UNIVERSITY OF CALIFORNIA,
IRVINE

Dual Catalytic Systems with Gold(I)

THESIS

submitted in partial satisfaction of the requirements
for the degree of

MASTER OF SCIENCE

in Chemistry

by

Joel Johnson

Thesis Committee:
Professor Chris D. Vanderwal, Chair
Professor Suzanne A. Blum
Professor Vy M. Dong

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Acknowledgments

There have been a number of people who have influenced my career choices and my decision to become a research scientist and I believe it is worth giving thanks to them here.

Prof. Peter Beak, my organic chemistry I co-professor. Because of you, I adopted the mindset of thinking of reactions in terms of their mechanisms instead of the reagents needed to facilitate the reaction. I honestly think that because of this, I was able to develop a good understanding of organic chemistry fairly quickly.

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Abstract Of Thesis

Dual Catalytic Systems with Gold(I)

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Joel Johnson

Master of Science in Chemistry

University of California, Irvine, 2015

Professor Chris D. Vanderwal, Chair

Chapter 1. Described herein is a study on the functional group tolerance of the gold/palladium dual catalyzed synthesis of 4-allylisocoumarins. A number of motifs commonly found in compounds with biological activity and intermediates towards such compounds were prepared and tested. The effect of silver on the product distribution was determined.

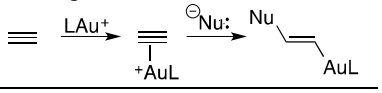
Chapter 2. A kinetic study of the alkoxyboration reaction showed the reaction is second order overall: first order with respect to both IPrAuTFA and NaTFA. NaTFA was determined to be both a Lewis base, by enhancing the nucleophilicity the B–O σ bond, and as a reagent needed to decrease the amount of IPrAuTFA converted to the catalytically inactive IPrAuCl. Increasing the amount of trifluoroacetate eventually lead to a decrease in the reaction rate. This effect is attributed to over addition of the Lewis base into the borate ester that is formed after the cyclization step. The rate-determining step was determined to be the transmetalation step.

Introduction

This introduction will present to those without an in depth knowledge of the chemical theory the information needed to understand the subsequent chapters. The subsequent chapters discuss a specific type of catalysis called *dual catalysis*, but first, a discussion of catalysis should occur. Catalysis is the field of study revolving around the development of reactions that use a reagent called a catalyst to increase the rate of the reaction. Catalysts work by either providing an alternative, lower energy pathway for a reaction to traverse or by lowering the activation energy of the rate-determining step of the reaction. The activation energy is inversely proportional to the rate of the reaction. Reactions with lower activation energies have faster rates. As the name suggests, dual catalysis involves a chemical transformation that is catalyzed by two catalysts. The advantage of a dual catalytic system is that otherwise impossible transformations and pathways become viable using this type of catalysis.

The dual catalytic system that is the main focus of research in the Blum group is one where gold(I) is one component of the dual catalytic system. Gold complexes are known to be carbophilic π acids, meaning electron density can be withdrawn from a π system, enabling them to accept electron density from a nucleophile. The gold catalyst can be regenerated in a number of ways, including transmetalation with another metal or acting as a nucleophile towards an electrophile. We seek to discover and develop these types of reactions.

Figure 0.1 Gold(I) catalyzed nucleophilic addition.



In addition to discovering new reactions, understanding the mechanistic underpinnings of how these reactions work is equally important. This is done by first forming a mechanistic hypothesis based on literature precedent and a thorough understanding of the principles that govern chemical reactions pathways. Determining both what reagents affect the rate and reaction intermediates are two ways in which one can aid in the determination of the true mechanism.

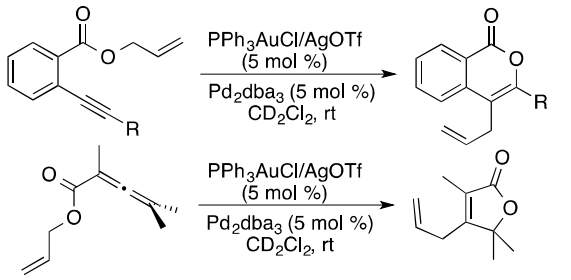
Chapter 1

Functional Group Tolerance and Silver Effect of Gold/Palladium Catalyzed Synthesis of 4-allylisocoumarins

Abstract: Described herein is a study on the functional group tolerance of the gold/palladium dual catalyzed synthesis of 4-allylisocoumarins. A number of motifs commonly found in compounds with biological activity and intermediates towards such compounds were prepared and tested. The effect of silver on the product distribution was determined.

INTRODUCTION

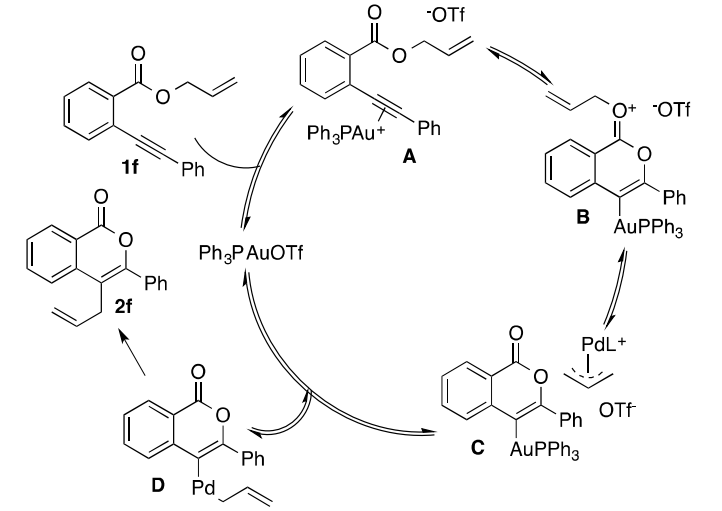
Figure 1.1 Work from Blum et al.



Dual metal catalyzed reactions can facilitate transformations that could not be reproduced otherwise.[1] The advantages of dual metal catalytic systems are usually counterbalanced by undesired redox chemistry, ligand exchange, and functional group incompatibility.[2] In 2009, Blum and coworkers reported the gold/palladium dual catalyzed cyclization of allyl allenoates and benzoates to form 4-allyl butenolides and isocoumarins respectively (Figure 1.1).[3] Figure 1.2 shows a plausible mechanism for the gold/palladium dual catalyzed cyclo-isomerization reaction.

Many of the intermediates in the putative mechanism can traverse alternative pathways, leading to the formation of side products. The organogold intermediates **B** and **C** can act as nucleophiles as opposed to participating in transmetalation with the palladium π allyl intermediate. This is the manner in which gold catalysts are typically regenerated, where the electrophile is a proton.[4] Intermediate **B** also contains an oxocarbenium fragment capable of acting as an electrophilic allylating agent as opposed to acting as the species capable of being oxidatively added into by palladium(0). Palladium π-allyl intermediates have also been reported to act as electrophiles, such as in the

Figure 1.2 Plausible mechanism of the reaction.

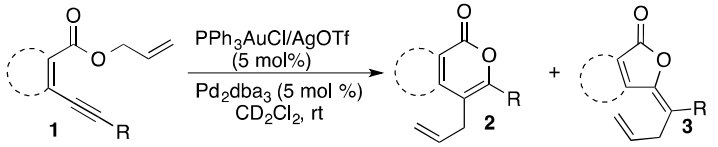


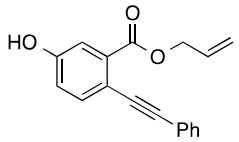
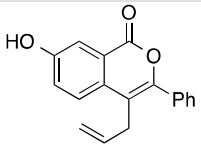
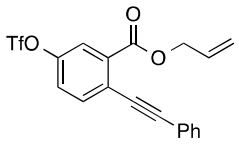
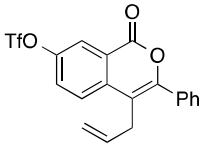
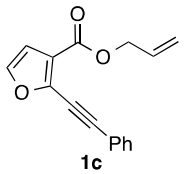
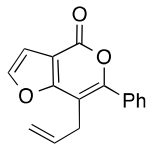
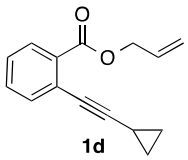
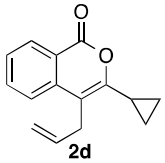
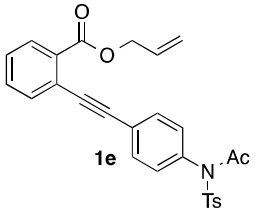
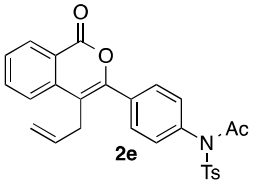
Tsuji-Trost reaction.[5]

In the seminal publication, no appreciable functional group tolerance study was conducted, however, it was reported that aryl bromides were tolerated by the reaction conditions. The following report shows a subset of the functional groups tolerated, a downstream functionalization reaction, along with the effect silver(I) has on the product distribution.

RESULTS AND DISCUSSION

Table 1.1 Gold and palladium dual-catalyzed synthesis of lactones 2a-2e[a].



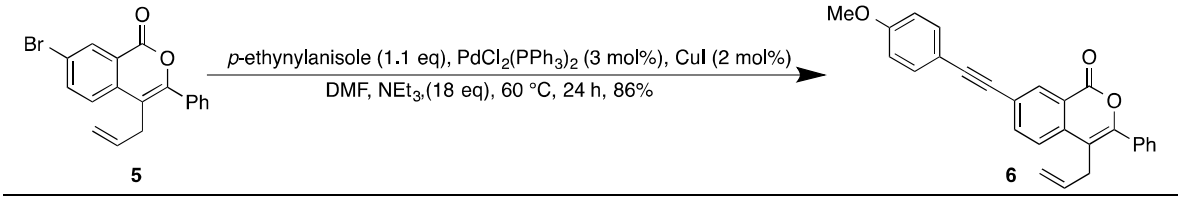
Entry	Starting Material	Product	Isolated Yield (%)	2:3[e]
1[b]	 1a	 2a	24	11:1
2[c]	 1b	 2b	33	10:1
3[d]	 1c	 2c	83	Only 2
4	 1d	 2d	71	12:1
5[b]	 1e	 2e	50	16:1

[a]Unless otherwise noted, reaction conditions: substrate **1** (1.0 equiv), PPh_3AuCl (5 mol%), AgOTf (5 mol%), and Pd_2dba_3 (5 mol%) in dry CD_2Cl_2 (0.1 M substrate) were stirred at ambient temperature. [b]Reaction was carried out at 60 °C in DCE-d_4. [c]Reaction was carried out at 40 °C in CD_2Cl_2. [d]Reaction was carried out at 50 °C in DCE-d_4. [e]The ratio was determined via analysis of the crude ^1H NMR spectrum.

The results from the functional group tolerance study are shown in Table 1.1. As stated in the previous section, each substrate has a functional group capable of undergoing an undesired chemical reaction with one of the catalysts or putative intermediates in the catalytic cycle (Figure 1.2). Substrates **1a**, **1c**, and **1e** all contain Lewis basic atoms capable of ligating to the cationic gold catalyst, which could lead to rate retardation or complete inhibition of product formation under nominal conditions. Notably, in order for the reaction to proceed at a viable rate using these substrates, higher temperatures were necessary. Also note that substrate **1a** can act as a proton source, which could lead to the protodeauration of intermediates **B** or **C**. The protodeaurated product was isolated in 10% yield. No allyl ethers were detected, suggesting that the phenol may not have acted as a nucleophile towards one of the electrophilic allyl species. The reaction with **1d**, which contains a propargylic cyclopropyl group capable of rearrangement under acidic conditions, proceeded at ambient temperature, affording the product in 71% yield.[6] Substrate **1b** contains an electrophilic cross coupling partner capable of undergoing oxidative addition with palladium(0). The reaction temperature using this substrate needed to be increased to 40 °C. The temperature increase may have been necessitated by the reversible oxidative addition removing the active palladium catalyst from the reaction mixture or due to the formation of palladium black. One potential selling point of this substrate is that it is an electrophilic cross coupling partner, which creates the opportunity for downstream functionalization.

As proof of concept, downstream functionalization reactions were conducted. Starting with the compound **5**, a Sonogashira Coupling with *p*-ethynylanisole produced the product, **6,** in 86% yield (Figure 1.3).

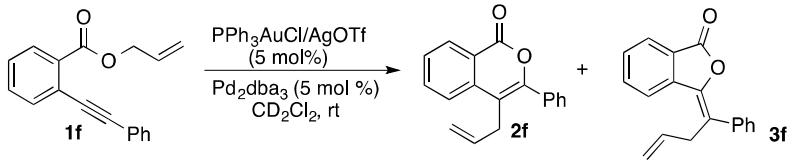
Figure 1.3 Down stream functionalization reaction.



A paper published by Shi and coworkers detailed the role silver(I) can play in gold catalysis.[7] The effect of silver on the reaction was determined (Table 1.2). It seems the product distribution is dependent on the silver content in the reaction medium.

In summary, a number of motifs are tolerated by the reaction conditions, including: Lewis basic atoms, electrophilic cross coupling partners, and motifs known to rearrange under acidic conditions, albeit, a small

Table 1.2 Effect of silver on the reaction.



Entry	Conditions[a]	^{1}H NMR yield (%)[b]	Product ratio 2:3
1	Ag(I) filtered[c]	96	8:1–16:1
2	Ag(I) unfiltered	98	8:1–>20:1
3	AgOTf only[d]	20	>20:1

[a]PPh_3AuCl (5 mol %), AgOTf (5 mol %), and Pd_2dba_3 (5 mol %) in CD_2Cl_2 at rt. [b]^{1}H NMR spectroscopy yield was determined after 24 h based on the ratio of product to mesitylene (the internal standard). [c]AgCl and AgOTf were removed via filtration through Celite or glass fiber paper. [d]In the absence of PPh_3AuCl.

modification in temperature was needed in order for the reaction to proceed at a viable rate in a number of cases. The tolerance of some functional groups can allow for down stream functionalization. Silver(I) also seems to have an effect on the product distribution of the reaction.

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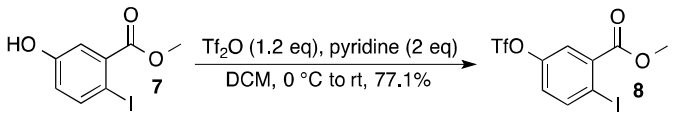
5.) I. Ibrahem; A. Córdova *Angew. Chem. Int. Ed.* **2006**, *45*, 1952 – 1956.
6.) Olah, G. A.; Reddy, V. P.; Prakash, G. K. S. *Chem. Rev.* **1992**, *92*, 69 – 95.
7.) Wang, D.; Cai, R.; Sharma, S.; Jirak, J.; Thummanapeli, S. K.; Akhmedov, N. G.; Zhang, H.; Liu, X.; Petersen, J. L.; Shi, X. *J. Am. Chem. Soc*. **2012**, *134*, 9012 − 9019.

EXPERIEMNTAL SECTION

General Procedure for transesterification:
To a flame dried round bottom flask equipped with a stir bar and activated four angstrom molecular sieves, allyl alcohol (10 mmol) was dissolved in dry THF (10 mL). The reaction flask was cooled to –78 °C. *n*-butyllithium (1.6 M, 5 mmol) was added, the mixture was allowed to warm to room temperature. The methyl ester (1 mmol) was then transferred to the reaction flask with minimal amounts of THF. The reaction was allowed to stir over night at room temperature under nitrogen. The reaction was added to water (10 mL) and extracted with dichloromethane (10 mL × 3). The combined organic layers were dried with $MgSO_4$ and concentrated. The compound was purified via chromatography (20% EtOAc in hexanes), unless stated otherwise. Like fractions were combined, concentrated, and dried under high vacuum.

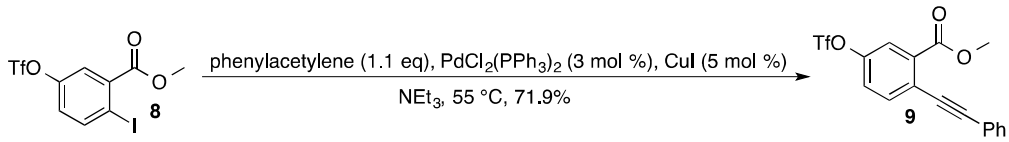
Synthesis of **8**:



Made according to literature precedent.[1] To a flame dried round bottom flask equipped with a stir bar, **7** (0.9653 g, 3.472 mmol, 1.000 equiv) and pyridine (0.56 mL, 6.9 mmol, 2.0 equiv) was dissolved in dry DCM (12 mL) under

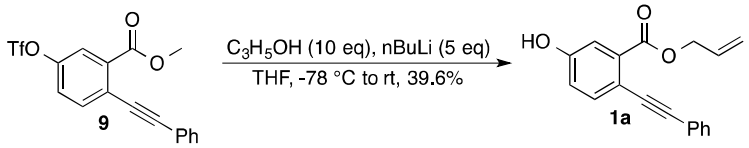
nitrogen. Triflic anhydride (1.0 mL, 4.2 mmol, 1.2 equiv) was added at 0 °C. The mixture was allowed to warm to room temperature and stir for six hours. The reaction mixture was quantitatively transferred to a separatory funnel and washed with saturated NH_4Cl (aq.). The organic layer was dried with $MgSO_4$, which was removed via gravity filtration. The solution was concentrated. The compound was purified by column chromatography (0 to 20% EtOAc in hexanes). The product, **8** (1.0974 g, 77.1%), was isolated in analytically pure form. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.09 (d, J = 8.7, 1H), 7.74 (d, J = 3.0 Hz, 1H), 7.10 (dd, J = 8.7 Hz, 3.0 Hz, 1H), 3.97 (s, 3H); ^{13}C ($CDCl_3$, 125 MHz) δ 165.00, 149.17, 143.34, 136.84, 125.55, 124.13, 118.69 (q, J = 319.1 Hz, 1C), 93.55, 53.11; ^{19}F ($CDCl_3$, 376 MHz) δ -72.6; HRMS *m/z* calcd for $C_9H_{10}O_5F_3ISN$ $(M + NH_4)^+$ 427.9276, found 427.9269.

Synthesis of **9**:



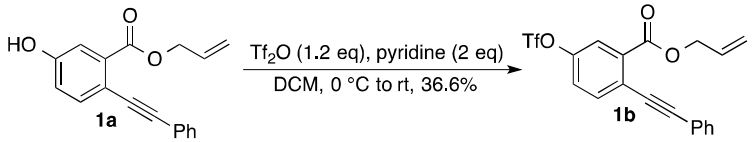
To a 25 mL round bottom flask equipped with a stir bar, **8** (1.0974 g, 2.6759 mmol, 1.0000 equiv), phenylacetylene (0.33 mL, 2.9 mmol, 1.1 equiv), $PdCl_2(PPh_3)_2$ (56.3 mg, 80.3 μmol, 0.03 equiv), CuI (25.4 mg, 80.3 μmol, 0.05 equiv) was dissolved in degassed triethylamine (8.9 mL). The mixture was allowed to stir under nitrogen overnight at 55 °C. The reaction mixture was concentrated under nitrogen and purified by column chromatography (0 to 20% EtOAc in hexanes). The product, **9** (0.7388 g, 71.9%), was isolated. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.90 (d, J = 2.6 Hz, 1H), 7.73 (d, J = 8.6 Hz, 1H), 7.58 (m, 2H), 7.42 (dd, J = 8.6 Hz, 2.7 Hz, 1H), 7.38 (m, 3H), 3.99 (s, 3H); ^{13}C NMR (CD_2Cl_2, 125 MHz) δ 165.32, 148.85, 136.47, 134.62, 132.40, 129.77, 129.19, 125.34, 124.86, 124.12, 123.28, 120.64, 119.27 (t, J = 318.4 Hz), 96.86, 87.14; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -72.7; HRMS *m/z* calcd for $C_{17}H_{11}O_5F_3SNa$ $(M + Na)^+$ 407.0177, found 407.0172.

Synthesis of **1a**:



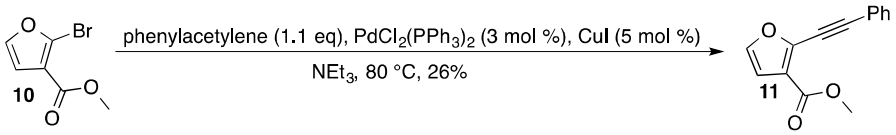
General procedure for transesterification followed. **9** (0.7388 g, 1.922 mmol, 1.000 equiv), allylic alcohol (1.31 mL, 19.2 mmol, 10.0 equiv), *n*-butyllithium (6.0 mL, 9.6 mmol, 5.0 equiv). The product, **1a** (0.2634 g, 39.6%), was isolated in analytically pure form. ^{1}H ($CDCl_3$, 600 MHz) δ 7.59 (m, 3H), 7.52 (d, J = 2.7 Hz, 1H), 7.39 (m, 3H), 7.05 (dd, J = 8.5 Hz, 2.7 Hz, 1H), 6.10 (ddt, J = 17.2 Hz, 10.4 Hz, 5.6 Hz, 1H), 5.49 (app-dq, J = 17.2, 1.4 Hz, 1H), 5.39 (s, 1H), 5.3230 (app-dq, J = 10.4 Hz, 1.4 Hz, 1H), 4.92 (app-dt, J = 5.6 Hz, 1.4 Hz, 2H); ^{13}C ($CDCl_3$, 125 MHz) δ 167.4, 155.8, 135.8, 132.9, 131.6, 128.4, 128.3, 123.6, 119.7, 117.5, 115.8, 92.7, 88.1, 52.6; HRMS *m/z* calcd for $C_{18}H_{14}O_3Na$ $(M + Na)^+$ 301.0841, found 301.0846.

Synthesis of **1b**:



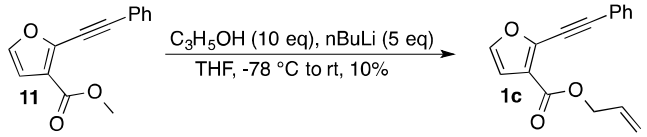
Same procedure used to make **8**. **1a** (124.1 mg, 0.4459 mmol, 1.000 equiv), pyridine (70. μL, 0.89 mmol, 2.0 equiv), triflic anhydride (0.11 mL, 0.67 mmol, 1.2 equiv), dry DCM (1.7 mL). The product, **1b** (67.0 mg, 36.6%), was isolated in analytically pure form. ^{1}H ($CDCl_3$, 600 MHz) δ 7.91 (d, J = 2.7 Hz, 1H), 7.73 (d, J = 8.6 Hz, 1H), 7.57 (m, 2H), 7.42 (dd, J = 8.6 Hz, 2.7 Hz, 1H), 7.38 (m, 3H), 6.05 (ddt, J = 17.1 Hz, 10.4 Hz, 5.8 Hz, 1H), 5.45 (app-dd, J = 17.1 Hz, 1.4 Hz, 1H), 5.30 (app-dd, J = 10.4 Hz, 1.4 Hz, 1H), 4.89 (dt, J = 5.8 Hz, 1.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 164.2, 148.3, 136.1, 134.0, 132.0, 131.8, 129.3, 128.6, 124.9, 124.6, 123.8, 122.8, 119.3, 118.9 (t, J = 319.0 Hz), 96.8, 86.7, 66.7; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -72.7; HRMS *m/z* calcd for $C_{19}H_{13}F_3O_5SNa$ $(M + Na)^+$ 433.0334, found 433.0326.

Synthesis of **11**:



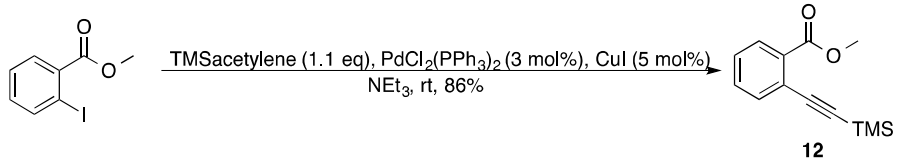
To an 5 mL one neck round bottom flask equipped a reflux condenser and stir bar, **10** (0.100 g, 0.487 mmol, 1.00 equiv), phenylacetylene (0.06 mL, 0.5 mmol, 1.1 equiv), $PdCl_2(PPh_3)_2$ (17.7 mg, 24.4 μmol, 0.050 equiv), and CuI (4.6 mg, 24 μmol, 0.050 equiv) was dissolved in NEt_3 (0.98 mL). The reaction was stirred under nitrogen at 80 °C. The reaction was allowed to cool to room temperature and then concentrated. The compound was isolated by column chromatography (0 to 10% EtOAc/hexanes). Compound **11** was purified via Prep TLC (5% EtOAc in hexanes). The product, **11** (29.0 mg, 26%), was isolated in analytically pure form. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.60 (m, 2H), 7.39 (m, 4H), 6.80 (d, J = 1.9 Hz, 1H) 3.91 (s, 3H); ^{13}C ($CDCl_3$, 125 MHz) δ 163.1, 143.5, 140.8, 132.0, 129.6, 128.7, 121.9, 121.3, 111.7, 98,1, 78.8, 52.0; HRMS *m/z* calcd for $C_{15}H_{14}O_2Na$ $(M + Na)^+$ 249.0892, found 249.0894.

Synthesis of **1c**:



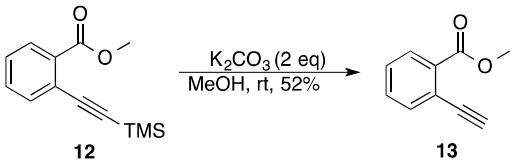
General procedure for transesterification followed. **11** (29.0 mg, 0.128 mmol, 1.00 equiv), allyl alcohol (90. μL, 1.3 mmol, 10. equiv), *n*-BuLi (1.6 M, 0.40 mL, 0.64 mmol, 5.0 equiv). The compound was purified via Prep TLC (2% EtOAc in hexanes). The product, **1c** (3.1 mg, 10 %) was isolated in analytically pure form. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.59 (m, 2H), 7.38 (m, 4H), 6.82 (d, J = 1.9 Hz, 1H) 6.03 (ddt, J = 17.2 Hz, 10.5 Hz, 5.6 Hz, 1H), 5.46 (app-dd, J = 17.2, 1.4 Hz, 1H), 5.28 (app-dd, J = 10.5 Hz, 1.4 Hz, 1H), 4.82 (app-d, J = 5.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 162.2, 143.4, 140.6, 132.1, 131.9, 129.4, 128.5, 121.7, 118.3, 111.6, 98.0, 78.8, 77.3, 65.4; HRMS *m/z* calcd for $C_{16}H_{12}O_3Na$ $(M + Na)^+$ 275.0684, found 275.0693.

Synthesis of **12**:



To a round bottom flask, methyl 2-iodobenozate (0.79 mL, 5.4 mmol, 1.0 eq), $PdCl_2(PPh_3)_2$ (113 mg, 0.161 mmol, 0.030 equiv), and CuI (30.7 mg, 0.161 mmol, 0.050 equiv) were added. The flask was capped and purged with nitrogen. Degassed triethylamine (5.4 mL) was added to dissolve the solids. Trimethylsilylacetylene (0.83 mL, 5.9 mmol, 1.1 equiv) was added slowly. The reaction mixture was allowed to stir at room temperature. The reaction was monitored by TLC until completion. The solution was concentrated under N_2. The compound was purified and isolated via column chromatography (0 to 20% over 10 column volumes). The product **12** (1.0790 g, 86.32%) was obtained in analytically pure form. ^{1}H NMR (CD_2Cl_2, 500 MHz) δ 7.87 (ddd, J = 7.9 Hz, 1.4 Hz, 0.5 Hz, 1H), 7.57 (ddd, J = 7.7 Hz, 1.3 Hz, 0.5 Hz) 7.47 (td, J = 7.5 Hz, 1.4 Hz) 7.39 (td, J = 7.8 Hz, 1.4 Hz, 1H), 3.89 (s, 3H), 0.26 (s, 9H); ^{13}C NMR (CD_2Cl_2, 125 MHz) δ 167.0353, 134.7105, 133.1035, 131.8509, 130.4719, 128.6152, 123.4034, 103.5347, 99.8476, 52.2508, -0.1093; HRMS *m/z* calcd for $C_{13}H_{16}O_2SiNa$ $(M + Na)^+$ 255.0817, found 255.0821. In agreement with literature precedent.[2]

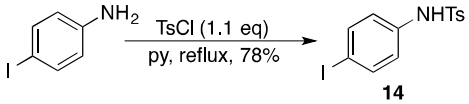
Synthesis of **13:**



12 **13**

Prepare according to literature precedent.[3] To a 5 mL round bottom flask **12** (1.08 g, 4.64 mmol, 1.00 equiv) and K_2CO_3 (1.29 g, 9.29 mmol, 2.00 equiv) were added. MeOH (2 mL) was added. The reaction was monitored by TLC until completion. The reaction was added to water (10 mL) and extracted with DCM (10 mL × 3). The combined organic layers were dried with $MgSO_4$ and concentrated. The compound was purified via column chromatography (0% to 20% EtOAc in hexanes). The product, **13** (390.1 mg, 52%), was isolated in analytically pure form. ^{1}H NMR (CD_2Cl_2, 500 MHz) δ 7.8952 (dd, J = 7.9 Hz, 1.6 Hz, 1H), 7.60 (dd, J = 7.7 Hz, 1.1 Hz, 1H), 7.48 (app-td, J = 7.6 Hz, 1.4 Hz, 1H), 7.41 (app-td, J = 7.7 Hz, 1.3 Hz, 1H), 3.88 (s, 3H), 3.39 (s, 1H); ^{13}C NMR (CD_2Cl_2, 125 MHz) δ 166.7, 135.3, 133.3, 132.1, 130.6, 129.0, 82.4, 82. 3, 52.4.

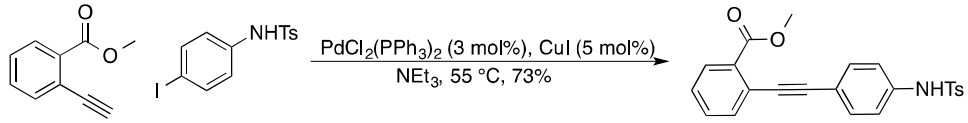
Synthesis of **14**:



14

Prepared according to a literature source.[4] To a flame dried round bottom flask, 4-iodoanilne (200. mg, 0.914 mmol, 1.00 equiv) and tosyl chloride (191 mg, 1.00 mmol, 1.10 equiv) were added. Pyridine (1.1 mL) was added to dissolve the solids. The reaction was stirred under nitrogen at reflux overnight. Upon cooling to room temperature the reaction mixture was added to EtOAc (5 mL) and washed with saturated NH_4Cl (aq) (3 × 5mL). The organic layer was dried with $MgSO_4$, which was removed via gravity filtration. The organic solution was concentrated. The compound was purified via column chromatography (0 to 30% EtOAc in hexanes over 15 column volumes). The product, **14** (266.5 mg, 78.27%), was isolated in analytically pure form. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.70 (d, J = 8.3, 2H), 7.59 (s, 1H), 7.49 (d, J = 8.8 Hz, 2H), 7.22 (d, J = 8.2 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H) 2.37 (s, 2H); HRMS *m/z* calcd for $C_{13}H_{16}O_2SiN_2$ $(M + NH_4)^+$ 390.9977, found 390.9974.

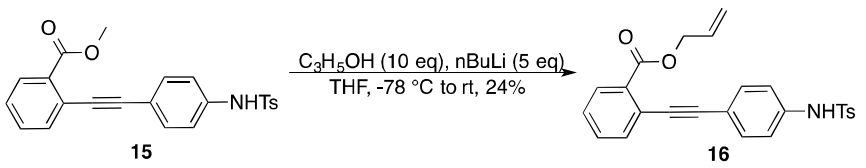
Synthesis of **15:**



13 **14** **15**

Compounds **14** (265.5 mg, 0.7117 mmol, 1.000 equiv), **13** (125.4 mg, 0.7829 mmol, 1.100 equiv), $PdCl_2(PPh_3)_2$ (15.0 mg, 21.4 μmol 0.030 equiv), and CuI (6.8 mg, 36 μmol, 0.050 equiv) were added to a 5 mL round bottom flask equipped with a stir bar. The flask was allowed to sit at room temperature while under dynamic nitrogen for 10 min. Degassed triethylamine (1.1 mL) was added. The reaction was heated to 55 °C and allowed to stir under nitrogen overnight. The reaction mixture was concentrated. The compound was purified and isolated via column chromatography (0 to 20% EtOAc in hexanes). The product, **15** (211.4 mg, 73.25%), was isolated in analytically pure form. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.97 (dd, J = 7.9 Hz, 1.0 Hz, 1H), 7.68 (d, J = 8.3 Hz, 2H), 7.5987 (dd, J = 7.8 Hz, 0.9 Hz, 1H), 7.48 (app-td, J = 7.5 Hz, 1.3 Hz, 1H), 7.42 (d, J = 8.6 Hz, 2H), 7.37 (app-td, J = 7.7 Hz, 1.3 Hz, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.07 (d, J = 8.6 Hz, 2H), 6.97 (s, 1H), 3.9405 (s, 3H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 166.7, 144.2, 136.8, 135.8, 134.0, 132.9, 131.8, 131.7, 130.6, 129.8, 128.0, 127.3, 123.7, 120.8, 120.0, 93.7, 88.6, 52.3, 21.6; HRMS *m/z* calcd for $C_{23}H_{18}NO_4S$ $(M - H)^-$ 404.0956, found 404.0948.

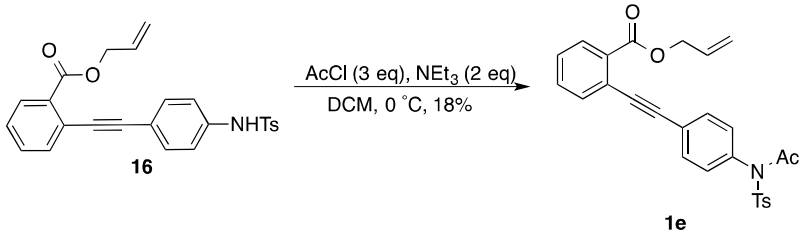
Synthesis of **16**:



15 16

General procedure for transesterification used. **13** (211 mg, 0.520 mmol, 1.00 equiv), allyl alcohol (0.35 mL, 5.2 mmol, 10. equiv), *n*-BuLi (1.6 M, 1.60 mL, 2.60 mmol, 5.00 equiv). The product **16** (53.7 mg, 24%) was isolated in analytically pure form. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.99 (dd, J = 7.9 Hz, 1.0 Hz, 1H), 7.71 (d, J = 8.3 Hz, 2H), 7.60 (m, 2H), 7.47 (app-td, J = 7.6 Hz, 1.3 Hz, 1H), 7.40 (d, J = 8.6 Hz, 2H), 7.36 (app-td, J = 7.6 Hz, 1.0 Hz, 1H), 7.22 (d, J = 8.3 Hz, 2H), 7.10 (d, J = 8.6 Hz, 1H), 6.03 (ddt, J = 17.2 Hz, 10.4 Hz, 5.6 Hz, 1H), 5.41 (dd, J = 17.2 Hz, 1.4 Hz, 1H), 5.24 (dd, J = 10.4 Hz, 1.4 Hz, 1H), 4.85 (app-dt, J = 5.6 Hz, 1.3 Hz, 2H), 2.36 (s, 3H); HRMS *m*/*z* calcd for $C_{25}H_{21}NO_4SNa$ $(M + Na)^+$ 454.1089, found 454.1087.

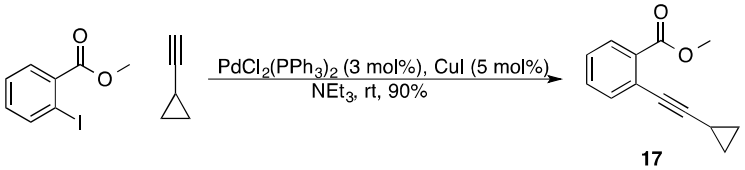
Synthesis of **1e**:



16 1e

To a flame dried 5 mL round bottom flask, **16** (19.4 mg, 44.9 μmol, 1.00 equiv) and triethylamine (12.5 μL, 89.9 μmol, 2.00 equiv) was dissolved in dry dichloromethane (0.45 mL). The reaction vessel was cooled to 0 °C. Acetyl chloride (14.4 μL, 0.20 mmol, 4.5 equiv) was added via a syringe. The reaction mixture was allowed to stir under N_2 over night. The reaction was quenched with saturated NH_4Cl (0.50 mL) and transferred to a 4 mL vial. The product was extracted with dichloromethane (3 × 5 mL). The organic layers were combined, dried with $MgSO_4$, and concentrated in vacuo. The compound was purified via Prep TLC (25% EtOAc in hexanes). The product, **1e** (3.8 mg, 18%), was obtained in analytically pure form. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.04 (dd, J = 7.9 Hz, 1.0 Hz, 1H), 7.91 (d, J = 8.0 Hz, 2H), 7.67 (app-d, J = 8.3 Hz, 3 H), 7.53 (app-td, J = 7.6 Hz, 1.3 Hz, 1H), 7.43 (app-td, J = 7.8 Hz, 1.3 Hz, 1H), 7.35 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 6.06 (ddt, J = 17.1 Hz, 10.3 Hz, 5.6 Hz, 1H), 5.45 (app-dq, J = 17.1 Hz, 1.4 Hz, 1H), 5.29 (app-dd, J = 10.4 Hz, 1.3 Hz, 1H), 4.88 (app-dt, J = 5.6 Hz, 1.3 Hz, 2H), 2.46 (s, 3H), 1.90 (s, 3H); HRMS *m*/*z* calcd for $C_{27}H_{23}NO_5SNa$ $(M + Na)^+$ 496.1195, found 496.1197.

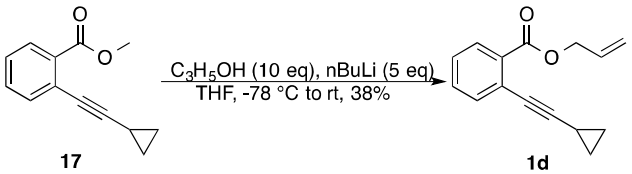
Synthesis of **17**:



17

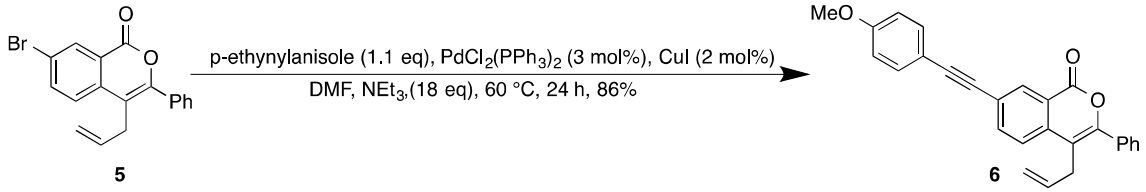
To a 5 mL round bottom flask equipped with a stir bar, methyl 2-iodobenozate (0.37 mL, 2.5 mmol, 1.0 equiv), $PdCl_2(PPh_3)_2$ (17.5 mg, 25.0 μmol, 0.010 equiv), and CuI (9.5 mg, 50. μmol, 0.020 equiv) were added and allowed to sit under N_2 for 10 minutes. Degassed triethylamine (2.5 mL) was added to the reaction vessel. Cyclopropylacetylene (0.23 mL, 2.7 mmol, 1.1 equiv) was added slowly. The reaction mixture was allowed to stir at room temperature, under N_2, over night. The reaction was concentrated under N_2. The compound was purified by column chromatography (0% to 20% EtOAc in hexanes). The product, **17** (488.7 mg, 90%), was isolated in analytically pure form. ^{1}H NMR (CD_2Cl_2, 500 MHz) 7.83 (d, J = 7.9 Hz, 1H), 7.45 (d, J = 7.5 Hz, 1H), 7.41 (t, J = 7.5 Hz, 1H), 7.30 (t, J = 7.7 Hz, 1H), 3.86 (s, 3H), 1.48 (m, 1H), 0.90 (m, 2H), 0.81 (m, 2H); ^{13}C NMR (CD_2Cl_2, 125 MHz), δ 167.1, 134.3, 132.6, 131.9, 130.5, 127.5, 124.7, 89.4, 74.7, 52.3, 9.1, 0.8; HRMS *m*/*z* calcd for $C_{13}H_{12}O_2Na$ $(M + Na)^+$ 223.0735, found 223.0736.

Synthesis of **1d**:



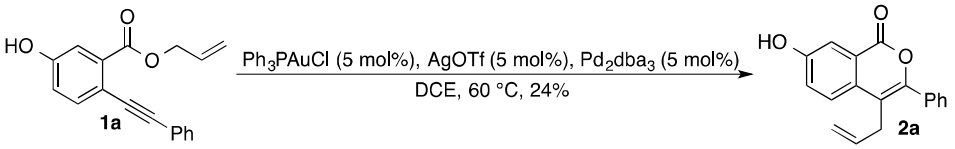
General procedure for transesterification followed. **17** (448.7 mg, 2.240 mmol, 1.00 equiv), allyl alcohol (1.52 mL, 22.4 mmol, 10. equiv), *n*-BuLi (1.6 M, 7.0 mL, 11 mmol, 5.0 equiv). The product, **1d** (193.5 mg, 38%), was isolated in analytically pure form. ^{1}H NMR (CD_2Cl_2, 500 MHz) δ 7.87 (d, J = 7.9 Hz, 1H), 7.47 (d, J = 7.7 Hz, 1H), 7.43 (app-t, J = 7.6 Hz, 1H), 7.32 (app-t, J = 7.4 Hz, 1H), 6.06 (ddt, J = 17.2 Hz, 10.4 Hz, 5.6 Hz, 1H), 5.43 (app-d, J = 17.2 Hz, 1H), 5.29 (app-d, J = 10.4 Hz, 1H), 4.80 (app-d, J = 5.6 Hz, 2H), 1.48 (m, 1H), 0.89 (m, 2H), 0.82 (m, 2H); ^{13}C NMR (CD_2Cl_2, 125 MHz) δ 166.4, 134.4, 132.8, 132.5, 131.9, 130.5, 127.5, 124.7, 118.3, 99.4, 74.8, 66.0, 9.0, 0.8; HRMS *m/z* calcd for $C_{15}H_{14}O_2Na$ $(M + Na)^+$ 249.0892, found 249.0884.

Synthesis of **6**:



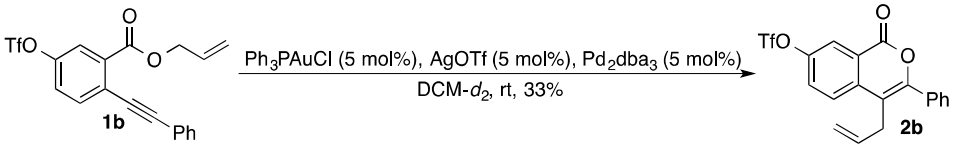
To a 5 mL round bottom flask equipped with a stir bar, **5** (45.3 mg, 0.133 mmol, 1.00 equiv), $PdCl_2(PPh_3)_2$ (2.8 mg, 40. μmol, 0.030 equiv), CuI (0.5 mg, 30 μmol, 0.020 equiv) were added. Degassed DMF (1 mL) was added via syringe. *p*-ethynylanisole (19 μL, 0.15 mmol, 1.1 equiv) and NEt_3 (0.33 mL) were added sequentially. The reaction was allowed to stir under nitrogen at 60 °C for 24 h. The reaction mixture was added to brine (5 mL) and extracted into DCM (3 × 5 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated. The product was crystallized with a mixture of hexanes and DCM, then isolated. The product, **6** (42 mg, 86%), was isolated and fully characterized ^{1}H NMR (CD_2Cl_2, 600 MHz) δ 8.44 (d, J = 1.7 Hz, 1H), 7.84 (dd, J = 8.3 Hz, 1.8 Hz, 1H) 7.64 (m, 2H), 7.60 (d, J = 8.4 Hz, 1H), 7.51 (d, J = 8.8 Hz, 2H), 7.48 (m, 3H), 6.92 (d, J = 8.9 Hz, 2H), 6.1238 (ddt, J = 17.2 Hz, 10.4 Hz, 5.6 Hz, 1H), 5.22 (app-dq, J = 10.4 Hz, 1.3 Hz, 1H), 5.08 (app-dq, J = 17.2 Hz, 1.3 Hz, 1H), 3.83 (s, 3H), 3.46 (app-dt, J = 5.6 Hz, 1.3 Hz, 2H); ^{13}C NMR (CD_2Cl_2, 125 MHz) δ 161.3, 160.1, 152.9, 137.1, 136.8, 135.6, 133.1, 133.0, 132.0, 129.7, 128.6, 128.3, 124.6, 123.4, 121.2, 116.9, 114.6, 114.1, 110.7, 91.5, 86.8, 55.4, 31.2; HRMS *m/z* calcd for $C_{27}H_{20}O_3Na$ $(M + Na)^+$ 415.1310, found 415.1302.

Synthesis of **2a**:



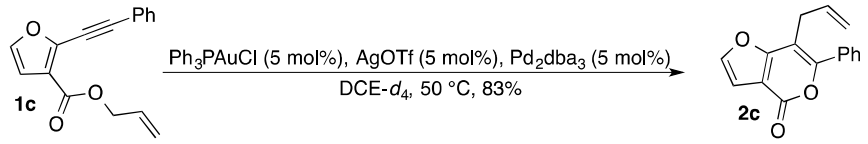
In a one dram vial, the active gold catalyst was generated with Ph_3PAuCl (1.9 mg, 3.8 μmol 0.050 equiv) and AgOTf (1.0 mg, 3.8 μmol, 0.050 equiv) in DCE (0.20 mL). The active gold catalysis solution was transferred to a one dram vial containing **1a** (21 mg, 76 μmol, 1.0 equiv) and mixed thoroughly. The solution containing the active gold catalyst and **1a** was transferred to a one dram vial containing Pd_2dba_3 (3.5 mg, 3.8 μmol, 0.050 equiv). The mixture was diluted to a total of 0.76 mL DCE. The reaction temperature was increased to 60 °C and the reaction was allowed to stir under an inert atmosphere for 8 h. The reaction mixture was concentrated in vacuo. The product was isolated and purified via silica gel column chromatography (0% to 40% EtOAc/hexanes). The product **2a** (5 mg, 24%) was fully characterized. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.98 (d, J = 2.6 Hz 1H), 7.62 (m, 2H), 7.54 (d, J = 8.9 Hz, 1H), 7.44 (m, 3H), 7.35 (dd, J = 8.9 Hz, 2.2 Hz, 1H), 6.71 (s, br, 1H), 6.10 (ddt, J = 17.8 Hz, 10.1 Hz, 3.5 Hz, 1H), 5.22 (d, J = 10.1 Hz, 1H), 5.09 (d, J = 17.8 Hz, 1H), 3.45 (d, J = 3.5, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 163.3, 156.4, 150.5, 136.0, 133.2, 131.5, 129.7, 128.9, 128.5, 126.6, 124.3, 122.3, 117.4, 114.3, 111.3, 31.6; HRMS *m/z* calcd for $C_{18}H_{14}O_3Na$ $(M + Na)^+$ 301.0841, found 301.0840.

Synthesis of **2b**:



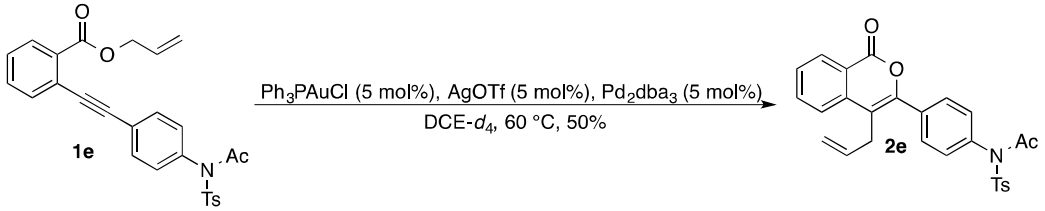
Ph_3PAuCl (1.4 mg, 2.8 μmol, 0.050 equiv) was dissolved in CD_2Cl_2 (0.10 mL) and thoroughly mixed with AgOTf (0.7 mg, 2.8 μmol, 0.050 equiv) to generate the active gold catalyst. The active gold catalyst was added to the **1b** (23 mg, 55 μmol, 1.0 equiv) and thoroughly mixed. The mixture was then added to Pd_2dba_3 (2.3 mg, 2.8 μmol, 0.050 equiv). The reaction was allowed to stir at room temperature for 24 h. Afterwards, the reaction temperature was raised to 40 °C, the reaction was allowed to stir for 8 h. An excess of dimethylaminoethanethiol and triethylamine was added to the reaction mixture. The reaction mixture was allowed to stir for an additional 24 h at room temperature. The product was isolated and purified via silica gel column chromatography. The product **2b** (7.6 mg, 33%) was fully characterized. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.26 (d, J = 2.5 Hz, 1H), 7.71 (d, J = 8.9 Hz, 1H), 7.63 (m, 3H), 7.47 (m, 3H), 6.11 (ddt, J = 17.5 Hz, 10.1 Hz, 5 Hz, 1H), 5.27 (d, J = 10.1, 1H), 5.10 (d, J = 17.5 Hz, 1H), 3.47 (d, J = 5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 160.7, 153.8, 148.2, 138.0, 135.0, 132.2, 130.1, 128.6, 128.3, 127.9, 126.9, 122.6, 122.0, 118.6 (t, J = 318 Hz, 1C), 117.7, 109.8, 31.4; ^{19}F NMR ($CDCl_3$, 376 MHz) δ –72.6; HRMS *m/z* calcd for $C_{19}H_{13}F_3O_5SNa$ $(M + Na)^+$ 433.0334, found 433.0339.

Synthesis of **2c:**



Ph_3PAuCl (1.6 mg, 3 μmol, 0.05 equiv) was dissolved in $C_2D_4Cl_2$ (0.10 mL) and thoroughly mixed with AgOTf (0.9 mg, 3 μmol, 0.05 equiv) to generate the active gold catalyst. The active gold catalyst was added to the **1c** (16.7 mg, 66 μmol, 1.0 equiv) and thoroughly mixed. The mixture was then added to Pd_2dba_3 (3.0 mg, 3 μmol, 0.05 equiv). The reaction mixture was diluted to 0.66 mL. The reaction temperature was increased to 50 °C. The reaction was allowed to stir for 6 h. The reaction was cooled to room temperature. An excess of dimethylaminoethanethiol and triethylamine was added and the reaction mixture was allowed to stir at room temperature over night. The product was isolated and purified via column chromatography (gradient from 0% to 10% EtOAc/hexanes). The product **2c** (13.9 mg, 83%) was fully characterized. ^{1}H NMR ($C_2D_4Cl_2$, 600 MHz) δ 7.61 (m, 3H), 7.47 (m, 3H), 6.91 (d, J = 1.8 Hz, 1H), 6.07 (ddt, J = 17.3 Hz, 11.0, 5.7 Hz, 1H), 5.16 (d, J = 11.0, 1H), 5.09 (d, J = 17.3 Hz, 1H), 3.42 (d, J = 5.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 162.3, 158.7, 156.1, 144.8, 135.0, 132.3, 130.1, 129.2, 128.7, 125.6, 116.6, 109.8, 107.8, 106. 5, 29.5; HRMS *m/z* calcd for $C_{16}H_{12}O_3Na$ $(M + Na)^+$ 275.0684, found 275.0693.

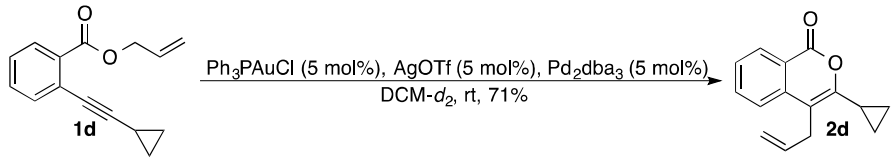
Synthesis of **2e**:



Ph_3PAuCl (1.5 mg, 3 μmol, 0.05 equiv) was dissolved in $C_2D_4Cl_2$ (0.10 mL) and thoroughly mixed with AgOTf (0.9 mg, 3 μmol, 0.05 equiv) to generate the active gold catalyst. The active gold catalyst was added to **1e** (30 mg, 64 μmol, 1 equiv) and thoroughly mixed. The mixture was then added to Pd_2dba_3 (3.0 mg, 3 μmol, 0.05 equiv). The reaction mixture was diluted to 0.64 mL. The reaction temperature was increased to 60 °C. The reaction was allowed to stir for 9 h. The reaction was cooled to room temperature. The product was isolated and purified via column chromatography (0% to 30% EtOAc/hexanes). The product **2e** (15 mg, 50%) was fully characterized. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.40 (d, J = 7.9 Hz, 1H), 7.93 (d, J = 8.1 Hz, 2H), 7.79 (m, 3H), 7.64 (d, J = 8.1 Hz, 1H), 7.58 (app-t, J = 7.4 Hz, 1H), 7.36 (app-t, J = 7.2, 4H), 6.17 (ddt, J = 17.5 Hz, 10.1 Hz, 2.4 Hz, 1H), 5.28 (d, J = 10.1 Hz, 1H), 5.10 (d, J = 17.5 Hz, 1H), 3.53 (d, J = 2.4 Hz, 2H), 2.47 (s, 3H), 1.92 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz)

δ 169.7, 162.0, 150.7, 145.2, 137.7, 137.5, 135.8, 135.3, 134.8, 134.5, 130.1, 129.9, 129.8, 129.5, 129.4, 129.2, 128.4, 124.4, 121.0, 117.5, 111.6, 31.3, 25.1, 21.7; HRMS *m*/*z* calcd for $C_{27}H_{23}NO_5SNa$ $(M + Na)^+$ 496.1195, found 496.1197.

Synthesis of **2d**:



Ph_3PAuCl (2.4 mg, 5 μmol, 0.05 equiv) was dissolved in CD_2Cl_2 (1 mL) and thoroughly mixed with AgOTf (1.3 mg, 5 μmol, 0.05 equiv) to generate the active gold catalyst. The active gold catalyst was added to **1d** (23 mg, 0.10 mmol, 1.0 equiv) and thoroughly mixed. The mixture was then added to Pd_2dba_3 (4.6 mg, 5 μmol, 0.05 eq). The reaction was allowed to stir at room temperature for 24 h. The products were purified by silica gel chromatography (0% to 10% EtOAc/hexanes). The product **2d** (16 mg, 71%) was fully characterized ^1H NMR ($CDCl_3$, 600 MHz) δ 8.28 (dd, J = 7.9 Hz, 1.1 Hz, 1H), 7.70 (app-td, J = 7.4 Hz, 1.4 Hz, 1H), 7.48 (d, J = 8.2 Hz, 1H), 7.42 (app-td, J = 7.2 Hz, 1.3 Hz, 1H), 5.99 (ddt, J = 17.1 Hz, 10.4 Hz, 5.7 Hz, 1H), 5.12 (app-dq, J = 10.5 Hz, 1.3 Hz, 1H), 5.10 (app-dq, J = 17.2, 1.4 Hz, 1H), 3.53 (app –dt, J = 5.6 Hz, 1.3 Hz, 2H), 1.97 (m, 1H), 1.18 (m, 2H), 0.94 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 162.6, 154.5, 138.3, 134.9, 134.8, 130.0, 126.9, 122.6, 116.5, 109.2, 29.8, 11.1, 7.3; HRMS *m*/*z* calcd for $C_{15}H_{14}O_2H$ $(M + H)^+$ 227.1072, found 227.1076.

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Chapter 2

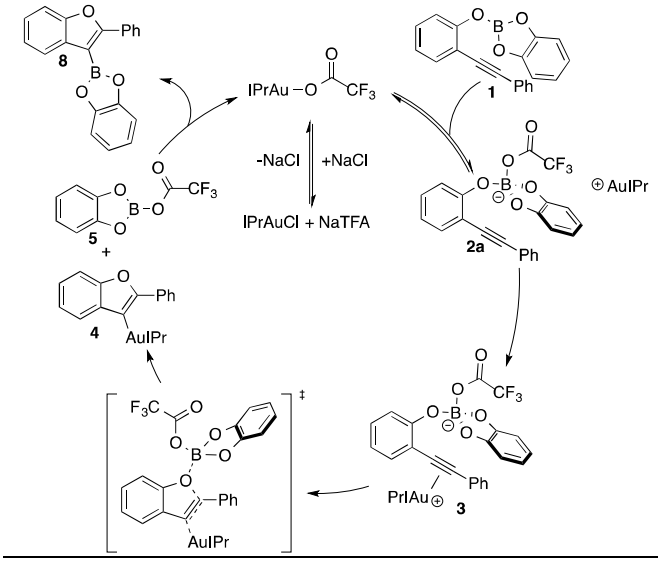
Mechanistic Studies of The Alkoxyboration Reaction

Abstract: A kinetic study of the alkoxyboration reaction showed the reaction is second order overall: first order with respect to both IPrAuTFA and NaTFA. NaTFA was determined to be both a Lewis base, by enhancing the nucleophilicity the B–O σ bond, and as a reagent needed to decrease the amount of IPrAuTFA converted to the catalytically inactive IPrAuCl. Increasing the amount of trifluoroacetate eventually lead to a decrease in the reaction rate. This effect is attributed to over addition of the Lewis base into the borate ester that is formed after the cyclization step. The rate-determining step was determined to be the transmetalation step.

INTRODUCTION

In 2014, the Blum group reported a gold catalyzed alkoxyboration reaction, allowing for the synthesis of 3-borylbenzofurans.[1] In the seminal publication, the authors proposed that the reaction was catalyzed by a bifunctional catalyst capable of activating both the B–O σ bond and C–C π bond. The proposed mechanism is shown in Figure 2.1. In this mechanism, the trifluoroacetate ion is transferred to the boric ester to form a gold borate ion pair, **2a**. Upon binding of the cationic gold complex to the alkyne, **3**, cyclization yields a vinyl organogold intermediate, **4**, and a borate ester, **5**. Transmetalation yields the desired product, **8**. The proposed mechanism is dissimilar to other reactions that are formal 1,3-transpositions due to the migration occurring in an intermolecular fashion.[2,3] The role of sodium trifluoroacetate (NaTFA) along with the manner in which transmetalation occurred remained unclear. The purpose of this study was to determine the mechanism of the alkoxyboration reaction.

Figure 2.1 The proposed mechanism from the seminal publication.



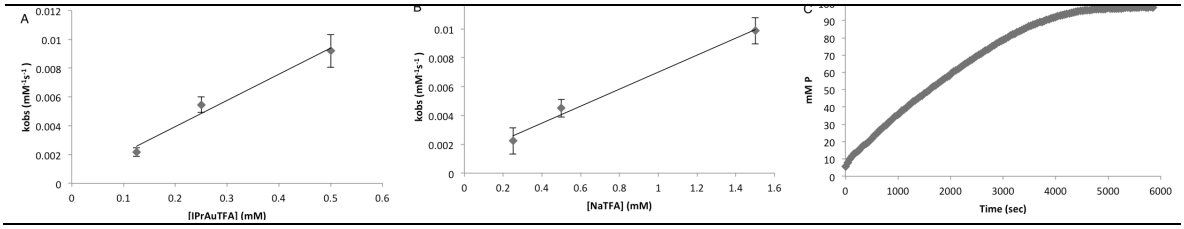
RESULTS AND DISCUSSION

Initial studies focused on determining the order with respect to IPrAuTFA, NaTFA, and **1**. The kinetic data (Figure 2.2) obtained is consistent with the rate equation shown in eq 1. Note, increasing the amount of NaTFA from 15 mol % (1.5 mM) to 30 mol % (3.0 mM) showed no statistically significant increase in rate.

$$\text{Rate} = k[\text{IPrAuTFA}][\text{NaTFA}] \quad (1)$$

Due to the enormous amount of literature precedent surrounding gold(I) complexes acting as carbophilic π acids, IPrAuTFA is thought to act as such.[4] However, the manner in which NaTFA affects the rate of the reaction is not as obvious.

Figure 2.2 (A) Rate dependence on IPrAuTFA concentration. (B) Rate dependence on NaTFA concentration. (C) The change in product concentration over time using 10 mol % IPrAuTFA and 30 mol% NaTFA at 70 °C.



In order to deconvolute the role of NaTFA, mass spectrometry and NMR spectroscopy were used. Saturation of a 100 mM solution of **1** in toluene with NaTFA followed by equilibration at 50 °C showed one small peak around the -75 ppm region in the ^{19}F NMR, a range consistent with compounds containing the TFA fragment.[5] A saturated solution of NaTFA in toluene produces no peaks consistent with NaTFA at 50 °C, suggesting NaTFA alone is not soluble. Mass spectrometry data suggests that NaTFA can be solubilized via complexation with the boric ester. Borate **6** (Figure 2.5) was observed via ESI-MS. Since the only source of the catecholborane fragment is the boric ester, the TFA ion must react with **1** in order to produce the observed species. A m/z value of 425.1 with a isotopic distribution indicative of a boron containing compound was observed in the MS spectrum, suggesting that there may be **2** in solution, but due to the low intensity nothing can be said definitively. It is also notable that tetrakis(2,2,2-trifluoroacetoxy)borate, $B(TFA)_4^-$, was also observed, suggesting that if the TFA concentration is too high over-addition can occur, which would lead to a decrease in yield and rate.

To test this hypothesis, tetrabutylammonium trifluoroacetate (TTFA) was synthesized and used as a substitute for NaTFA. The rate decreased dramatically in the case where TTFA was used (Table 2.1). This result is consistent with the hypothesis that there exists an ideal concentration of TFA, such that solutions with higher concentrations of TFA may open an alternative pathway where the catecholborane fragment can be removed from

the reaction medium and solutions with lower concentrations may suffer from both catalyst quenching by exogenous chloride and a lack of borate in solution. Ion pairs suspended in solution may also have a detrimental effect on the rate of the reaction. The active gold catalyst (presumably $IPrAu^+$) can be quenched by NaCl to generate IPrAuCl (observed by ESI-MS). The concentration of chloride can be reduced via the common ion effect. Also, a metathesis reaction can regenerate the precatalyst from IPrAuCl. Based on this reasoning, it is reasonable to believe that Na^+ may have an effect on the rate.

Table 2.1 Observed rate constants shown for comparison.

Conditions	k_{obs} ($mM^{-1}s^{-1}\times10^{-3}$)
5 mol % IPrAuTFA, 15 mol % NaTFA	9.9 ± 0.9
5 mo l% IPrAuTFA, 15 mol % TTFA	0.096 ± 0.111
5 mol % IPrAuTFA, 15 mol % SHFA	0.72 ± 0.62
5 mol % IPrAuTFA	0.015 ± 0.059
5 mol % IPrAuTFA (No NaCl)	55 ± 7

In order to determine the rate dependence of Na^+ on the reaction, the reaction without any additional salt (outside the NaCl generated by the reaction) was used as the control experiment for comparison. Replacing NaTFA with sodium hexafluoroantimonate (SHFA) led to a major decrease in yield relative to the case where NaTFA was present (Table 2.1). However, comparison of the control and experimental rate constants suggest that Na^+ may have a favorable effect on the rate. Due to the low precision of the calculated rate constants, there is ambiguity that lies in whether or not the increase in rate in statistically significant. Using the T.TEST function in Microsoft Excel, the probability that the difference in the rate constants is insignificant was determined to be 0.09. To rephrase for clarity, there is a 91% chance that the differences in the rate constants are statistically significant and that Na^+ concentration influences the rate of the reaction.

The common ion effect and a metathesis may be occurring simultaneously. The common ion effect seems to play a minor role in reducing the amount of catalyst quenching (assuming NaTFA and SHFA have similar solubility products in toluene). A metathesis reaction may account for the low rate when SHFA is used as a co-catalyst.

$$IPrAuCl + NaSbF_6 \rightarrow IPrAuSbF_6 + NaCl \quad (2)$$

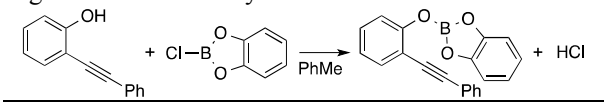
A metathesis reaction to produce $IPrAuSbF_6$ would not produce a bifunctional catalyst capable of enhancing both the electrophilicity and nucleophilicity of the substrate (eq 2).

The nature of the transmetalation step may also be discerned by analysis of the rate constants shown in Table 2.1. The experimentally determined rate constant for the reaction with 5 mol % IPrAuTFA in the presence of NaCl is 660 times slower than the reaction with 5 mol % IPrAuTFA and 15 mol % NaTFA. If the transmetalation occurred via a four centered transition state, the relative rate would not be as large because every turnover would

result in the formation of the precatalyst. A metathesis reaction with NaCl may lead to a decrease in rate due to formation of IPrAuCl, but the likelihood of a reaction with NaCl relative to a reaction with the catalyst is low due to the low solubility of NaCl in toluene. An alternative explanation is that putative organogold intermediate, **4**, may act as a nucleophile towards the borate ester, **5,** resulting in a gold borate ion pair, **7**. Dissociation of TFA would produce the desired product. This hypothesis is consistent with the data obtained from a recent study from the Blum group.[6]

The rate retardation attributed to NaCl can easily be discerned via its elimination from the reaction medium. The reaction of chlorocatehcolborane and 2-(phenylethynyl)phenol generated the desired boric ester and hydrogen chloride gas (Figure 2.3). The container was evacuated to remove hydrogen chloride.

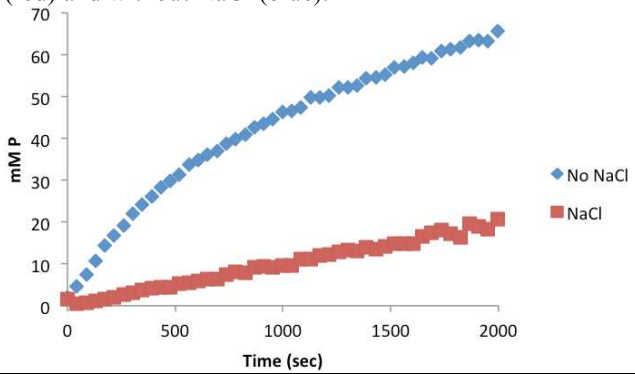
Figure 2.3 NaCl free synthesis of boric ester.



The kinetic studies using the boric ester synthesized in this fashion show a different kinetic profile than what is observed under nominal conditions. Using 5 mol % IPrAuTFA, the initial rate (Table 2.1, Figure 2.4) is about 5.5 times higher than the initial rate using 5 mol % IPrAuTFA and 15 mol % NaTFA in the presence of NaCl (Table 2.1, Figure 2.4). The rate quickly decreases about 40% of the initial rate after about 20% conversion to product (figure 2.4).

The rate decrease may be due to the manner in which NaCl affects the electronic nature of the solvent. When NaCl is present, ions are more stable. After the formation of complex **2,** the species is persistent enough to allow the cationic gold catalyst to form the π complex, **3**. When NaCl is absent, ionic species are not as stable. Upon formation of **2**, disproportionation occurs to form **5** and a phenolate. The phenolate can then bind to the cationic gold complex, resulting a lower amount of gold catalyst to induce cyclization, which would result in a lower, steady rate after equilibration.

Figure 2.4 Change in product concentration over time with (red) and without NaCl (blue).



Notably, in absence of NaCl, NaTFA retards the rate. The active catalyst and precatalyst could be in equilibrium. Introduction of more TFA in solution would lead to a shift in the equilibrium resulting in less active

catalyst in solution. A greater amount of the TFA in the reaction medium could result in increased amounts of borate **6** in solution, which may not be a reactive partner in gold to boron transmetalation. It appears that doubling the concentration of TFA in the reaction medium cuts the rate in half. The current data suggest that the reaction is inverse first order with respect to TFA when NaCl is absent.

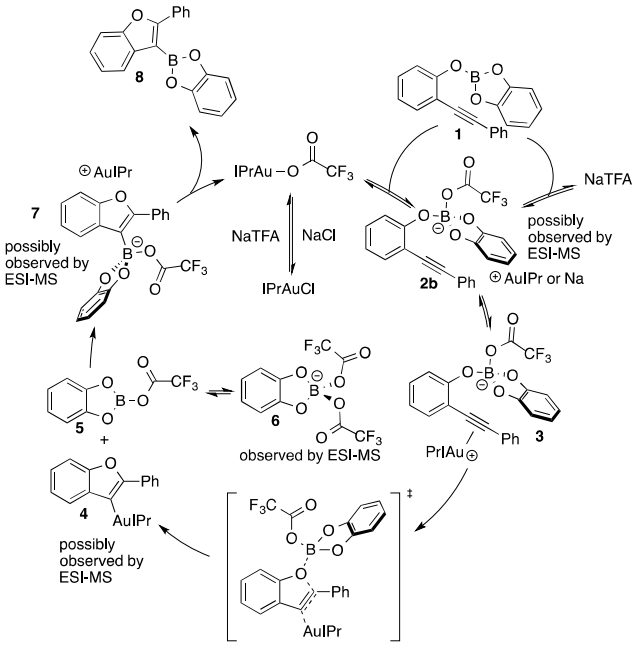
Table 2.2. The activation parameters from the Eyring analysis.

$\Delta G^{\ddagger}$ (kcal mol^{-1})	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (cal K^{-1} mol^{-1})
26.34 ± 1.47	13.44 ± 1.47	- 39.96 ± 4.58

An Eyring analysis was carried out to discern the rate-determining step (RDS) of the reaction. The thermodynamic values are listed in Table 2.2. The entropy of activation is consistent with a bimolecular RDS.[7] There are two bimolecular steps in the proposed mechanism, substrate binding and transmetalation. The positive enthalpy of activation indicates that energy is required for the transformation to occur. In the case of substrate binding, the enthalpy of activation should be negative, also if substrate binding was the RDS, the reaction would not be zero order with respect to substrate. The data from the Eyring analysis suggests the transmetalation is the RDS of the reaction.

The data obtained in this study is consistent with the mechanism shown in Figure 2.5, which takes into account the ability of NaTFA to act as a source of TFA for **1** and **5**. The intermediate after the transmetalation step is also included. In conclusion, the alkoxyboration reaction is second order overall, first order with respect to both IPrAuTFA and NaTFA. NaTFA acts as both a species that reduces the degree of catalyst quenching and acts as a source of TFA that can produce the borate necessary for cyclization to occur. The rate of the reaction seems to be sensitive to the amount of TFA present in solution. Solutions with higher concentrations of TFA had lower observed rate constants. The data obtained from the Eyring analysis suggests the RDS is the transmetalation.

Figure 2.5 The Proposal mechanism based on the data obtained.



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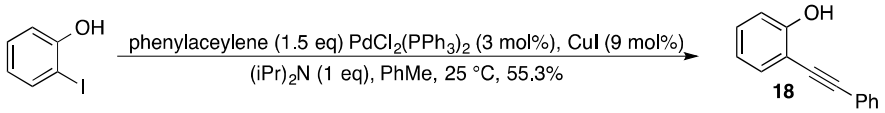
6.) Hirner, J. J.; Blum, S.A. *Tetrahedron* **2015**, *71*, 4445 – 4449.
7.) Denmark S. E.; Bui, T. *J. Org. Chem.* **2005**, *70*, 10393 – 10399.

EXPERIMENTAL

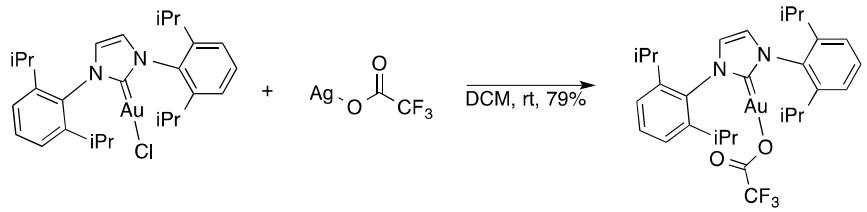
I. Synthetic Procedures

Synthesis of 2-(phenylethynyl)phenol **18** (Conducted by Darius J. Faizi)



A flame dried 1-L round bottomed flask equipped with a stir bar was charged with 2-iodophenol (14.0 g, 3.60 mmol, 1.00 equiv), copper iodide (1.09 g, 5.71 mmol, 0.08980 equiv), and bis(triphenylphosphine)palladium dichloride (1.33 g, 1.89 mmol, 0.0297 equiv). Toluene (320 mL), diisopropylamine (8.90 mL, 63.6, 1.00 equiv), and phenylacetylene (10.5 mL, 95.4 mmol, 1.50 equiv) were added sequentially. The reaction mixture was stirred for 8.5 h at 25 °C. Ethyl acetate (100 mL) was added and the mixture was washed with saturated ammonium chloride (50 mL × 1) then brine (50 mL × 1). The organic layer was isolated and dried with sodium sulfate. Upon concentration of the solution, a dark brown oil was obtained. The material was purified via column chromatography (12% EtOAc in hexanes). Like fractions were collected, concentrated and dried under high vacuum. The resultant oil was recrystallized from hexanes to afford a brown crystalline material (6.82 g, 55.3%). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.57–7.55 (m, 2H), 7.44 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.40–7.38 (m, 3H), 7.30–7.27 (m, 1H), 7.03 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.96 (td, *J* = 7.5, 1.0 Hz, 1H), 5.90 (s, 1H). Spectral Information is in agreement with literature precedent.[1]

Synthesis of IPrAuTFA



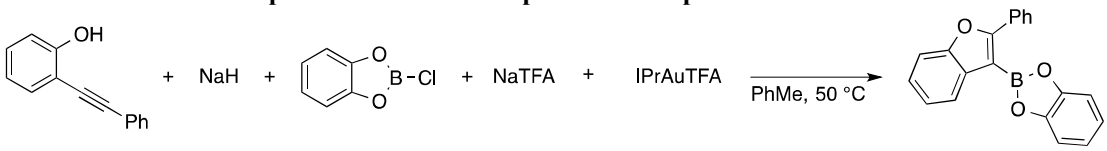
IPrAuCl (124. mg, 0.200 mmol, 1.00 equiv) and AgTFA (44.2 mg, 0.200 mmol, 1.00 equiv) were weighed in separate vials. IPrAuCl was dissolved in DCM (1 mL). The solution was transferred to the vial with AgTFA. DCM (1 mL) was used to rinse the IPrAuCl vial, washings were transferred to the vial with AgTFA. The reaction mixture was then capped with a telfon coated cap and covered in aluminum foil and allowed to stir for 30 h in a glovebox. The reaction mixture was then filtered through glass fiber filter paper. The resultant solution was concentrated inside the glovebox. No further purification was performed, a colorless solid was isolated (110.4 mg, 79%). ^{1}H (PhMe-d_8, 400 MHz) δ 7.13 (t, J = 8 Hz, 2H), 6.30 (s, 2H), 2.46 (app-sep, J = 7 Hz, 4H), 1.35 (d, J = 7 Hz, 12H), 1.02 (d, J = 7 Hz, 12H). Spectral Information is in agreement with literature precedent.[2]

Synthesis of Tetrabutylammonium Trifluoroacetate

The product was prepared according to literature precedent.[3] Trifluoroacetic acid (0.04 mL, 0.5 mmol, 1 equiv) was added to a 10 mL round bottom flask with trimethyl phosphate (0.7 mL, 6.0 mmol, 12 equiv) dropwise. While stirring tetrabutylammonium bromide (161 mg, 0.500 mmol, 1.00 equiv) was added. The reaction was allowed to stir at 60 °C overnight. Excess trimethylphosphate was removed via vacuum distillation at 85 °C. The resultant residue was dissolved in DCM (2 mL), 25 drops of a 10% (w/v) NH_4OH aqueous solution was added. The pH of the

solution was checked while stirring. Water (2 mL) was added when pH = 7. The layers were separated. The aqueous layer was extracted with DCM (2 mL × 2). The organic fractions were combined, concentrated, and dried under high vacuum at 100 °C overnight. No further purification was performed, the product was isolated as a beige solid (133.3, 75%). ^{1}H ($CDCl_3$, 600 MHz) δ 3.30 (t, J = 8 Hz, 8H), 1.65 (app-quin, J = 8 Hz, 8H), 1.44 (app-sex, J = 8 Hz, 8H), 1.01 (t, J = 8 Hz, 12H); ^{19}F ($CDCl_3$, 376 MHz) δ 75.10.

II. General Procedure for Preparation of Kinetic Experiment Samples



2-(phenylethynyl)phenol (34.0 mg, 0.175 mmol, 1.00 equiv), 89% w/w NaH (4.7 mg, 0.18 mmol, 1.0 equiv), B-chlorocatecholborane (27.0 mg, 0.175 mmol, 1.00 equiv), Sodium trifluoroacetate (7.2 mg, 0.053 mmol, 0.30 equiv), IPrAuTFA (12.3 mg, 0.018 mmol, 0.10 equiv) were weighed in separate 4 mL vials. 2-(phenylethynyl)phenol was dissolved in toluene-d_8 (250 μL) and transferred to the vial with NaH. The mixture was stirred by hand briefly and allowed to sit for 15 min. The mixture was then transferred to the vial with B-chlorocatecholborane. Toluene-d_8 (250 μL × 2) was used to rinse through the first two vials. The mixture was allowed to stir for 30 min with occasional stirring by hand. Toluene-d_8 was added to NaTFA to create a suspension, which was then transferred to the reaction mixture. This process was repeated until the total volume of solvent added to the reaction container was 1400 μL. The IPrAuTFA was dissolved in toluene-d_8 (350 μL). From the boric ester stock solution, 400 μL was transferred to a J-Young tube and capped with a rubber septum. This was repeated a total of three times.

III. General Procedure for Kinetic Experiments

One J-Young tube and one 250 μL capped (with a rubber stopper) gas tight syringe with 100 μL of the IPrAuTFA solution were removed from the glovebox. The rubber spectrum on the J-Young tube was wrapped in parafilm. The sample in the J-Young tube was immediately transported to the NMR spectrometer, which underwent temperature calibration before sample injection. The contents of the syringe were injected into the J-Young tube. The J-Young was shaken and inserted into the NMR spectrometer. Acquisition of spectra immediately followed. The acquisition time was set to 6 s. A 90° pulse was used. The line broadening was set to 1 Hz. The number of scans per experiment = 1. The number of dummy scans = 0. Fifty experiments were conducted sequentially with 34 s delays between experiments.

IV. Raw Kinetic Data

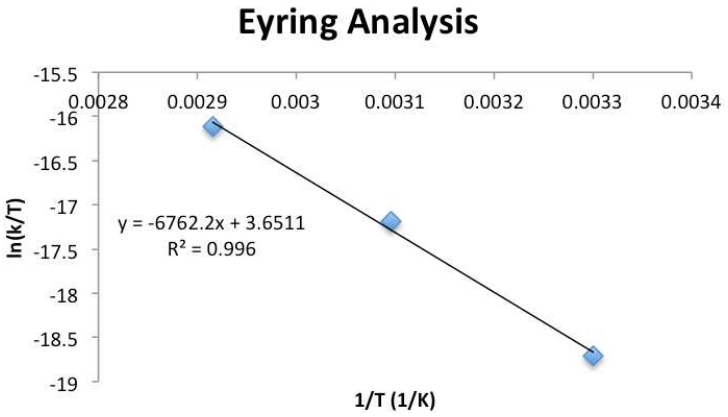
Catalyst Loadings	average rate ($mM/s \times 10^{-3}$)	St. Dev. ($mM/s \times 10^{-3}$)
7.5 mol % IPrAuTFA, 30 mol % NaTFA	11	0.1
5 mol % IPrAuTFA, 30 mol % NaTFA	9.2	1.1
5 mol % IPrAuTFA, 15 mol % NaTFA	9.9	0.9
5 mol % IPrAuTFA, 5 mol % NaTFA	4.5	0.6
2.5 mol % IPrAuTFA, 30 mol % NaTFA	5.5	0.6
5 mol % IPrAuTFA, 15 mol % NaBArF	0	0
5 mol % IPrAuTFA, No salt	0.015	0. 059
5 mol % IPrAuTFA, 15 mol % $NaSbF_6$	0. 72	0. 6
5 mol % IPrAuTFA, 15 mol % NBu_4TFA	0.096	0.111
1.25 mol % IPrAuTFA, 30 mol % NaTFA	2.2	0.3
5 mol % IPrAuTFA, 2.5 mol % NaTFA	2.2	0.9
5 mol % IPrAuTFA, No NaTFA/NaCl	55	6
5 mol % IPrAuTFA, 5 mol % NaTFA, no NaCl	20	1

5 mol % IPrAuTFA, 10 mol % NaTFA, no NaCl	23	7

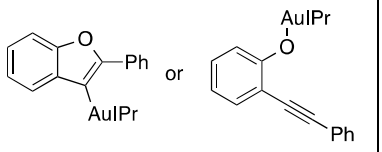
V. EYRING ANALYSIS DATA

Temperature (°C)	Average rate (M/s × 10^{-5})	St. Dev. (M/s × 10^{-5})
70	3.4	0.2
50	1.1	0.1
30	0.23	0.04

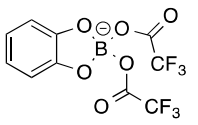
Raw Eyring Analysis Data		Activation Parameters		
1/T (K^{-1})	ln(k/T)	Parameter	Value	St. Dev.
0.0029	-16.11	$\Delta G^{\ddagger}$ (kcal mol^{-1})	26.3	1.5
0.0031	-17.19	$\Delta S^{\ddagger}$ (cal K^{-1} mol^{-1})	-40.0	4.6
0.0033	-18.71	$\Delta H^{\ddagger}$ (kcal mol^{-1})	13.4	1.5



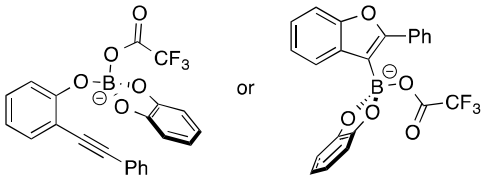
VI. Reaction Intermediates Found By High Resolution Mass Spectrometry



Theoretical m/z $(M+H)^+$: 779.3276
Observed m/z $(M+H)^+$: 779.3294

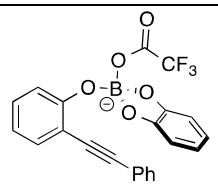


Theoretical m/z (M^-): 345.0007
Observed m/z (M^-): 345.0024

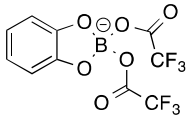


Theoretical m/z (M^-): 425.0812
Observed m/z (M^-): 425.0820

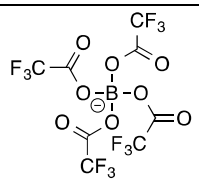
VII. Species Found in NaTFA Solubility Study by Low Resolution Mass Spectrometry



Observed m/z (M^-): 425.1



Observed m/z (M^-): 345.0

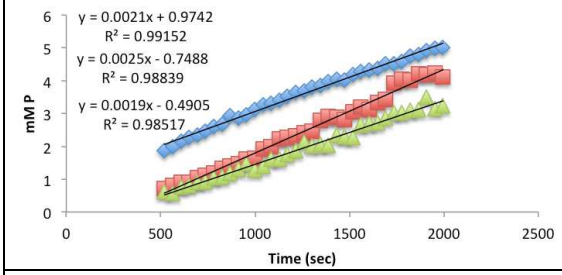


Observed m/z (M^-): 463

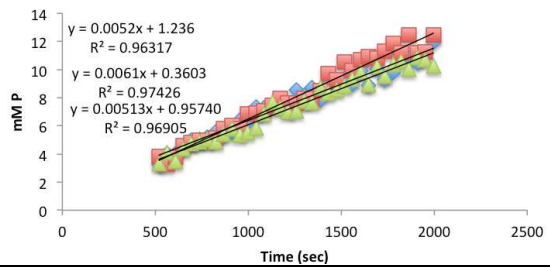
IX. Kinetic Plots

Note: 1.25% Au = 1.25 mol % IPrAuTFA

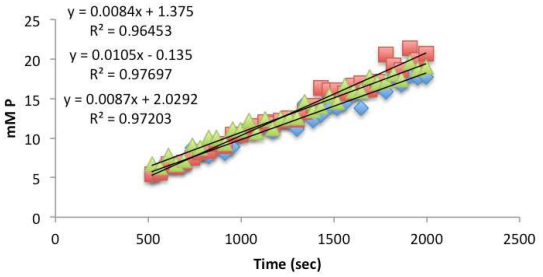
1.25% Au, 30% NaTFA



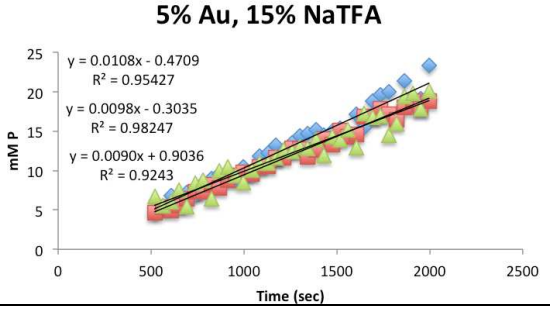
2.5% Au, 30% NaTFA



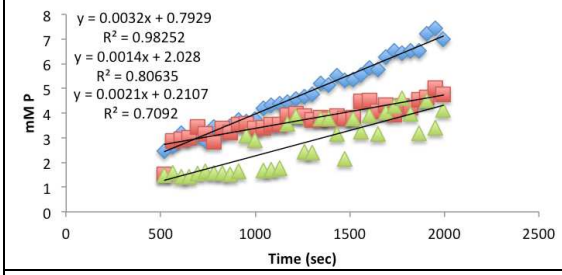
5% Au, 30% NaTFA



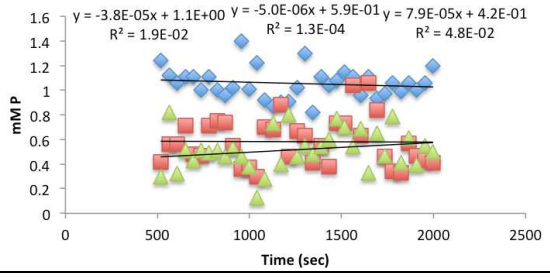
5% Au, 15% NaTFA



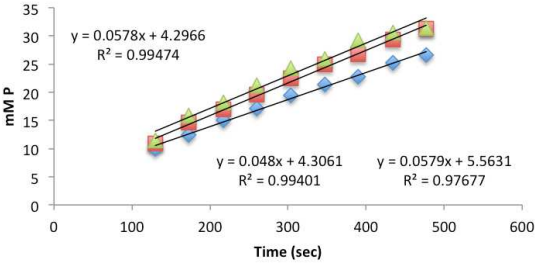
5% Au, 2.5% NaTFA



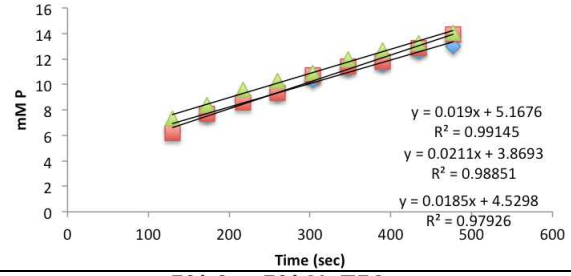
5% Au



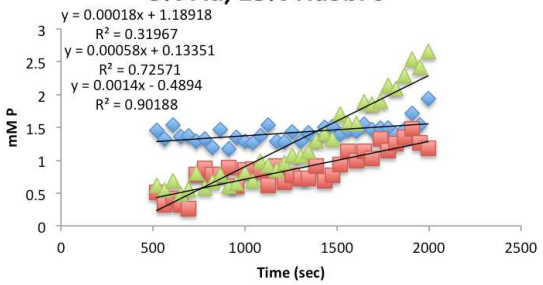
5% Au, No NaCl



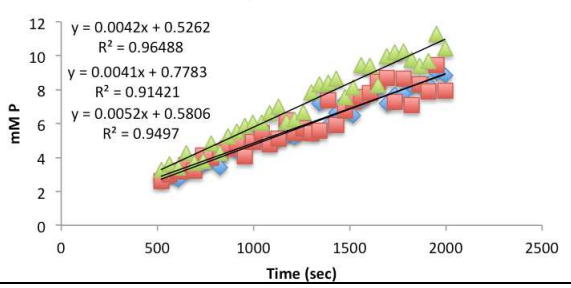
5% Au, 5% TFA, No NaCl

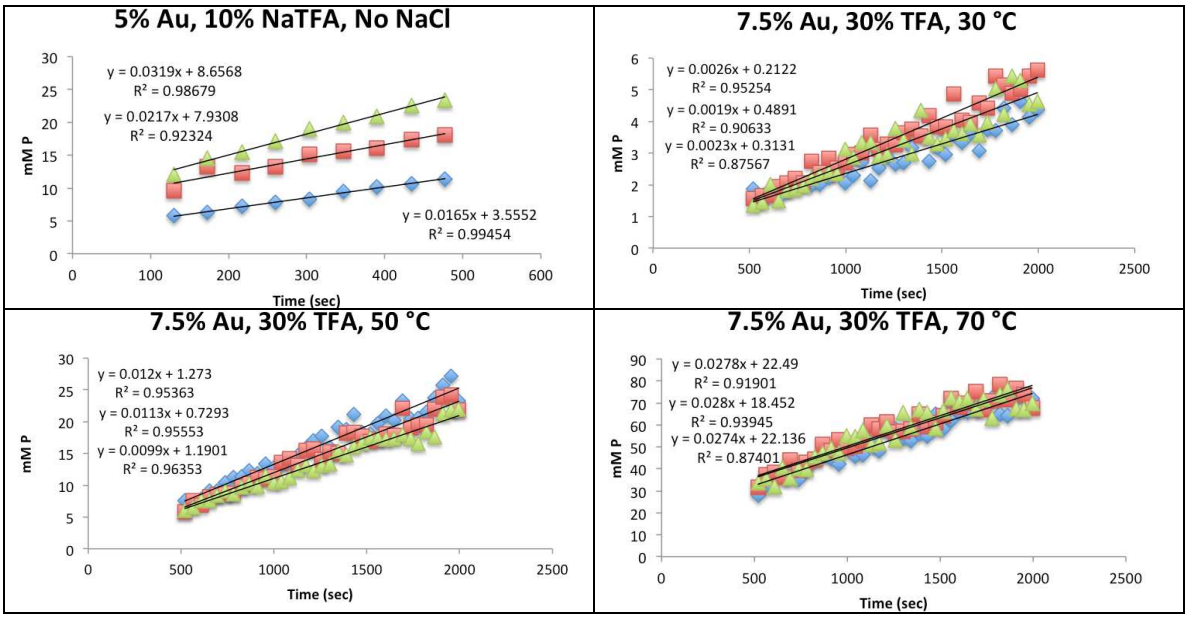


5% Au, 15% NaSbF6



5% Au, 5% NaTFA

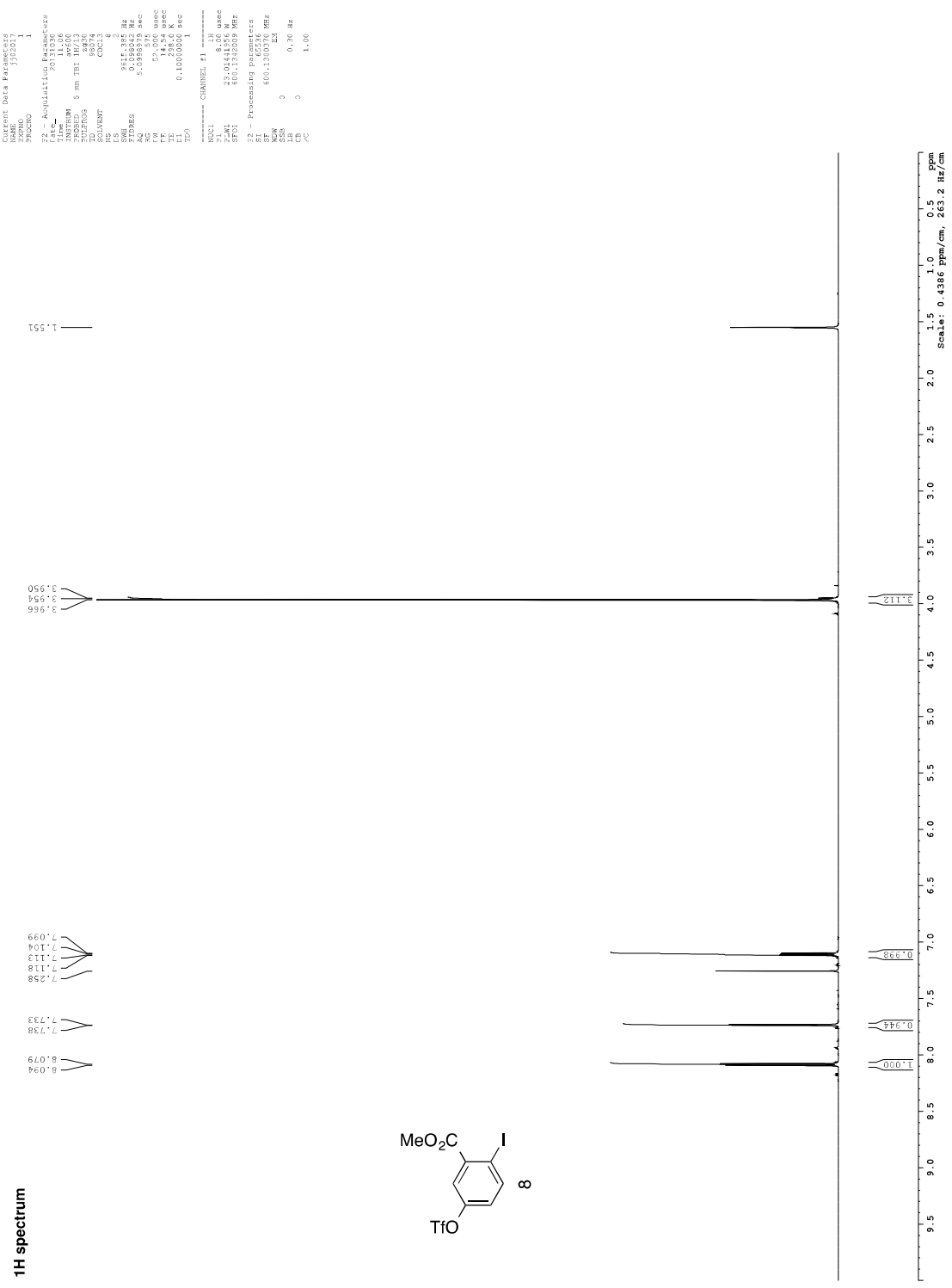




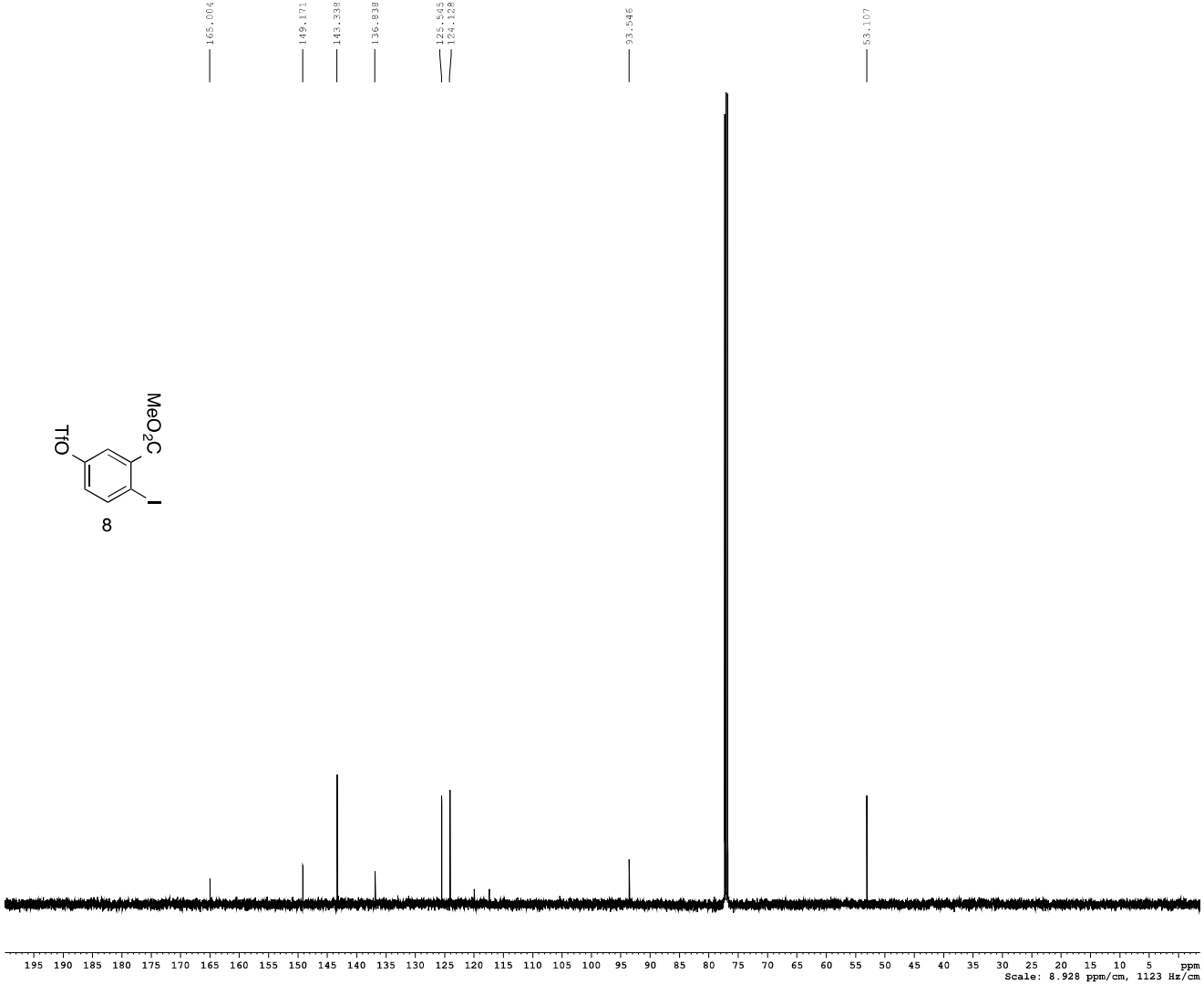
REFERENCES FOR EXPERIMENTAL SECTION

1.) Hirner, J. J.; Faizi, D. J.; Blum, S. A. *J. Am. Chem. Soc.* **2014**, *136*, 4740 – 4745.
2.) Chong, E.; Blum, S. A. *J. Am. Chem. Soc.* **2015**, *137*, 10144 − 10147.
3.) Jeon, J. Y.; Varghese, J. K.; Park, J. H.; Lee, S.; Lee, B. Y. *Eur. J. Org. Chem.* **2012**, *2012*, 3566 – 3569.

Appendix A: NMR Spectra



Z–restored spin–echo 13C spectrum with 1H decoupling



8

```
Current Data Parameters
NAME                  jj044
EXPNO                     3
PROCNO                    1

F2 - Acquisition Parameters
Date_              20130429
Time                  18.37
INSTRUM              cryo500
PROBHD     5 mm CPTCI 1H-
PULPROG    SpinEchopg30gp.prd
TD                    65536
SOLVENT               CDCl3
NS                     1024
DS                       16
SWH               30303.031 Hz
FIDRES            0.462388 Hz
AQ                1.0813940 sec
RG                   7298.2
DW                  16.500 usec
DE                   6.00 usec
TE                  298.0 K
D1                0.25000000 sec
D11               0.03000000 sec
D16               0.00020000 sec
D17               0.00019600 sec
MCREST     0 sec
MCWRK             0.01500000 sec
P2                   31.00 usec

======== CHANNEL f1 ========
NUC1                    13C
P1                    15.50 usec
P11                  500.00 usec
P12                 2000.00 usec
PL0                  120.00 dB
PL1                   -1.00 dB
SFO1           125.7942548 MHz
SF1                   3.20 dB
SF2                   3.20 dB
SPNAM1     Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SPOFF1     0 Hz
SPOFF2     0 Hz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2                100.00 usec
PL2                   1.60 dB
PL12                 24.80 dB
SFO2           500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1              SINE.100
GPNAM2              SINE.100
GPX1       0 %
GPX2       0 %
GPY1       0 %
GPY2       0 %
GPZ1                 30.00 %
GPZ2                 50.00 %
p19                 500.00 usec
p16                1000.00 usec

F2 - Processing parameters
SI                    65536
SF             125.7804188 MHz
WDW                      EM
SSB       0
LB                    1.00 Hz
GB        0
PC                    2.00
```

19F spectrum

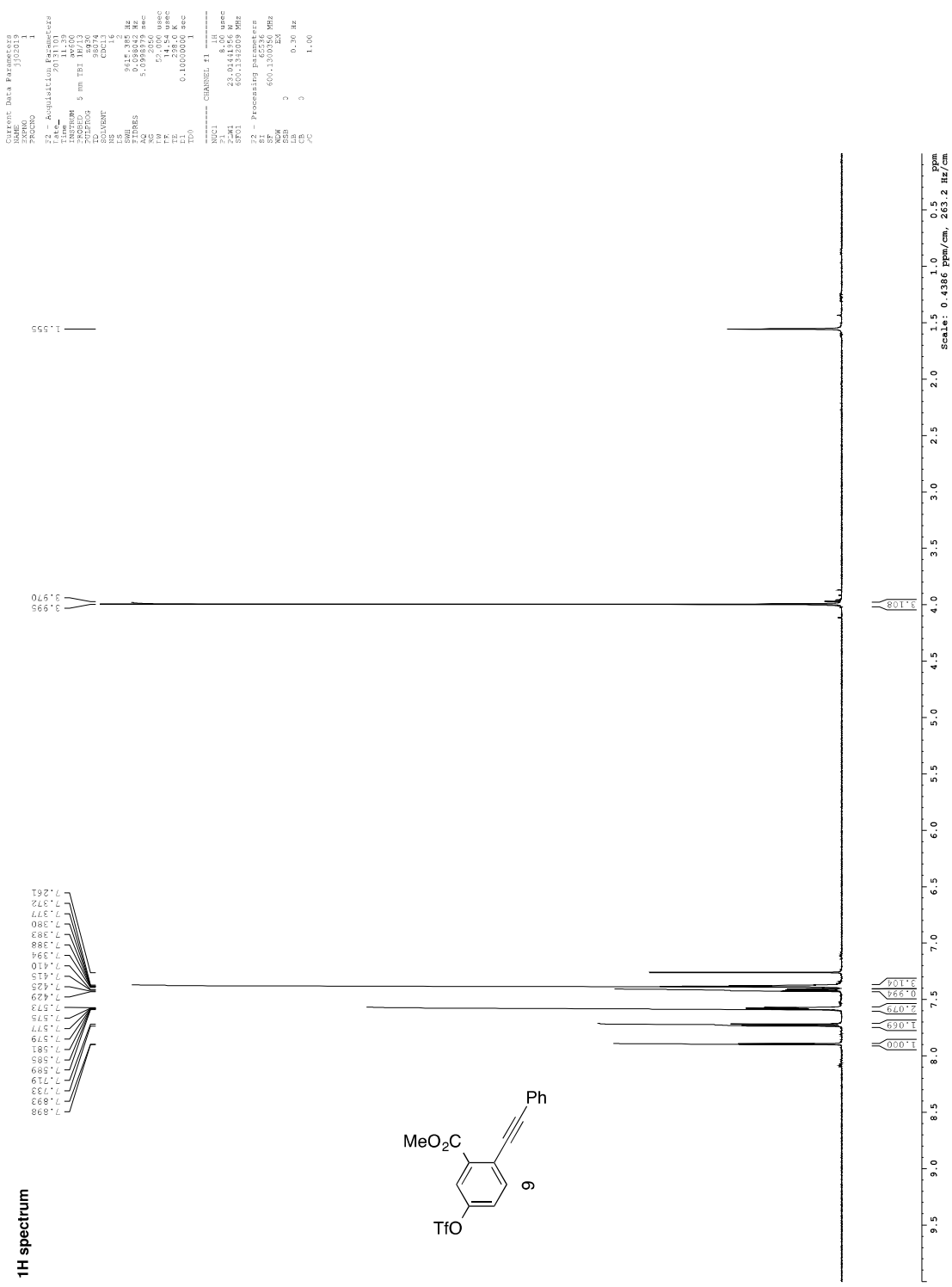
8

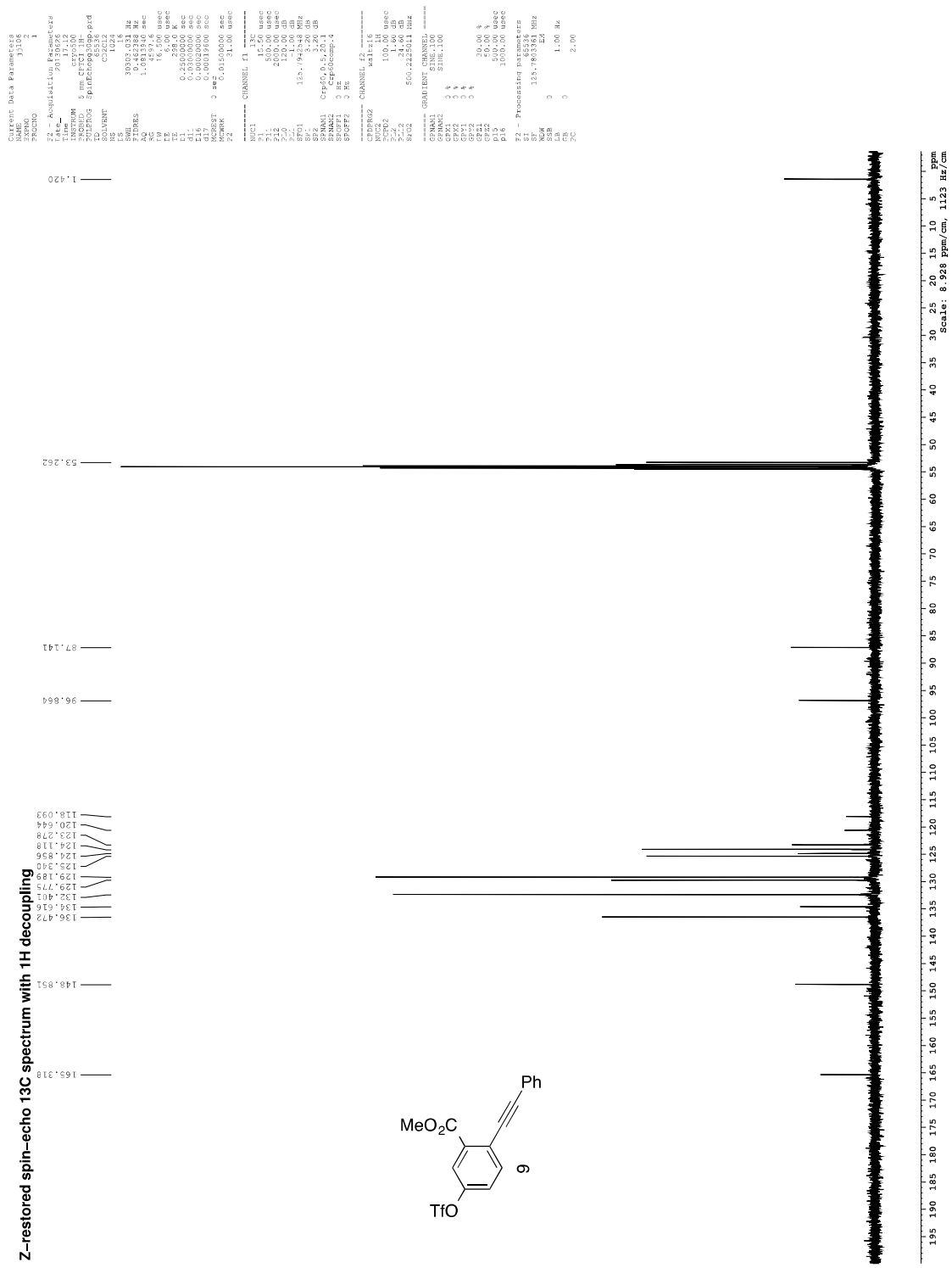

```
Current Data Parameters
NAME                  jj022017
EXPNO                        3
PROCNO                       1

F2 - Acquisition Parameters
Date_              20131030
Time                   11.32
INSTRUM                drx400
PROBHD   5 mm CNP H/F/C
PULPROG             zgflqn30
TD                     65536
SOLVENT                CDCl3
NS                        55
DS                         2
SWH                75187.969 Hz
FIDRES                 1.147277 Hz
AQ                     0.4358644 sec
RG                      1824.6
DW                        6.650 usec
DE                        9.46 usec
TE                      298.0 K
D1                   2.00000000 sec

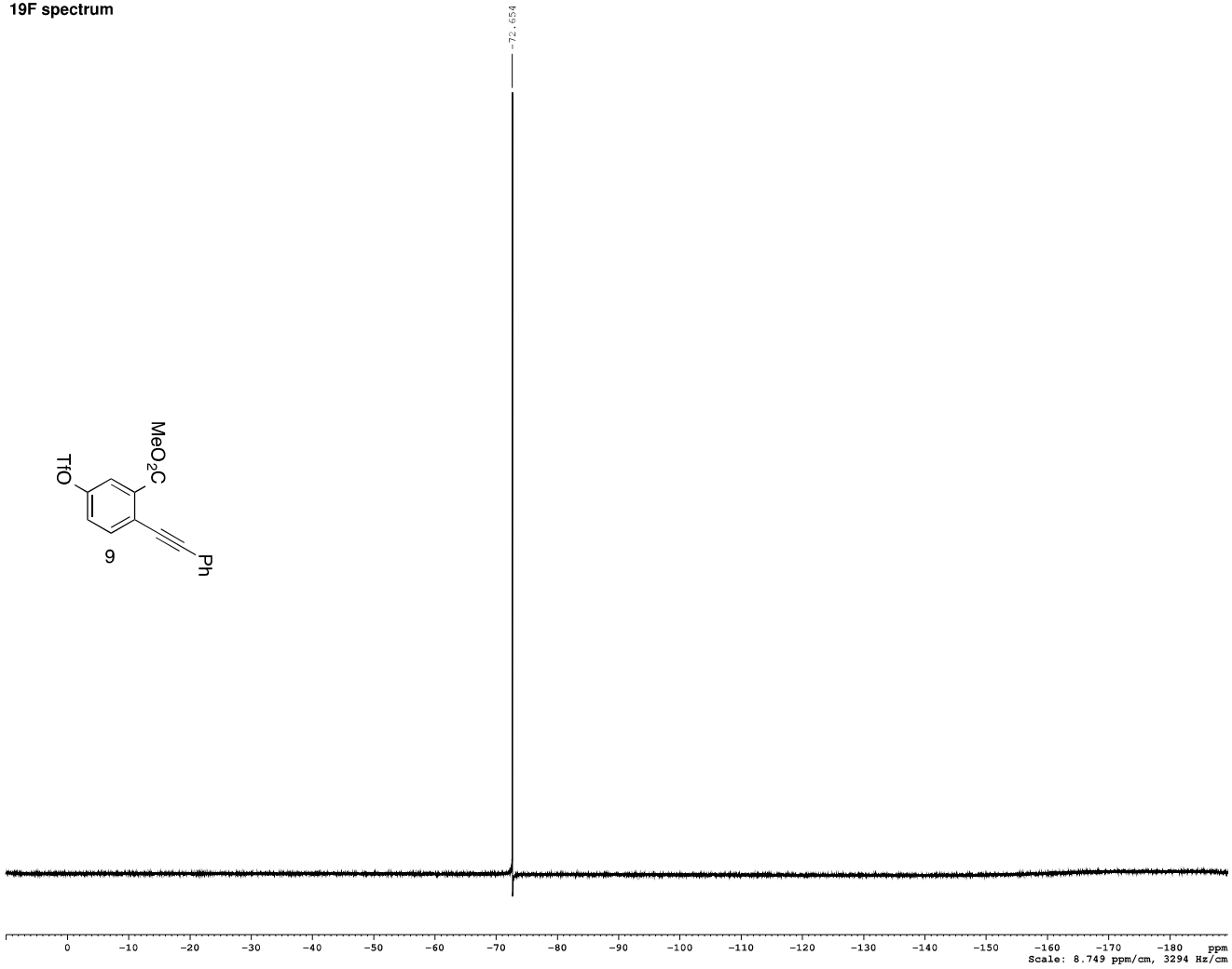
======== CHANNEL f1 ========
NUC1                      19F
P1                      22.50 usec
PL1                     -6.00 dB
SFO1                376.4646491 MHz

F2 - Processing parameters
SI                        65536
SF                  376.4983832 MHz
WDW                        EM
SSB          0
LB                      1.00 Hz
GB           0
PC                      1.00
```


1H spectrum
Ph
MeO2C
TfO
6
Scale: 0.4386 ppm/cm, 263.2 Hz/cm
ppm


Z–restored spin–echo 13C spectrum with 1H decoupling
MeO2C
Ph
TfO
6
Scale: 8.928 ppm/cm, 1123 Hz/cm

19F spectrum

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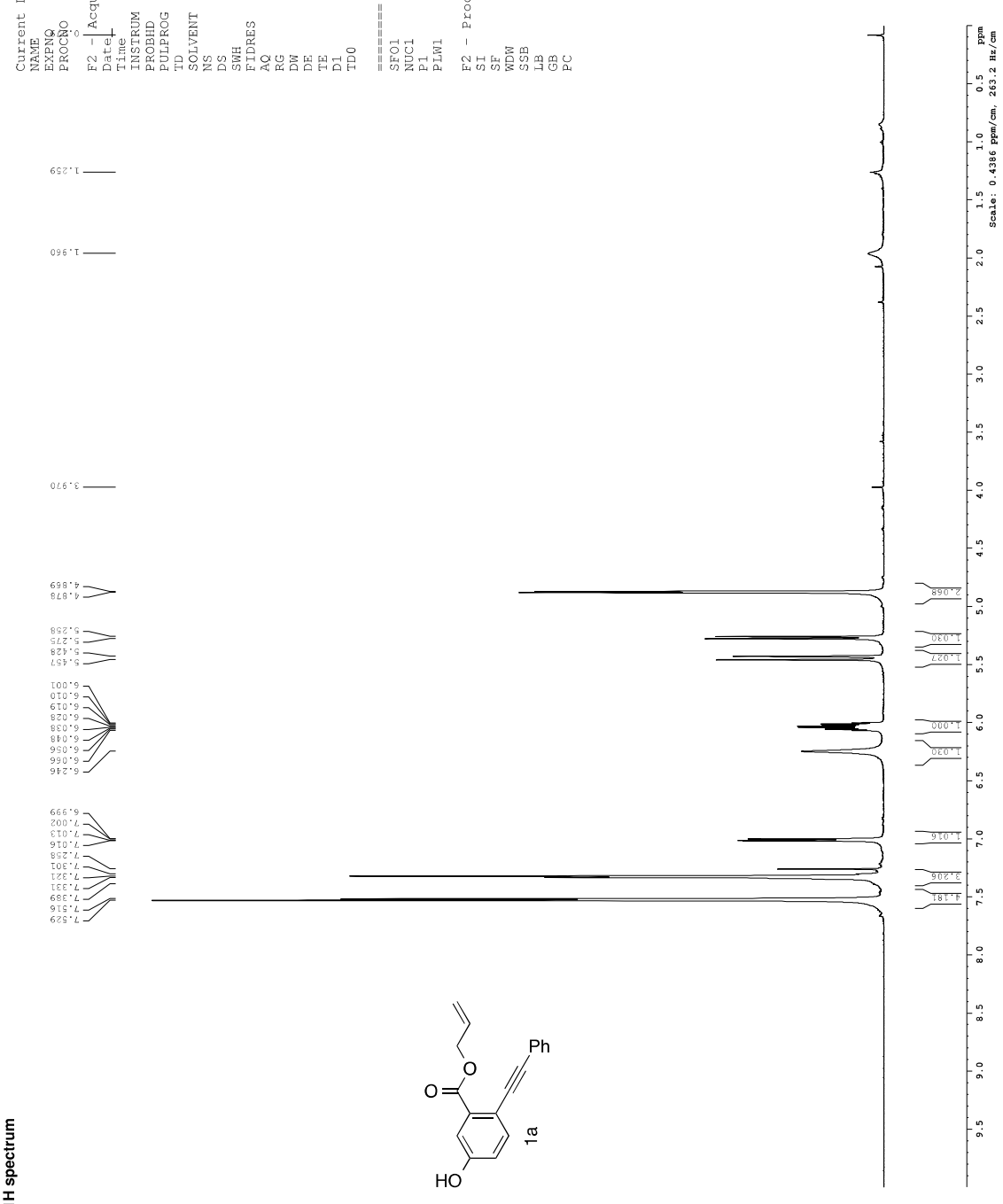
Current Data Parameters
NAME                  jj02019
EXPNO                       3
PROCNO                      1

F2 - Acquisition Parameters
Date_              20131101
Time                   12.01
INSTRUM                drx400
PROBHD   5 mm CNP H/F/C
PULPROG             zgflqn30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                75187.969 Hz
FIDRES                 1.147277 Hz
AQ                     0.4358644 sec
RG                      1449.2
DW                        6.650 usec
DE                        9.46 usec
TE                       298.0 K
D1                  2.00000000 sec

======== CHANNEL f1 ========
NUC1                       19F
P1                       22.50 usec
PL1                      -6.00 dB
SFO1                376.4646491 MHz

F2 - Processing parameters
SI                         65536
SF                  376.4983829 MHz
WDW                           EM
SSB                0
LB                        1.00 Hz
GB                 0
PC                        1.00
```

1H spectrum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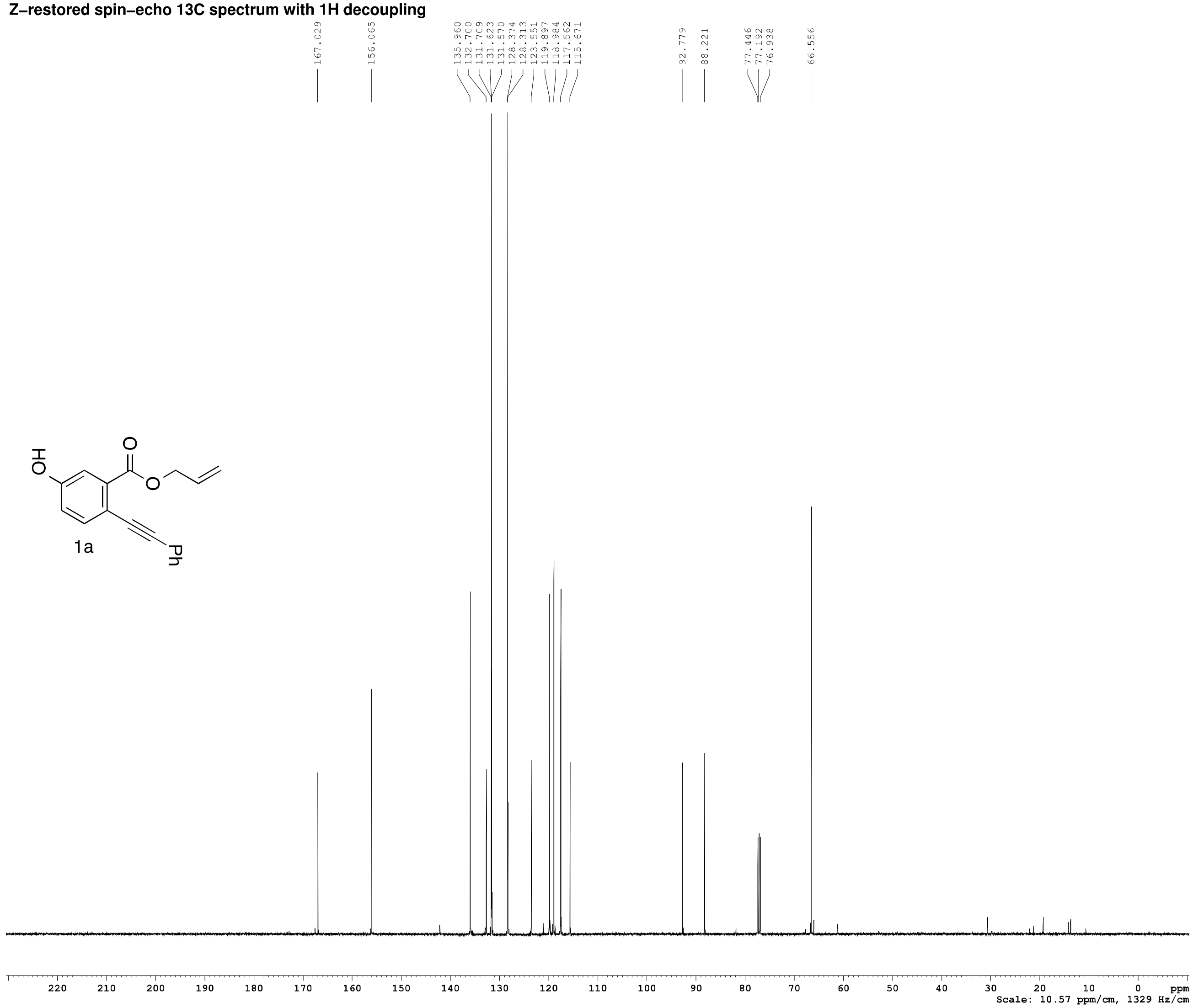
NAME jj02136
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140522
Time 11.07
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 406
DW 52.000 use
DE 14.54 use
TE 298.1 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 use
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300355 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1.259
1.960
3.970
4.878
4.869
5.457
5.428
5.275
5.258
6.001
6.019
6.028
6.038
6.048
6.056
6.066
6.246
6.999
7.002
7.015
7.016
7.258
7.301
7.321
7.331
7.389
7.516
7.529
2.068
1.030
1.027
1.000
1.030
1.016
3.206
4.181
O
O
Ph
HO
1a
Scale: 0.4386 ppm/cm, 263.2 Hz/cm
ppm

Z–restored spin–echo 13C spectrum with 1H decoupling

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EXPNO                 4
PROCNO                1

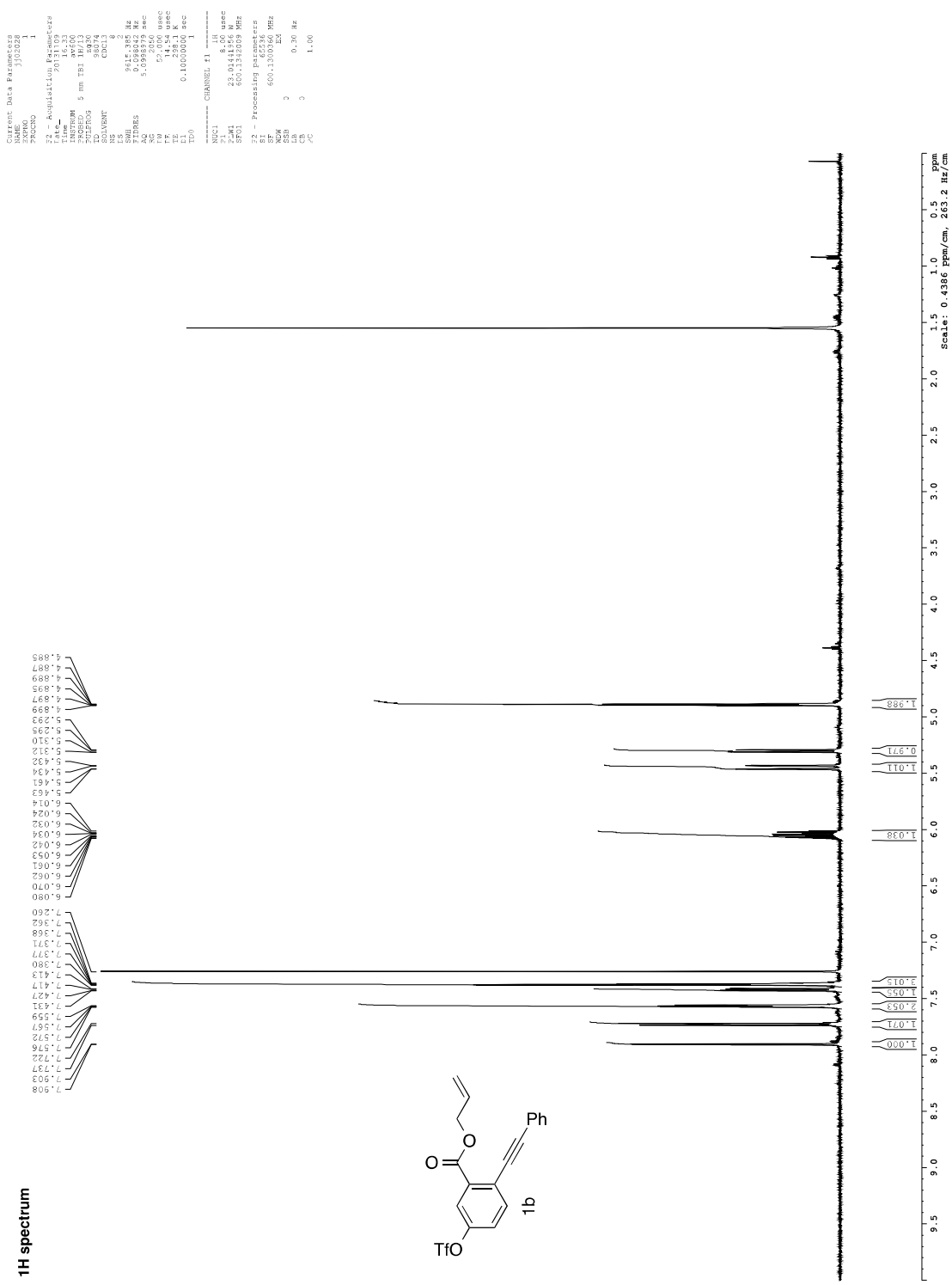
F2 - Acquisition Parameters
Date_          20131106
Time              10.53
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  524
DS                   16
SWH           30303.031 Hz
FIDRES         0.462388 Hz
AQ            1.0813940 sec
RG                13004
DW               16.500 usec
DE                 6.00 usec
TE                298.0 K
D1           0.25000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST   0 sec
MCWRK        0.01500000 sec
P2                31.00 usec

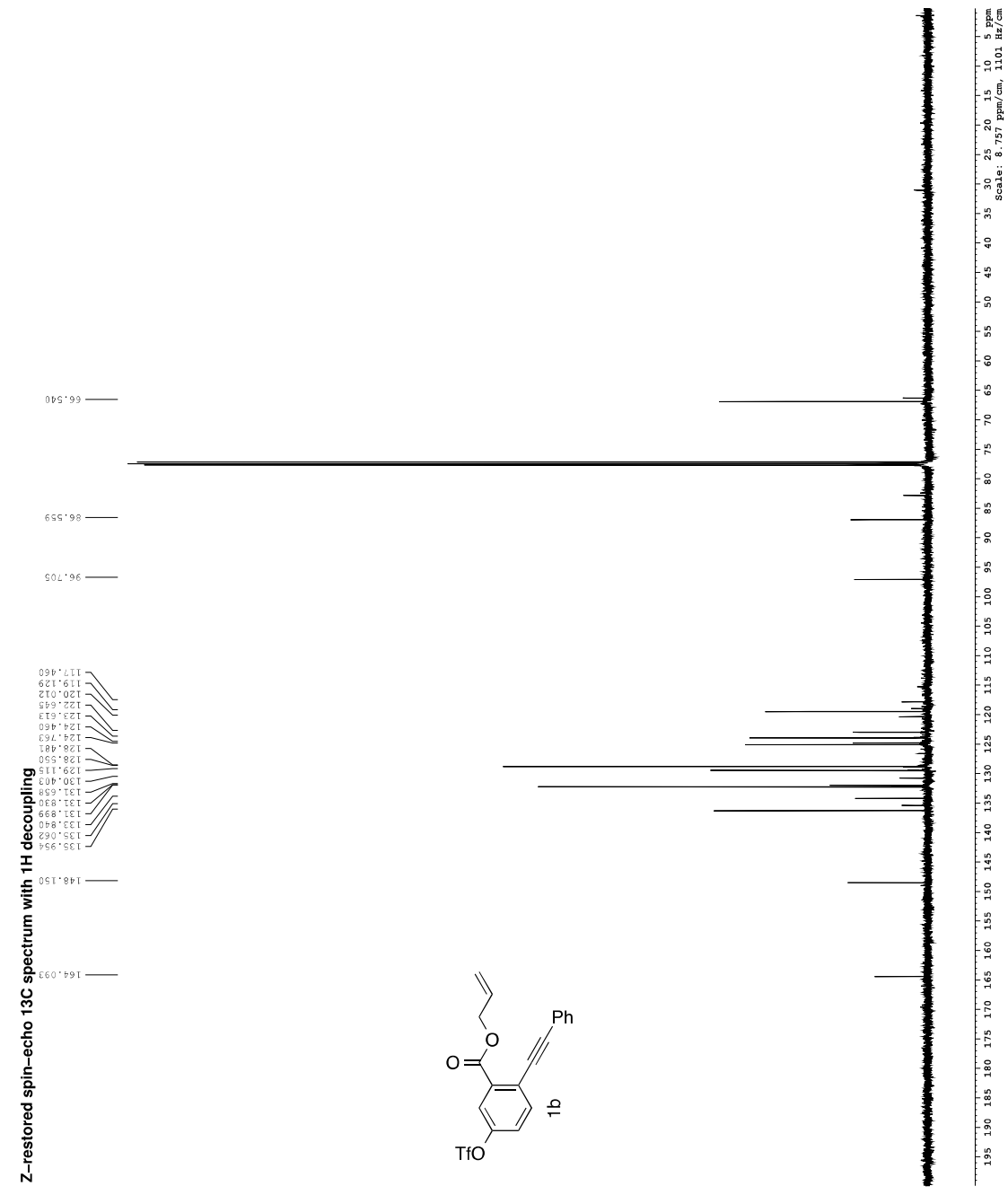
======== CHANNEL f1 ========
NUC1                13C
P1                15.50 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MHz
SP1                3.20 dB
SP2                3.20 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1   0 Hz
SPOFF2   0 Hz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                 1H
PCPD2            100.00 usec
PL2                1.60 dB
PL12              24.60 dB
SFO2        500.2225011 MHz

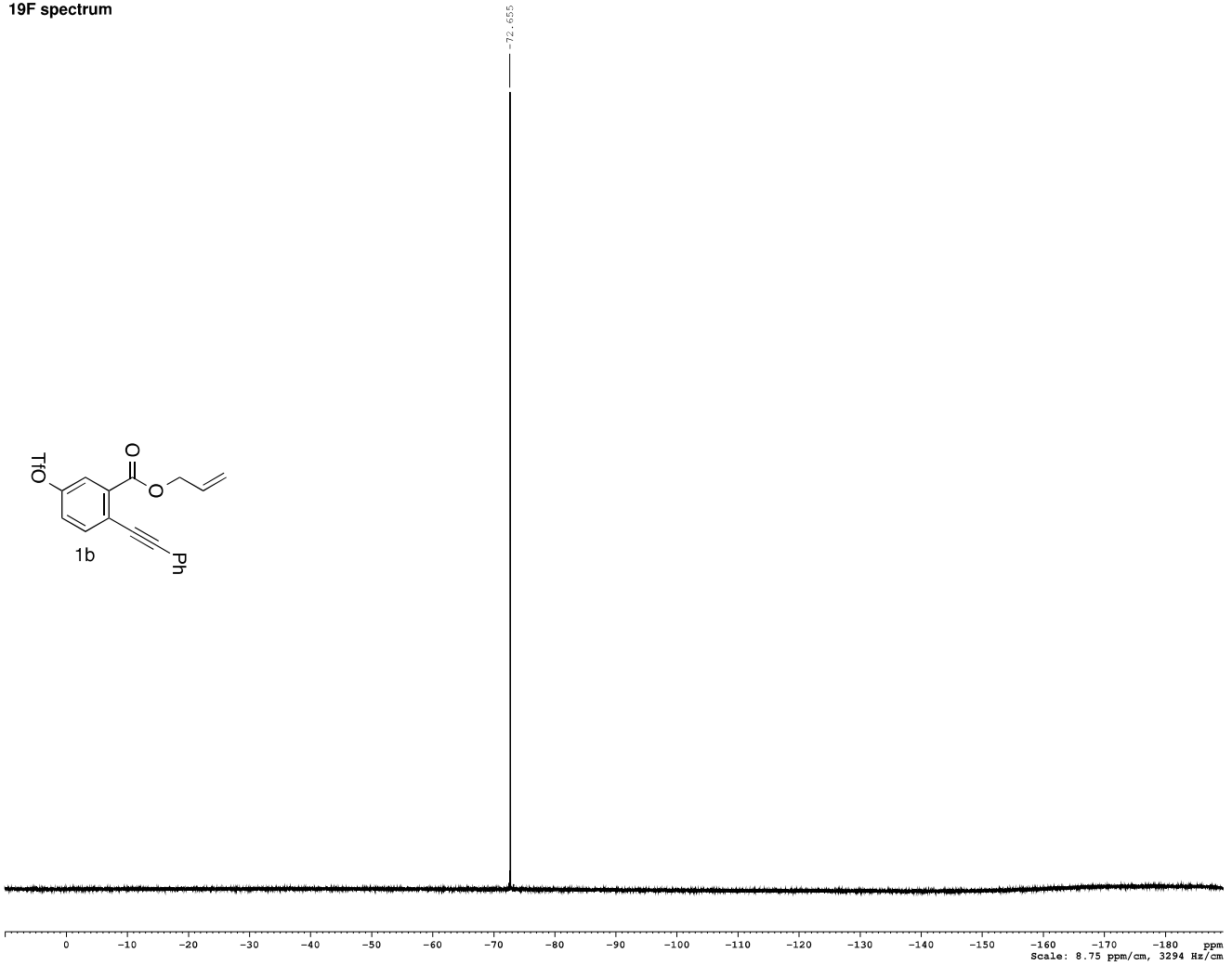
====== GRADIENT CHANNEL =====
GPNAM1         SINE.100
GPNAM2         SINE.100
GPX1     0 %
GPX2     0 %
GPY1     0 %
GPY2     0 %
GPZ1              30.00 %
GPZ2              50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                65536
SF          125.7804190 MHz
WDW                  EM
SSB      0
LB                 1.00 Hz
GB       0
PC                 2.00
```


1H spectrum
Ph
O
O
TfO
1b
ppm
Scale: 0.4386 ppm/cm, 263.2 Hz/cm


Z–restored spin–echo 13C spectrum with 1H decoupling
Ph
O
O
TfO
1b
Scale: 8.757 ppm/cm, 1101 Hz/cm

19F spectrum

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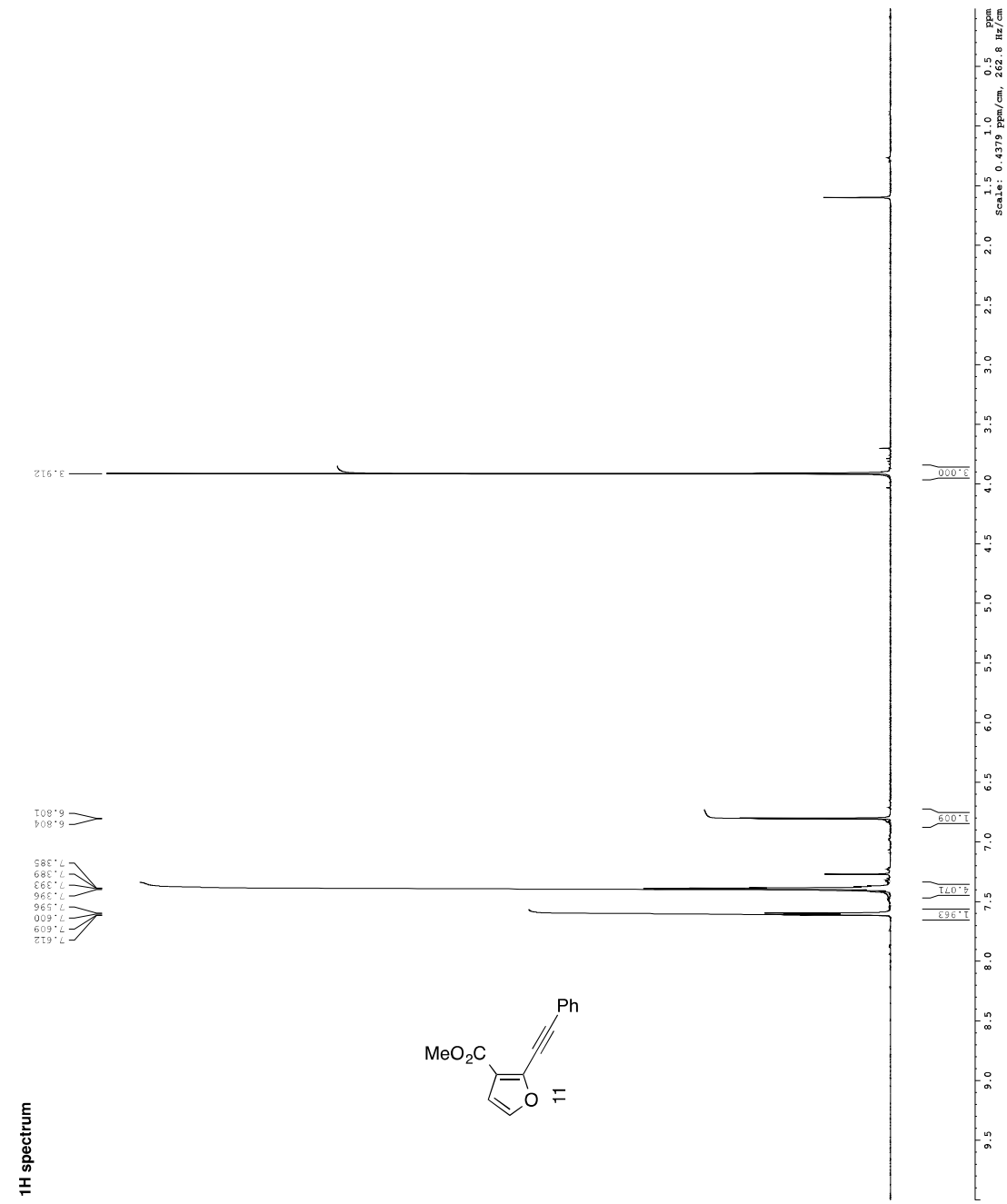
Current Data Parameters
NAME                  jj02028
EXPNO                       3
PROCNO                      1

F2 - Acquisition Parameters
Date_              20131109
Time                   16.51
INSTRUM                drx400
PROBHD   5 mm CNP H/F/C
PULPROG             zgflqn30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                75187.969 Hz
FIDRES                 1.147277 Hz
AQ                     0.4358644 sec
RG                        3251
DW                     6.650 usec
DE                     9.46 usec
TE                     298.0 K
D1                  2.00000000 sec

======== CHANNEL f1 ========
NUC1                      19F
P1                     22.50 usec
PL1                    -6.00 dB
SFO1               376.4646491 MHz

F2 - Processing parameters
SI                        65536
SF                 376.4983831 MHz
WDW                        EM
SSB          0
LB                      1.00 Hz
GB           0
PC                      1.00
```


Current Data Parameters
NAME JJ02025
EXPNO 3
PROCNO 1
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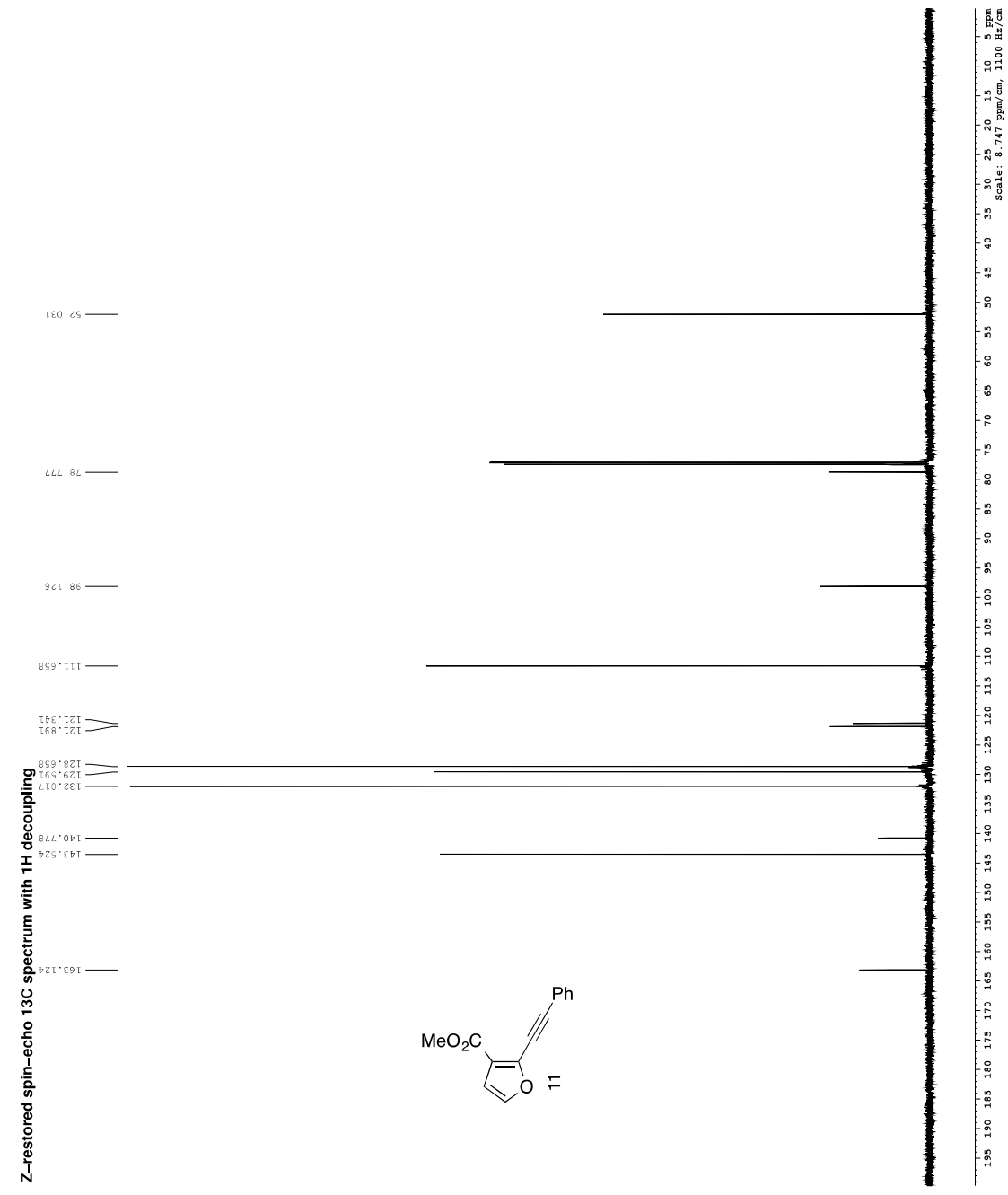
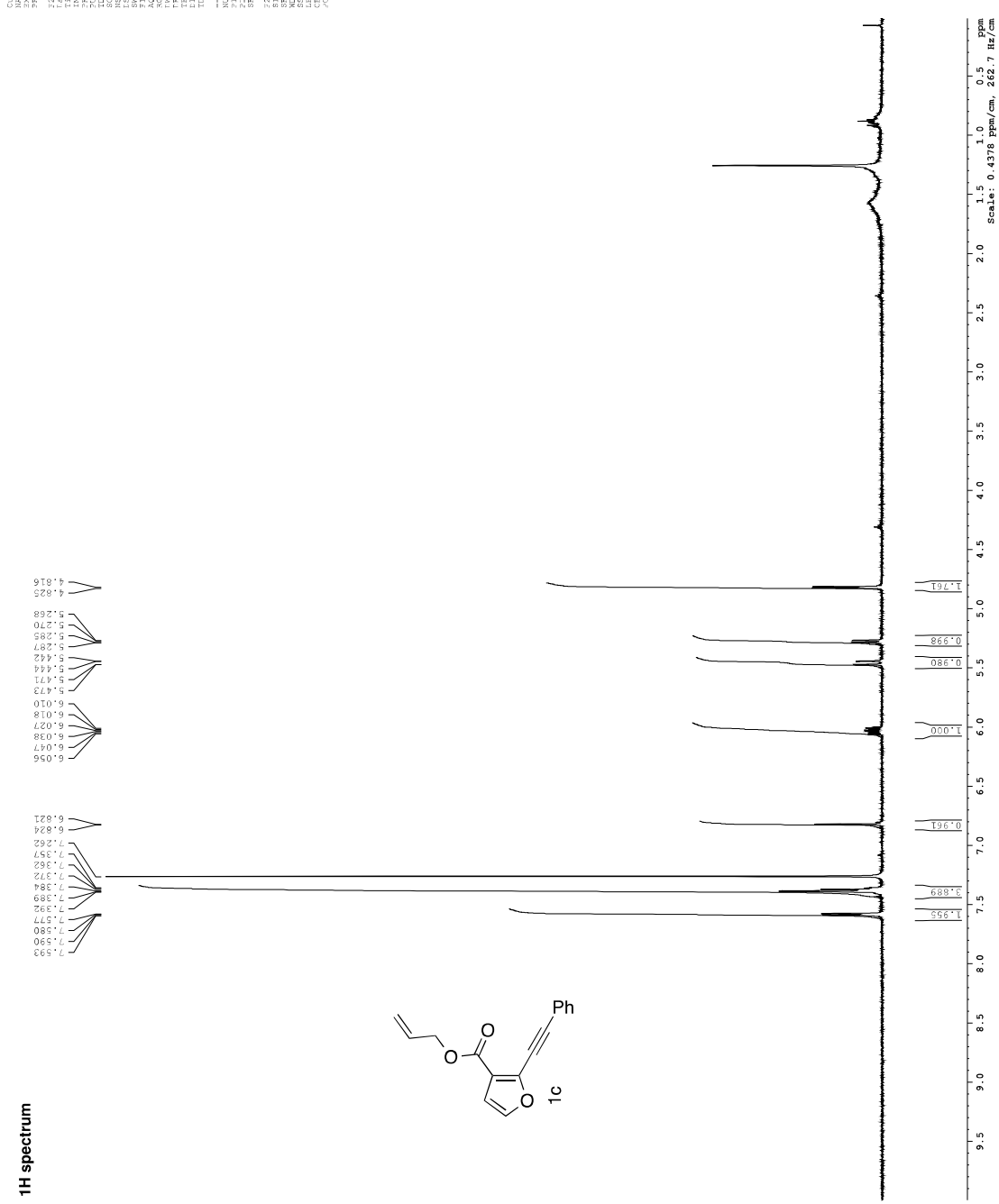
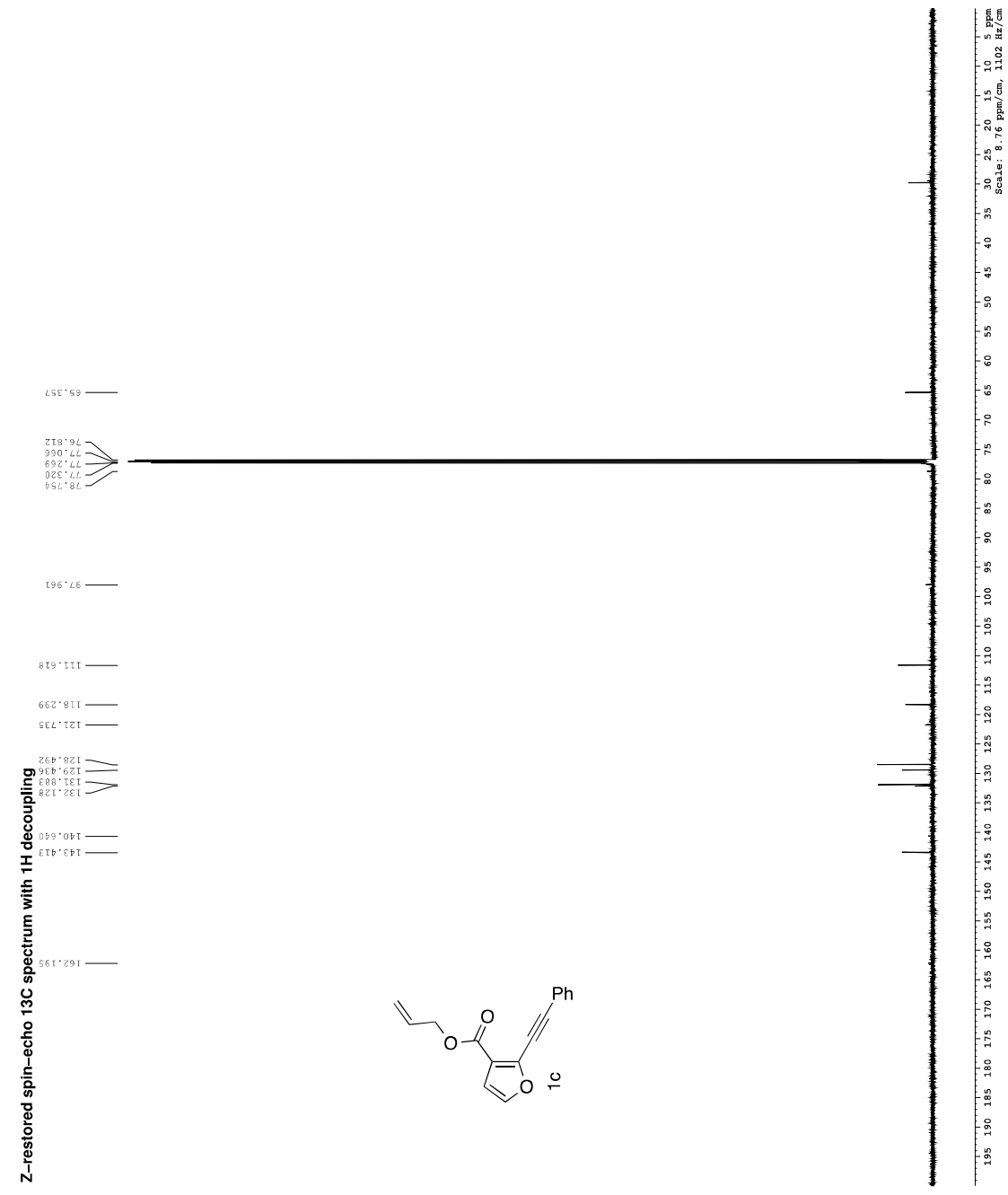
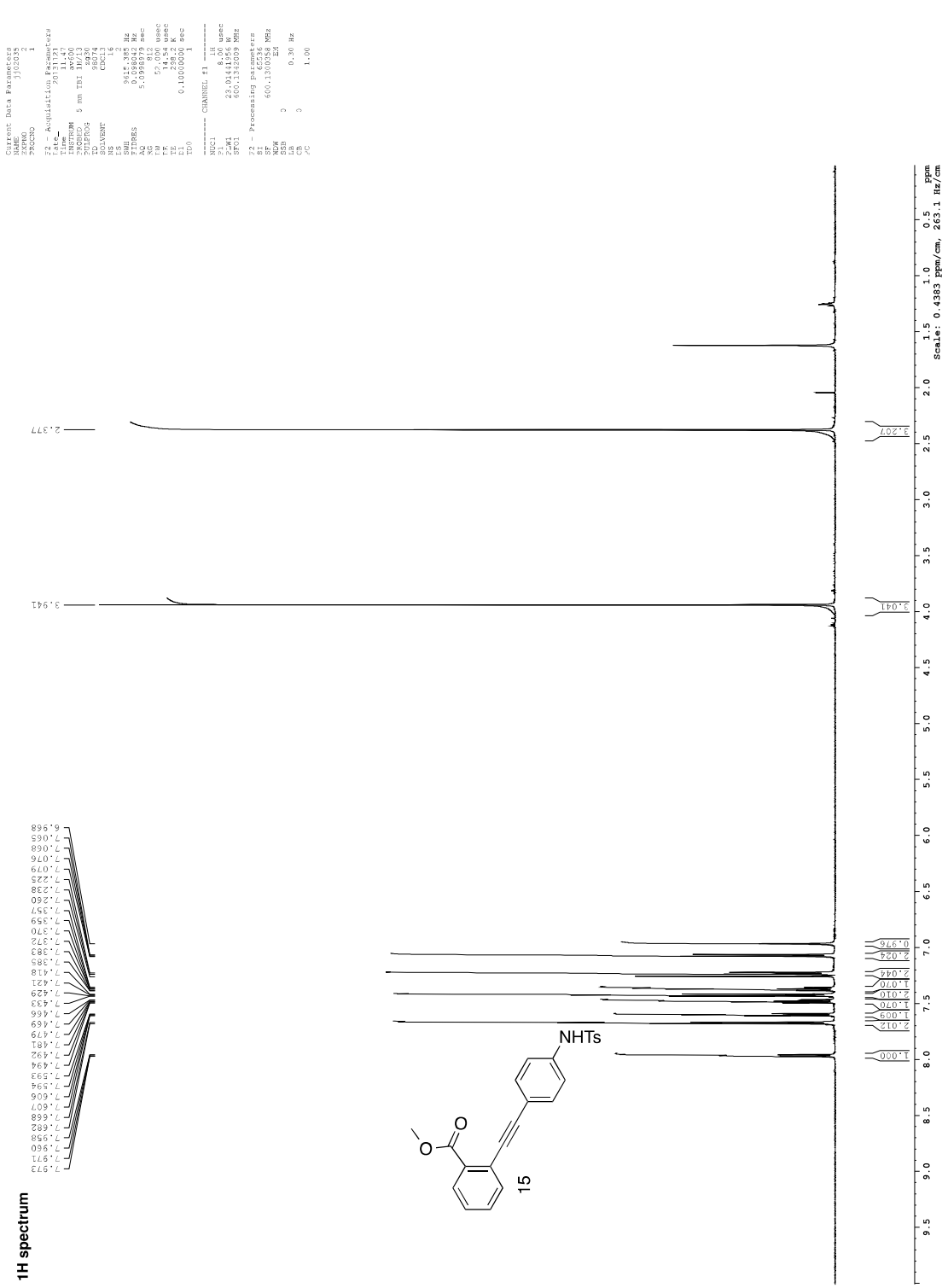
Date_ 20171109
Time 16.38
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 88074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998879 sec
RG 812.82
DW 52.000 usec
DE 14.54 usec
TE 298.1 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PL1 23.01411156 W
SFO1 600.1342009 MHz
F2 - Processing parameters
SI 65536
SF 600.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.612
7.609
7.600
7.596
7.396
7.393
7.389
7.385
6.804
6.801
3.912
1.963
4.071
1.009
3.000
MeO2C
Ph
O
11
1H spectrum
Scale: 0.4379 ppm/cm, 262.8 Hz/cm
ppm


Z–restored spin–echo 13C spectrum with 1H decoupling
163.124
143.524
140.778
132.017
129.591
128.658
121.891
121.341
111.658
98.126
78.777
52.031
MeO2C
Ph
O
11
Scale: 8.747 ppm/cm, 1100 Hz/cm

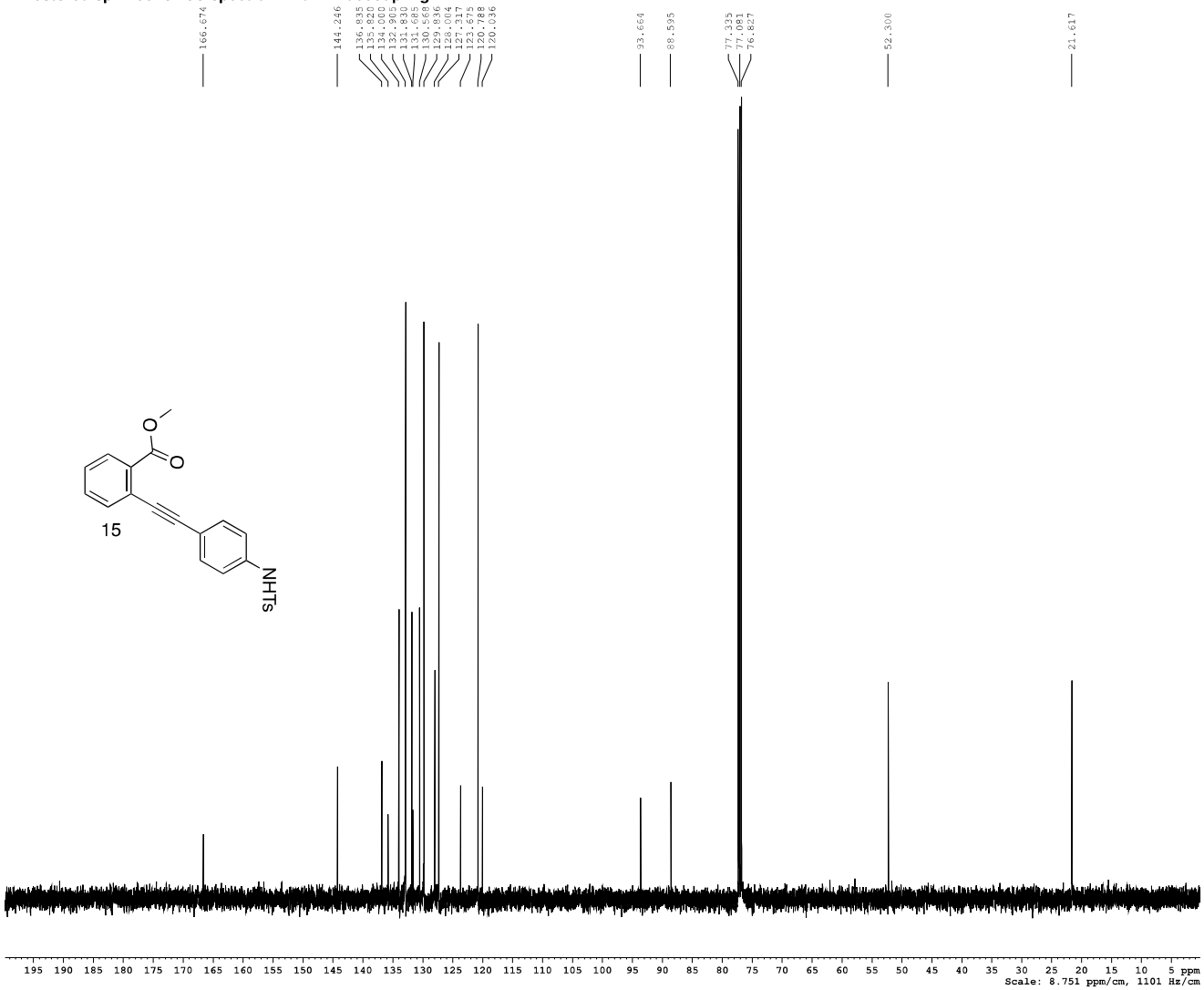
1H spectrum


Current Data Parameters
NAME
EXPNO
PROCNO
F2 - Acquisition Parameters
Date_
Time
INSTRUM
PROBHD
PULPROG
TD
SOLVENT
NS
DS
SWH
FIDRES
AQ
RG
DW
DE
TE
D1
TD0
======== CHANNEL f1 ========
NUC1
P1
SFO1
F2 - Processing parameters
SI
SF
WDW
SSB
LB
GB
PC
7.593
7.580
7.577
7.392
7.389
7.384
7.372
7.362
7.357
7.262
6.824
6.821
6.056
6.047
6.038
6.027
6.018
6.010
5.473
5.471
5.444
5.442
5.287
5.285
5.270
5.268
4.825
4.816
1.761
0.998
0.980
1.000
0.961
3.889
1.955
Ph
O
O
O
1c
ppm
Scale: 0.4378 ppm/cm, 262.7 Hz/cm


Z–restored spin–echo 13C spectrum with 1H decoupling
Ph
O
O
O
1c
Scale: 8.76 ppm/cm, 1102 Hz/cm


1H spectrum
NHTs
O
O
15
Scale: 0.4383 ppm/cm, 263.1 Hz/cm
ppm

Z–restored spin–echo 13C spectrum with 1H decoupling




```
Current Data Parameters
NAME                  jj02035
EXPNO                       3
PROCNO                      1

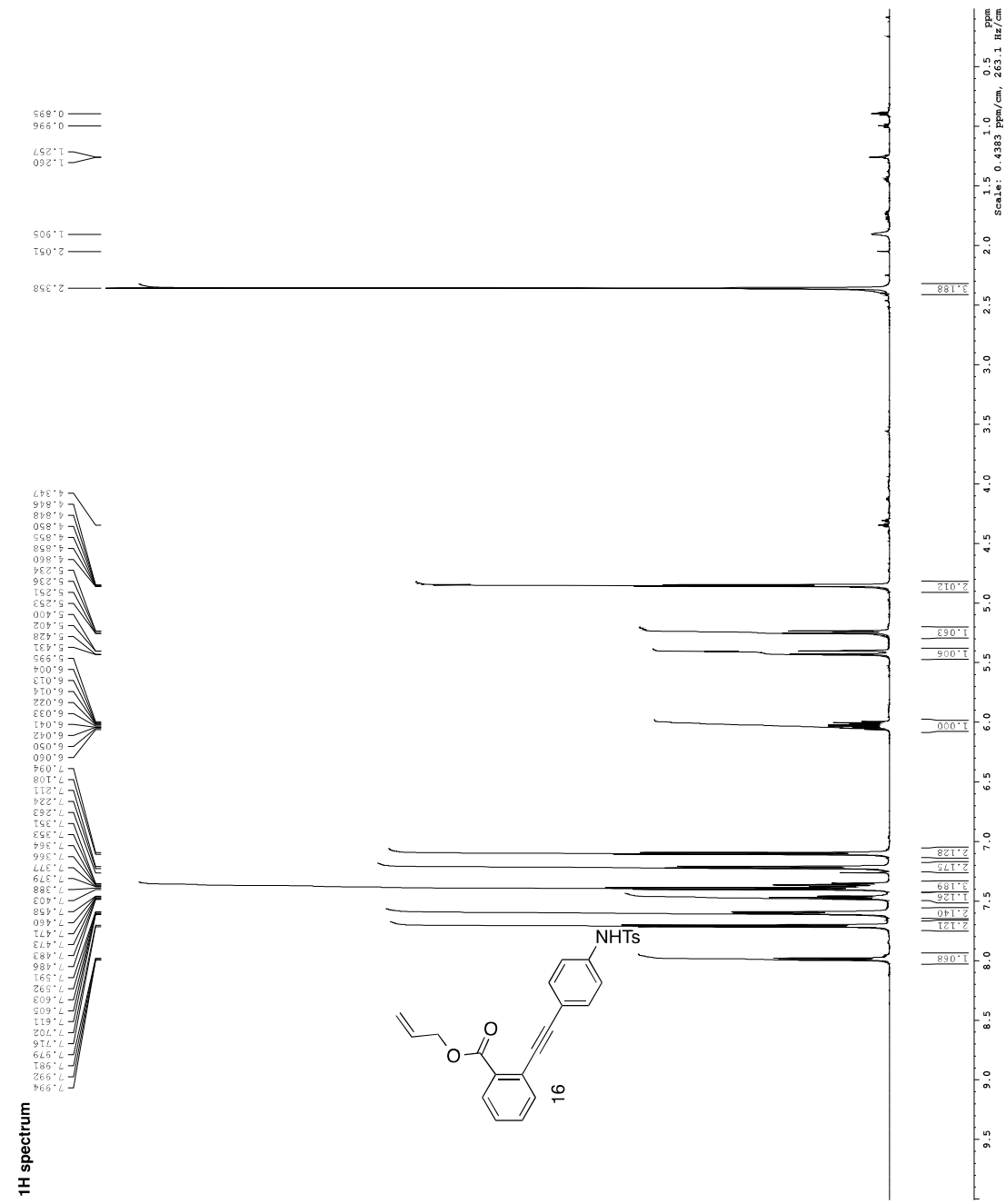
F2 - Acquisition Parameters
Date_              20131121
Time                   12.01
INSTRUM                cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30qp.prd
TD                      65536
SOLVENT                 CDCl3
NS                        434
DS                         16
SWH                30303.031 Hz
FIDRES             0.462388 Hz
AQ                 1.08113940 sec
RG                     7298.2
DW                    16.500 usec
DE                     6.00 usec
TE                     298.0 K
D1                 0.25000000 sec
d11                0.03000000 sec
D16                0.00020000 sec
d17                0.00019600 sec
MCREST    0 sec
MCWRK              0.01500000 sec
P2                    31.00 usec

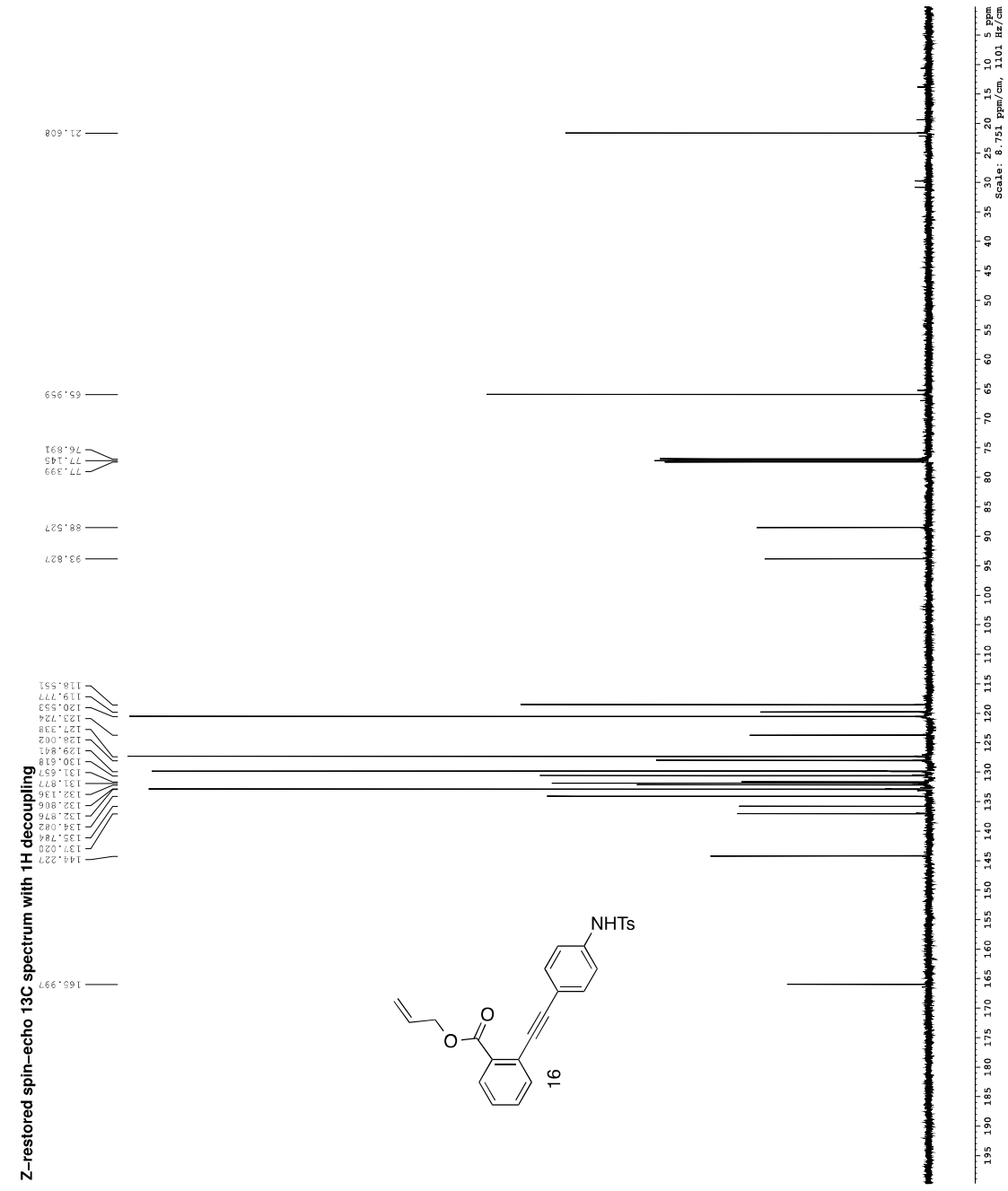
======== CHANNEL f1 ========
NUC1                      13C
P1                      15.50 usec
PL1                    500.00 usec
PL2                   2000.00 usec
PL0                    120.00 dB
PL1                     -1.00 dB
SFO1              125.7942548 MHz
SP1                     3.20 dB
SP2                     3.20 dB
SPNAM1     Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SPOFF1    0 Hz
SPOFF2    0 Hz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                        1H
PCPD2                  100.00 usec
PL2                      1.60 dB
PL12                    24.80 dB
SFO2              500.2225011 MHz

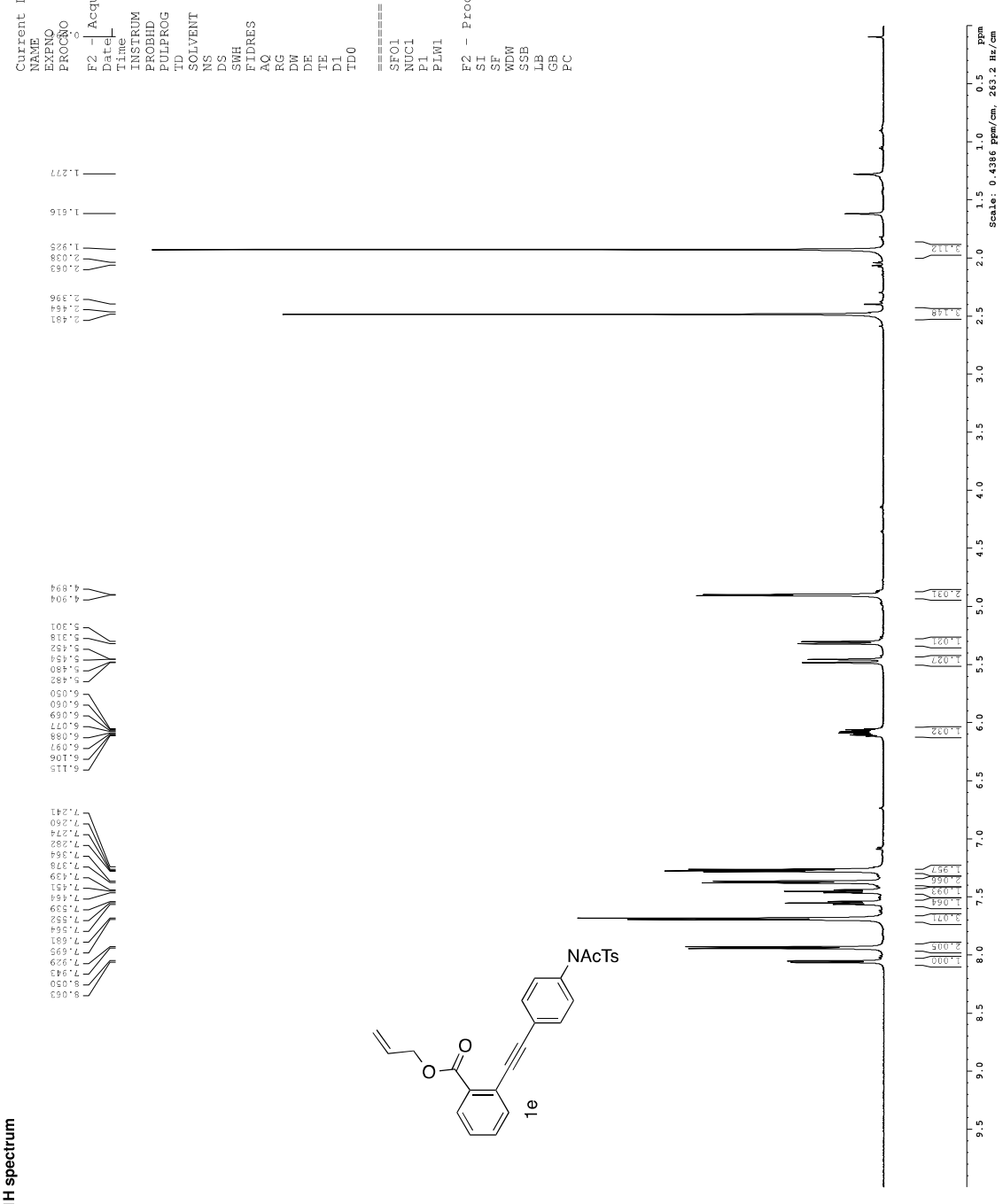
====== GRADIENT CHANNEL =====
GPNAM1                SINE.100
GPNAM2                SINE.100
GPX1      0 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1                    30.00 %
GPZ2                    80.00 %
p19                    500.00 usec
p16                   1000.00 usec

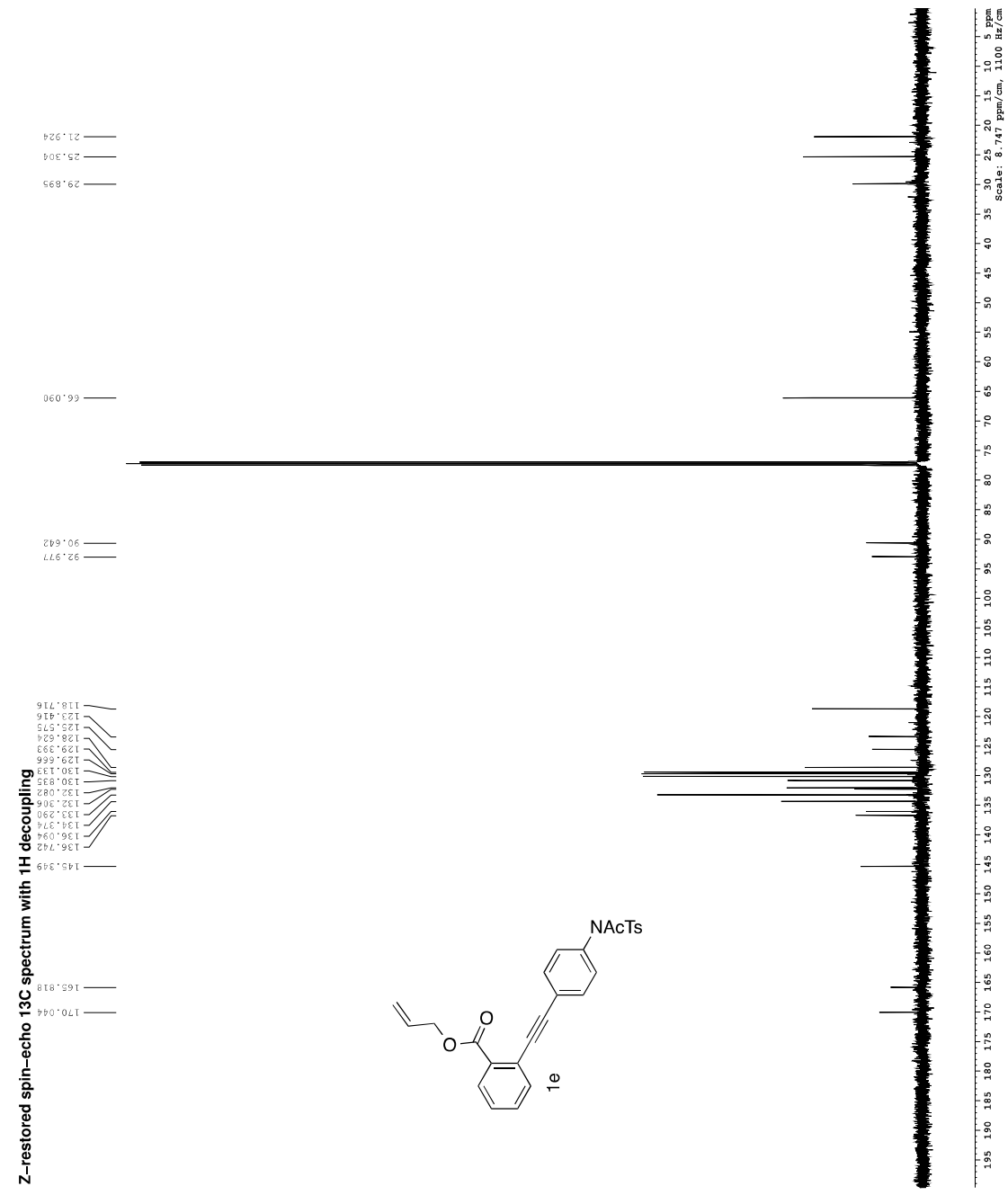
F2 - Processing parameters
SI                        65536
SF                125.7804188 MHz
WDW                          EM
SSB       0
LB                       1.00 Hz
GB        0
PC                       2.00
```


1H spectrum
NHTs
O
O
16

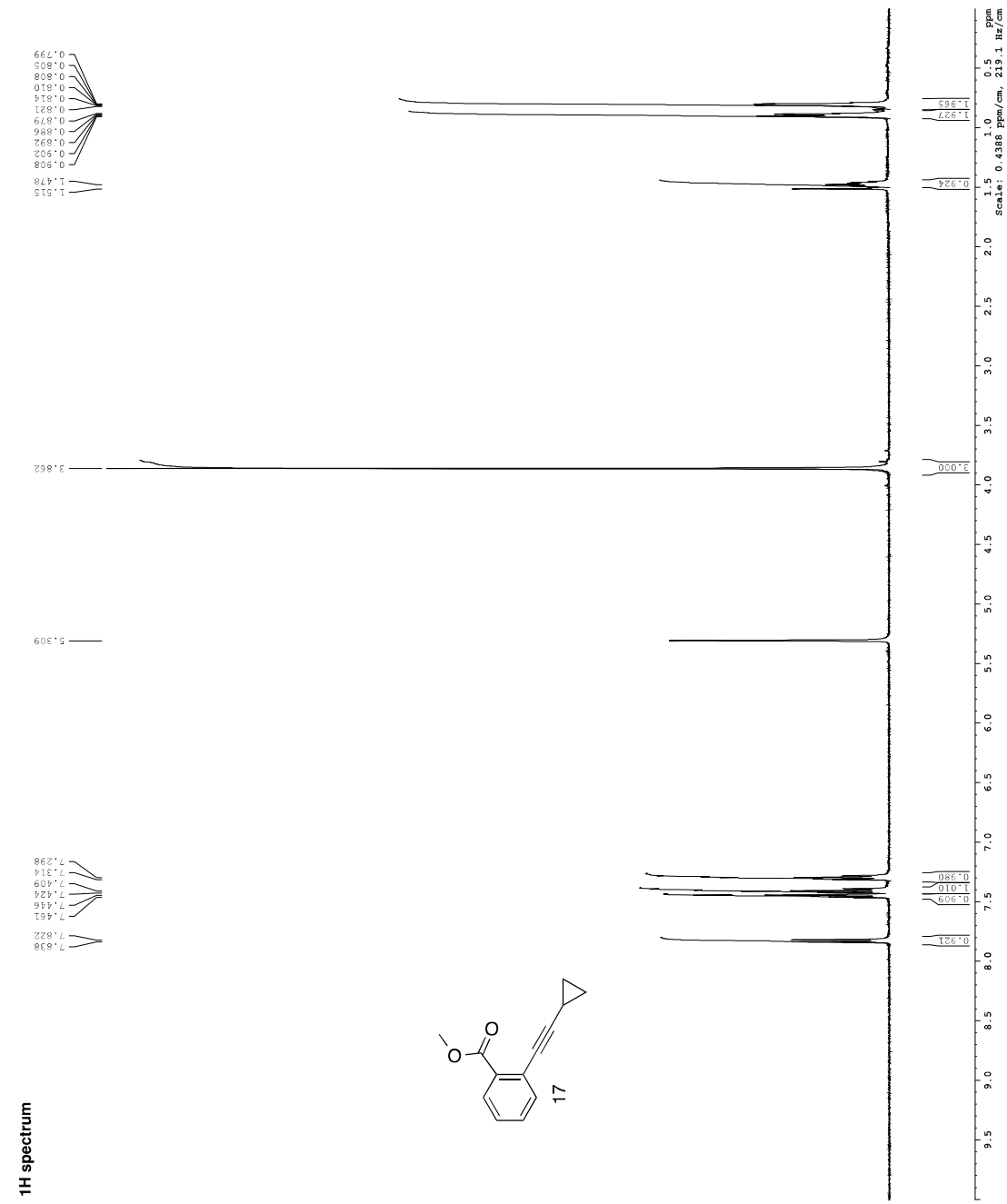

Z–restored spin–echo 13C spectrum with 1H decoupling
NHTs
16
Scale: 8.751 ppm/cm, 1101 Hz/cm

1H spectrum

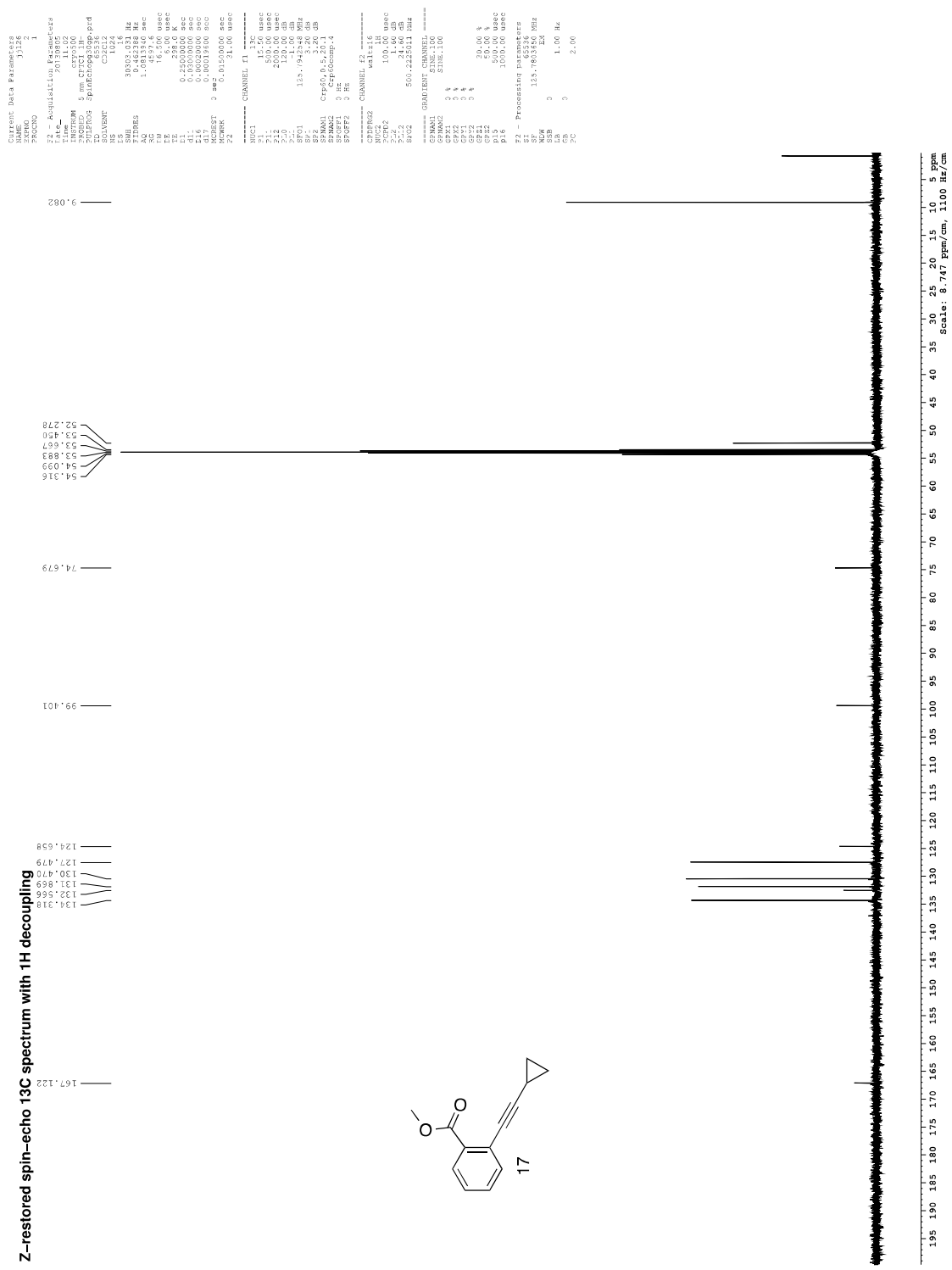

Current Data Parameters
NAME jj02145
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140617
Time 7.27
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 724
DW 52.000 use
DE 14.54 use
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 use
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300211 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
NAcTs
1e
Scale: 0.4386 ppm/cm, 263.2 Hz/cm
ppm

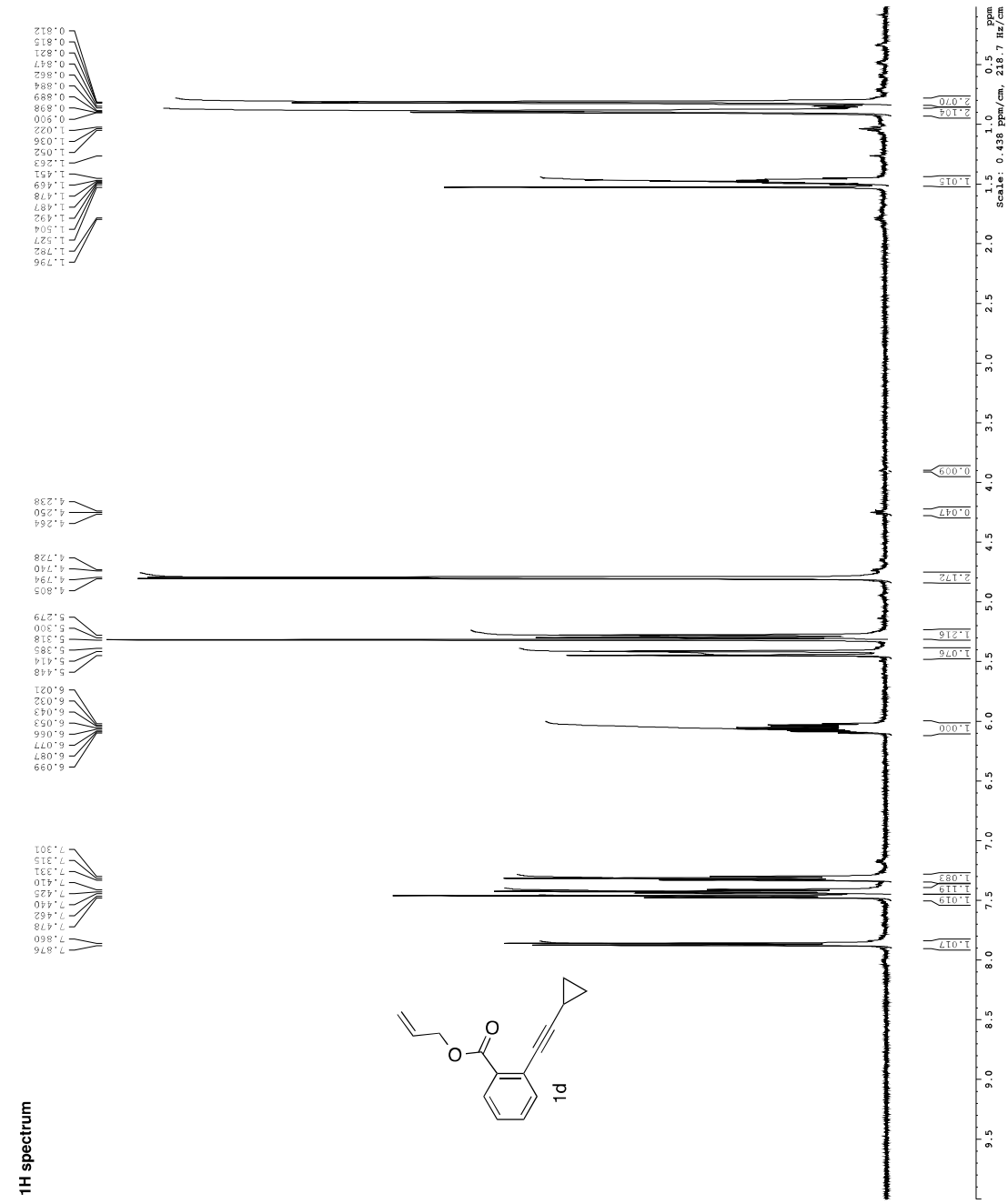

Z–restored spin–echo 13C spectrum with 1H decoupling
NAcTs
1e
Scale: 8.747 ppm/cm, 1100 Hz/cm

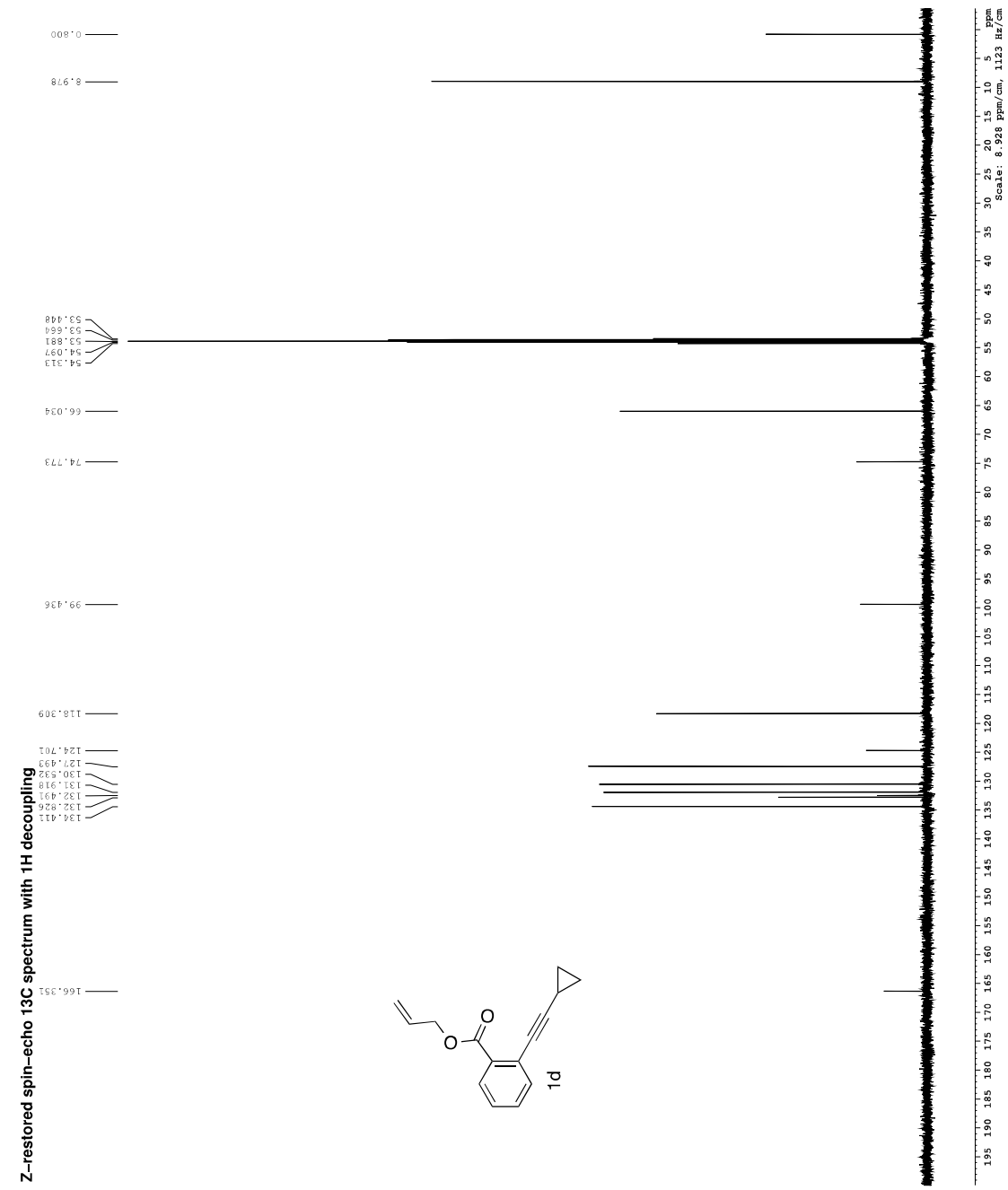
1H spectrum

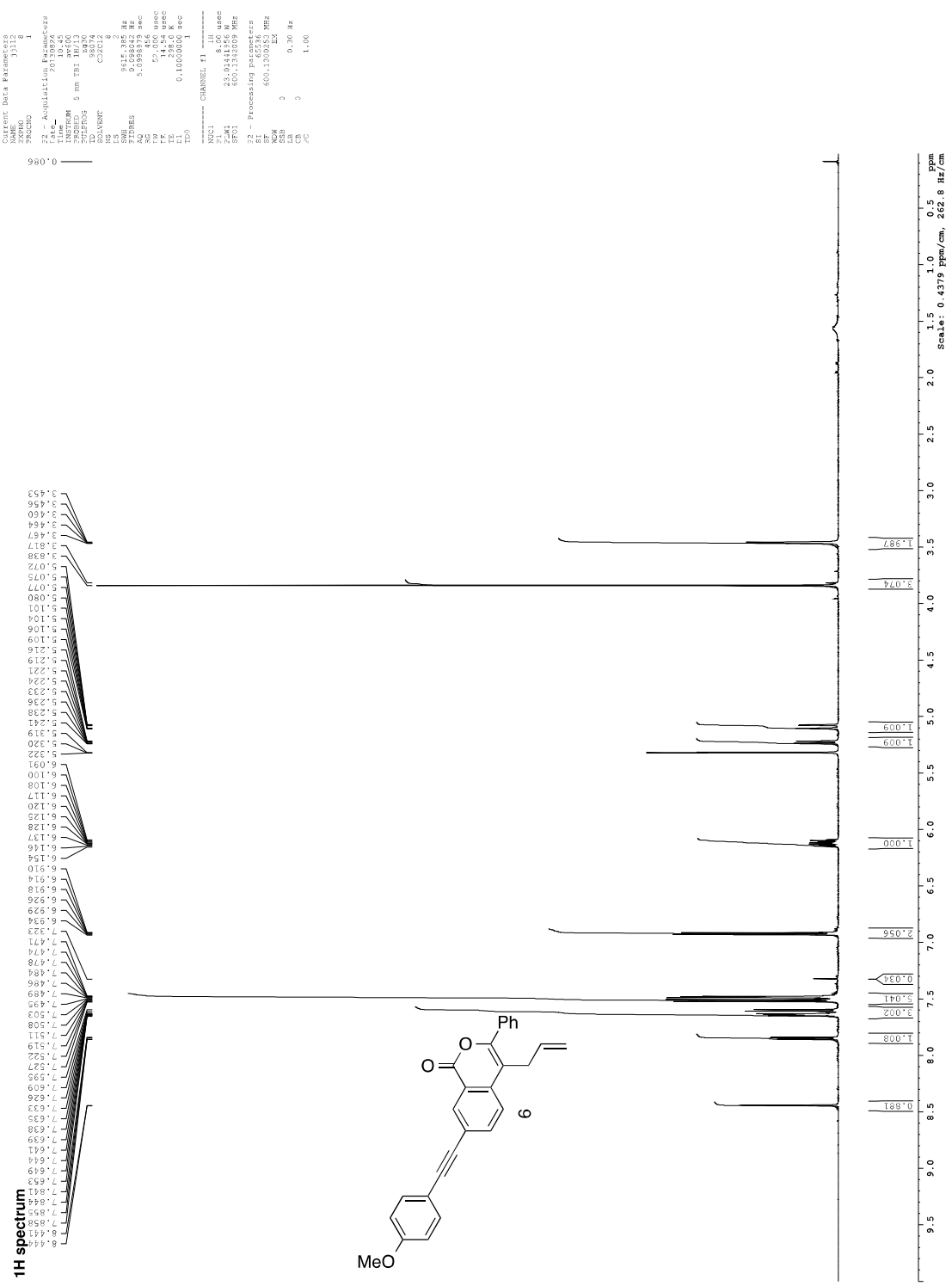


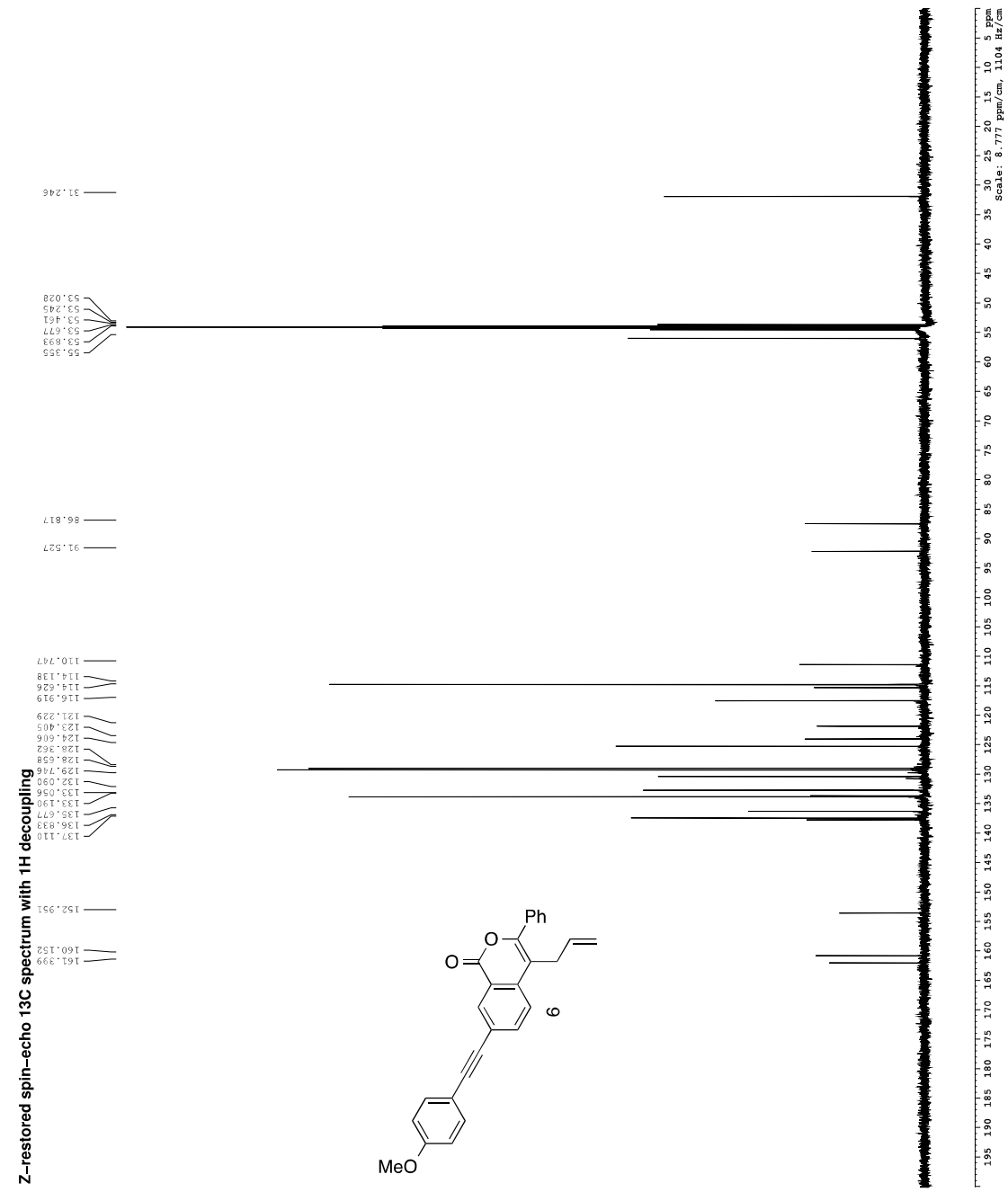
17

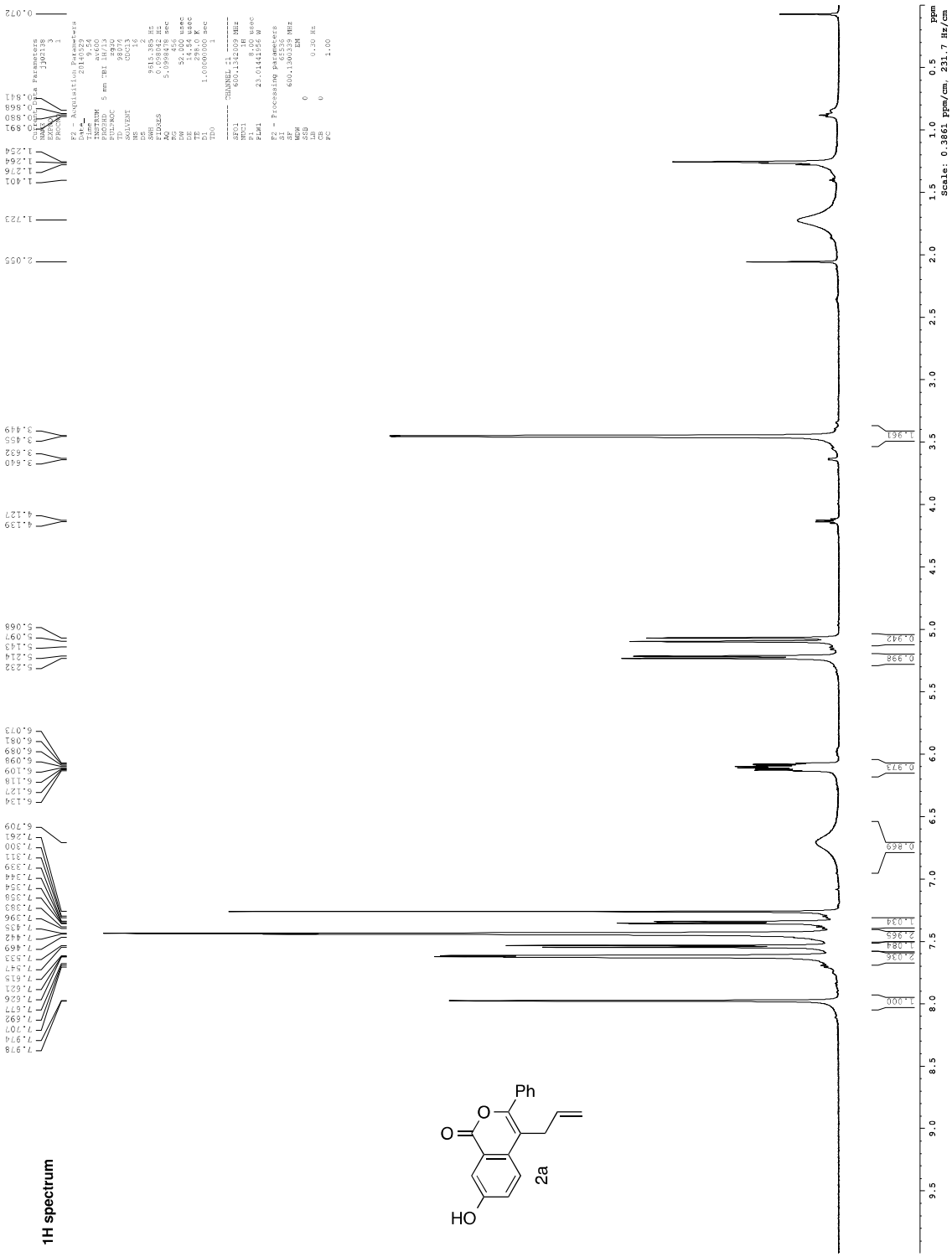

Z–restored spin–echo 13C spectrum with 1H decoupling
167.122
134.318
132.566
131.869
130.470
127.479
124.658
99.401
74.679
54.316
54.099
53.883
53.667
53.450
52.278
9.082
17
Scale: 8.747 ppm/cm, 1100 Hz/cm

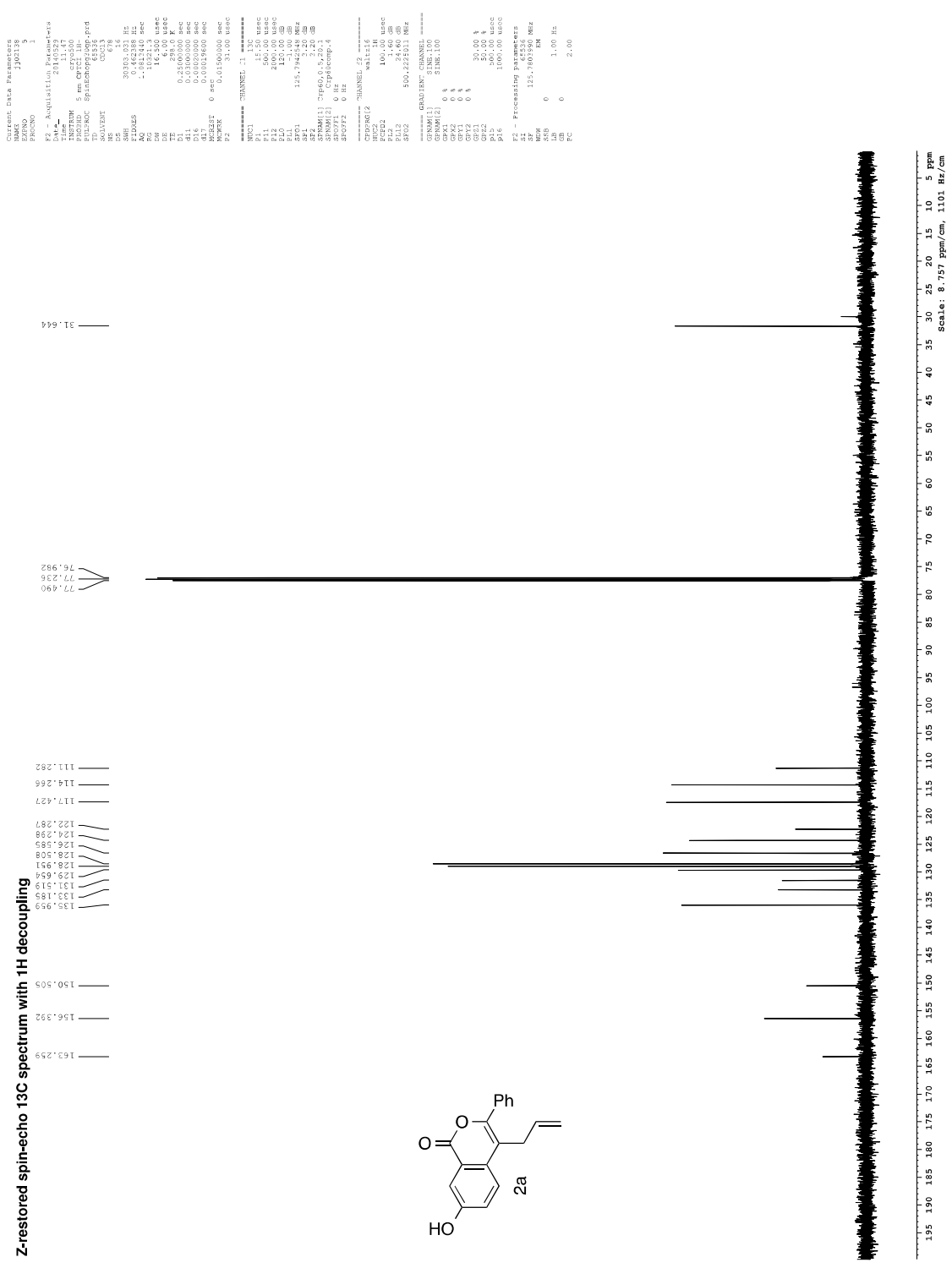

1H spectrum
1d
Scale: 0.438 ppm/cm, 218.7 Hz/cm
ppm

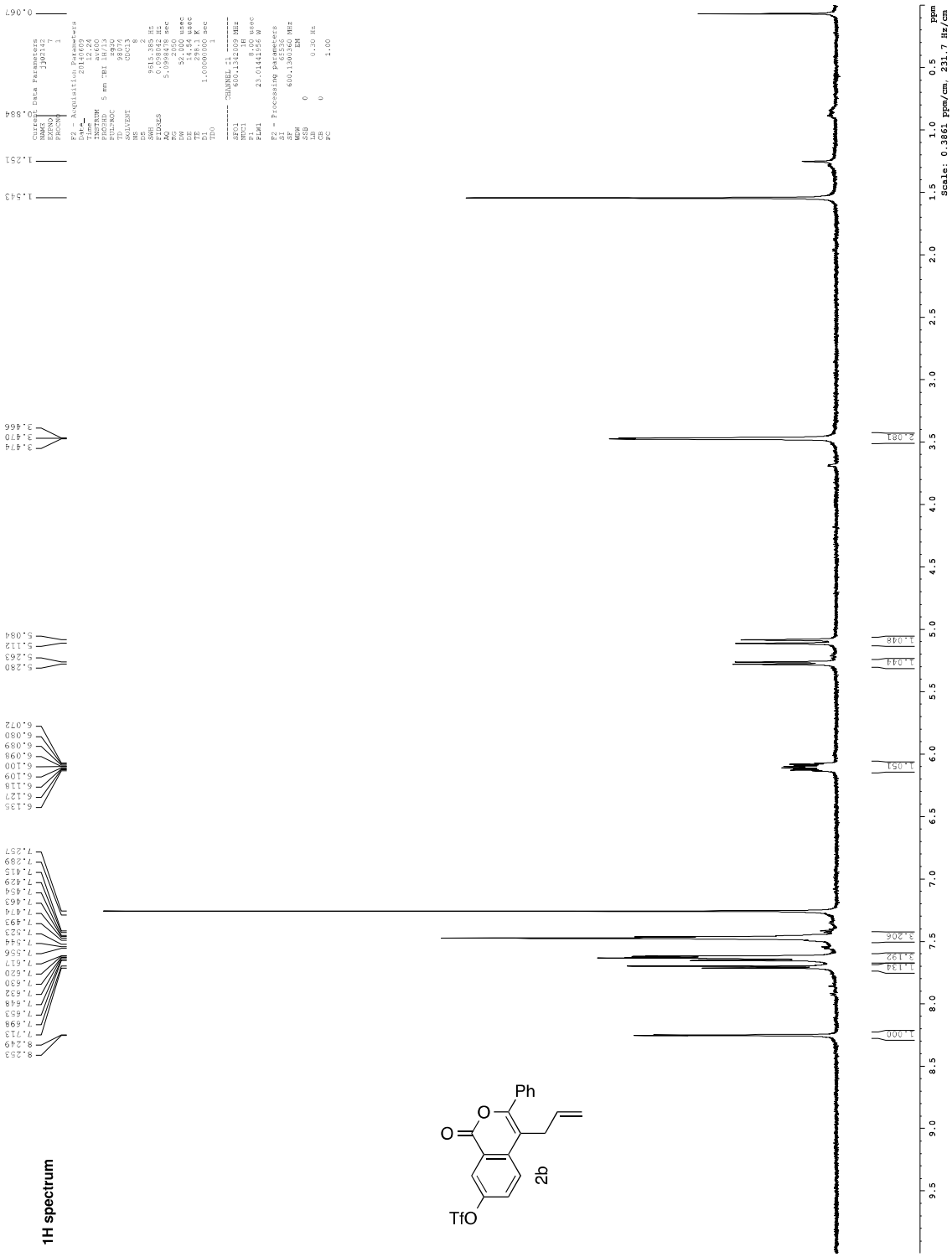

Z–restored spin–echo 13C spectrum with 1H decoupling
1d
Scale: 8.928 ppm/cm, 1123 Hz/cm
ppm

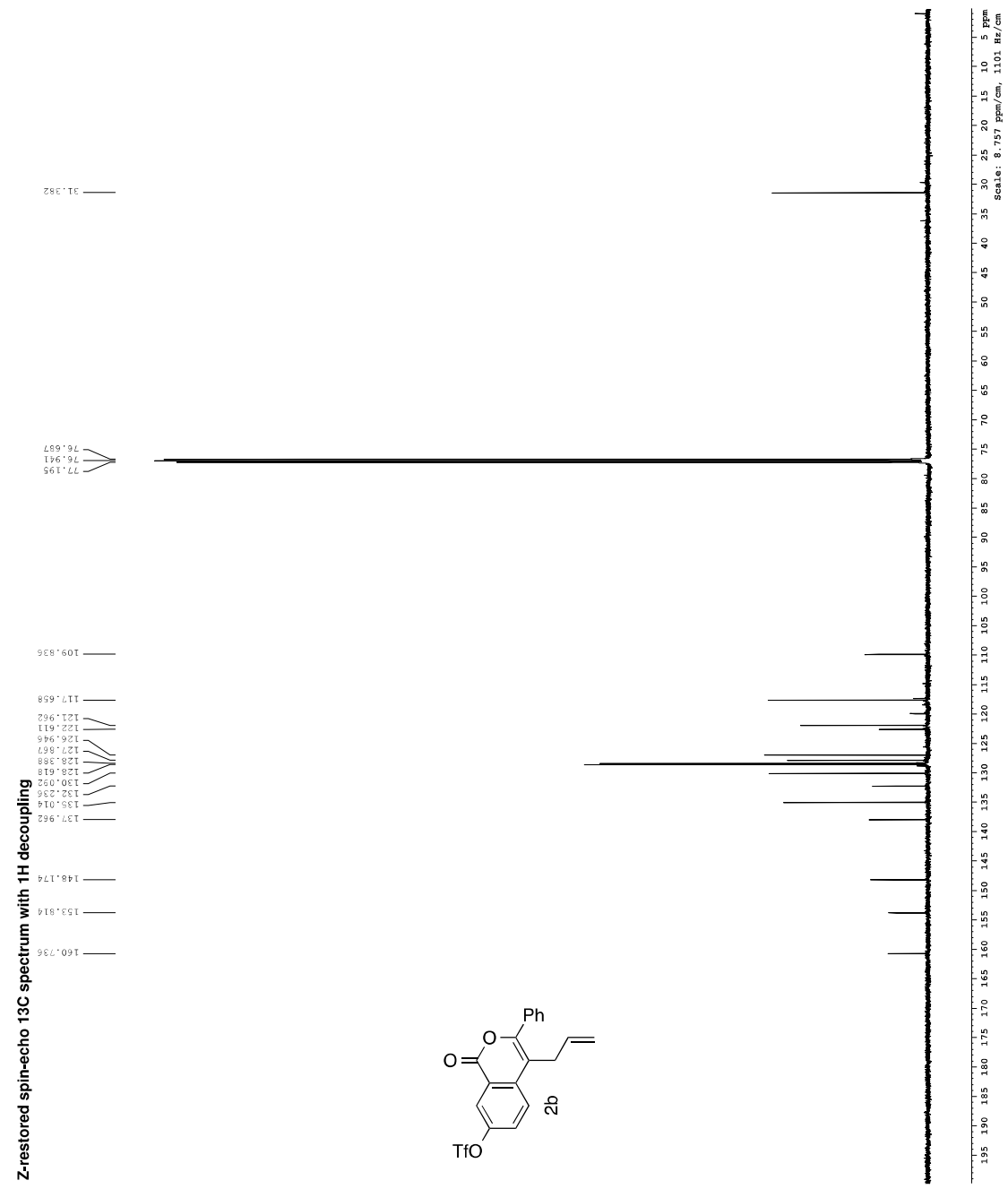

1H spectrum
Ph
O
O
MeO
9
Scale: 0.4379 ppm/cm, 262.8 Hz/cm
ppm


Z–restored spin–echo 13C spectrum with 1H decoupling
Ph
O
O
MeO
9
Scale: 8.777 ppm/cm, 1104 Hz/cm

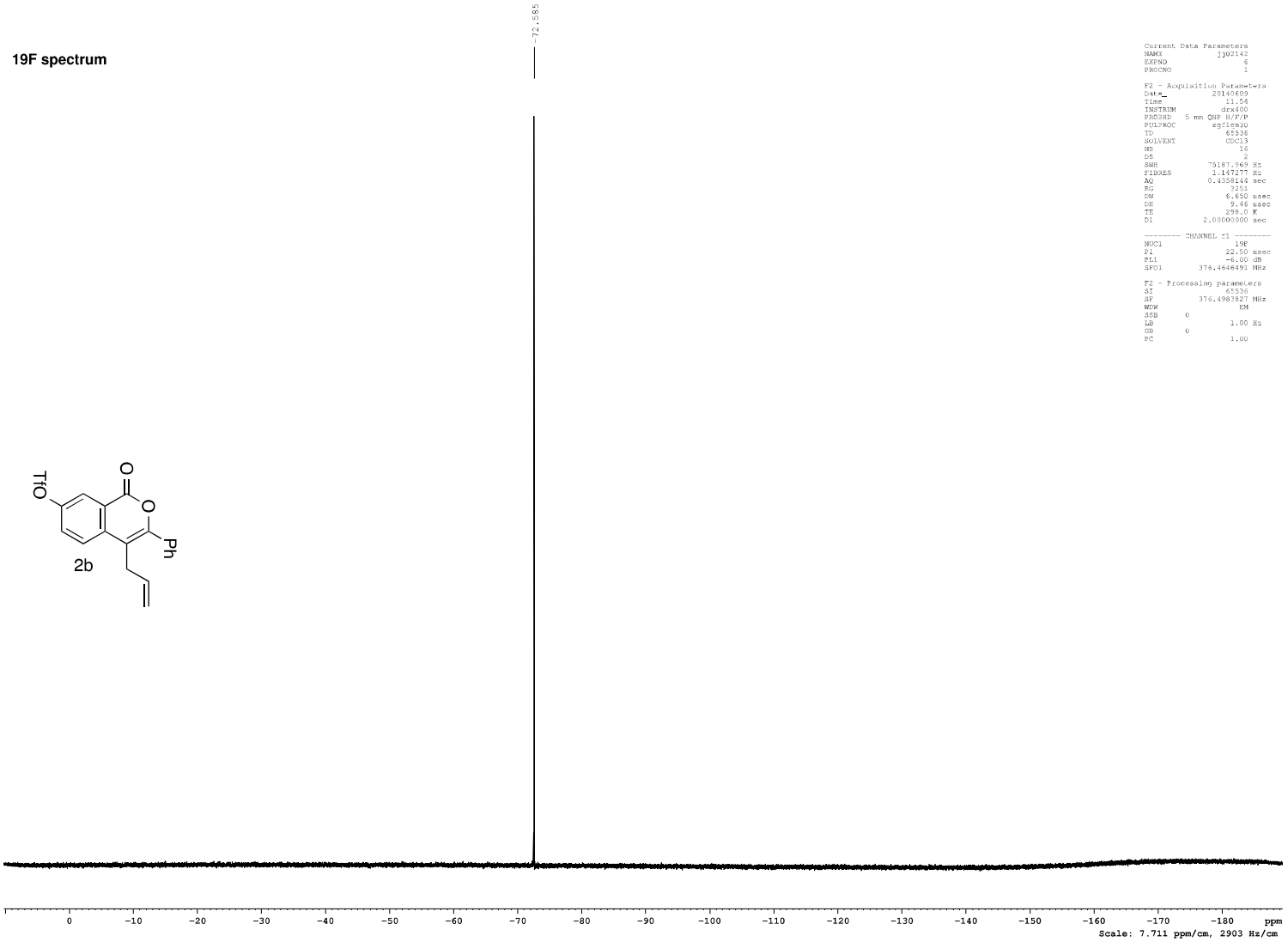

1H spectrum
Ph
O
O
HO
2a
ppm
Scale: 0.3861 ppm/cm, 231.7 Hz/cm


Z-restored spin-echo 13C spectrum with 1H decoupling
Ph
O
O
HO
2a
Scale: 8.757 ppm/cm, 1101 Hz/cm


1H spectrum
Ph
O
O
TfO
2b


Z-restored spin-echo 13C spectrum with 1H decoupling
Ph
O
O
TfO
2b
Scale: 8.757 ppm/cm, 1101 Hz/cm

19F spectrum

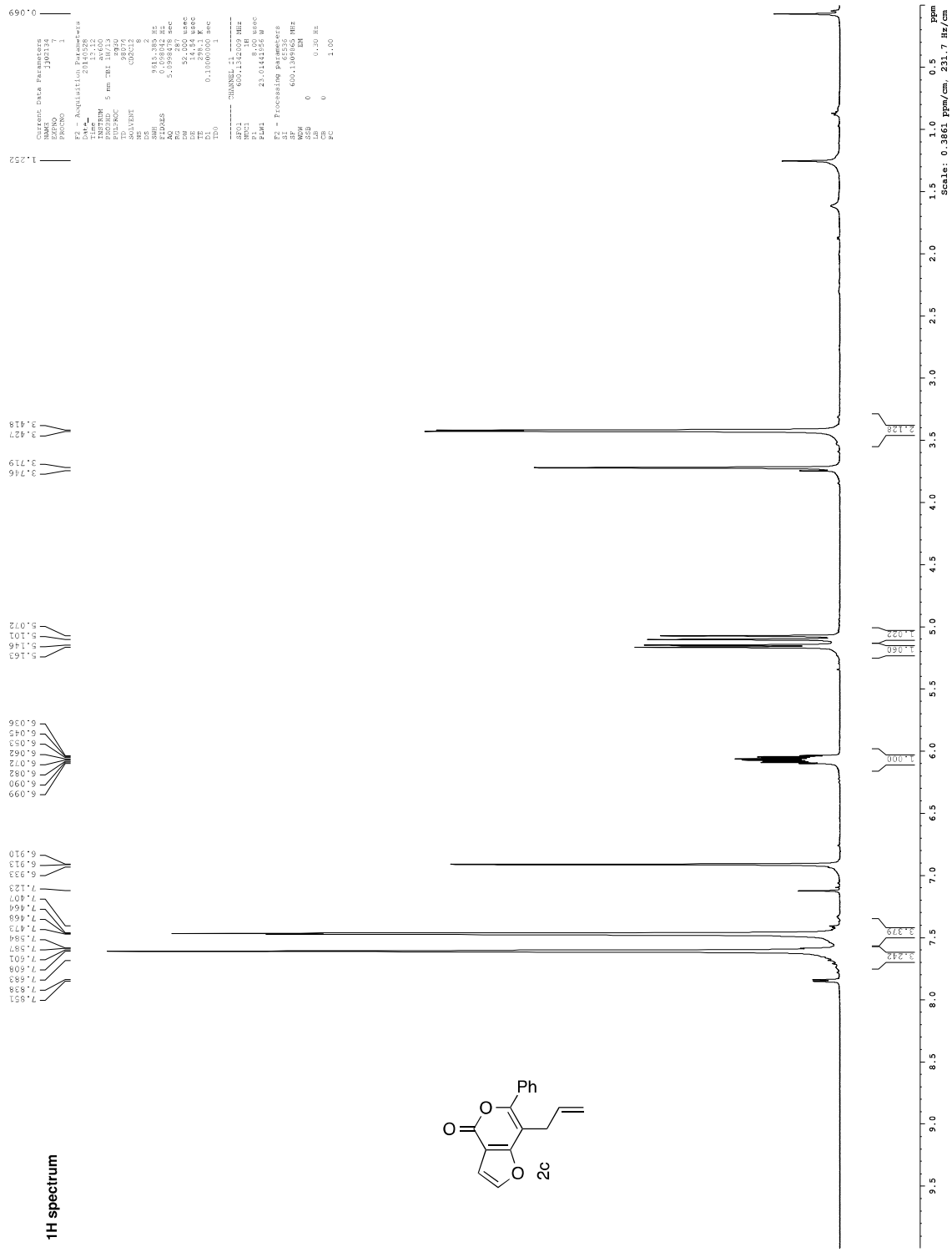


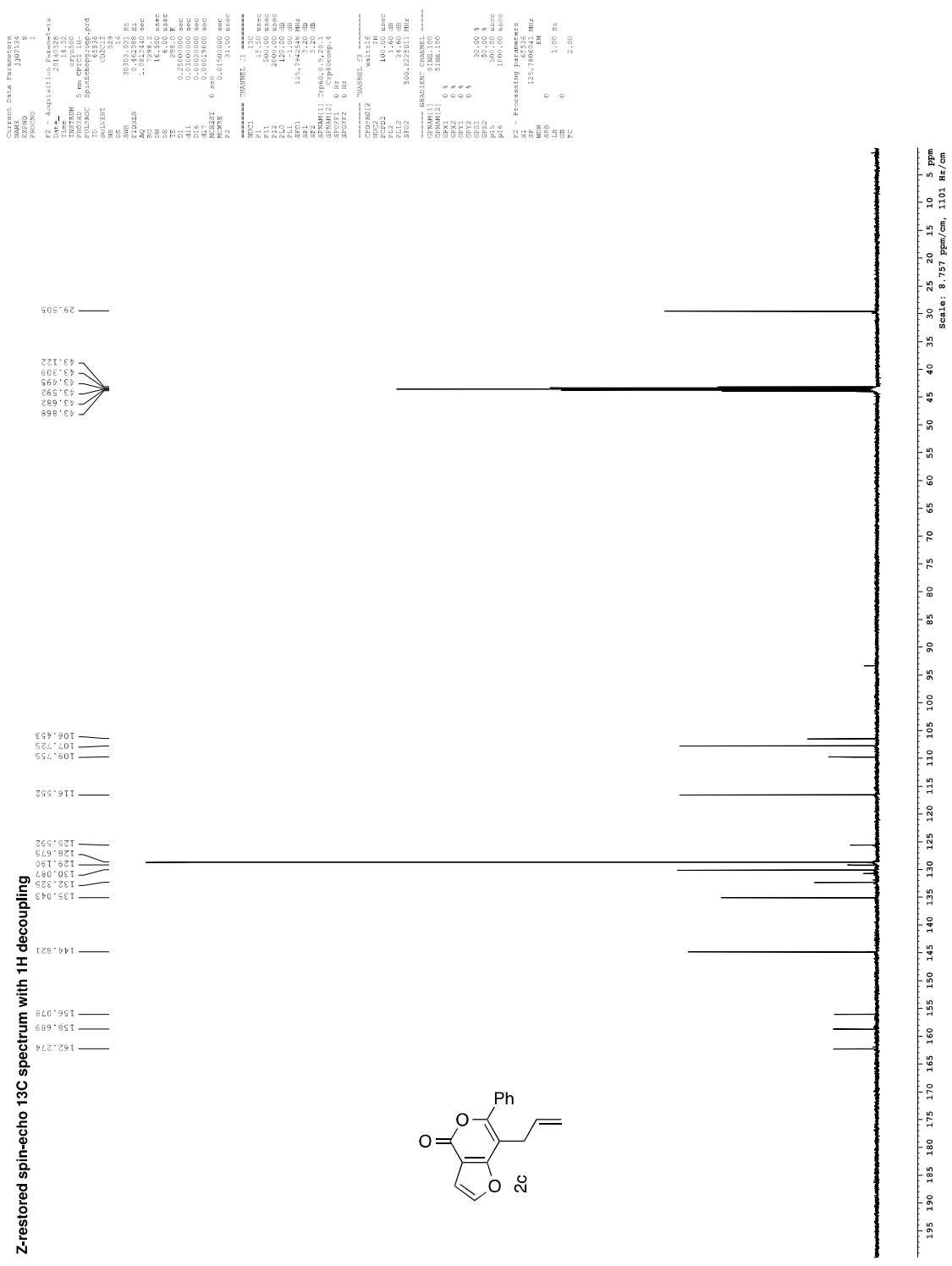

```
Current Data Parameters
NAME                  jj02142
EXPNO                       6
PROCNO                      1

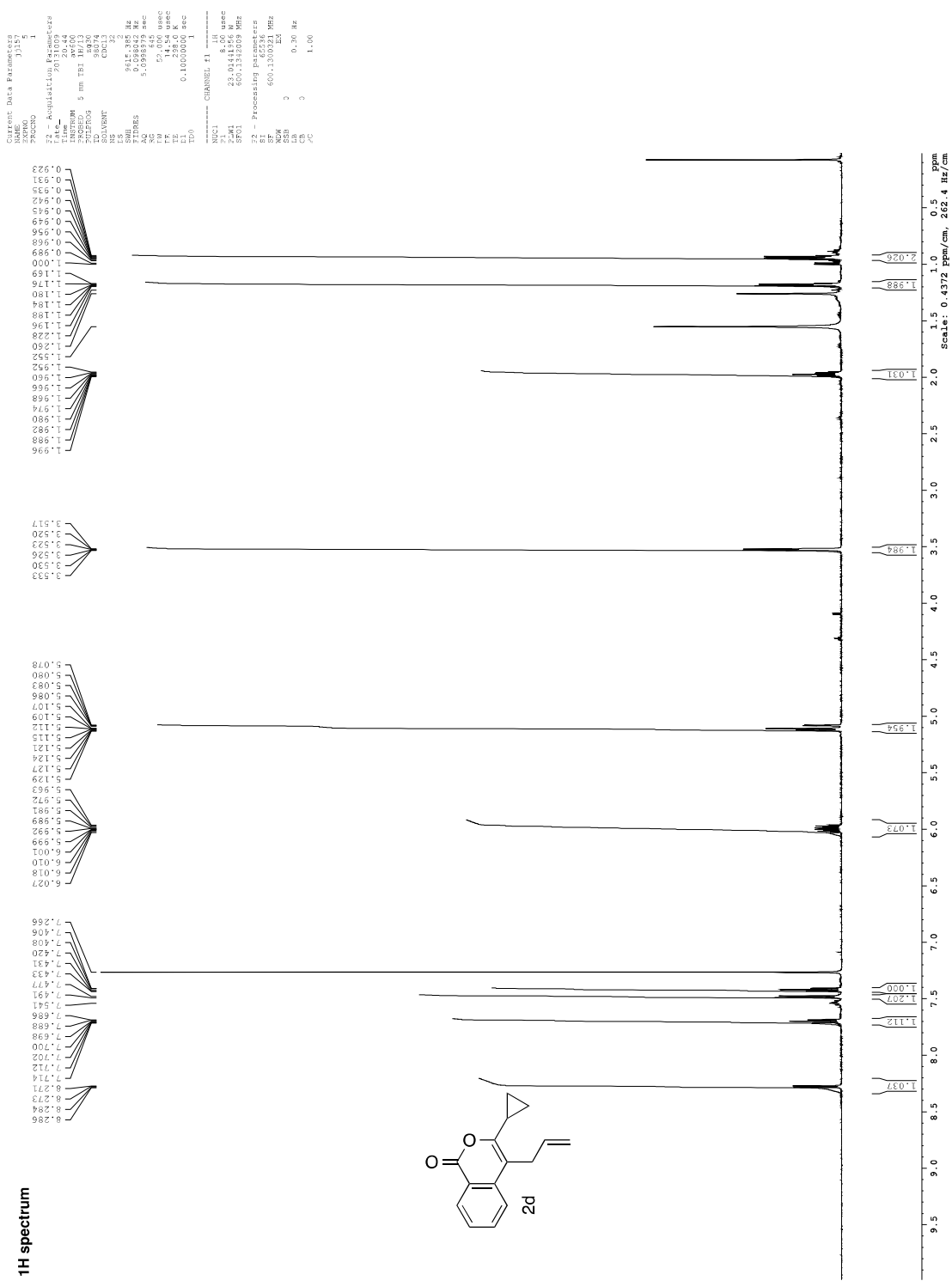
F2 - Acquisition Parameters
Date_              20140609
Time                   11.54
INSTRUM                drx400
PROBHD    5 mm QNP H/F/P
PULPROG             zgflqn30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                75187.969 Hz
FIDRES             1.147277 Hz
AQ                 0.43581440 sec
RG                       2253
DW                     6.650 usec
DE                     9.46 usec
TE                     298.0 K
D1                2.00000000 sec

-------- CHANNEL f1 --------
NUC1                      19F
P1                      22.50 usec
PL1                     -6.00 dB
SFO1              376.4646491 MHz

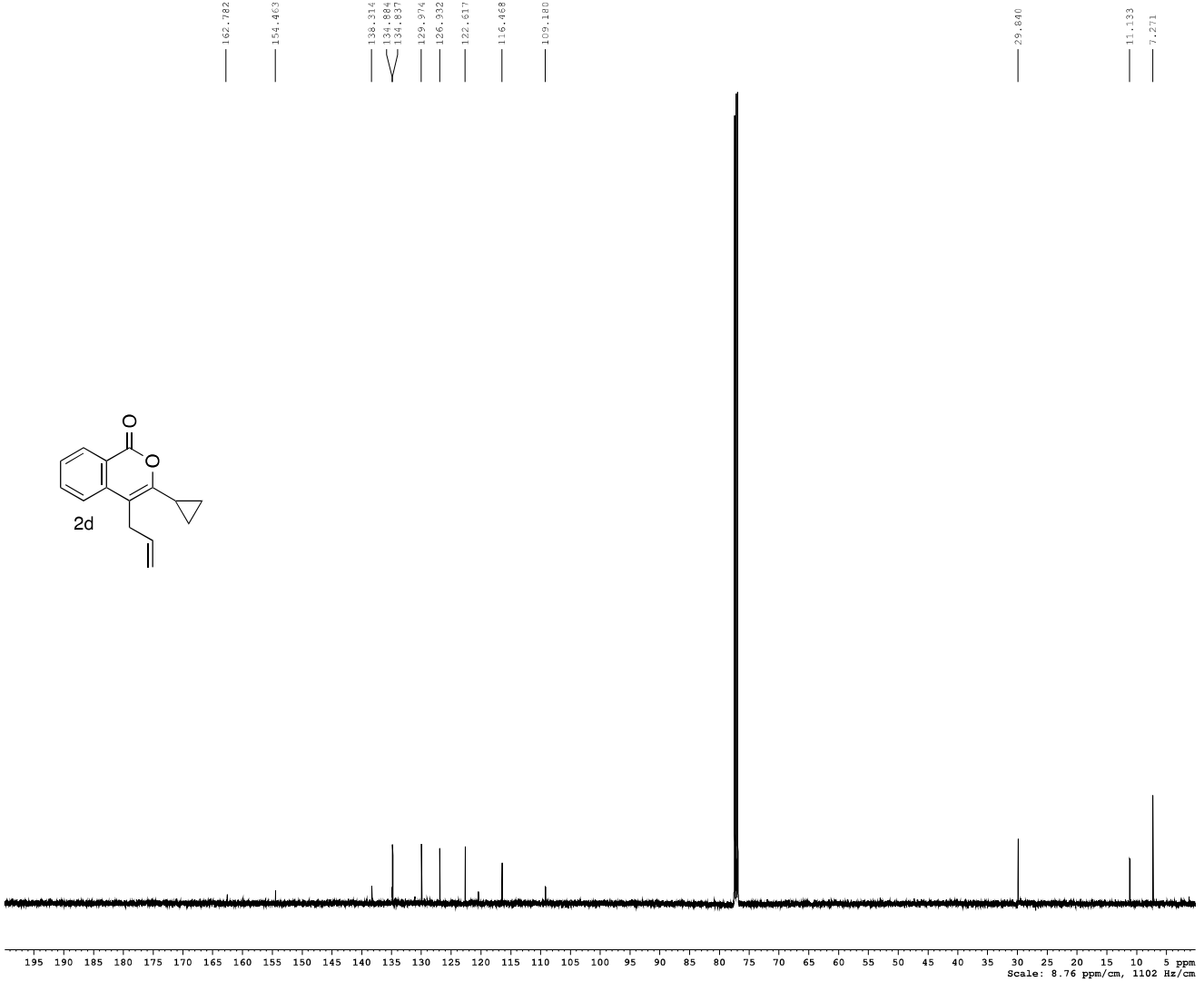
F2 - Processing parameters
SI                        65536
SF                376.4983827 MHz
WDW                          EM
SSB          0
LB                      1.00 Hz
GB           0
PC                      1.00
```


Ph
O
O
O
2c
1H spectrum
ppm
Scale: 0.3861 ppm/cm, 231.7 Hz/cm


Z-restored spin-echo 13C spectrum with 1H decoupling
29.505
43.122
43.308
43.495
43.592
43.682
43.868
106.453
107.725
109.755
116.552
125.592
128.675
129.190
130.087
132.325
135.043
144.821
156.078
158.689
162.274
Ph
O
O
O
2c
Scale: 8.757 ppm/cm, 1101 Hz/cm


1H spectrum
2d
Scale: 0.4372 ppm/cm, 262.4 Hz/cm
ppm

Z–restored spin–echo 13C spectrum with 1H decoupling




```
Current Data Parameters
NAME                  yj157
EXPNO                     6
PROCNO                    1

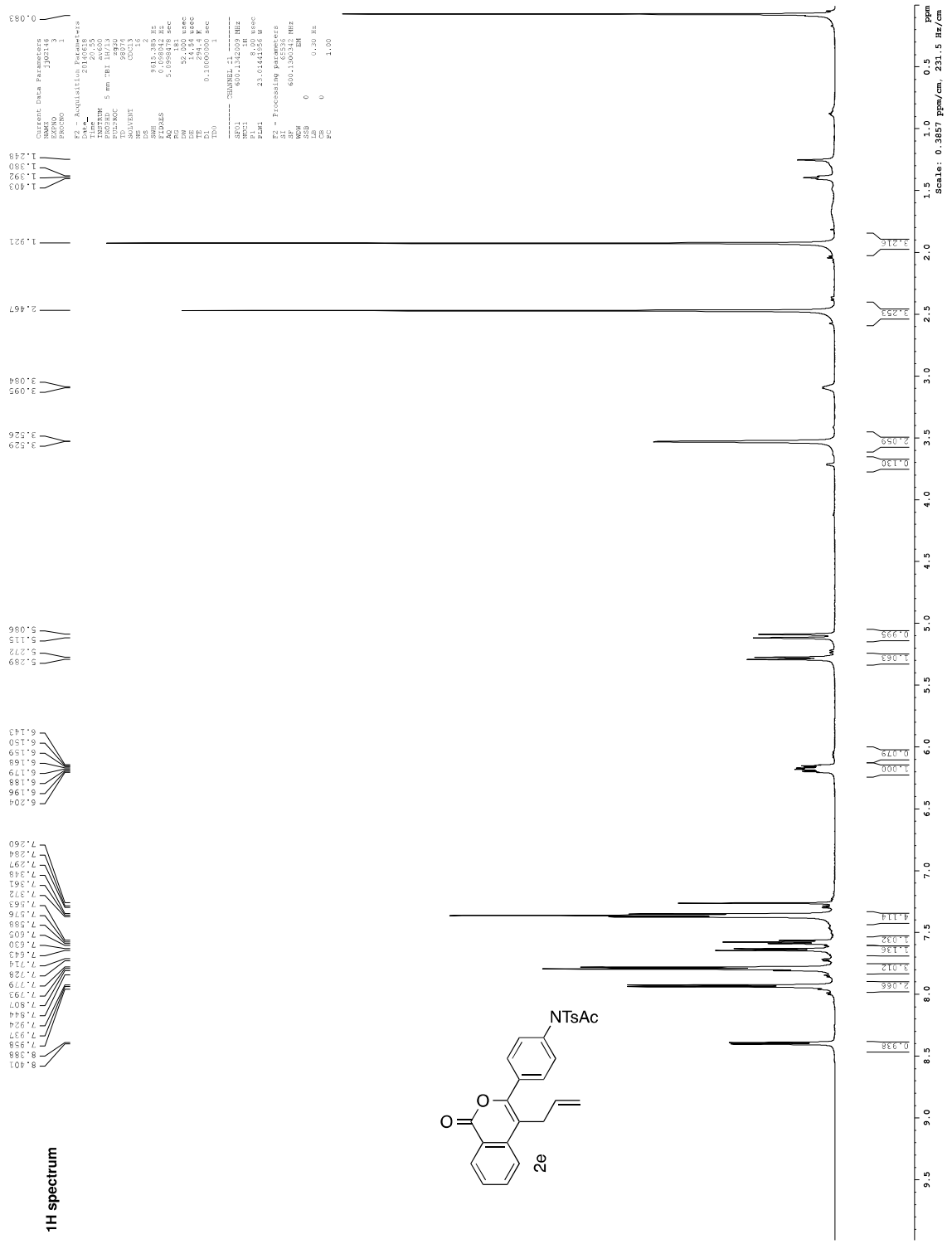
F2 - Acquisition Parameters
Date_              20131009
Time                  22.53
INSTRUM               cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                    65536
SOLVENT               CDCl3
NS                      5120
DS                        16
SWH               30303.031 Hz
FIDRES            0.462388 Hz
AQ                1.0813940 sec
RG                   7298.2
DW                  16.500 usec
DE                   6.00 usec
TE                  298.0 K
D1                0.25000000 sec
D11               0.03000000 sec
D16               0.00020000 sec
D17               0.00019600 sec
MCREST    0 sec
MCWRK             0.01500000 sec
P2                  31.00 usec

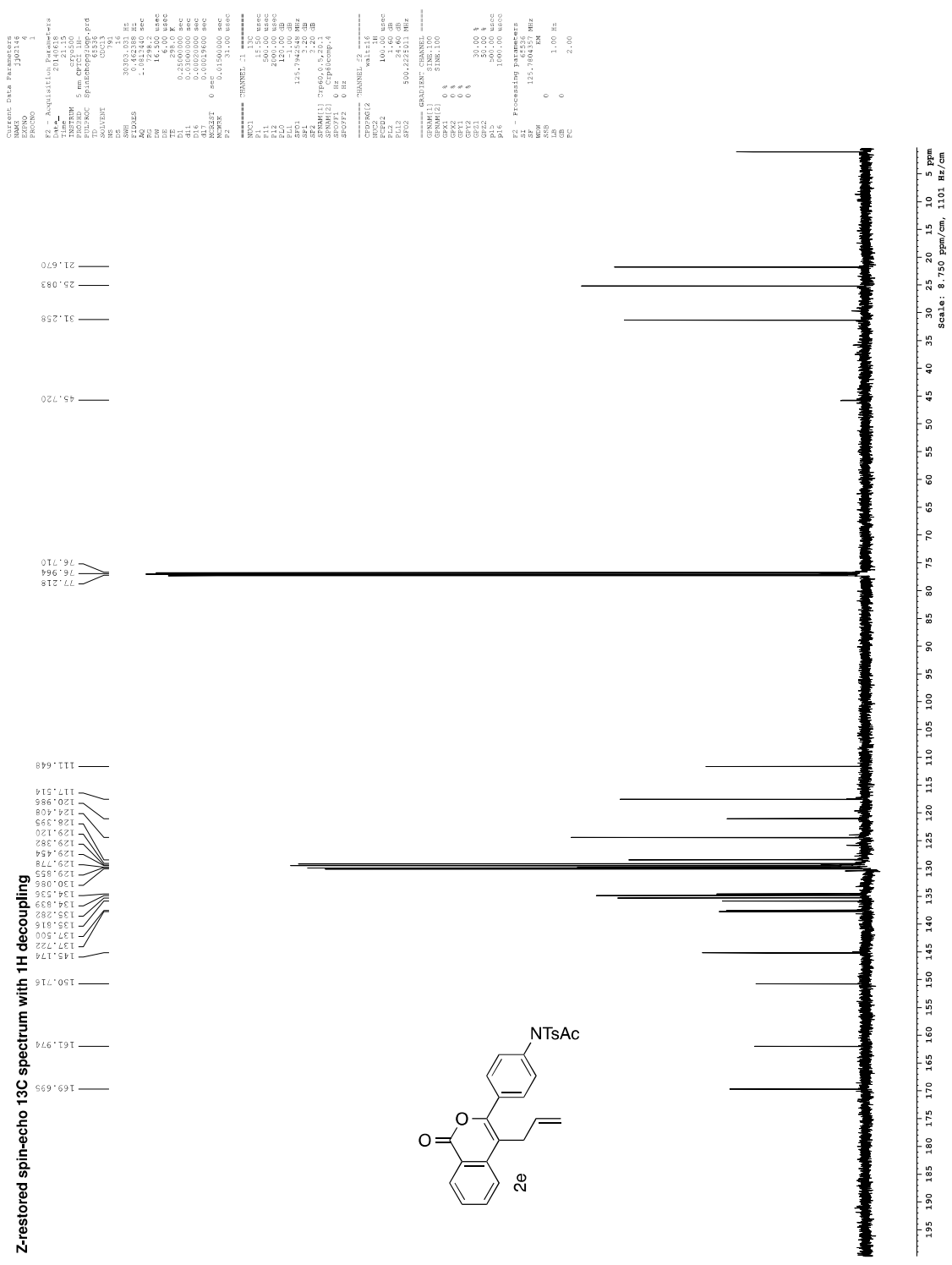
======== CHANNEL f1 ========
NUC1                    13C
P1                    15.50 usec
P11                  500.00 usec
P12                 2000.00 usec
PL0                  120.00 dB
PL1                   -1.00 dB
SFO1          125.7942548 MHz
SP1                   3.20 dB
SP2                   3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1    0 Hz
SPOFF2    0 Hz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2                100.00 usec
PL2                   1.60 dB
PL12                 24.60 dB
SFO2          500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1              SINE.100
GPNAM2              SINE.100
GPX1      0 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1                 30.00 %
GPZ2                 50.00 %
p19                 500.00 usec
p16                1000.00 usec

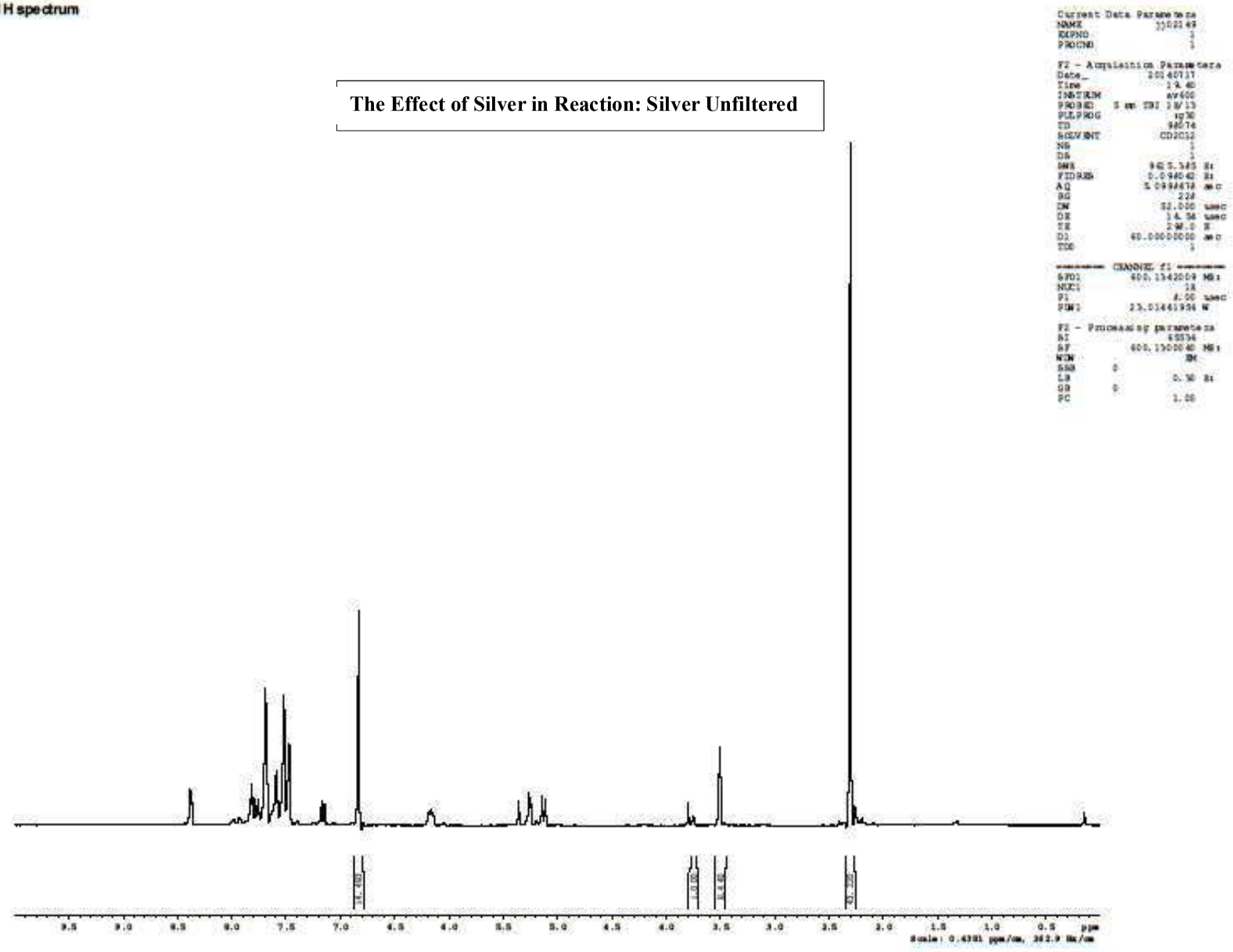
F2 - Processing parameters
SI                    65536
SF            125.7804015 MHz
WDW                     EM
SSB       0
LB                    1.00 Hz
GB        0
PC                    2.00
```


NTsAc
O
O
2e
1H spectrum


Z-restored spin-echo 13C spectrum with 1H decoupling
NTsAc
O
O
2e
21.670
25.083
31.258
45.720
76.710
76.964
77.218
111.648
117.514
120.986
124.408
129.120
129.382
129.454
129.778
129.855
130.086
134.535
134.839
135.282
135.816
137.500
137.722
145.174
150.716
161.974
169.695
Scale: 8.750 ppm/cm, 1101 Hz/cm

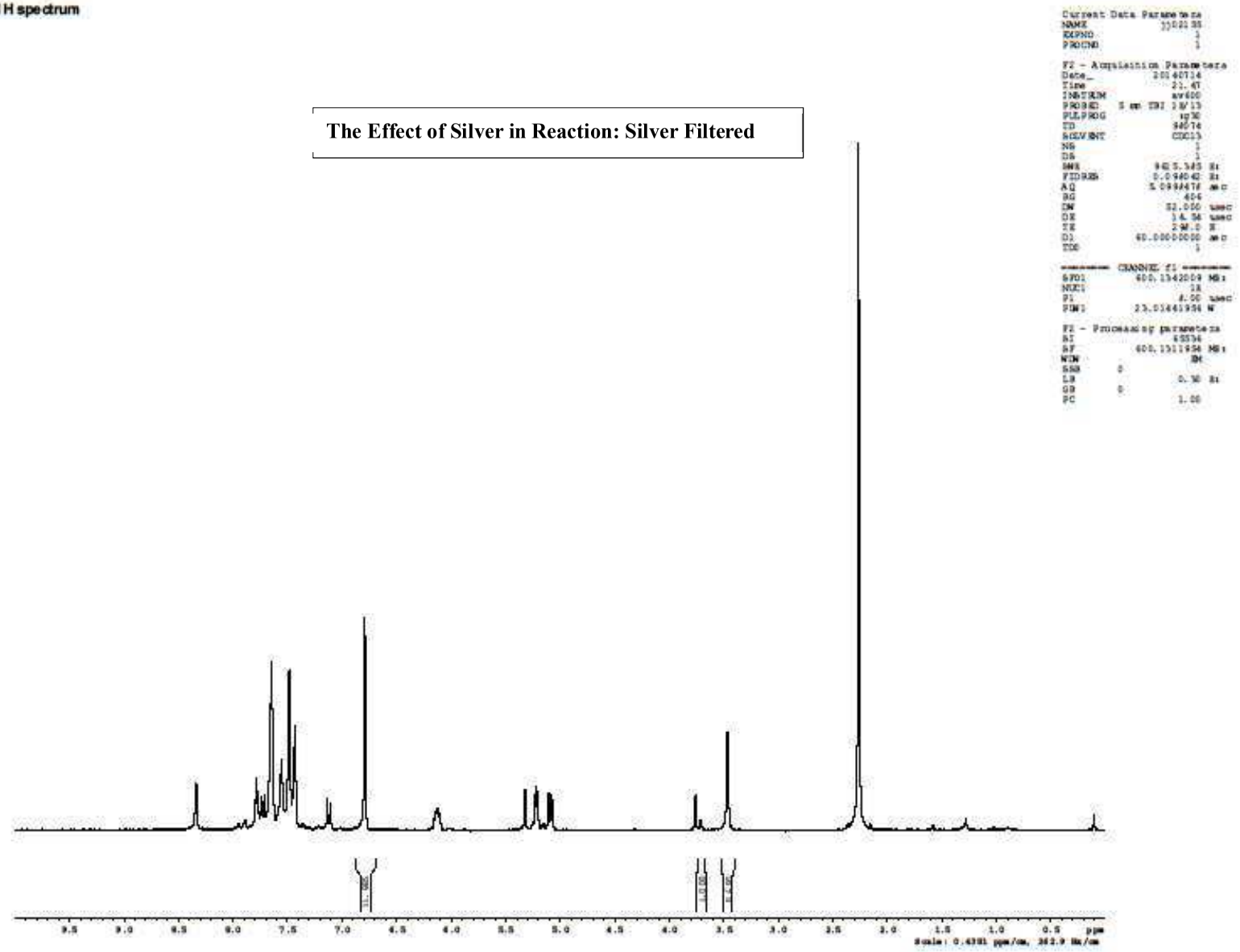
1H spectrum

The Effect of Silver in Reaction: Silver Unfiltered



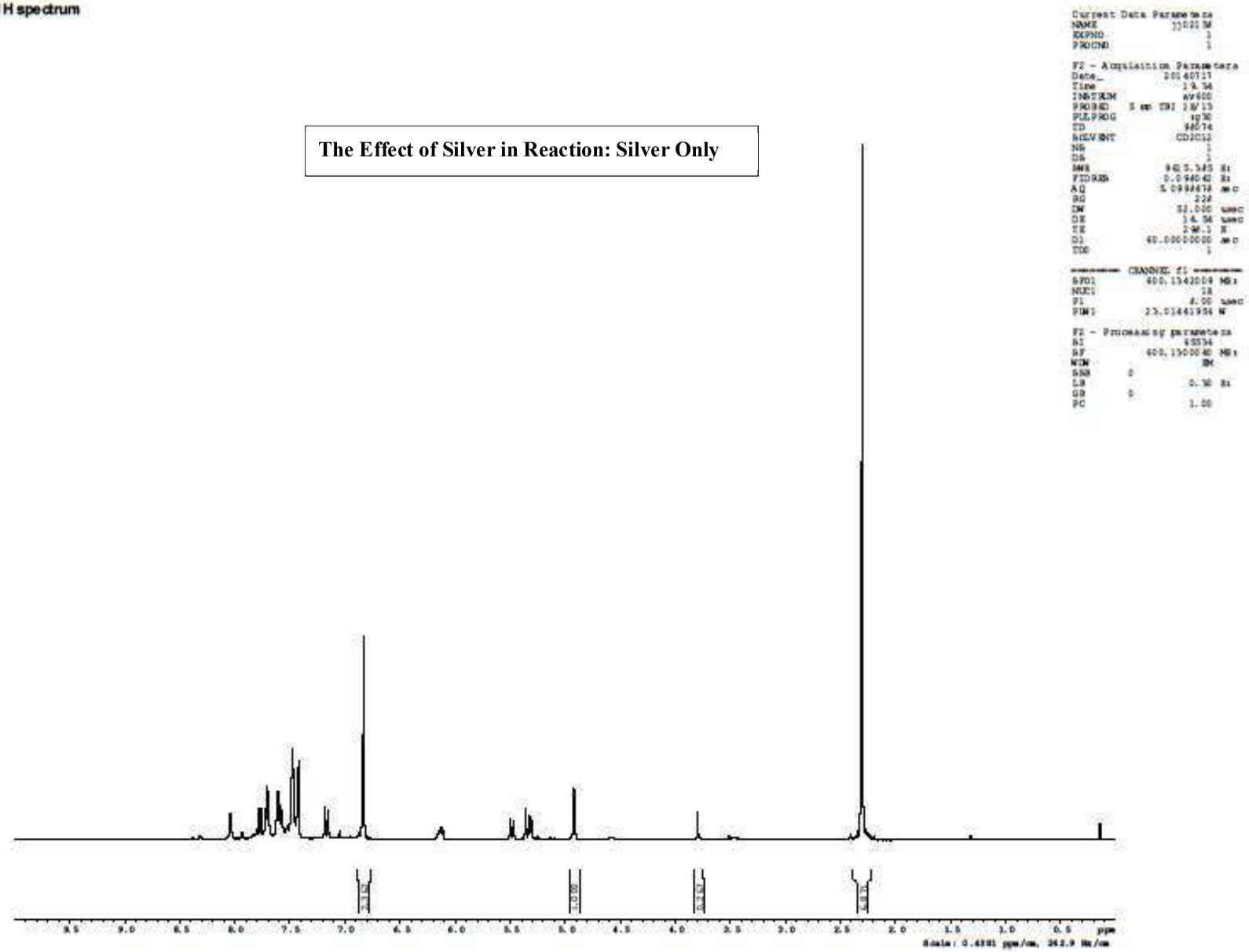
1H spectrum

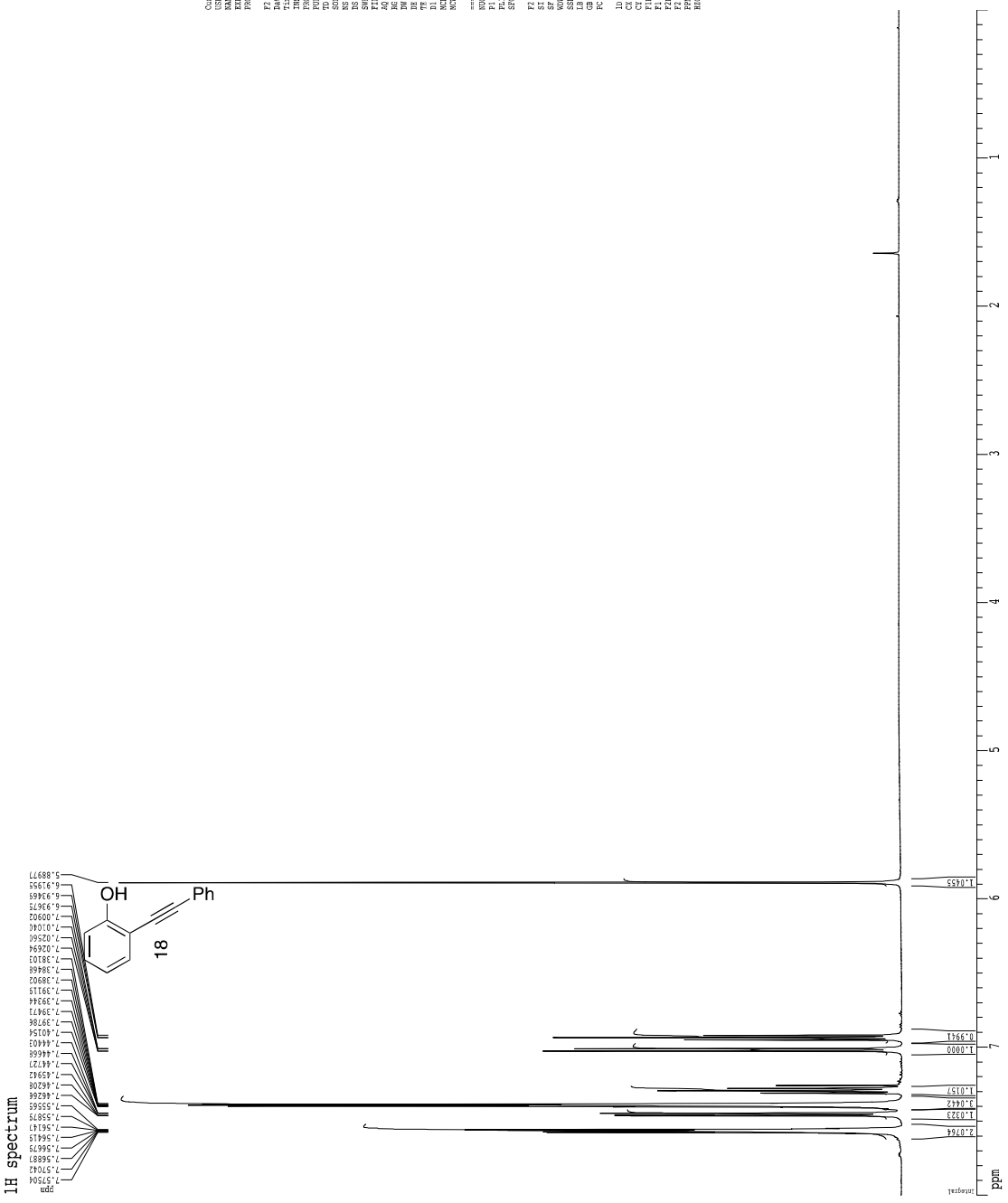
The Effect of Silver in Reaction: Silver Filtered

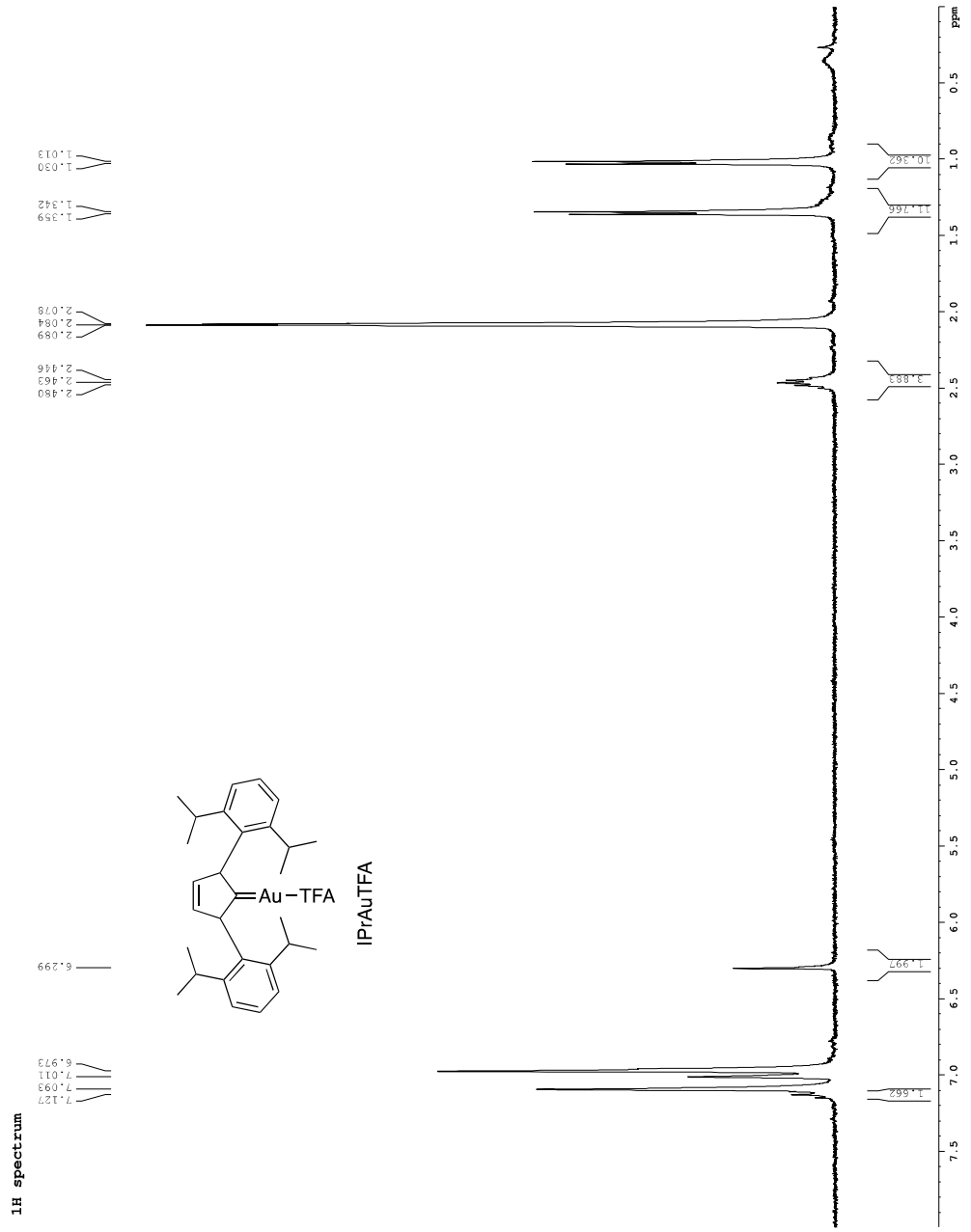


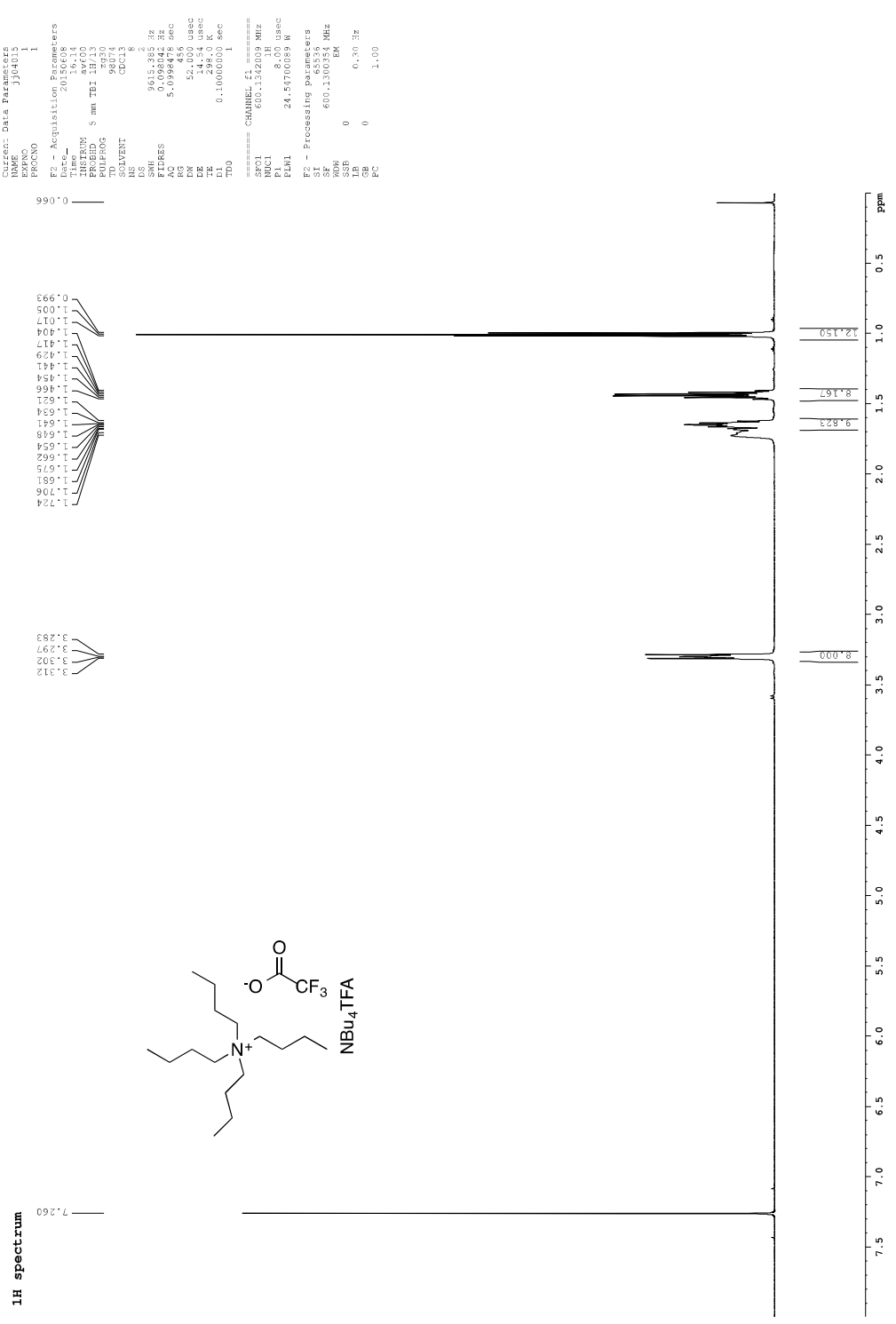
1H spectrum

The Effect of Silver in Reaction: Silver Only



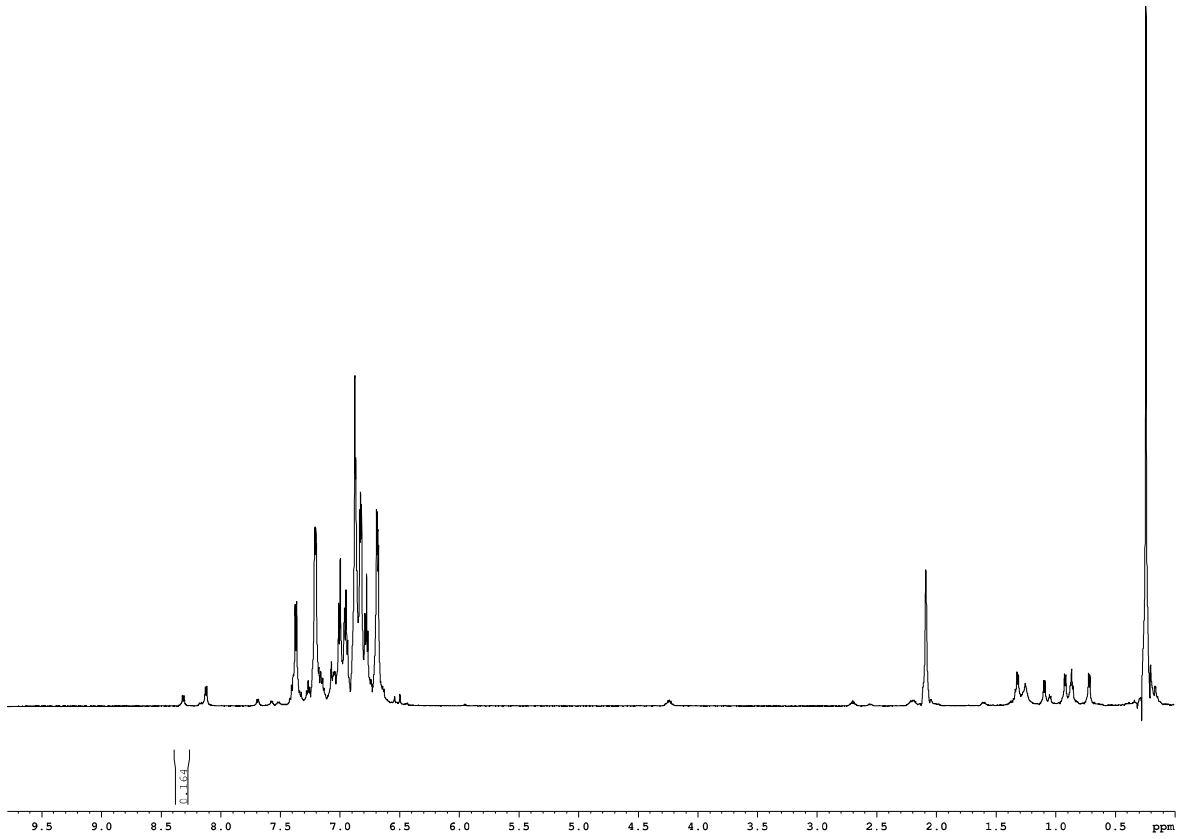

1H spectrum
OH
Ph
18
ppm


1H spectrum
Current Data Parameters
NAME jj03152
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150412
Time 11.13
INSTRUM dtx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097814 Hz
AQ 5.1118078 sec
RG 1024
DW 78.000 usec
DE 4.50 usec
TE 294.1 K
D1 0.10000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
CHANNEL f1
NUC1 1H
P1 12.00 usec
PL1 0 dB
SFO1 400.1328009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300071 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 2.00
7.127
7.093
7.011
6.973
6.299
2.480
2.463
2.446
2.089
2.084
2.078
1.359
1.342
1.030
1.013
1.662
1.997
3.883
11.766
10.362
Au−TFA
IPrAuTFA
ppm


1H spectrum
Current Data Parameters
NAME jj04015
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150608
Time 16.14
INSTRUM avr00
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 88274
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.108944 Hz
AQ 5.0998447 sec
RG 456
DW 52.000 usec
DE 6.50 usec
TE 298.1 K
D1 0.10000000 sec
TD0 1
CHANNEL f1
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 24.54700089 W
F2 - Processing parameters
SI 65536
SF 600.1300354 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.260
3.312
3.302
3.297
3.283
1.724
1.706
1.681
1.675
1.662
1.654
1.648
1.641
1.634
1.621
1.466
1.454
1.441
1.429
1.417
1.404
1.017
1.005
0.993
12.150
8.167
9.823
8.000
ppm
NBu4TFA

1H spectrum

Sample Spectrum at T = 130 s




```
Current Data Parameters
NAME                  jj04007
EXPNO                       4
PROCNO                      1

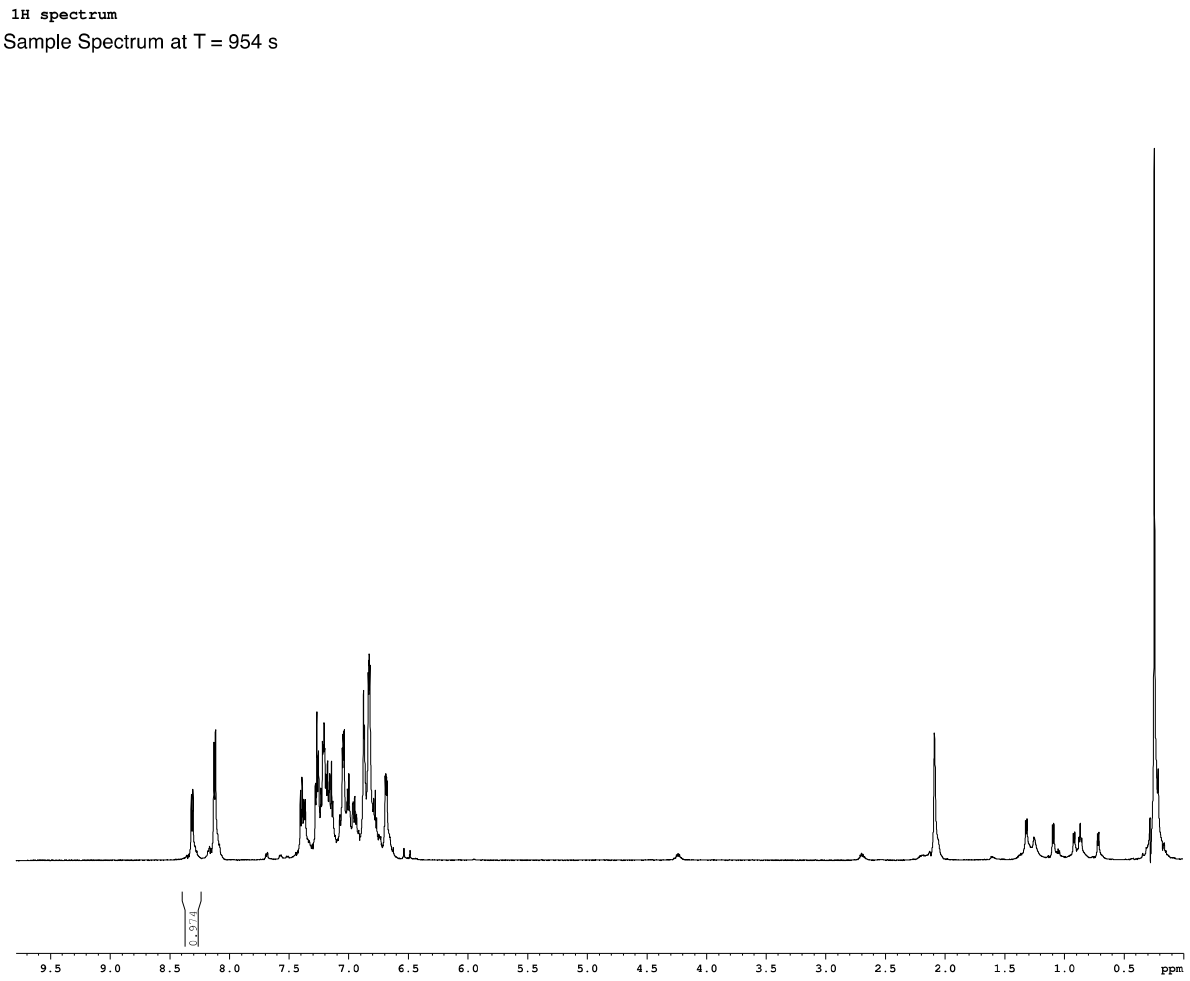
F2 - Acquisition Parameters
Date_              20150509
Time                  21.33
INSTRUM                av600
PROBHD    5 mm BBO BB-1H
PULPROG                   zg
TD                    115382
SOLVENT                CDCl3
NS                          1
DS                          0
SWH                9615.385 Hz
FIDRES            0.083335 Hz
AQ                5.9998641 sec
RG                        114
DW                   52.000 usec
DE                   10.50 usec
TE                   340.6 K
D1                0.10000000 sec
TD0                         1

======== CHANNEL f1 ========
SFO1           600.1342009 MHz
NUC1                      1H
P1                    9.00 usec
PLW1          60.25600052 W

F2 - Processing parameters
SI                      65536
SF             600.1331355 MHz
WDW                        EM
SSB       0
LB                    1.00 Hz
GB        0
PC                    1.00
```

1H spectrum

Sample Spectrum at T = 954 s




```
Current Data Parameters
NAME                  jj04007
EXPNO                      23
PROCNO                      1

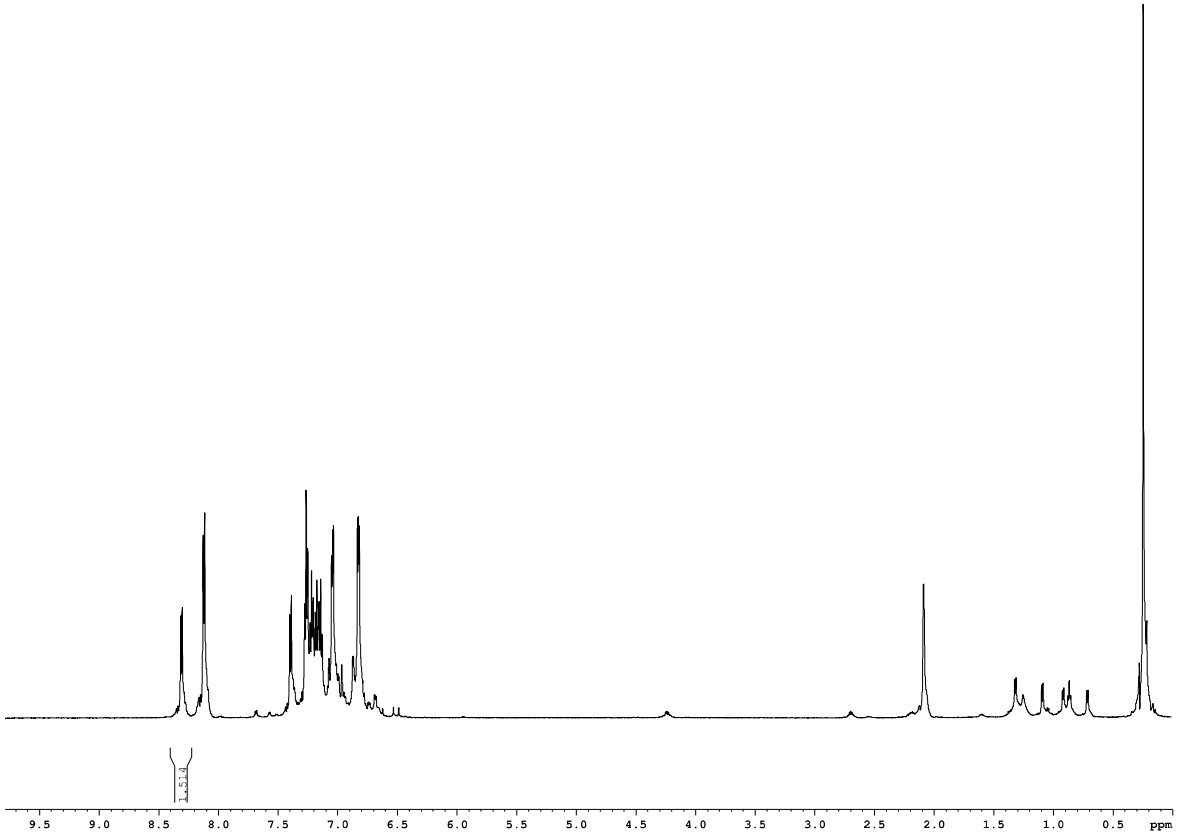
F2 - Acquisition Parameters
Date_              20150509
Time                  21.47
INSTRUM                av600
PROBHD    5 mm BBO BB-1H
PULPROG                   zg
TD                    115382
SOLVENT                CDCl3
NS                          1
DS                          0
SWH                9615.385 Hz
FIDRES            0.083335 Hz
AQ                5.9998641 sec
RG                        114
DW                   52.000 usec
DE                   10.50 usec
TE                   341.1 K
D1               0.10000000 sec
TD0                         1

======== CHANNEL f1 ========
SFO1            600.1342009 MHz
NUC1                      1H
P1                     9.00 usec
PLW1           60.25600052 W

F2 - Processing parameters
SI                      65536
SF              600.1331349 MHz
WDW                        EM
SSB       0
LB                     1.00 Hz
GB        0
PC                     1.00
```

1H spectrum

Sample Spectrum at T = 1995 s




```
Current Data Parameters
NAME                  jj04007
EXPNO                      47
PROCNO                      1

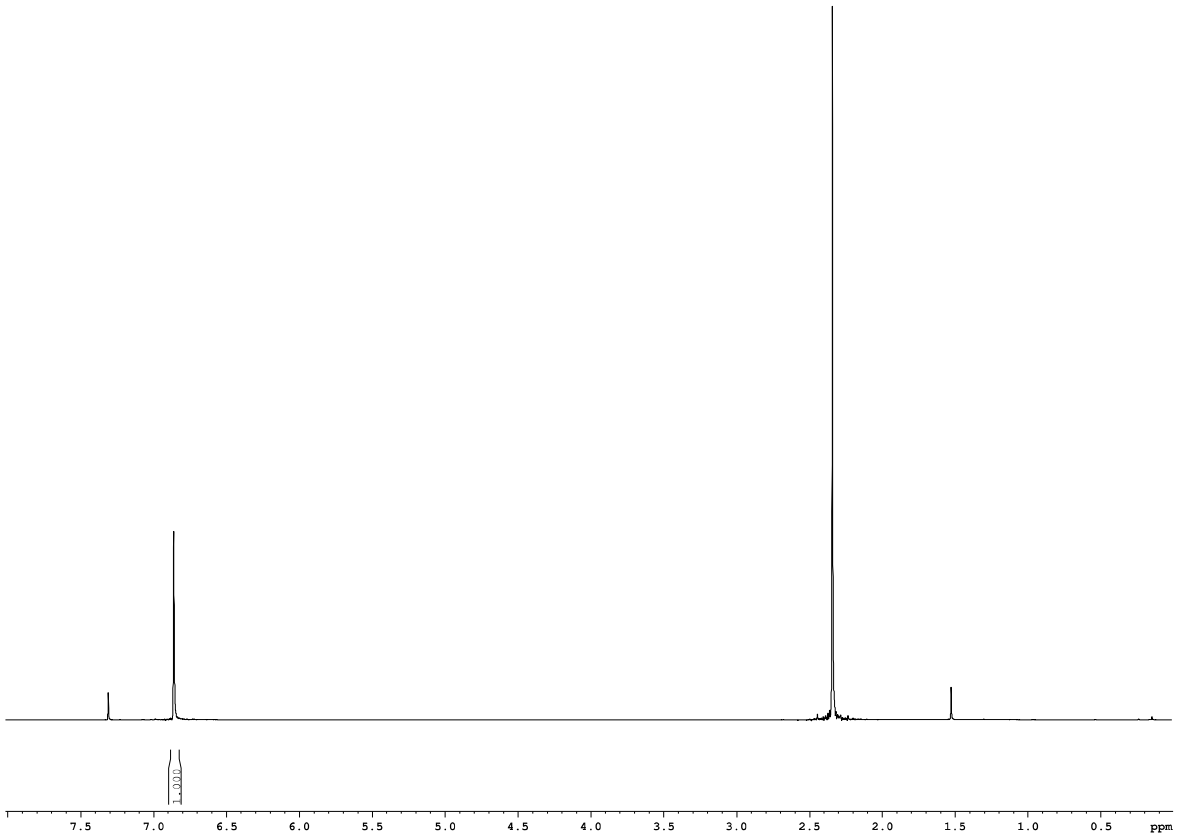
F2 - Acquisition Parameters
Date_              20150509
Time                  22.06
INSTRUM                av600
PROBHD    5 mm BBO BB-1H
PULPROG                   zg
TD                    115382
SOLVENT                CDCl3
NS                          1
DS                          0
SWH                9615.385 Hz
FIDRES             0.083335 Hz
AQ                 5.9998641 sec
RG                        114
DW                   52.000 usec
DE                   10.50 usec
TE                    339.8 K
D1                 0.10000000 sec
TD0                         1

======== CHANNEL f1 ========
SFO1            600.1342009 MHz
NUC1                      1H
P1                     9.00 usec
PLW1           60.25600052 W

F2 - Processing parameters
SI                      65536
SF              600.1331355 MHz
WDW                        EM
SSB       0
LB                     1.00 Hz
GB        0
PC                     1.00
```

1H spectrum

Mesitylene ERETIC Reference Spectrum




```
Current Data Parameters
NAME      mes eretic 50 degree tbi
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20150601
Time              12.14
INSTRUM           av600
PROBHD   5 mm TBI 1H/13
PULPROG             zg
TD                115382
SOLVENT            CDCl3
NS                    1
DS                    0
SWH            9615.385 Hz
FIDRES        0.083335 Hz
AQ            5.9998641 sec
RG                  144
DW               52.000 usec
DE               11.13 usec
TE                323.5 K
D1           34.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1         600.1342009 MHz
NUC1                 1H
P1                8.00 usec
PLW1         24.54700089 W

F2 - Processing parameters
SI                65536
SF           600.1300040 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.00
```