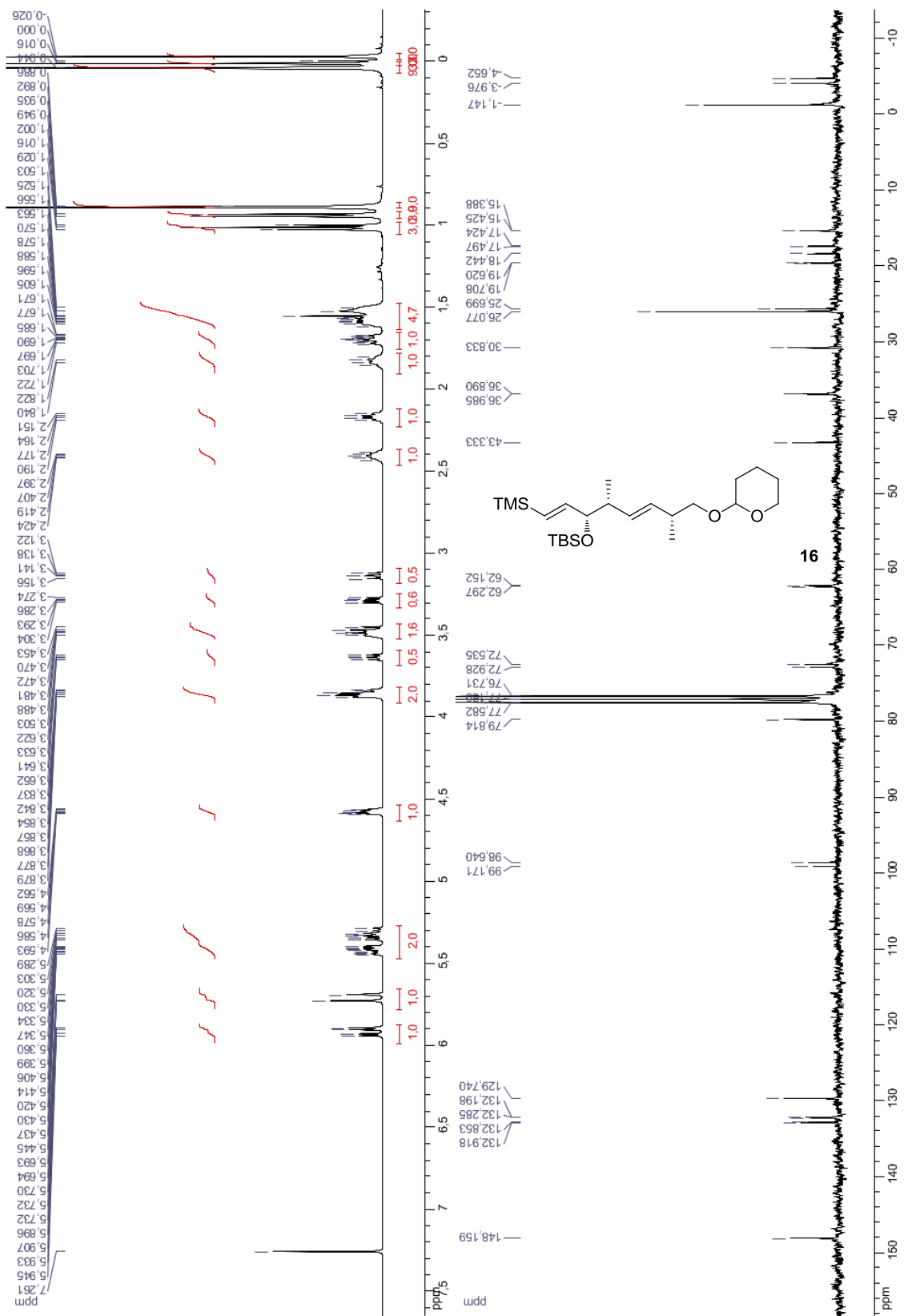


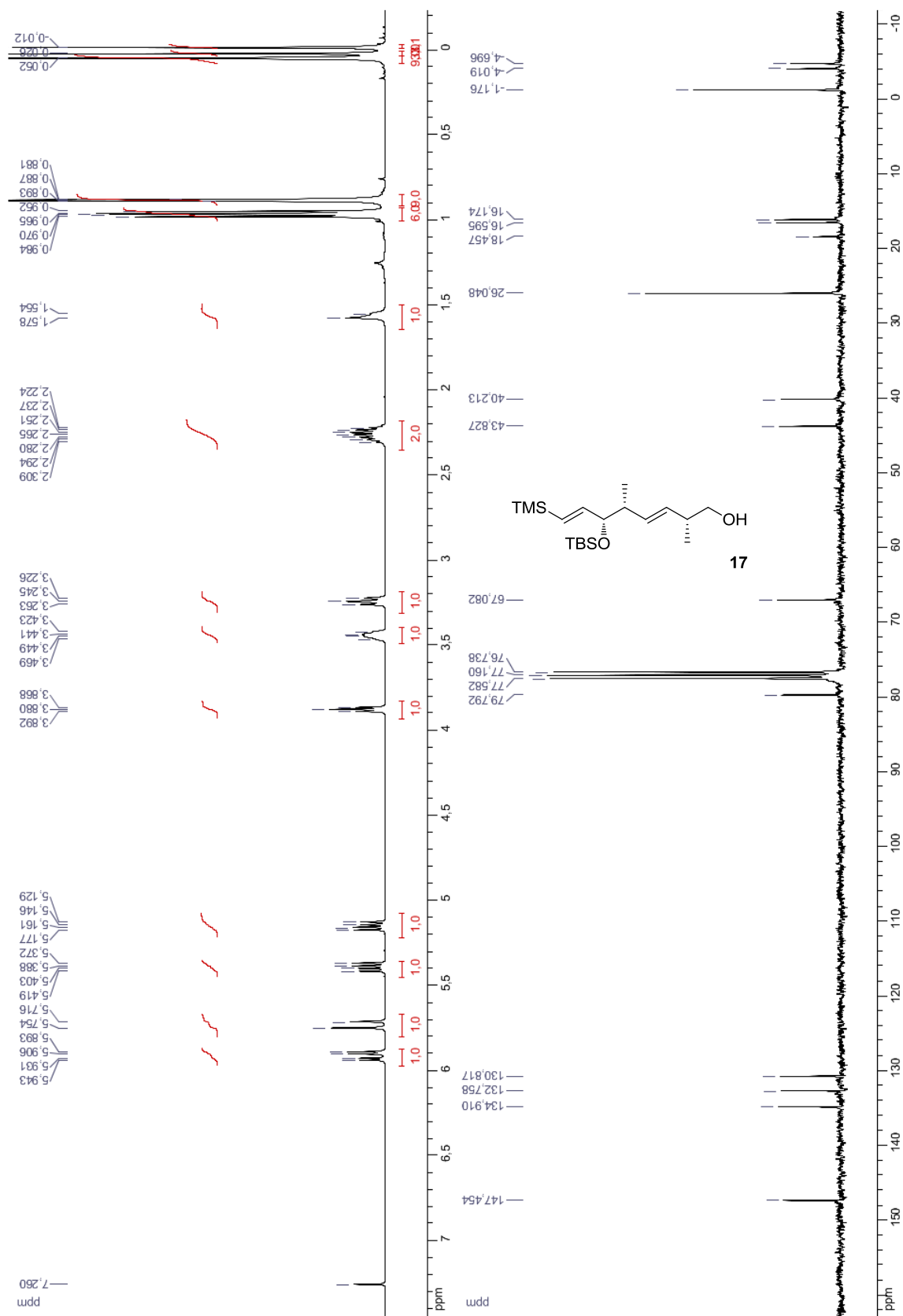


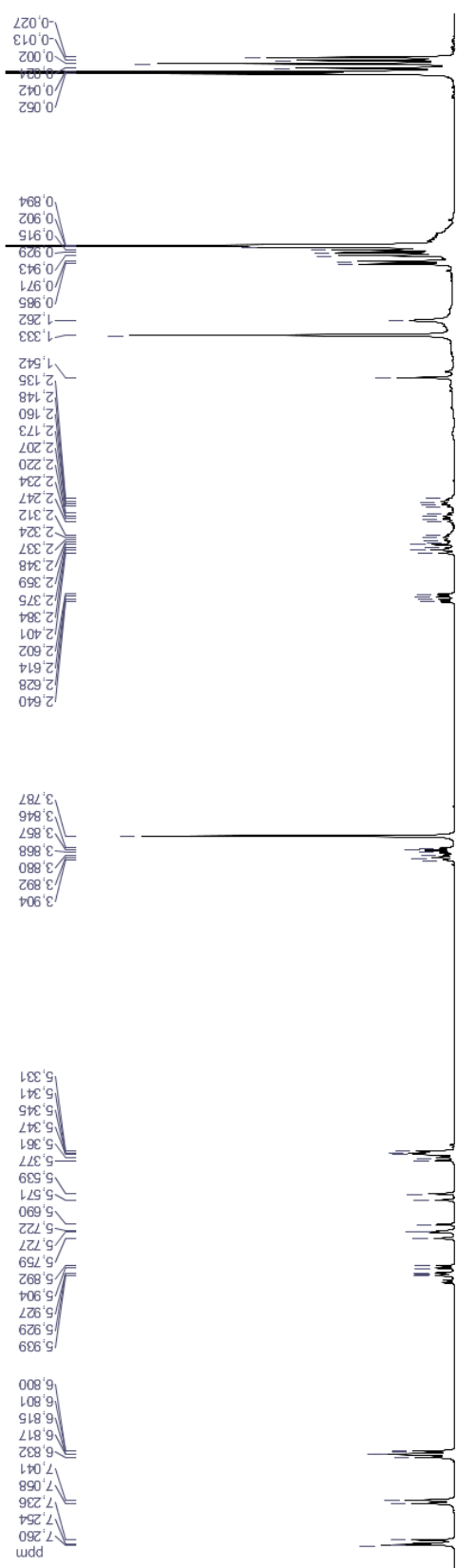
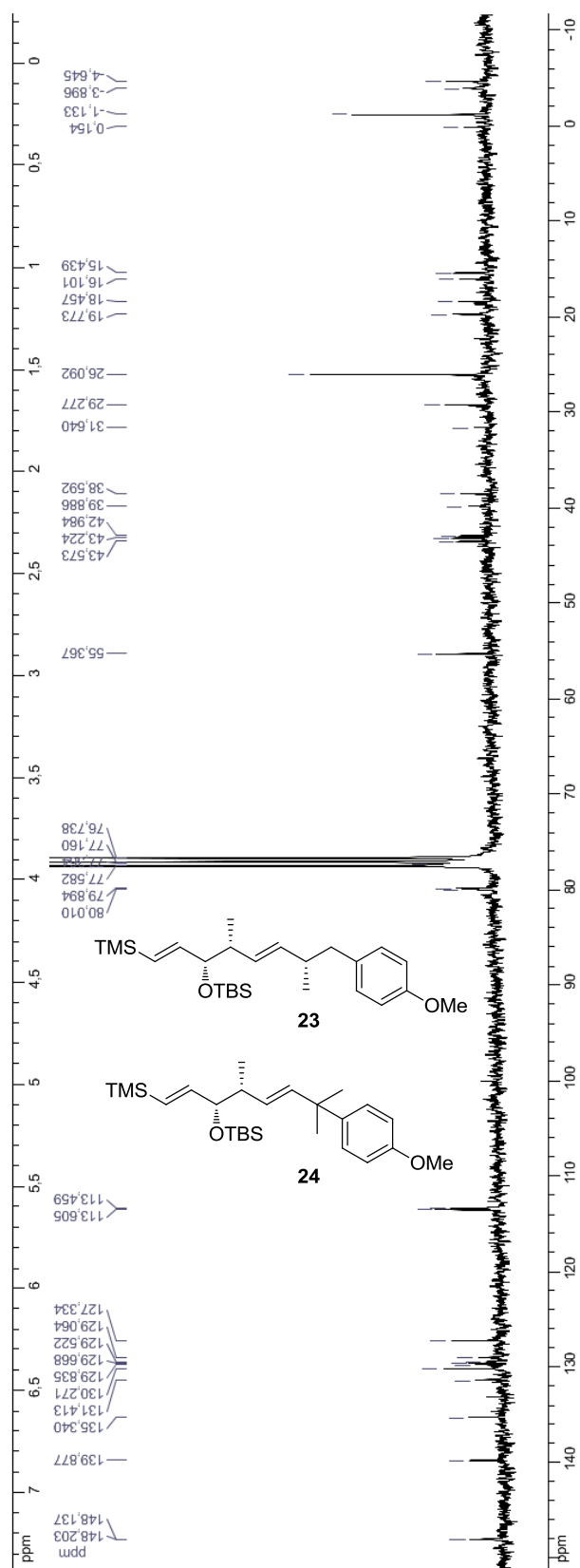


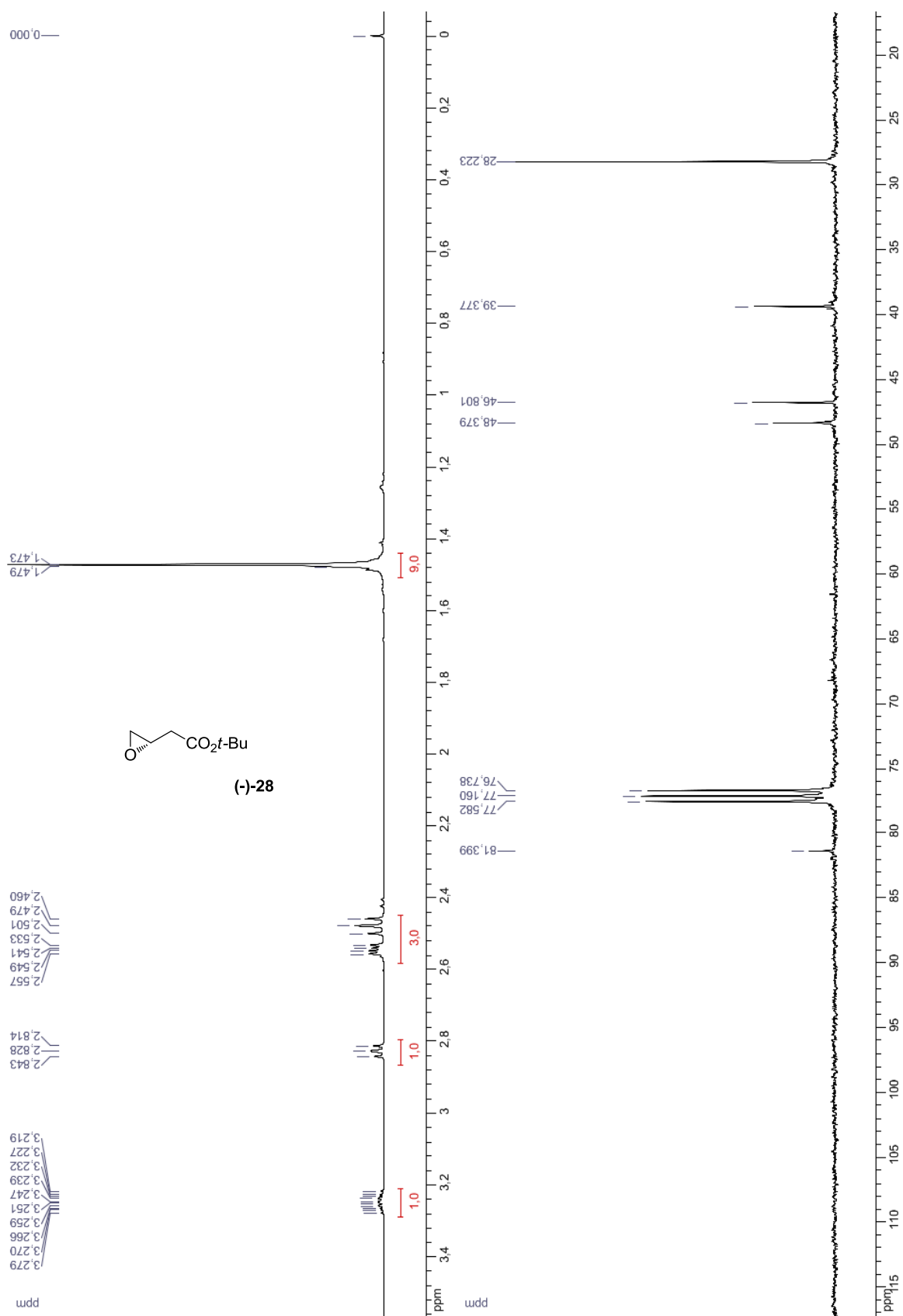


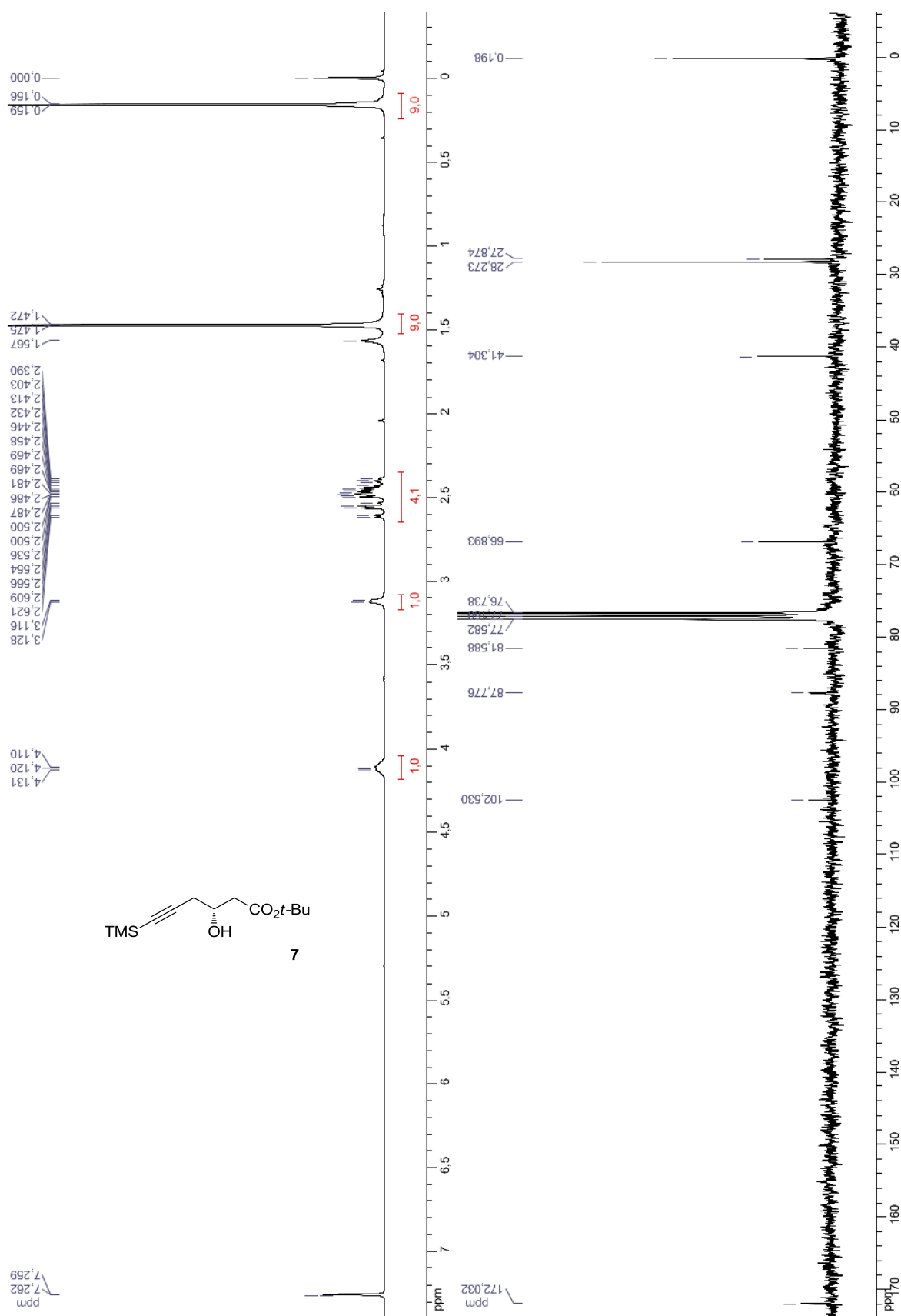


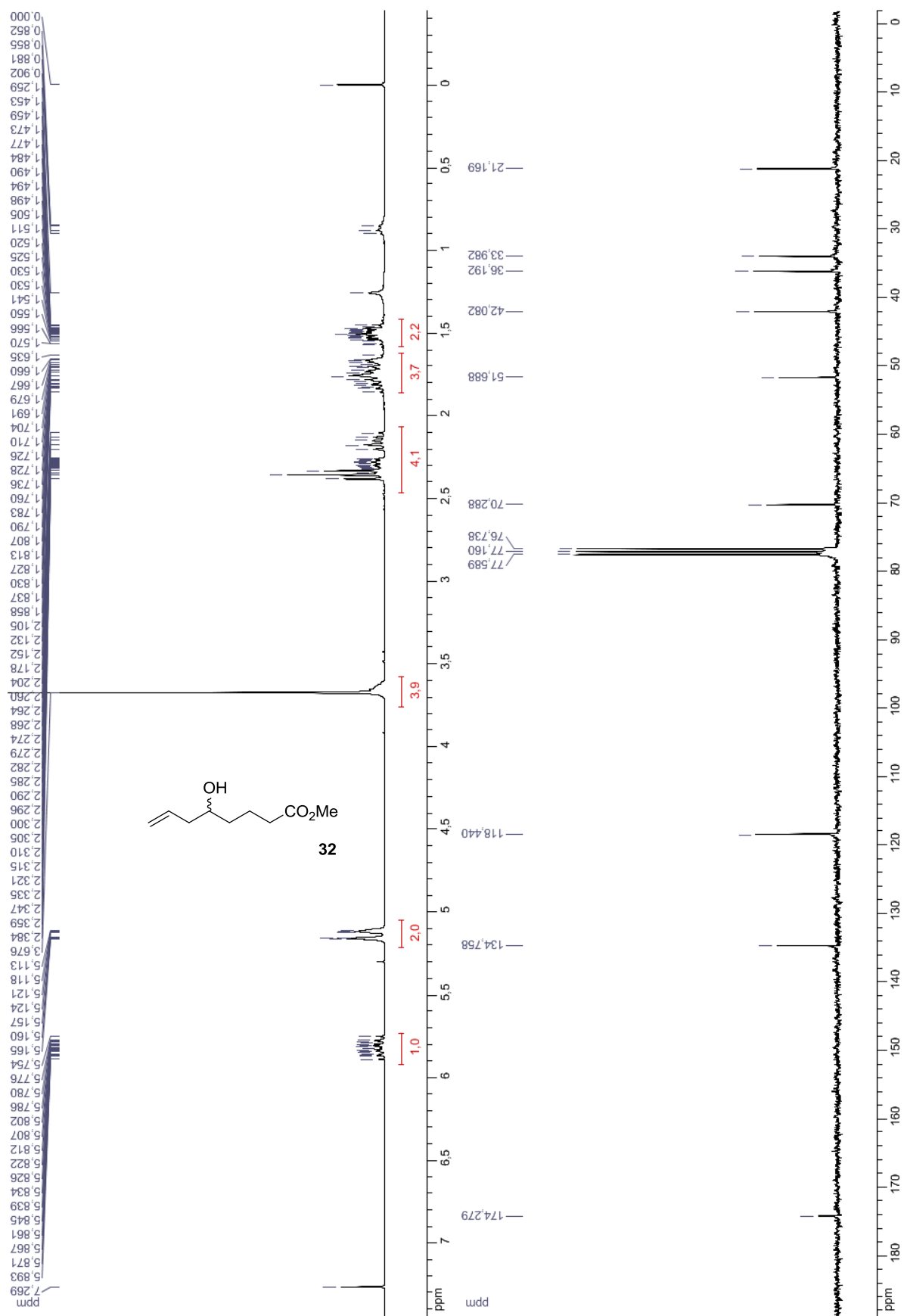


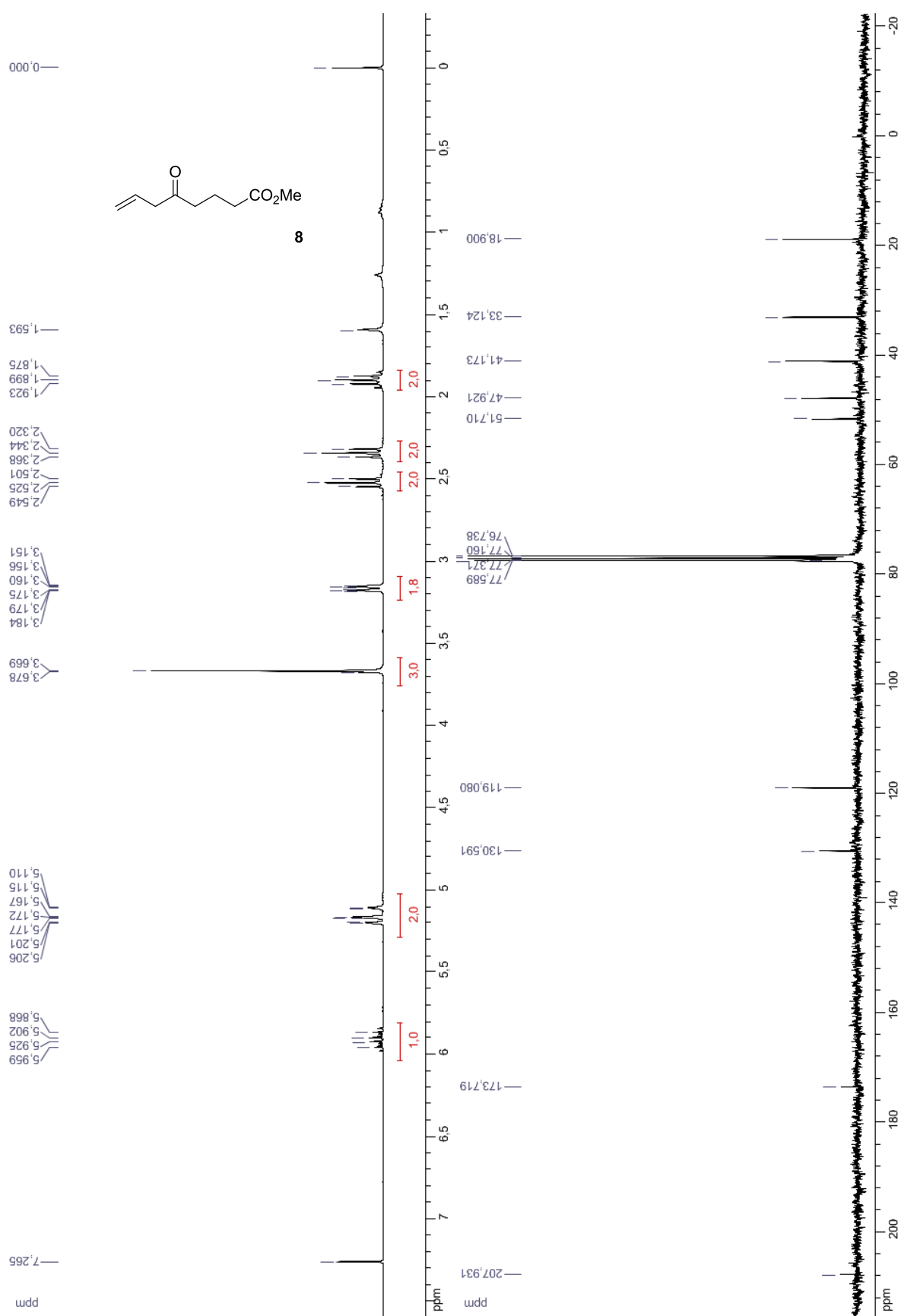


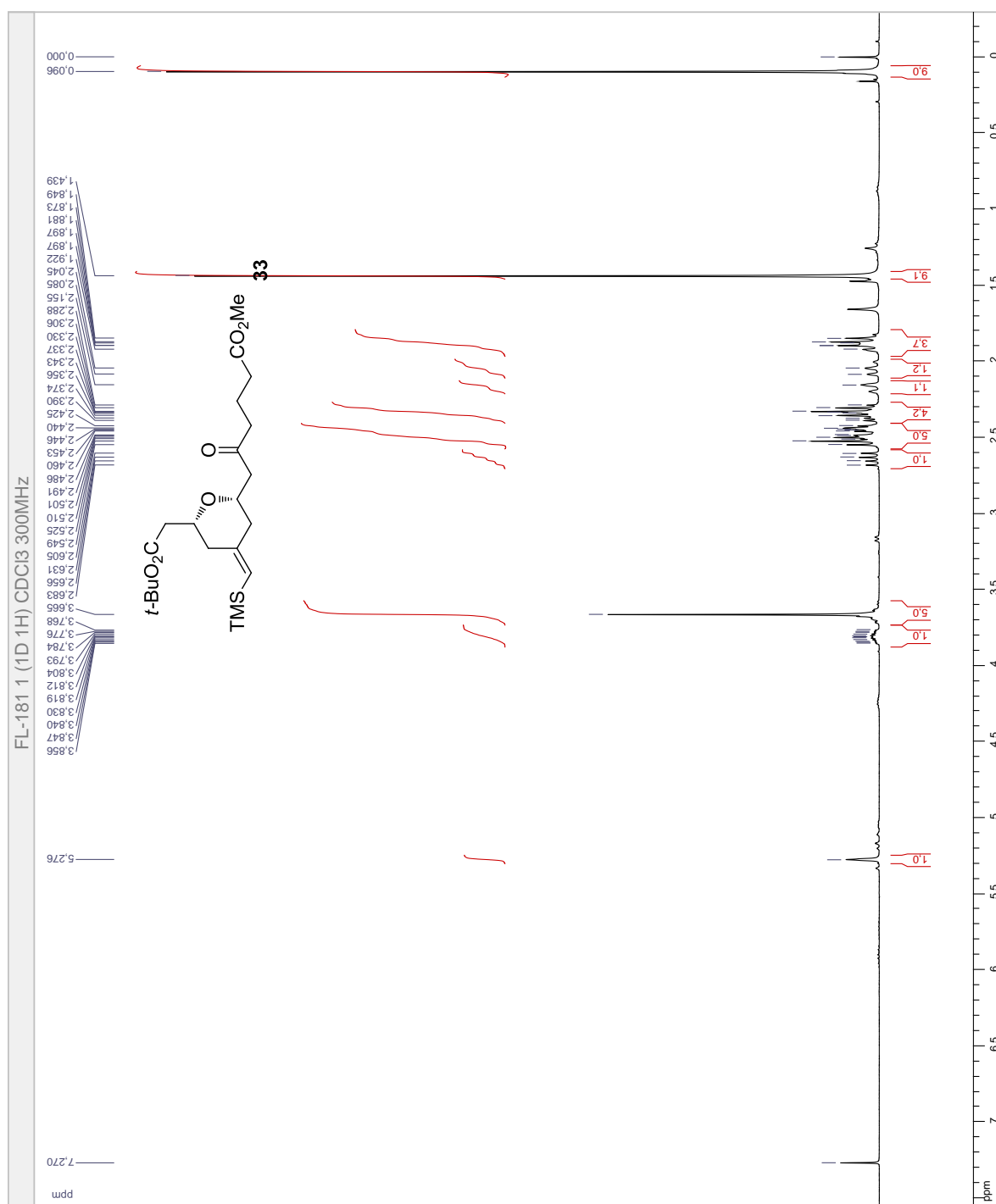


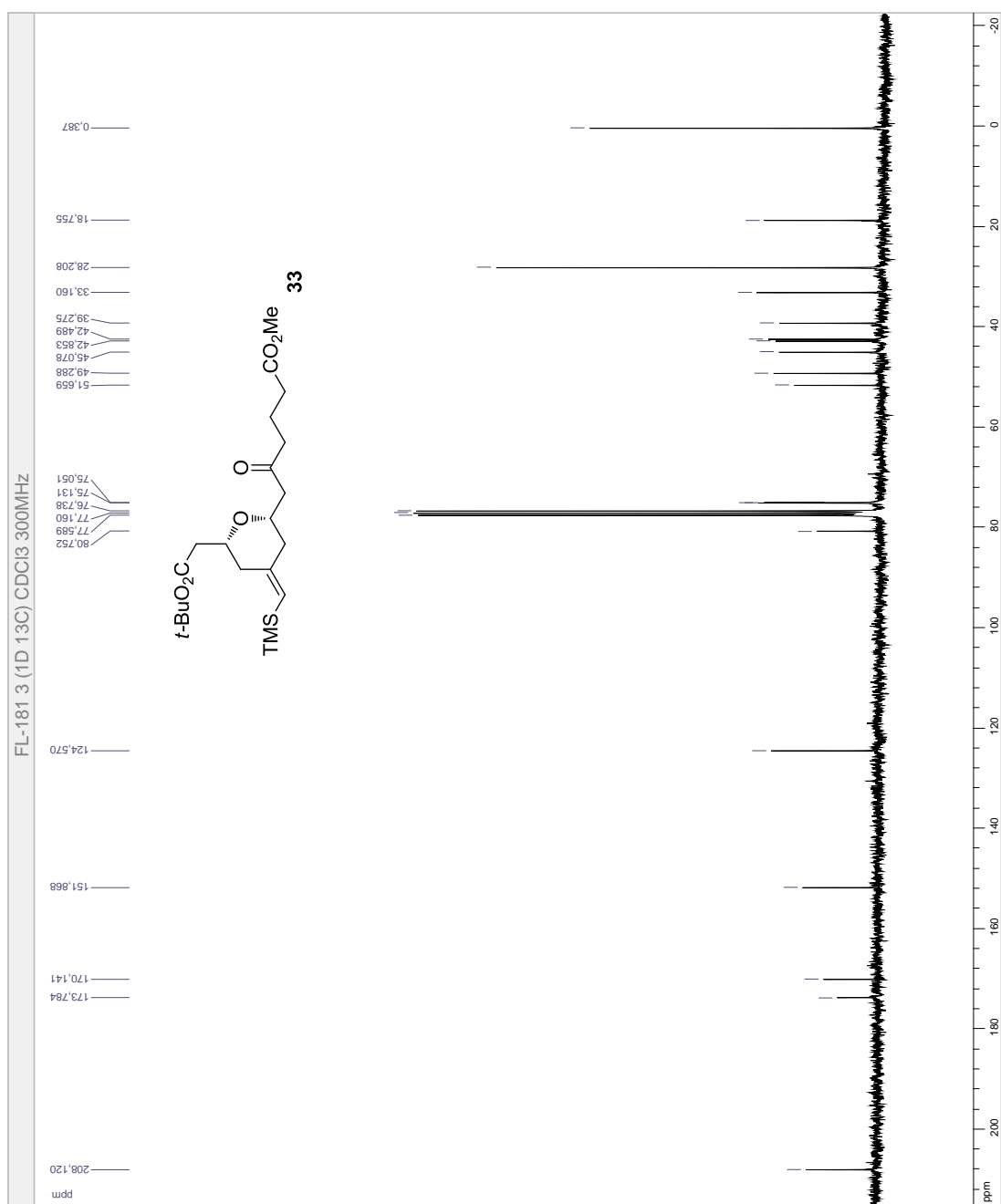


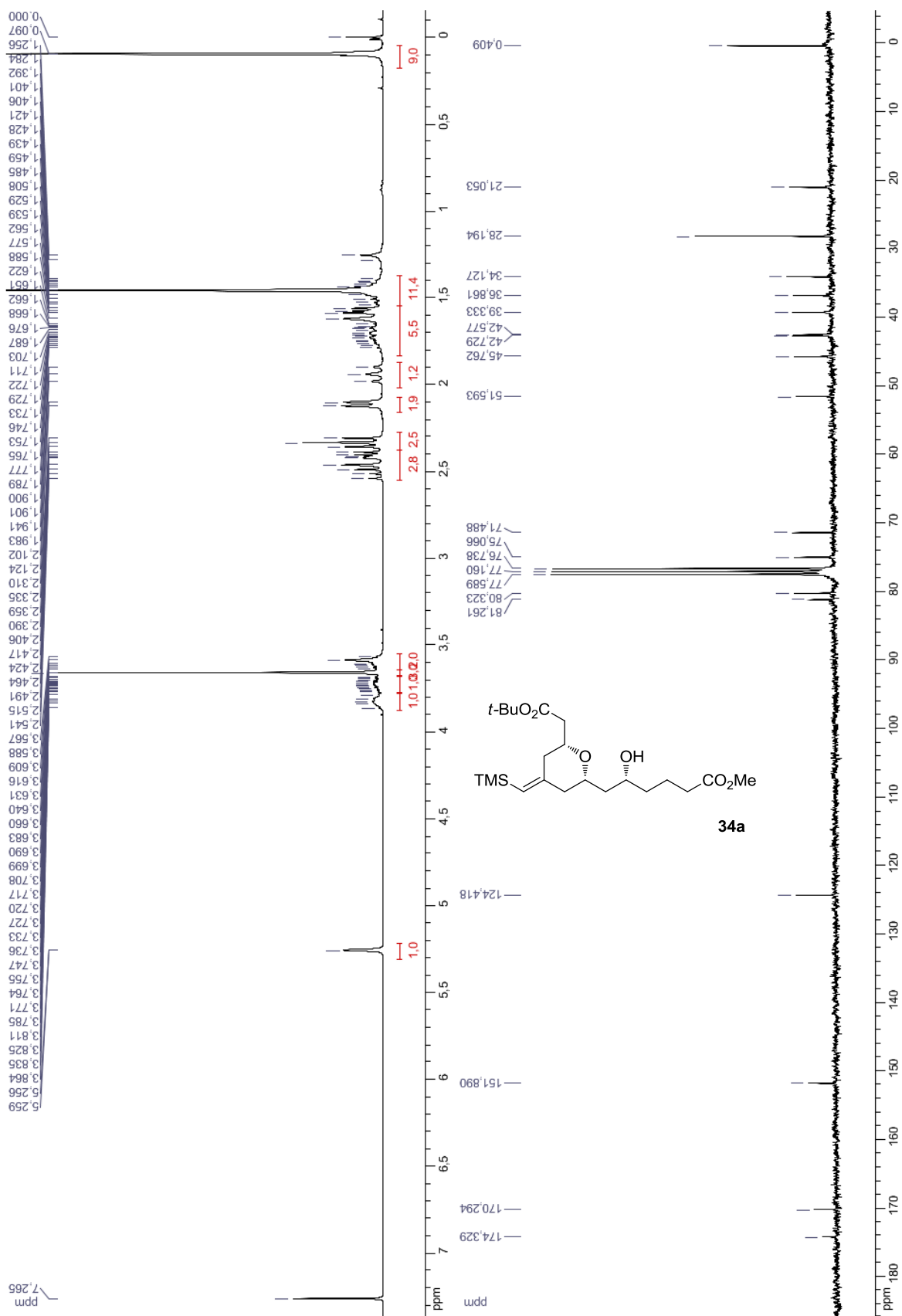


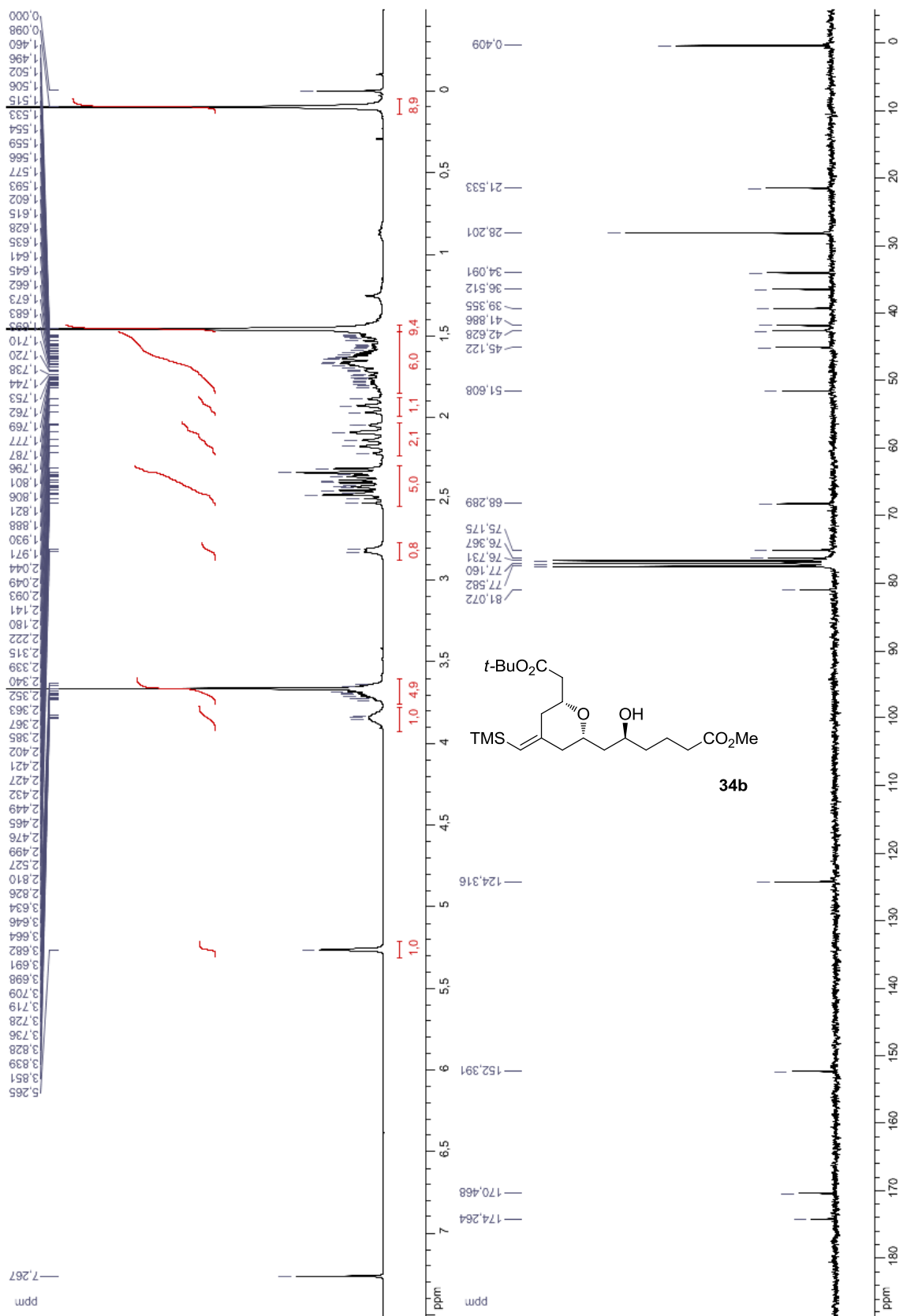


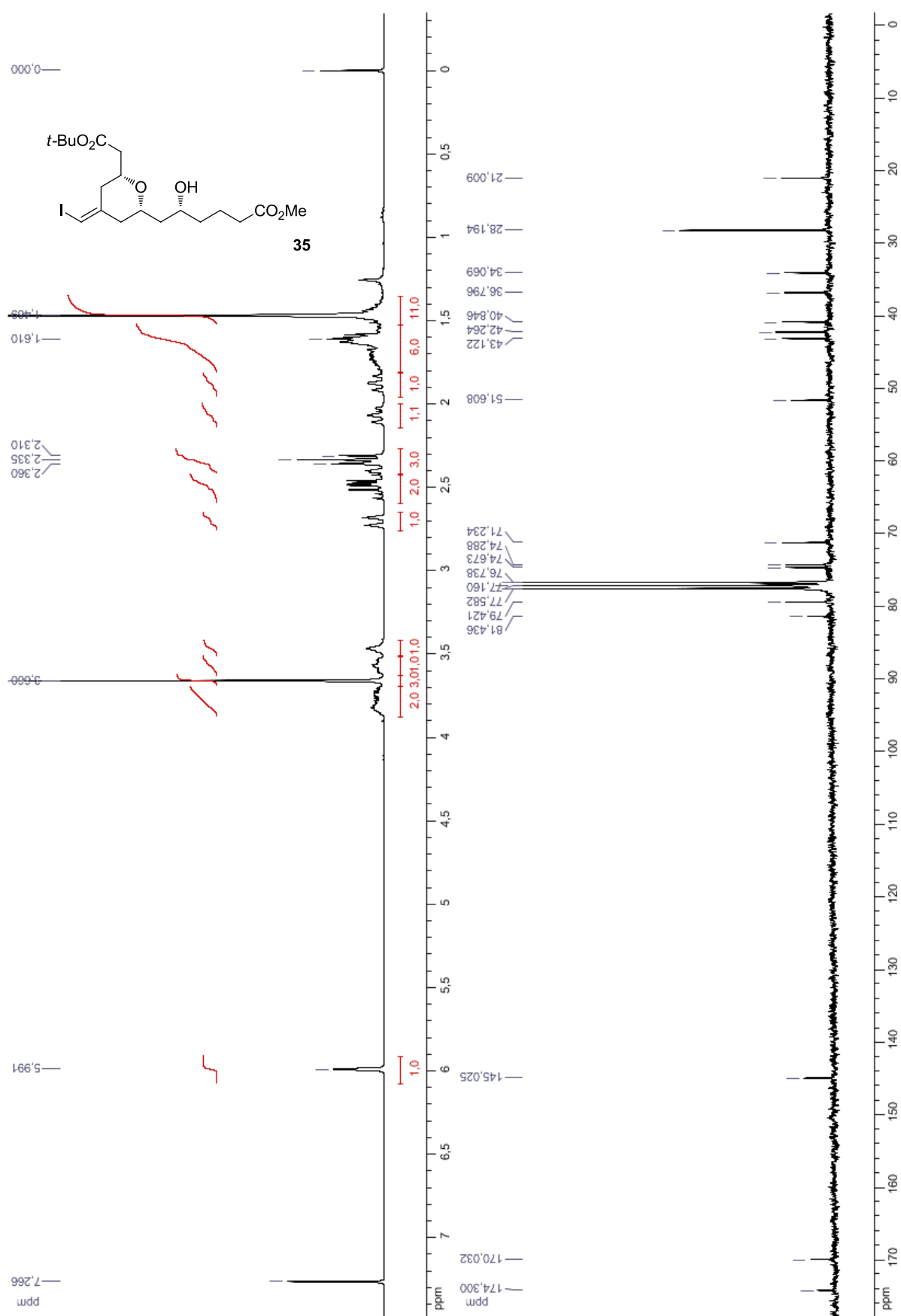


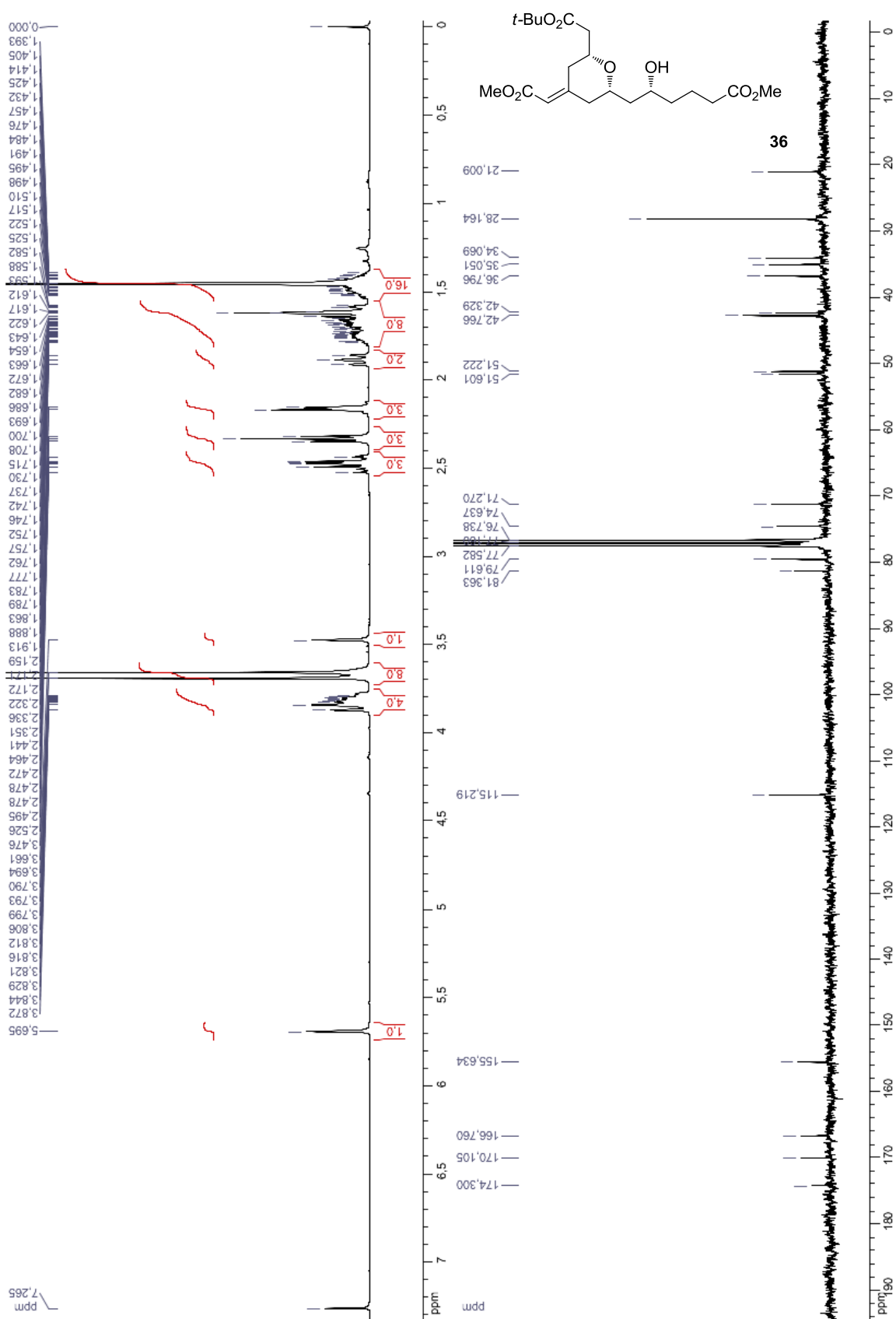


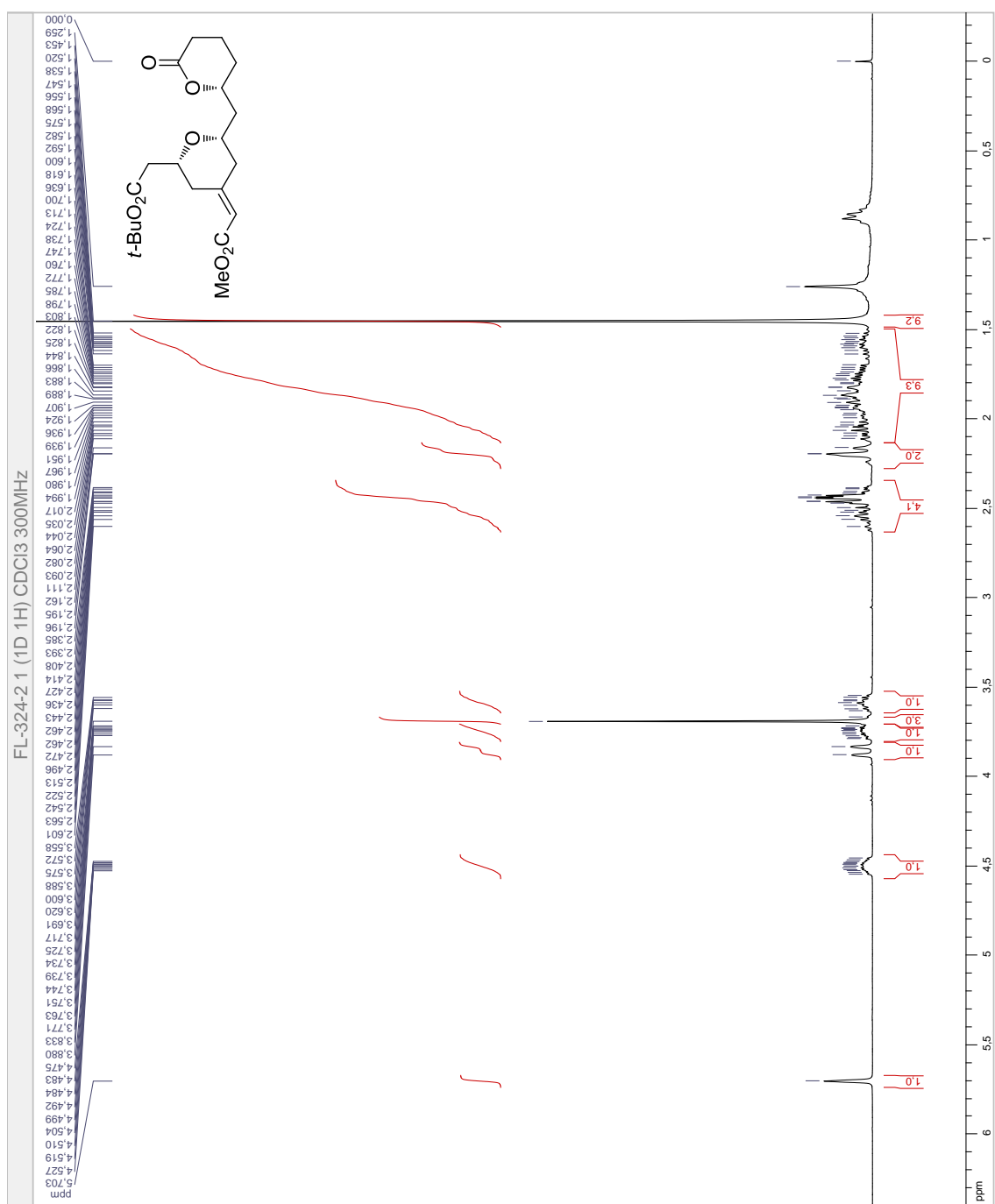












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