Organic Syntheses

Preparation of Cyclopent-2-enone Derivatives via the Aza-Piancatelli Rearrangement

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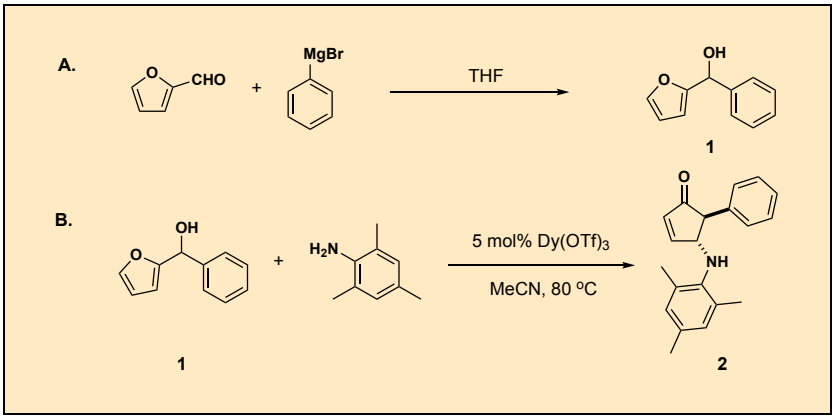
Checked by Feng Peng and Kevin Campos



Procedure (Note 1)

A. *Furan-2-yl(phenyl)methanol (**1**).* An oven-dried 500 mL three-necked, round-bottomed flask equipped with an egg-shaped, Teflon-coated magnetic stir bar (3 cm x 1.5 cm) is capped on all necks with rubber septa. Phenylmagnesium bromide (57.4 mL, 57.4 mmol, 1.0 equiv, 1M in THF) (Note 2) is charged into this flask under an atmosphere of nitrogen at 5 °C (ice-water bath). Furfural (4.76 mL, 57.4 mmol, 1.0 equiv) (Note 3) is added over the course of 30 min via syringe into the cooled reaction through a side neck while maintaining internal temperature below 25 °C. Once all furfural is added the reaction stirs for 4 h. The reaction is monitored by thin-layer

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chromatography (TLC) analysis on silica gel with 70% hexanes in ethyl acetate as eluent and visualized under 254 nm UV light and stained with *p*-anisaldehyde (Note 4). Upon confirmation of product formation the reaction is quenched with saturated aqueous ammonium chloride (1 x 100 mL) and transferred to a 1 L separatory funnel and extracted with ethyl acetate (3 x 100 mL). The combined organic layers are dried over $MgSO_4$, filtered and concentrated to produce a yellow-orange oil. The product of the crude reaction mixture is purified via column chromatography (Note 5) to afford furan-2-yl(phenyl)methanol (**1**) as a yellow oil (9.71 g, 94%) (Notes 6, 7, and 8).

B. *4-(Mesitylamino)-5-phenylcyclopent-2-en-1-one* (**2**). An oven-dried 500 mL single-necked, round-bottomed flask equipped with an egg-shaped, Teflon-coated magnetic stir bar (3 cm x 1.5 cm) is capped with a rubber septum. While cooling to ambient temperature under an atmosphere of nitrogen, an oil bath is preheated to 80 °C. Once the flask is cooled, furan-2-yl(phenyl)methanol (**1**) (3.95 g, 22.7 mmol, 1.1 equiv) (Note 9) and acetonitrile (200 mL) (MeCN) (Notes 10 and 11) are added along with 2,4,6-trimethylaniline (2.78 g, 20.5 mmol, 1.0 equiv) (Note 12), resulting in a pale brown homogeneous mixture (Figure 1).

Figure 1. Homogenous mixture of furan-2-yl(phenyl)methanol and 2,4,6-trimethylaniline

Dysprosium(III) trifluoromethanesulfonate ($Dy(OTf)_3$, 0.628 g, 1.03 mmol, 0.05 equiv) is added (Notes 13 and 14). Immediately following addition, the flask is fitted with a water reflux condenser, placed under an atmosphere of nitrogen, and submerged in the oil bath that is preheated to 80 °C and stirred for 4 h (Note 15).

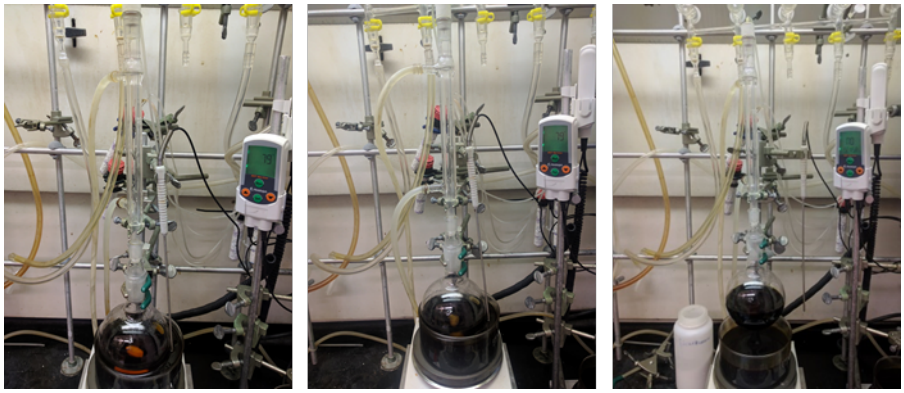

Figure 2. Reaction mixture 15 minutes into heating (left), 30 minutes into heating (center), and after 3 hours of heating (right)

The reaction mixture becomes dark brown in color upon heating (Figure 2). The reaction is followed by TLC analysis on silica gel with 85% hexanes in ethyl acetate as eluent and visualized with under 254 nm UV light and stained with *p*-anisaldehyde (Note 16). Upon confirmation that no 1,3,5-trimethylaniline remains, the stirring is stopped and the reaction mixture is allowed to cool to ambient temperature under an atmosphere of nitrogen. The cooled reaction mixture is quenched with saturated aqueous sodium bicarbonate (1 x 150 mL) and transferred to a 1 L separatory funnel and extracted with ethyl acetate (3 x 150 mL) (Figure 3).

Figure 3. Reaction mixture being quenched with sodium bicarbonate (left) and the final extraction with ethyl acetate (right)

The combined organic layers are dried over $MgSO_4$, filtered and concentrated (25 °C, 10 mmHg) to produce a dark brown oil. The product of the crude reaction mixture is purified via column chromatography (Note 17) to afford the cyclopentenone product (**2**) as a brown oil (4.97 g, 83%) (Notes 18, 19, 20, 21, and 22) (Figure 4).

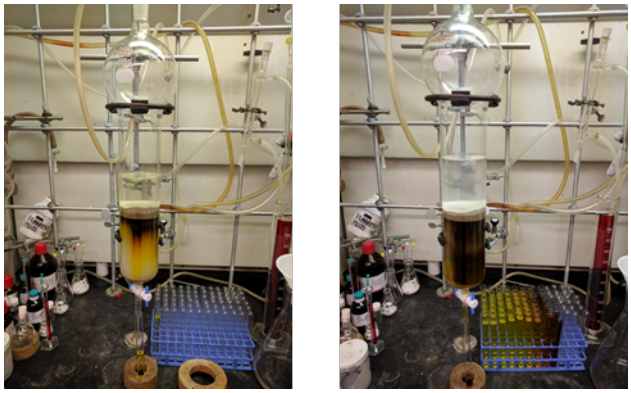

Figure 4. Column chromotagraphy on crude product (left) and the final dark brown oil cyclopentenone product (right)

Notes

1. Prior to performing each reaction, a thorough hazard analysis and risk assessment should be carried out with regard to each chemical substance and experimental operation on the scale planned and in the context of the laboratory where the procedures will be carried out. Guidelines for carrying out risk assessments and for analyzing the hazards associated with chemicals can be found in references such as Chapter 4 of "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at https://www.nap.edu/catalog/12654/prudent-practices-in-the-laboratory-handling-and-management-of-chemical). See also "Identifying and Evaluating Hazards in Research Laboratories" (American Chemical Society, 2015) which is available via the associated website "Hazard Assessment in Research Laboratories" at https://www.acs.org/content/acs/en/about/governance/committees/chemicalsafety/hazard-assessment.html. In the case of this procedure,

the risk assessment should include (but not necessarily be limited to) an evaluation of the potential hazards associated with magnesium, bromobenzene, tetrahydrofuran, phenylmagnesium bromide, furfural, ethyl acetate, ammonium chloride, hexane, silica gel, acetonitrile, furan-2-yl(phenyl)methanol, dysprosium(III) trifluoromethanesulfonate, and 2,4,6-trimethylaniline.

2. The reagent solution was purchased from Sigma-Aldrich, although the same yield was obtained using phenylmagnesium bromide made from bromobenzene and magnesium turnings.
3. Furfural (99%) was purchased from Acros and distilled prior to use. The furfural can be stored in the freezer for up to 2 months.
4. When stained with *p*-anisaldehyde, furan-2-yl(phenyl)methanol stains a dark blue-brown color with a R_f of 0.46.
5. The product can be purified using column chromatography with a gradient of hexanes:ethyl acetate from 100% hexane to a 3:2 eluent. To a column (2″ in diameter) 165 g of silica (Geduran Si 60, Silicagel 60, 0.040-0.063 mm) was added and prepared with a 9:1 eluent solution. The unpurified product was dry loaded onto celite and loaded on the column. The product was eluted with 500 mL of 100% hexane eluent followed by 750 mL of 4:1 eluent, and lastly 500 mL of 3:2 eluent. The fractions containing the product were identified by TLC (Note 4), and the fractions were combined. The solvent was removed by rotatory evaporation (25 °C, 10 mmHg).
6. The product (**1**) has been characterized as follows: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.40 (s, 1H), 5.85 (s, 1H), 6.13 (d, 1H), 6.33 (m, 1H), 7.39 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 70.2, 107.4, 110.2, 126.6, 128.1, 128.5, 140.8, 142.5, 155.9; IR (film) 3364, 3054, 3022, 2874, 1595, 1492, 1451, 1224, 1196, 1140, 1140, 1073, 1007, 939, 926, 884, 812, 728, 697, 625 cm^{-1}. HRMS (ESI+): [M + H] calcd for $C_{11}H_{11}O_2$: 175.0759 Found: 175.0739
7. The purity was determined to be >97% wt. by quantitative ^{1}H NMR spectroscopy in $CDCl_3$ using 174.2 mg of **1** and 168.6 mg of 1,3,5-trimethoxylbenzene as an internal standard (D1 = 10 s).
8. A second reaction on 0.85X scale provided 7.61 g (94%) of the product (**1**).
9. Furan-2-yl(phenyl)methanol is freshly synthesized using a Grignard reaction between bromobenzene and furfural. If prepared freshly, the compound is a yellow oil after column purification and it becomes a dark black tar upon one week storage at room temperature. It is

recommended that the freshly prepared furan-2-yl(phenyl)methanol will be used for step 1B in less than one week upon fridge storage.

10. Acetonitrile was dried using a solvent purification system from a JC Meyer solvent dispensing system (content of water: 20-50 ppm). Reagent grade acetonitrile (Sigma Aldrich, anhydrous, 99.8%) can also be used.
11. Acetonitrile (35 mL) is added first to ensure any furan-2-yl(phenyl)methanol is washed down the sides of the flask before 4-iodoaniline addition. The final 5 mL is added after the addition of dysprosium triflate.
12. 2,4,6-Trimethylaniline (97%) was purchased from Acros Organics and used as received.
13. Dysprosium triflate (98%) was obtained from Strem Chemicals, stored in a desiccator and used as received.
14. Dysprosium triflate is added by quickly removing the rubber septum and adding the powdered catalyst to the stirring reaction mixture.
15. Reaction time may slightly vary between 3–5 h and can be determined by TLC analysis.
16. The reaction is considered complete when there is no 2,4,6-trimethylaniline is detected by TLC analysis. The R_f of the furan-2-yl(phenyl)methanol was 0.14, the R_f of the 2,4,6-trimethylaniline was 0.19, and the R_f of the product was 0.09. When stained with *p*-anisaldehyde, the furan-2-yl(phenyl)methanol starting material appears as a dark blue, the 2,4,6-trimethylaniline appears yellow, and the product appears as an olive brown color.
17. The product can be purified using column chromatography with a gradient of hexanes:ethyl acetate from 19:1 to 1:1. To a column (3" diameter column) 275 g of silica (Geduran Si 60, Silicagel 60, 0.040-0.063 mm) was added and prepared with a 19:1 eluent solution. The unpurified product was dry loaded onto celite and loaded on the column. The product was eluted with 1 L of 95:5 eluent followed by 1.5 L of 85:15 eluent, then 1 L of 70:30 eluent, and lastly 0.5 L of 1:1 eluent. The fractions containing the product by TLC were combined and solvent was removed by rotatory evaporation (25 °C, 10 mmHg).
18. The product (**2**) has been characterized as follows: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.14 (s, 6H), 2.26 (s, 3H), 3.20 (br s, 1H), 3.43 (d, 1H), 4.46 (s, 1H), 6.36 (dd, 1H), 6.84 (s, 2H), 7.06 (m, 2H), 7.31 (m, 3H), 7.67 (dd, 1H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ: 18.6, 20.5, 60.4, 67.5, 127.0, 127.9, 128.7, 129.6, 132.3, 133.5, 137.9, 140.7, 162.8, 206.8; IR (film or solvent): 3346,

2914, 1704, 1585, 1481, 1452, 1373, 1335, 1230, 1155, 1109, 1040, 914, 854, 735, 697 cm^{-1}; HRMS (ESI+): calcd for $C_{20}H_{20}NO$ [M + H] [M + H] calcd for $C_{20}H_{22}NO$: 292.1701 Found: 292.1704

19. The purity was determined to be >98% wt. by quantitative ^1H NMR spectroscopy in $CDCl_3$ using 128.1 mg of the compound 6 and 102.0 mg of trimethoxylbenzene as an internal standard (D1 = 10 s).
20. A second reaction on 0.85X scale provided 4.03 g (84%) of the product.
21. Alternatively, product was isolated as (*s*)-CSA salt via crystallization in MeCN: After workup of the reaction (scale of reaction based on furan-2-yl(phenyl)methanol: 10.0 g, 57.4 mmol, 1.1 equiv), the combined organic layers are dried over $MgSO_4$, filtered and concentrated to produce a dark brown oil. This dark oil was re-dissolved in 100 mL of dry MeCN. The resulting dark solution was dried until KF < 150 ppm water via constant volume distillation with dry MeCN (KF = 80 ppm). The dark mixture was then filtered to remove solid $MgSO_4$, and the resulting dark solution was heated to 50 °C. To the solution was charged (S)-CSA (10.8 g, 46.5 mmol, 0.9 equiv). The mixture was agitated at 50 °C until CSA dissolved. MeCN (50 mL) was removed by vacuum distillation (50 mmHg). During this process, the product crystallized as white solid. The slurry was cooled to room temperature and agitated for 2 h at rt. The slurry was filtered and the wet cake was washed with MeCN (2 x 10 mL). The cake was dried under vacuum (24.5 g, 80%, 98.5%purity).
22. Compound 6-CSA salt was characterized as follows: ^1H NMR (500 MHz, CD_2Cl_2) δ: 0.82 (s, 3H), 1.04 (s, 3H), 1.38 (m, 1H), 1.63 (m, 1H), 1.87 (d, 1H), 1.99 (m, 1H), 2.06 (t, 1H), 2.30 (s, 3H), 2.34 (s, 6H), 2.51 (ddd, 1H), 2.76 (dd, 1H), 3.27 (d 1H), 4.00 (d, 1H), 4.85 (m, 1H), 6.54 (m, 1H), 6.90 (m, 4H), 7.27 (m, 3H), 7.98 (m, 1H), 9.78 (s, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ: 18.8, 20.09, 20.11, 21.0, 25.3, 27.4, 43.2, 43.4, 48.3, 48.5, 53.6, 53.8, 54.0, 54.2, 54.4, 55.16, 55.24, 58.9, 69.1, 69.2, 128.1, 128.2, 128.5, 129.3, 129.4, 130.5, 131.4, 131.5, 132.7, 136.9, 137.7, 137.9, 139.8, 156.8, 156.9, 203.6, 203.7, 217.2; IR 3558, 3416, 3267, 3055, 2960, 2724, 2463, 1740, 1725, 1714, 1604, 1454, 1182, 1169, 1157, 1038 cm^{-1}; HRMS (ESI+): calcd for $C_{20}H_{22}NO$ [M + H] 292.1701, found 292.1704.

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The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

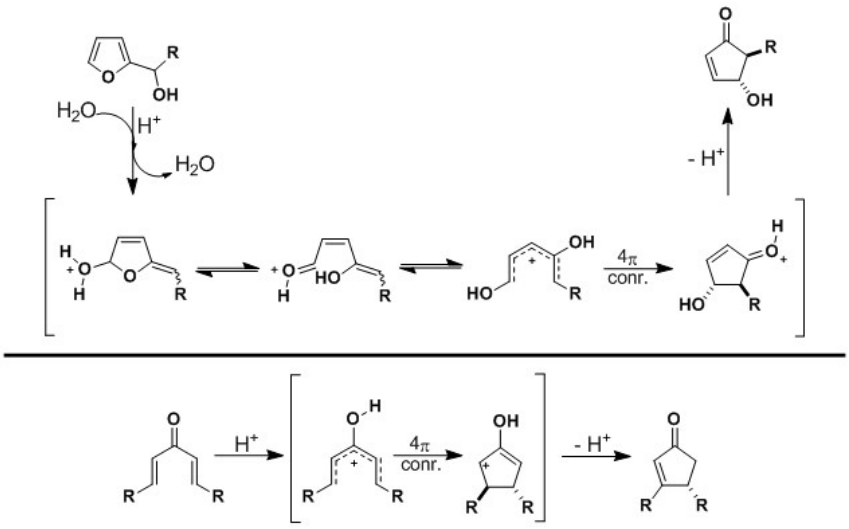
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

Discussion

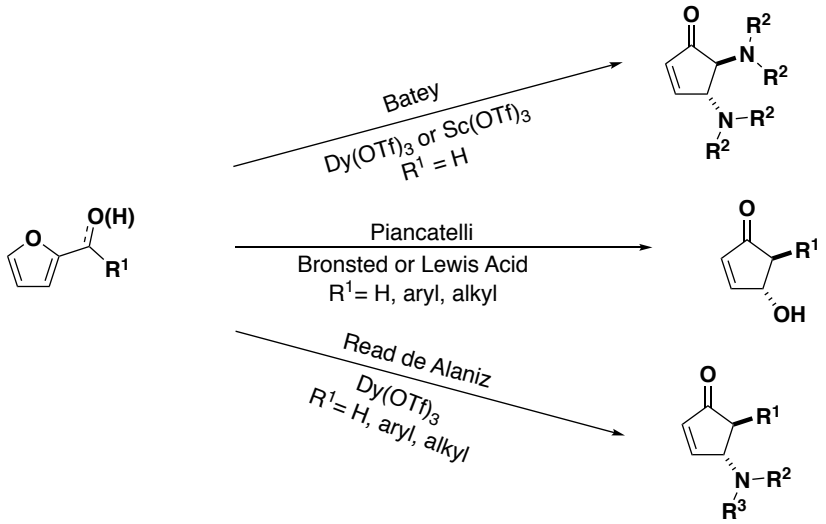
The cyclopentenone framework, often present in natural product architectures, has inspired the development of a number of elegant synthetic approaches.[2] One particularly attractive approach developed in 1976 when Piancatelli and co-workers constructed 4-hydroxycyclopentanone derivatives via an acid-catalyzed rearrangement of 2-furylcarbinols.[3] The transformation is highly diastereoselective and

believed to proceed through a cascade sequence that terminates with an electrocyclic ring closure, analogous to the Nazarov cyclization (Scheme 1).[4,5]



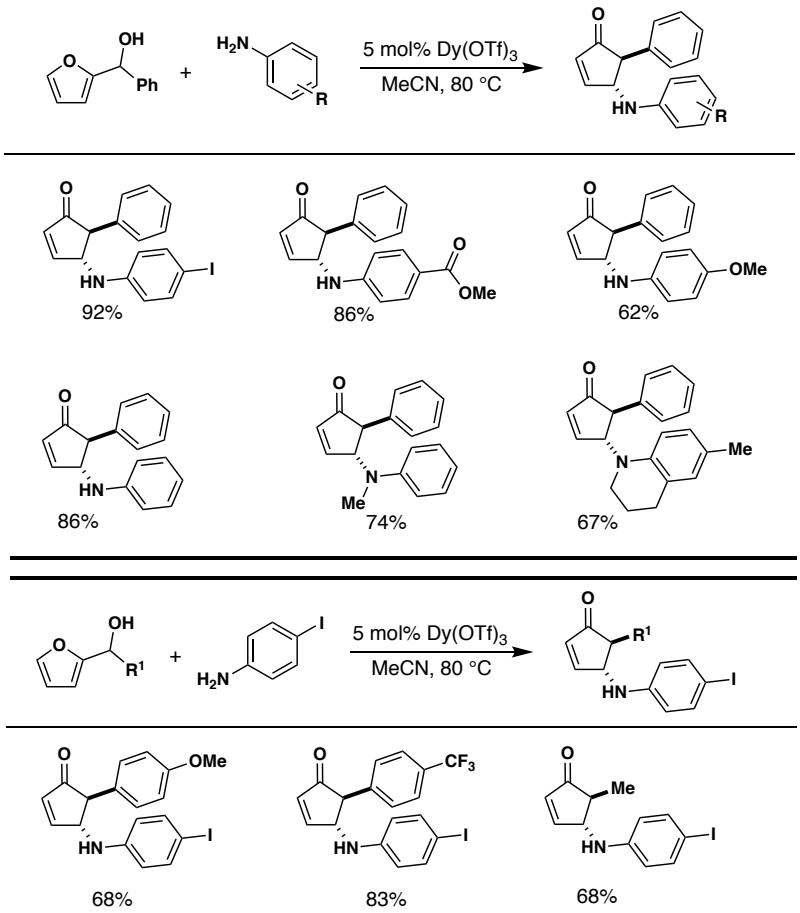
Scheme 1. Proposed Piancatelli mechanism (top) similar to a Nazarov 4π electrocyclization (bottom)

Although the Piancatelli rearrangement offers one of the most direct routes to 4-hydroxycylopentenones, its use in synthesis was largely driven by the synthesis of prostaglandins.[6] However, over the years rapid access to substituted cyclopentenones has played a critical role in a wide array of natural product synthesis.[7,8] Despite tremendous progress, a literature survey in 2009 revealed a lack of methods available for the direct synthesis of 4-aminocyclopentenone derivatives, with most relying on multistep approaches.[9] Two notable exceptions were reported independently by Denisov[10] and Batey[11] (Scheme 2) in 1993 and 2007, respectively. Inspired by these reports and Piancatelli's work we envisioned that an efficient catalytic aza-Piancatelli rearrangement could serve as a powerful general method to biologically active molecules bearing nitrogen functionality. Because furfural, the precursor to furylcarbinols, is produced from agricultural waste products like bagasse, oat hulls, and corncobs, it also provides chemists with a route to this key building block without relying on petrochemical feedstock.



Scheme 2. Research performed by various groups on acid-catalyzed rearrangements of furfural

Our investigation into an efficient aza-Piancatelli rearrangement began with the use of $Dy(OTf)_3$ in catalytic amounts (5 mol %) to facilitate the cascade rearrangement of furylcarbinols with aniline nucleophiles (Scheme 3).[12,13] While using $Dy(OTf)_3$ in our rearrangement we found the reaction was efficient in producing a trans-selective product that turned out to be adaptable with various functional groups present on either the furylcarbinol or aniline. Subsequent to our initial reports[14], a number of groups have demonstrated that other acids such as phosphomolybdic acid (PMA)[15], $In(Otf)_3$[15], $La(OTf)_3$[11], $Ca(NTf_2)_2$[16], $In(Br)_3$[15,17], and PPh_3 with DEAD[18] could also be used to catalyze the aza-Piancatelli reaction. The aza-Piancatelli reaction has also been extended to other amine nucleophiles such as hydroxylamine[14e] and tethered alkyl amines,[14a,18,19] as well as alcohol nucleophiles.[13,14b,14c] Recently the aza-Piancatelli reaction has been rendered asymmetric using chiral phosphoric acid to control the absolute stereochemistry.[2g,20,21,22]



Scheme 3. Scope of rearrangement with multiple substituted anilines (top) as well as various 2-furylcarbinols (bottom)

References

1. Department of Chemistry and Biochemistry, University of California, Santa Barbara, CA 93106-9510, USA. Email: javier@chem.ucsb.edu.
2. (a) Tius, M. A. *Eur. J. Org. Chem.* **2005**, 2193–2206; (b) Pellissier, H. *Tetrahedron* **2005**, *61*, 6479–6517; (c) Frontier, A. J.; Collison, C. *Tetrahedron* **2005**, *61*, 7577–7606; (d) Grant, T. N.; Rieder, C. J.; West, F. G. *Chem. Commun.* **2009**, 5676–5688; (e) Blanco-Urgoiti, J.; Anorbe, L.;

Perez-Serrano,L.; Dominguez, G.; Perez-Castells, J. *Chem. Soc. Rev.* **2004**, *33*, 32–42; (f) Gibson, S. E.; Mainolfi, N. *Angew. Chem.* **2005**, *117*, 3082–3097; *Angew. Chem. Int. Ed.* **2005**, *44*, 3022–3037; (g) Simeonov, S. P.; Nunes, J. P. M.; Guerra, K.; Kurteva, V. B.; Alfonso, C. A. M. *Chem. Rev.* **2016**, *116*, 5744–5893.
3. Piancatelli, G.; Scettri, A.; Barbadoro, S. *Tetrahedron Lett.* **1976**, *17*, 3555–3558.
4. Faza, A. N.; Lopez, C. S.; Alvarez, R.; de Lera, I. R. *Chem. Eur. J.* **2004**, *10*, 4324–4329.
5. Wenz, D. R.; Read de Alaniz, J. *Eur. J. Org. Chem.* **2015**, 23–37.
6. Piancatelli, G.; Dauria, M.; Donofrio, F. *Synthesis* **1994**, 867–889.
7. Touré, B. B.; Hall, D. G. *Chem. Rev.* **2009**, *109*, 4439–4486.
8. Roche, S. P.; Aitken, D. J. *Eur. J. Org. Chem.* **2010**, 5339–5358.
9. For select examples, see: (a) Davis, F. A.; Wu, Y. Z. *Org. Lett.* **2004**, *6*, 1269–1272; (b) Dauvergne, J.; Happe, A. M.; Jadhav, V.; Justice, D.; Matos, M. C.; McCormack, P. J.; Pitts, M. R.; Roberts, S. M.; Singh, S. K.; Snape, T. J.; Whittall, J. *Tetrahedron* **2004**, *60*, 2559–2562; (c) Dauvergne, J.; Happe, A. M.; Roberts, S. M. *Tetrahedron* **2004**, *60*, 2551–2557; (d) Zaja, M.; Blechert, S. *Tetrahedron* **2004**, *60*, 9629-9634.
10. Denisov, V. R.; Shustitskaya, S.E.; Karpov, M. G. *Zh. Org. Khim.* **1993**, *29*, 249–252.
11. Li, S. W.; Batey, R. A. *Chem. Commun.* **2007**, 3759–3761.
12. Veits, G. K.; Wenz, D. R.; Read de Alaniz, J. *Angew. Chem Int. Ed.* **2010**, *49*, 9484–9487.
13. Read de Alaniz, J.; Palmer, L.; *Synlett* **2014**, *25*, 8–11.
14. (a) Palmer, L. I.; Read de Alaniz, J. *Angew. Chem. Int. Ed.* **2011**, *50*, 7167–7170; (b) Palmer, L. I.; Read de Alaniz, J. *Org. Lett.* **2013**, *15*, 476–479; (c) Fisher, D.; Palmer, L. I.; Cook, J. E.; Davis, J. E.; Read de Alaniz, J. *Tetrahedron* **2014**, *70*, 4105–4110; (d) Chung, R.; Yu, D.; Thai, V. T.; Jones, A. F.; Veits, G. K.; Read de Alaniz, J.; Hein, J. E. *ACS Catal.* **2015**, *5*, 4579–4585; (e) Veits, G. K.; Wenz, D. R.; Palmer, L. I.; St. Amant, A. H.; Hein, J. E.; Read de Alaniz, J. *Org. Biomol.Chem.* **2015**, *13*, 8465–8469.
15. Reddy, B. V. S.; Reddy, Y. V.; Lakshumma, P. S.; Narasimhulu, G.; Yadav, J. S.; Sridhar, B.; Reddy, P. P.; Kunwar, A. C. *RSC Advances* **2012**, *2*, 10661–10666.
16. Leboeuf, D.; Schulz, E.; Gandon, V. *Org. Lett.* **2014**, *16*, 6464–6467.
17. Aitken, D. J.; Eijsberg, H.; Frongia, A.; Ollivier, J.; Piras, P. P. *Synthesis* **2014**, *46*, 1–24.
18. Xu, Z. L.; Xing, P.; Jiang, B. *Org. Lett.* **2017**, *19*, 1028–1031.

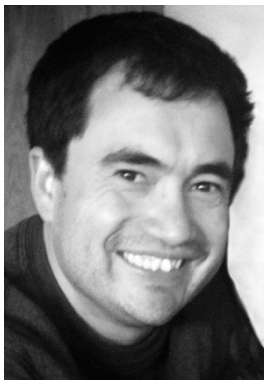
19. Piutti, C.; Quartieri, F. *Molecules* **2013**, *18*, 12290–12312.
20. Cai, Y.; Tang, Y.; Atodiresei, I.; Rueping, M. *Angew. Chem. Int. Ed.* **2016**, *55*, 14126–14130.
21. Li, H.; Tong, R.; Sun, J. *Angew. Chem. Int. Ed.* **2016**, *55*, 15125–15128.
22. Gade, A. B.; Patil, N. T. *Synlett* **2017**, *28*, 1096–1100.

Appendix
Chemical Abstracts Nomenclature (Registry Number)

Furan-2-yl(phenyl)methanol: 2-Furyl(phenyl)methanol; (4484-57-5)
MeCN: acetonitrile; (75-05-8)
4-Iodoaniline: 4-Iodo-benzenamine; (540-37-4)
$Dy(OTf)_3$: Dysprosium(III) trifluoromethanesulfonate; (139177-62-1)

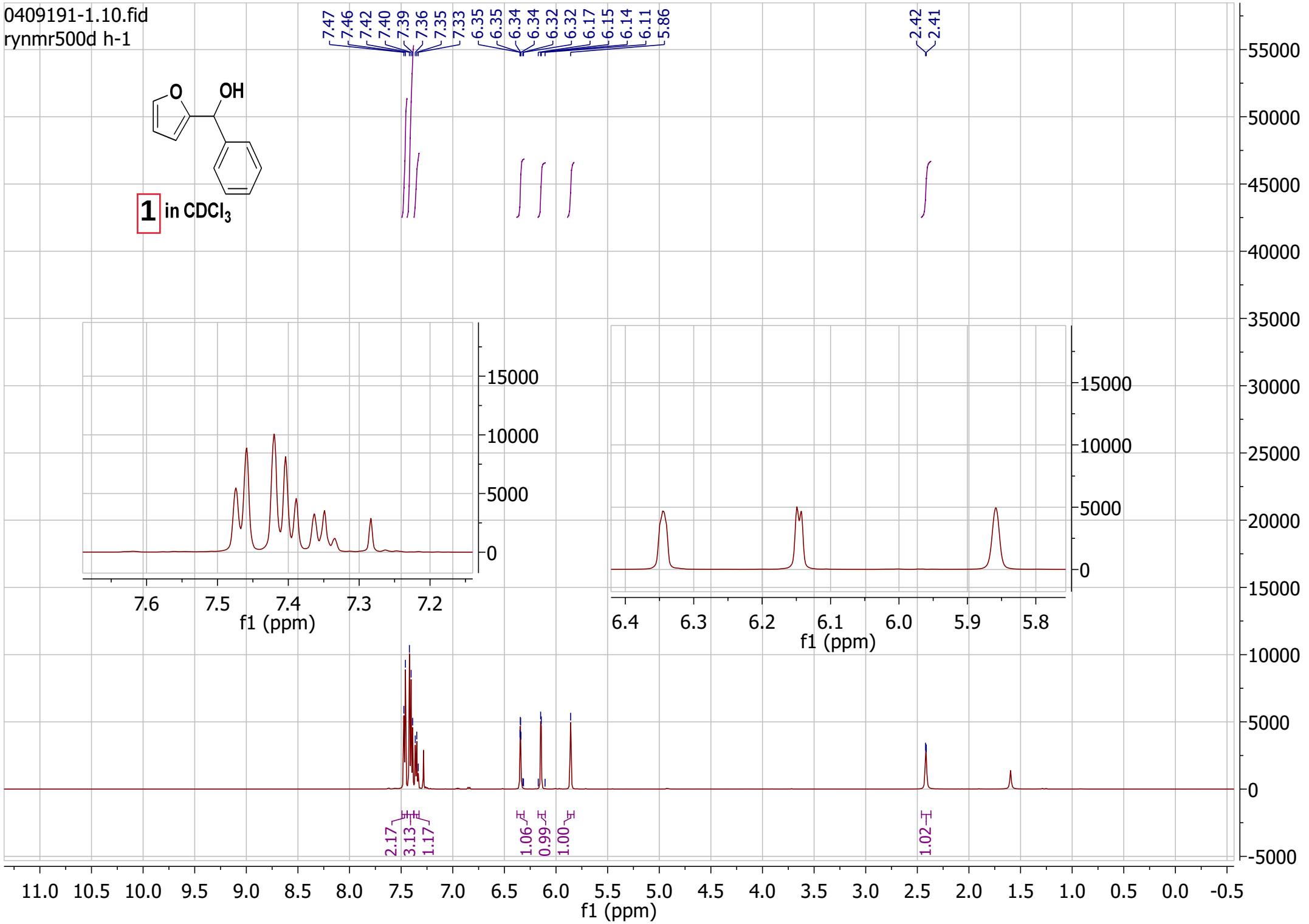
Meghan F. Nichol came to the University of California at Santa Barbara in 2015 and began work in the group of Dr. Read de Alaniz. She earned her B. S. degree in chemical physics from Lewis University (Romeoville, IL) in 2015 where she conducted undergraduate research under the direction of Dr. Jason J. Keleher. Meghan then moved to Santa Barbara where she is pursuing work in self-immolative polymer trigger systems.

Luis Limon is an undergraduate researcher at the University of California at Santa Barbara pursuing his B. S. degree in chemistry. He joined the Read de Alaniz group in the summer of 2016 and is currently working on development of new methodology for small molecule synthesis.



Javier Read de Alaniz joined the department of Chemistry and Biochemistry at University of California at Santa Barbara in 2009 as an Assistant Professor. He received his B. S. degree from Fort Lewis College (Durango, Colorado) in 1999 where he conducted undergraduate research under the direction of Professor William R. Bartlett. He obtained his Ph. D. in 2006 under the supervision of Professor Tomislav Rovis at Colorado State University with a research focus on asymmetric catalysis. Javier then moved to California, where he worked in the area of total synthesis with Professor Larry E. Overman at the University of California, Irvine.

Feng Peng joined the Process Research Department of Merck & Co., Inc. in 2012. His research focuses on using state-of-art organic chemistry to address critical problems in drug development. He received his B. S. degree from Beijing Normal University. He obtained his M.S. under the supervision of Professor Dennis Hall at University of Alberta with a research focus on Boron Chemistry. Feng then moved to New York City, where he obtained Ph.D. in the area of total synthesis (maoecrystal V) with Professor Samuel Danishefsky at Columbia University.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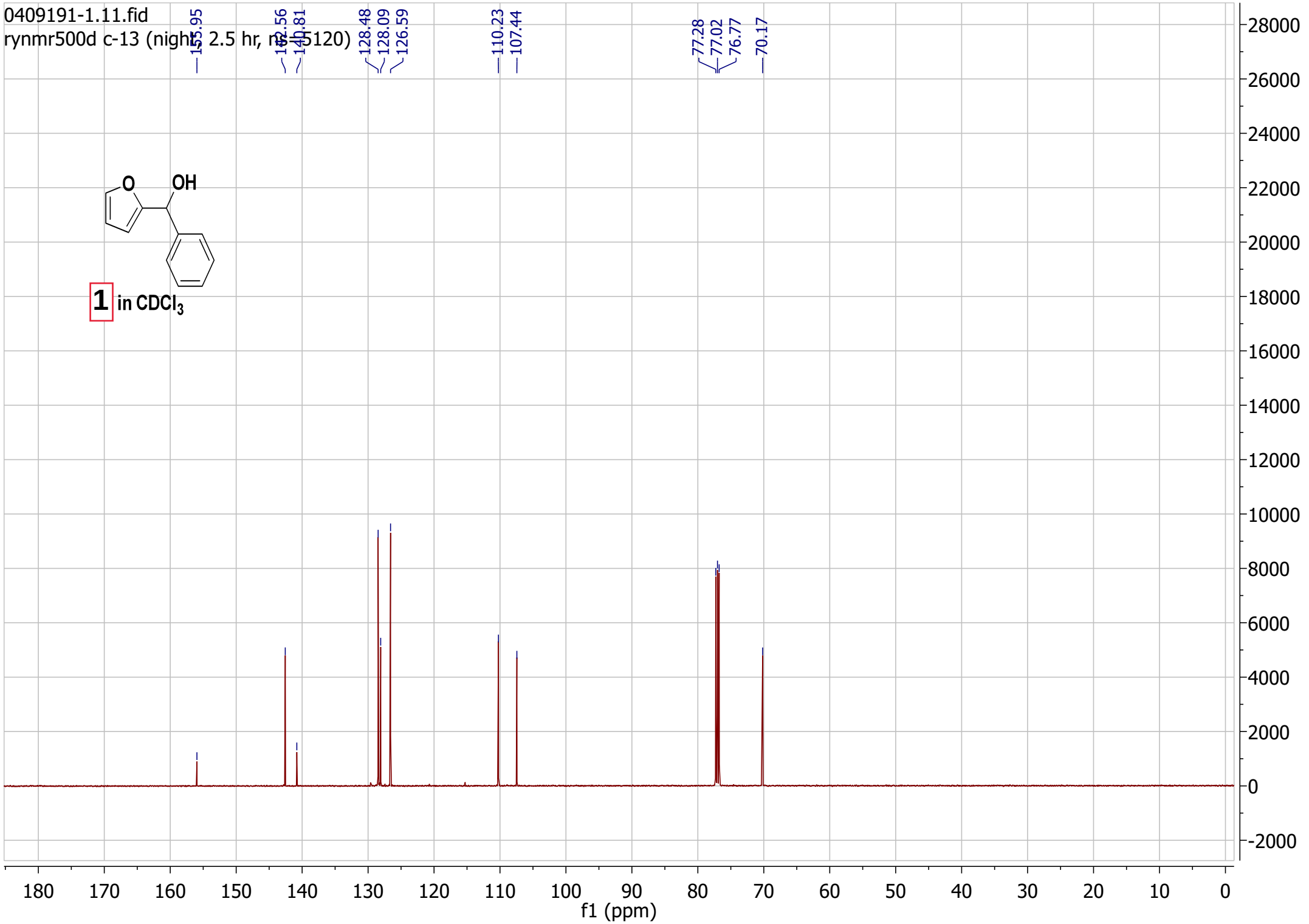
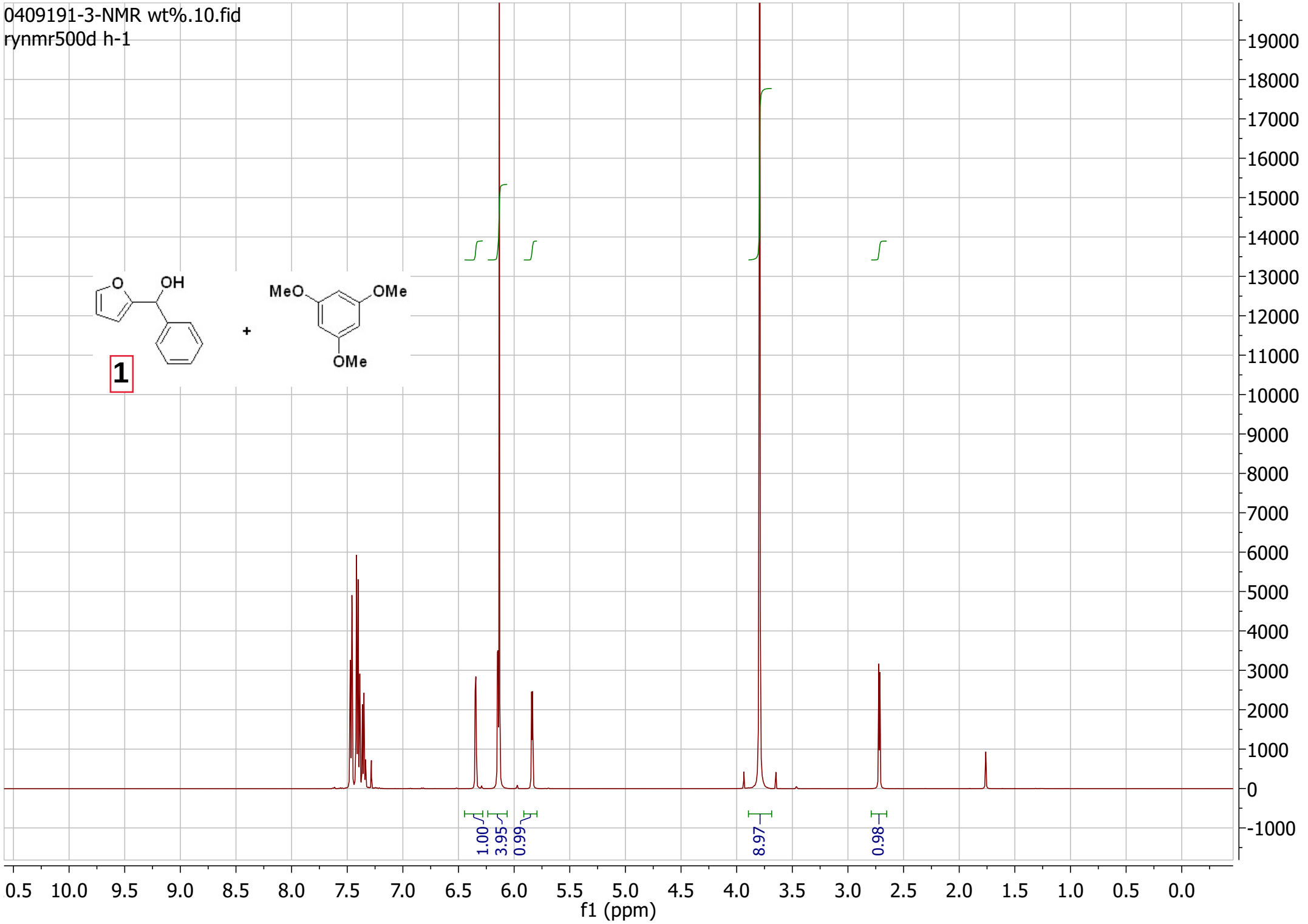
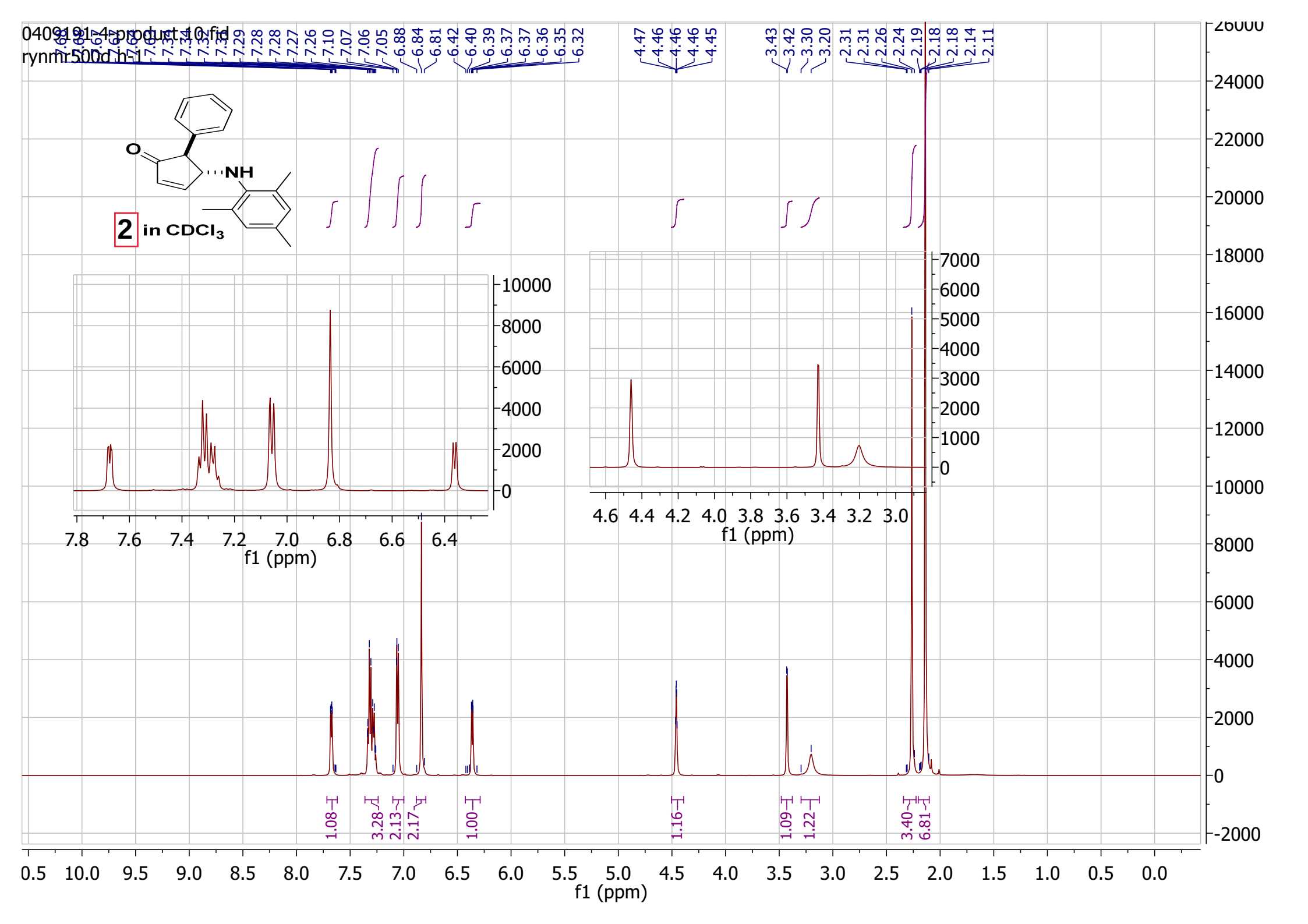
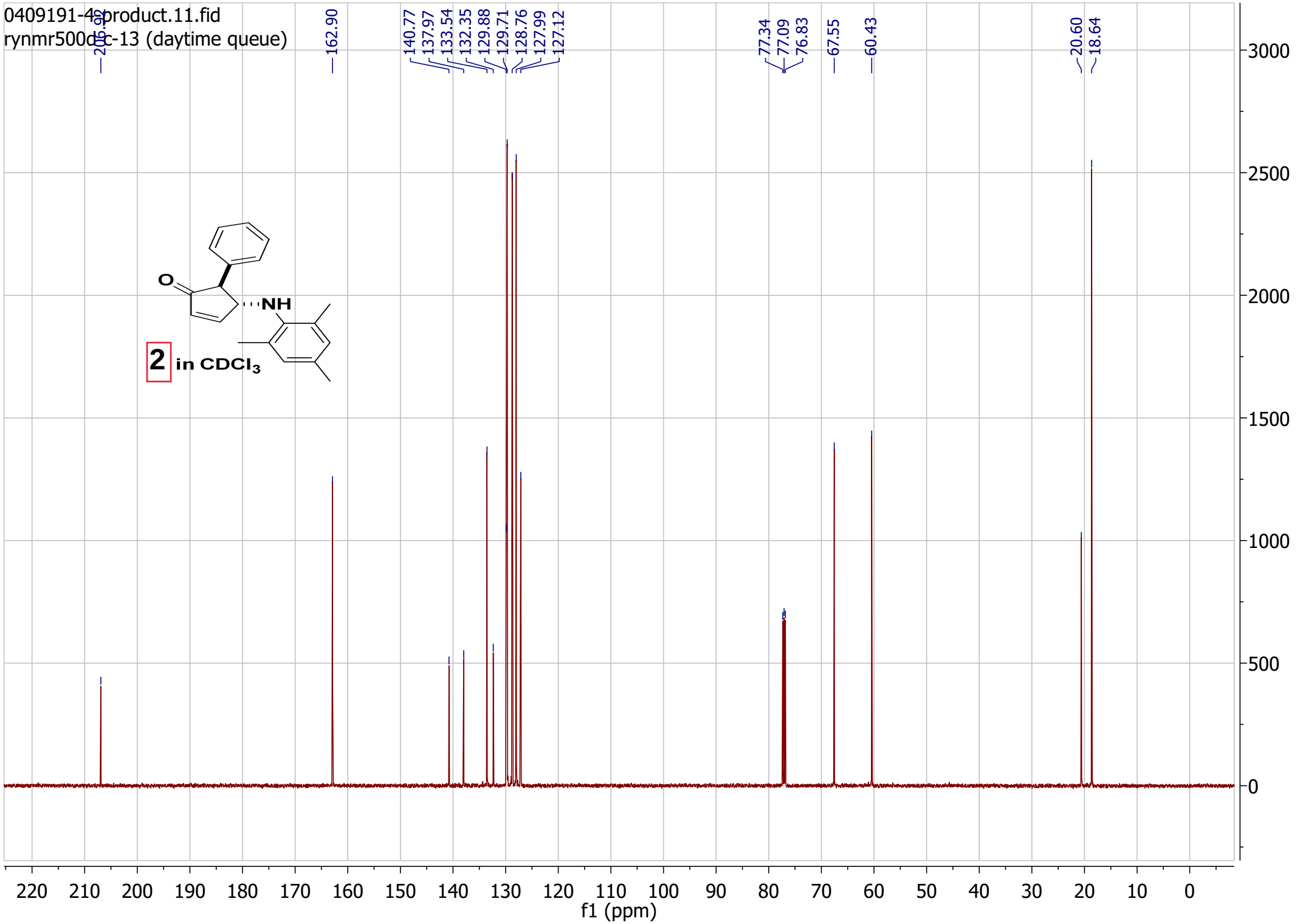
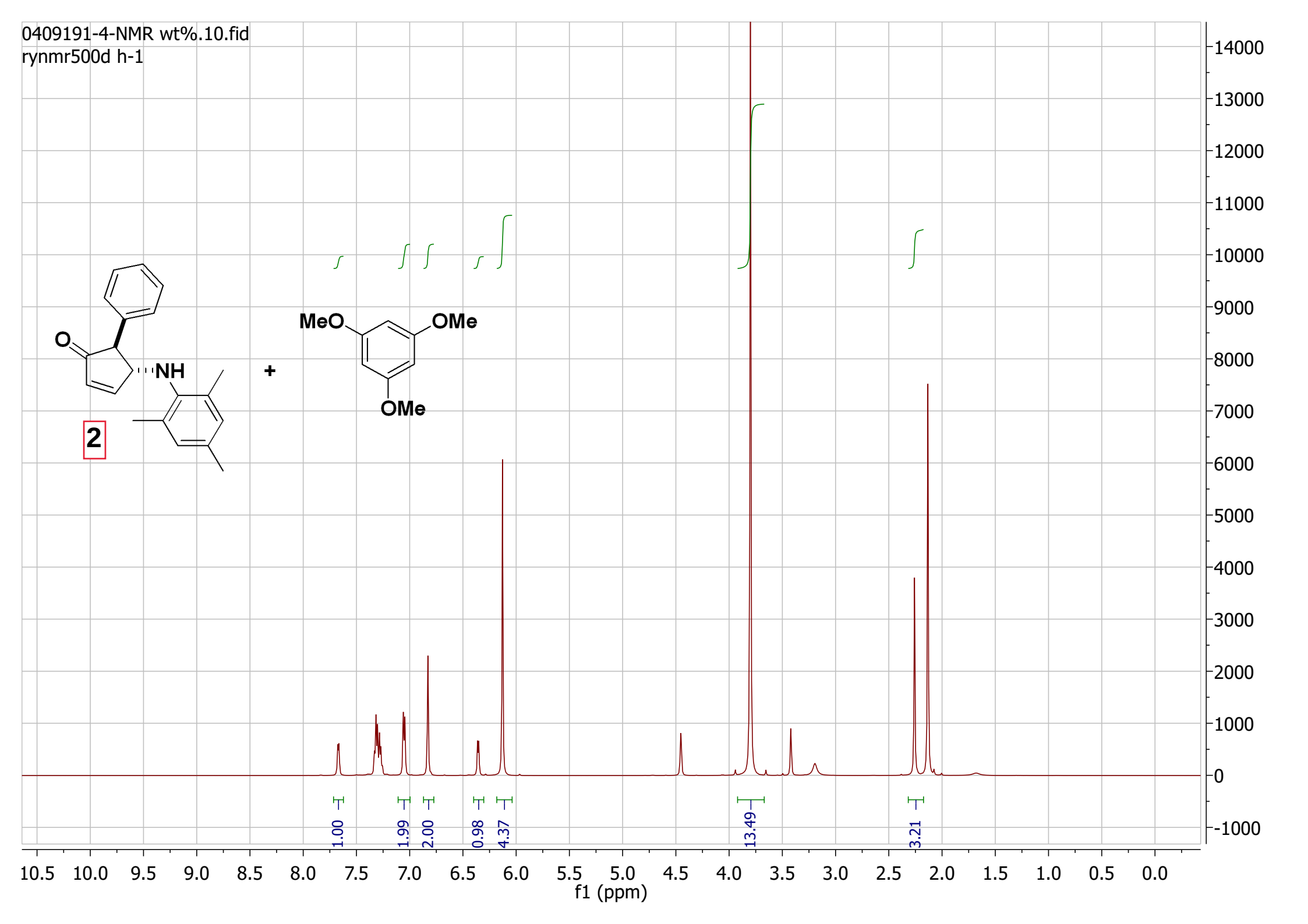
6.34
6.32
6.32
6.17
6.15
6.14
6.11
5.86
2.42
2.41
O
OH
1 in CDCl3
15000
10000
5000
0
7.6
7.5
7.4
7.3
7.2
f1 (ppm)
15000
10000
5000
0
6.4
6.3
6.2
6.1
6.0
5.9
5.8
f1 (ppm)
2.17
3.13
1.17
1.06
0.99
1.00
1.02
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

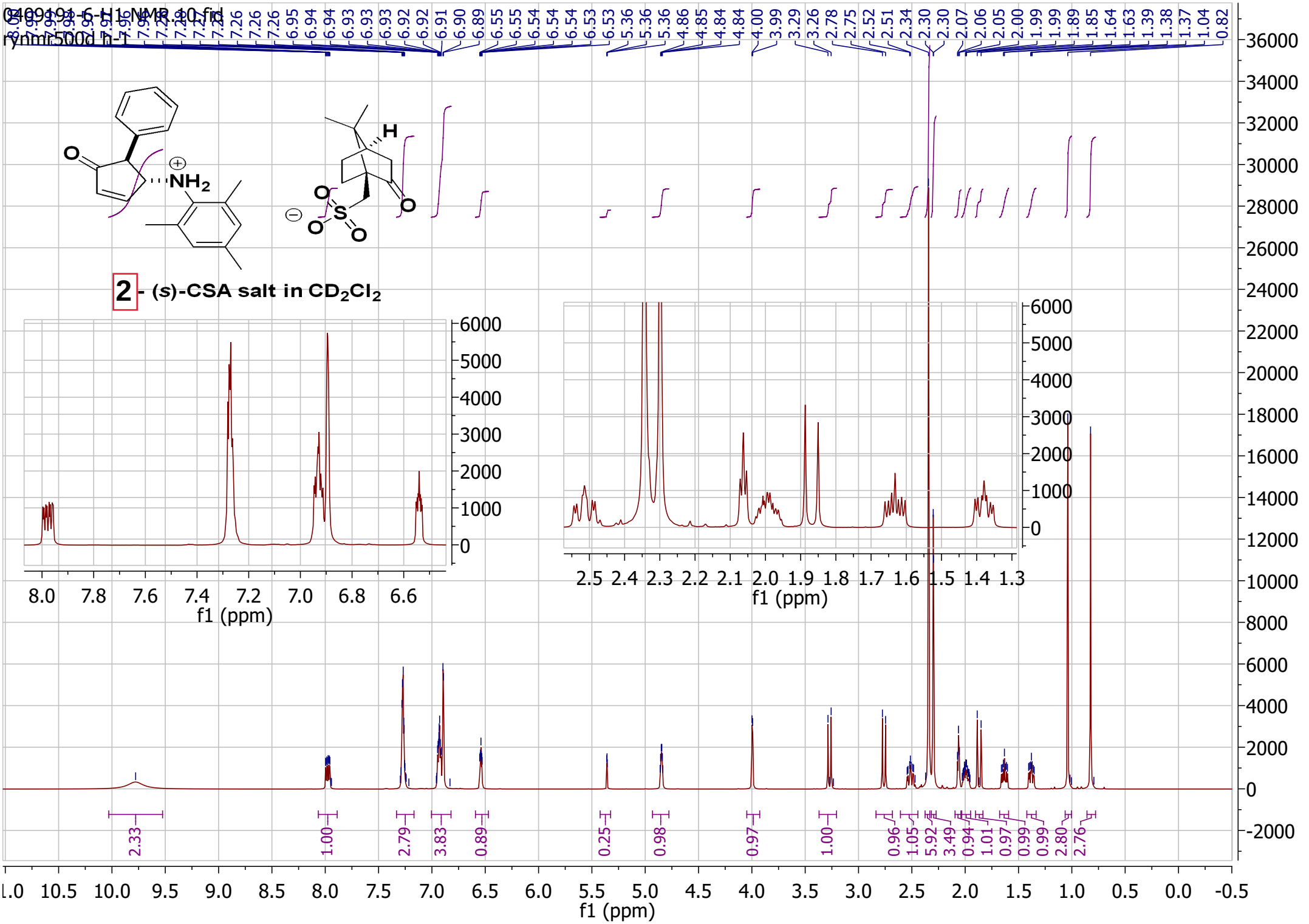

0409191-1.11.fid
rynmr500d c-13 (night 2.5 hr, rd 5120)
155.95
142.56
140.81
128.48
128.09
126.59
110.23
107.44
77.28
77.02
76.77
70.17
O
OH
1 in CDCl3
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

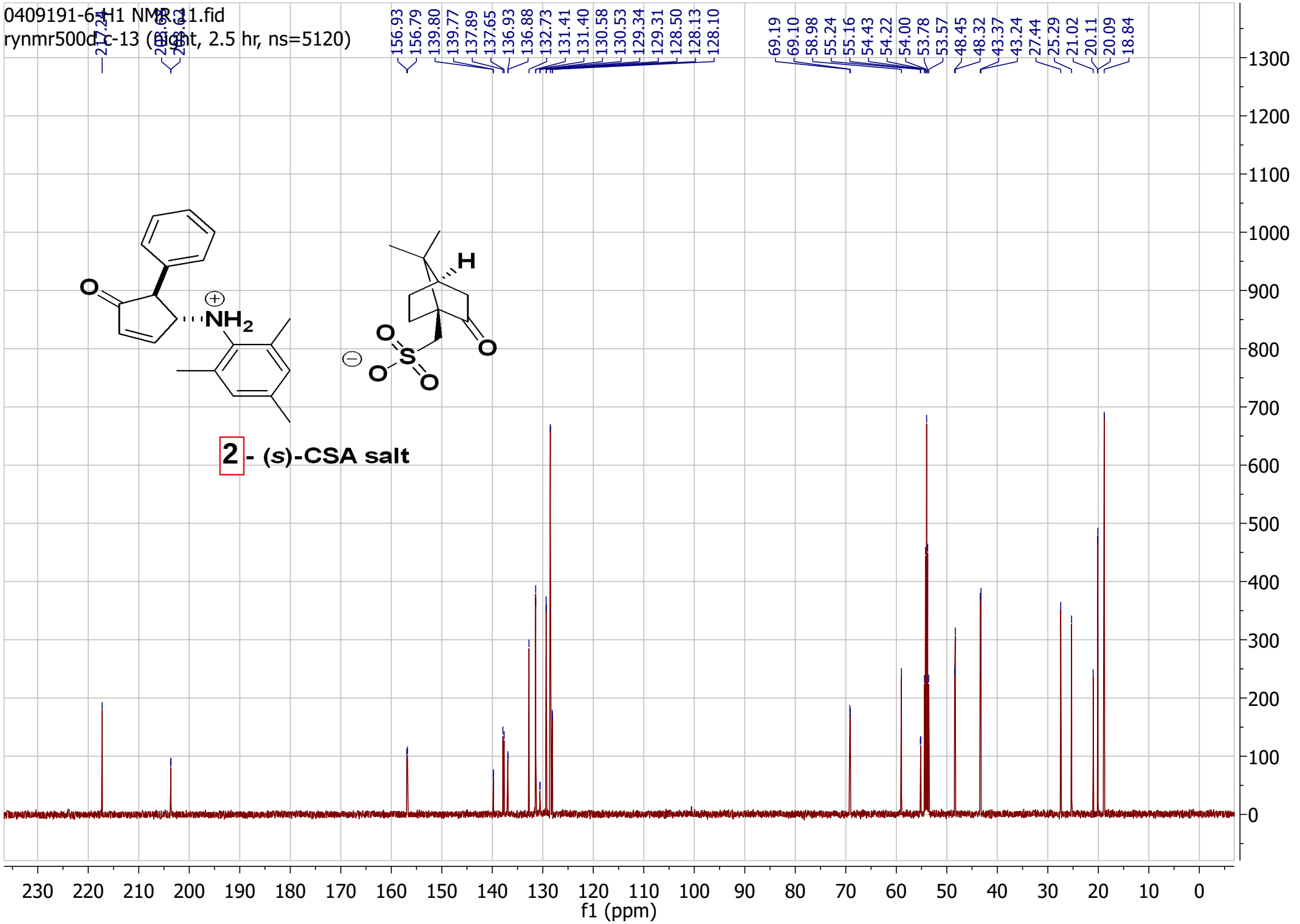

0409191-3-NMR wt%.10.fid
rynmr500d h-1
O
OH
1
+
MeO
OMe
OMe
1.00
3.95
0.99
8.97
0.98
f1 (ppm)


040919-1-4-product-10.fid
rynmr500d h-1
O
NH
2 in CDCl3
f1 (ppm)
f1 (ppm)
f1 (ppm)

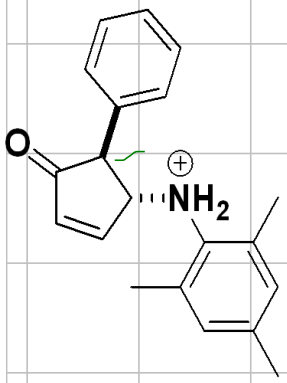

0409191-4-product.11.fid
rynmr500dcc-13 (daytime queue)
206.91
162.90
140.77
137.97
133.54
132.35
129.88
129.71
128.76
127.99
127.12
77.34
77.09
76.83
67.55
60.43
20.60
18.64
O
NH
2 in CDCl3
3000
2500
2000
1500
1000
500
0
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

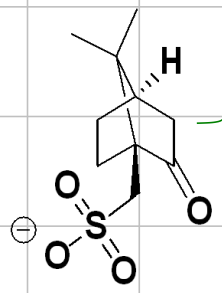

0409191-4-NMR wt%.10.fid
rynmr500d h-1
O
NH
2
+
MeO
OMe
OMe
1.00
1.99
2.00
0.98
4.37
13.49
3.21
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


0409191-6-H1_NMR.10.fid
rynmr500d h-1
2 - (s)-CSA salt in CD2Cl2
f1 (ppm)

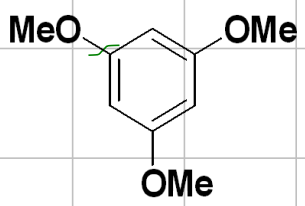

0409191-6-H1 NMR.11.fid
rynmr500d_c-13 (night, 2.5 hr, ns=5120)
156.93
156.79
139.80
139.77
137.89
137.65
136.93
136.88
132.73
131.41
131.40
130.58
130.53
129.34
129.31
128.50
128.13
128.10
69.19
69.10
58.98
55.24
55.16
54.43
54.22
54.00
53.78
53.57
48.45
48.32
43.37
43.24
27.44
25.29
21.02
20.11
20.09
18.84
O
NH2
H
O
S
O
O
O
2 - (s)-CSA salt
f1 (ppm)

0409191-6-NMR wt%.10.fid
rynmr500d h-1





+



2 - (*s*)-CSA salt

1.00 11.21 1.15 32.78 1.12 1.07 10.78 3.25 3.23

f1 (ppm)