

Synthesis of 2,5-Diaryl-1,5-Dienes from Allylic Bromides Using Visible-Light Photoredox Catalysis

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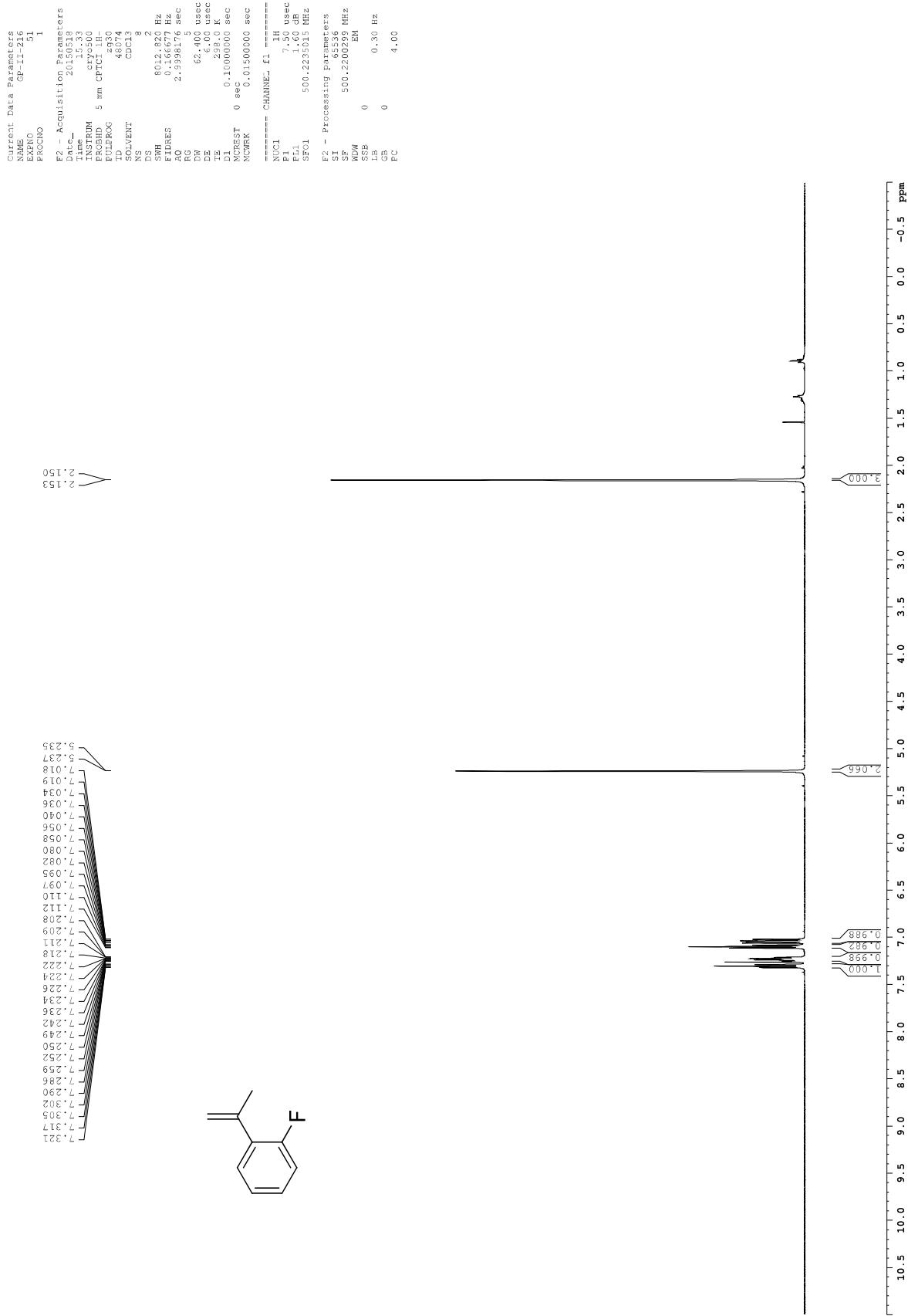
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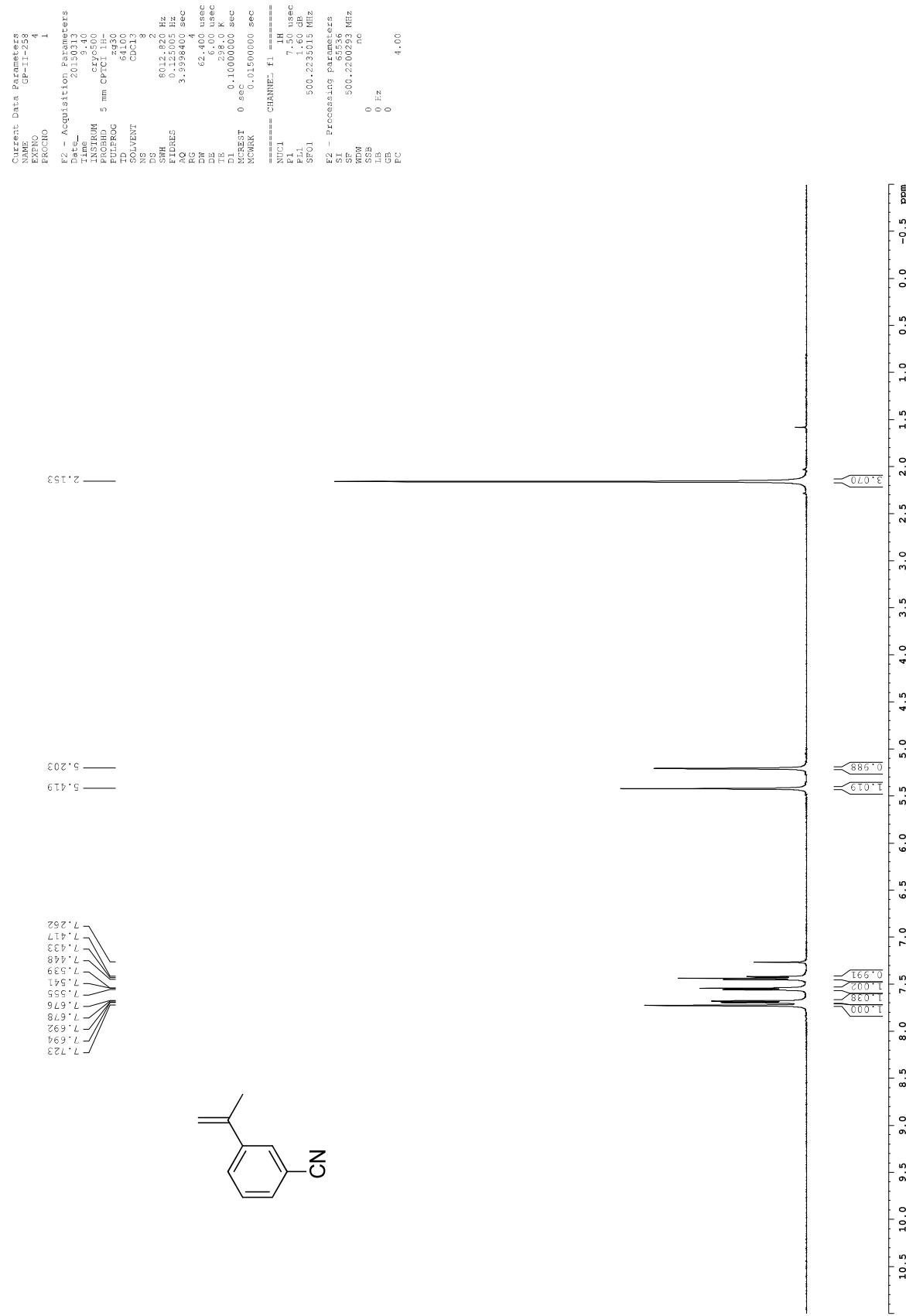
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Optimization of Allylic Bromination of α -Methylstyrene Derivatives.

The well-known allylic bromination turned out to be more complex and, in comparison to the Wittig olefination, highly substrate-dependent. Generally, three different approaches starting from α -methylstyrene derivatives can be found in literature: most commonly used are procedures where the starting material and NBS are heated in chlorinated solvents (such as carbon tetrachloride, chloroform or chlorobenzene) in absence¹ or presence of a radical initiator.² Regarding the investigated substrates, yields of the desired product were typically low and the separation from the complex mixture of by-products were often difficult. However, the combination of NBS and dibenzoyl peroxide in refluxing carbon tetrachloride proved to be the only method enabling a successful allylic bromination of electron-rich ortho- and para-methoxy substituted α -methylstyrenes in moderate yields.² Mukherjee *et al.* reported a *p*-toluenesulfonic acid-catalyzed allylic bromination of several α -methylstyrene derivatives with NBS.³ Unfortunately, synthetically useful yields are only obtained for a limited number of substrates. However, we have never been able to reproduce the unusually high reported yields (e.g. 47-65% vs 89% for the preparation of **2a**) and found a significant dependence of the reaction outcome on the nature of the employed sample of *p*-toluenesulfonic acid. The formation of isomeric and double-bromination products additionally complicated the purification which finally excluded this method for our purposes. The broadly applicable and most reliable procedure in our hands was published by Nakagawa and coworkers in 2002.⁴ The allylic bromination with NBS occurs in the presence of catalytic $\text{Yb}(\text{OTf})_3$ and TMS-Cl at room temperature in less than one hour (see Article Scheme 1). Although the reported yields were not fully reproducible (e.g. 43% vs 84% for the preparation of **2a**), this method led to fairly clean product formation of α -(bromomethyl)styrene derivatives **2** in consistent yields up to 60% for a wide array of substituents with only minor modifications necessary.⁵ Even alkyl substitution at the allylic scaffold was tolerated. As mentioned in the original publication, electron-rich ortho- and para-methoxy substituted α -methylstyrenes are incompatible substrates likely due to oligomerization.

^1H NMR Spectra

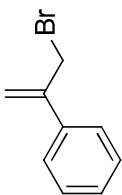
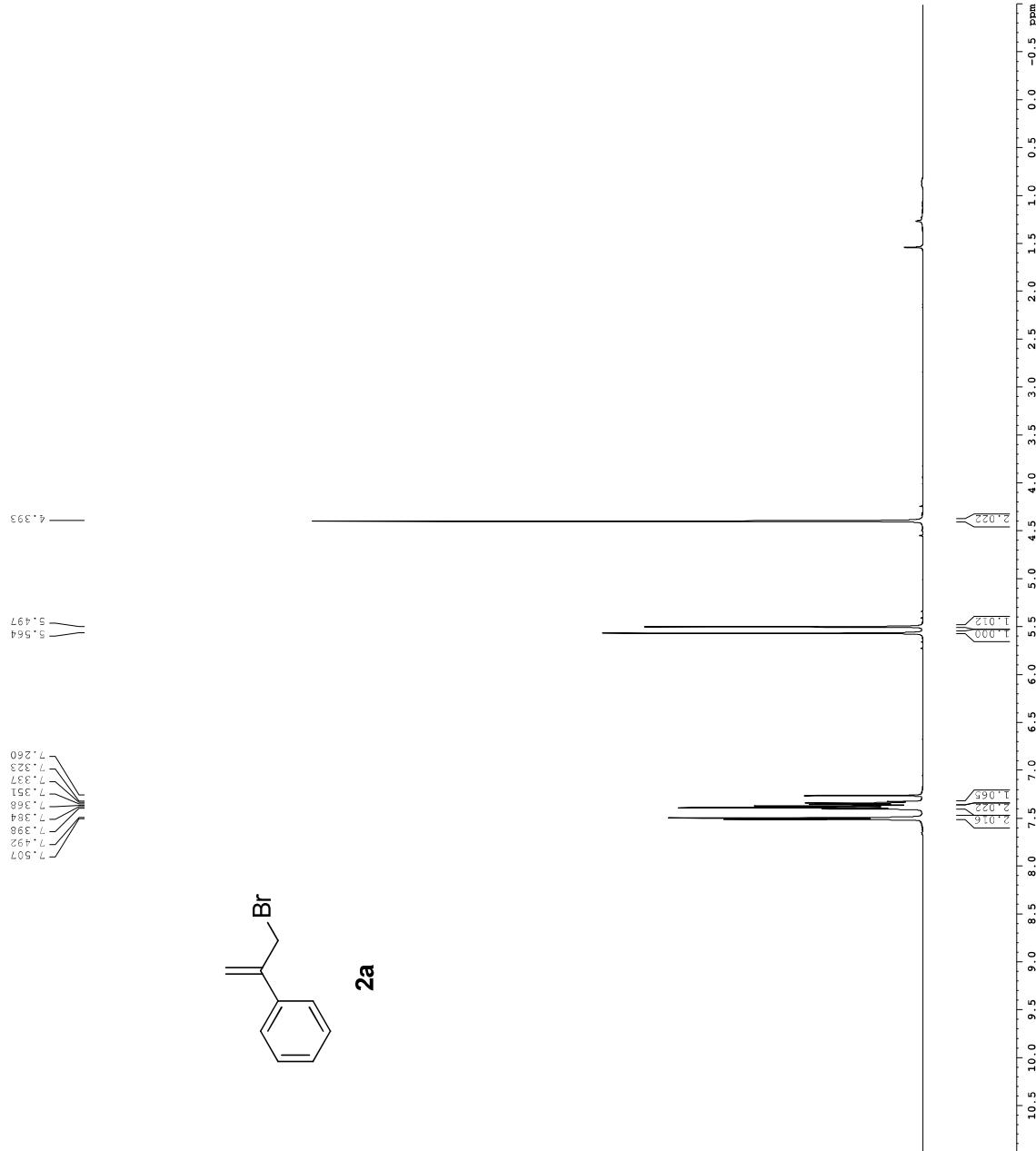


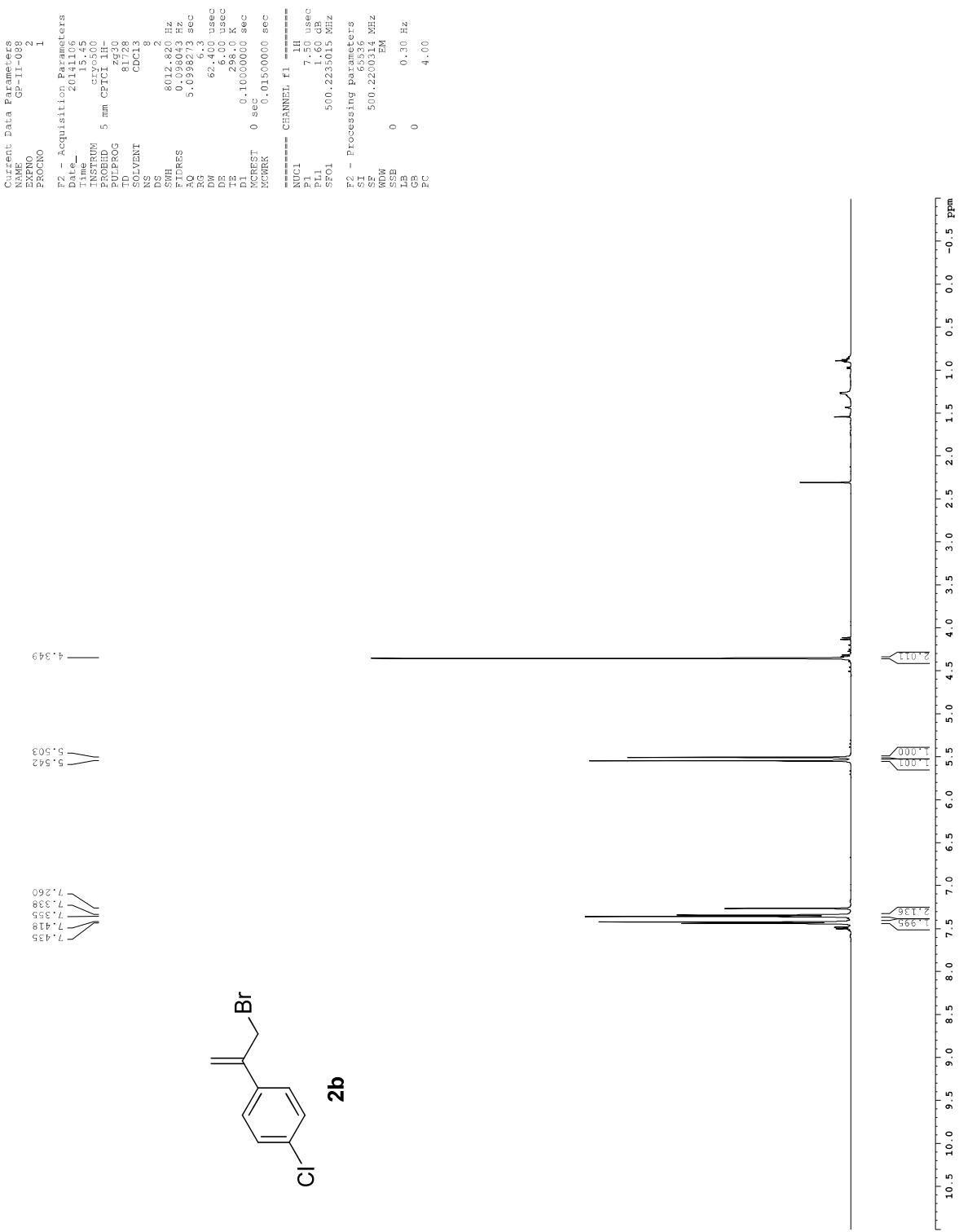


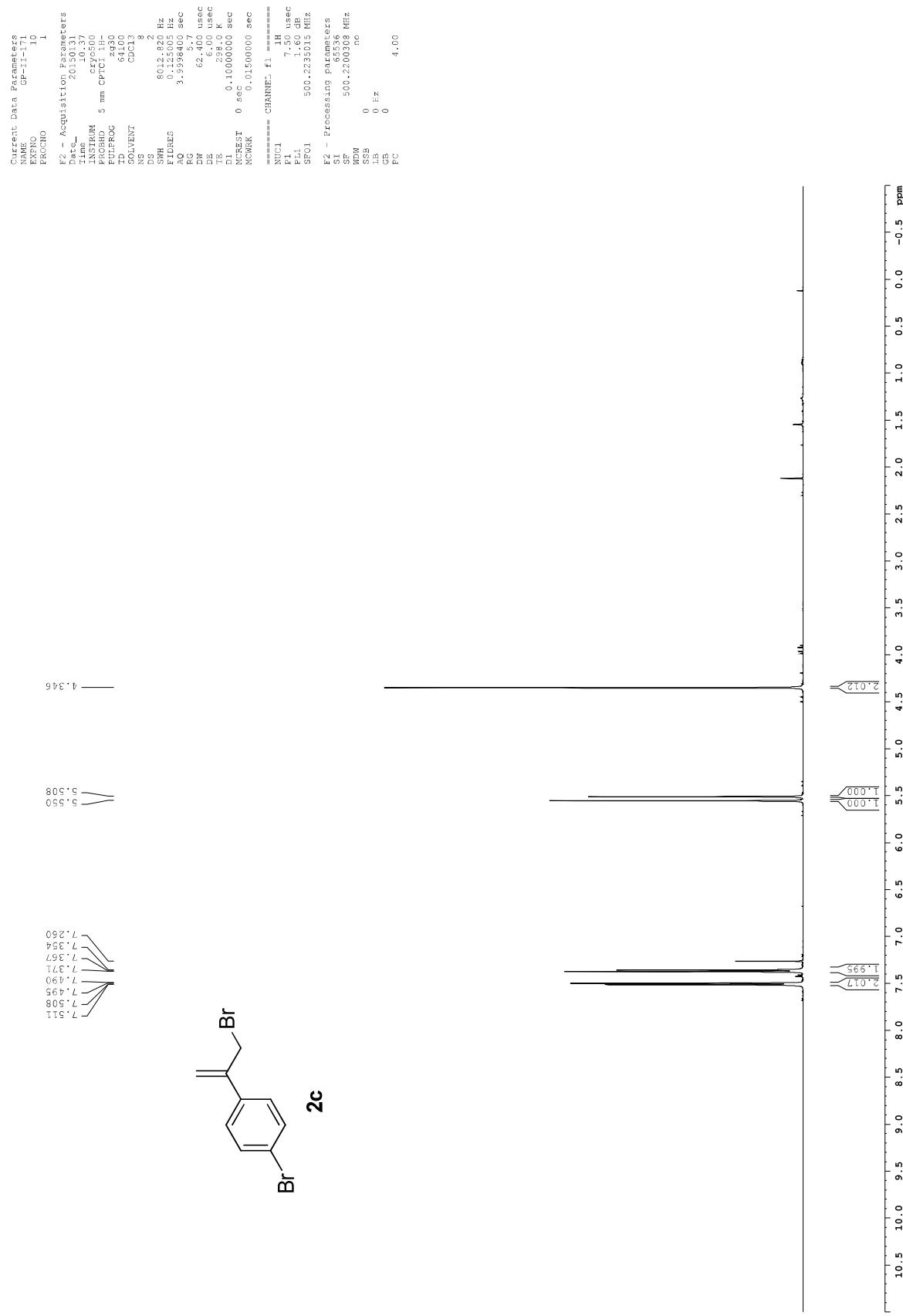
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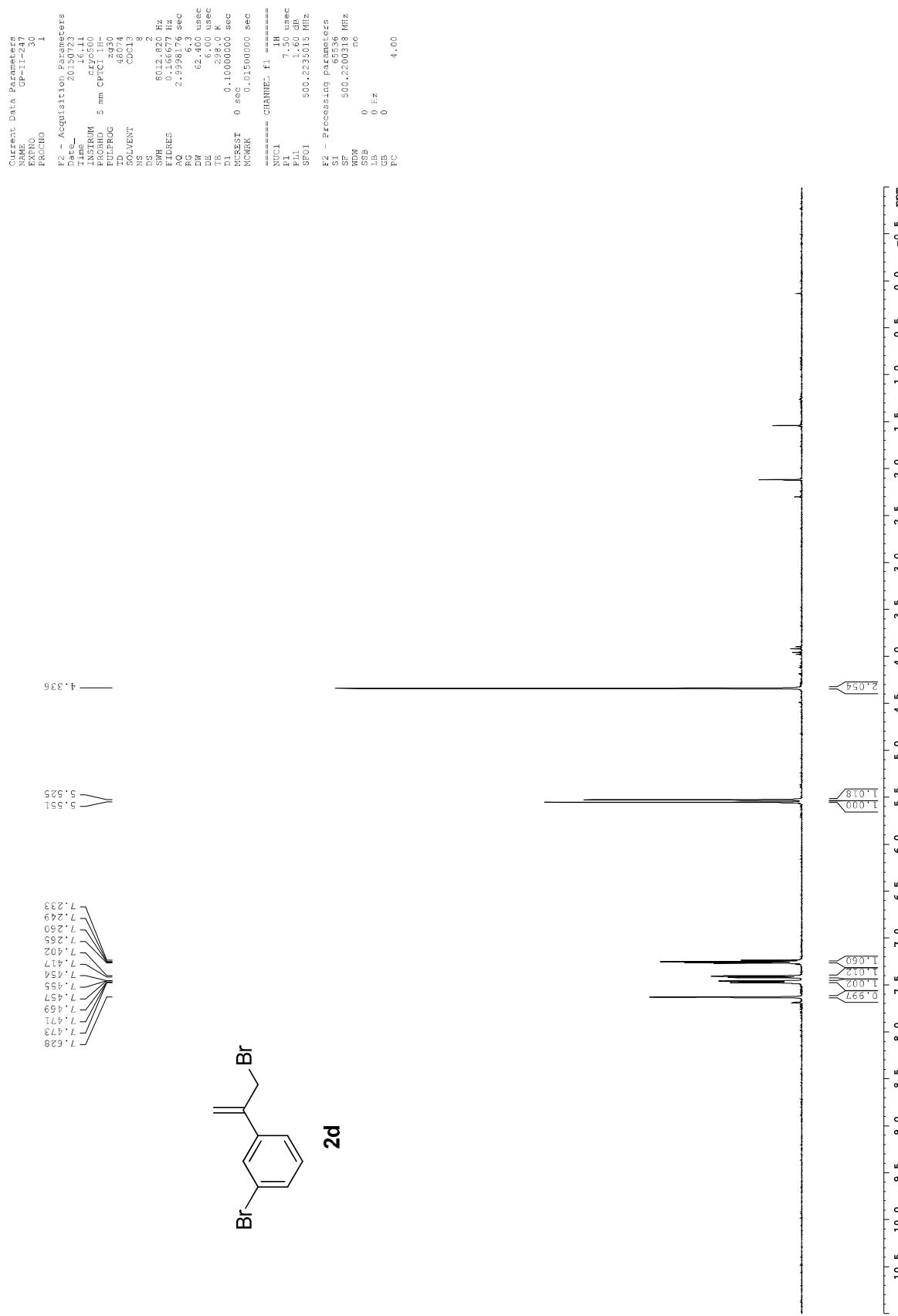
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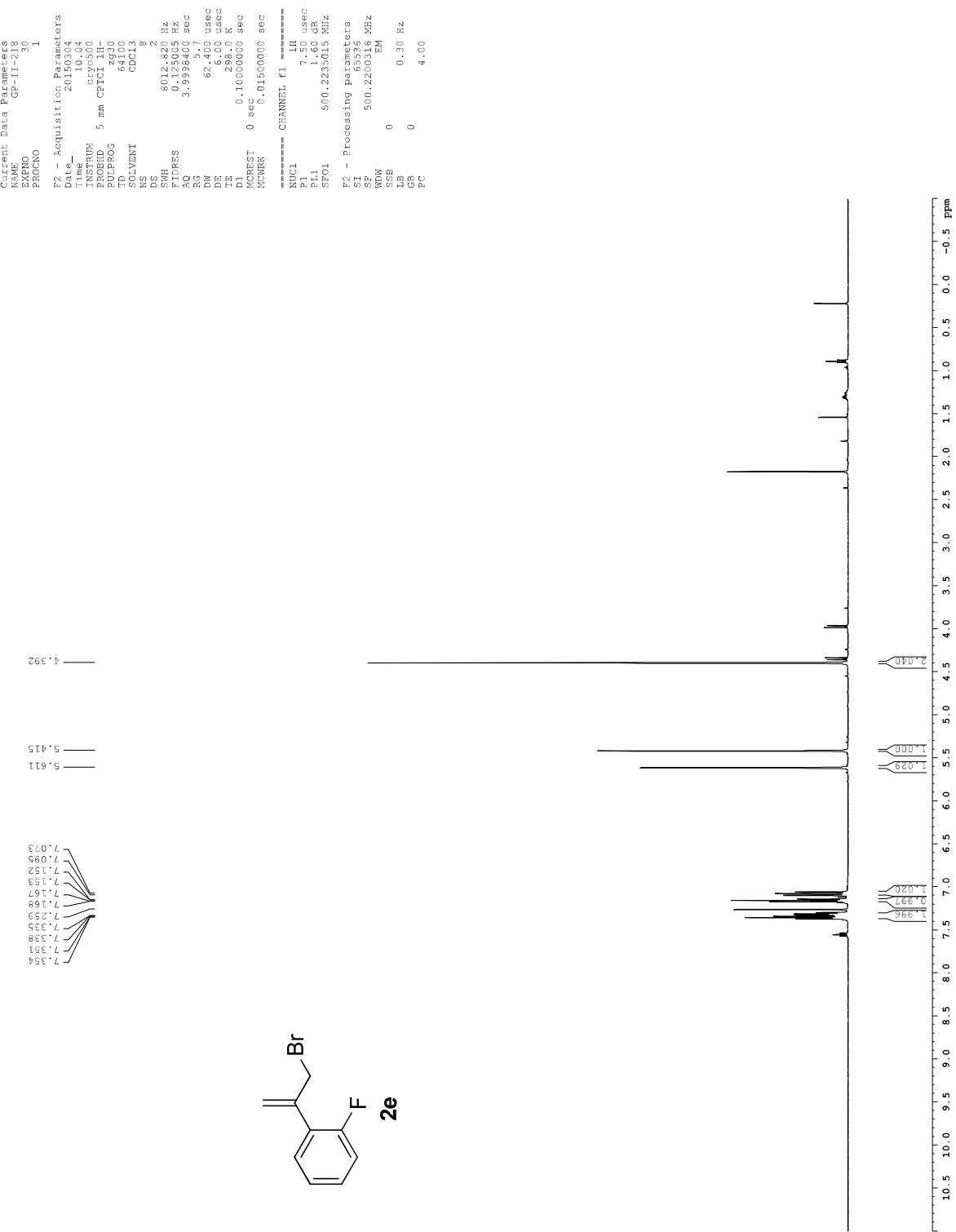
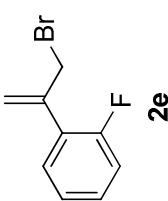
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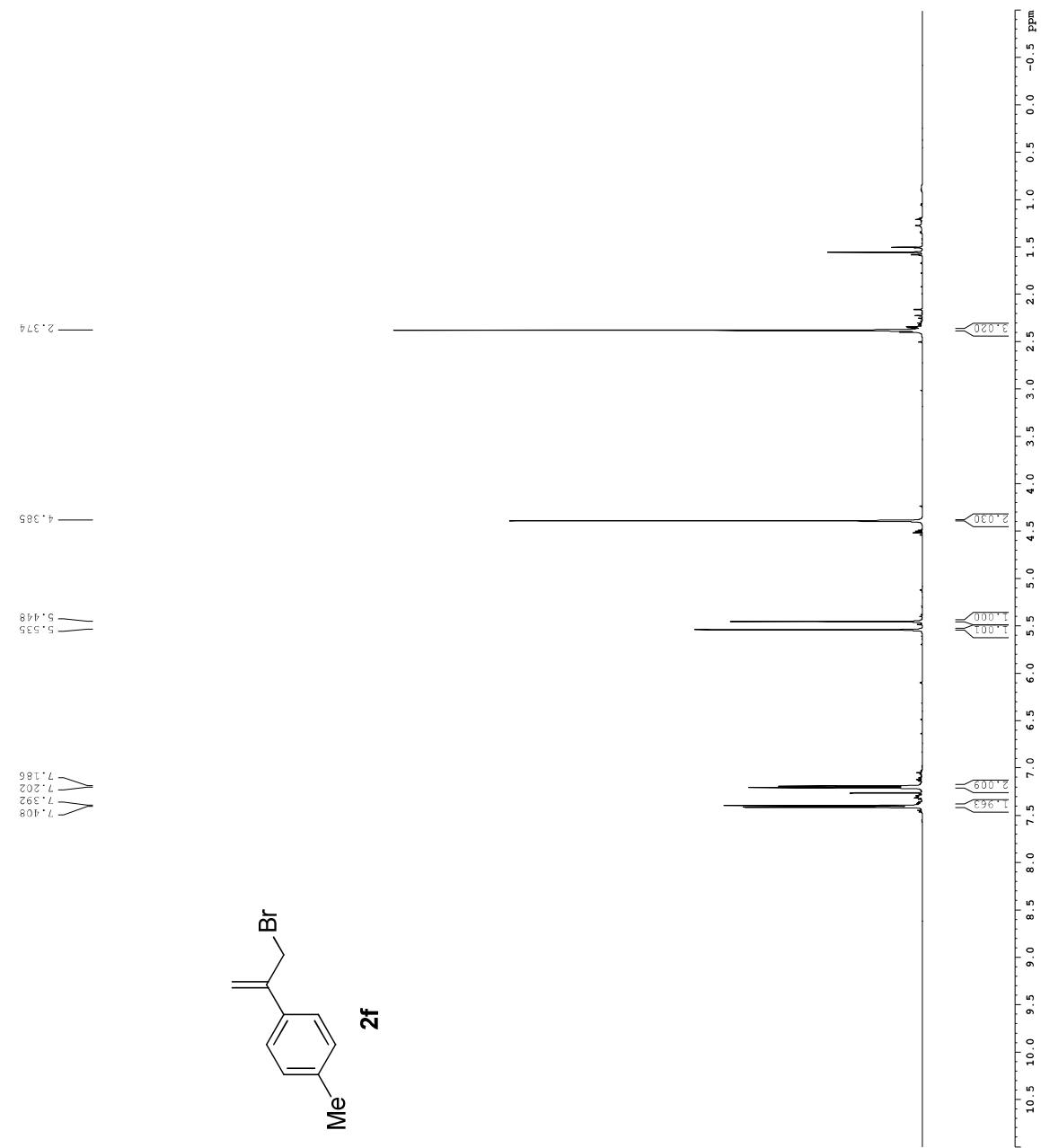
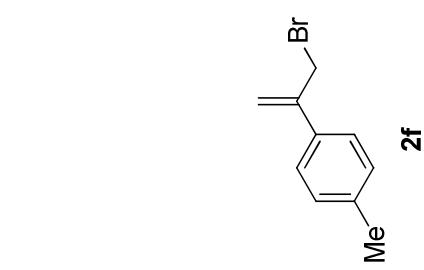












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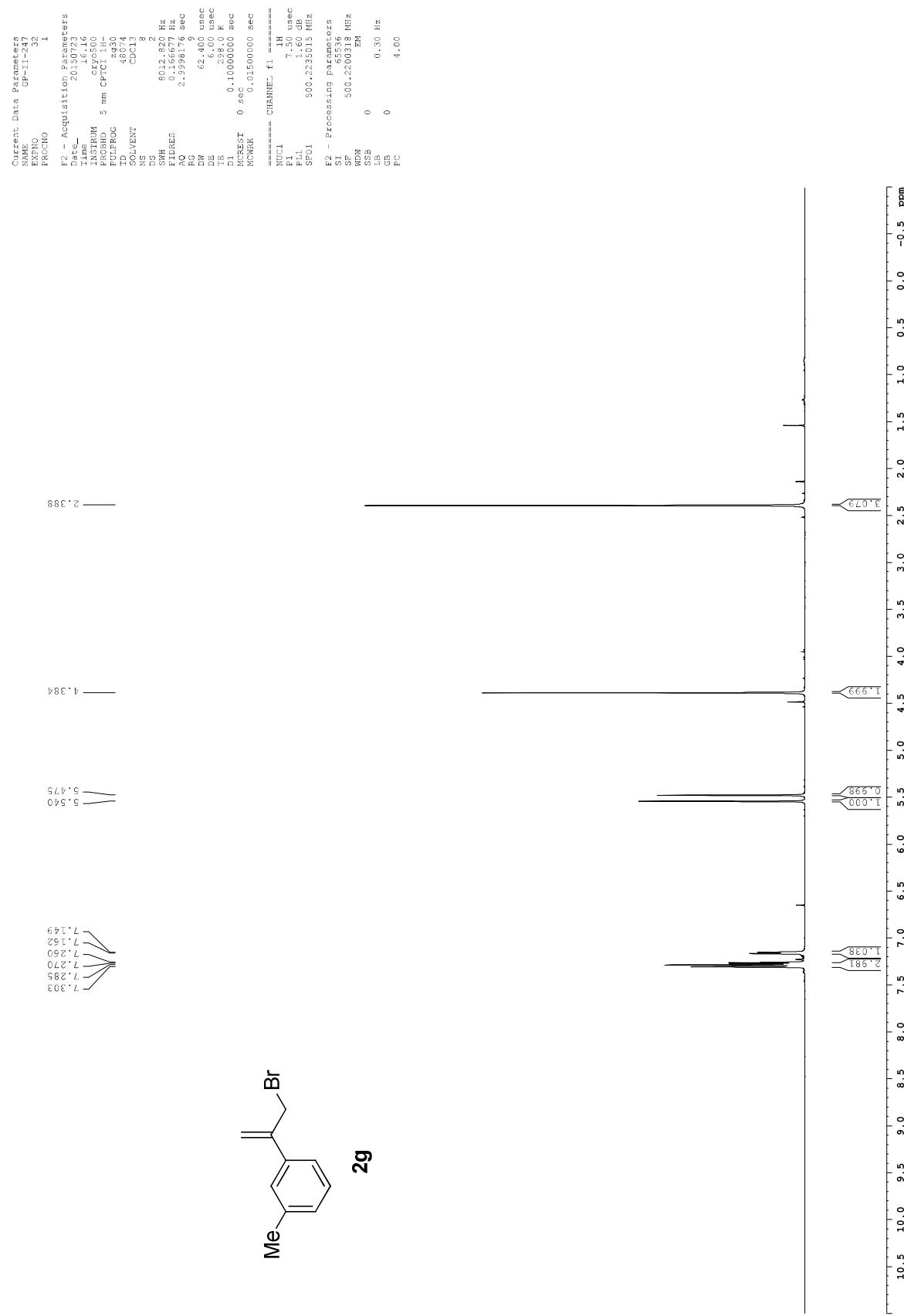
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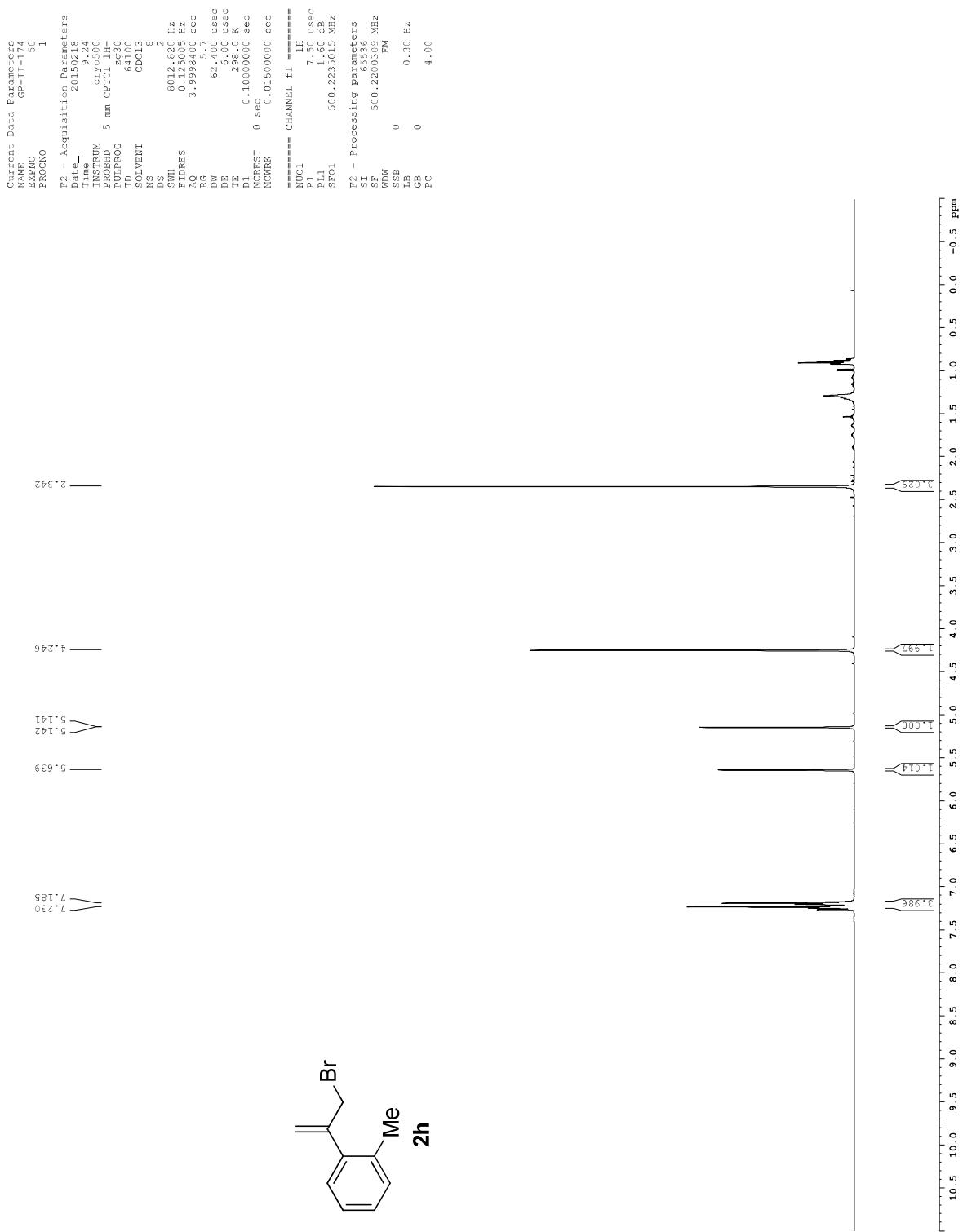
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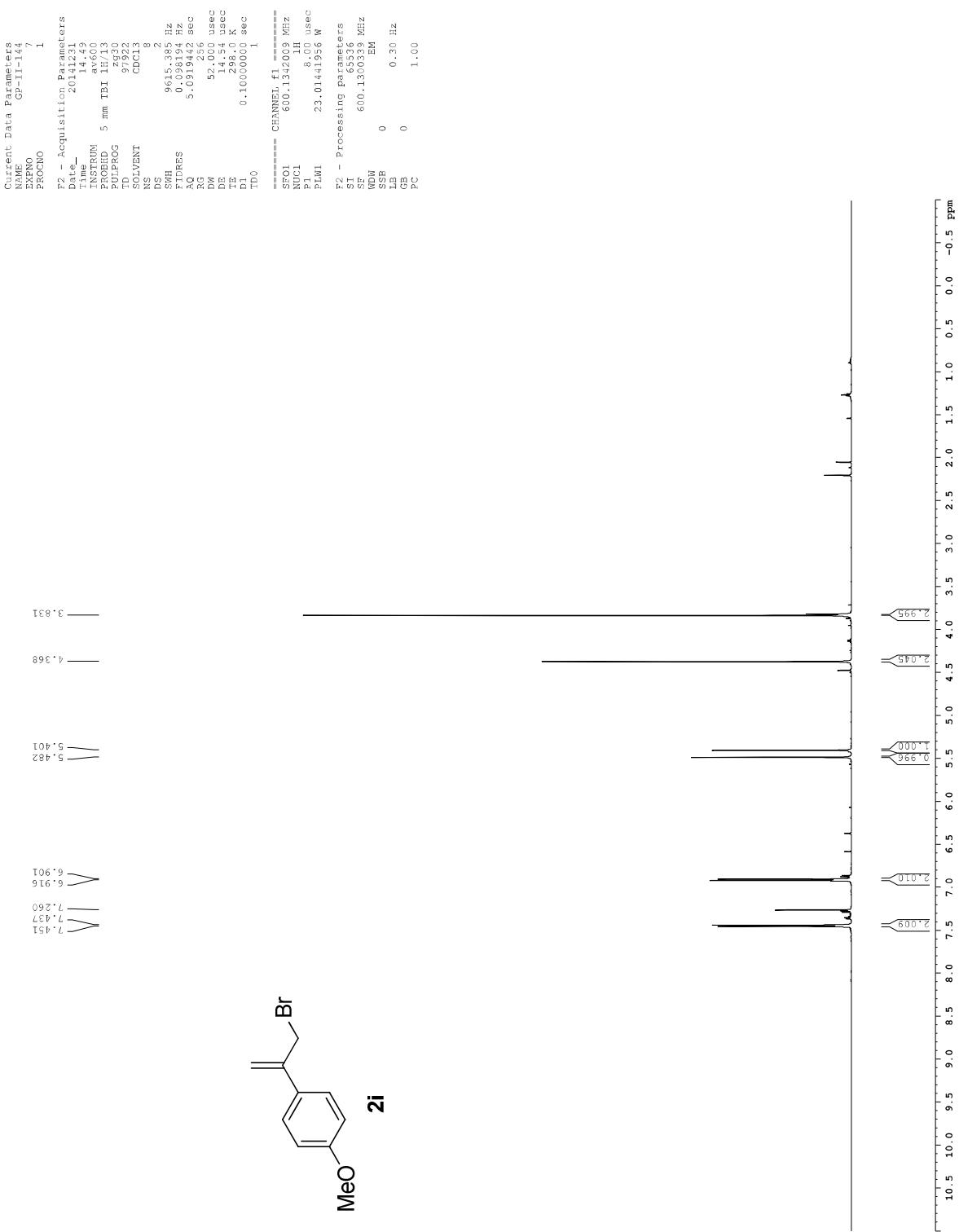
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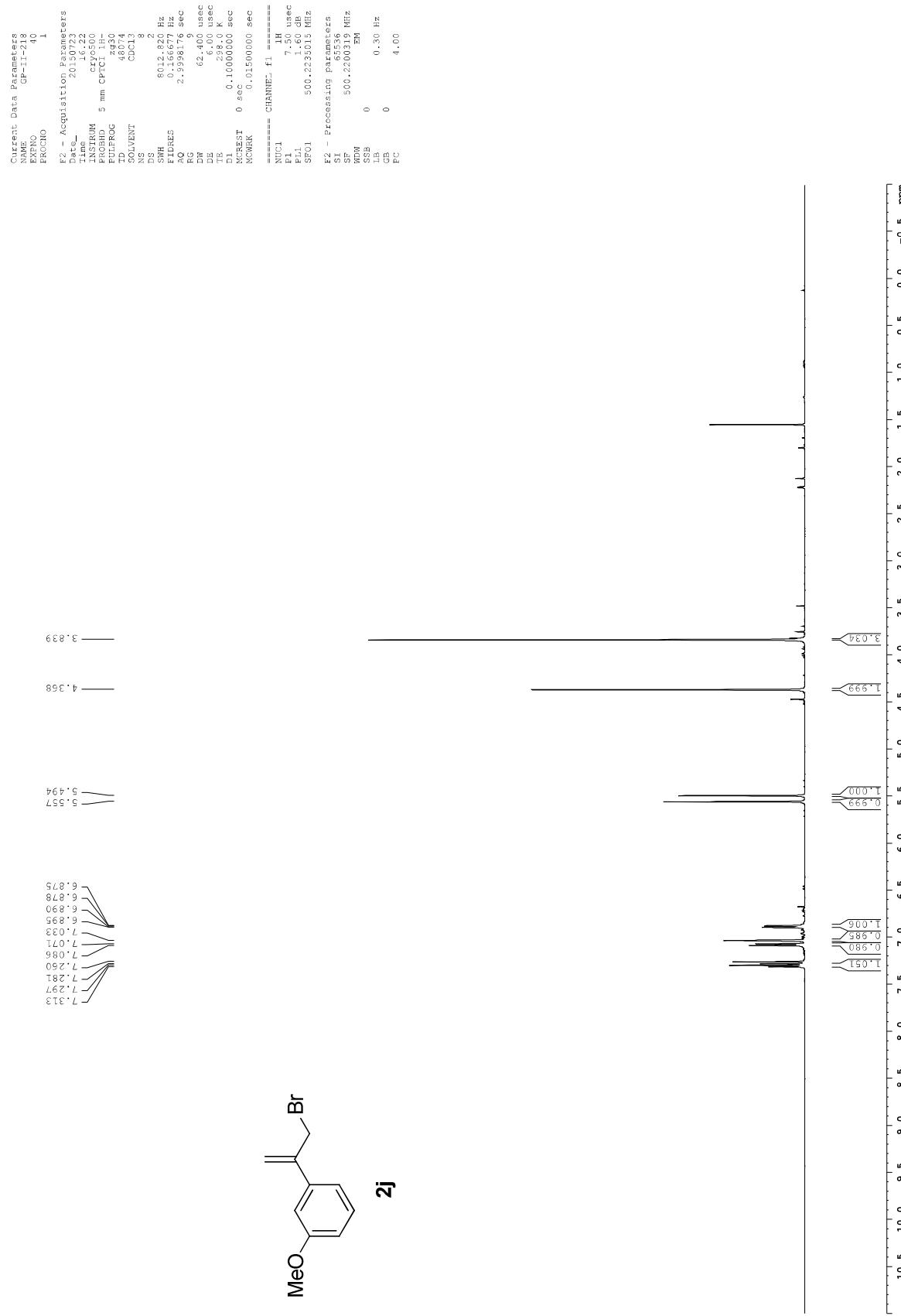
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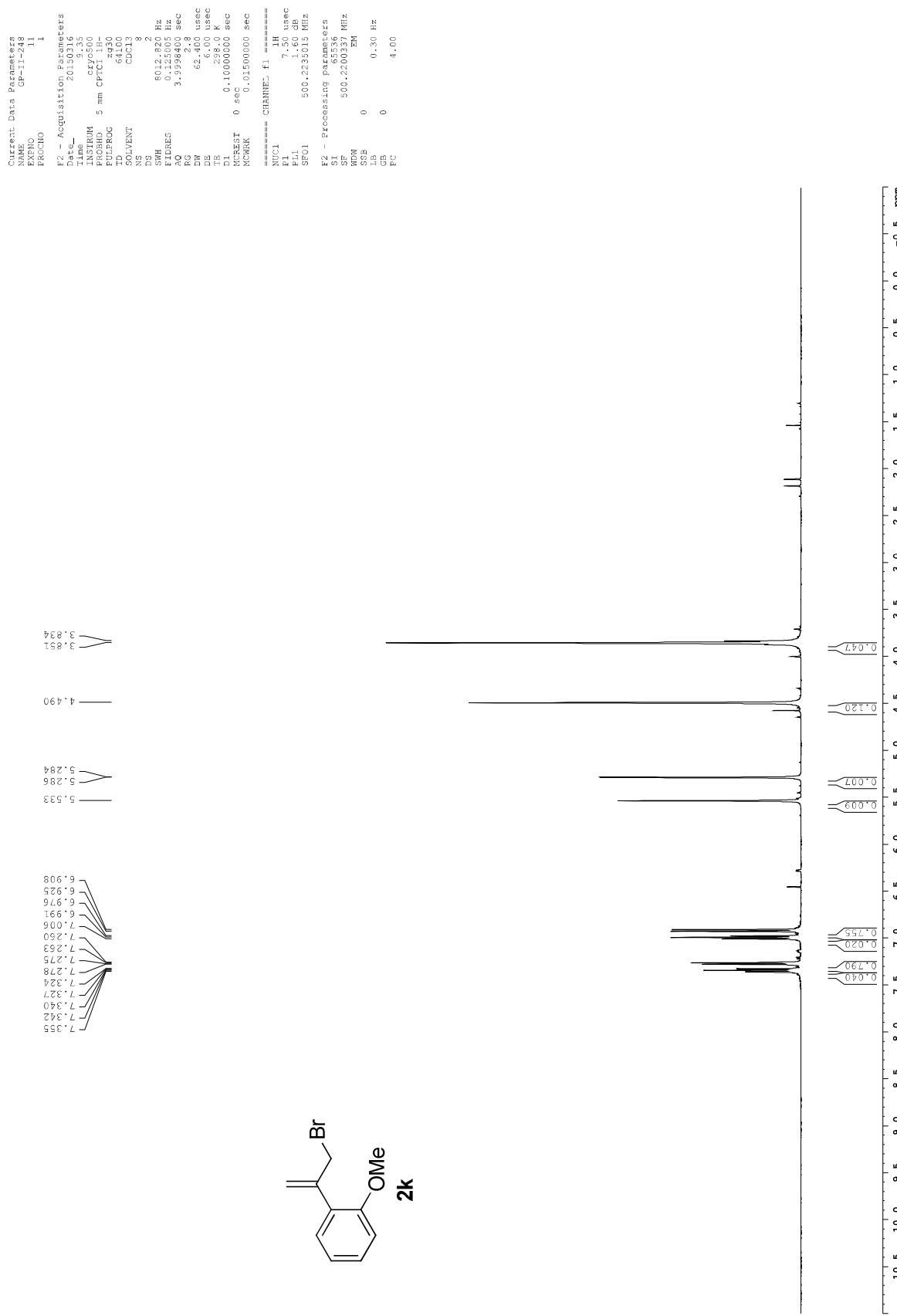
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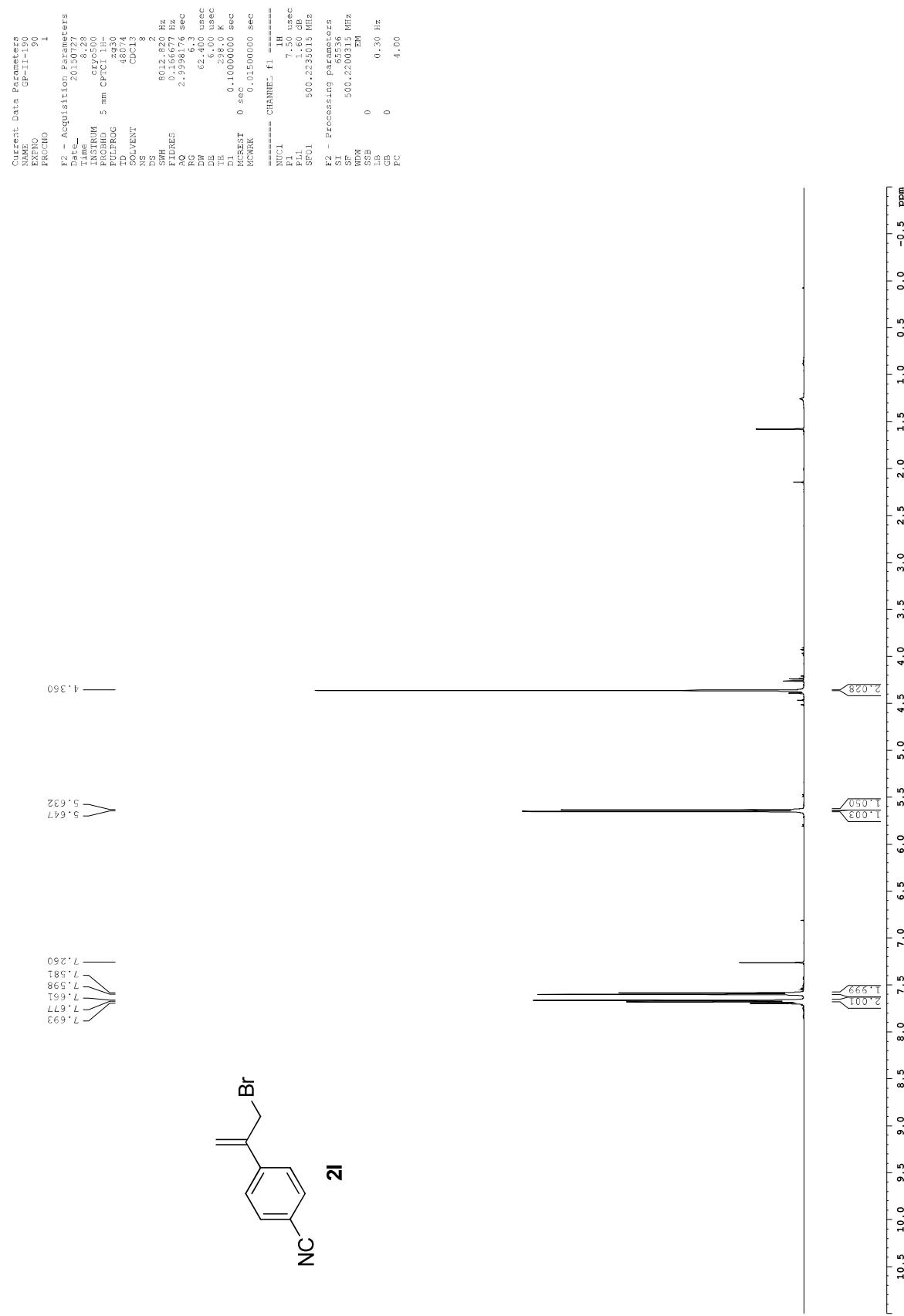


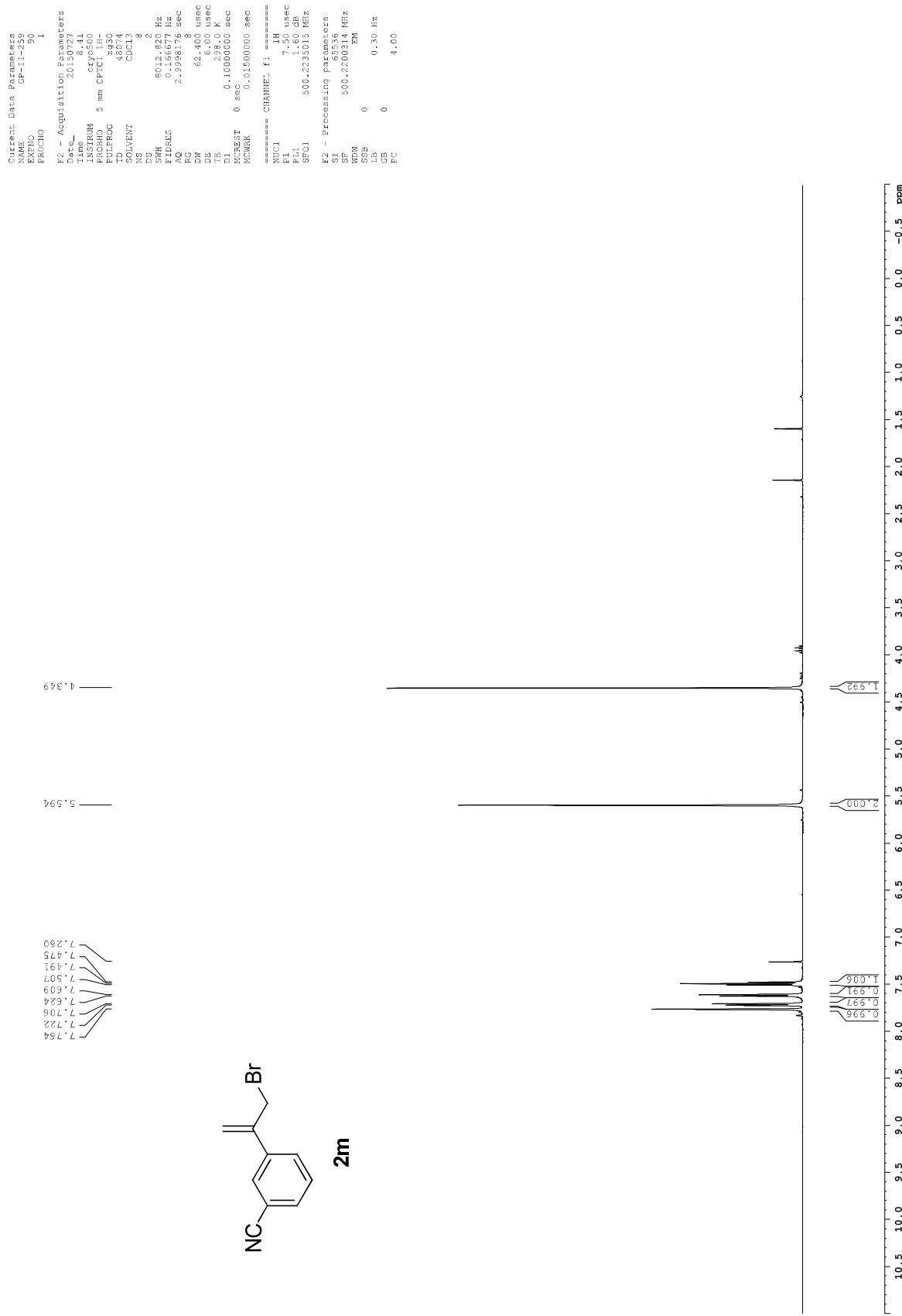


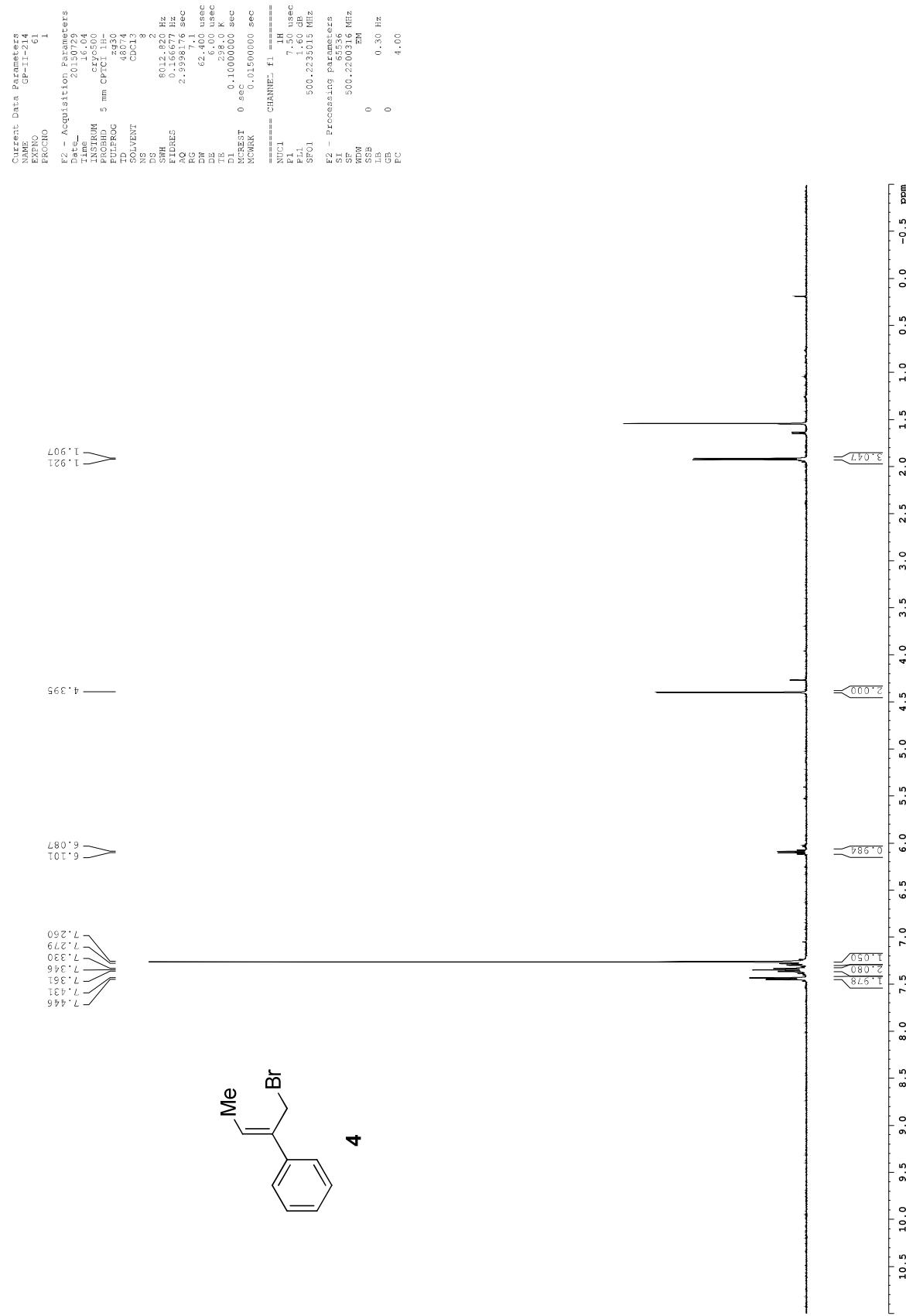


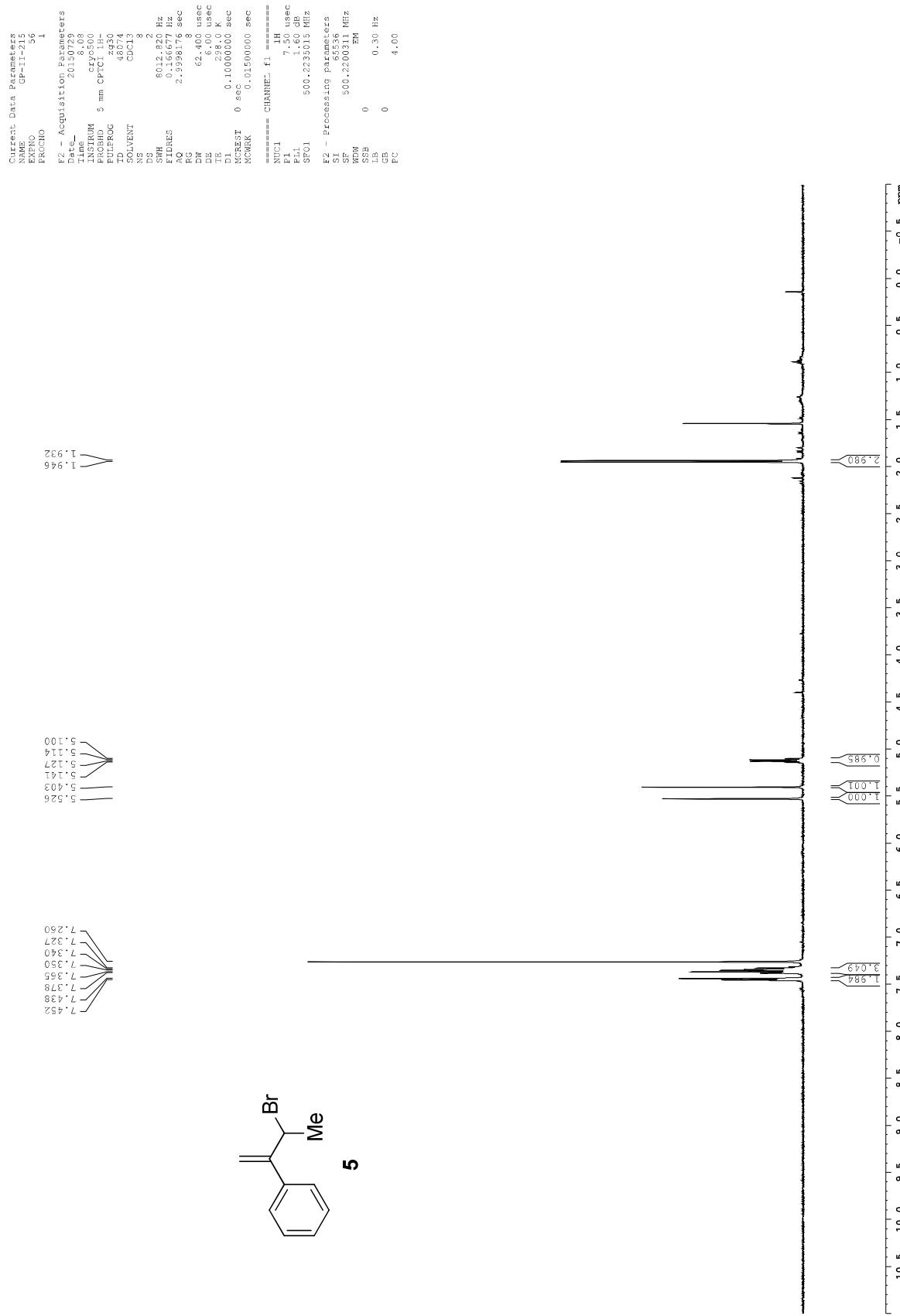
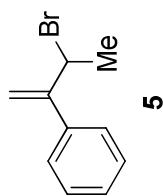


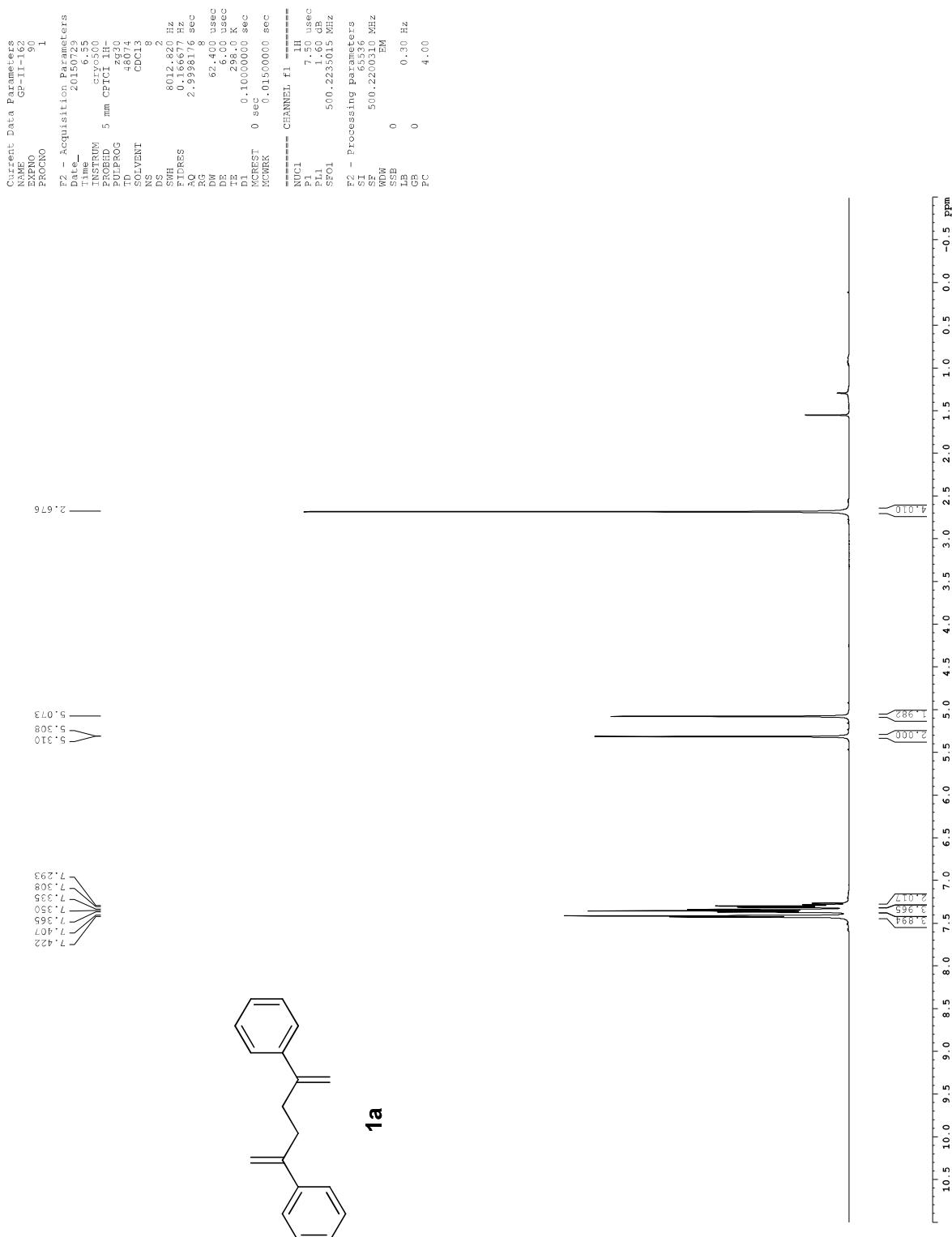


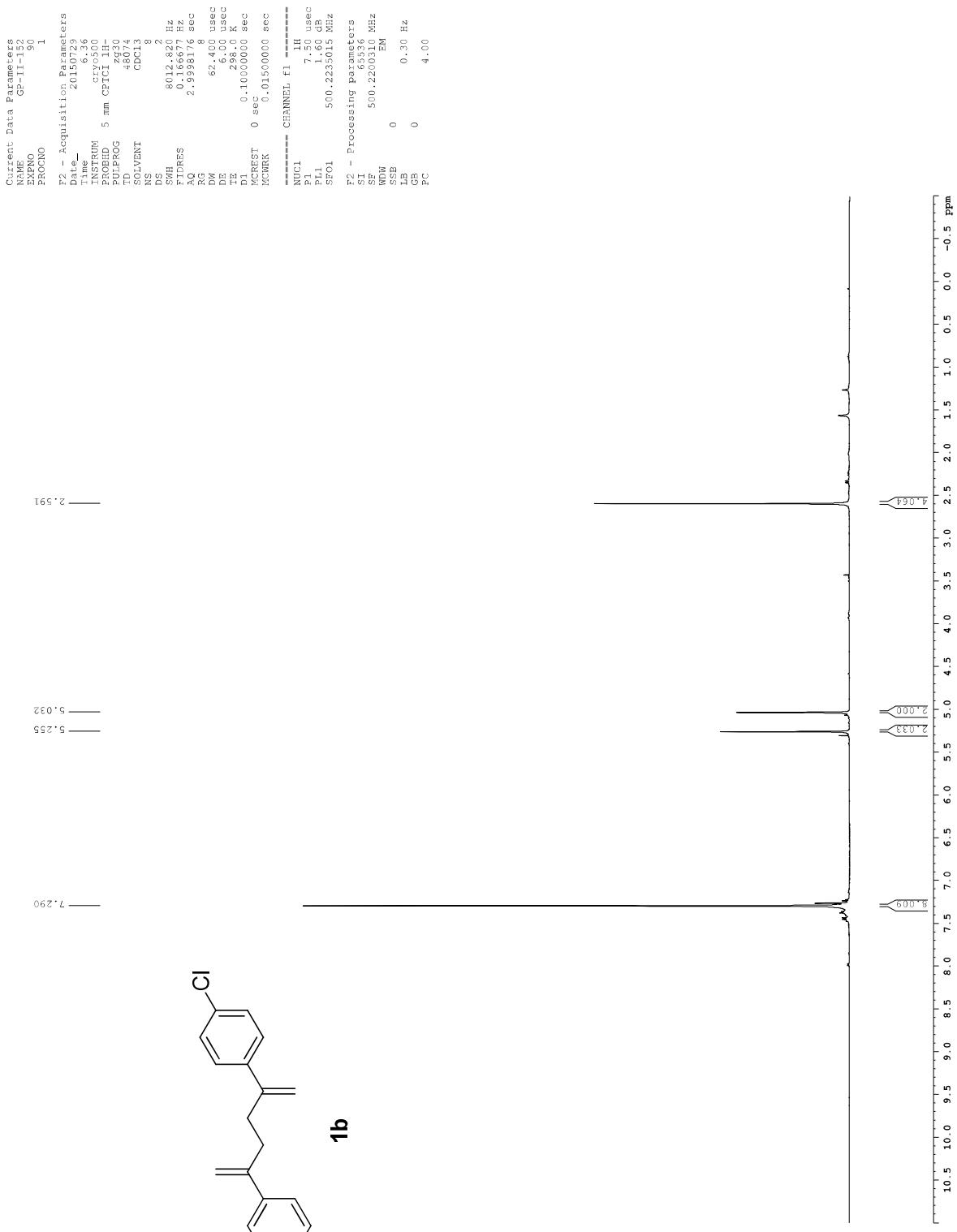


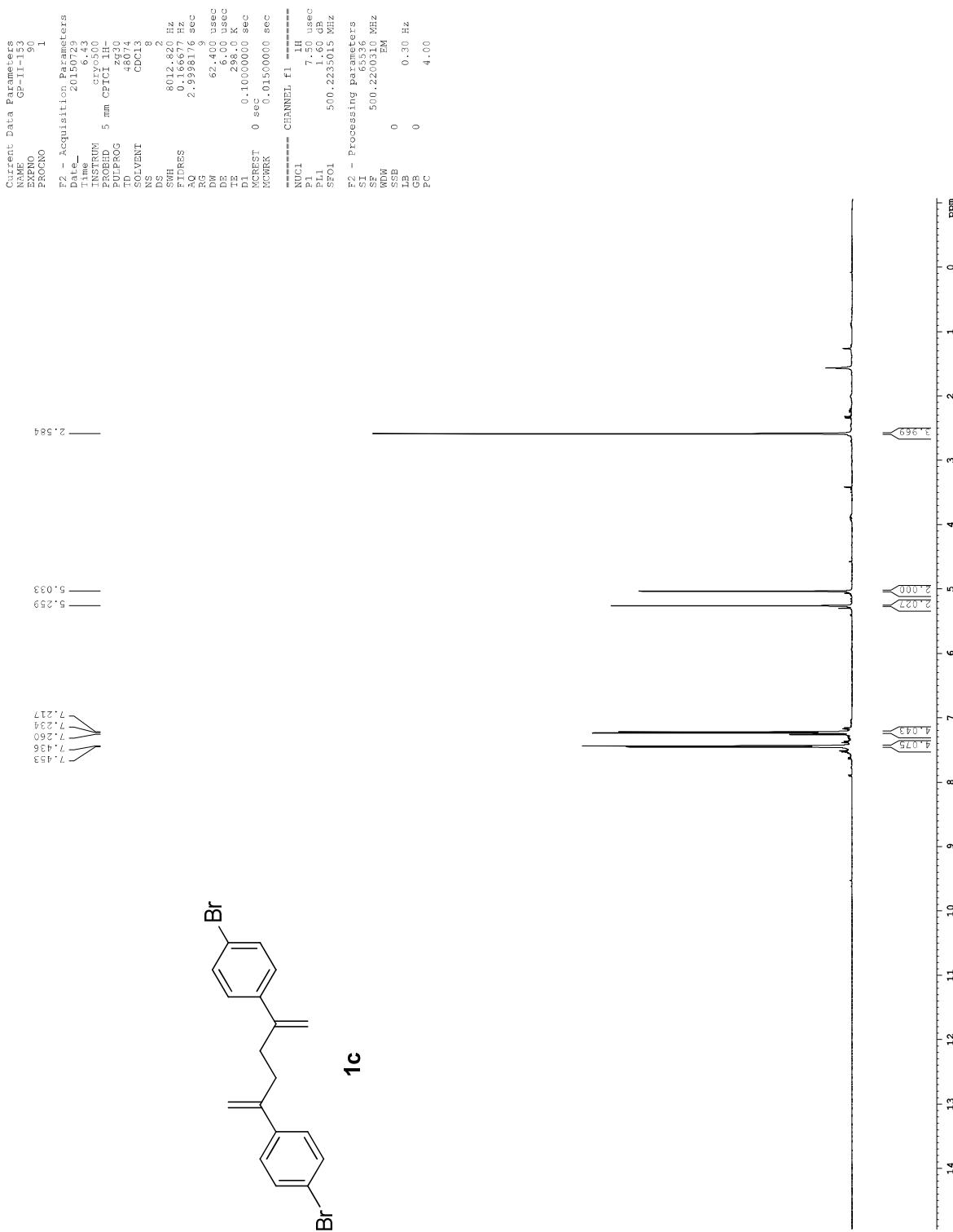




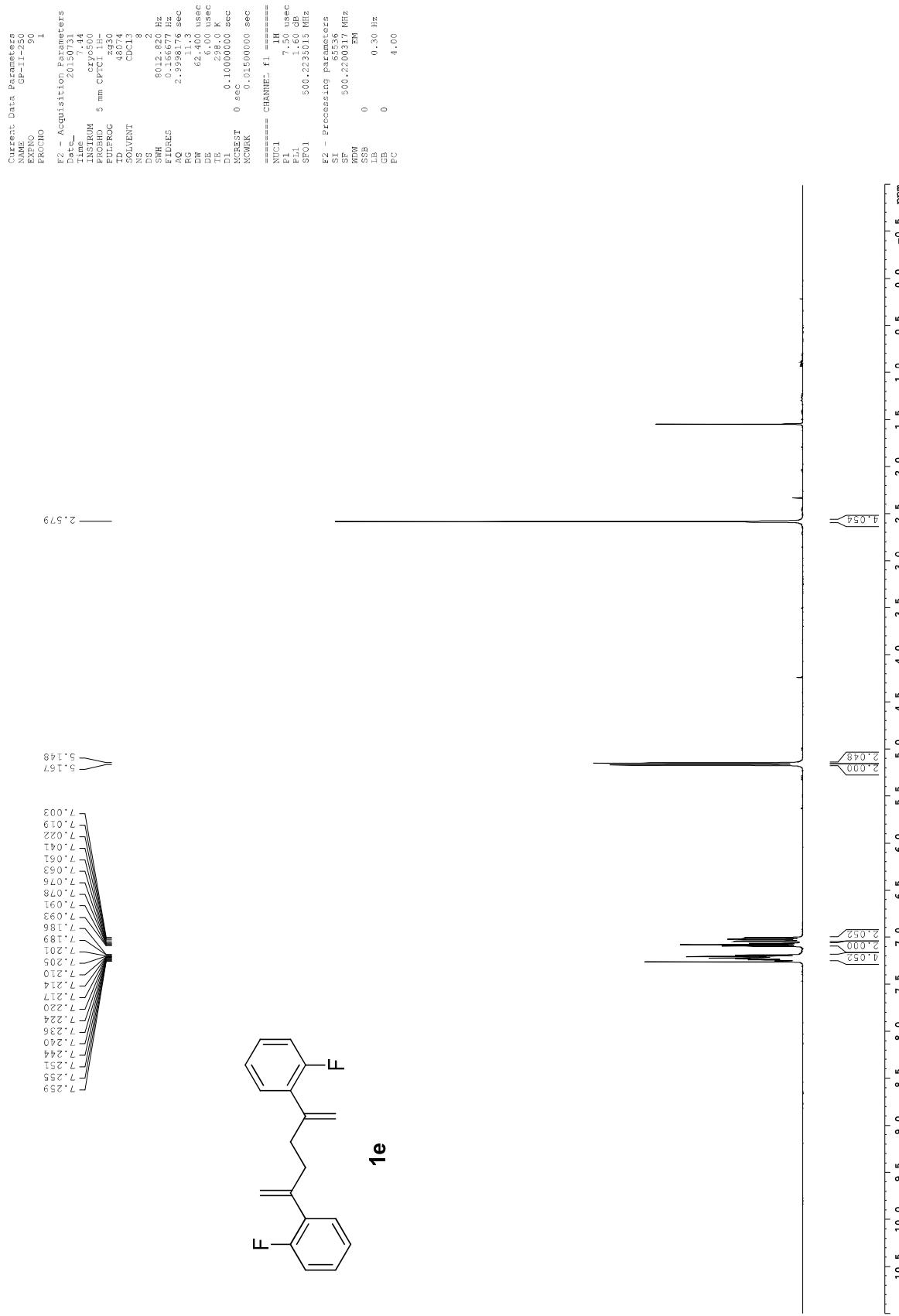


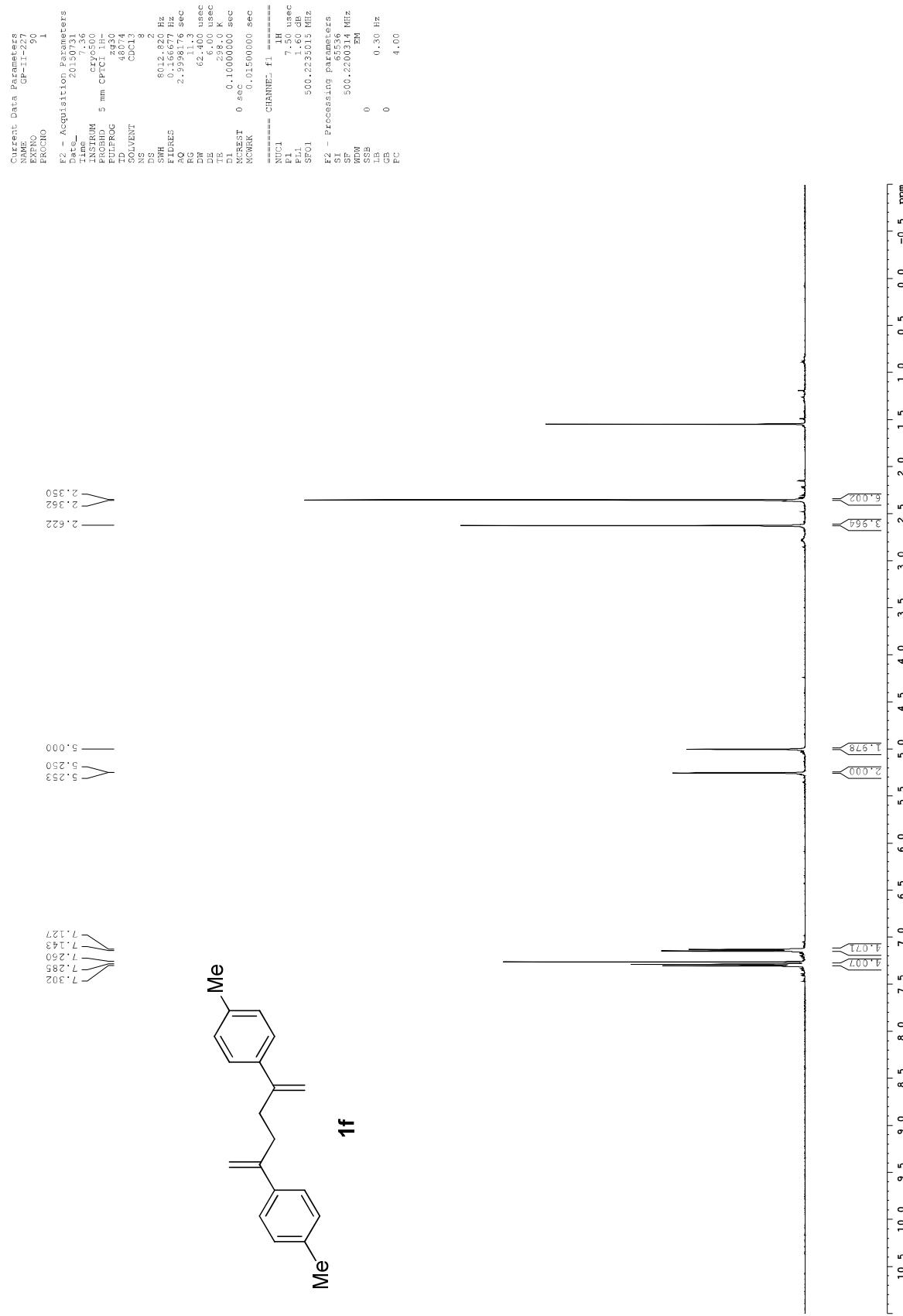


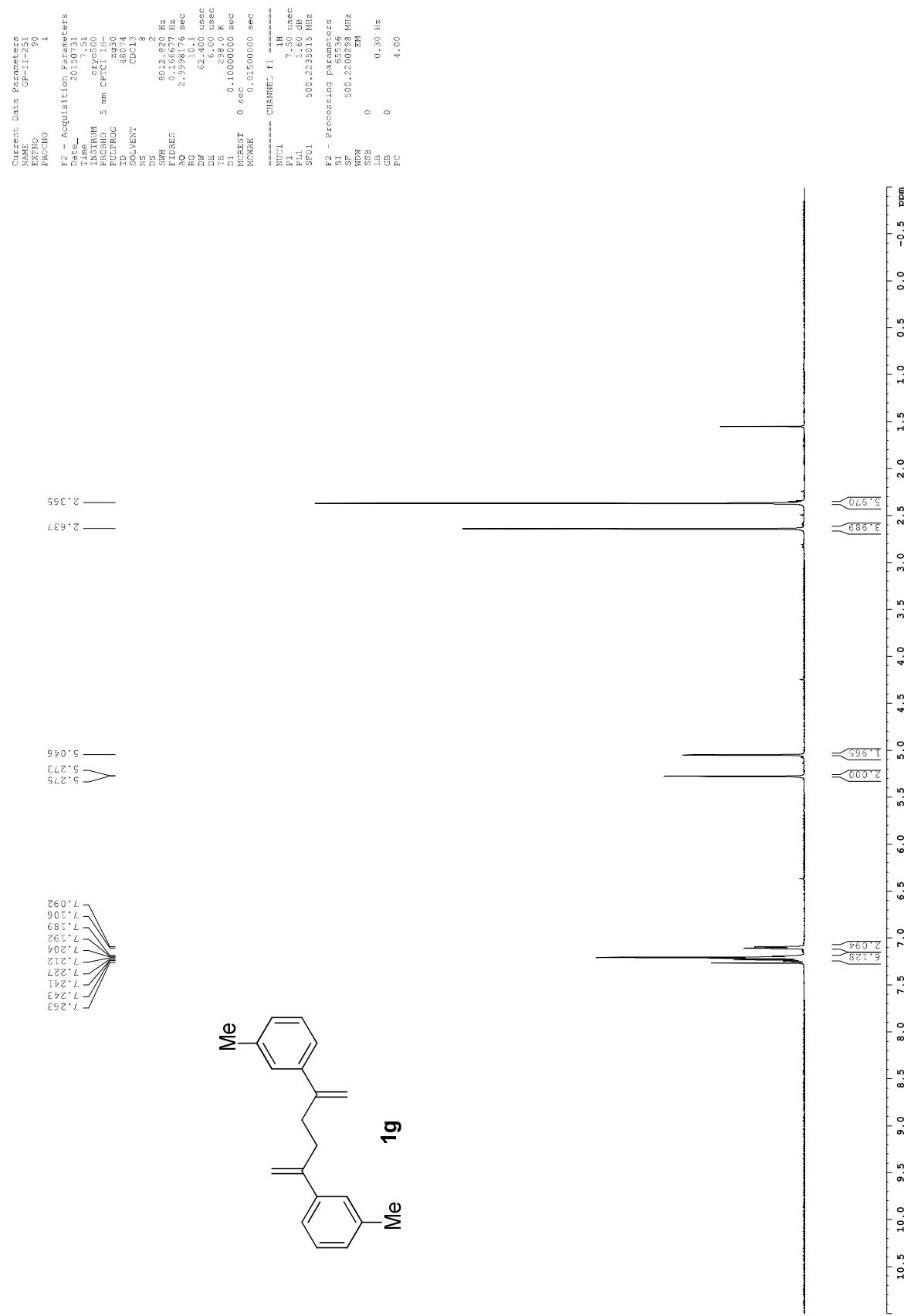


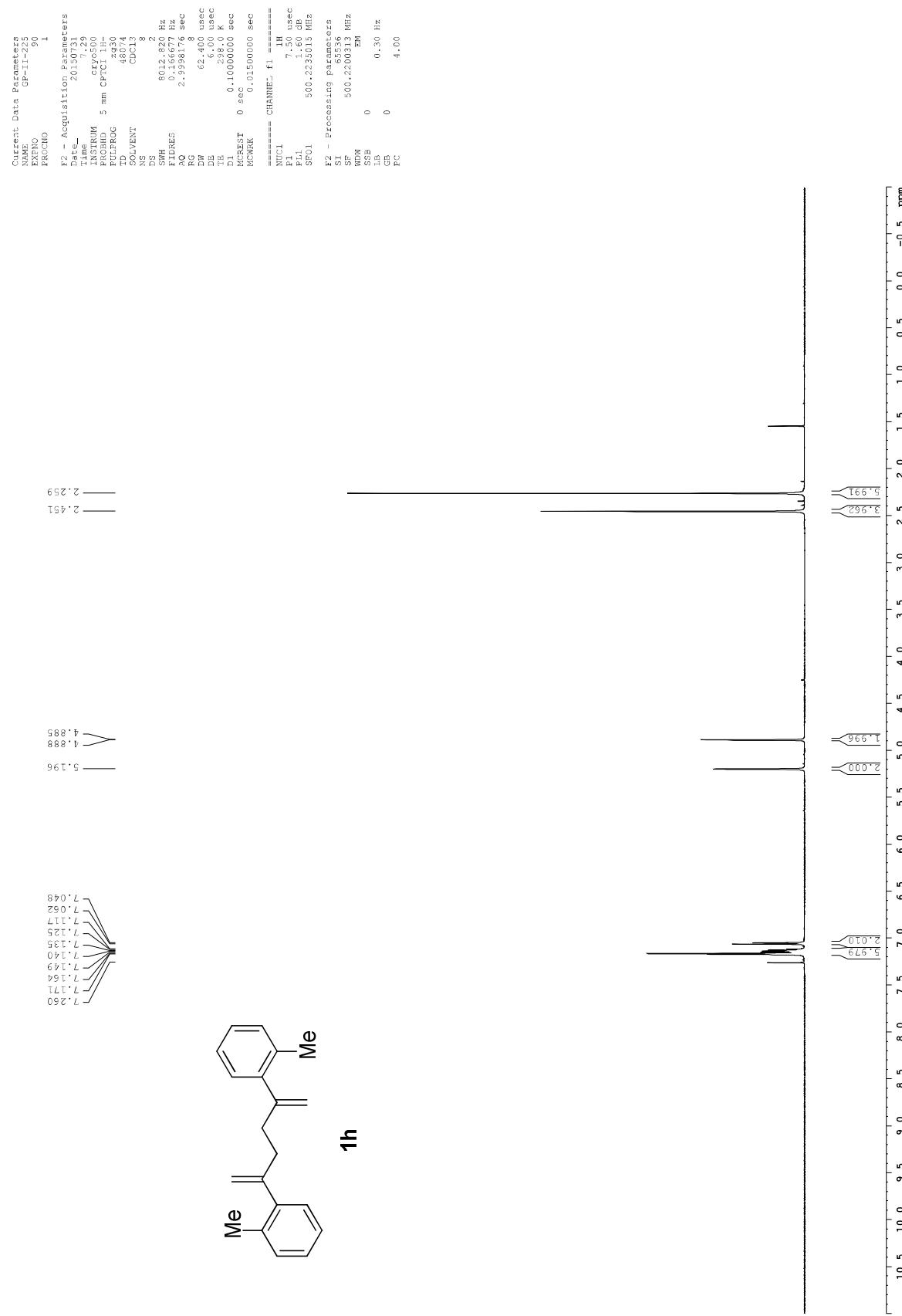


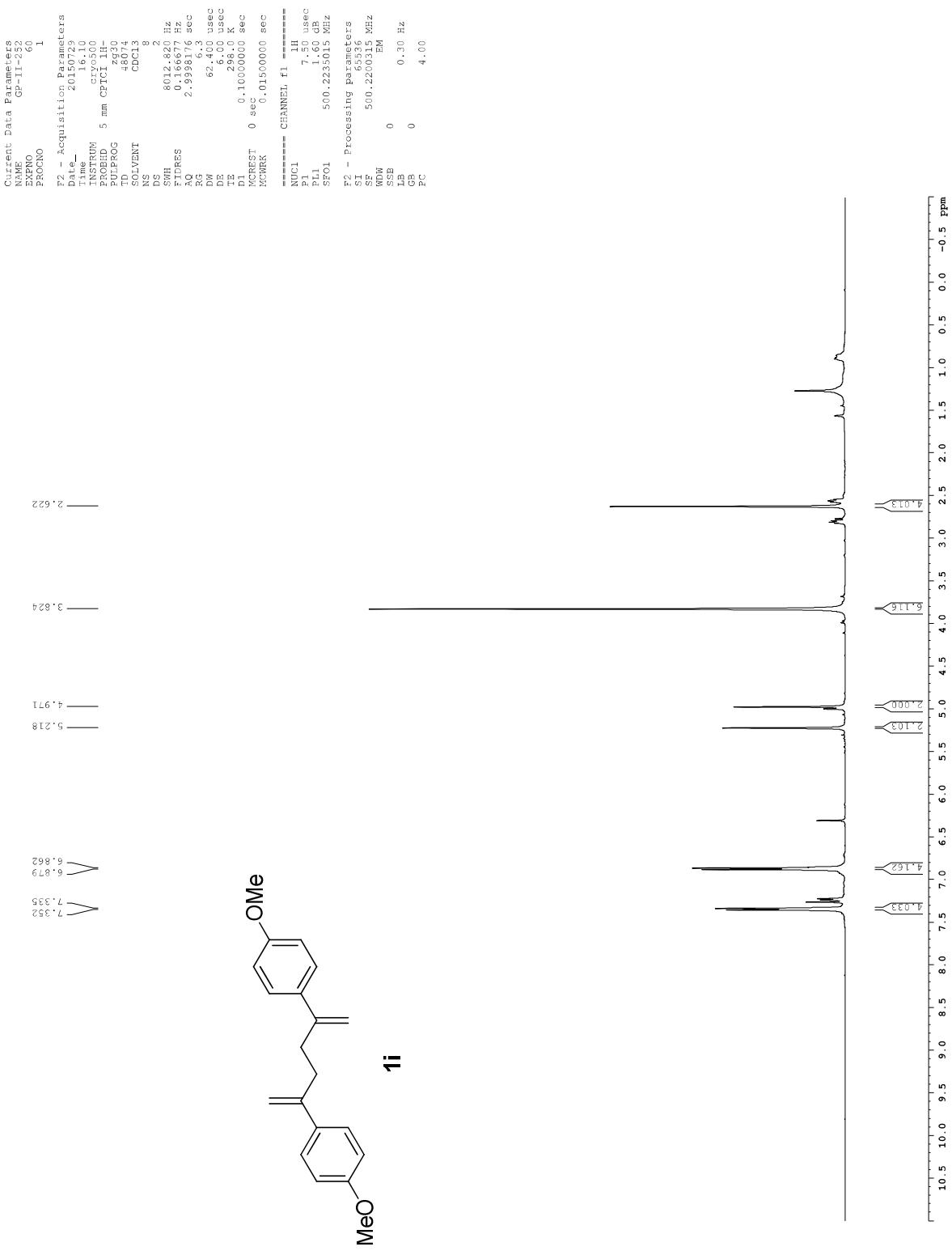


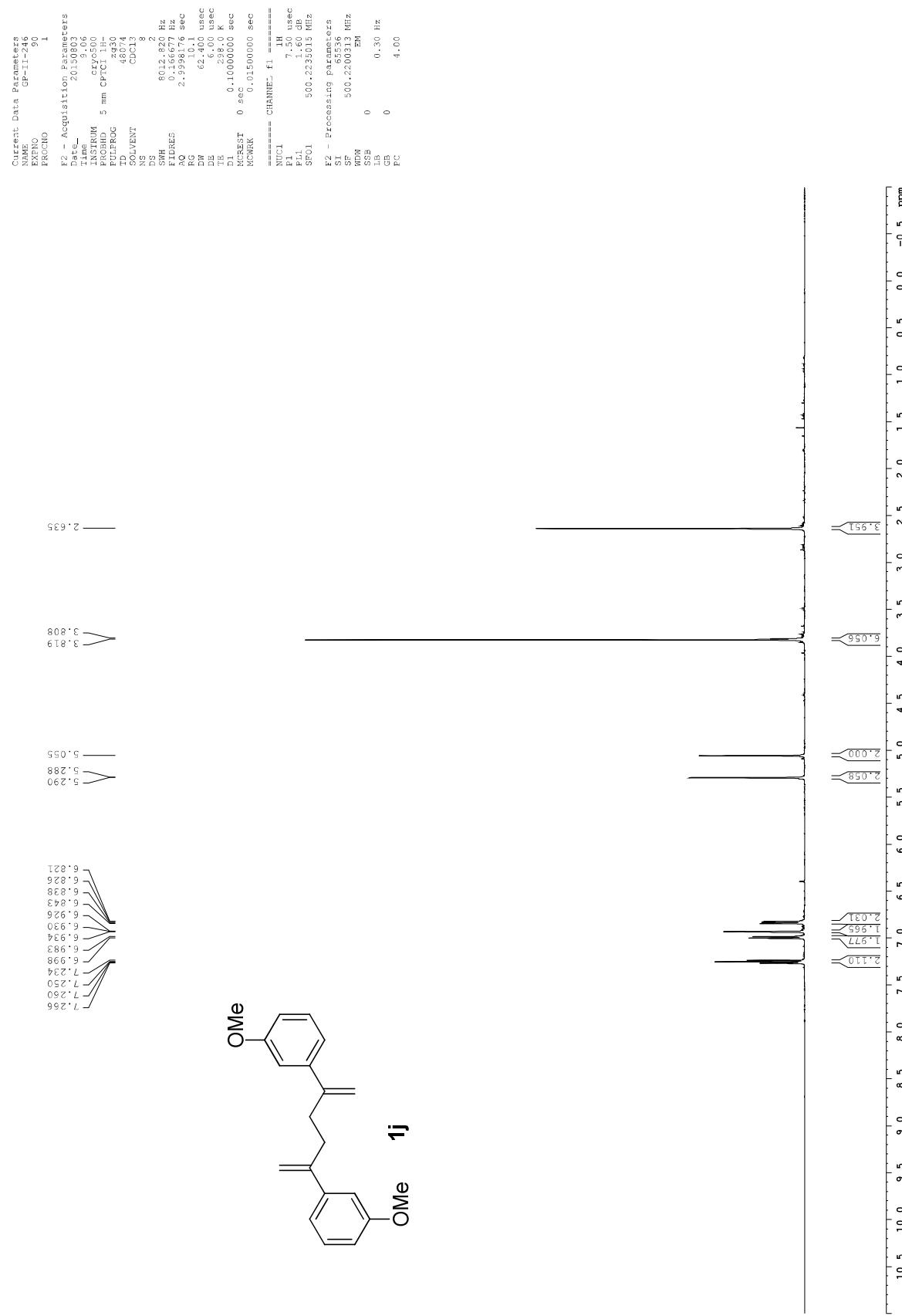


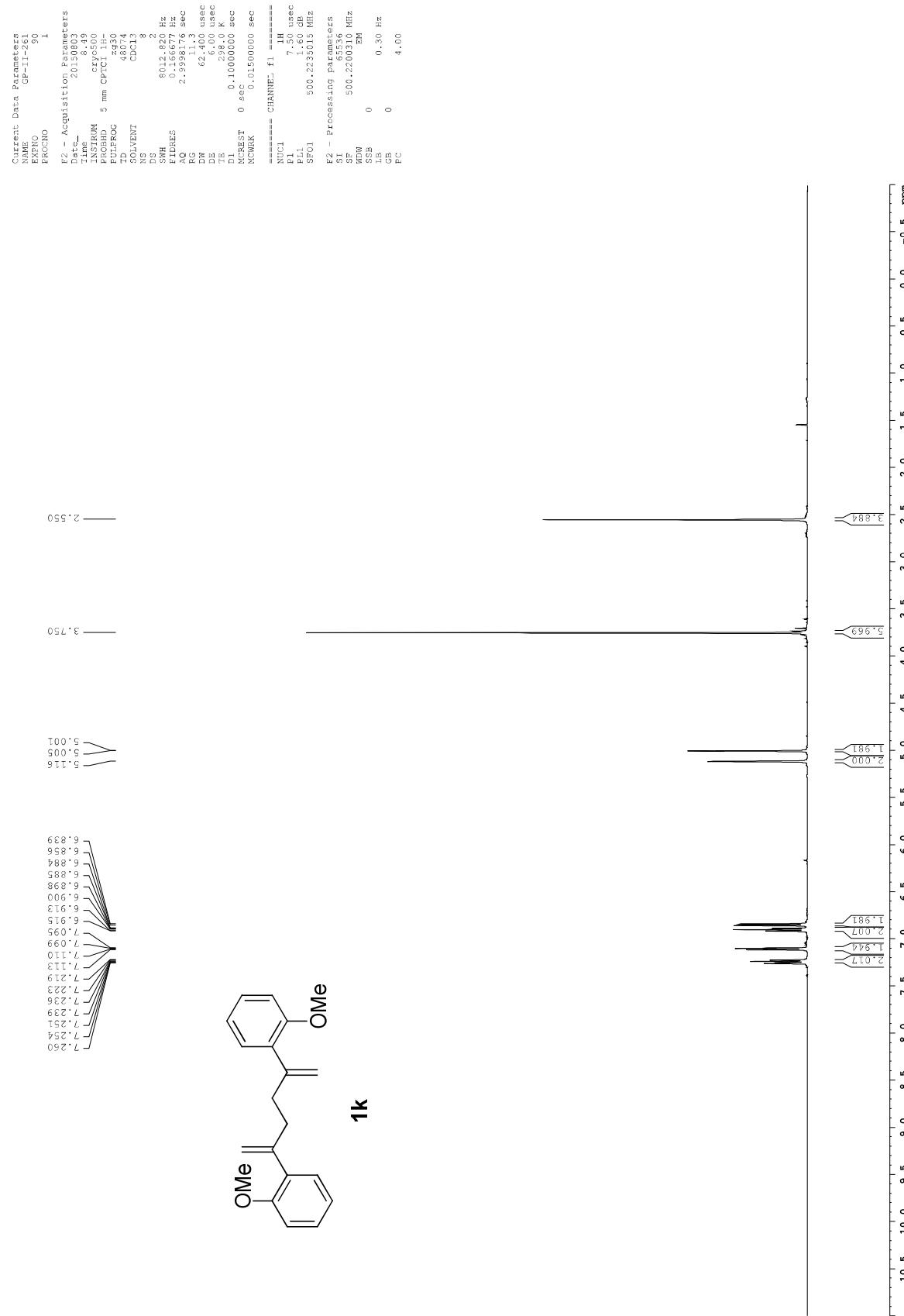














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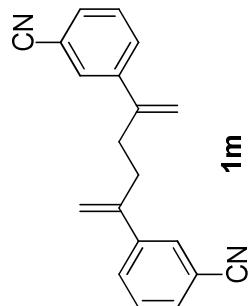
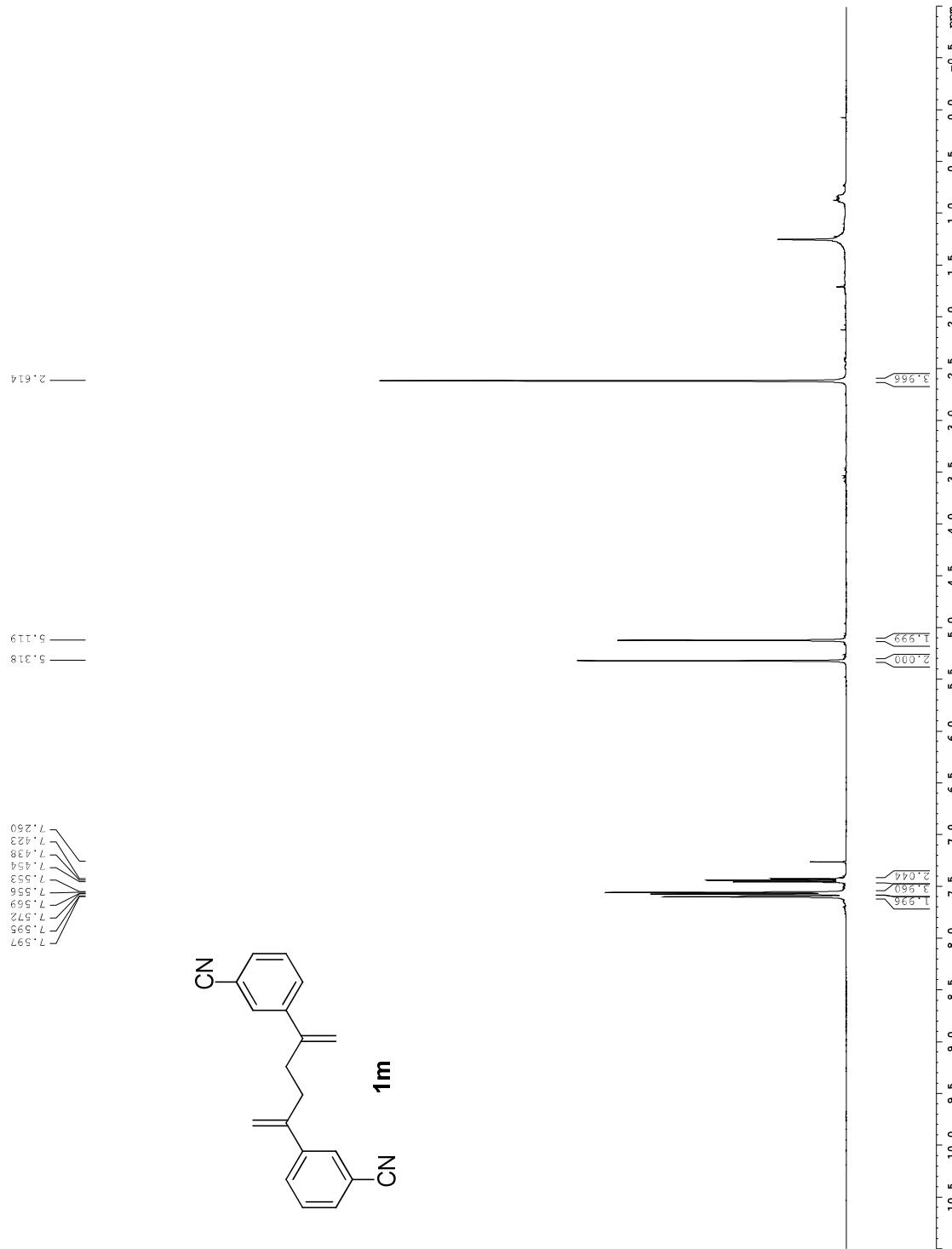
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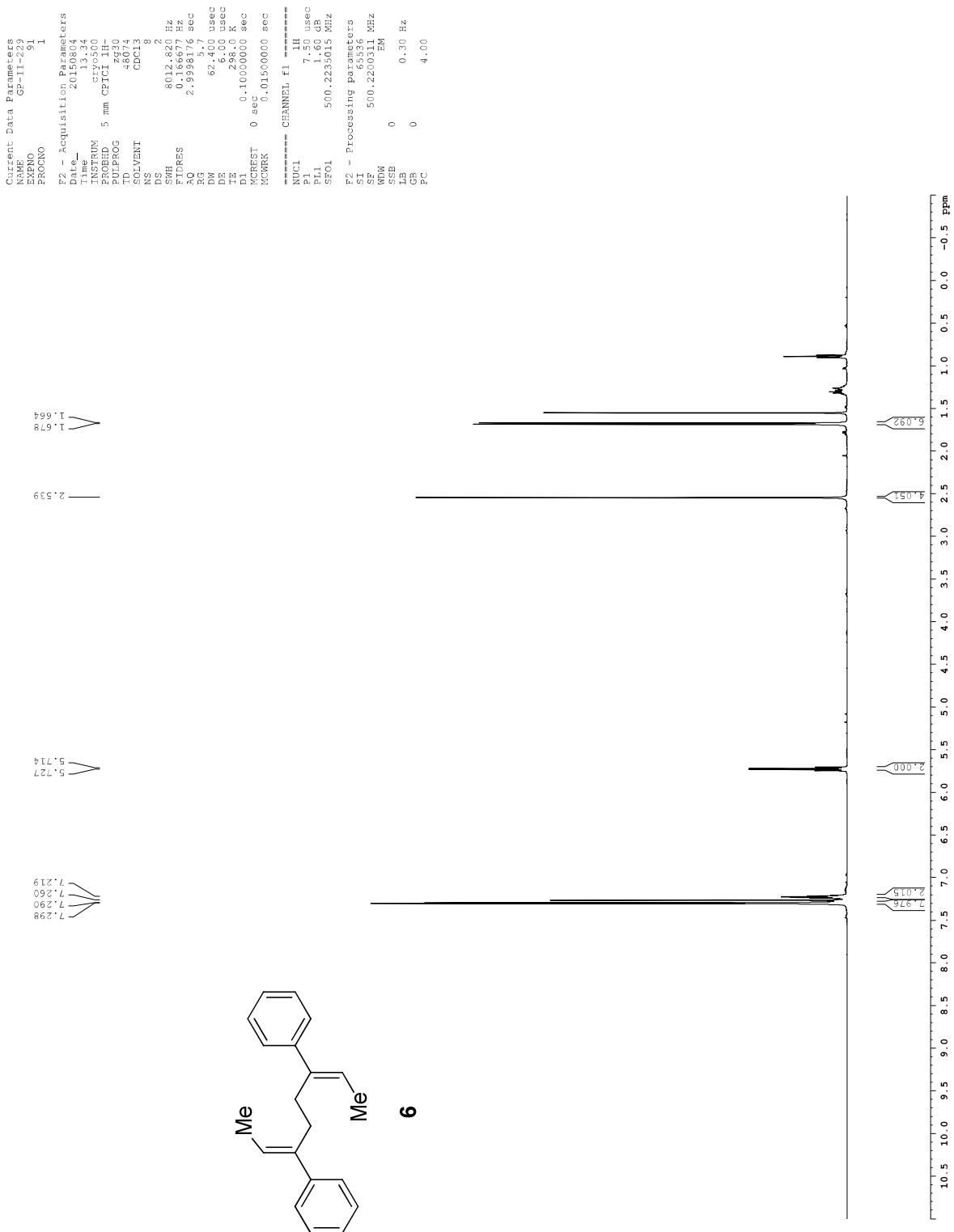
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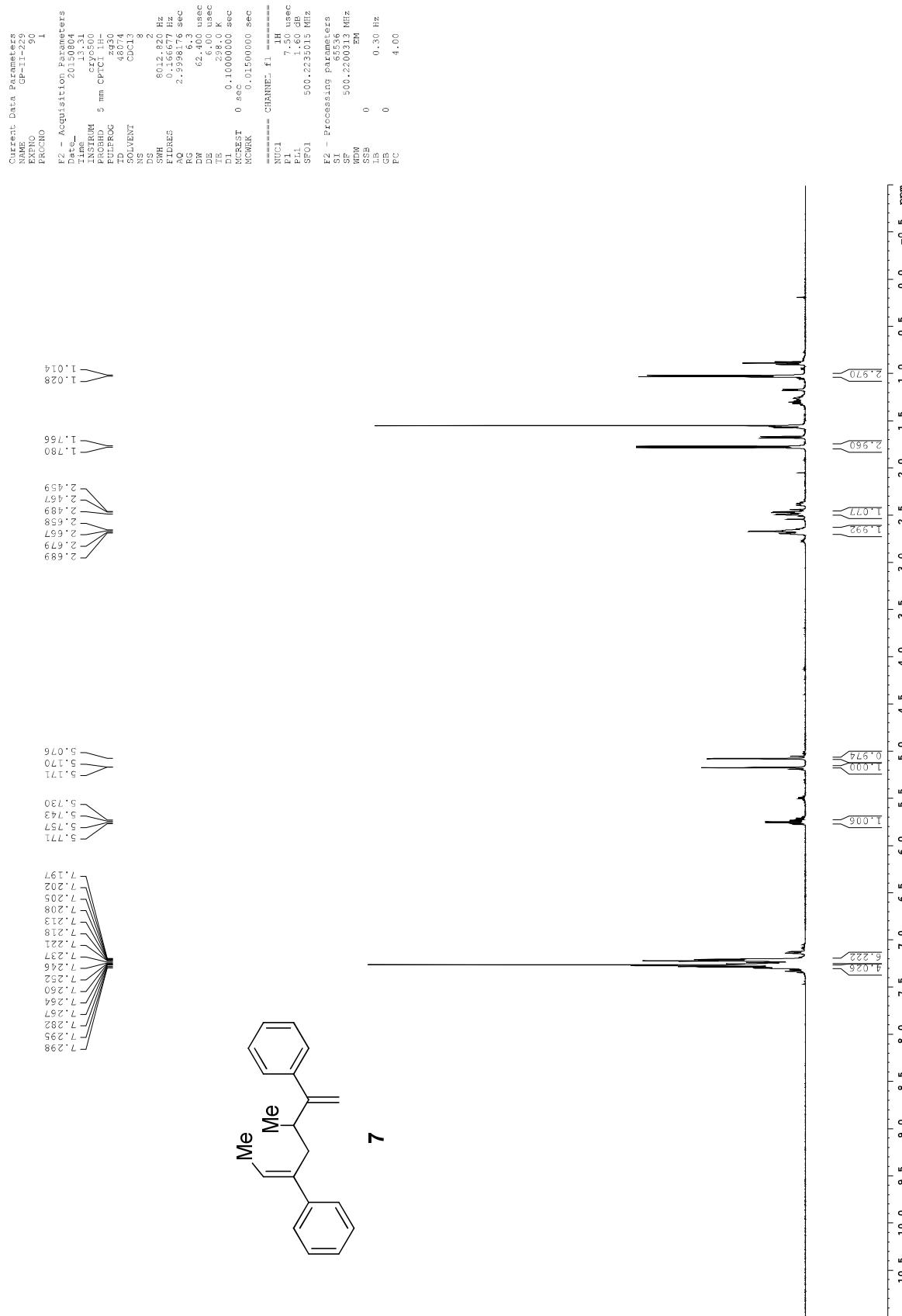
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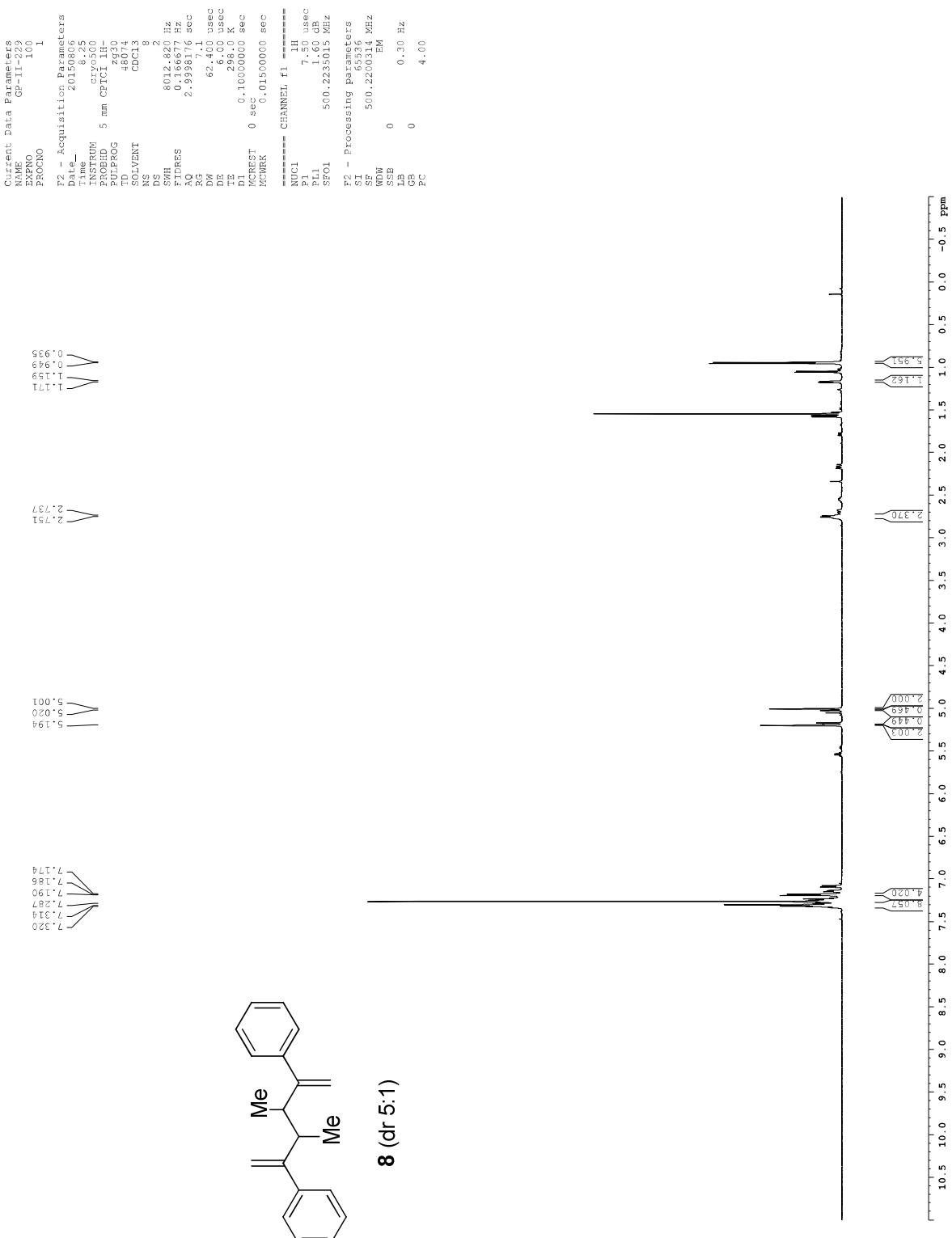
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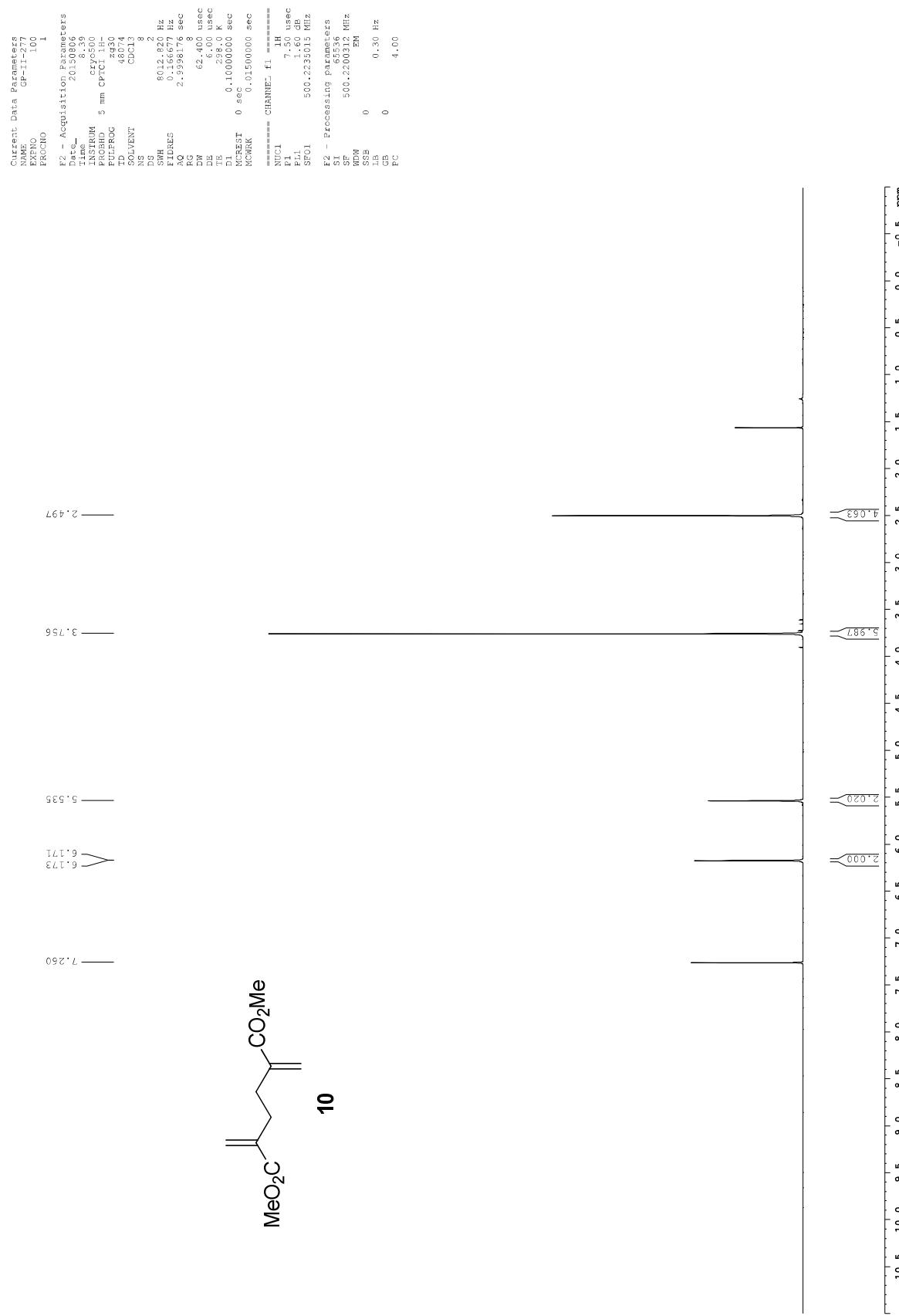
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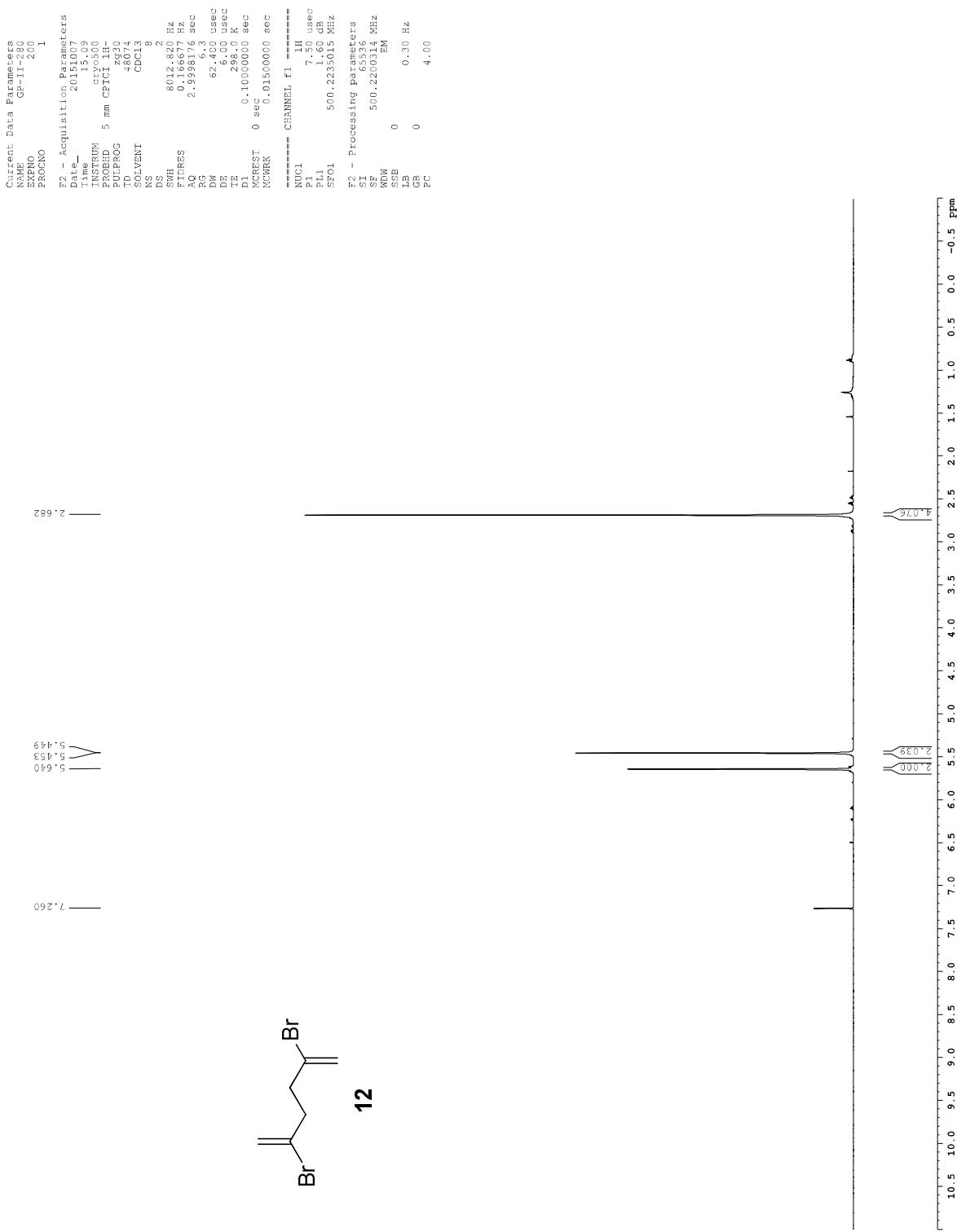


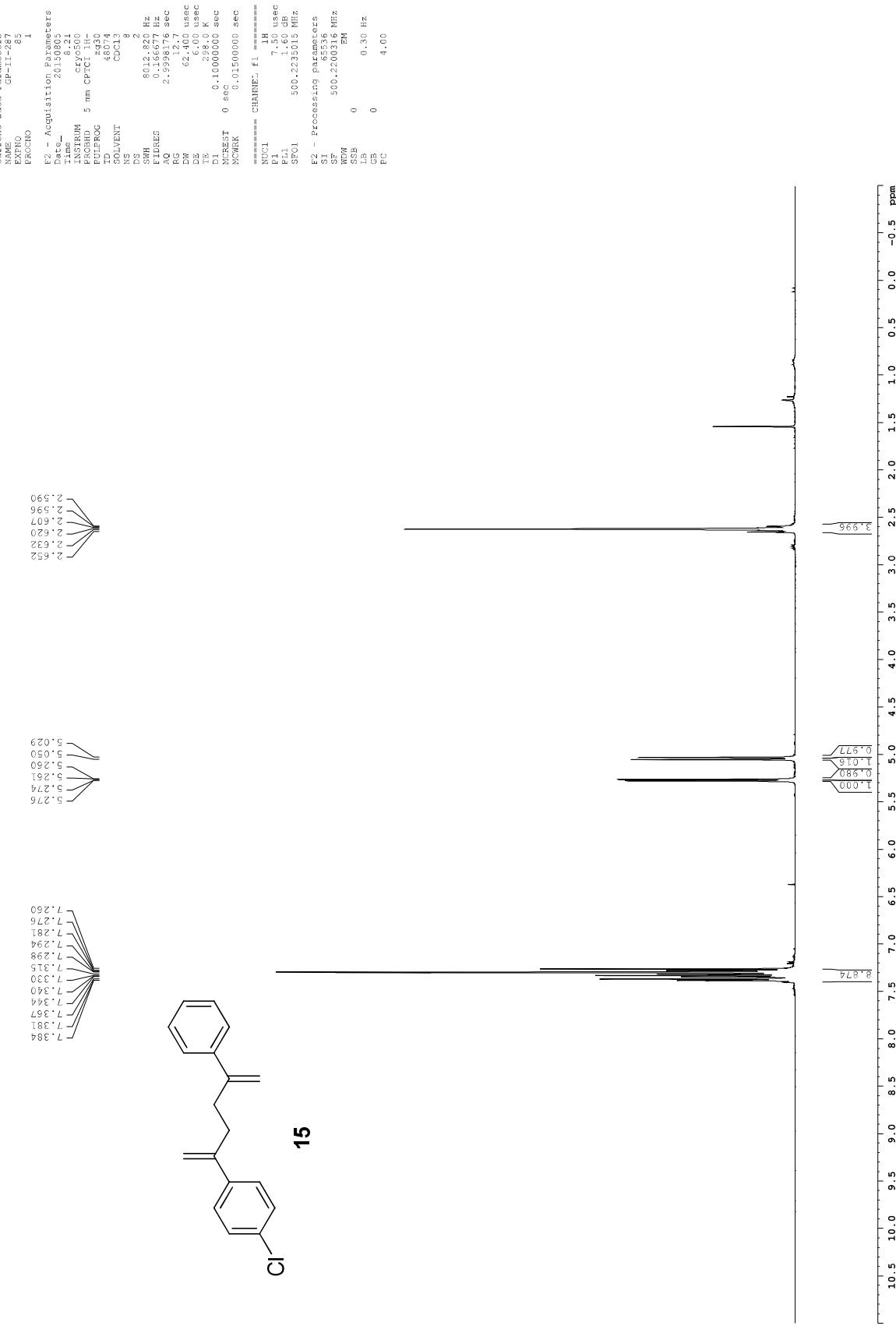




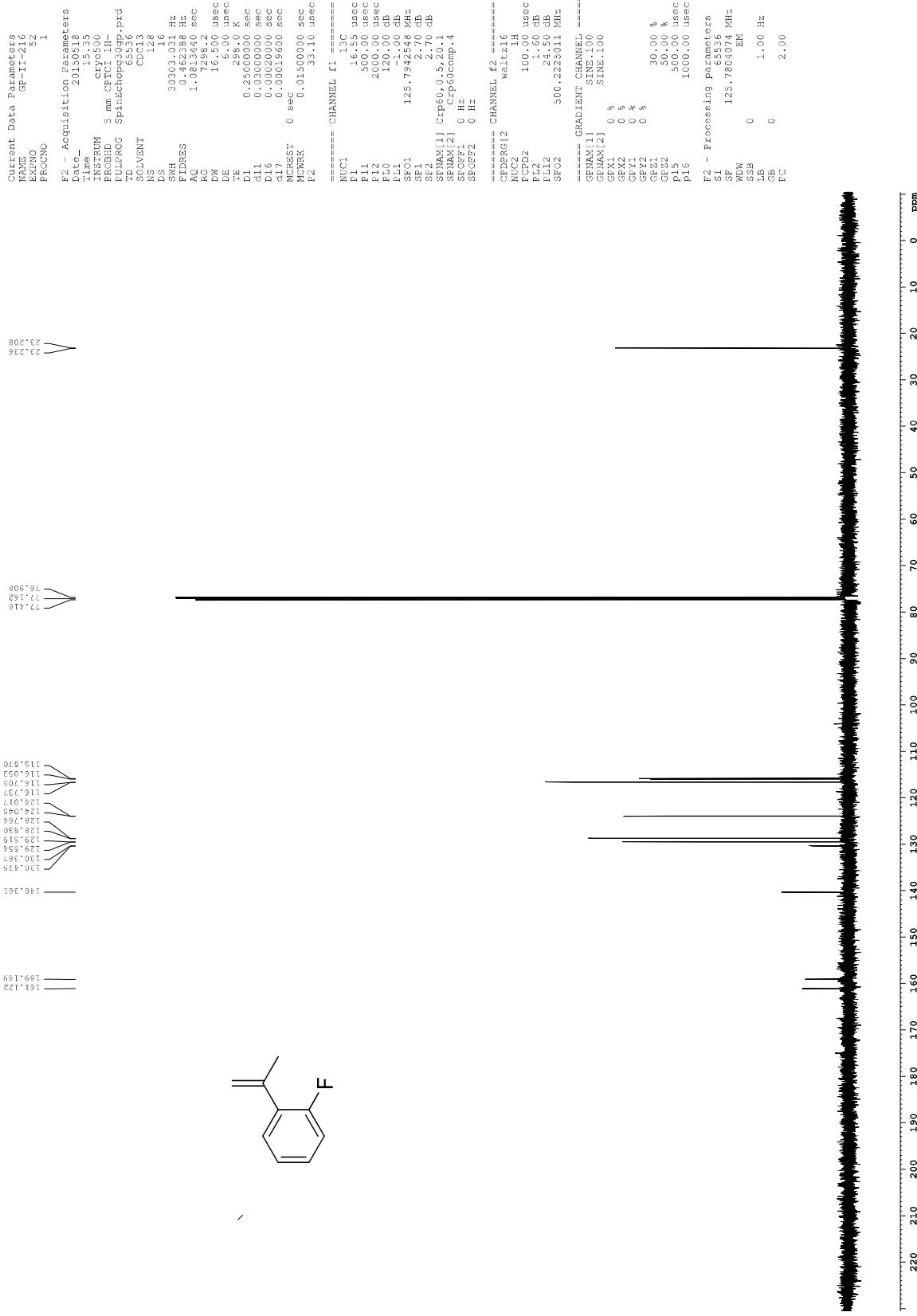


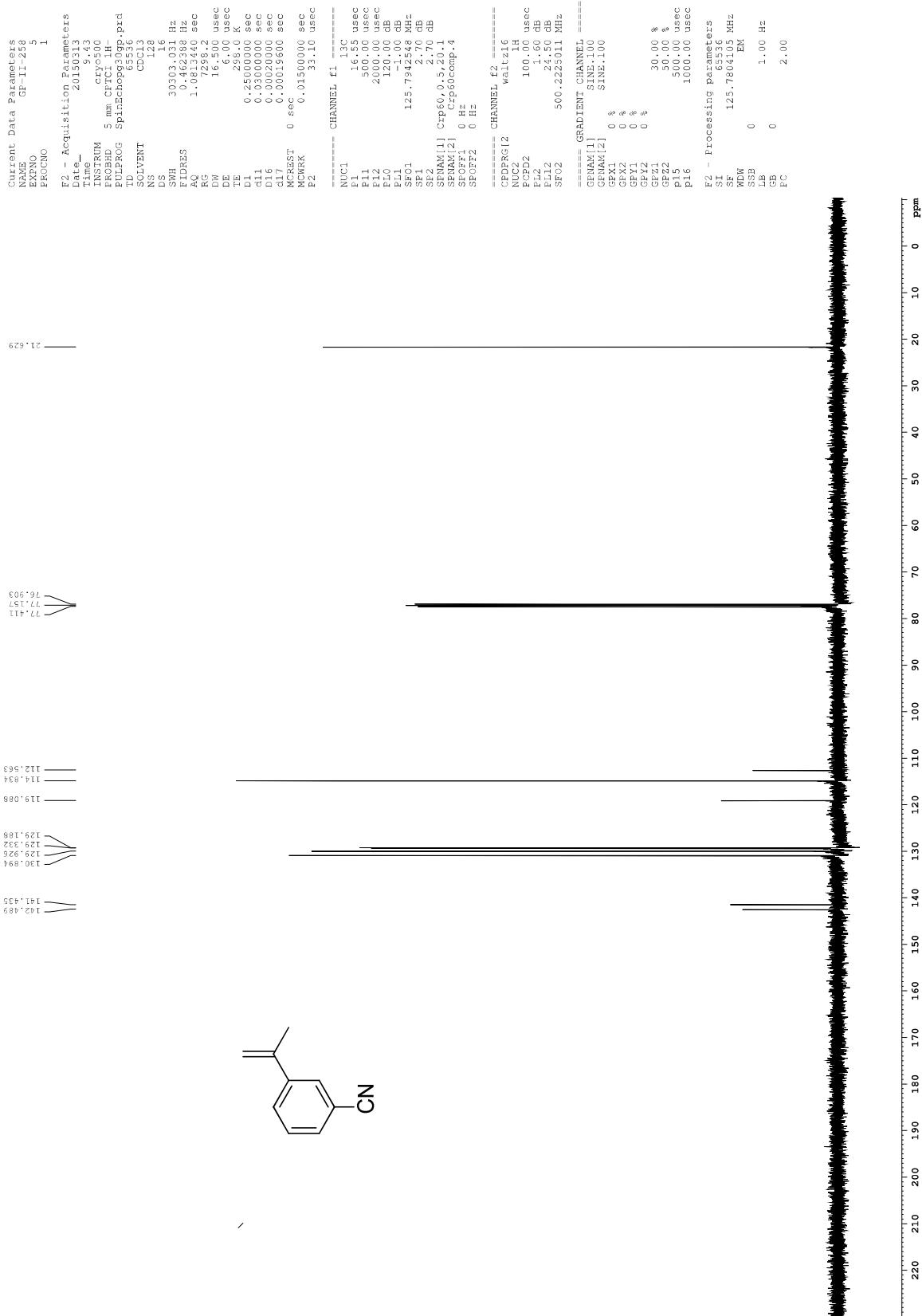


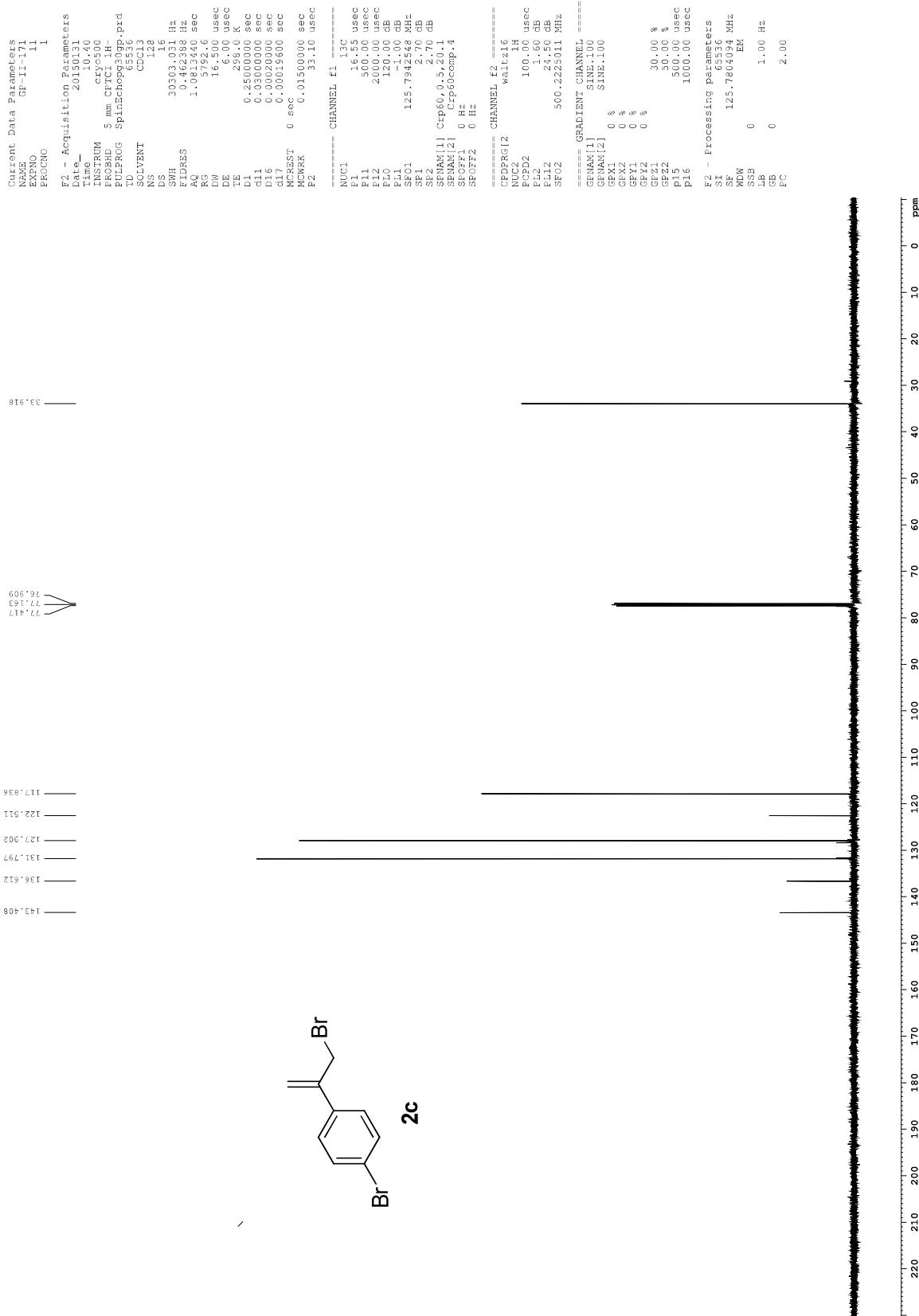


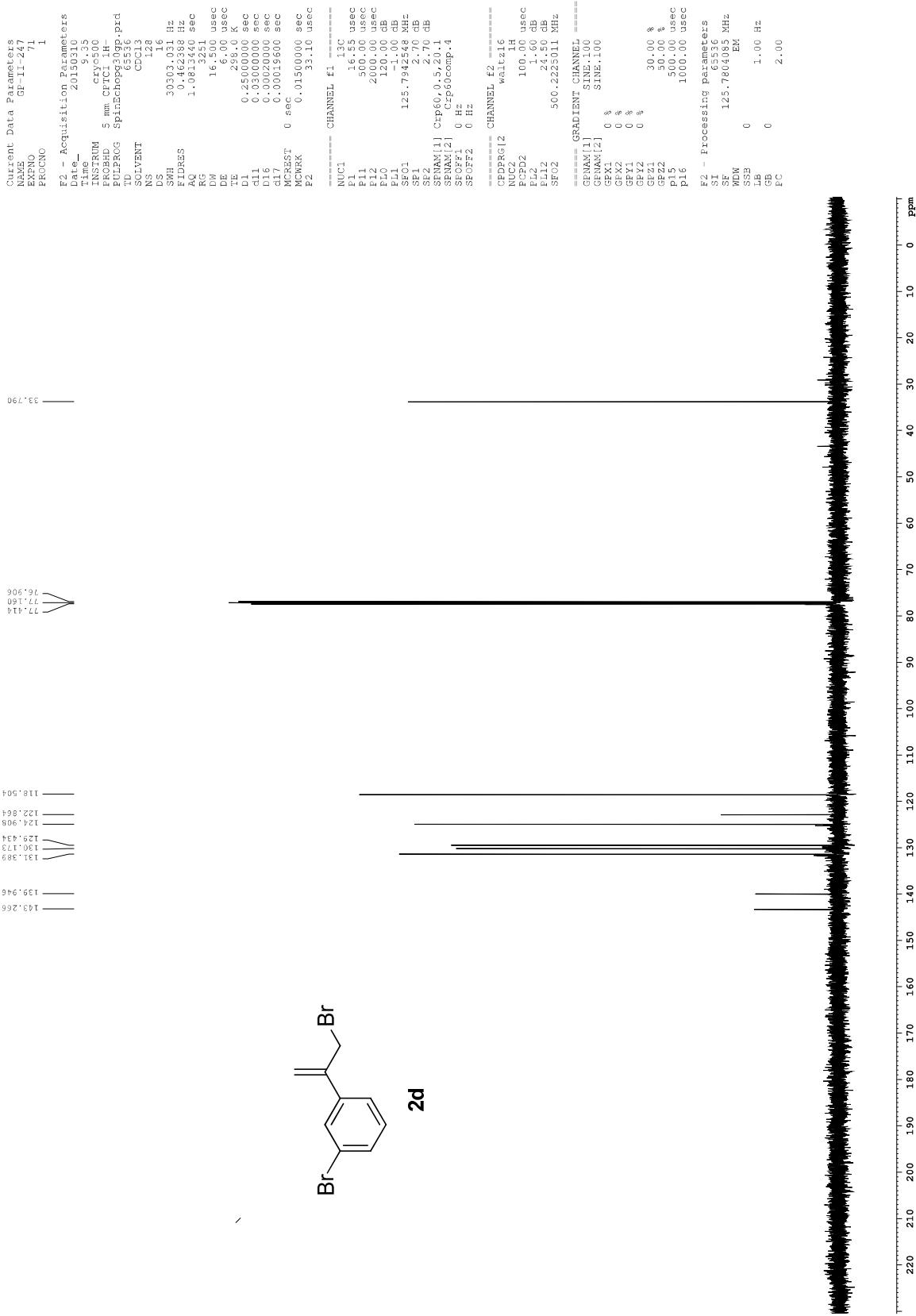


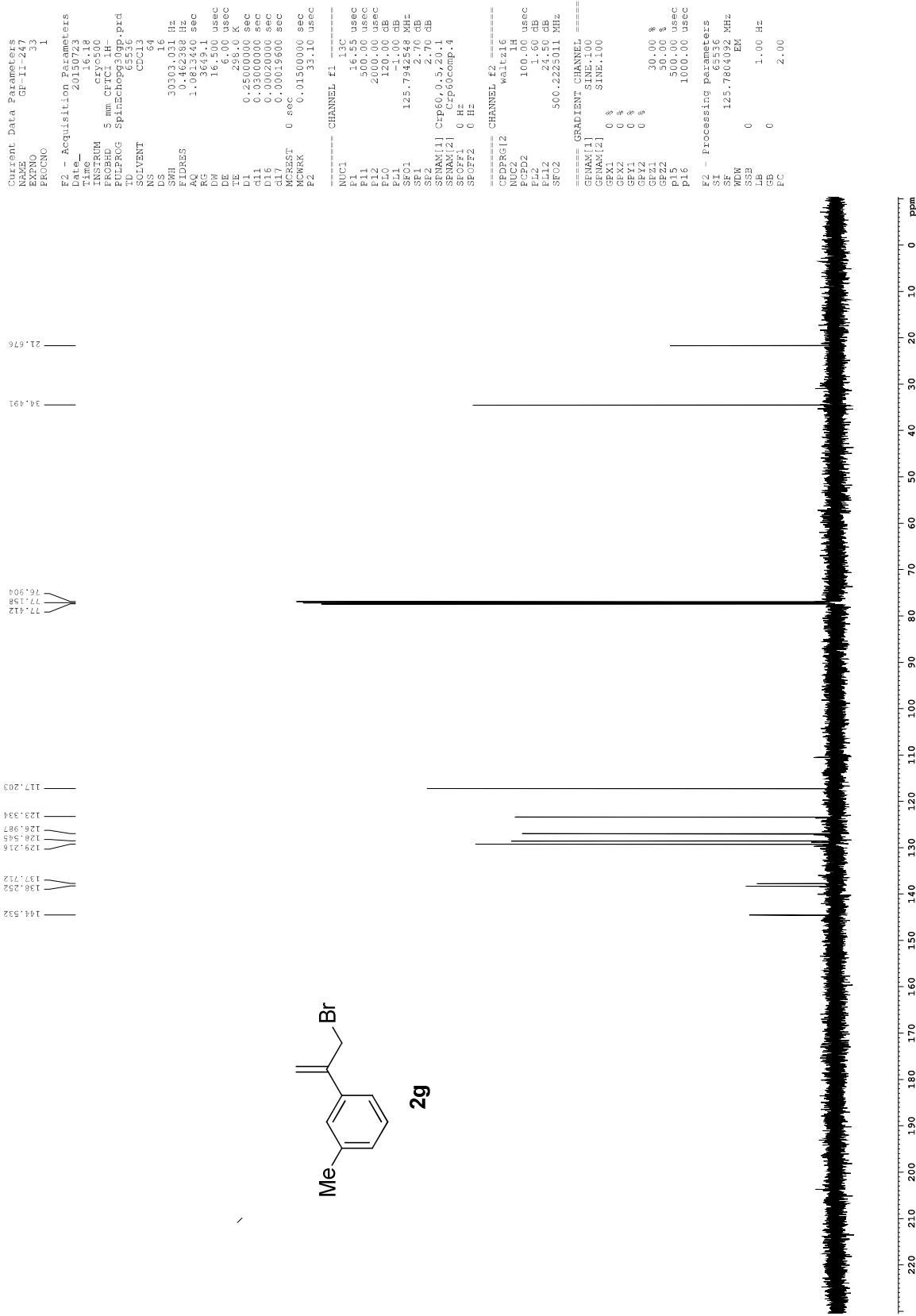
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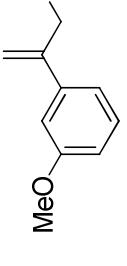
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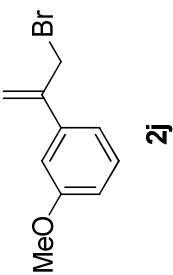
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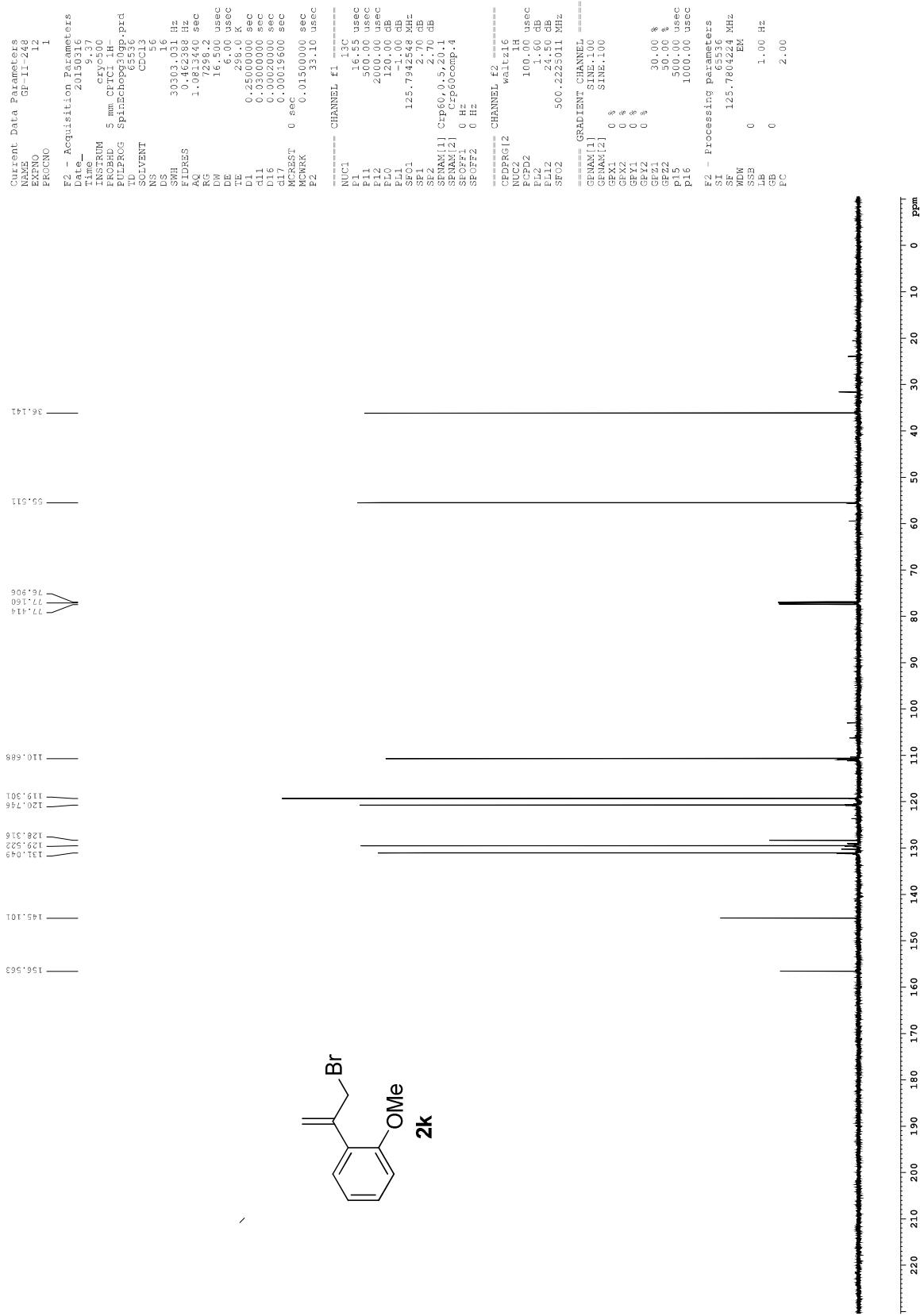
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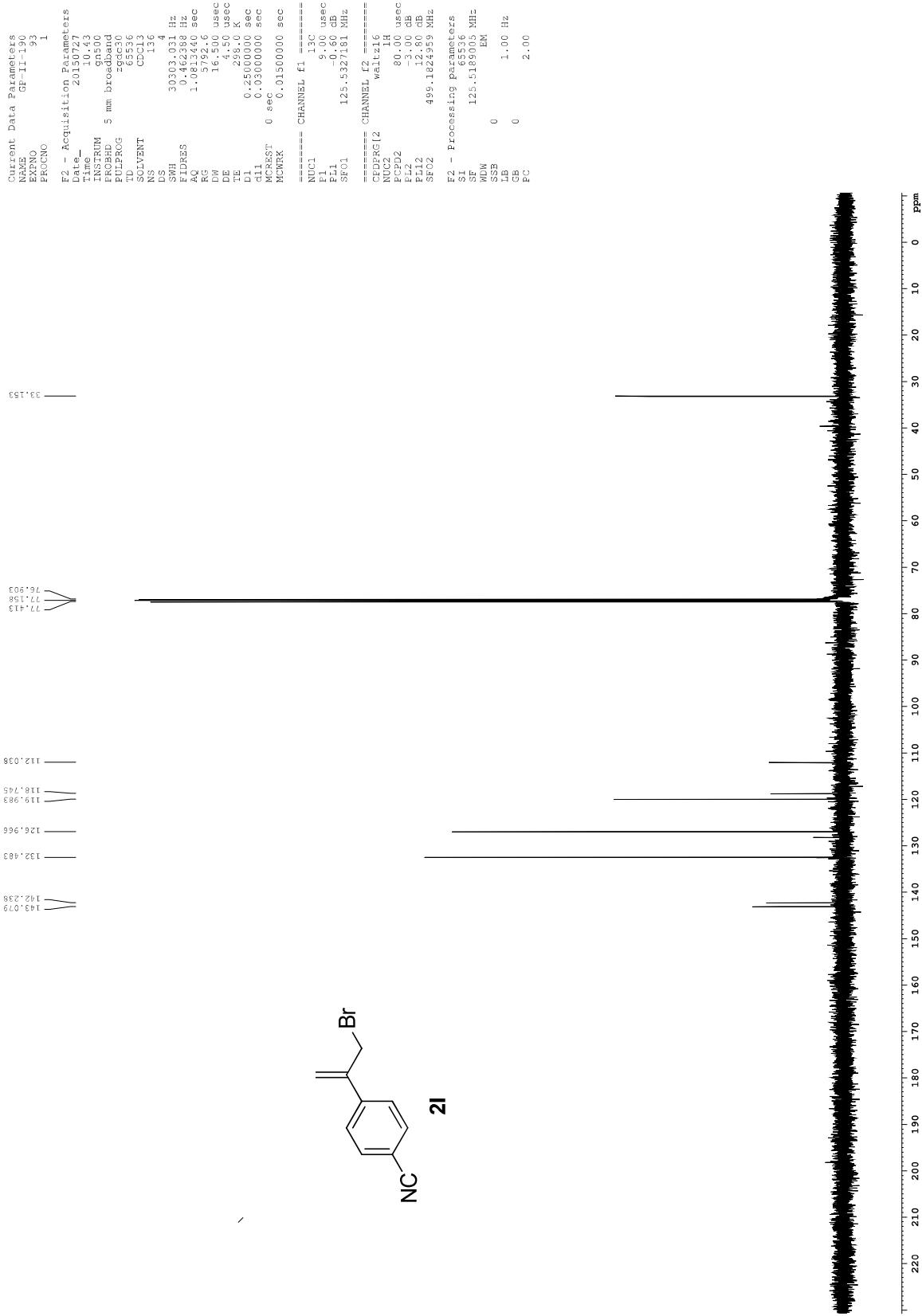
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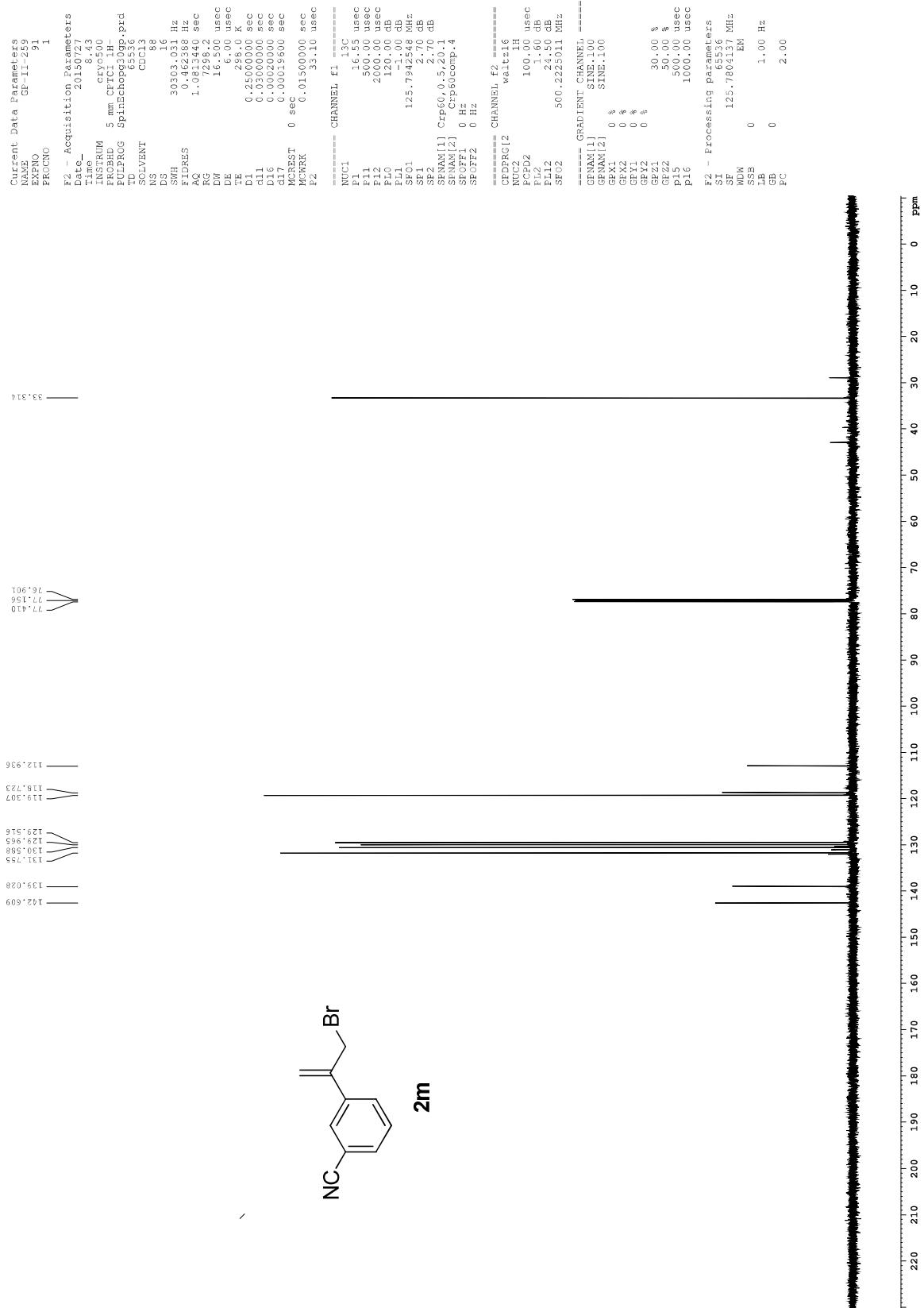
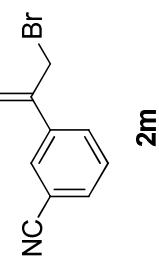
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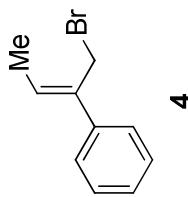


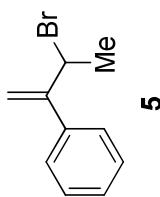
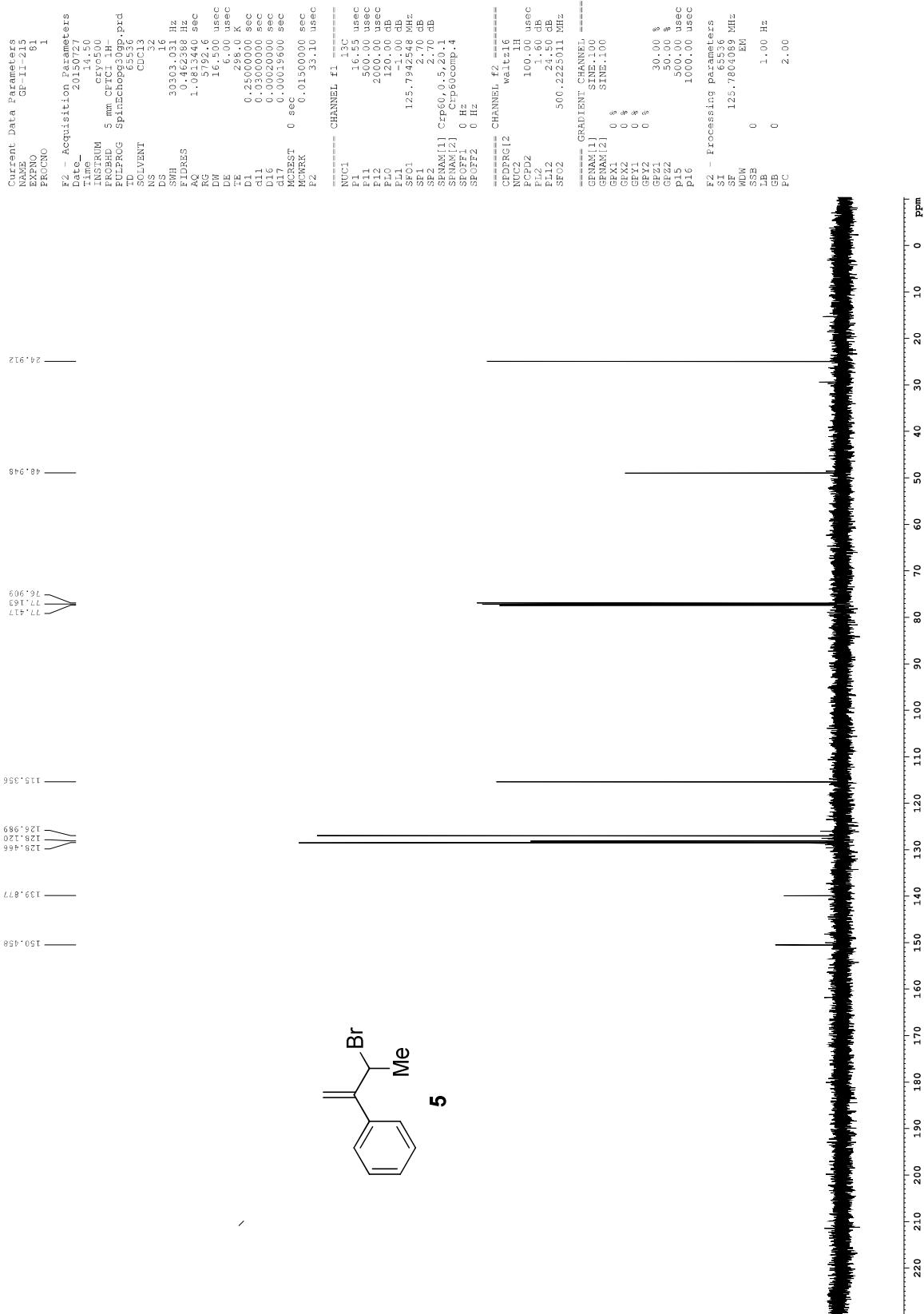


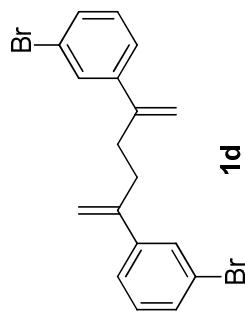


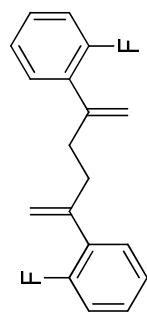






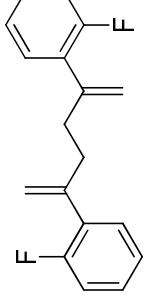




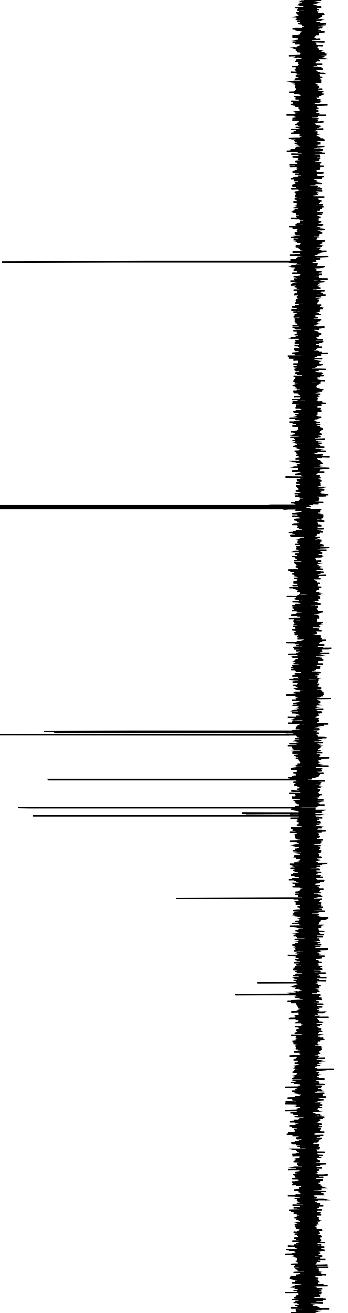


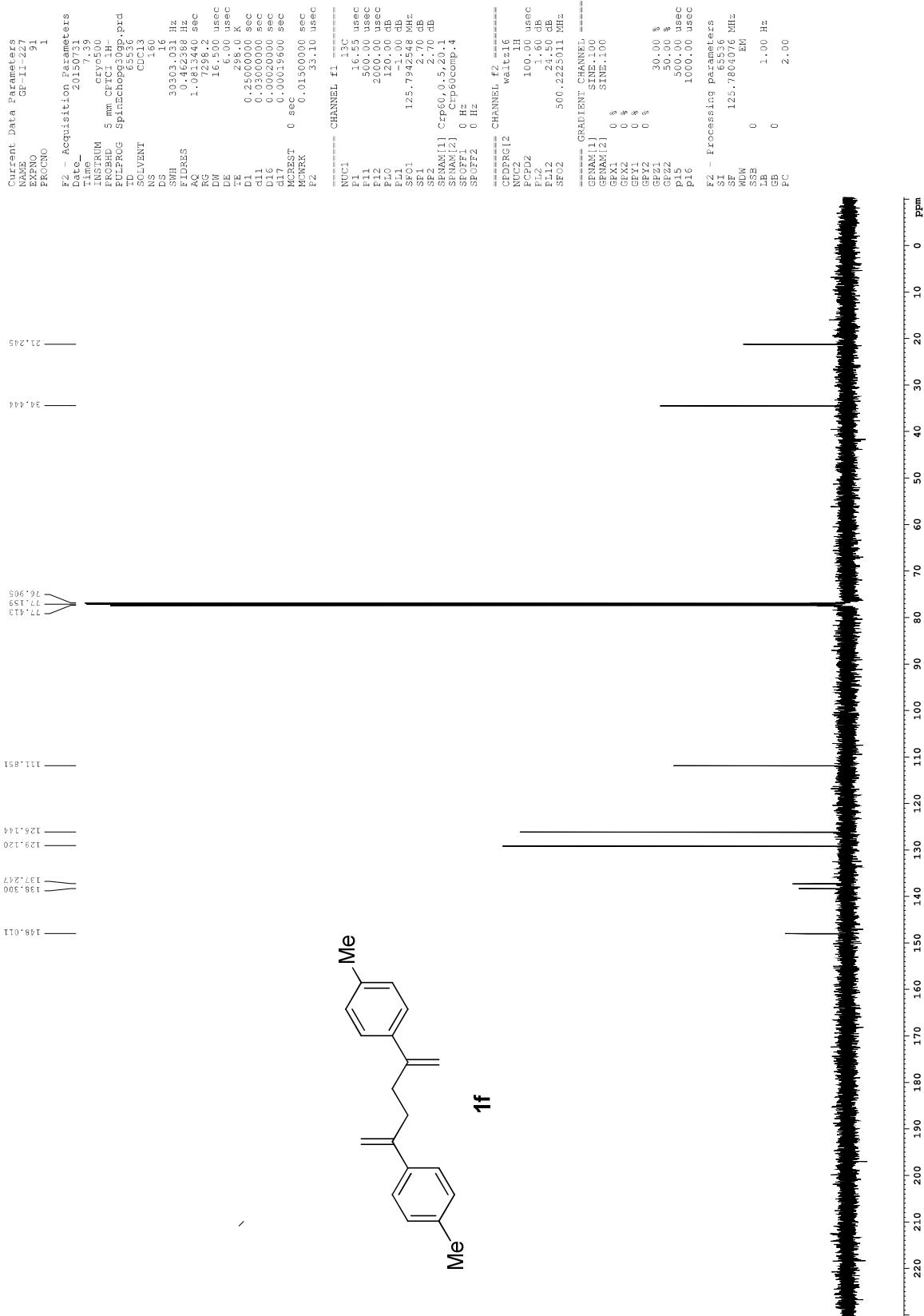
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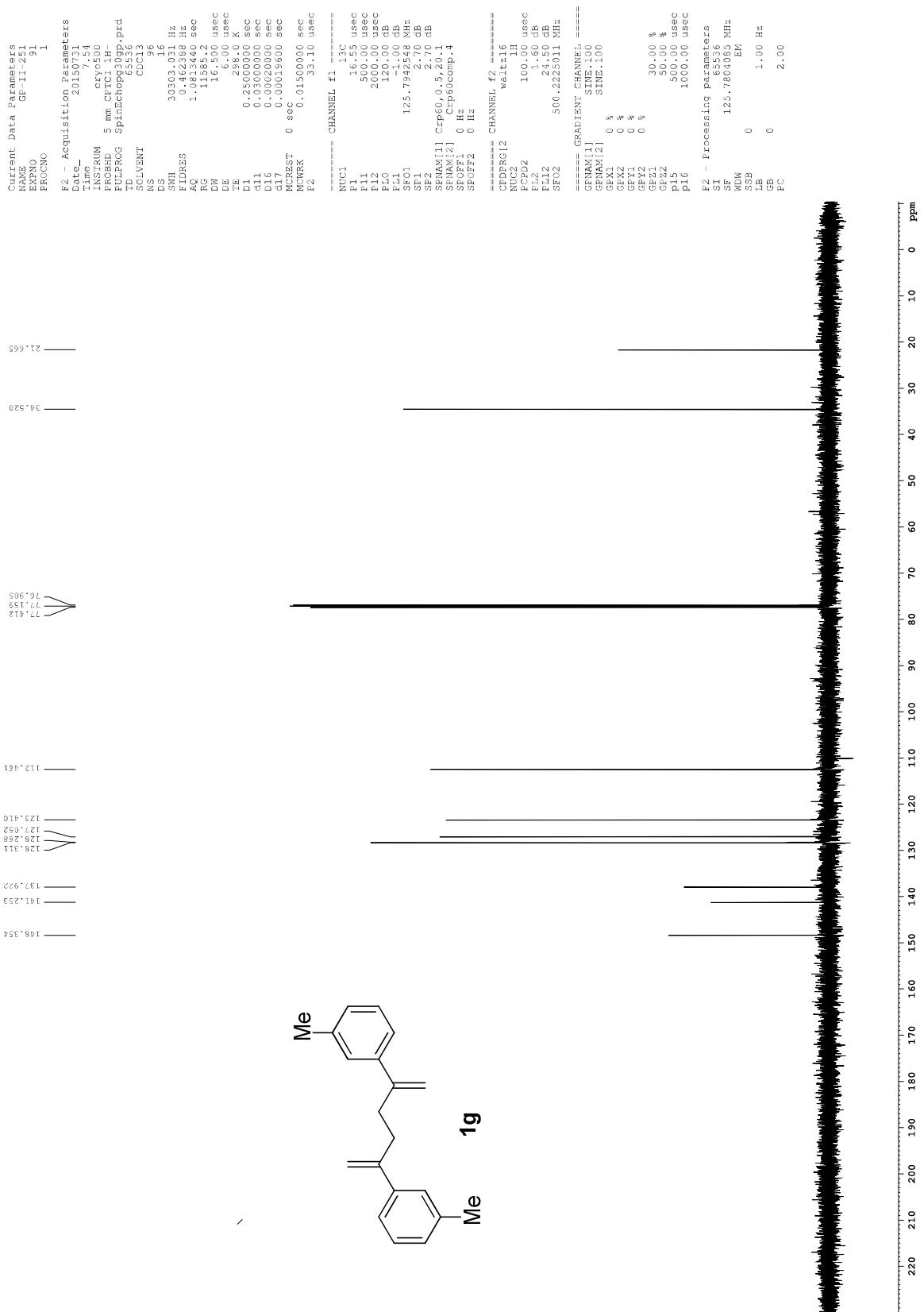
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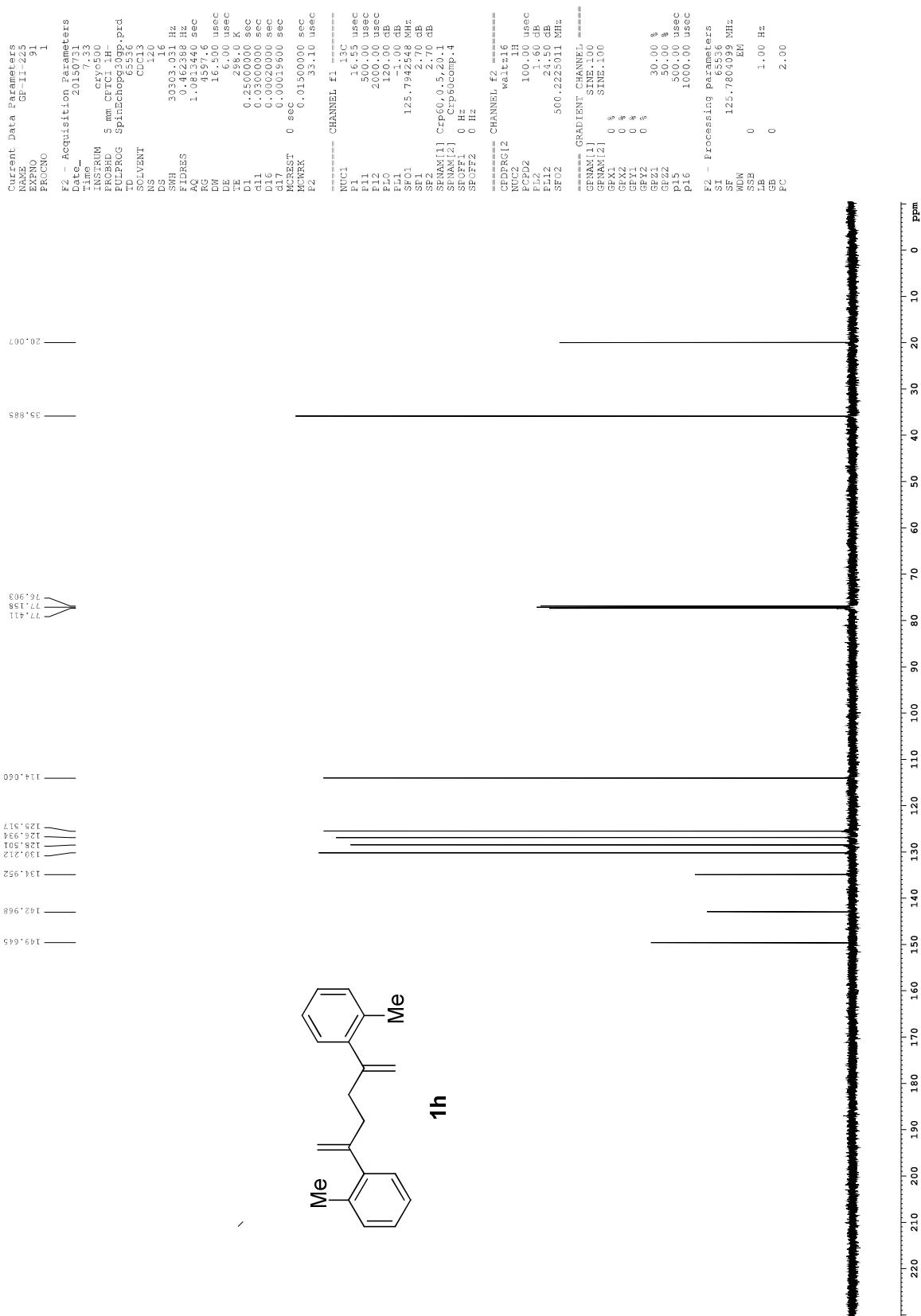


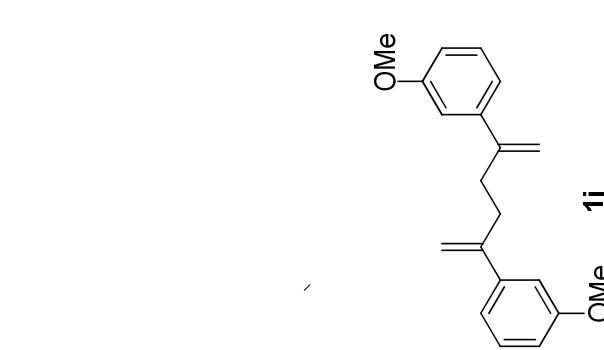
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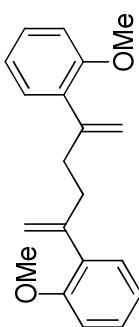




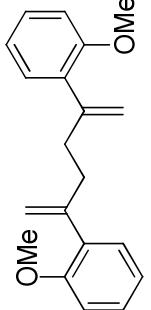


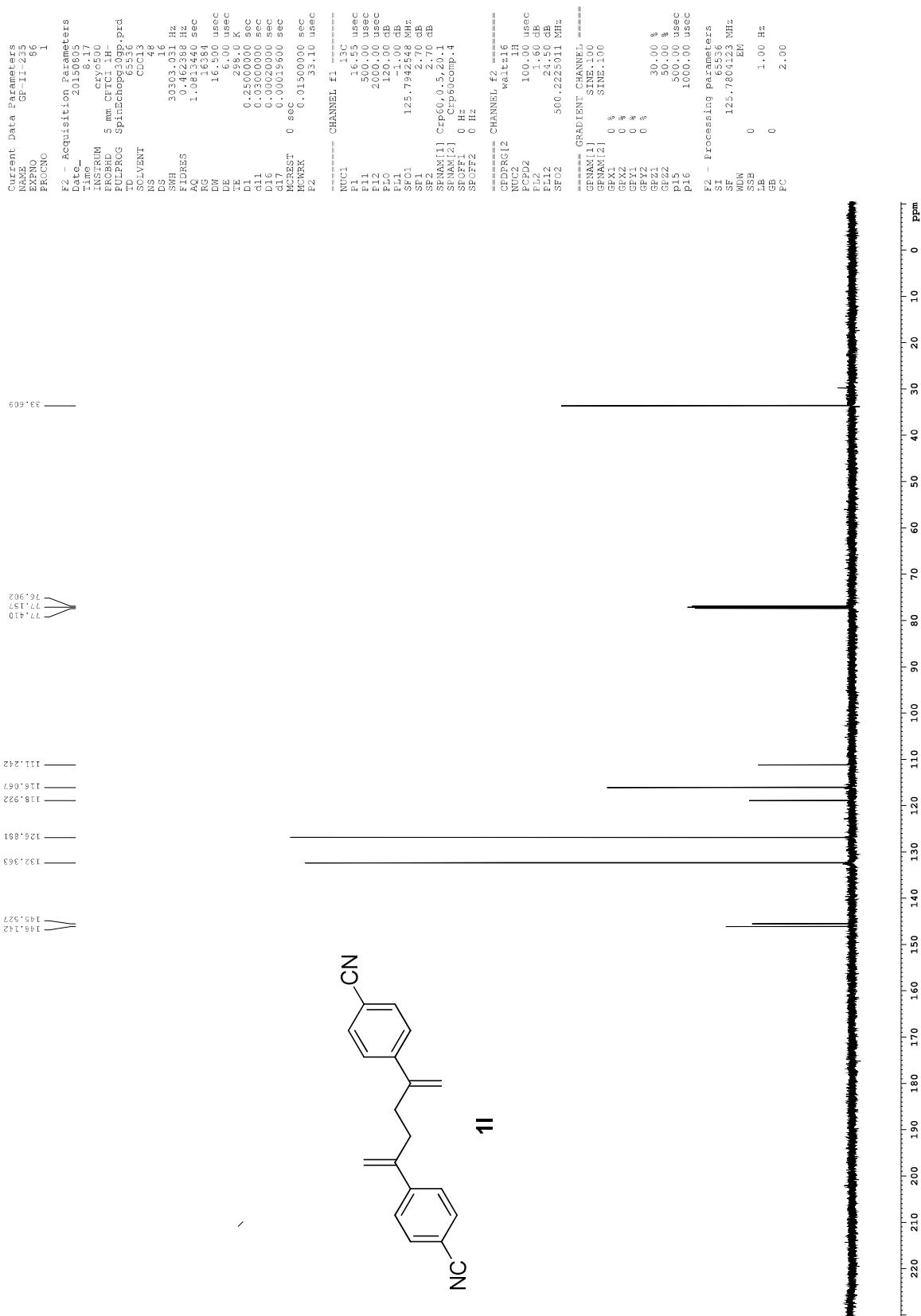


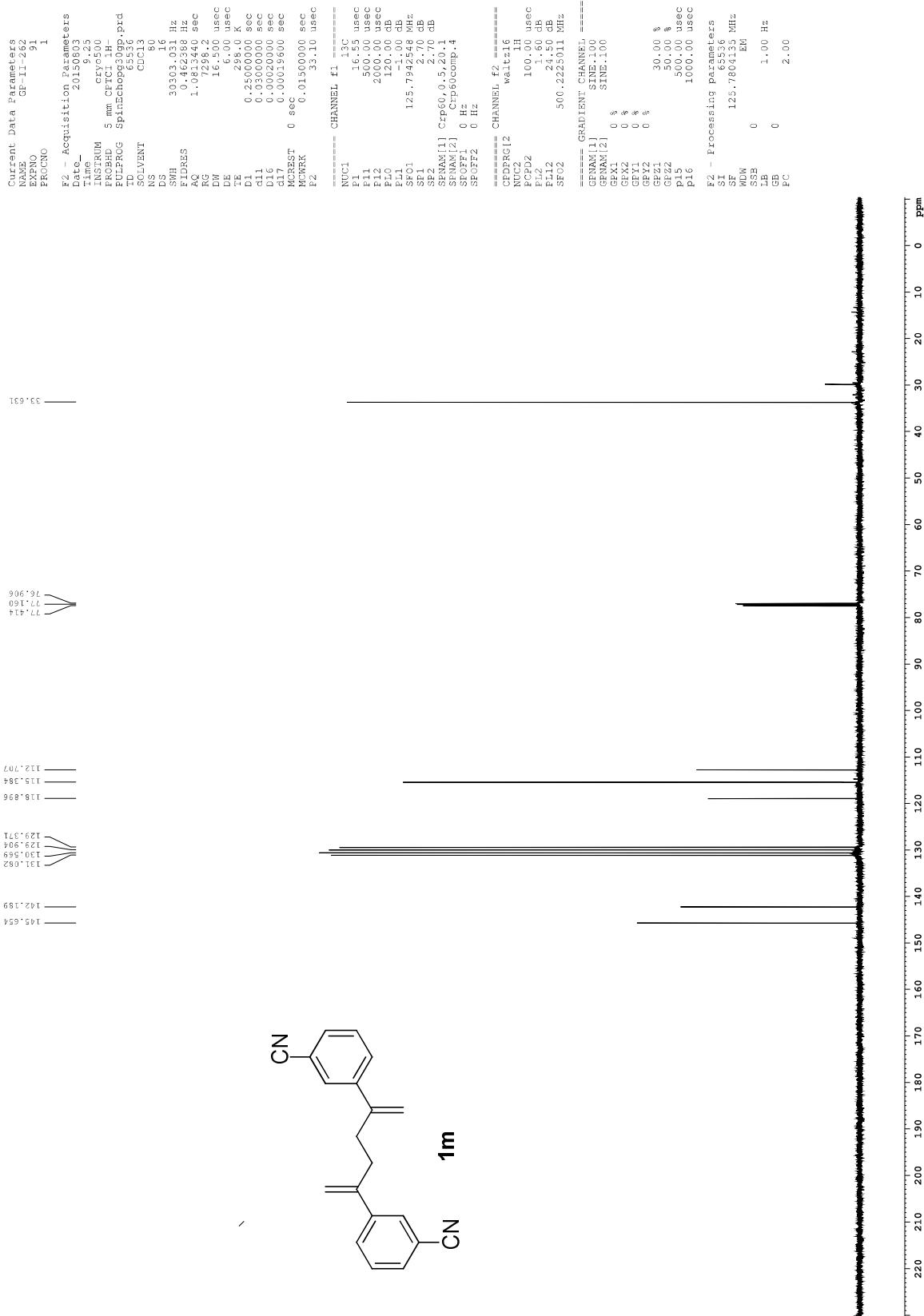


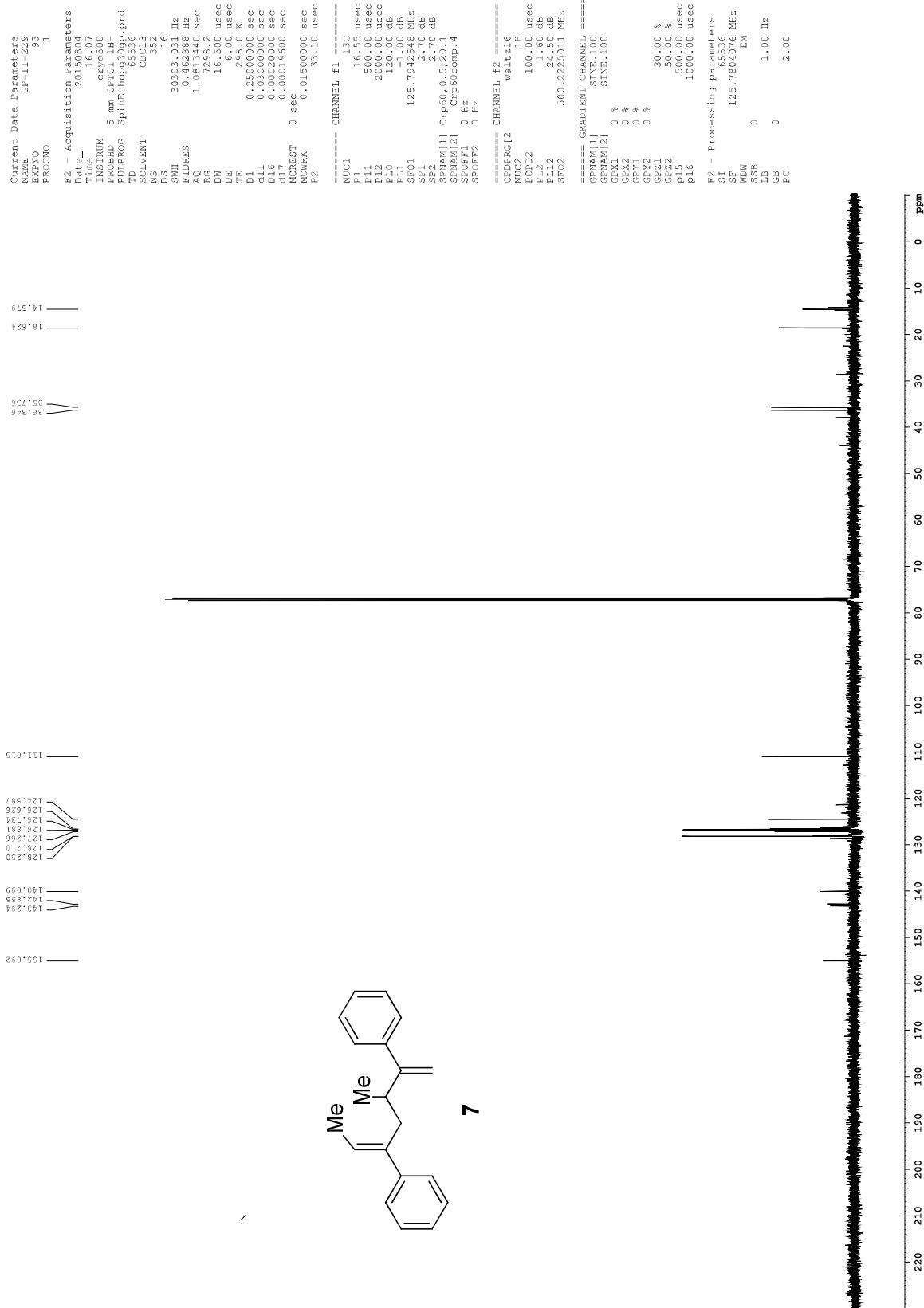


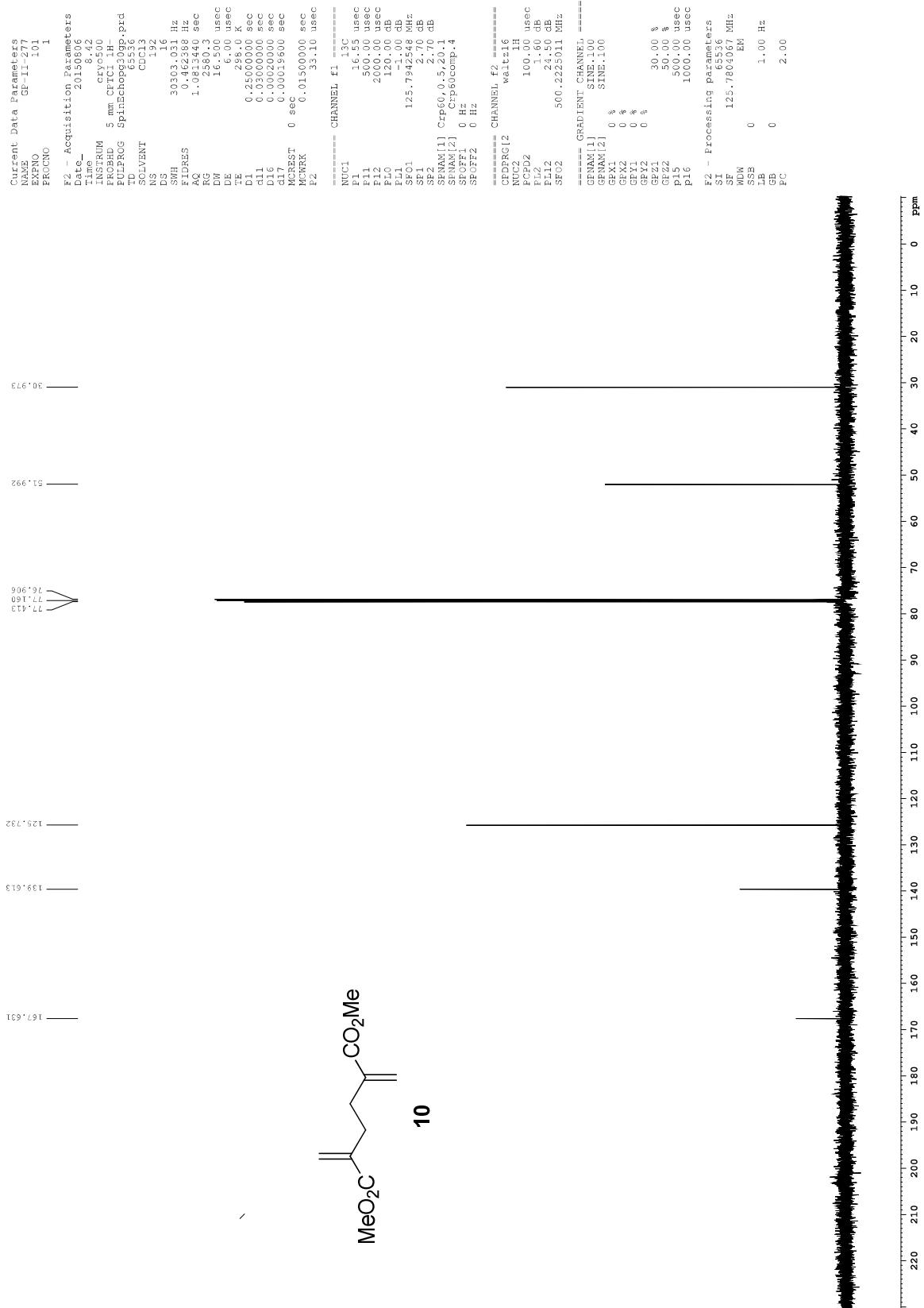
1k

Current Data Parameters
 F2 - Acquisition Parameters
 Date_ 20150803
 Time 08:52
 INSTRUM 5 mm ORCI 1H
 PRBHD Spindchopg10P.prd
 PULPROG 6536
 SOLVENT CIC13
 D1 112
 D1S 30303.00 Hz
 D1Q 1.981440 sec
 F2W 16.500 usc
 F2E 6.00 usc
 F2T 0.250000 sec
 D11 0.0300000 sec
 D16 0.0002000 sec
 Q17 0.0001600 sec
 MCEST 0 sec
 MCERK 0.0150000 sec
 F2 33.10 usc
 ===== CHANNEL f1 =====
 NUC1 F11 16.55 usc
 F11 500.00 usc
 F12 F10 120.00 dB
 F11 125.774548 MHz
 SFO1 SP1 2.70 dB
 SP11 Cpp0.0-0.5,20.1
 SP1M[2] Cpp0comp.4
 SP1FF1 0 Hz
 SP1FF2 0 Hz
 ===== CHANNEL f2 =====
 CPDPRG[2] NUC2 waltz16
 PCP2 100.00 usc
 F112 F112 24.50 dB
 SF12 500.02225011 MHz
 ===== GRADIENT CHANNEL =====
 CPDAM[1] SINE100
 CPDAM[2] SINE100
 GPR1 0 %
 GPR2 0 %
 GPR3 0 %
 GPR4 0 %
 GPR5 0 %
 GPR6 0 %
 GPR7 0 %
 GPR8 0 %
 GPR9 0 %
 GPR10 0 %
 GPR11 0 %
 GPR12 0 %
 GPR13 0 %
 GPR14 0 %
 GPR15 50.00 usc
 F116 1000.00 usc
 F2 - Processing parameters
 SI 6536
 SF 125.780005 MHz
 WDW EN
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 2.00
 35.474
 55.474
 77.147
 76.969
 110.659
 114.233
 120.522
 128.580
 130.387
 132.222
 146.923
 156.643


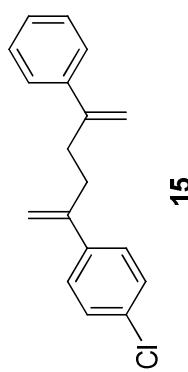








Current Data Parameters
 RF1 11.245
 RF2 9.66
 F2NUC 1
 F2PROB 1
 F2ACQNO 1
 F2 - Acquisition Parameters
 Date 20150605
 Time 08:24
 INSTRUM cry500
 PROBHD 5 mm QFTCI 1H
 PULPROG SpinEchopp10p.prd
 TD 65536
 SW1 CUC13
 SOLVENT NS
 D1 160
 SWH 20303.0381 Hz
 FIDRES 0.461389 Hz
 AQ 1.081440 sec
 RG 16.500 usc
 DW 16.500 usc
 DE 0.500 usc
 E1 0.250000 usc
 E11 0.0500000 sec
 E12 0.0002000 sec
 MC17 0 sec
 MCEST 0 sec
 MCTRK 0.0150000 sec
 F2 33.10 usc
 ===== CHANNEL f1 =====
 NUC1 13C
 F11 16.5 usc
 F12 500.00 usc
 F10 2000.00 usc
 FLL1 120.00 dB
 SP01 123.794548 MHz
 SP1 2.70 dB
 SP2 2.70 dB
 SPFW1[1] CPMG 0.5,0.1
 SPFW1[2] CPMG 0.5,0.1
 SPFW2 0 Hz
 SPJF2 0 Hz
 ===== CHANNEL f2 =====
 CEPFR12 wall16
 NUC2 1H
 FC1D 100.00 usc
 FLL2 1.60 dB
 SF12 500.222.011 MHz
 ===== GRADIENT CHANNEL =====
 GPRAM1[1] SINE,100
 GPRAM1[2] SINE,100
 CPX1 0 %
 CPX2 0 %
 GRY1 0 %
 GRY2 0 %
 GRZ1 30.00 %
 GRZ2 50.00 %
 F115 500.00 usc
 F116 1000.00 usc
 F2 - Processing Parameters
 ST 165536
 SF 125.780000 MHz
 WDW 0
 SS2 0
 LB 1.00 Hz
 PC 0
 2.00



5

References.

¹ For an example of heating the substrate with NBS in chlorobenzene without a radical initiator, see:

Vaccher, B.; Flouquet, D. *Synth Commun.* **1993**, *23*, 671–679.

² For an example of heating the substrate with NBS in carbon tetrachloride in the presence of dibenzoyl peroxide, see: Baird, L. J.; Timmer, M. S. M.; Teesdale-Spittle, P. H.; Harvey, J. E. *J. Org. Chem.* **2009**, *74*, 2271–2277.

³ Tripathi, C. B.; Mukherjee, S. *Angew. Chem., Int. Ed.* **2013**, *52*, 8450–8453. For the original publication of the herein described procedure for allylic bromination of α -methylstyrene derivatives, see: Harrison, C. R. *US Patent No. 5474998 (1995)*.

⁴ Yamanaka, M.; Arisawa, M.; Nishida, A.; Nakagawa, M. *Tetrahedron Lett.* **2002**, *43*, 2403–2406.

⁵ The yield of product formation is dependent on the combination of substituents on the aromatic core and the amount of $\text{Yb}(\text{OTf})_3$ (0.1-10 mol%) added to the reaction mixture. The optimized conditions for all substrates depicted in Scheme 1 (Article) are summarized in the Experimental Section.