Boronate titanium alkylidene reagents for the diversity-based synthesis of benzofurans

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Supporting Information

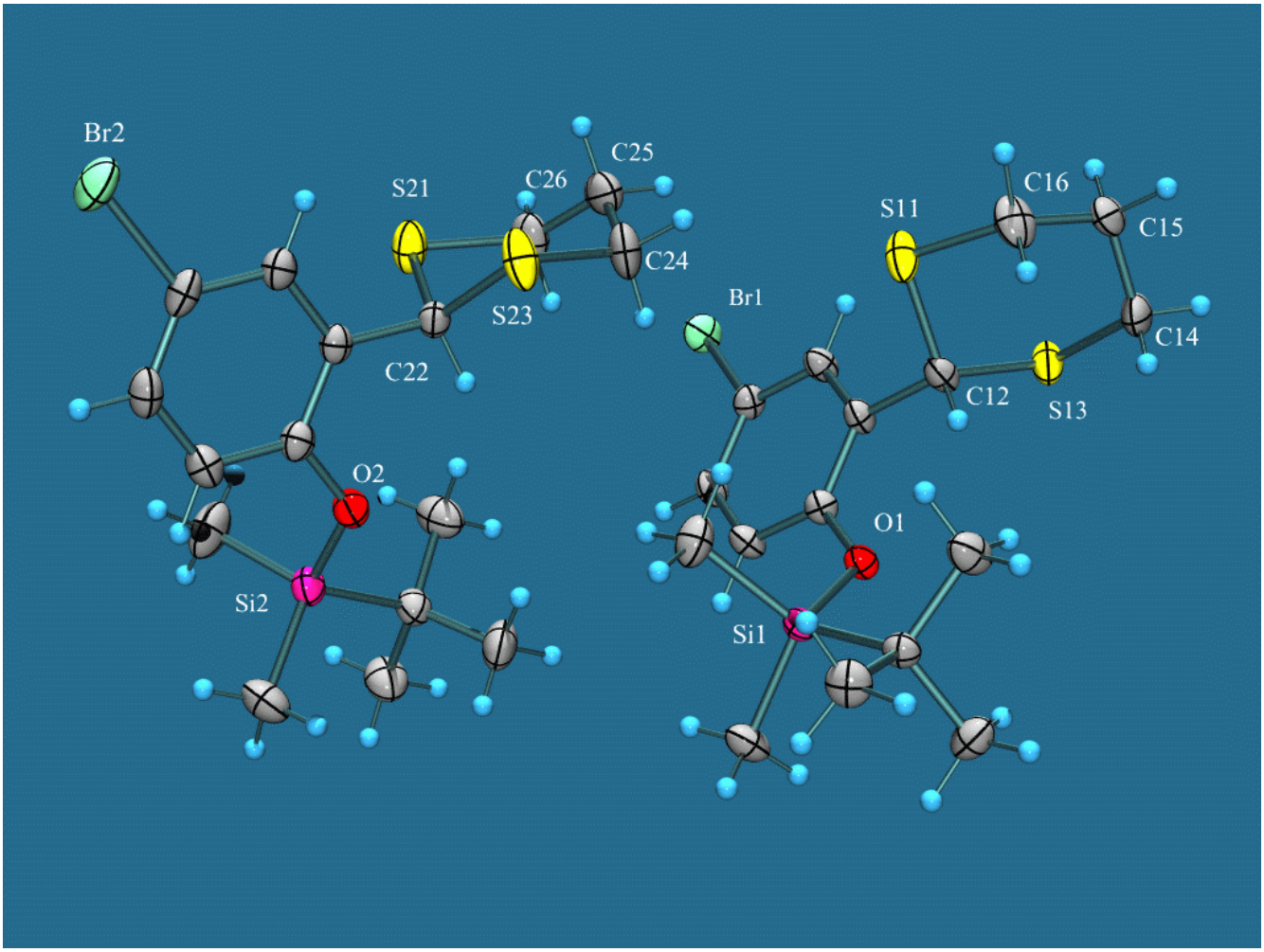
General considerations: All experiments were performed under an atmosphere of Ar or N_2. THF was distilled from sodium/benzophenone; $P(OEt)_3$ was distilled from CaH_2 prior to use and DMF was distilled from CaH_2 then stored over activated 4Å MS. Bis(cyclopentadienyl)titanium dichloride was purchased from Lancaster and used without further purification. Merrifield resin was purchased from Polymer laboratories and had a loading of 1.83 mmol/g. Resin-bound esters were synthesised according to the procedure of Frenette and Friesen.[1]

Example procedure: Bis(cyclopentadienyl)titanium dichloride (0.93g , 3.74 mmol, 12 eq), magnesium turnings (0.10 g, 4.12 mmol, 13.2 eq) and 4Å MS (0.20 g) were heated gently by heat-gun for 1 min, under reduced pressure. Once cooled, THF (4 ml) and $P(OEt)_3$ (1.30 ml, 8.07 mmol, 24 eq) were added and the mixture stirred at room temperature. After 3 h, a solution of [1,3]dithiane **23** (0.38 g, 0.933 mmol, 3 eq) in THF (10 ml) was added and the mixture stirred for a further 15 min before addition of Merrifield resin-bound ester **12b** (0.311 meq, contained within an IRORI macrokan). The mixture was heated to reflux. After 3 h, the reaction was allowed to cool, the resin removed and washed: THF (5 x 30 ml); MeOH and DCM alternately (4 x 30 ml each); and finally MeOH and DCM (30ml each). The resin-bound enol ether was dried *in vacuo*.

The IRORI macrokan containing resin-bound enol ether **31b** (0.311 meq) was treated with Cs_2CO_3 (0.52 g, 1.56 mmol, 5 eq), $Pd(PPh_3)_4$ (14.7 mg, 4 mol%) and iodotoluene (0.33 g, 1.56 mmol, 5 eq) in dry DMF (8 ml) and distilled water (5.6 μl, 0.311 mmol, 1 eq) was added. The mixture was heated to 80 ˚C. After 20 h, the reaction was cooled and the resin washed: (9:1) DMF–H_2O (3 x 30 ml); THF (5 x 30 ml); MeOH and DCM alternately (4 x 30 ml each); and finally, MeOH and DCM (30 ml each). The resin was dried *in vacuo* then treated with 1%TFA-DCM for 30 min. The DCM solution was decanted then the resin washed with DCM (3 x 5 ml); all DCM solutions were combined, neutralised/dried over solid anhydrous K_2CO_3 and concentrated *in vacuo* to give the *ketone* **32ba'** as an orange oil (57 mg, 0.177 mmol, 57% based on loading of chloromethylpolystyrene). The orange oil (54 mg, 0.166 mmol after characterisation) was taken-up in 10% conc. HCl–MeOH (5 ml) and heated to reflux for 5 min. MeOH was removed *in vacuo* and the residue taken-up in DCM (50 ml) and dried/neutralised over solid K_2CO_3 then concentrated *in vacuo* to give the *benzo[*b*]furan* **33ba'**as a yellow solid (41.5 mg, 0.158 mmol, 95%).

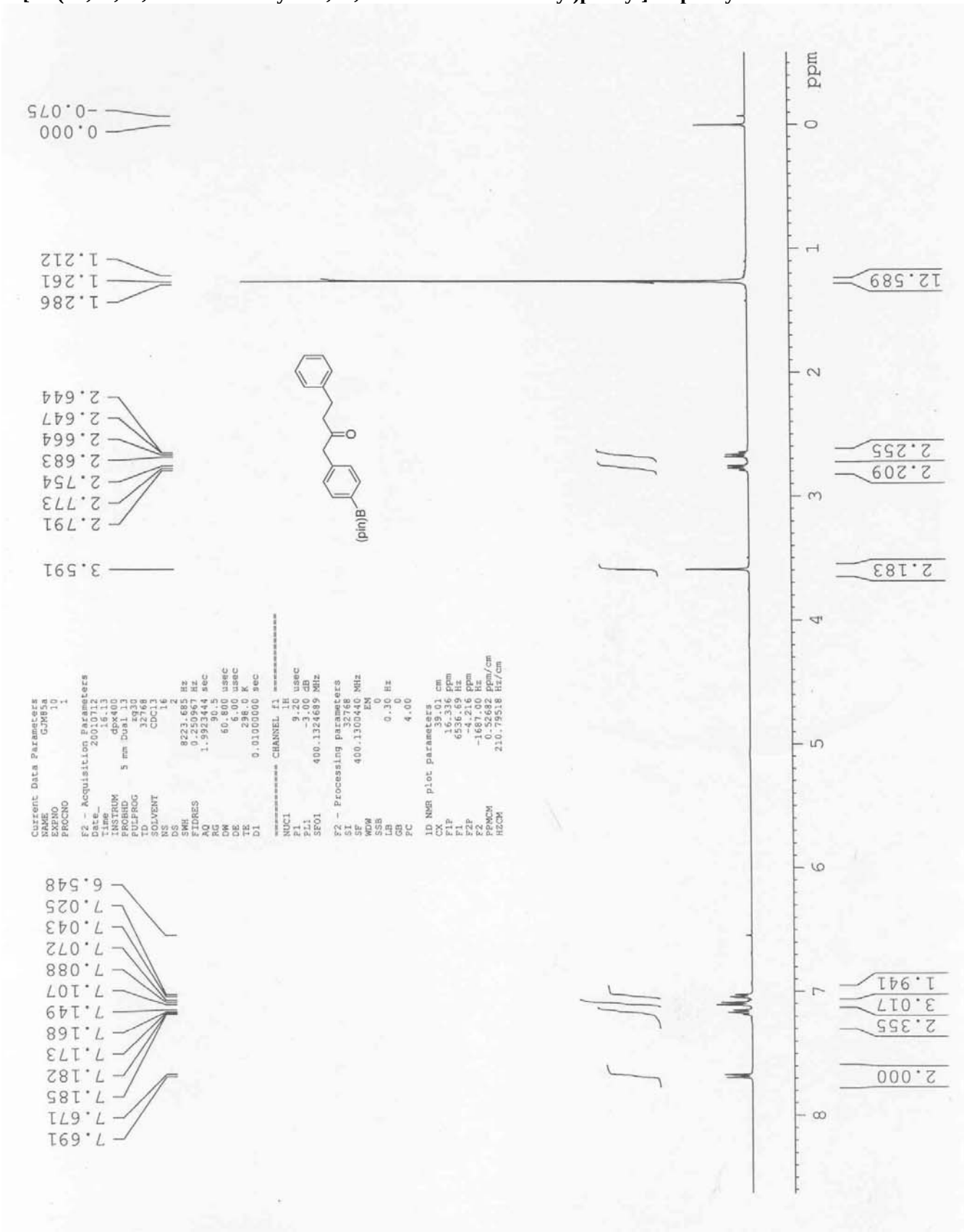
[1] 1. Frenette, R.; Friesen, R.W.; *Tetrahedron Lett.* **1994**, *35*, 9177

Crystal stucture of (5'-Bromophenyl-2'-*tert*-butyldimethylsiloxyphenyl)-[1,3]dithiane 24:

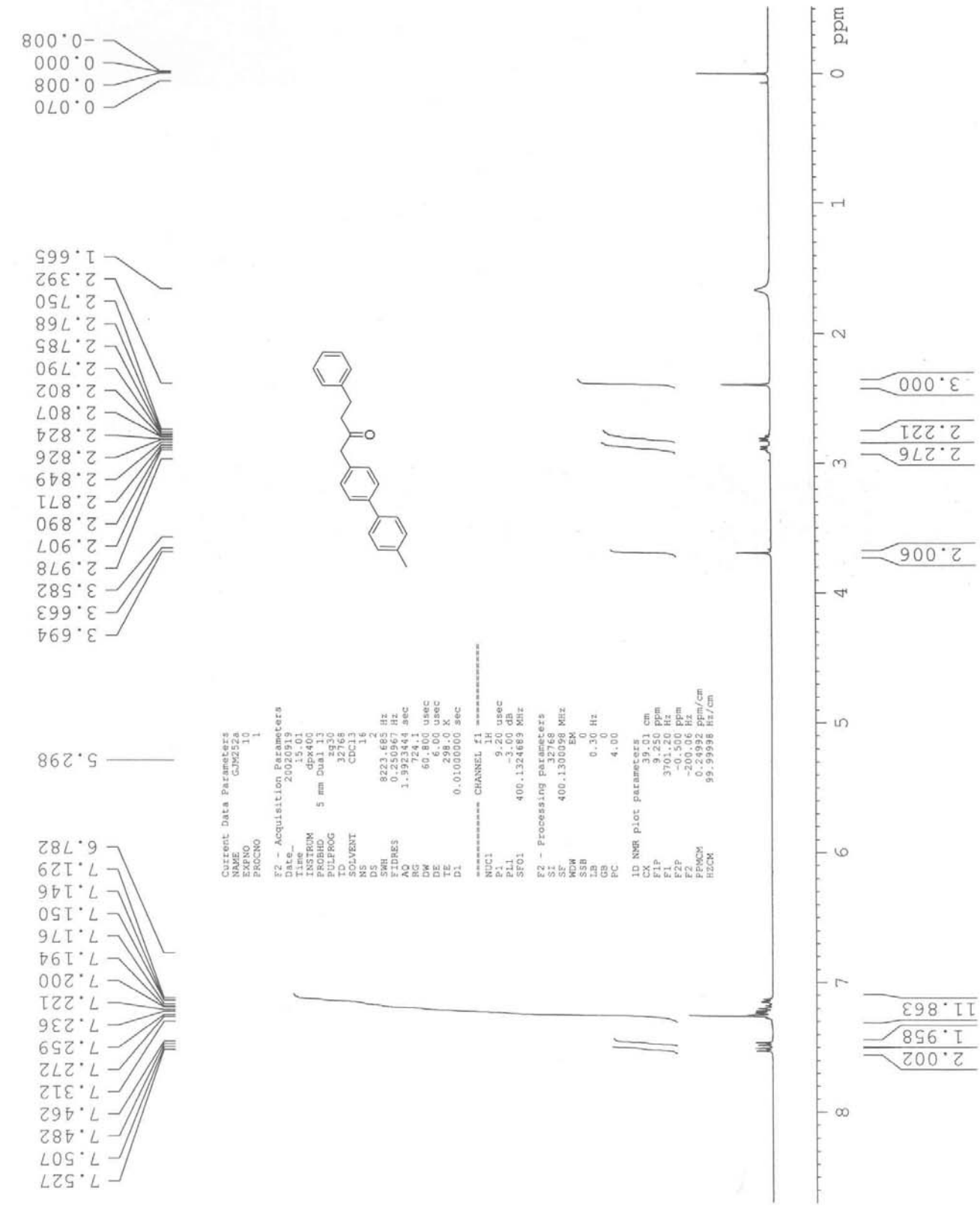


^{1}H NMR spectra of 14–16, 28a–c, 29a–c and 32aa'–cc'

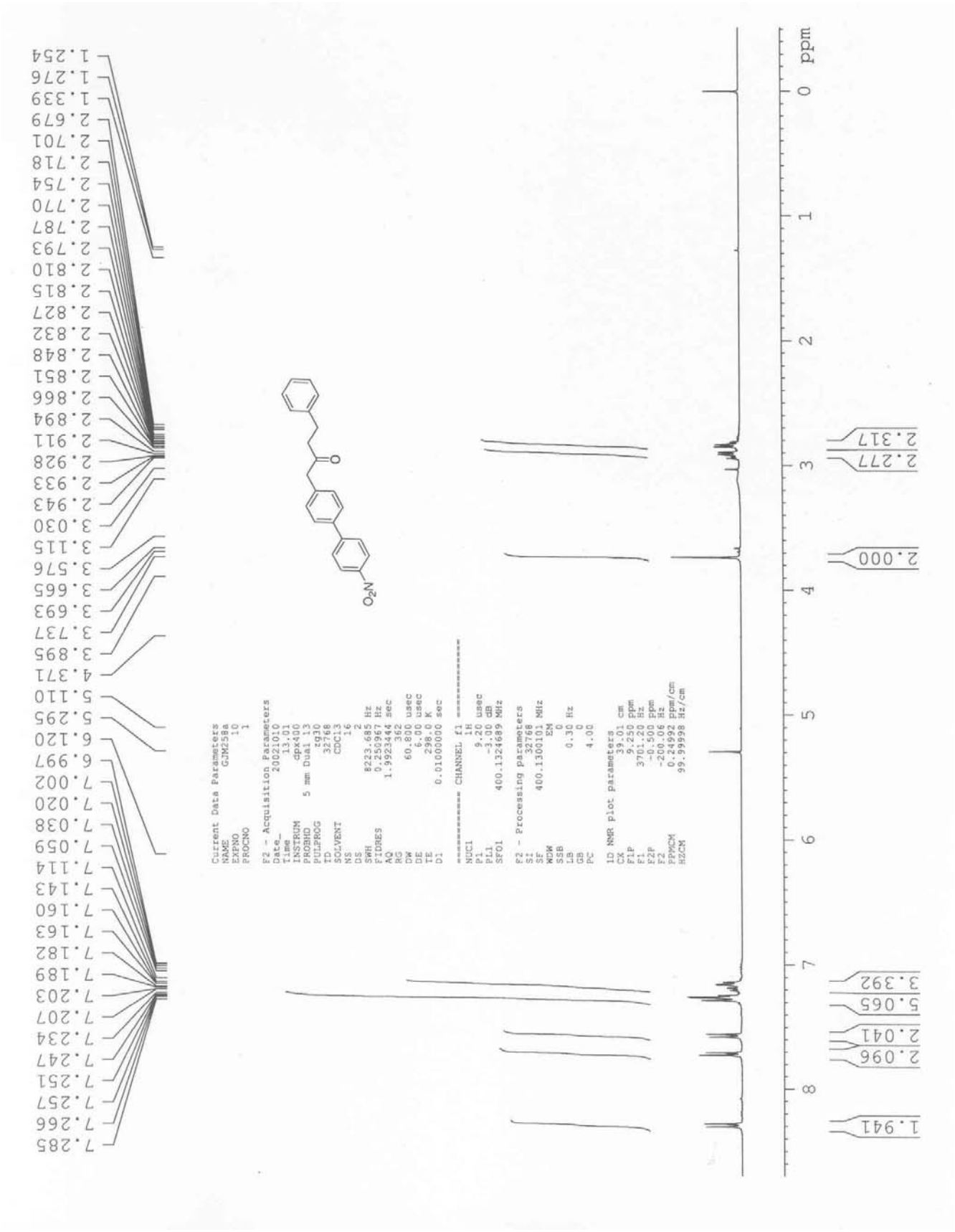
1–[4'–(4'',4'',5'',5''–Tetramethyl–1'',3'',2''–dioxaborolan–2''–yl)phenyl]–4–phenylbutan–2–one 14



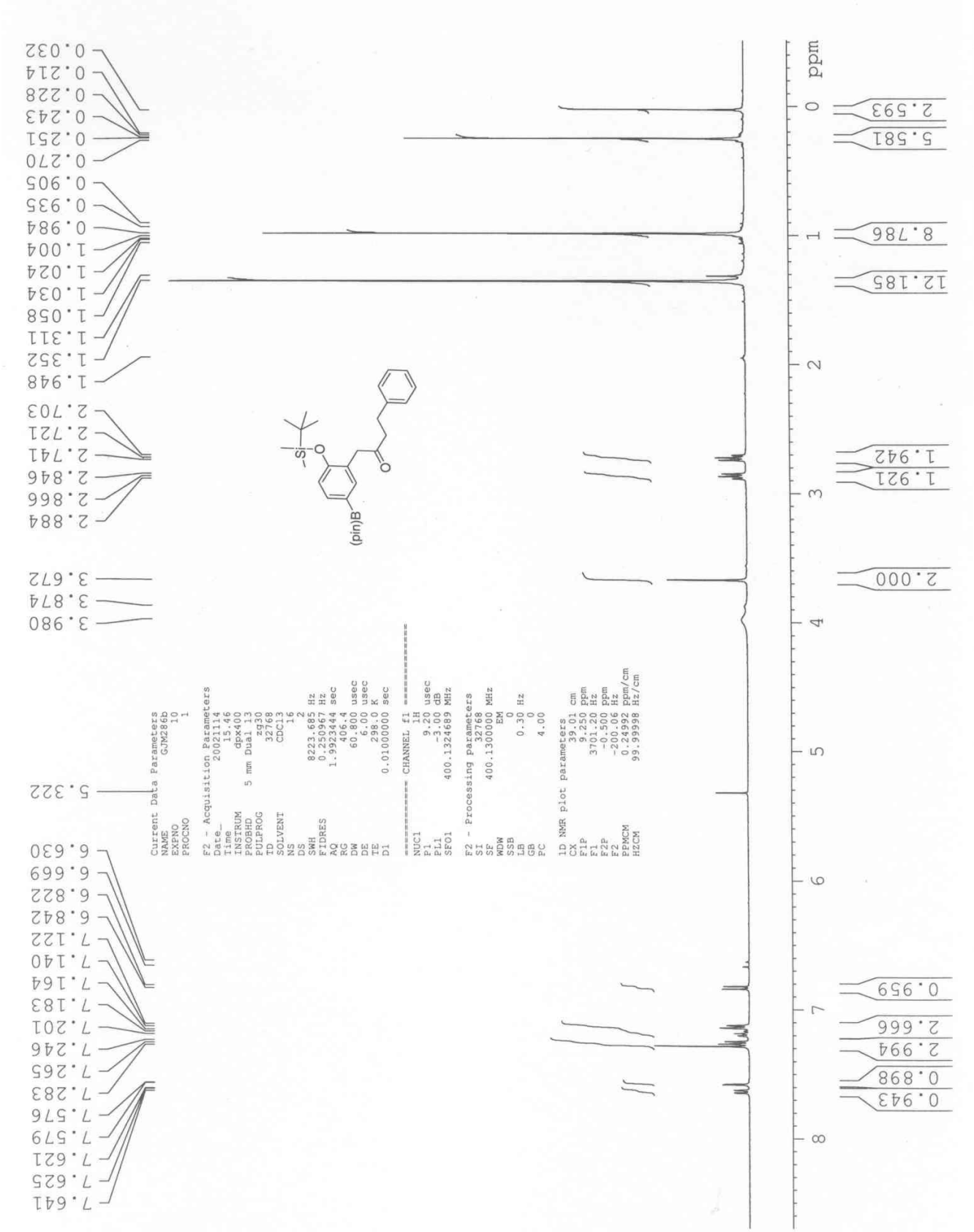
1–(4'–methylphenyl)phenyl–4–phenylbutan–2–one 15



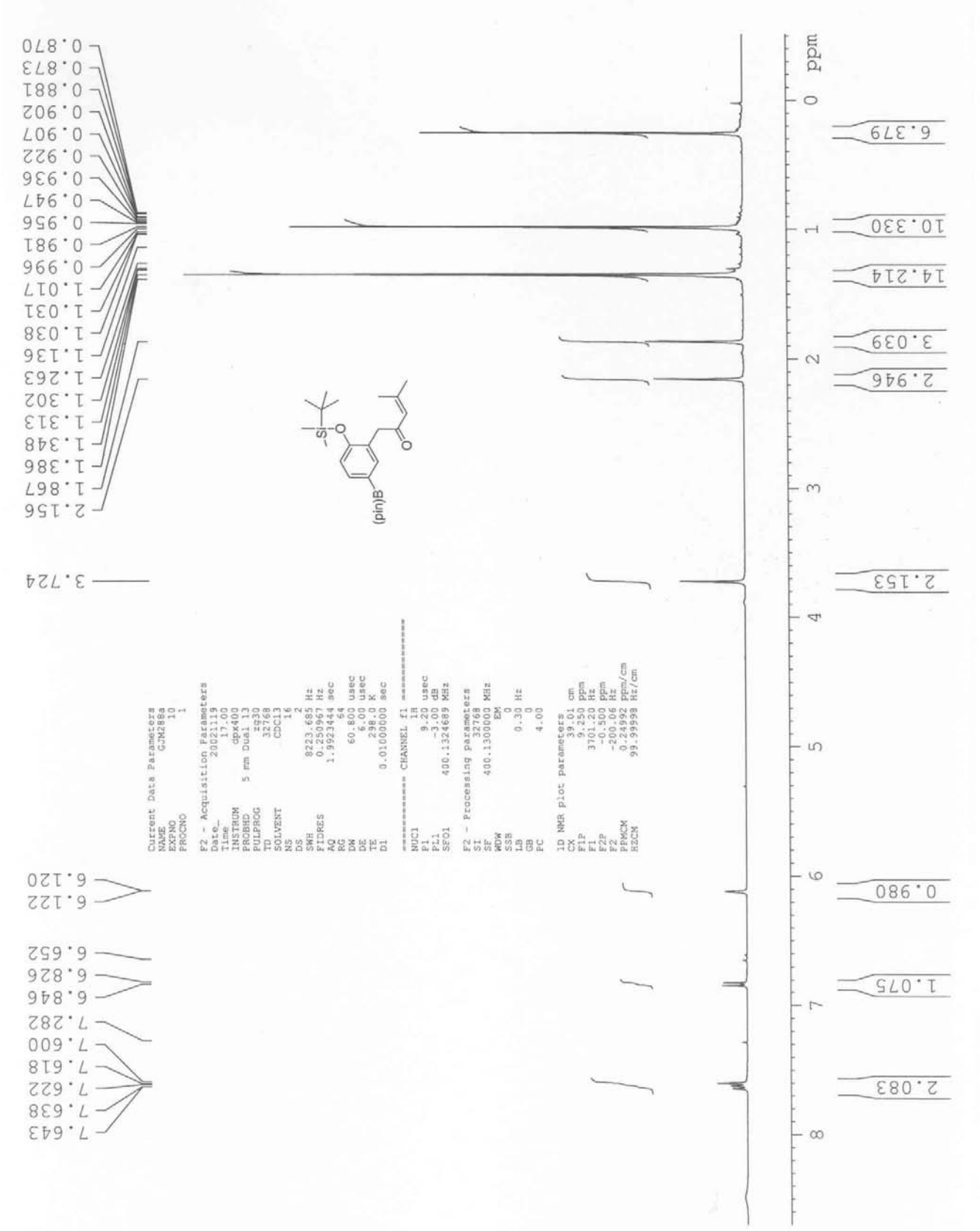
1–(4'–nitrophenyl)phenyl–4–phenylbutan–2–one 16



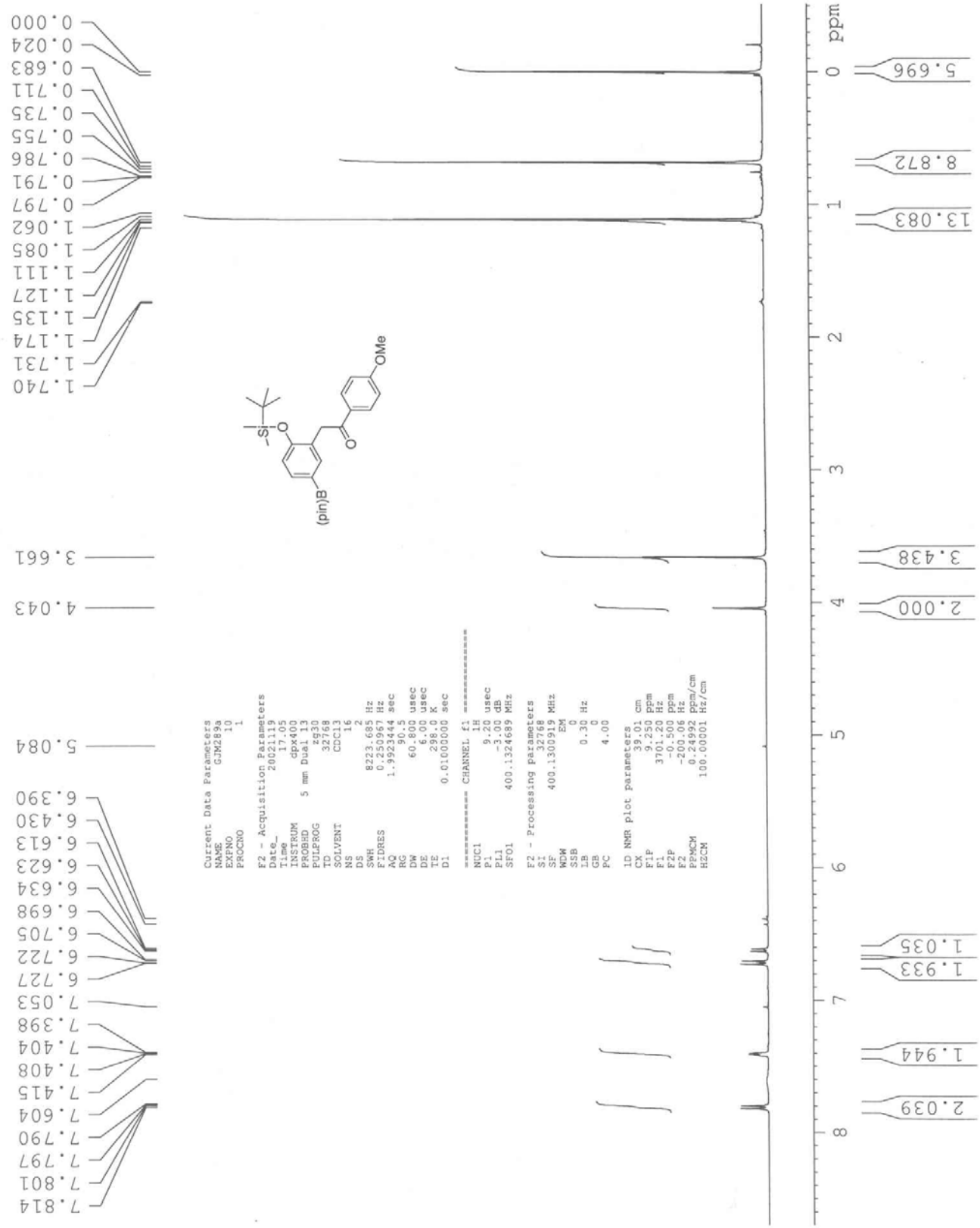
1–[5'–(4'',4'',5'',5''–Tetramethyl–1'',3'',2''–dioxaborolan–2''–yl)–2'–*tert*–butyldimethylsiloxyphenyl] –4–phenylbutan–2–one 28a



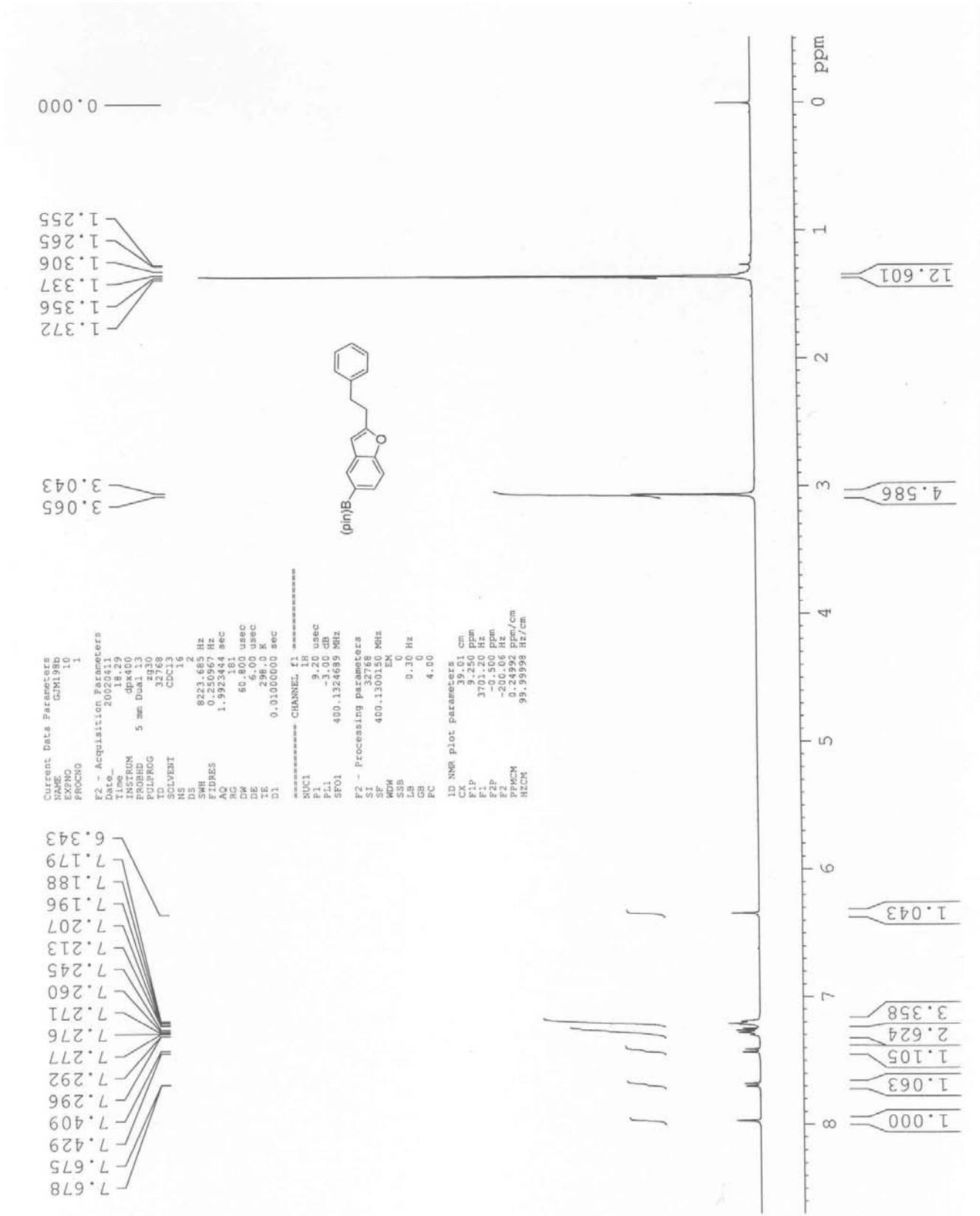
1–[5'–(4'',4'',5'',5''–Tetramethyl–1'',3'',2''–dioxaborolan–2''–yl)–2'–*tert*–butyldimethylsiloxyphenyl] –3,3–dimethoxyacrylone 28b



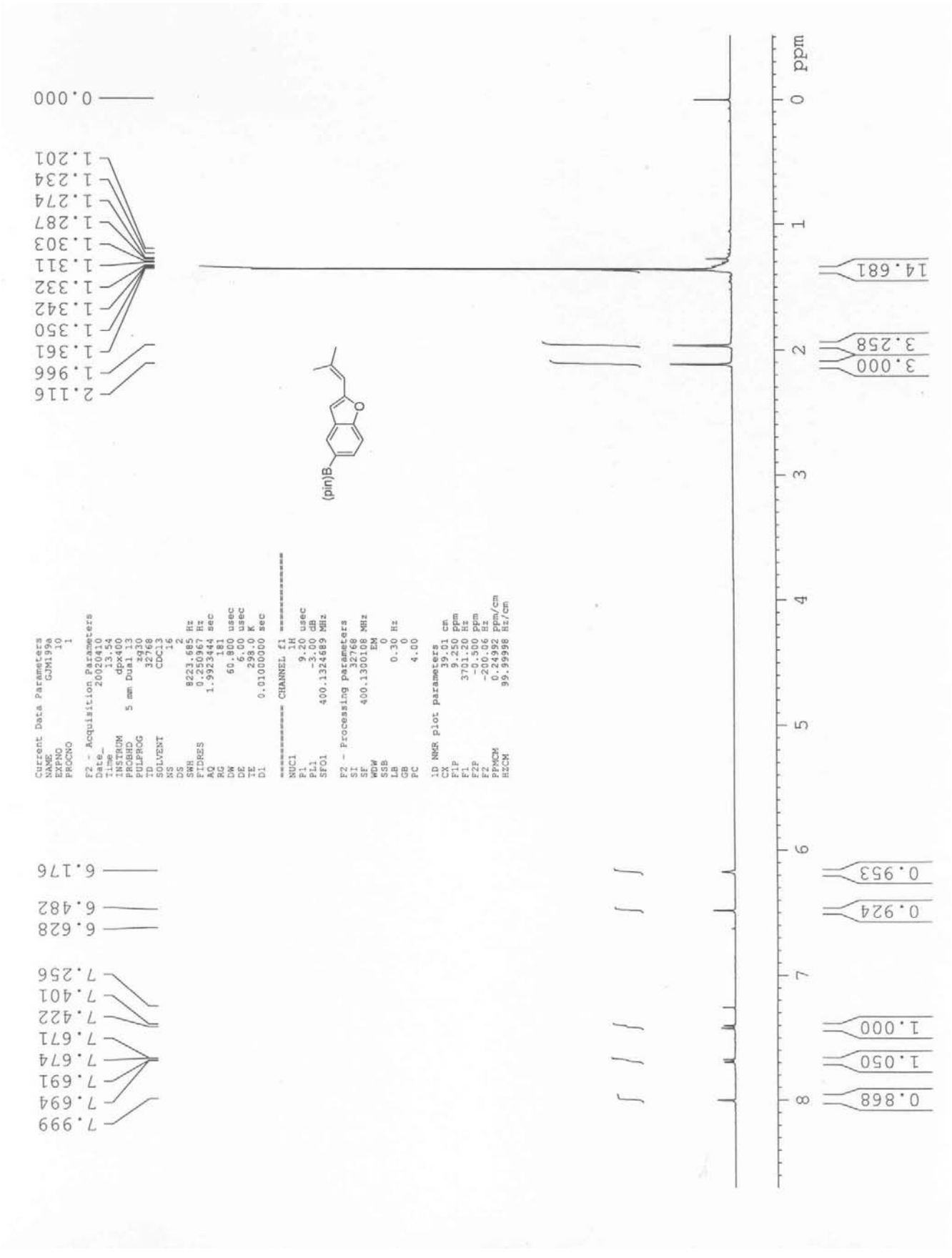
1–[5'–(4'',4'',5'',5''–Tetramethyl–1'',3'',2''–dioxaborolan–2''–yl)–2'–*tert*–butyldimethylsiloxyphenyl] –*para*–methoxyacetophenone 28c



5–(4'',4'',5'',5''–Tetramethyl–1'',3'',2''–dioxaborolan–2''–yl)–2–(2'–phenylethyl)benzo[*b*]furan 29a



5–(4'',4'',5'',5''–Tetramethyl–1'',3'',2''–dioxaborolan–2''–yl)–2–(2',2'–dimethylethenyl)benzo[*b*]furan 29b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1.311
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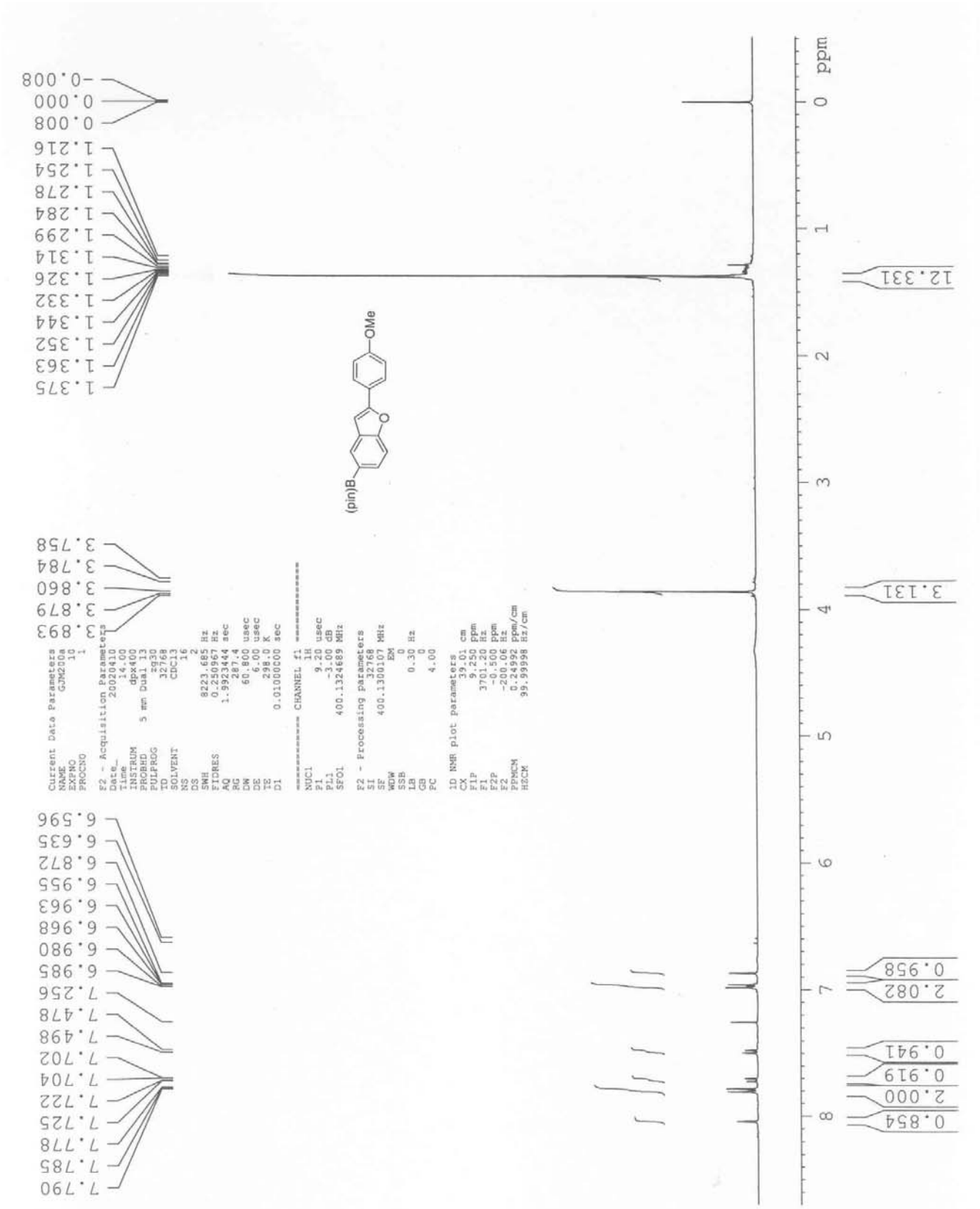
1.350
1.361
1.966
2.116

5–(4'',4'',5'',5''–Tetramethyl–1'',3'',2''–dioxaborolan–2''–yl)–2–(4'–*para*–methoxyphenyl)benzo[*b*]furan
29c



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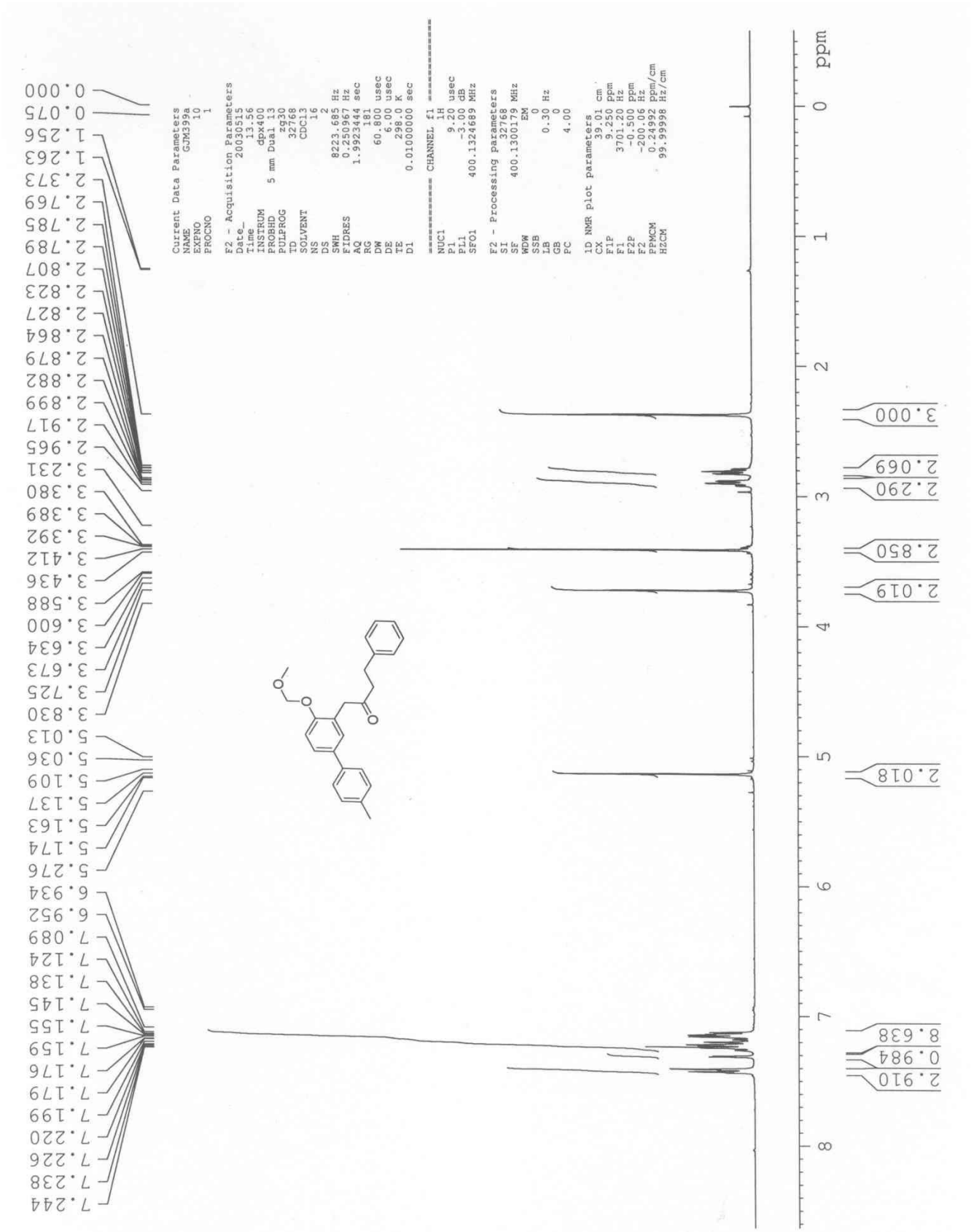

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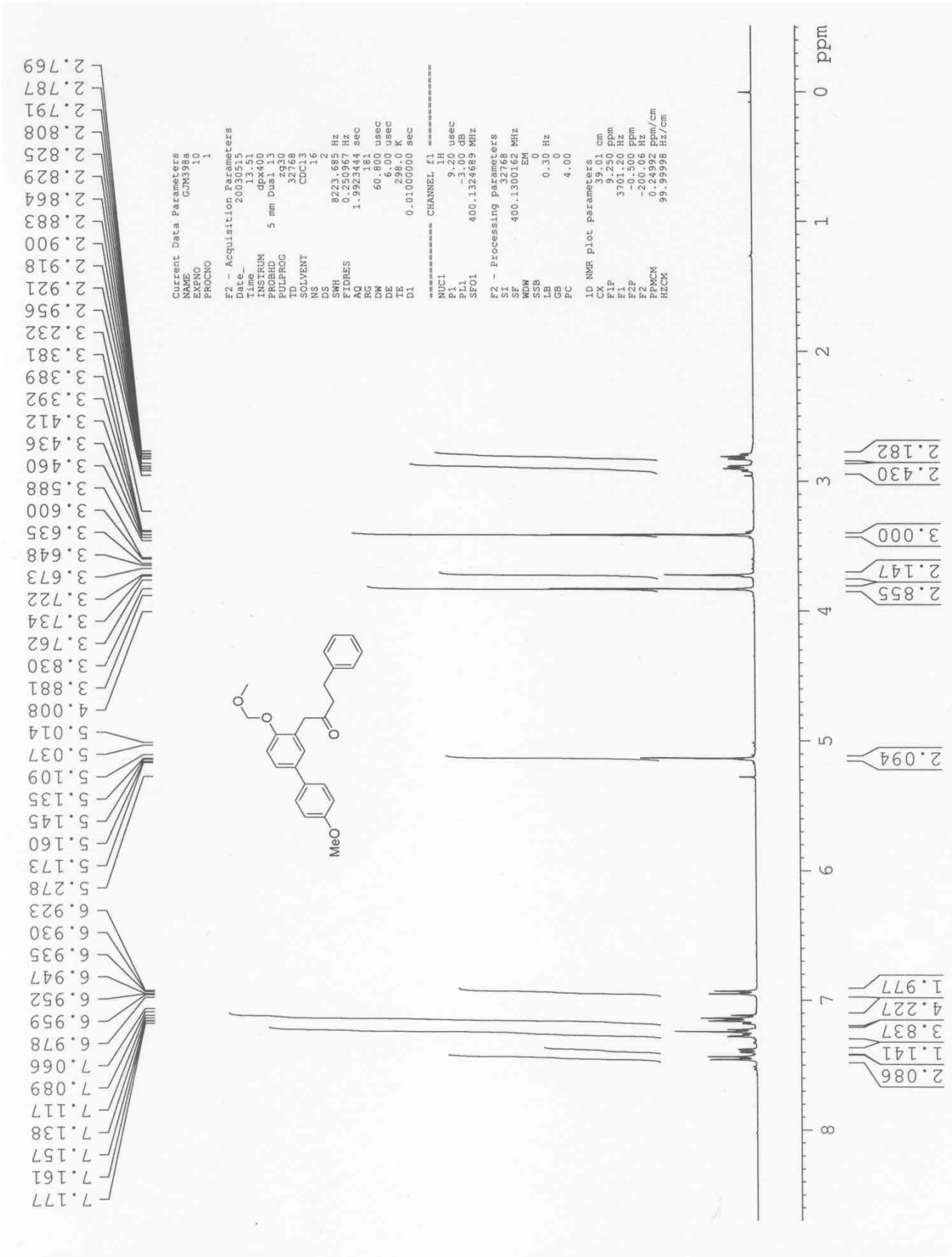

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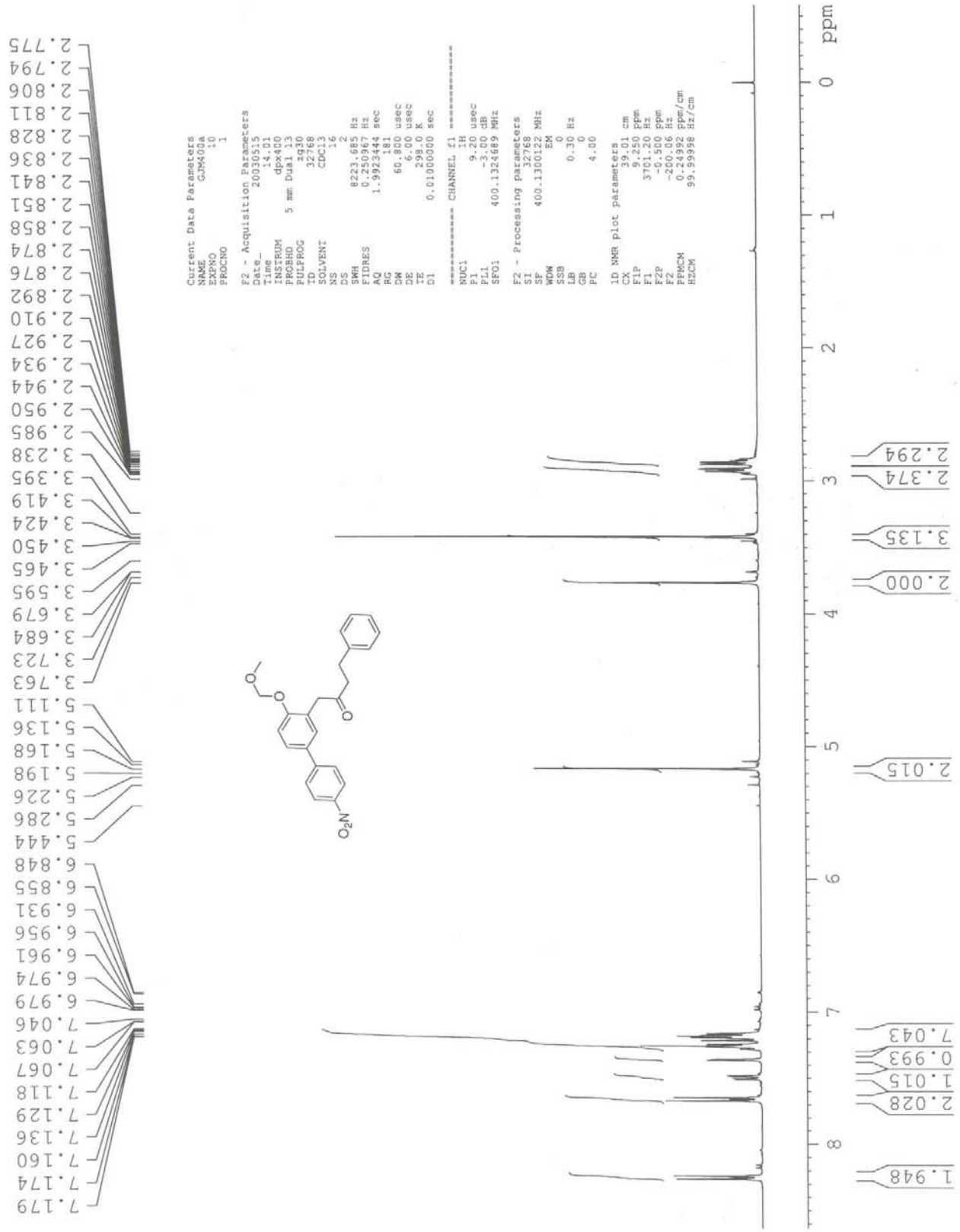

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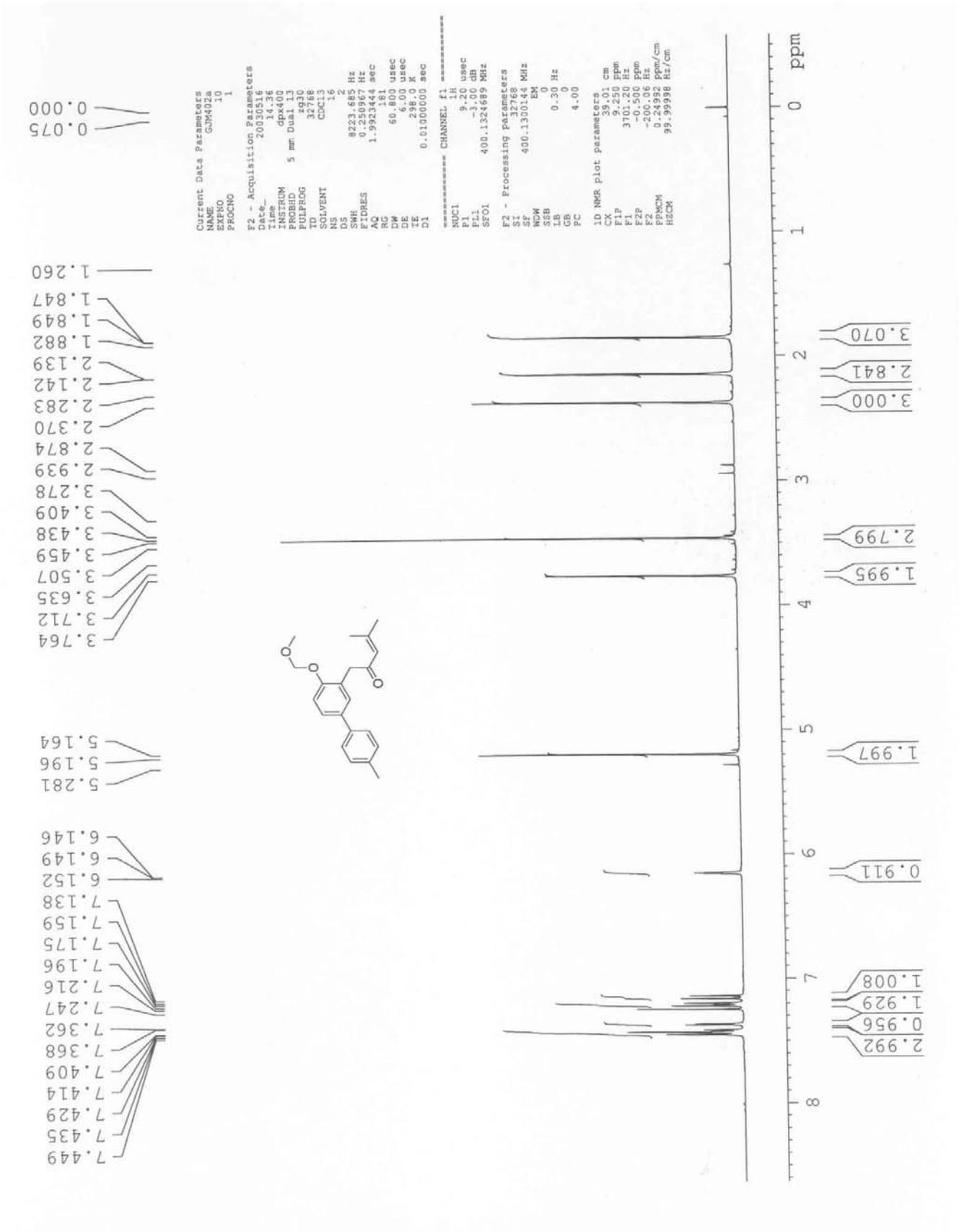

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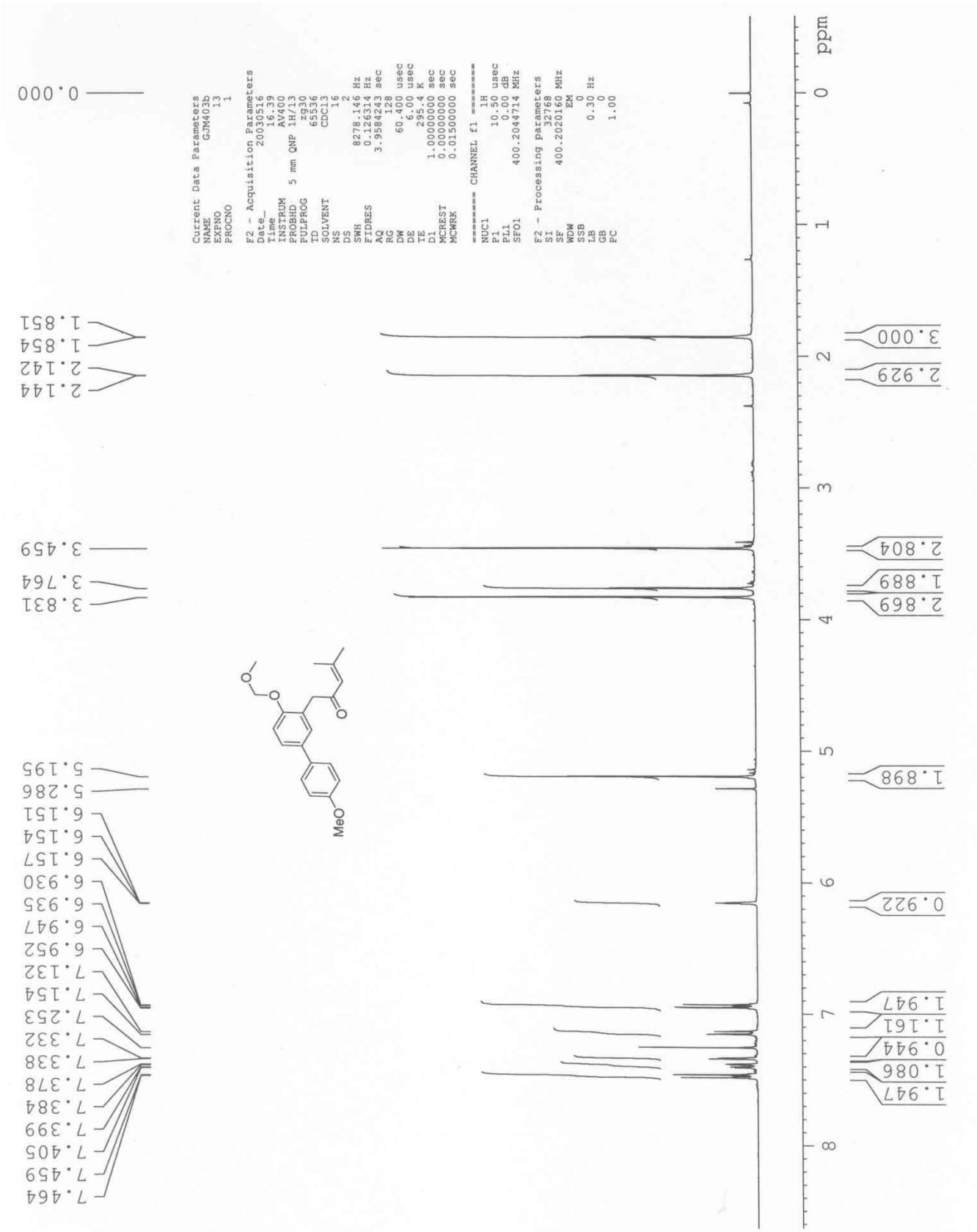

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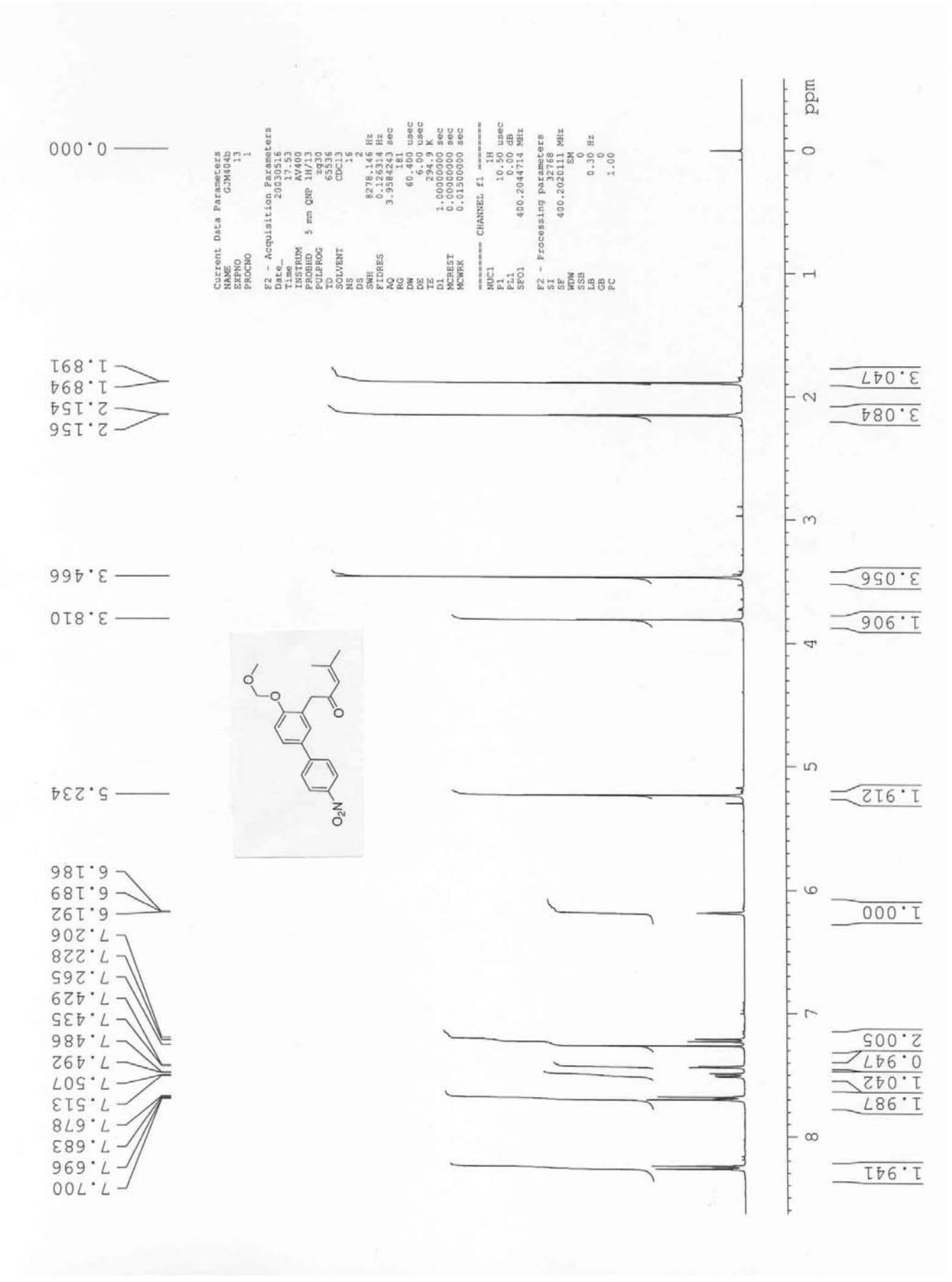

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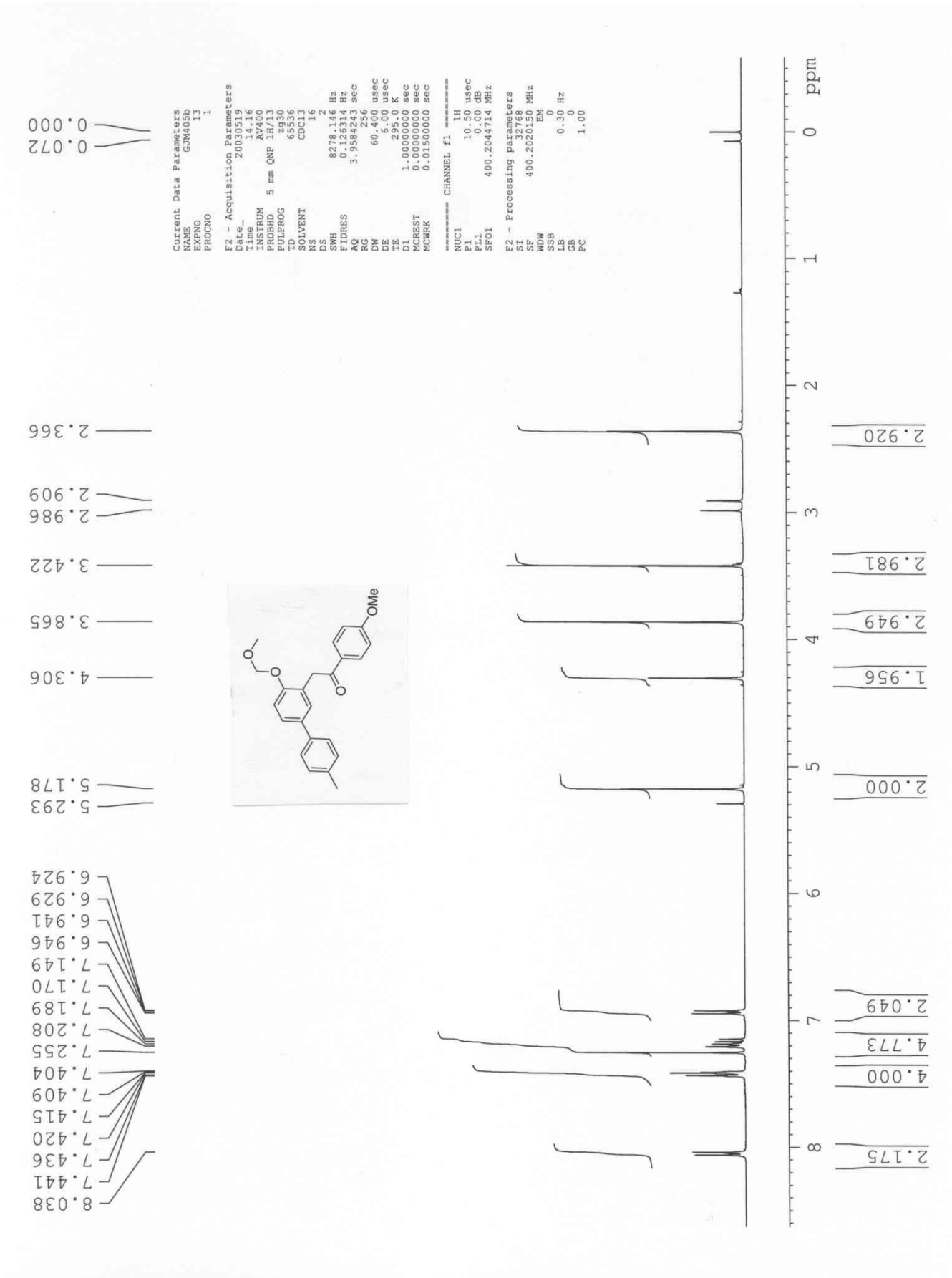

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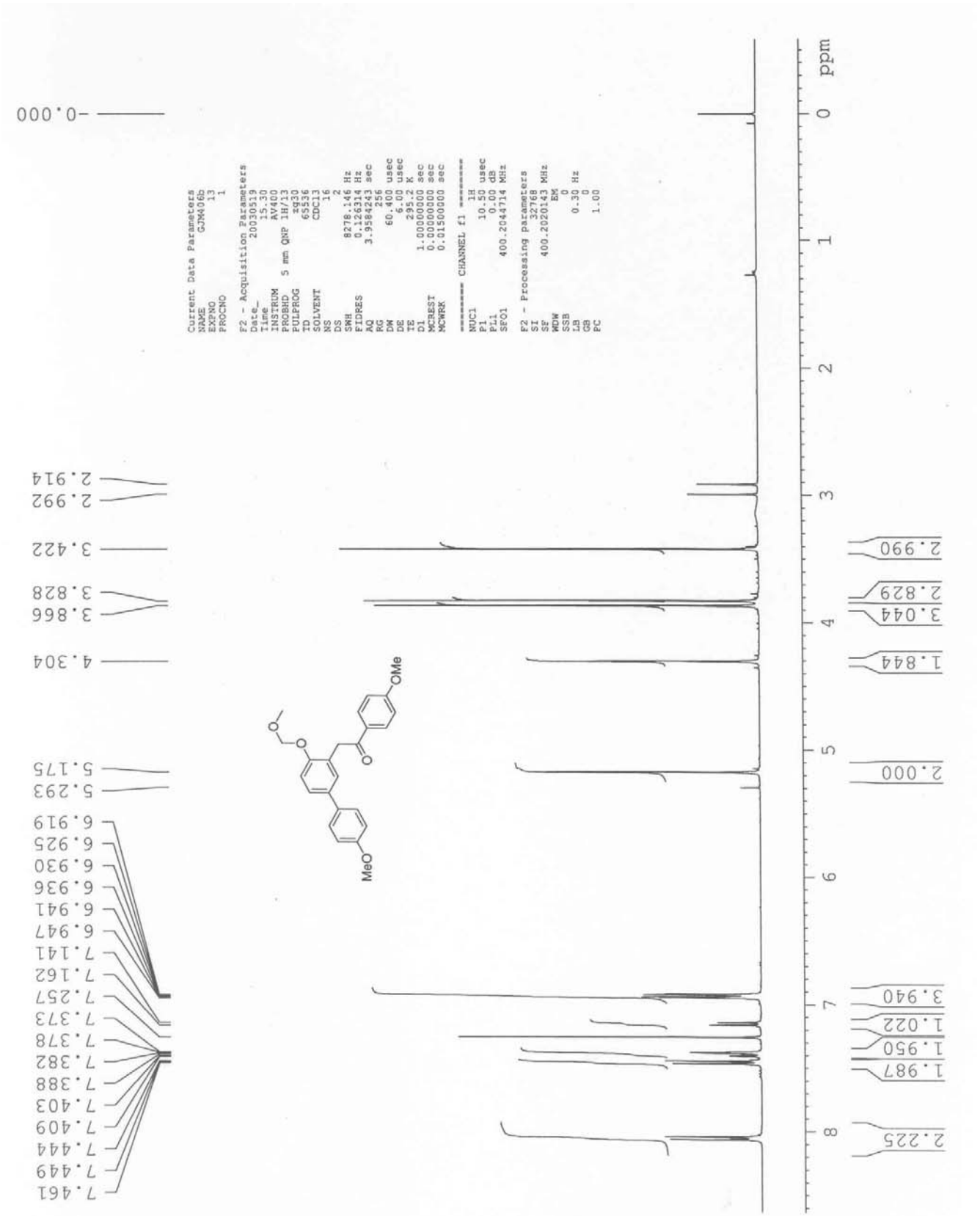

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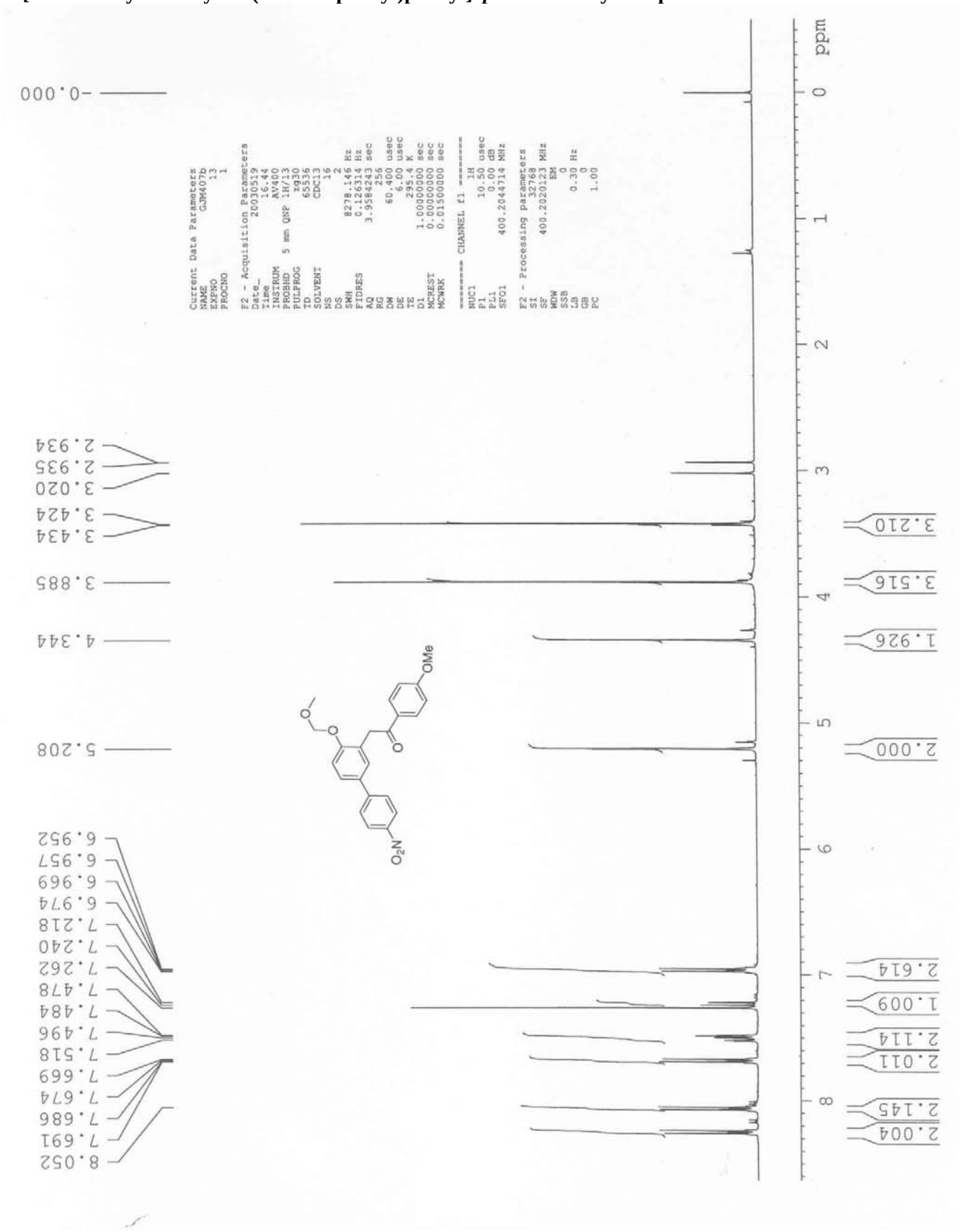

^{1}H NMR spectra of benzo[*b*]furans 33aa'–cc'

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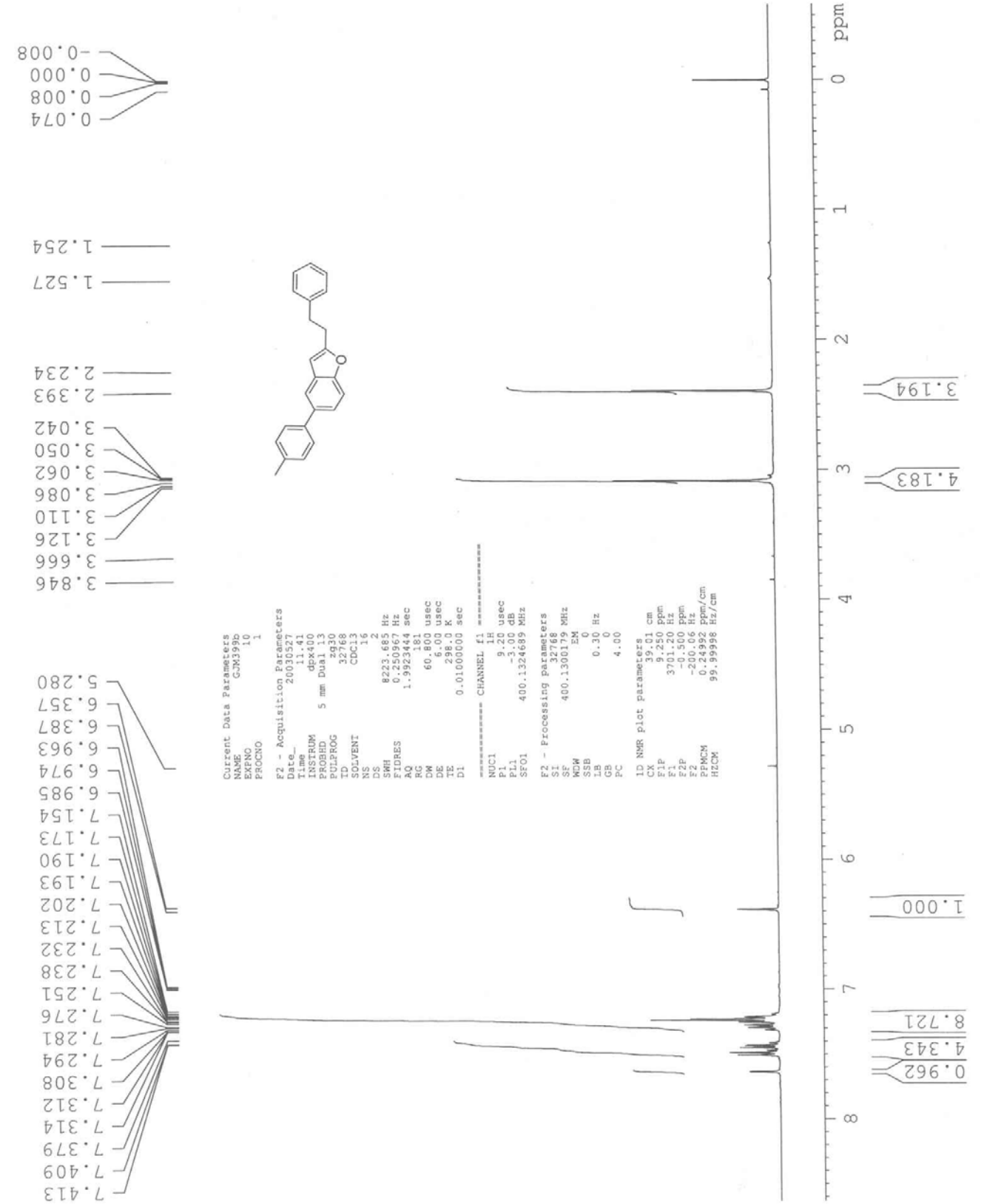

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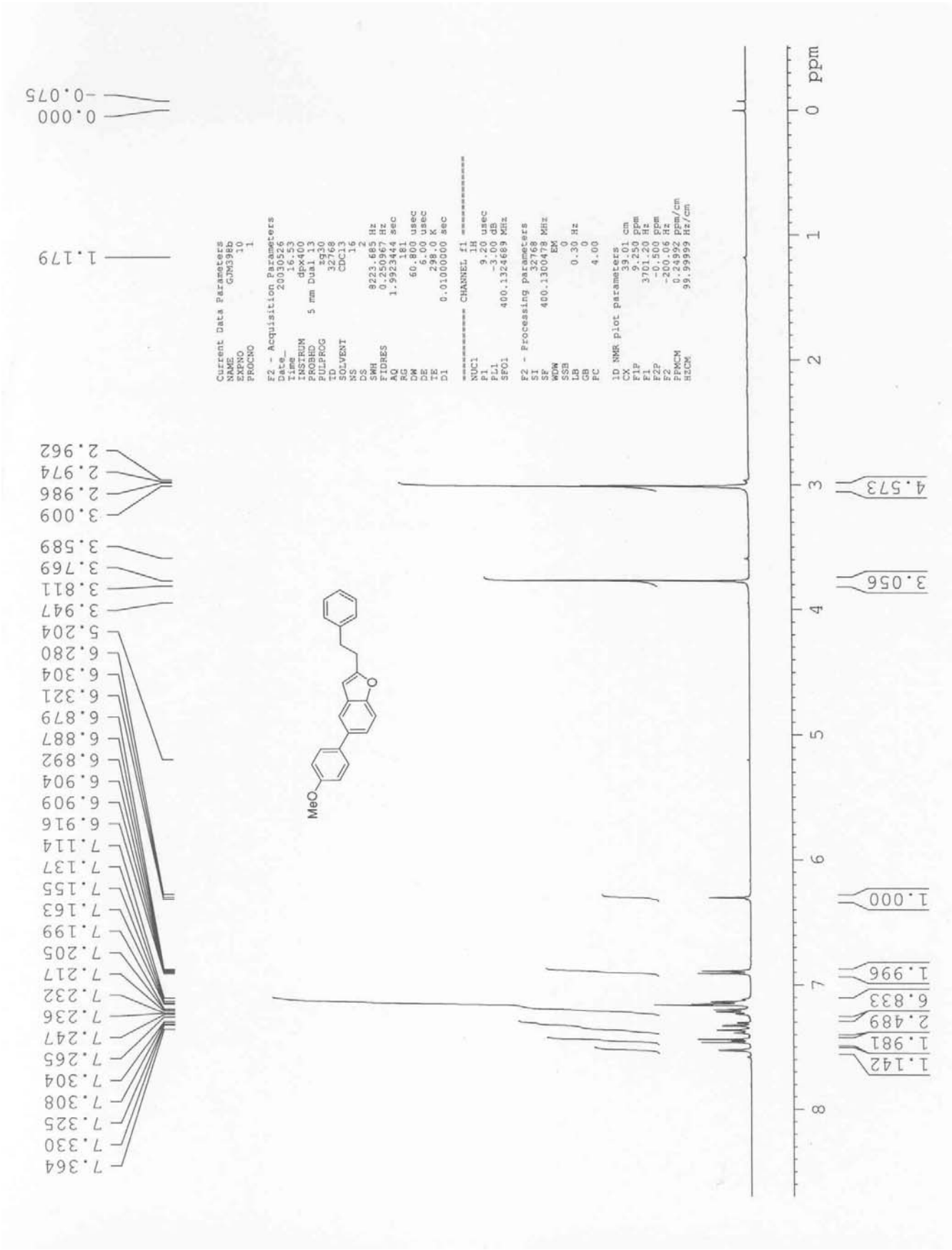

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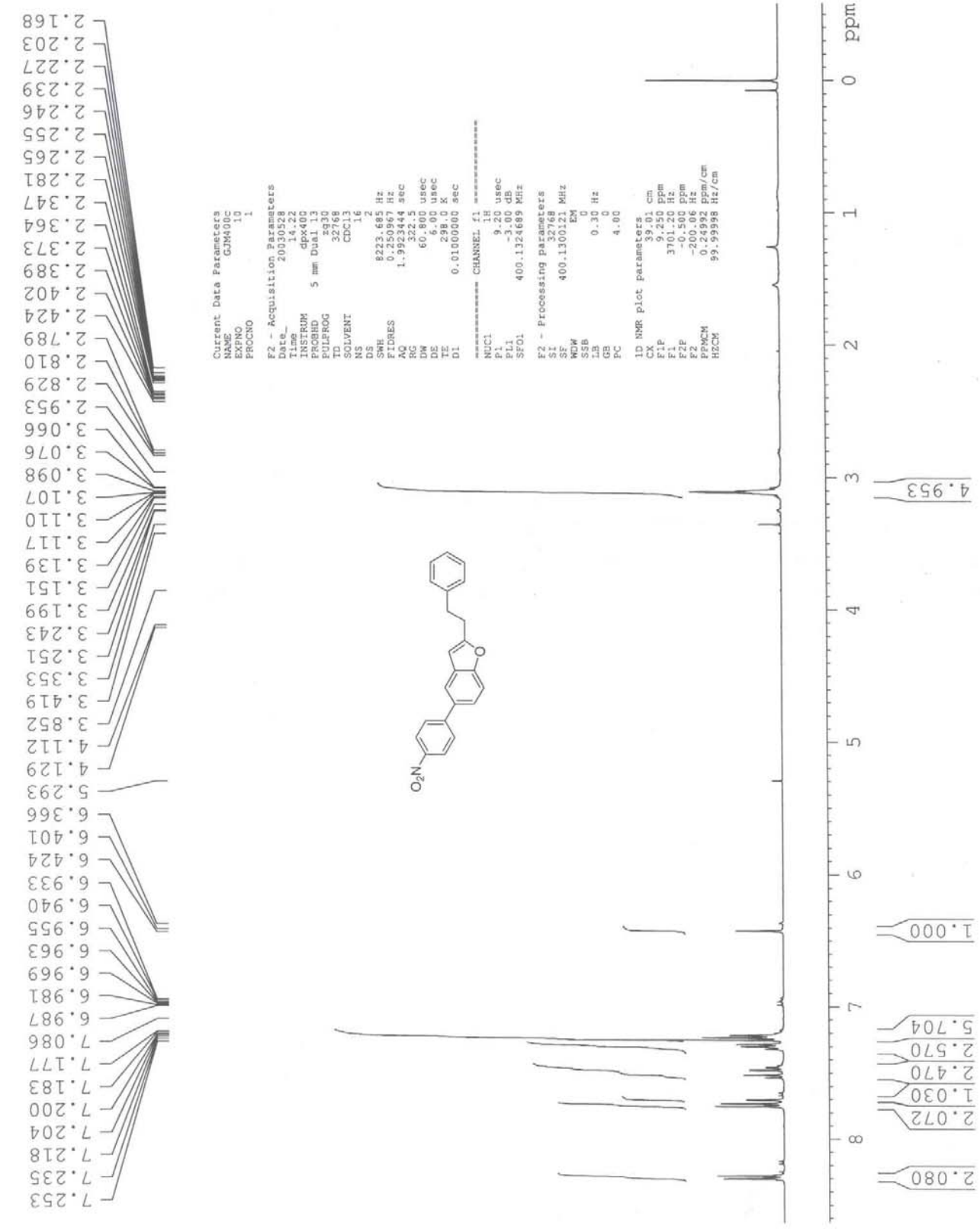
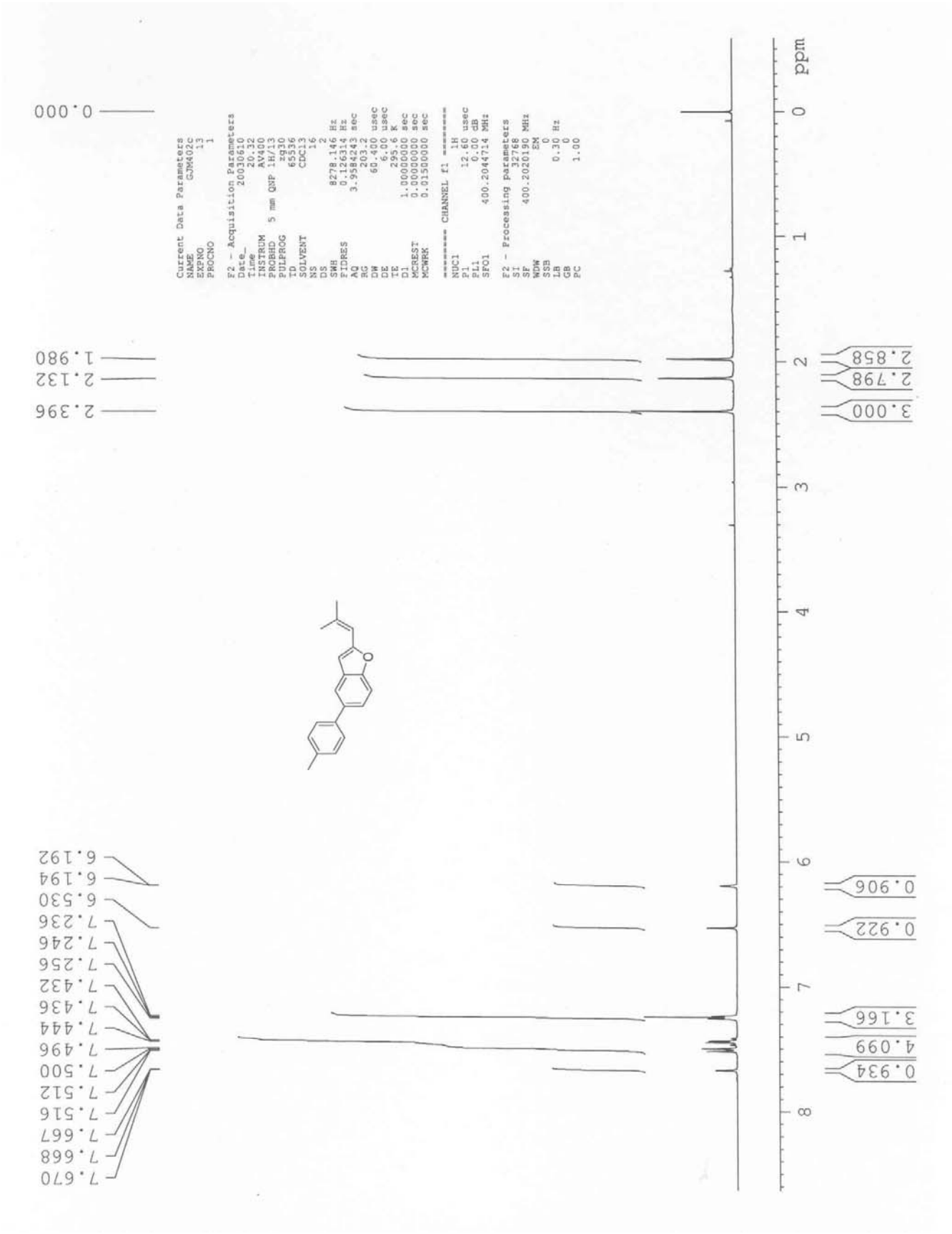


5–(4''–Methylphenyl)–2–(2',2'–dimethylethenyl)benzo[*b*]furan 33ba'



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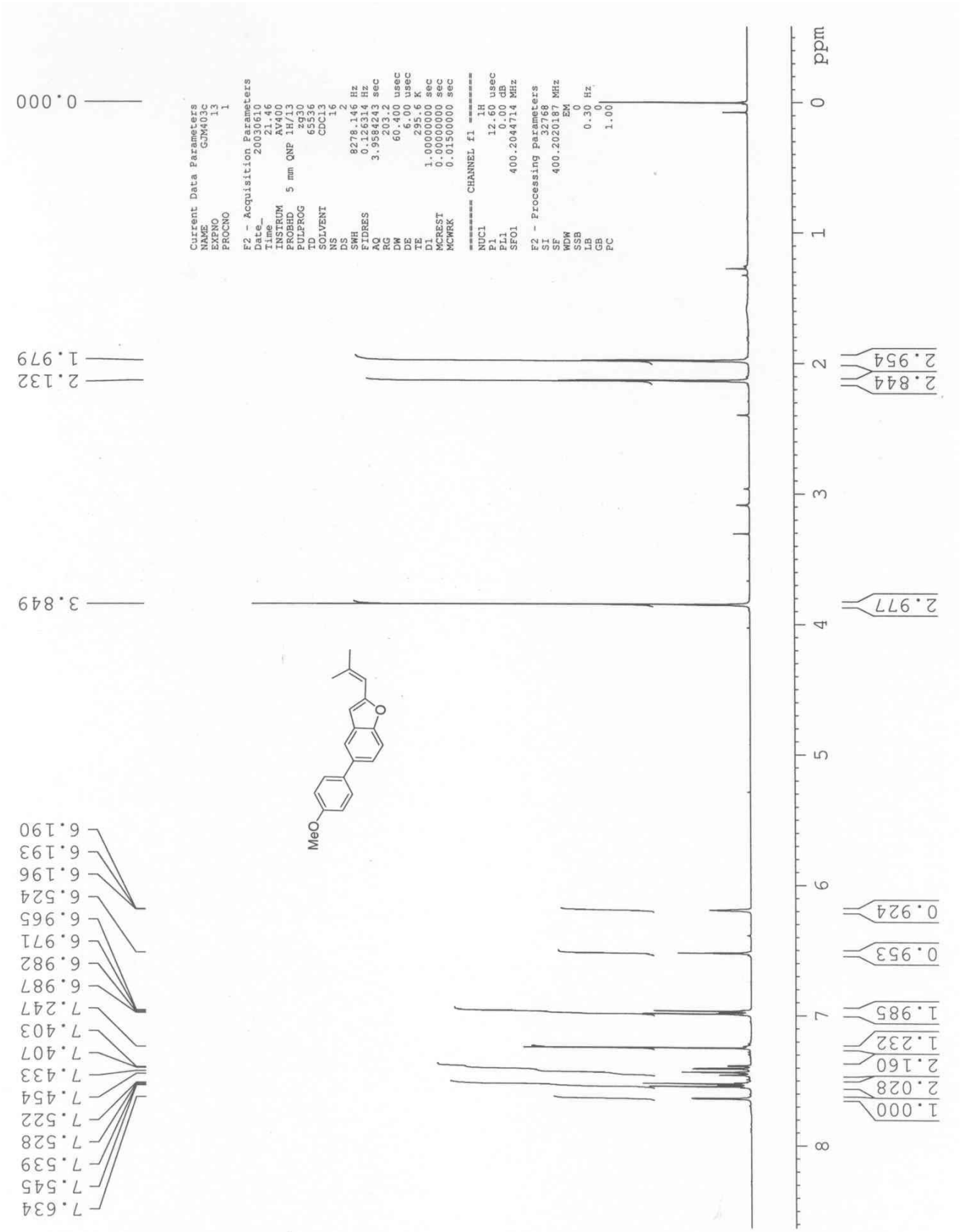

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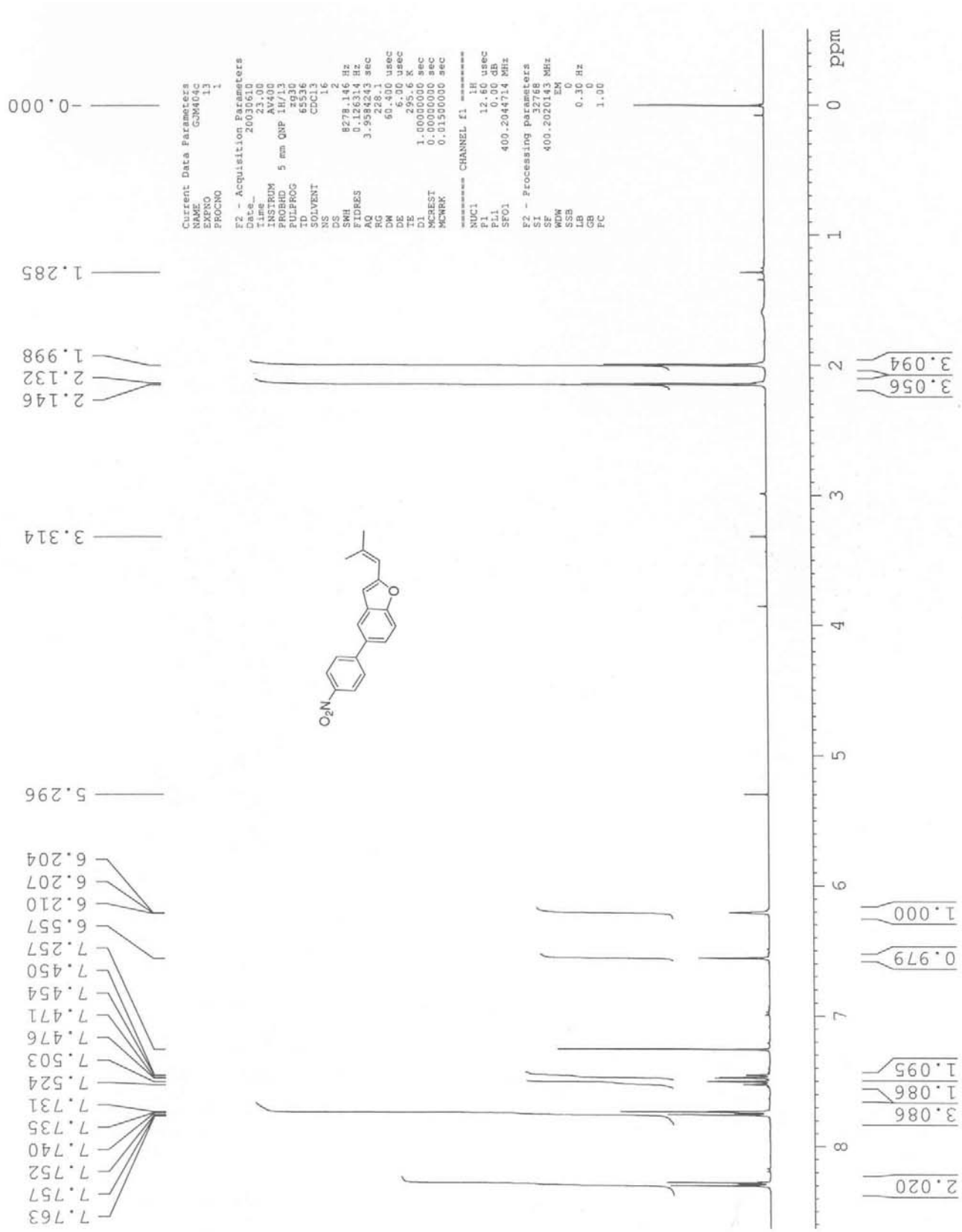

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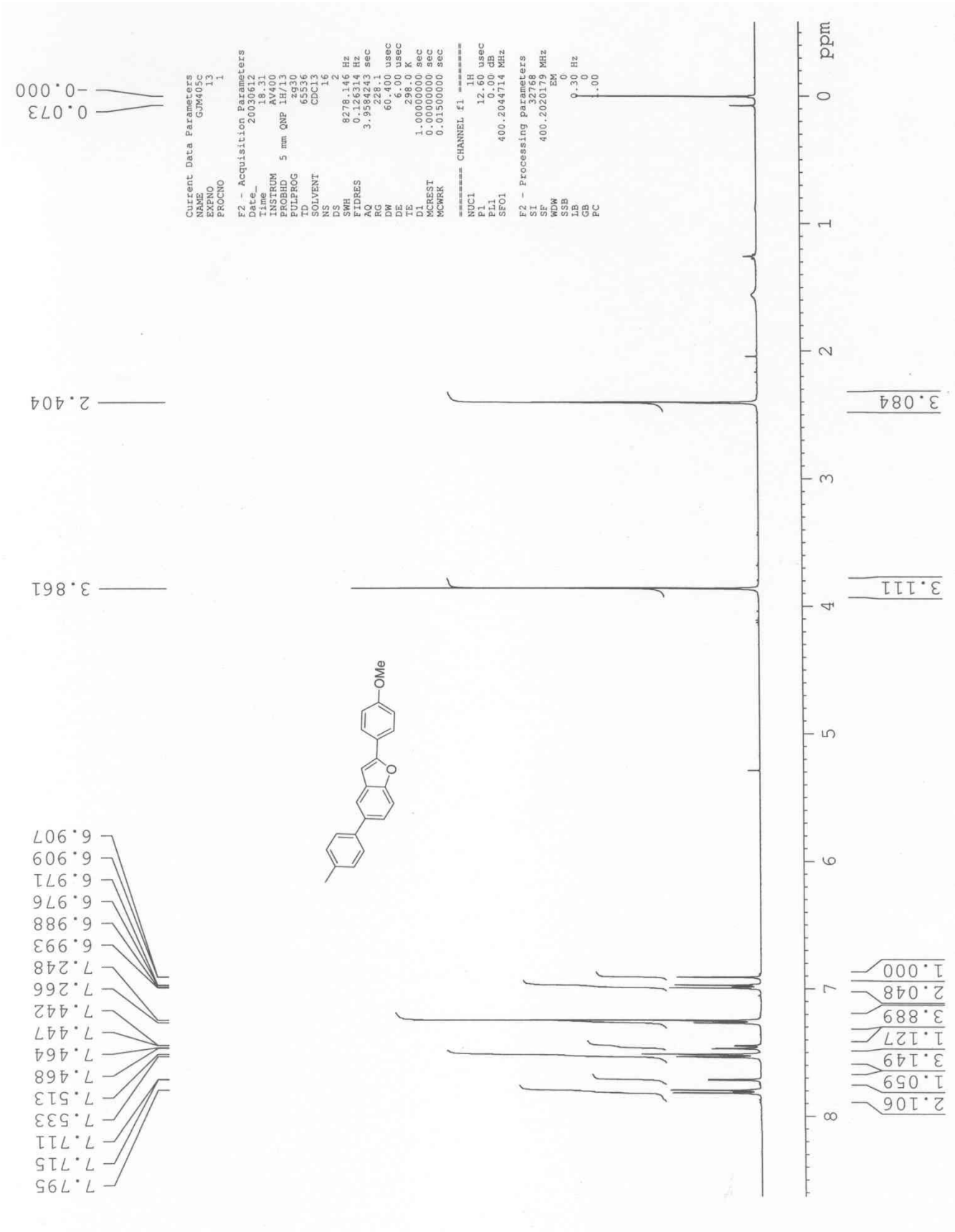

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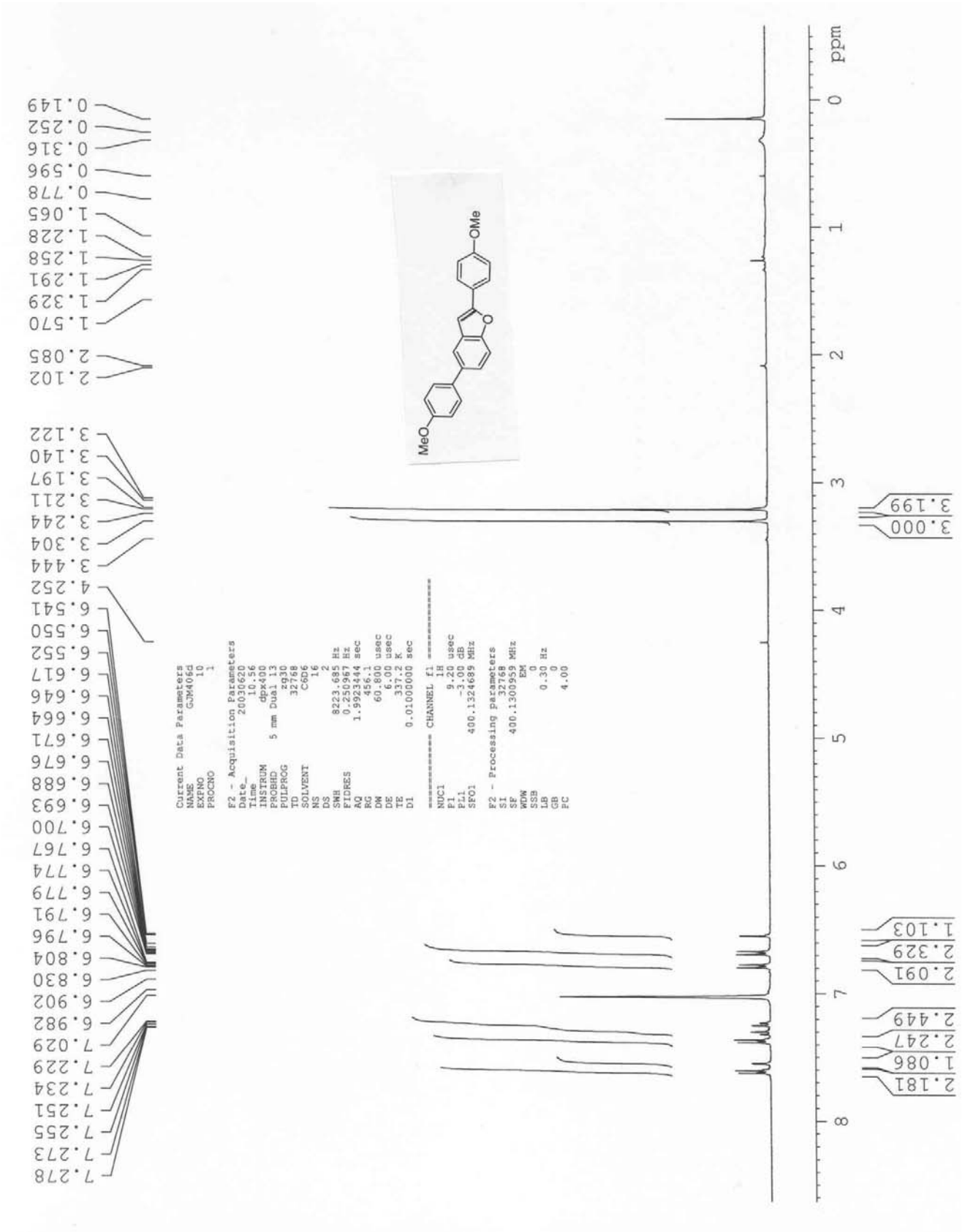

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