Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

THE PREPARATION OF (2*R*,5*S*)-2-*t*-BUTYL-3,5-DIMETHYLIMIDAZOLIDIN-4-ONE

A.

B.
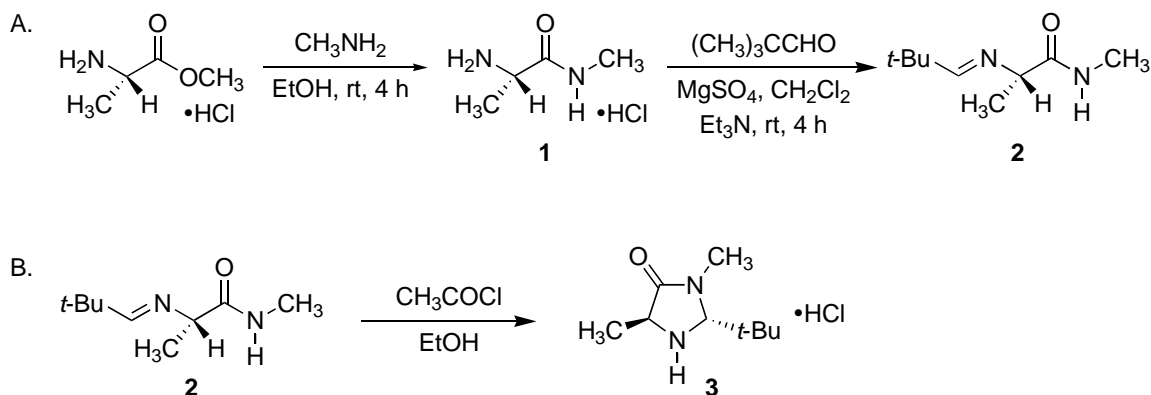
Submitted by Thomas H. Graham, Benjamin D. Horning and David W. C. MacMillan.[1]

Checked by David Hughes.[2]

1. Procedure

A. *(S,E)-2-(2,2-dimethylpropylidenamino)-N-methylpropanamide (2)*. A tared 1-L round-bottomed flask (Note 1) equipped with a 3-cm oval PTFE-coated magnetic stir bar is charged with a 31 wt% solution of methylamine in ethanol (112 mL, 85 g, 0.85 mol, 3.0 equiv) (Note 2) and placed in a room temperature water bath. To the stirred solution is added L-alanine methyl ester hydrochloride (40.0 g, 0.287 mol, 1.0 equiv) (Note 3) via a powder funnel followed by a rinse with ethanol (10 mL). The flask is fitted with a rubber septum through which is inserted both an 18-gauge needle connected to a nitrogen inlet with a gas bubbler and a thermocouple probe (Note 4). The mixture is stirred at 20–22 °C for 4 h (Notes 5 and 6). The stir bar is removed, and the mixture is concentrated by rotary evaporation (20 mm Hg, 45 °C bath temperature) to provide a wet solid (60 g). Toluene (100 mL) (Note 7) is added to the mixture, which is concentrated by rotary evaporation (20 mm Hg, 45 °C bath temperature) to provide a wet solid (65 g). The toluene (100 mL) flush is repeated, and the mixture is concentrated to 49 g of solids, which are dried in a vacuum oven (20 mmHg, 45 °C) for 4 h to afford the crude L-alanine-*N*-methylamide **1** as a pasty solid (45 g) (Notes 8 and 9).

The 1-L flask containing the crude L-alanine-*N*-methylamide **1** is equipped with a 3-cm oval PTFE-coated magnetic stirring bar. The solids

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are scraped off the walls using a spatula (Note 10). The flask is immersed in a room temperature water bath and charged with anhydrous magnesium sulfate (30 g) and dichloromethane (140 mL) (Note 11). The mixture is stirred at ambient temperature and treated sequentially with triethylamine (60.0 mL, 43.6 g, 0.425 mol, 1.5 equiv) and pivaldehyde (95% purity, 35 mL, 28 g, 0.31 mmol, 1.07 equiv corrected for purity) (Notes 11 and 12). The flask is fitted with a rubber septum through which is inserted both an 18-gauge needle connected to a nitrogen inlet with a gas bubbler and a thermocouple probe (Note 4). The reaction mixture is stirred for 4 h at ambient temperature (Notes 13 and 14). Additional pivaldehyde (3 mL) and magnesium sulfate (5 g) are added, and the mixture is stirred for an additional 30 min at ambient temperature. The septum is removed and replaced with a 250-mL addition funnel. Toluene (200 mL) is added over 10 min, and the mixture is stirred for an additional 15 min. The mixture is then filtered through a 350-mL medium porosity sintered glass funnel to remove the triethylamine hydrochloride and magnesium sulfate. The filter cake is washed with toluene (3 x 50 mL). The combined filtrate is concentrated by rotary evaporation (100 mmHg initially to 20 mmHg, 45 °C bath temperature) to 70 g. Additional triethylamine hydrochloride precipitates during this concentration, so additional toluene (100 mL) is added and the mixture is filtered through a 60-mL medium porosity sintered glass funnel. The filtrate is concentrated by rotary evaporation (20 mmHg, 50 °C bath temperature), then vacuum dried (0.1 mmHg, 23 °C) for 4 h to afford (*S,E*)-2-(2,2-dimethylpropylidenamino)-*N*-methylpropanamide (**2**) (44.2–46.5 g, 95% purity, 86–90% yield) as a pale yellow oil. (Notes 15 and 16)

B.   *(2R,5S)-2-tert-butyl-3,5-dimethylimidazolidin-4-one (3)*.   A 500-mL round-bottomed, three-necked flask, equipped with a 3-cm oval PTFE-coated magnetic stirring bar, is fitted with two septa and a 100-mL pressure-equalizing addition funnel connected to a nitrogen inlet with a gas bubbler. A thermocouple probe is inserted through one septum (Note 4). The flask is charged with ethanol (140 mL), placed in an ice-water bath, and cooled to 1–3 °C. The addition funnel is charged with acetyl chloride (22.3 mL, 24.5 g, 0.312 mol, 1.1 equiv) (Note 17). The acetyl chloride is added dropwise over 15 min to the stirred ethanol solution, resulting in a temperature rise to 18 °C. The solution is cooled to 5 °C with an ice bath. The addition funnel is replaced with a standard tapered glass funnel, and maintaining ice bath cooling, the crude imine (**2**) (45.7 g, 95% pure, 0.255 mol) is poured into the HCl/ethanol solution as one portion over 30 s. The

flask that contained **2** is rinsed with ethanol (3 x 10 mL), and the rinses are added to the HCl/ethanol solution via the tapered glass funnel. The glass funnel is removed and replaced with an inlet adapter connected to a nitrogen line and gas bubbler. The reaction temperature rises from 5 °C to 30 °C over a 3 min period after addition of the imine, and crystallization occurs within 10 min (Note 18). The ice-bath is removed and replaced with a heating mantle, and the stirred mixture is warmed to 70 ± 2 °C over 30 min and held at this temperature for 20 min (Note 19). The mixture remains heterogeneous. The heating mantle is removed, and the stirred mixture is allowed to cool to 23 °C over 1.5 h, and stirring is continued for 2 h at ambient temperature. The resulting crystals are vacuum filtered using a 350-mL sintered glass funnel. The filter cake is washed with ethanol (2 x 30 mL) and air-dried to afford (2*R*,5*S*)-2-*tert*-butyl-3,5-dimethylimidazolidin-4-one (**3**) (43.2 g) as white crystalline material (Note 20). The mother liquors are concentrated to 80 mL by rotary evaporation (20 mmHg, 50 °C bath temperature) in a 500-mL round-bottomed flask, and the crystallization process is repeated to afford a second batch of **3** (3.9 g) as white crystalline material (Note 21). The first and second batches are combined to afford 47.1 g of **3** (89% yield for this step, 77–80% for 3 steps) (Notes 22-26).

2. Notes

1. A 1-L flask was used to minimize bumping during concentration after completion of the reaction.

2. Methylamine (33 wt% in ethanol) was purchased from Sigma-Aldrich and used as received. ^{1}H NMR analysis with a 5 second delay indicated the reagent contained 31 wt% methylamine and 69 wt% ethanol. The use of less than 3 equiv of methylamine led to incomplete conversion to the *N*-methyl amide.

3. L-Alanine methyl ester hydrochloride (**1**) was purchased from Sigma-Aldrich (99%) and Alfa Aesar (99%) and used as received. The hydrochloride salt is hygroscopic and was weighed into a bottle that was capped after weighing to avoid exposure to air prior to addition to the reaction. ^{1}H NMR analysis of this starting material is recommended as one sample contained 15% of the diketopiperazine impurity. Water content was measured by Karl-Fischer titration and ranged from 0.2 to 1.0% for the various lots of material used.

4. The internal temperature was monitored using a J-Kem Gemini digital thermometer with a Teflon-coated T-Type thermocouple probe (12-inch length, 1/8 inch outer diameter, temperature range –200 to +250 °C).

5. The mixture warms from 21 °C to 29 °C within 5 min of solids addition, then cools to 20-22 °C over 15 min in the water bath. In the hands of the checker the reaction solution remained heterogeneous throughout. In one experiment, an aliquot of the reaction mixture was filtered at the end of the reaction. The solids were determined to be methylamine hydrochloride by ^{1}H NMR analysis (CD_3OD).

6. The reaction progress is monitored by ^{1}H NMR analysis (CD_3OD) of aliquots of the reaction mixture. The starting material resonances at 3.74 (s, 3 H, O**CH$_3$**) and 1.34 (d, 3 H, CHC**H$_3$**) are monitored vs. product at 2.78 (s, 3 H, NHC**H$_3$**) and 1.29 (d, 3 H, CHC**H$_3$**). The reaction is complete after 1.5 h (<1% starting material based on a spiking experiment with starting material).

7. Toluene (ACS reagent grade, >99.5%) was purchased from Sigma-Aldrich and used as received

8. The solids are a mixture of methylamine and L-alanine-*N*-methylamide. The level of methylamine was typically ~40 mol% vs. product. The solids are vacuum dried until the level of ethanol and toluene are <3 mol% by ^{1}H NMR analysis. One experiment in which the toluene flushes were omitted afforded material that contained 15 mol% ethanol and 70 mol% methylamine relative to amide product. This material resulted in a 10 % lower yield in the imine formation.

9. Spectroscopic data for crude L-alanine-*N*-methylamide hydrochloride: ^{1}H NMR (400 MHz, CD_3OD) δ: 1.49 (d, *J* = 7.1 Hz, 3 H, CHC**H$_3$**), 2.79 (s, 3 H, NHC**H$_3$**), 3.93 (q, *J* = 7.0 Hz, 1 H, C**H**CH$_3$); ^{13}C NMR (100 MHz, CD_3OD) δ: 17.8, 26.5, 50.4, 171.6. Methylamine: ^{1}H NMR (400 MHz, CD_3OD) δ: 2.55 (s); ^{13}C NMR (100 MHz, CD_3OD) δ: 25.5.

10. Material dried on the walls of the flask tends not to react so optimum yields are obtained when this material is dislodged from the walls. L-Alanine-*N*-methylamide that is chunky or pasty in consistency performs well in the imine formation. The submitters report that thoroughly dried amide must be ground to a powder for optimum results.

11. The following reagents and solvents were used as received for the imine formation: anhydrous magnesium sulfate powder (Fisher), toluene (Sigma-Aldrich, ACS reagent grade, >99.5%), triethylamine (Sigma-

Aldrich, 99%), and dichloromethane (Fisher Optima, >99.5%). Pivaldehyde (96%) was purchased from Sigma-Aldrich; ^{1}H NMR analysis revealed a number of low level impurities that collectively integrated to ~5%. The material was charged based on 95% purity.

12. The mixture warms from 24 °C to 30 °C over a 5 min period after addition of pivaldehyde.

13. The reaction progress is followed with ^{1}H NMR by adding an aliquot of the reaction mixture to CDCl$_3$ and filtering the sample. To determine the level of pivaldehyde remaining, the sample is analyzed directly, comparing the aldehyde proton (9.5 ppm) of pivaldehyde to the corresponding proton of the imine (7.6 ppm). To accurately measure unreacted amide, the solution is evaporated to remove dichloromethane, then taken up in CDCl$_3$ for analysis (imine **CH**CH$_3$ quartet at 3.7 ppm compared to amide at 3.5 ppm).

14. Complete consumption of pivaldehyde typically occurs within a two hour reaction time but depends on the consistency of the amide (chunky material takes longer to react). The reaction typically stalls at 91-94% conversion, requiring an additional charge of pivaldehyde and magnesium sulfate. Addition of 10% more pivaldehyde or 25% more magnesium sulfate at the beginning of the reaction does not lead to increased conversion.

15. By ^{1}H NMR analysis, the imine contained 1.5 wt% unreacted amide and 3.5 wt% toluene. Toluene levels up to 8% were used with no impact for the next step. Amide levels up to 8% were used for the next step with no impact for the first and second crop isolations but co-crystallized with product if a third crop was isolated. The submitters stored the imine under vacuum. The checker stored the imine in a flask sealed with a septum and observed approximately 2% hydrolysis to the amide in a week at room temperature.

16. Spectroscopic data for **2**: ^{1}H NMR (400 MHz, CDCl$_3$) δ: 1.08 (s, 9 H, C(**CH**$_3$)$_3$), 1.31 (d, J = 7.1 Hz, 3 H, CH**CH**$_3$), 2.84 (d, J = 5.0 Hz, 3 H, N**CH**$_3$), 3.68 (q, J = 7.0 Hz, 1 H, **CH**CH$_3$), 6.9 (bs, 1 H, **H**NCH$_3$), 7.52 (s, 1 H, (CH$_3$)$_3$C**H**N); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 21.6, 26.0, 26.9, 36.6, 67.7, 173.2, 174.8.

17. Ethanol (ACS reagent, >99.5%, water content 0.37 mg/mL based on Karl Fischer titration) and acetyl chloride (reagent grade, 98%) were purchased from Sigma-Aldrich and used as received.

18. The reaction progress is monitored by ^{1}H NMR of a sample dissolved in CD$_3$OD. The reaction is complete within 10 min of imine addition with no resonances corresponding to the imine detectable.

19. The cyclization reaction forms a 3:1 mixture of trans:cis (**3:4**) diastereomers. Warming to 70 °C for 20 min results in equilibration to the thermodynamic ratio of 5:1 (this thermodynamic ratio in ethanol is also established starting with pure **3**). At the same time, decomposition of the diastereomers to amide **1** and the diethyl acetal of pivaldehyde occurs. At reflux (79 °C), the equilibration occurs within 5 – 10 min but degradation is also relatively rapid; therefore, the equilibration time and temperature were selected to afford complete equilibration with minimal decomposition (about 2%). The equilibration and decomposition of **3** is likely occurring via a reversible reaction with the imine as outlined below. Equilibration directly between **3** and **4** is unlikely as neither of the protons at positions 2 or 5 is exchanged in CD$_3$OD during equilibration, indicating that a deprotonation/ protonation process is not occurring. Starting with pure **3** in either methanol or ethanol solution, the equilibration of **3** and **4**, and their decomposition to amide **1** and the acetal of pivaldehyde, were followed by ^{1}H and ^{13}C NMR.
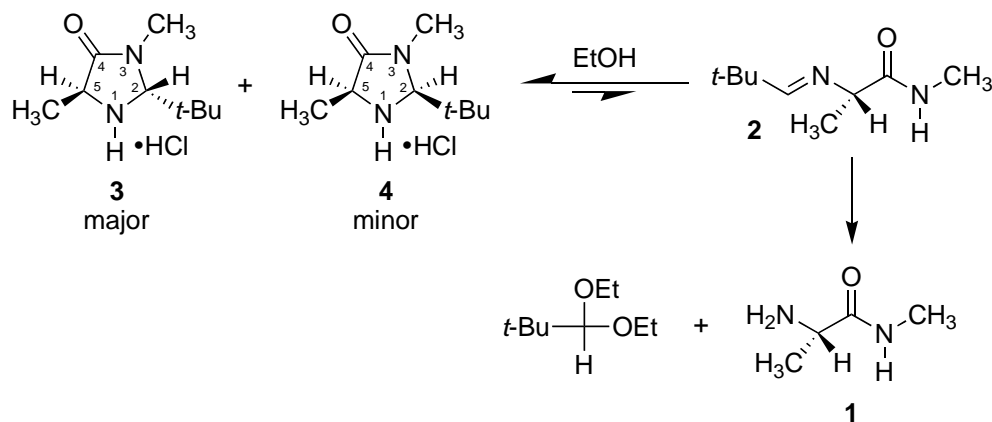
20. In the lab of the submitters, cooling the solution at a more rapid rate resulted in the entrainment of the minor diastereomer, (2*S*,5*S*)-2-*tert*-butyl-3,5-dimethylimidazolidin-4-one **4**. In addition, the submitters report cooling the solution below 20 °C, or allowing **3** to age with the mother liquors for >6 h, caused the minor diastereomer to begin crystallizing. In the lab of the checker, the minor diastereomer **4** was never detected in crystalline **3** (<0.2% by NMR) even with >12 h crystallization age times. It is important to adequately wash the filter cake to ensure that the mother liquors are not entrained.

21. ^{1}H NMR (CD$_3$OD) analysis of an evaporated sample of the mother liquors indicated a ratio of **3:4:1** of 49:37:12. Heating at 70 ± 2 °C for 20 min resulted in equilibration to a 5:1 ratio of **3:4**.

22. A third crop of **3** can be obtained by concentrating the remaining mother liquors to 40 mL and repeating the equilibration/crystallization procedure to afford 1.1 g of **3**.

23. (2*R*,5*S*)-2-*tert*-Butyl-3,5-dimethylimidazolidin-4-one (**3**) has the following physical and spectroscopic data: mp 211–216 °C with decomposition (ethanol); $[\alpha]_D$ -43.4 (*c* 1.0, CH$_3$OH, 23 °C); IR (solid) 2873, 2641, 2514, 1719, 1584 cm^{-1}; ^{1}H NMR (400 MHz, CD$_3$OD) δ: 1.19 (s, 9 H, (C**H**$_3$)$_3$C), 1.59 (d, *J* = 7.0 Hz, 3 H, CHC**H**$_3$), 3.09 (s, 3 H, NC**H**$_3$), 4.28 (q, *J* = 7.0 Hz, 1 H, C**H**CH$_3$), 4.79 (s, 1 H, (CH$_3$)$_3$CC**H**); ^{13}C NMR (100 MHz, CD$_3$OD) δ: 14.9, 25.5, 32.5, 37.7, 54.9, 82.0, 171.3; HRMS (ESI-TOF) *m/z* calcd for C$_9$H$_{19}$N$_2$O ([M+H]$^+$) 171.1492, found 171.1492; Karl Fischer titration: 0.1% water; elemental analysis calcd. for C$_9$H$_{19}$ClN$_2$O: C, 52.29; H, 9.26; N, 13.55; found: C, 52.53; H, 9.51; N, 13.51; chloride titration (AgNO$_3$) calcd: Cl, 17.15; found Cl, 17.16.

24. The minor diastereomer, (2*S*,5*S*)-2-*tert*-butyl-3,5-dimethyl-imidazolidin-4-one (**4**), has the following spectroscopic data: ^{1}H NMR (400 MHz, CD$_3$OD) δ: 1.19 (s, 9 H, (C**H**$_3$)$_3$C), 1.59 (d, *J* = 7.2 Hz, 3 H, CHC**H**$_3$), 3.04 (s, 3 H, NC**H**$_3$), 4.13 (q, *J* = 7.1 Hz, 1 H, C**H**CH$_3$), 4.71 (s, 1 H, (CH$_3$)$_3$CC**H**); ^{13}C NMR (100 MHz, CD$_3$OD) δ: 14.9, 25.4, 31.5, 35.3, 54.8, 81.8, 171.6.

25. Imidazolidinone **3** is converted, as follows, to (2*S*,5*S*)-benzyl-2-*tert*-butyl-3,5-dimethyl-4-oxoimidazolidine-1-carboxylate for assessing the enantiopurity:
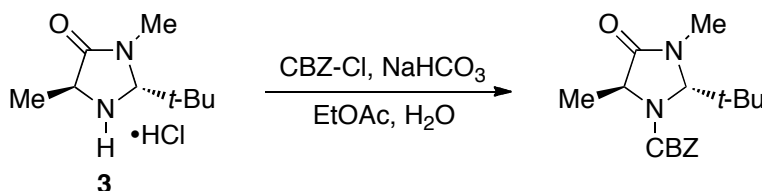
An 8 mL vial is charged with **3** (100 mg, 0.48 mmol, 1.0 equiv), solid NaHCO$_3$ (200 mg, 2.4 mmol, 5.0 equiv), ethyl acetate (1.0 mL) and water (1.0 mL). The mixture is treated with benzyl chloroformate (100 μL, 0.72 mmol, 1.5 equiv) and stirred at ambient temperature for 16 h. The layers are separated and the aqueous layer is extracted with ethyl acetate (2 mL). The combined organic layers are concentrated and purified on SiO$_2$ (10 g),

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eluent: 25% ethyl acetate/ hexanes, 10 mL fractions. Fractions 8-13 are concentrated to afford (2*S*,5*S*)-benzyl-2-*tert*-butyl-3,5-dimethyl-4-oxoimidazolidine-1-carboxylate (130 mg, 88%) as a clear, colorless syrup: R_f 0.4 (40% ethyl acetate/ hexanes); $[\alpha]_D$ –15.3 (*c* 1.00, CH_2Cl_2, 22 °C); IR (neat) 2966, 1699, 1411, 1392, 1251, 1119, 698 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) matches reported spectrum (Seebach, D.; Juaristi, E.; Miller, D. D.; Schickli, C.; Weber, T. *Helv. Chim. Acta* **1987**, *70*, 237-261) δ: 0.97 (s, 9 H, C(C**H**$_3$)$_3$, 1.55 (bs, 3 H, CHC**H**$_3$), 3.01 (s, 3 H, NC**H**$_3$), 4.04-4.06 (m, 1 H, C**H**CH$_3$), 5.05-5.21 (m, 3 H, C**H**C(CH$_3$)$_3$, PhC**H**$_2$O), 7.33-7.39 (m, 5 H, Ar**H**); ^{13}C NMR (125 MHz, CDCl$_3$) δ: 18 (br), 26.5, 32.2, 40.7, 56.0, 67.7, 81.2, 128.6, 128.80, 128.81, 136.0, 155 (br), 173.0; HRMS (ESI-TOF) *m/z* calcd for $C_{17}H_{25}N_2O_3$ ([M+H]$^{+}$) 305.1865, found 305.1865. Since both enantiomers were required to develop a chiral assay, the enantiomer of **3** was prepared from *D*-alanine methyl ester hydrochloride. Submitters chiral HPLC analysis: AD-H (250 x 4.6 mm, 5µm particle size), isocratic elution with 15% ethanol/hexanes, 1.0 mL/min, 254 nm), R_t(major) = 8.47 min, R_t(minor) = 6.87 min; checkers chiral SFC analysis: AD-H (250 x 4.6 mm, 5µm particle size), isocratic elution with 4% MeOH containing 25 mM isobutylamine, 3.0 mL/min, 200 bar, 35 °C, 215 nm, 6 min total run time; R_t(major) = 3.9 min, R_t(minor) = 4.5 min. None of the minor enantiomer was detected; spiking experiments indicated the ee was >99%.

26. Imidazolidinone **3** is non-hygroscopic at ambient humidity conditions and can be stored in a closed container at ambient temperature with no additional precautions.

Safety and Waste Disposal Information

All hazardous materials should be handled and disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

Over the past decade, organocatalysis has emerged as a versatile method for the enantioselective preparation of organic molecules.[3] Among the numerous organocatalysts developed, the imidazolidinone family is one of the most versatile catalysts, mediating a variety of transformations including Diels-Alder,[4] 1,3-dipolar cycloadditions,[5] 1,4-conjugate additions,[6]

α-oxidations,[7] α-chlorinations, α-fluorinations,[8] hydride reductions,[9] and epoxidations.[10] In addition, the mild reaction conditions and selectivity of the imidazolidinone organocatalysts allow for efficient cascade catalysis.[11] A new mode of activation, SOMO catalysis, involving the oxidative coupling of enamines and nucleophiles (SOMO-philes) allows for unprecedented enantioselective transformations including α-allylations,[12] α-enolations,[13] α-vinylation,[14] α-nitroalkylation,[15] α-arylations[16] and the carbo-oxidation of styrenes.[17]

Recently, (2R,5S)-2-*tert*-butyl-3,5-dimethylimidazolidin-4-one (**3**) has emerged as a privileged organocatalyst that mediates a variety of useful asymmetric transformations (Scheme 1). The α-chlorination of aldehydes occurs in 75-95% yield and 91-96% ee and the α-chloroaldehydes can be transformed into a variety of enantio-enriched epoxides, aziridines, α-chloro alcohols, α-cyano alcohols, α-hydroxy acids, and α-amino acids (Scheme 1, eq 1).[18] The α-trifluoromethylation of aldehydes occurs in 62-86% yield and 93-99% ee using visible light and 0.5 mol% of an iridium photoredox catalyst (Scheme 1, eq 2).[19] Similarly, bromoalkanes will add to the aldehyde with visible light and 0.5 mol% of a ruthenium photoredox catalyst (Scheme 1, eq 3).[20]

Scheme 1.
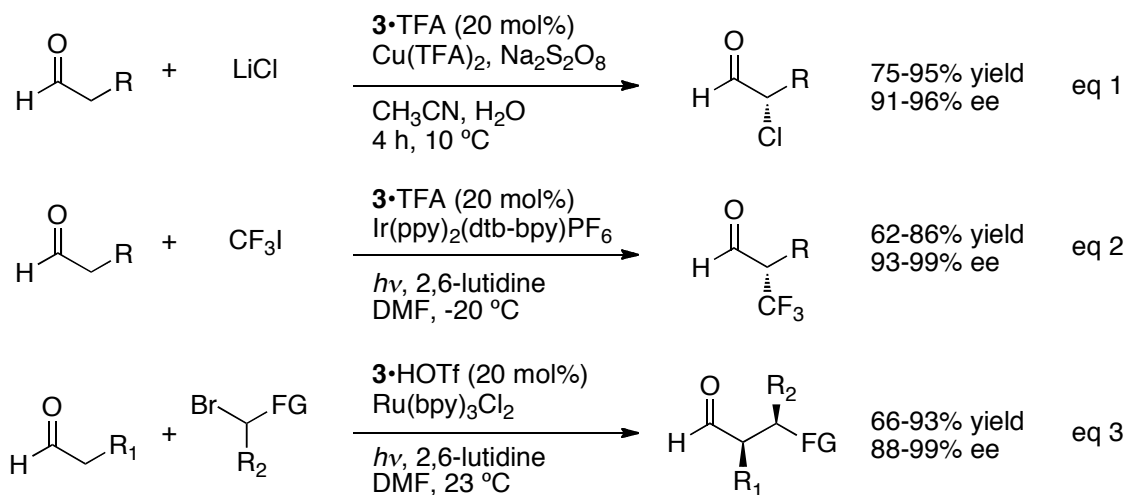
The procedure describes the preparation of (2R,5S)-2-*tert*-butyl-3,5-dimethylimidazolidin-4-one (**3**) from L-alanine methyl ester hydrochloride.[21] The present method consistently affords **3** as white crystals in good yield (77–80% for 3 steps) and high enantiomeric purity (>99% ee), without intermediate purifications or chromatography.

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2. The checker thanks Zainab Pirzada for development of the chiral assay of the CBZ derivative of compound **3**, Mirlinda Biba for the rotation and chloride analyses, and Robert Reamer for NMR support.

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Appendix
Chemical Abstracts Nomenclature (Registry Number)

Acetyl chloride: (75-36-5)

L-Alanine methyl ester hydrochloride: (2491-20-5)

Benzyl chloroformate, carbobenzoxy chloride: (501-53-1)

Methylamine: (74-89-5)

Pivaldehyde, trimethylacetaldehyde: (630-19-3)

Triethylamine, *N*,*N*-diethyl-ethanamine: (121-44-8)

David W. C. MacMillan received his B.S. degree in chemistry in 1990 from the University of Glasgow, Scotland, and his Ph.D. degree in 1996 from the University of California, Irvine, where he worked under the direction of Professor Larry E. Overman. David then moved to Harvard University and completed his postdoctoral studies with Professor David A. Evans. In 1998, David joined the faculty at the University of California, Berkeley. In 2000, he moved to the California Institute of Technology, where, in 2003, he was promoted to the rank of full professor and the following year, he became the Earle C. Anthony Chair in Organic Chemistry. In 2006, David moved to Princeton University where he is the A. Barton Hepburn Professor of Chemistry, the Director of the Merck Center for Catalysis at Princeton and the Chairperson of the Department of Chemistry.

Thomas H. Graham received his B.S. in Chemical Engineering from Virginia Tech in 1995. He completed his undergraduate research in the laboratory of Professor Neal Castagnoli, Jr. He then moved to Research Triangle Park, North Carolina, where he worked for Eli Lilly and was involved in chemical synthesis, laboratory automation and technology development. From 2000 to 2006, he completed his graduate studies in organic chemistry with Professor Peter Wipf at the University of Pittsburgh. From 2006 to 2008, he was a postdoctoral fellow with Professor David MacMillan at Princeton University. He is currently employed at Merck Research Laboratories in Rahway, New Jersey.
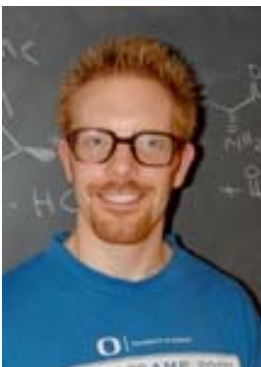
Benjamin D. Horning received his B.S. in Biochemistry at the University of Oregon in Eugene, Oregon in 2007. He did undergraduate research with Professor Michael Haley studying metalla-benzenes. He is currently a graduate student at Princeton University with Professor David MacMillan studying natural product synthesis and cascade catalysis.

Current Data Parameters
NAME   2010-137
EXPNO   3
PROCNO   1

F2 - Acquisition Parameters
Date_   20100703
Time   15.52
INSTRUM   spect
PROBHD   5 mm QNP 1H/1
PULPROG   zg30
TD   32768
SOLVENT   MeOD
NS   64
DS   2
SWH   6578.947 Hz
FIDRES   0.200774 Hz
AQ   2.4904180 sec
RG   181
DW   76.000 usec
DE   7.00 usec
TE   300.0 K
D1   0.10000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   11.20 usec
PL1   6.00 dB
SFO1   399.8724694 MHz

F2 - Processing parameters
SI   16384
SF   399.8700107 MHz
WDW   no
SSB   0
LB   0.00 Hz
GB   0
PC   1.00

MeNH2
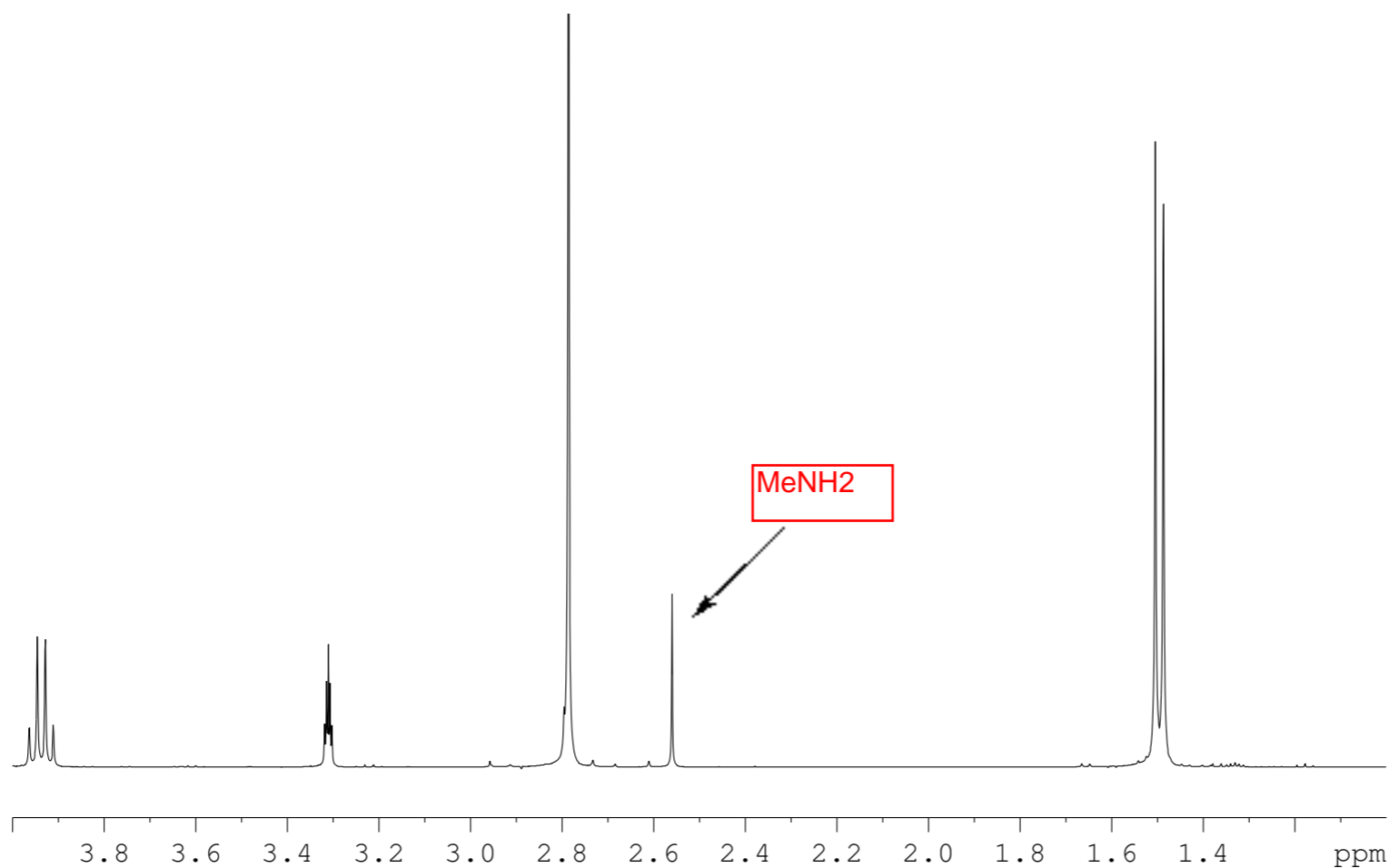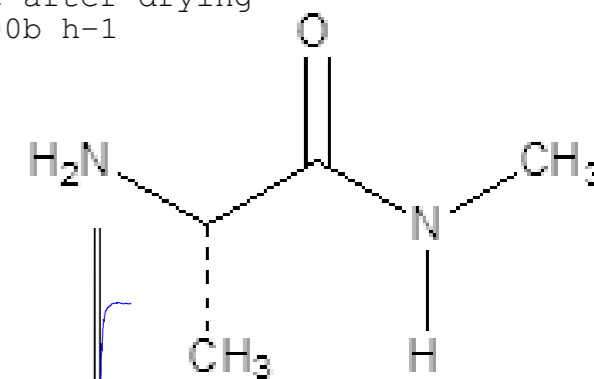
Peak	?(F1) [ppm]	?(F1) [Hz]	Intensity
1	3.9640	1585.0847	0.78
2	3.9464	1578.0470	2.50
3	3.9288	1571.0093	2.51
4	3.9112	1563.9716	0.81
5	3.3189	1327.1286	0.83
6	3.3149	1325.5291	1.64
7	3.3109	1323.9296	2.36
8	3.3068	1322.2902	1.61
9	3.3028	1320.6907	0.80
10	2.7956	1117.8766	1.16
11	2.7864	1114.1978	20.00
12	2.5598	1023.5873	3.34
13	1.5053	601.9243	11.99
14	1.4876	594.8466	11.18
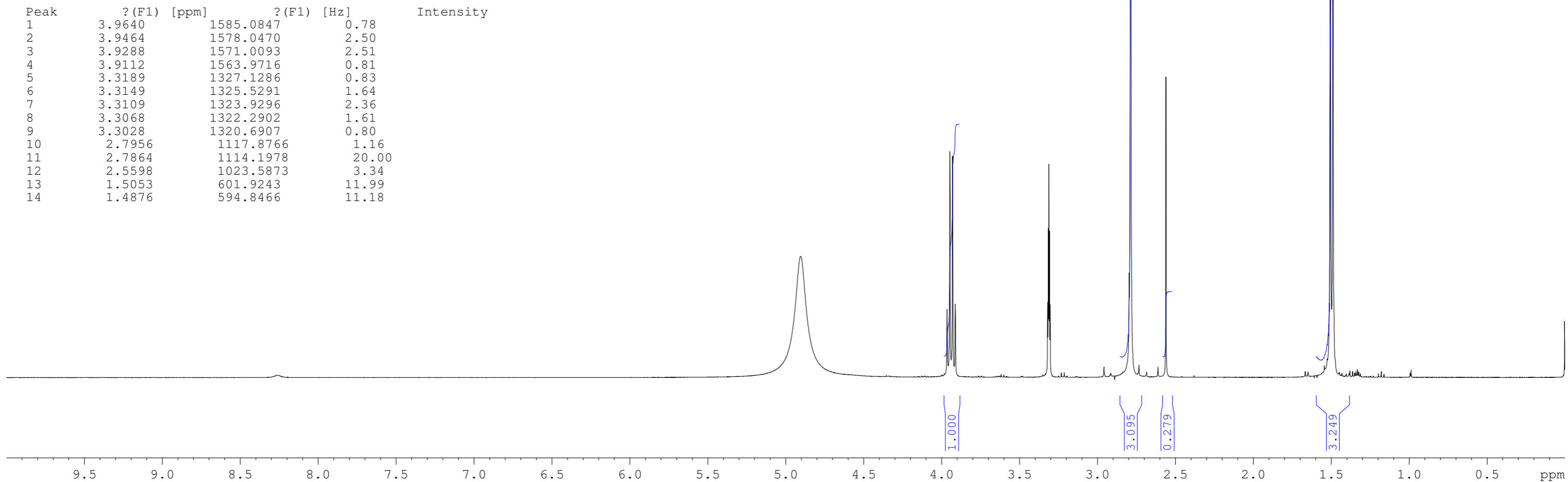
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NAME   2010-137
EXPNO   4
PROCNO   1

F2 - Acquisition Parameters
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Time   16.01
INSTRUM   spect
PROBHD   5 mm QNP 1H/1
PULPROG   zgdc
TD   65536
SOLVENT   CDCl3
NS   1306
DS   4
SWH   26315.789 Hz
FIDRES   0.401547 Hz
AQ   1.2452340 sec
RG   8192
DW   19.000 usec
DE   7.00 usec
TE   300.0 K
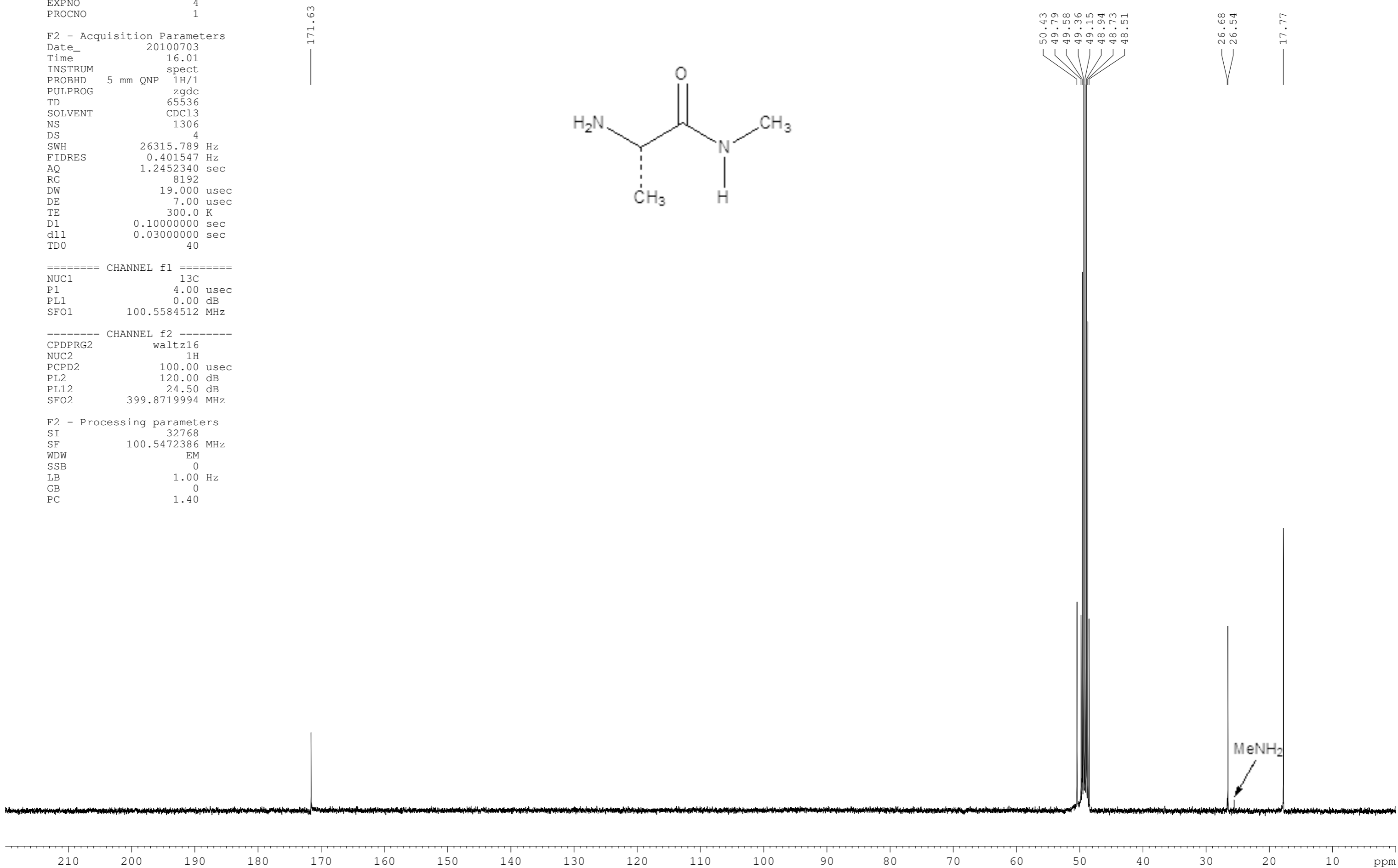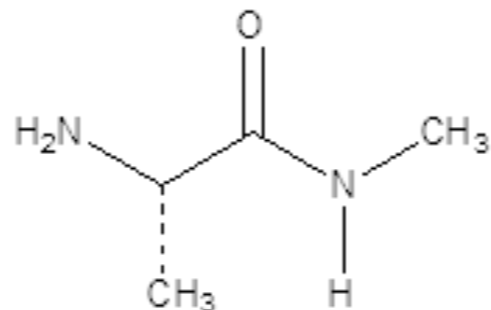D1   0.10000000 sec
d11   0.03000000 sec
TD0   40

======== CHANNEL f1 ========
NUC1   13C
P1   4.00 usec
PL1   0.00 dB
SFO1   100.5584512 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   100.00 usec
PL2   120.00 dB
PL12   24.50 dB
SFO2   399.8719994 MHz

F2 - Processing parameters
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SF   100.5472386 MHz
WDW   EM
SSB   0
LB   1.00 Hz
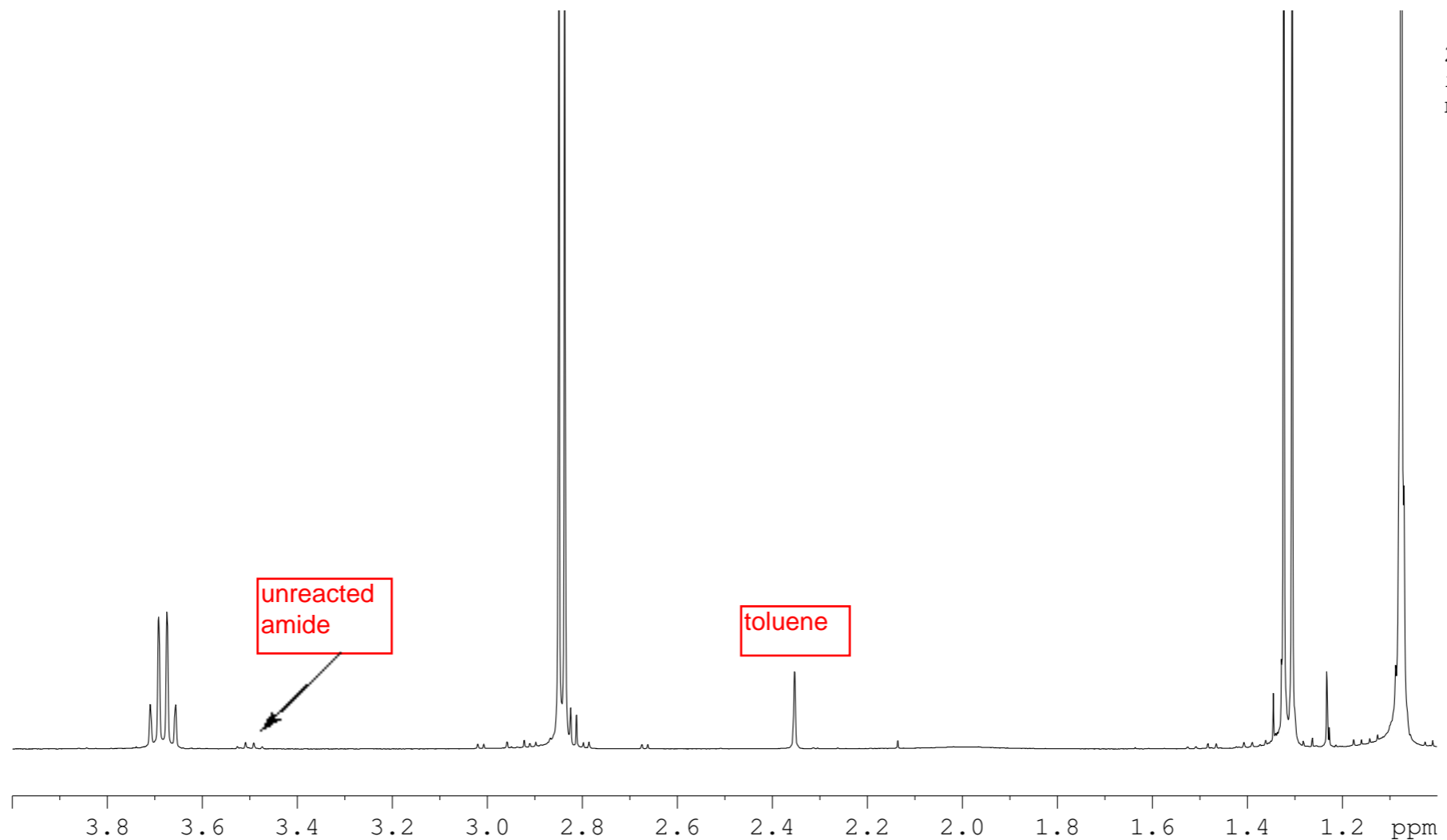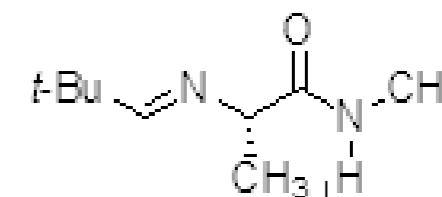GB   0
PC   1.40

171.63

50.43
49.79
49.58
49.36
49.15
48.94
48.73
48.51

26.68
26.54

17.77

MeNH$_2$

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

2010-143
imine vacuum dried
nmr400b h-1

Current Data Parameters
NAME   2010-143
EXPNO   5
PROCNO   1

F2 - Acquisition Parameters
Date_   20100724
Time   10.39
INSTRUM   spect
PROBHD   5 mm QNP 1H/1
PULPROG   zg30
TD   32768
SOLVENT   CDCl3
NS   70
DS   2
SWH   6578.947 Hz
FIDRES   0.200774 Hz
AQ   2.4904180 sec
RG   287.4
DW   76.000 usec
DE   7.00 usec
TE   300.0 K
D1   0.10000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   11.20 usec
PL1   6.00 dB
SFO1   399.8724694 MHz

F2 - Processing parameters
SI   16384
SF   399.8700086 MHz
WDW   no
SSB   0
LB   0.00 Hz
GB   0
PC   1.00

unreacted amide

toluene

Peak	?(F1) [ppm]	?(F1) [Hz]	Intensity
1	7.5220	3007.8222	1.38
2	7.2707	2907.3349	0.55
3	3.7095	1483.3178	0.14
4	3.6919	1476.2801	0.41
5	3.6743	1469.2424	0.42
6	3.6567	1462.2047	0.14
7	2.8497	1139.5096	2.67
8	2.8372	1134.5112	2.72
9	2.8250	1129.6328	0.13
10	2.8123	1124.5544	0.11
11	2.3535	941.0941	0.24
12	1.3457	538.1051	0.17
13	1.3283	531.1473	0.29
14	1.3237	529.3079	3.27
15	1.3062	522.3102	2.99
16	1.2329	492.9997	0.25
17	1.0882	435.1385	0.27
18	1.0763	430.3801	20.00
19	1.0709	428.2208	0.83
20	0.9711	388.3138	0.10
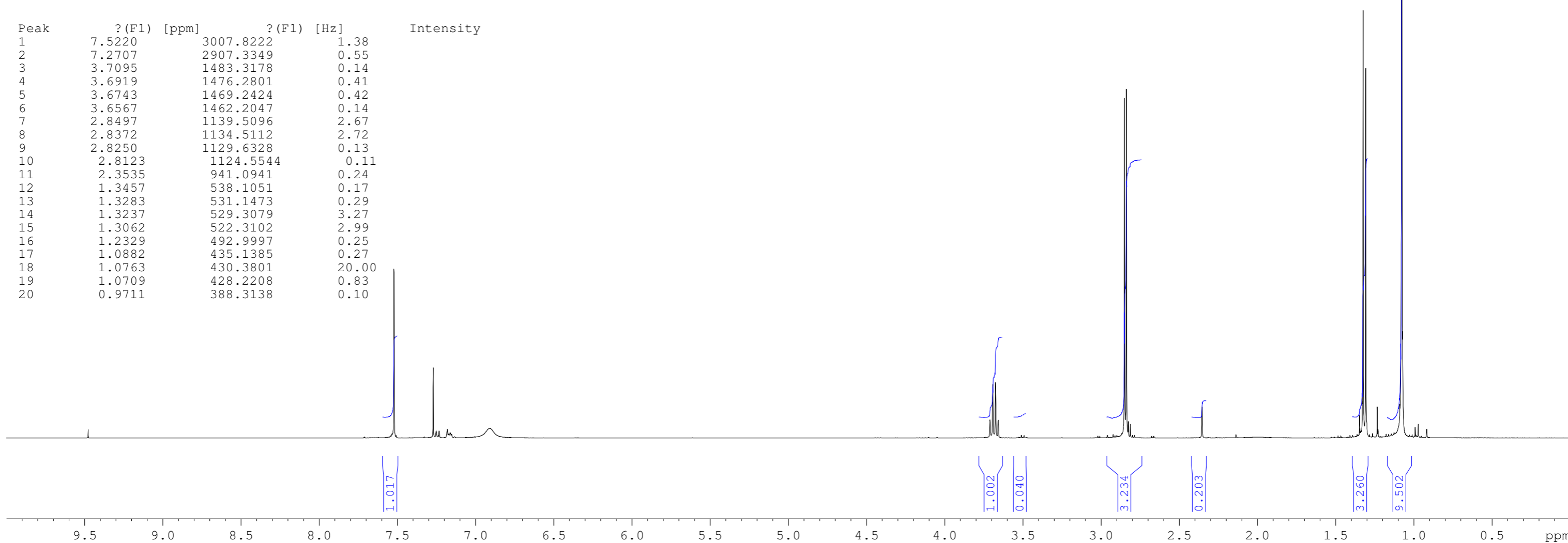
Peak	?(F1) [ppm]	?(F1) [Hz]	Intensity
1	174.7988	17575.5598	0.95
2	173.1683	17411.6173	3.65
3	77.5538	7797.8307	7.20
4	77.2357	7765.8466	7.39
5	76.9175	7733.8524	7.25
6	67.7379	6810.8678	3.62
7	36.5891	3678.9378	1.53
8	26.9085	2705.5789	15.00
9	26.0384	2618.0927	2.76
10	21.5512	2166.9165	4.37
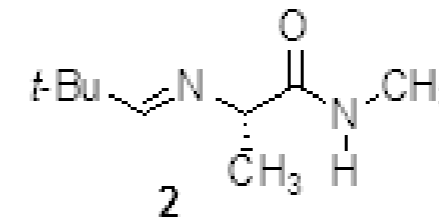
Current Data Parameters
NAME   2010-143
EXPNO   6
PROCNO   1

F2 - Acquisition Parameters
Date_   20100724
Time   10.46
INSTRUM   spect
PROBHD   5 mm QNP 1H/1
PULPROG   zgdc
TD   65536
SOLVENT   CDCl3
NS   2990
DS   4
SWH   26315.789 Hz
FIDRES   0.401547 Hz
AQ   1.2452340 sec
RG   8192
DW   19.000 usec
DE   7.00 usec
TE   300.0 K
D1   0.10000000 sec
d11   0.03000000 sec
TD0   40
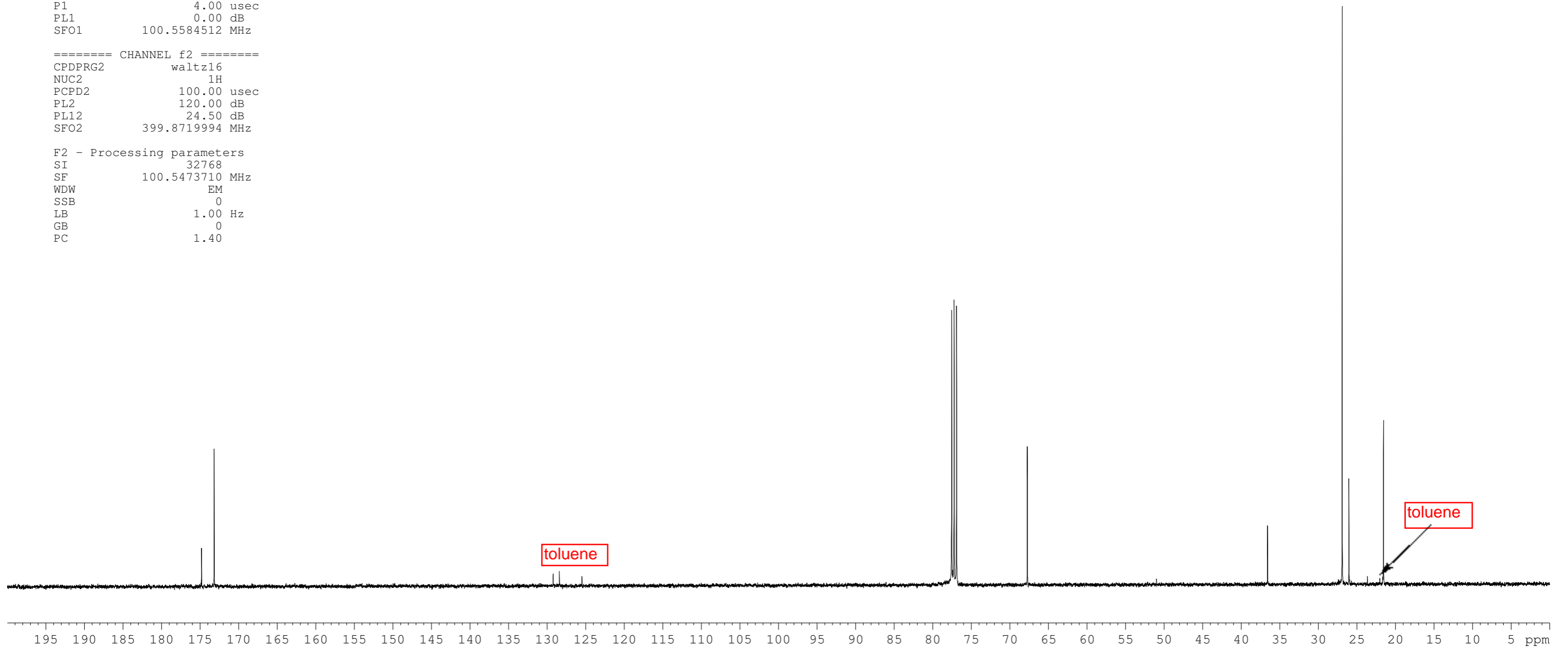
======== CHANNEL f1 ========
NUC1   13C
P1   4.00 usec
PL1   0.00 dB
SFO1   100.5584512 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   100.00 usec
PL2   120.00 dB
PL12   24.50 dB
SFO2   399.8719994 MHz

F2 - Processing parameters
SI   32768
SF   100.5473710 MHz
WDW   EM
SSB   0
LB   1.00 Hz
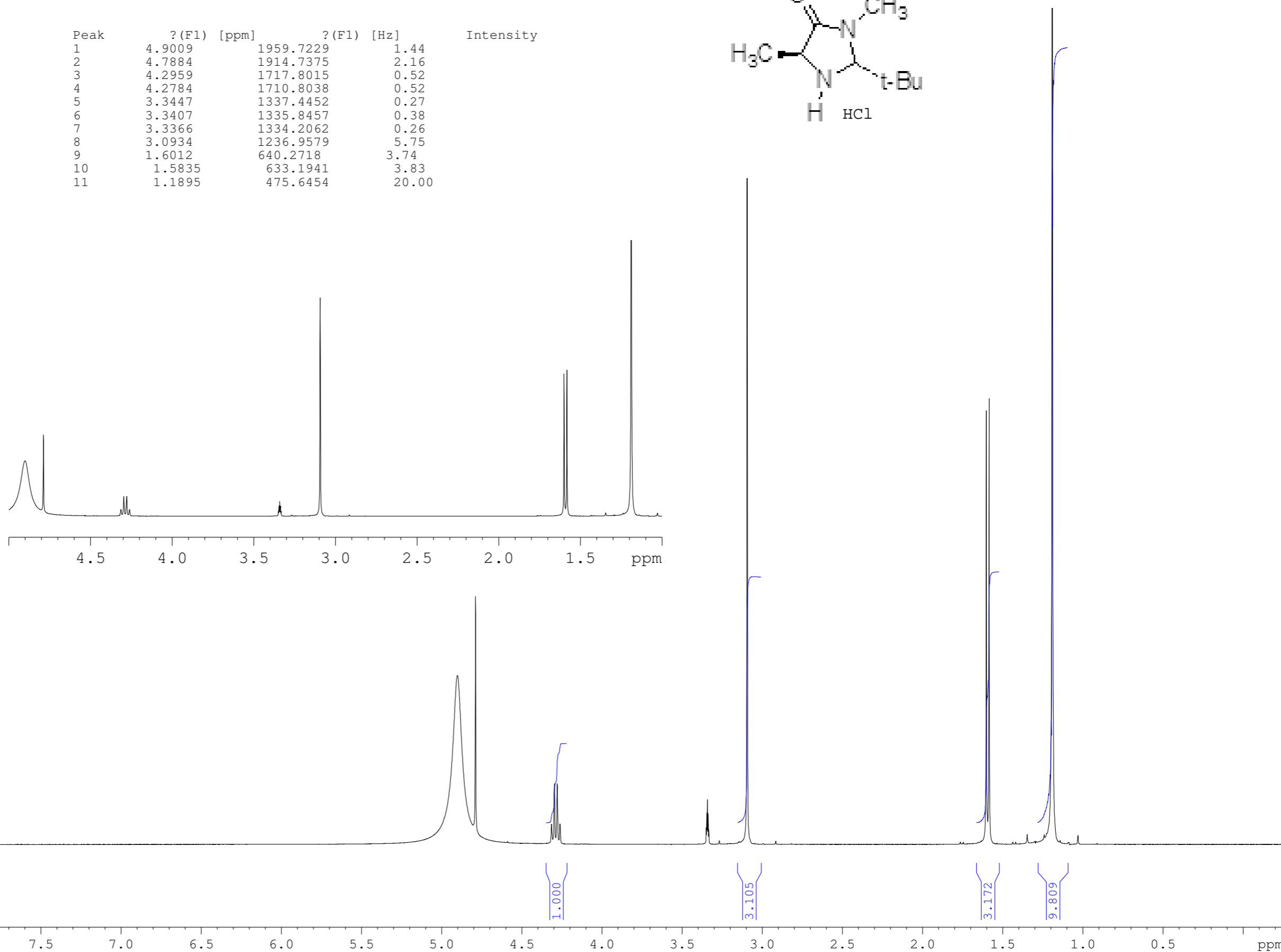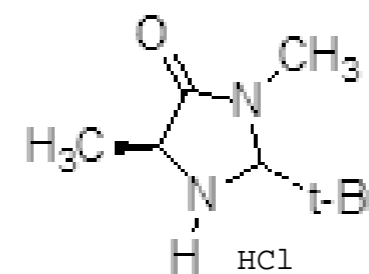GB   0
PC   1.40

77.55
77.24
76.92
67.74
36.59
26.91
26.04
21.55

toluene

toluene

2010-128
imidazilinone
nmr400b h-1

Peak	?(F1) [ppm]	?(F1) [Hz]	Intensity
1	4.9009	1959.7229	1.44
2	4.7884	1914.7375	2.16
3	4.2959	1717.8015	0.52
4	4.2784	1710.8038	0.52
5	3.3447	1337.4452	0.27
6	3.3407	1335.8457	0.38
7	3.3366	1334.2062	0.26
8	3.0934	1236.9579	5.75
9	1.6012	640.2718	3.74
10	1.5835	633.1941	3.83
11	1.1895	475.6454	20.00

Current Data Parameters
NAME   2010-128
EXPNO   11
PROCNO   1

F2 - Acquisition Parameters
Date_   20100612
Time   12.18
INSTRUM   spect
PROBHD   5 mm QNP 1H/1
PULPROG   zgdc
TD   65536
SOLVENT   CDCl3
NS   2354
DS   4
SWH   26315.789 Hz
FIDRES   0.401547 Hz
AQ   1.2452340 sec
RG   8192
DW   19.000 usec
DE   7.00 usec
TE   300.0 K
D1   0.10000000 sec
d11   0.03000000 sec
TD0   40
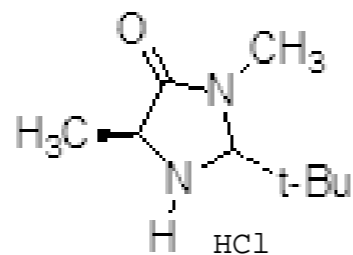
======== CHANNEL f1 ========
NUC1   13C
P1   4.00 usec
PL1   0.00 dB
SFO1   100.5584512 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   100.00 usec
PL2   120.00 dB
PL12   24.50 dB
SFO2   399.8719994 MHz

F2 - Processing parameters
SI   32768
SF   100.5472413 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

81.95

54.95
49.58
49.37
49.16
48.94
48.73

37.66

32.54

25.47

14.85
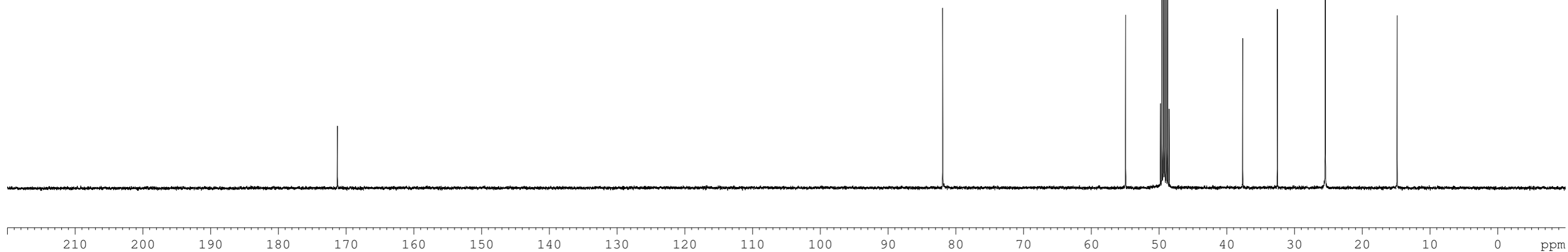
Current Data Parameters
NAME   2010-133A
EXPNO   10
PROCNO   1

F2 - Acquisition Parameters
Date_   20100731
Time   11.01
INSTRUM   spect
PROBHD 5 mm QNP 1H/13
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   51
DS   4
SWH   13020.833 Hz
FIDRES   0.198682 Hz
AQ   2.5166707 sec
RG   161.3
DW   38.400 usec
DE   6.50 usec
TE   300.0 K
D1   0.10000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   12.00 usec
PL1   -4.00 dB
SFO1   500.1330885 MHz

F2 - Processing parameters
SI   32768
SF   500.1300079 MHz
WDW   no
SSB   0
LB   0.00 Hz
GB   0
PC   1.00

Peak	?(F1) [ppm]	?(F1) [Hz]	Intensity	Annotation
1	7.3846	3693.2601	4.46	
2	7.3823	3692.1098	3.24	
3	7.3752	3688.5588	10.69	
4	7.3713	3686.6083	0.61	
5	7.3688	3685.3580	0.53	
6	7.3660	3683.9576	0.73	
7	7.3589	3680.4067	1.23	
8	7.3519	3676.9058	1.21	
9	7.3479	3674.9053	0.39	
10	7.3422	3672.0545	0.72	
11	7.3382	3670.0540	0.23	
12	7.3352	3668.5536	0.38	
13	7.3320	3666.9532	0.24	
14	7.2701	3635.9952	3.25	
15	5.2073	2604.3270	0.67	
16	5.1834	2592.3739	1.16	
17	5.1221	2561.7159	0.26	
18	5.0548	2528.0572	0.34	
19	4.0559	2028.4773	0.40	
20	4.0438	2022.4257	0.38	
21	3.0584	1529.5976	0.31	
22	3.0297	1515.2439	0.23	
23	3.0104	1505.5914	13.13	
24	2.1725	1086.5324	0.21	
25	2.0468	1023.6661	0.53	
26	1.6889	844.6696	0.34	
27	1.5478	774.1012	1.02	
28	1.2770	638.6660	0.20	
29	1.2627	631.5142	0.43	
30	1.2484	624.3623	0.20	
31	1.0356	517.9346	0.28	
32	0.9979	499.0797	0.19	
33	0.9742	487.2267	0.99	
34	0.9579	479.0745	20.00	