Organic Syntheses

α-Oxamination of Amides *via* Electrophilic Activation

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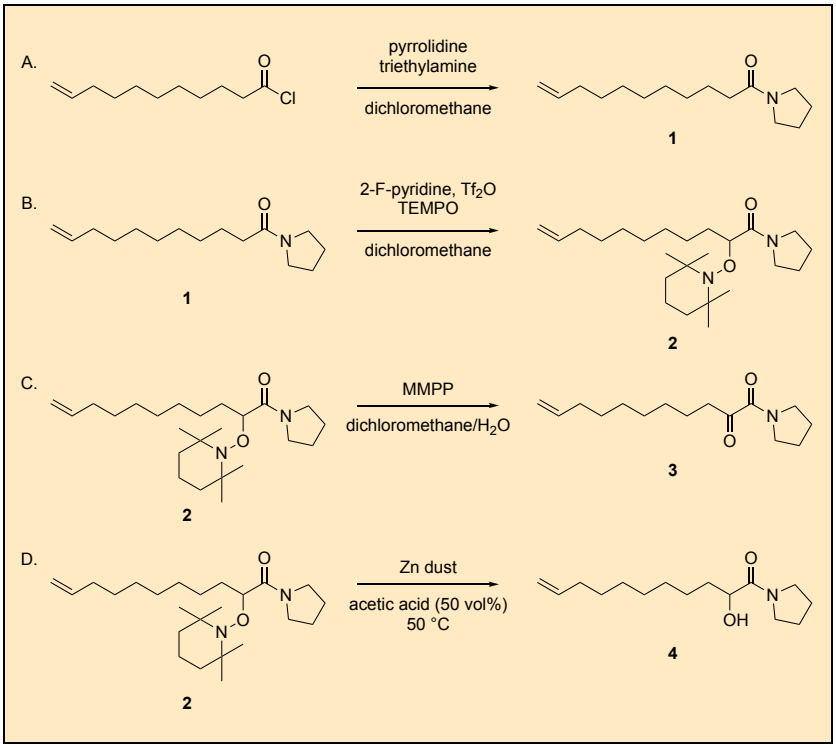

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Procedure (Note 1)

A. *1-(Pyrrolidin-1-yl)undec-10-en-1-one* (**1**). An oven-dried (at 150 °C) 250 mL one-necked, round-bottomed flask, equipped with an egg-shaped, PTFE-coated magnetic stir bar (3 cm), is charged with pyrrolidine (Note 2) (7.11 g, 100 mmol, 1.0 equiv) and Et_3N (Note 3) (21.0 mL, 150 mmol, 1.50 equiv) (Figure 1A). Anhydrous dichloromethane (Note 4) (100 mL) is added, the flask is sealed with a rubber septum (fitted with a 0.8 mm ⌀ needle) and then cooled to between 0 and 5 °C in a water-ice bath. While stirring (>800 rpm), 10-undecenoyl chloride (Notes 5 and 6) (23.6 mL, 110 mmol, 1.10 equiv) is added dropwise (50 mL syringe fitted with a 0.8 mm ⌀ needle) over the course of 15 min. The cooling bath is removed (Figure 1B), and the reaction mixture is allowed to warm to room temperature (23 °C) and stirred at this temperature for 16 h.

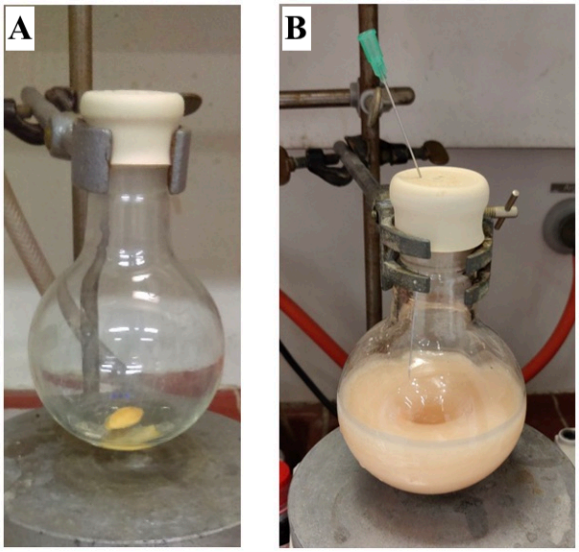

Figure 1. Reaction setup: A) After addition of pyrrolidine; B) After removal of cooling bath (photos provided by submitters)

After this time, the mixture is diluted with Et_2O (Note 7) (200 mL) and the organic phase is washed sequentially with 1 M HCl (Note 8) (50 mL), saturated aqueous $NaHCO_3$ (Note 9) (50 mL) and brine (Note 10) (50 mL). The washed organic layer is dried over anhydrous $MgSO_4$ (Note 11) (5 g) and

filtered *via* gravitational filtration using a glass funnel equipped with filter paper (Note 12). The filtrate is concentrated by rotary evaporation (450 mmHg at 40 °C, followed by 7.5 mmHg at 40 °C), affording a thick yellow oil. The oil is mixed with heptane (Note 13) (5 mL) and loaded onto a silica gel column (300 ± 10 g; column dimensions: 6 x 30 cm, equilibrated with heptane) (Note 14), and 80 mL fractions are collected (Figure 2A). The column is initially eluted with 1 L of a 30% EtOAc (Note 15) in heptane mixture, which is switched to 100% EtOAc once the compound of interest starts to elute (Figure 2B). The compound of interest is collected in fractions 13-34, the solvent is removed by rotary evaporation (120 mmHg mbar at 40 °C, and 0.8 mmHg at 40 °C, followed by high vacuum (ca. 0.05 mmHg) at room temperature (23 °C) for 6 h) to obtain the product **1** as a colorless oil (22.2 g, 94%) (Figure 2C) (Notes 16 and 17).

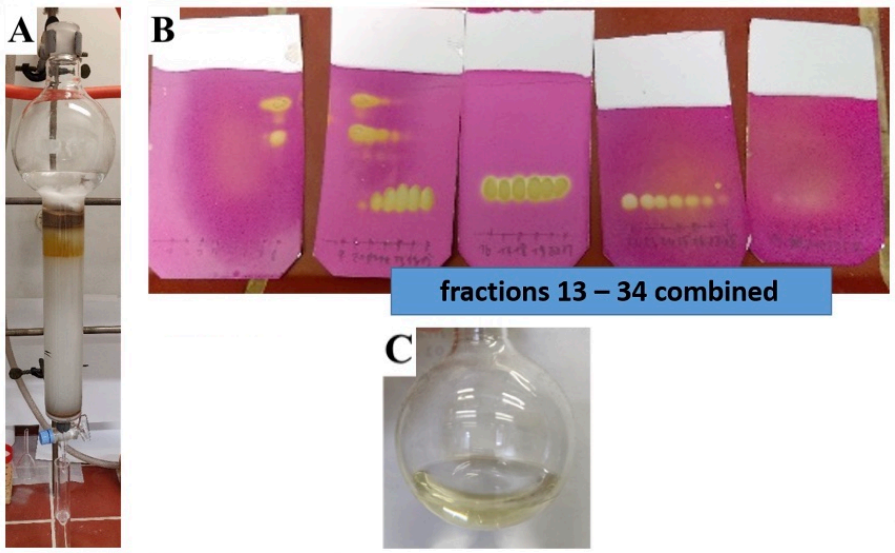

Figure 2. A) Chromatography setup; B) TLC analysis of collected fractions; C) Product in a 100 mL flask (photos provided by submitters)

B. *1-(Pyrrolidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy) undec-10-en-1-one* (**2**). An oven-dried (at 150 °C) 1 L round-bottomed Schlenk flask, equipped with an egg-shaped, PTFE-coated magnetic stir bar (3 cm), is charged with 1-(pyrrolidin-1-yl)undec-10-en-1-one (**1**) (18.5 g, 78.0 mmol, 1.00 equiv) and TEMPO (26.8 g, 172 mmol, 2.20 equiv) (Figure 3A) (Note 18).

The flask, which is connected to a vacuum-nitrogen manifold (Schlenk line) using rubber tubing, is sealed with a rubber septum. The flask is subsequently evacuated and refilled with nitrogen three times, after which anhydrous dichloromethane (Note 4) is added via cannula (0.8 ⌀ mm) (Figure 3B), followed by 2-fluoropyridine (Note 19) (7.60 g, 6.70 mL, 78.0 mmol, 1.00 equiv) in one portion *via* syringe (10 mL syringe with a 0.8 ⌀ mm needle). The flask is then cooled in a water-ice bath, while being kept under positive pressure of nitrogen (connected to the Schlenk line). Trifluoromethanesulfonic anhydride (14.4 mL, 86.0 mmol, 1.10 equiv) (Notes 6, 20 and 21) is added dropwise via syringe (20 mL syringe with a 0.8 ⌀ mm needle) over the course of 10 min while stirring (500 rpm) (Figure 3C), after which the mixture is allowed to warm to room temperature (23 °C) and is stirred at this temperature for 14 h (Note 22). After this time, water (500 mL) is added in one portion and stirring (1000 rpm) is continued for an additional 15 min (Figure 3D).

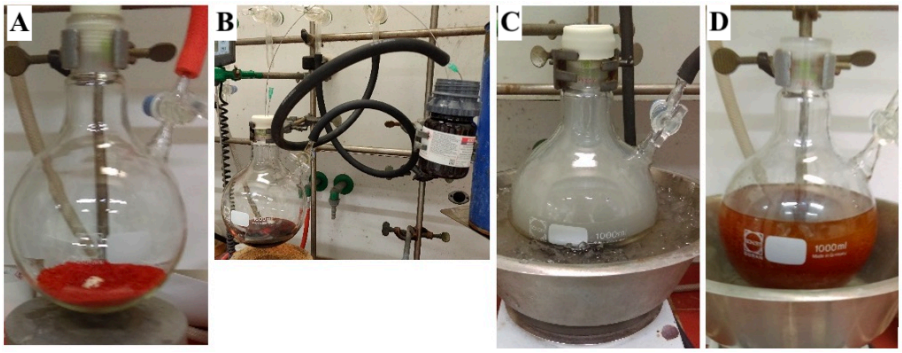

Figure 3. Reaction setup: A) after TEMPO addition; B) During CH_2Cl_2 addition; C) After trifluoromethanesulfonic anhydride addition; D) After water addition (photos provided by submitters)

Diethyl ether (300 mL) is added, the phases are separated, and the organic phase is sequentially washed with saturated aqueous $NaHCO_3$ (250 mL) and brine (100 mL). The washed solution is dried over anhydrous $MgSO_4$ (5 g) and filtered *via* gravitational filtration using a glass funnel equipped with filter paper. The filtrate is concentrated by rotary evaporation (450 mmHg at 40 °C, followed by 8 mmHg mbar at 40 °C), affording a thick orange oil. The oil mixed with heptane (5 mL) is loaded onto a silica gel column (approximately 500 ± 20 g, column dimensions: 8.5 x 25 cm,

equilibrated with heptane) and ca. 100 mL fractions are collected (Figure 4A). The column is first eluted with pure heptane (1 L), which is discarded, followed by an eluent of 10% EtOAc in heptane (4 L) and then 20% EtOAc in heptane for the remainder of the separation (6 L). Fractions 22-95 (Figure 4B) are combined (Note 23), and the solvent is removed by rotary evaporation (120 mmHg at 40 °C and followed by 0.8 mmHg at 40 °C) and by high vacuum (ca. 0.05 mmHg) at room temperature (23 °C) for 6 h to obtain the product **2** as an orange oil (25.1 g, 82%) (Figure 4C) (Notes 17, 24 and 25).

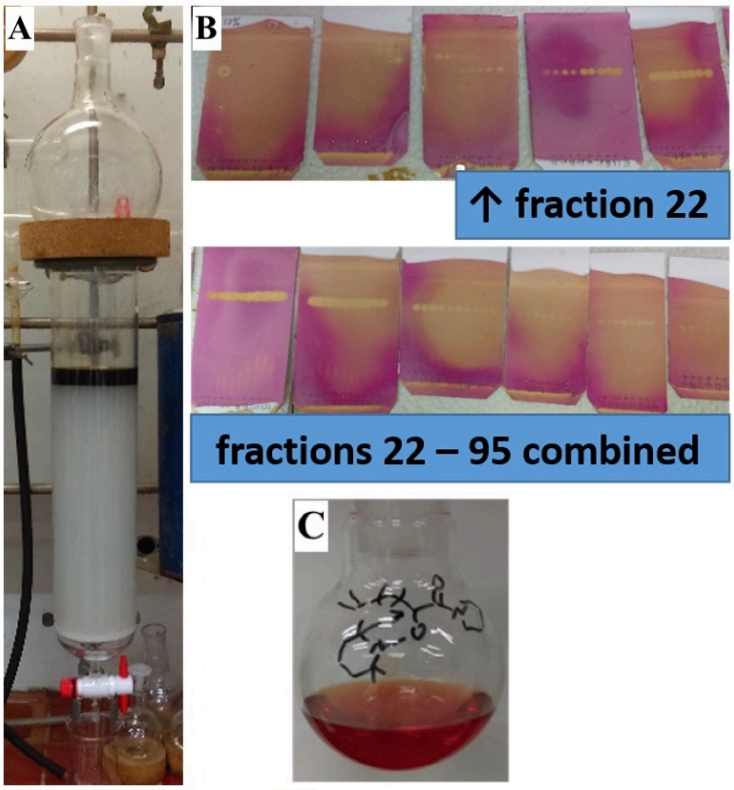

Figure 4. A) Chromatography setup; B) TLC analysis of collected fractions; C) Product in a 100 mL flask (photos provided by submitters)

C. *1-(Pyrrolidin-1-yl)undec-10-ene-1,2-dione* (**3**). A 250 mL, round-bottomed flask that is open to air is equipped with an egg-shaped, PTFE-coated magnetic stir bar (3 cm). the flask is charged with 1-(pyrrolidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)undec-10-en-1-one **2** (9.80 g,

25.0 mmol, 1.00 equiv), dichloromethane (50 mL) and deionized water (50 mL). The resulting mixture is stirred (800 rpm) and magnesium monoperoxyphthalate hexahydrate (Note 26) (30.9 g, 80% purity, 50.0 mmol, 2.00 equiv) is added in 10 portions over the course of 5 min. The resulting suspension is stirred under air at room temperature (23 °C) for 3 h (Note 27). The reaction mixture is diluted with EtOAc (250 mL) and a saturated aqueous solution of Na_2SO_3 (150 mL) (Note 28) is added while stirring is continued for 10 min. The phases are then separated, and the organic phase is sequentially washed with saturated aqueous Na_2CO_3 (2 x 150 mL) (Note 29), 1 M HCl (2 x 150 mL) and brine (100 mL). The washed solution is dried over anhydrous $MgSO_4$ (5 g) and filtered *via* gravitational filtration using a glass funnel equipped with filter paper (Note 12). The filtrate is concentrated by rotary evaporation (450 mmHg at 40 °C, followed by 120 mmHg at 40 °C), affording a thick orange oil. The oil is mixed with heptane (5 mL) and then loaded onto a silica gel column (approximately 200 ± 10 g, column dimensions: 6 x 18 cm, equilibrated with heptane) (Figure 5B). The column is then eluted with heptane (500 mL) and a mixture of 10% EtOAc in heptane (500 mL), with all the eluent being discarded. At this point 80 mL fractions are collected as the column is eluted with a mixture of 10% EtOAc in heptane (800 mL), followed by a mixture of 20% EtOAc in heptane (2 L) for the remainder of the separation. Fractions 22-38 (confirmed by TLC, 20% EtOAc in heptane, silica on aluminum, R_f = 0.63, $KMnO_4$ stain) (Figure 5C) are collected and the solvent is removed by rotary evaporation (120 mmHg at 40°C, followed by 0.8 mmHg at 40 °C). The residue is exposed to high vacuum (ca. 0.05 mmHg) at room temperature (23 °C) for 6 h to obtain product **3** as a slightly yellow oil (3.62 g, 58%) (Figure 5D) (Notes 17 and 30).

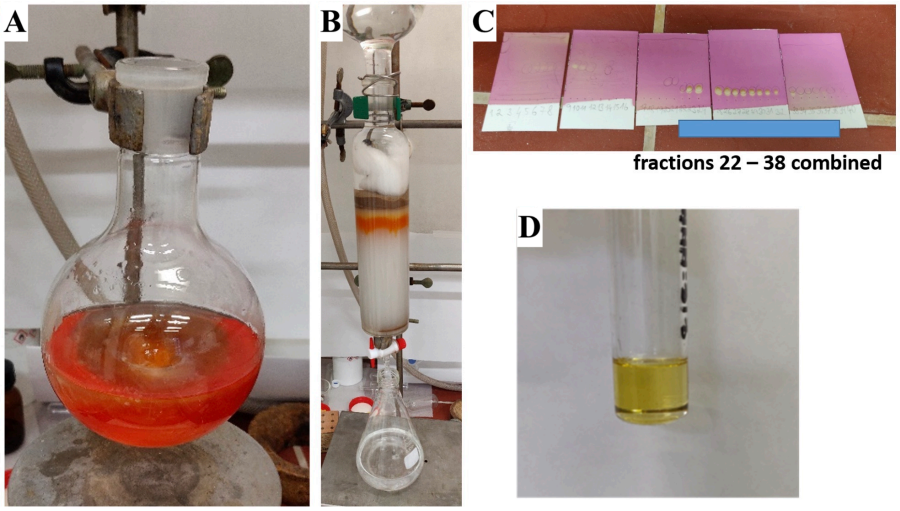

Figure 5. A) Reaction setup after Na_2SO_3 addition; B) Chromatography setup; C) TLC analysis of collected fractions; D) Product in a 16 mL vial (photos provided by submitters)

D. *2-Hydroxy-1-(pyrrolidin-1-yl)undec-10-en-1-one* (**4**). A 250 mL, round-bottomed flask that is open to air is equipped with an egg-shaped, PTFE-coated magnetic stir bar (3 cm) and charged with 1-(pyrrolidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)undec-10-en-1-one **2** (9.80 g, 25.0 mmol, 1.00 equiv) (Figure 6A), water (50 mL) and acetic acid (50 mL) (Note 31) (Figure 6B). The resulting mixture is stirred (600 rpm) open to air, and zinc dust (16.3 g, 250 mmol, 10.0 equiv) (Note 32) is added in 8 portions over the course of 5 min. The flask is loosely fitted with a PE stopper (Note 33) and stirred at 50 °C for 2 h under air (Figure 6C).

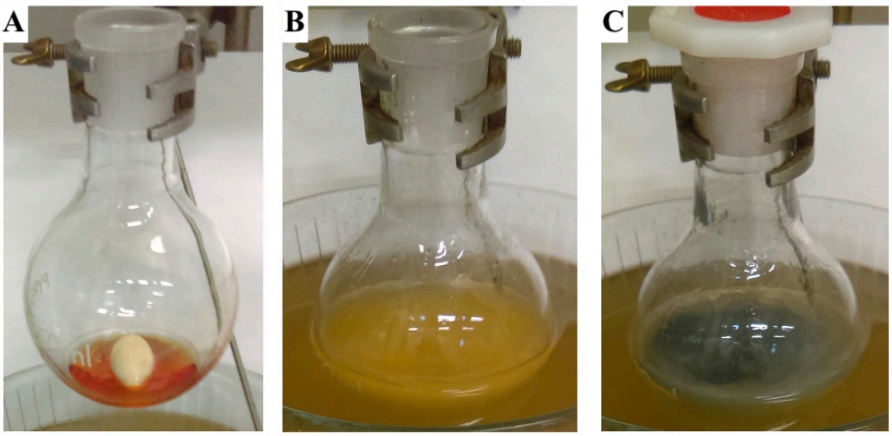

Figure 6. Reaction setup: A) After substrate addition; B) After acetic acid addition; C) After zinc addition (photos provided by submitters)

After cooling to room temperature (23 °C), excess zinc dust is filtered off *via* gravitational filtration, into a 500 mL round-bottomed flask, using a glass funnel equipped with filter paper (Note 12) (Figure 7A) and the reaction flask is rinsed with aqueous acetic acid (1:1 v/v, 2 x 10 mL). Then, the volume of the filtrate is reduced by approximately two thirds by rotary evaporation (55 mmHg at 50 °C) (Figure 7B). Dichloromethane (150 mL) is added, and the mixture is carefully neutralized by addition of saturated $NaHCO_3$ (ca. 70 mL) until pH 4 is reached (Note 34). The phases are separated through use of a separatory funnel, and a half-saturated sodium potassium tartrate solution (200 mL) (Note 35) is added to the organic layer (in a 500 mL round-bottomed flask). The biphasic mixture is stirred for 3 h at room temperature, during which time a precipitate forms. The phases are separated using a separatory funnel (whereby the precipitate is collected together with the dichloromethane phase), and the aqueous phase is extracted with dichloromethane (3 x 100 mL) (Figure 7C) (Notes 17 and 36).

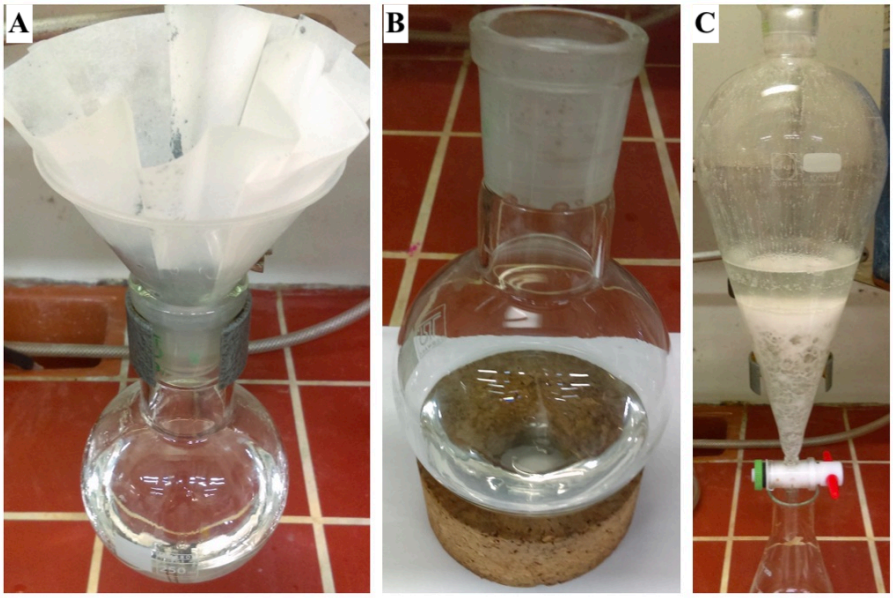

Figure 7. A) Filtration of excess zinc; B) After partial evaporation; C) After treatment with tartrate solution (photos provided by submitters)

The combined organic solutions (still containing the precipitate) are dried over anhydrous $MgSO_4$ (5 g) and the solids are filtered off *via* gravitational filtration using a glass funnel equipped with filter paper (Note 12). The filtrate is concentrated by rotary evaporation (450 mmHg at 40 °C and followed by 0.8 mmHg at 40 °C, followed by high vacuum (ca. 0.05 mmHg) at room temperature (23 °C) for 14 h), to afford product **4** as an-off white solid (5.46 g, 86%) (Figure 8) that requires no further purification (Note 37).

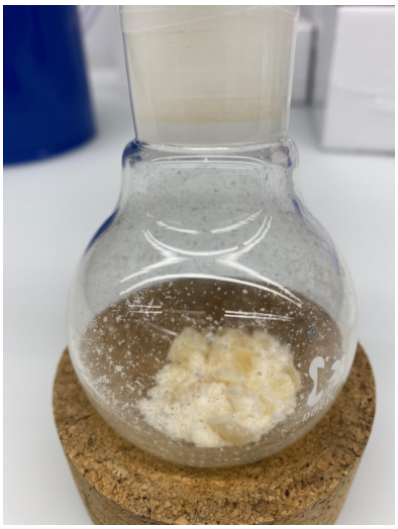

Figure 8. Product 4 (photo provided by submitters)

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 10-undecenoyl chloride, pyrrolidine, trimethylamine, 2-fluoropyridine,

trifluoromethanesulfonic anhydride, 2,2,6,6-tetramethylpiperidine 1-oxyl, magnesium monoperoxyphthalate hexahydrate, zinc, acetic acid dichloromethane, diethyl ether, sodium bicarbonate, sodium carbonate, hydrochloric acid, sodium potassium tartrate, heptane, ethyl acetate and silica gel.

2. Pyrrolidine was purchased from Merck (purity >99.0) and used as received.
3. Triethylamine was purchased from Fischer Chemicals, AG (purity >99.0) and used as received.
4. Dichloromethane (>99.9%) was purchased from Honeywell (dried by mBraun SPS) and stored under argon.
5. 10-Undecenoyl chloride was purchased from TCI (purity >98.0) and used as received.
6. Excess reagent remaining in the needle was quenched with water.
7. Diethyl ether was purchased from Honeywell (ACS reagent, purity >99.8) and used as received.
8. Aqueous HCl (32%) was purchased from VWR and diluted to 1M.
9. Saturated aqueous $NaHCO_3$ was purchased from Honeywell (purity >99.7) and used as received.
10. Brine was purchased from Honeywell (purity >99.5) and used as received.
11. Anhydrous $MgSO_4$ was purchased from Merck (purity >98.0) and used as received.
12. Filter paper (MN 615 ¼, >4 μm) was purchased from Macherey-Nagel.
13. Heptane was purchased from Honeywell (purity >99.7) and used as received.
14. Silica gel was purchased from Merck (0.063-0.200 mm).
15. Ethyl acetate was purchased from Honeywell (purity >99.7) and used as received.
16. Characterization data for **1**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.80 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H), 5.00 – 4.85 (m, 2H), 3.41 (dt, J = 20.4, 6.70 Hz, 4H), 2.28 – 2.20 (m, 2H), 2.03 (dd, J = 14.3, 6.9 Hz, 2H), 1.96 – 1.88 (m, 2H), 1.86 – 1.78 (m, 2H), 1.70 – 1.58 (m, 2H), 1.40 – 1.21 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 171.9, 139.3, 114.2, 46.7, 45.6, 34.9, 33.9, 29.6, 29.6, 29.5, 29.2, 29.0, 26.2, 25.0, 24.5. IR (neat) ν_{max}: 2973, 2925, 2870, 1650, 1439, 1132, 991, 909, 712 cm^{-1}. HRMS (ESI$^+$, m/z): $[M+H]^+$ calculated for $[C_{15}H_{28}NO]^+$: 238.2165, found: 238.2168. TLC R_f = 0.25 (50% EtOAc in heptane, silica on aluminum, (Note 17) $KMnO_4$ stain). Purity was

assessed at >99% by quantitative ^{1}H NMR spectroscopy using ethylene carbonate (>99%) as an internal standard.

17. TLC analysis is performed on TLC plates purchased from Merck (TLC Silica gel 60 F_{254}).
18. TEMPO was purchased from Fluorochem (purity 99%) and used as received.
19. 2-Fluoropyridine was purchased from Fluorochem (purity 98%) and used as received.
20. Trifluoromethanesulfonic anhydride was purchased from Fluorochem (purity 99%) and used as received.
21. Trifluoromethanesulfonic anhydride hydrolyses under air but can be reformed and purified according to a procedure reported by Stang and Dueber in *Org. Synth.* **1974**, *54*, 79.
22. Maximum conversion was confirmed via ^{1}H NMR analysis of the crude reaction mixture.
23. The product elution can be monitored by TLC (50% EtOAc in heptane, R_f = 0.70, silica on aluminum, $KMnO_4$ stain). The product is closely followed by an unidentified by-product. The TLC analysis should be conducted and evaluated carefully, so as to not collect the by-product in the pooled fractions.
24. Slight changes in color might be observed between different runs through small amounts of an unidentified impurity.
25. Characterization data for **2**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.81 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 4.96 (ddd, *J* = 13.6, 10.2, 1.4 Hz, 2H), 4.40 (dd, *J* = 10.2, 4.7 Hz, 1H), 3.94 (dt, *J* = 10.2, 6.6 Hz, 1H), 3.59 – 3.36 (m, 3H), 2.03 (dd, *J* = 14.4, 7.0 Hz, 2H), 1.98 – 1.90 (m, 2H), 1.90 – 1.73 (m, 4H), 1.46 – 0.97 (m, 28H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 171.3, 138.9, 113.8, 83.3, 60.2, 58.9, 46.5, 45.4, 40.3, 40.0, 33.4, 33.1, 32.4, 31.3, 29.4, 29.0, 28.7, 28.5, 25.8, 24.8, 23.8, 20.0, 19.7, 16.8.IR (neat) ν_{max}: 2973, 2925, 2870, 2853, 1650, 1439, 1375, 1339, 1132, 991, 909, 711 cm^{-1}. HRMS (ESI^+, *m*/*z*): $[M+H]^+$ calculated for $[C_{24}H_{45}N_2O_2]^+$: 393.3476, found: 393.3479. R_f = 0.70 (50% EtOAc in heptane, silica on aluminum, (Note 17) $KMnO_4$ stain). Purity was assessed at >99% by quantitative ^{1}H NMR using ethylene carbonate (>99%) as an internal standard. TLC
26. Magnesium monoperoxyphthalate hexahydrate is purchased from Fluorochem (purity 80%) and used as received.
27. Full conversion is reached after 3 h. TLC analysis was not used for analysis since the starting material and the product possess similar R_f values.

28. Sodium sulfite was purchased from Merck (>98%) and used to prepare the saturated solution.
29. Sodium carbonate was purchased from Merck (>99.5%) and used to prepare the saturated solution.
30. Characterization data for **3**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.78 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.02 – 4.86 (m, 2H), 3.58 (t, *J* = 7.4, Hz, 2H), 3.50 (t, *J* = 6.9 Hz, 2H), 2.82 (t, *J* = 7.4 Hz, 2H), 2.02 (dd, *J* = 14.4, 6.9 Hz, 2H), 1.96 – 1.90 (m, 2H), 1.90 – 1.83 (m, 2H), 1.62 – 1.55 (m, 2H), 1.40 – 1.25 (m, 8H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 201.2, 163.3, 139.2, 114.3, 47.4, 46.4, 39.4, 33.9, 29.3, 29.2, 29.0, 28.9, 26.5, 23.7, 23.1. IR (neat) ν_{max}: 3074, 2974, 2926, 2854, 1713, 1635, 1440, 1339, 1225, 995, 909 cm^{-1}. HRMS (ESI$^+$, *m*/*z*): $[M+H]^+$ calculated for $[C_{15}H_{26}NO_2Na]^+$: 252.1958, found: 252.1957. TLC R_f = 0.63 (50% EtOAc in heptane, silica on aluminum, (Note 17) $KMnO_4$ stain). Purity was assessed at >99% by quantitative ^{1}H NMR spectroscopy using ethylene carbonate (>99%) as an internal standard.
31. Acetic acid (glacial, 100%) was purchased from Merck and used as received.
32. Zinc dust was purchased from Merck (dust < 10 μm, purity >98%) and used as received.
33. Slow evolution of hydrogen gas can be observed.
34. Higher pH can lead to lower yields.
35. Sodium potassium tartrate was purchased from Merck (99%) and used as received to prepare the solution.
36. It can take several minutes until the two phases have separated in the separatory funnel.
37. Characterization data for **4**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.77 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.02 – 4.82 (m, 2H), 4.14 (dd, *J* = 7.5, 2.8 Hz, 1H), 3.62 – 3.49 (m, 1H), 3.50 – 3.38 (m, 2H), 3.32 (dt, *J* = 10.2, 6.8 Hz, 1H), 2.05 – 1.78 (m, 6H), 1.67 – 1.16 (m, 13H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 173.1, 139.2, 114.2, 69.4, 46.3, 46.0, 34.5, 33.8, 29.4 (2C), 29.1, 29.0, 26.1, 25.1, 23.9. IR (neat) ν_{max}: 3441, 2919, 2850, 1625, 1453, 1385, 1197, 1078, 992, 923, 732, 463 cm^{-1}. HRMS (ESI$^+$, *m*/*z*): $[M+H]^+$ calculated for $[C_{15}H_{28}NO_2]^+$: 254.2115, found: 254.2115. TLC R_f = 0.23 (50% EtOAc in heptane, silica on aluminum, (Note 17) $KMnO_4$ stain). Purity was assessed at >99% by quantitative ^{1}H NMR using ethylene carbonate (>99%) as an internal standard.

Working with Hazardous Chemicals

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.

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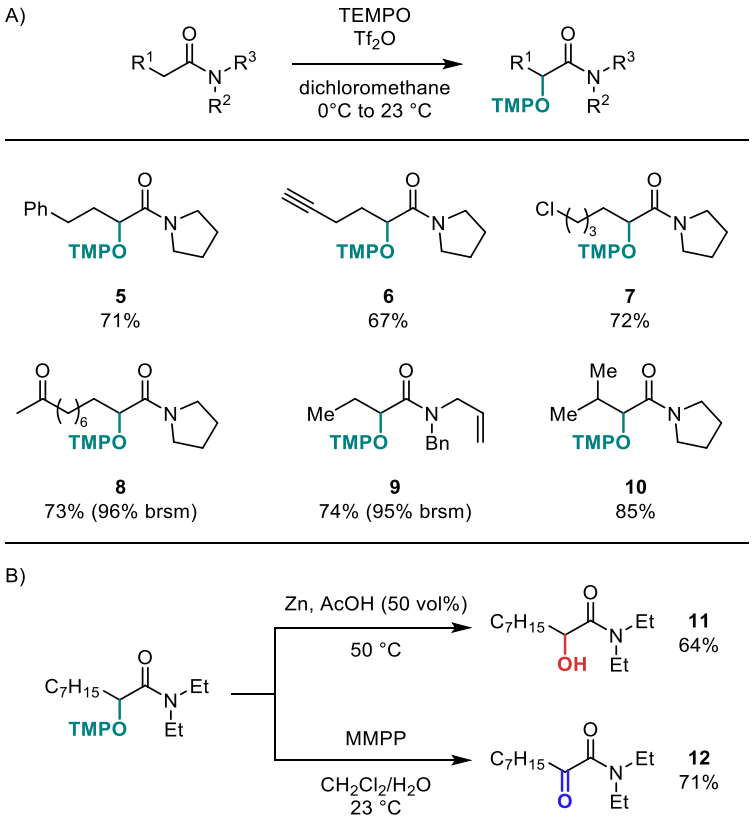
Discussion

Selective oxidation reactions are valuable transformations in organic synthesis.[2] Particularly, the α-keto amide functionality has observed a spike in popularity in the synthetic chemistry community in recent years.[3] Additionally, the α-hydroxy carbonyl moiety represents a useful template for further synthetic development.[4] Direct oxidation methodologies to access α-keto amides are scarce and limited to specific substrates,[5] whereas α-hydroxy carbonyl derivatives are generally obtained from the parent compounds

utilizing enol/enolate chemistry.[4b,6] This effectively limits the availability of amides as substrates for such transformations, due to their limited susceptibility to enolization.

Amide activation using triflic anhydride is a distinctive synthetic approach employed by multiple research groups in order to transform amides *via* chemoselective cycloaddition or nucleophilic addition processes.[7] Furthermore, formation of an electrophilic enolonium species under certain conditions can trigger Umpolung reactivity at the α-position of amides activated under this paradigm.[8] We have previously developed a chemoselective oxidation of amides to α-keto amides and α-hydroxy amides. Specifically, the use of TEMPO (2,2,6,6-tetramethylpiperidin-1-oxyl) during triflic anhydride-mediated amide activation provides the corresponding α-(tetramethylpiperidin-1-yl)oxyamides (Scheme 1A).[9] Reductive cleavage conditions lead to the corresponding α-hydroxy amides, thus positioning the tetramethylpiperidine (TMP) moiety as a "protecting group" for the hydroxy function. Alternatively, oxidative treatment of the oxyaminated amides provides access to α-keto amides (Scheme 1B). This synthetic strategy, based on chemoselective amide activation using triflic anhydride along with the use of an oxidant, represents a useful tool potentially applicable to virtually any type of tertiary amide. The utility of such an approach is showcased by further transformations of the oxyaminated amides into synthetically useful building blocks accessible employing commonly used reagents.



Scheme 1. A) Amide scope in α-OTMP amide oxidation; B) Synthesis of α-hydroxy and α-keto amides from α-OTMP amide

References

1. Department of Organic Chemistry, University of Vienna, Währinger Straße 38, 1090 Vienna, Austria. E-Mail: nuno.maulide@univie.ac.at, Homepage: http://maulide.univie.ac.at. Generous support of this research by the EU (VINCAT CoG 682002 to N.M.), the Austrian Science Fund (P32607), Covestro AG, and the University of Vienna (Uni:docs fellowship to M.L.) is acknowledged. We are grateful to the University of Vienna for its continued and generous support of our research programs.
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Appendix
Chemical Abstracts Nomenclature (Registry Number)

10-Undecenoyl chloride; (38460-95-6)
Pyrrolidine; (123-75-1)
Triethylamine; (121-44-8)
2-Fluoropyridine; (372-48-5)
Trifluoromethanesulfonic anhydride; (358-23-6)
2,2,6,6-Tetramethylpiperidine 1-oxyl; (2564-83-2)
Magnesium monoperoxyphthalate hexahydrate; (84665-66-7)
Zinc; (7440-66-6)

Miran Lemmerer studied chemistry at the University of Vienna. During his studies he performed an Erasmus exchange semester in Lund, Sweden where he focused his studies on organic- and biological chemistry. Under the supervision of Prof. Maulide, he completed his Masters thesis in 2018, developing a protocol for α-amination of amides *via* Umpolung. Currently, he is pursuing his Ph.D. degree in the group of Prof. Maulide, investigating novel methods based on the electrophilic activation of amides.

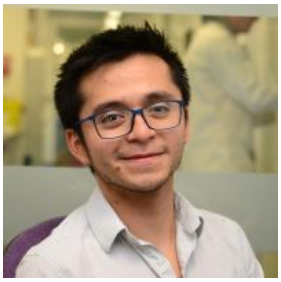
Ján Matyašovský was born in Partizanske, Slovakia. He received his Engineering Degree at the Slovak Technical University in Bratislava, specializing in organic chemistry. In 2020, he obtained his Ph.D. degree at the Charles University in Prague for his work on synthesis of modified nucleic acids at the Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences under supervision of Prof. Michal Hocek. He currently occupies a post-doctoral position in the research group of Professor Nuno Maulide at the University of Vienna. His current research interests focus on the development of new methodologies for organic synthesis.

Roberto Tinelli received his MSc from the University of Pavia in 2020, where, under the supervision of Prof. Ravelli, he worked on the development of new substrates for the Paternò-Büchi reaction. He is currently pursuing his Ph.D. studies at the University of Vienna under the supervision of Prof. Maulide. His current research focuses on the chemistry of thioalkynes and related high-energy intermediates.

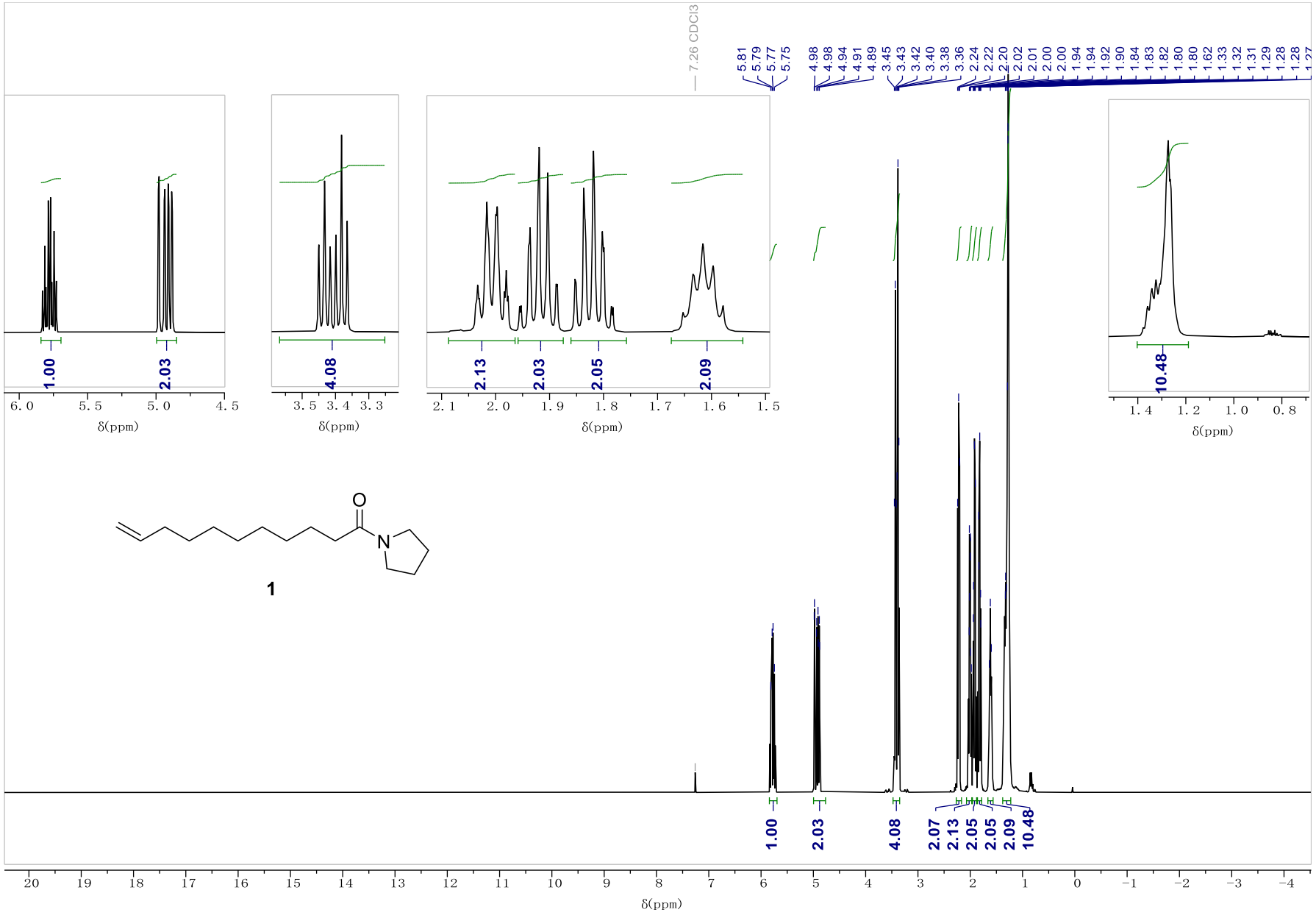
After obtaining his Ph.D. at the Université catholique de Louvain under the supervision of Prof. István E. Markó in 2007 Nuno Maulide pursued a postdoctoral position in the group of Prof. Barry M. Trost at Stanford University. In 2009, he started his independent career at the Max-Planck Institut für Kohlenforschung and only 4 years later, in 2013 he became a Full Professor at the University of Vienna. His research interests are broadly spread in the field of organic chemistry and include the development of new reaction methods, the total synthesis of natural compounds and medicinal chemistry driven investigations. He is a member of the Board of Editors for Organic Syntheses (2018) as well as an Associate Editor of Organic Letters (2018) and JACS AU (2020). Beyond his scientific endeavors, for which he received 3 ERC grants and multiple awards like the Tetrahedron Young Investigator Award (2020), he is also heavily involved in knowledge transfer to the public. For his great conveyance of Science, also coupled with his other passion, the piano, he was appointed Scientist of the Year in Austria (2018).

Colin Knus was born in Switzerland and joined the Nevado group in 2022 as a Lab Technician. He is currently a second-year student of his Apprenticeship course. He enjoys chemistry, travelling around on his motorbike and snowboarding.

Dr. Jaime Martín was born In León, Spain. In 2020, he obtained his Ph.D. in Inorganic Chemistry at the University of Zaragoza. Thereafter, he joined the group of Prof. Cristina Nevado at the University of Zurich as a Postdoctoral Associate. His main research interest is focused on the study of new gold(III) complexes, their reactivity and their application in catalysis.



Jorge A. González was born in Xalapa, Mexico. He completed his Undergraduate Degree in Chemistry at the National and Autonomous University of Mexico in 2011. He obtained his Ph.D. at the University of Edinburgh in 2016. He is currently a postdoctoral associate research associate in the group of Prof. Cristina Nevado.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3.40
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1.31
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1.28
1.28
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2.03
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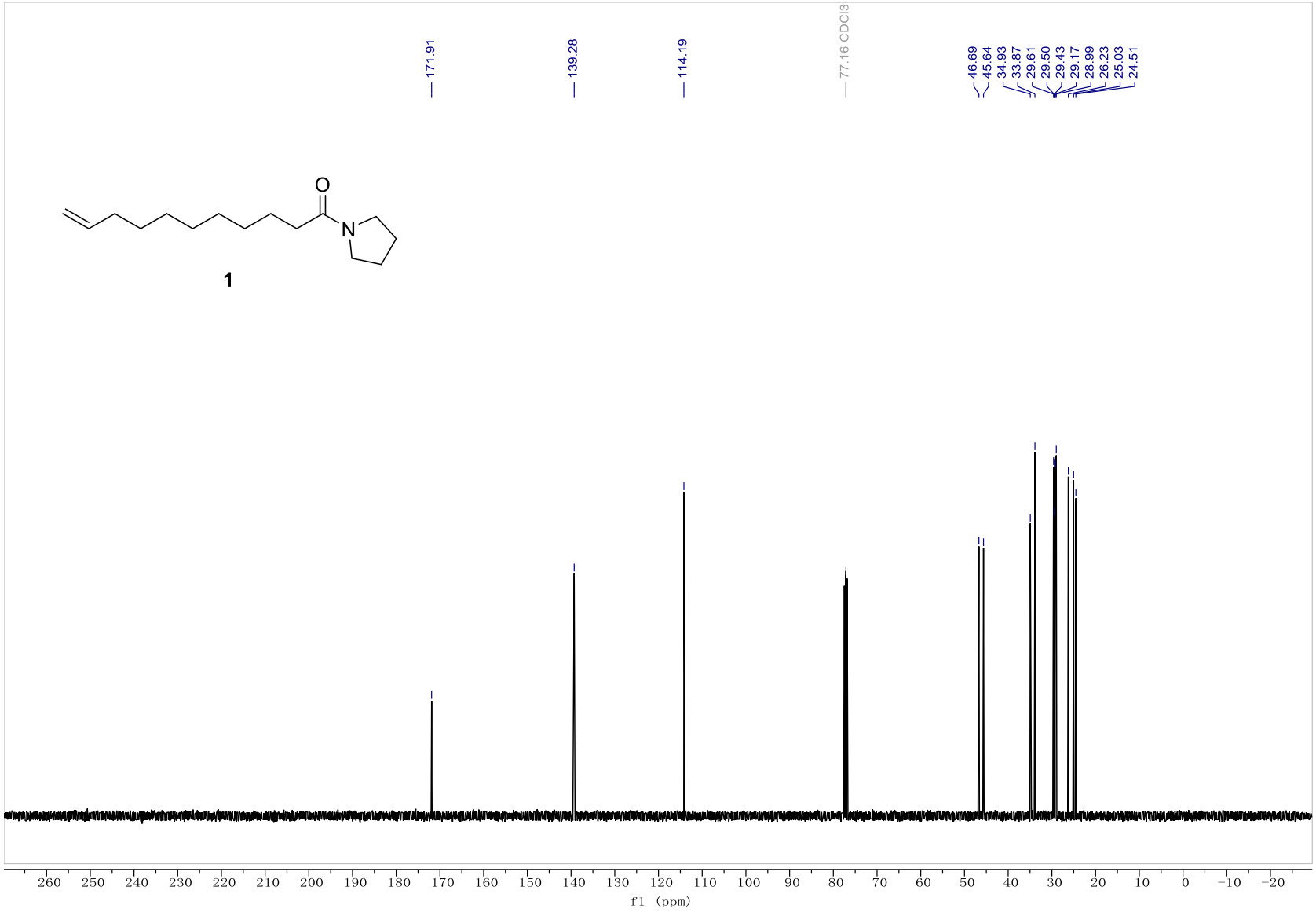
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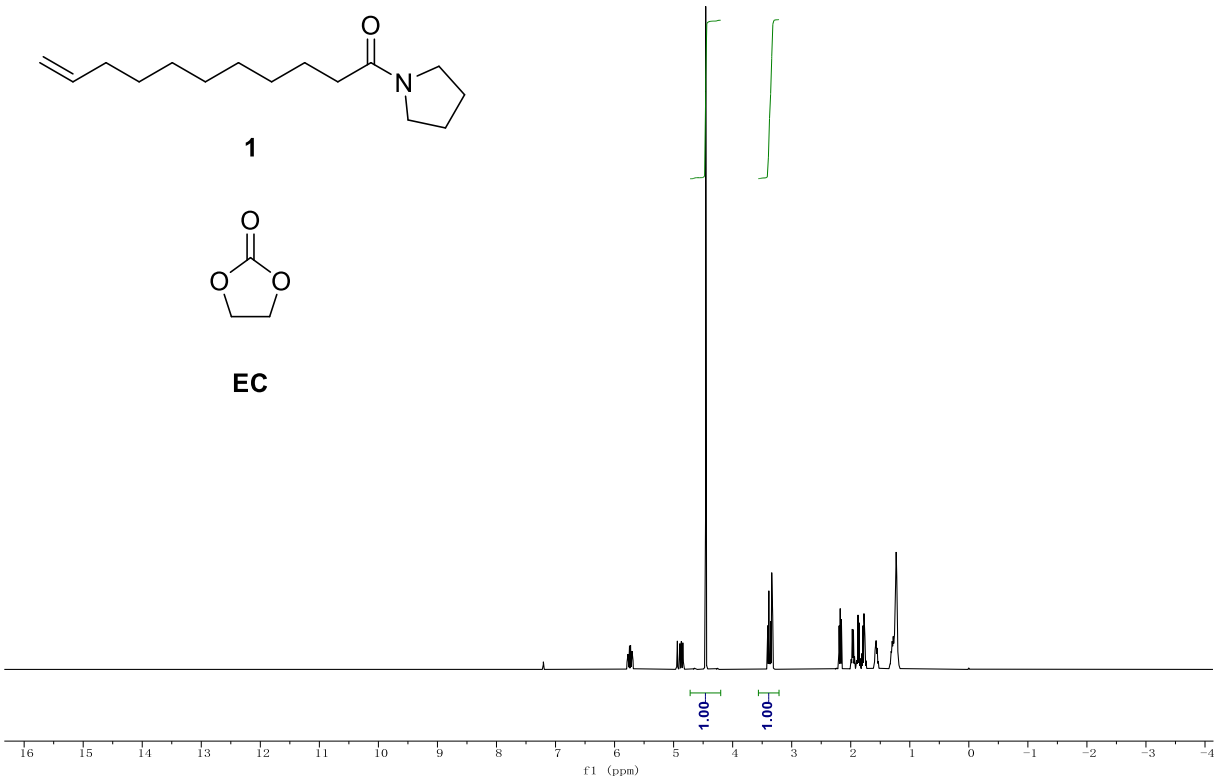
f1 (ppm)

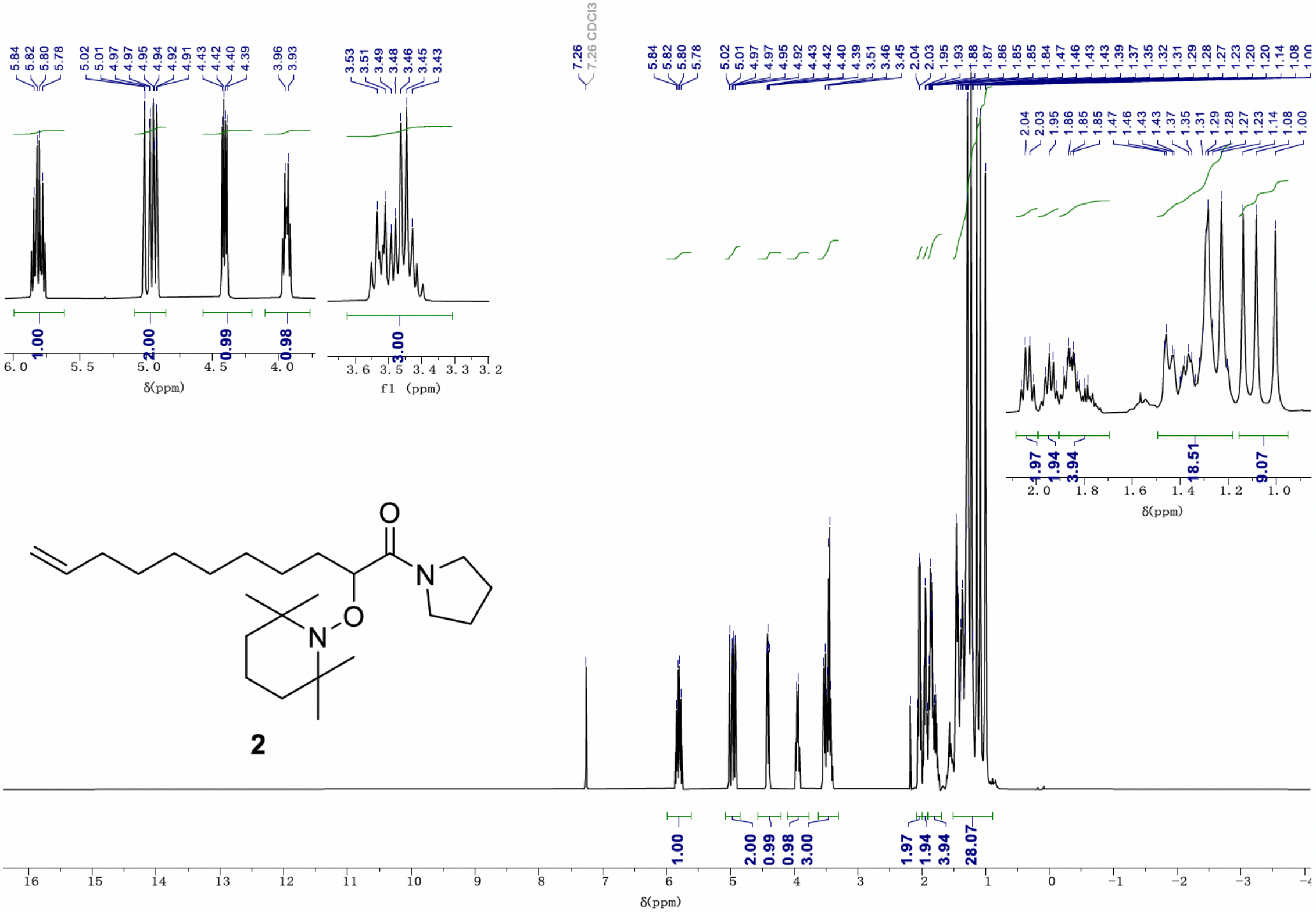


^{1}H NMR (400 MHz, $CDCl_3$) of compound 1 + EC as internal standard

Int= average of normalized integrals values
MW =molecular weight
P =Purity (as percent value)
m = mass
n= number of protons giving rise to a given NMR signal (The total number of protons is set to one because an average of all normalized integrals is carried out)

$n_{EC} = 1$	$n_1 = 1$
$Int_{EC} = 1.00$	$Int_1 = 1.0$
$MW_{Ec} = 88.06$	$MW_1 = 237.39$
$M_{EC} = 4.3$ mg	$m_1 = 11.5$ mg
$P_{EC} > 99$ %	

$$P(\%) = \left(\frac{n_{EC} \cdot Int_1 \cdot MW_1 \cdot m_{EC}}{n_1 \cdot Int_{EC} \cdot MW_{EC} \cdot m_1}\right) \cdot P_{EC} = 99.8\%$$



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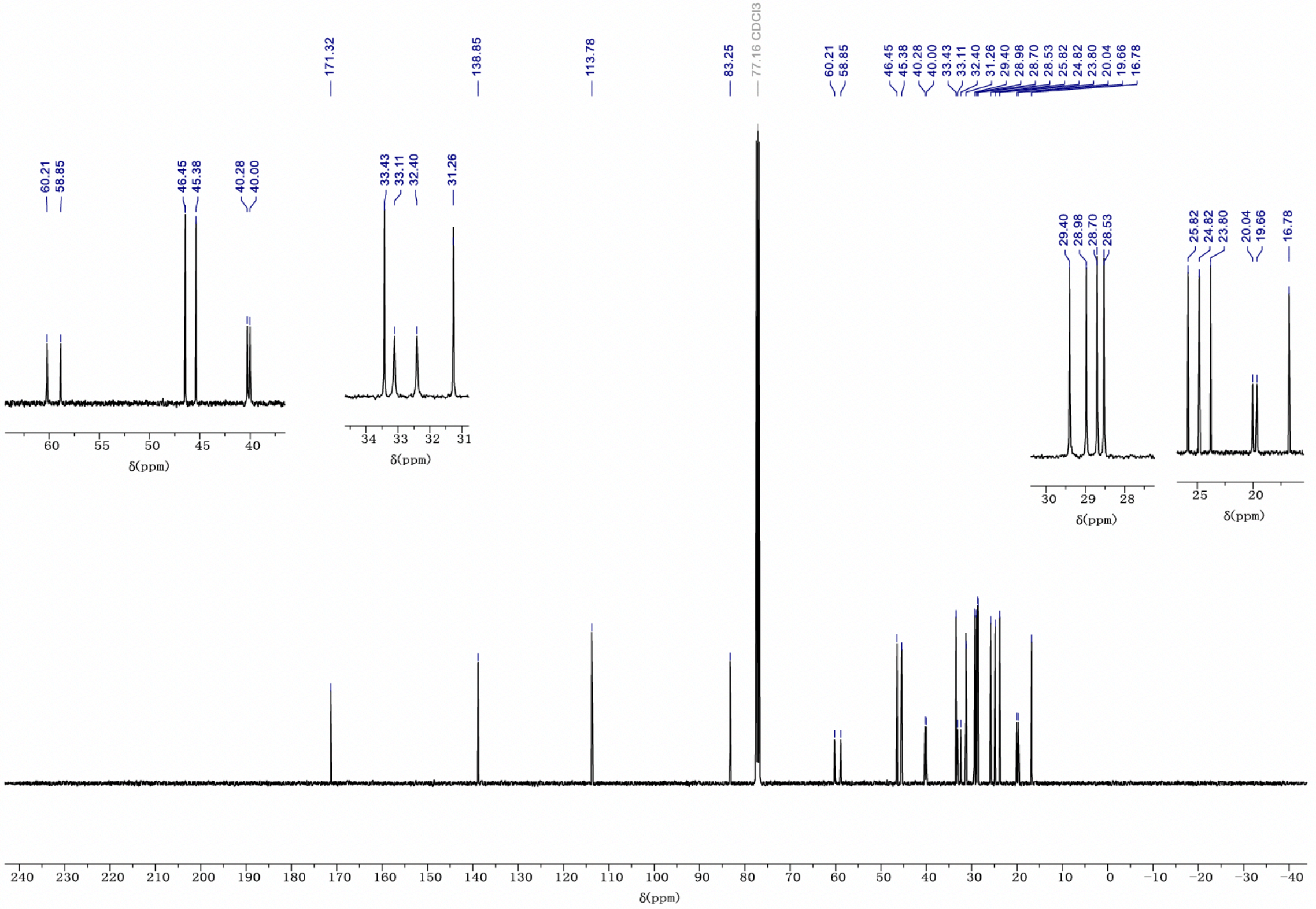

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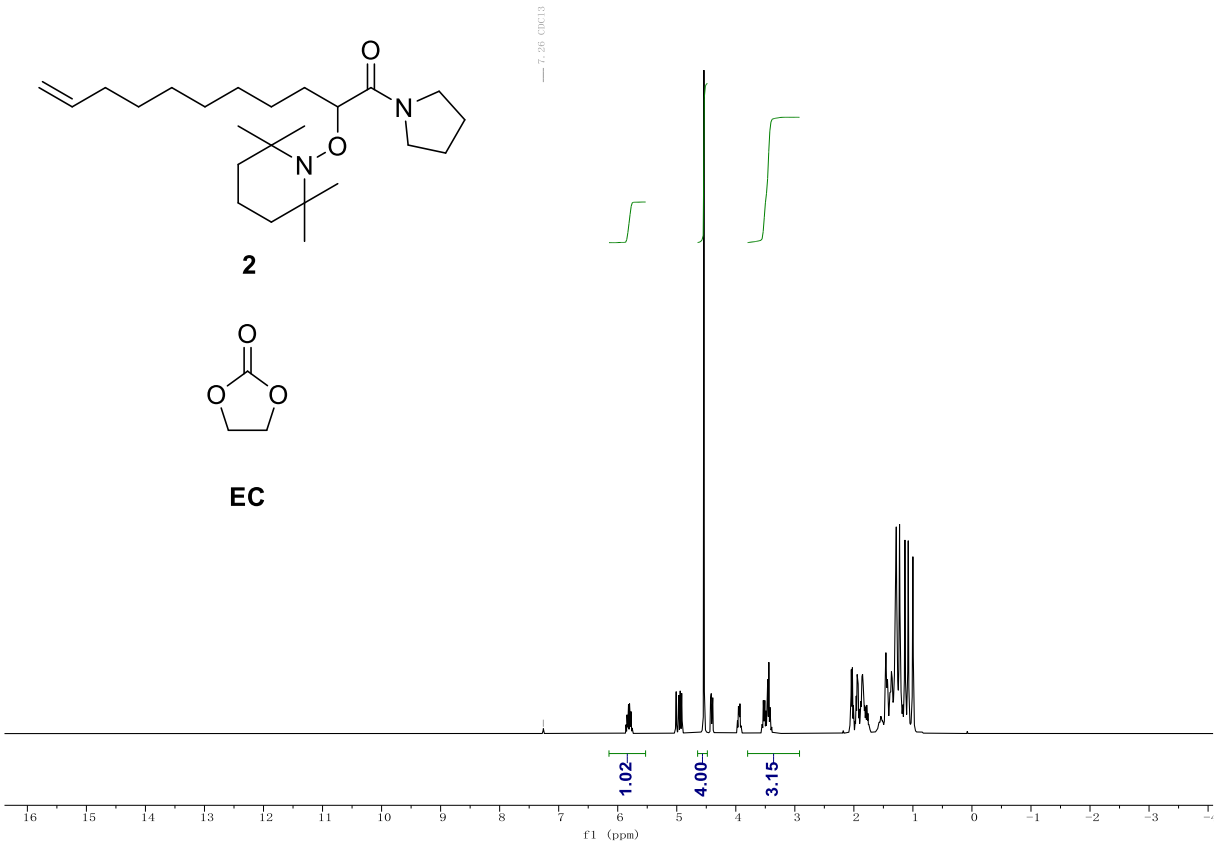

^{1}H NMR (400 MHz, $CDCl_3$) of compound 2 + EC as internal standard

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P =Purity (as percent value)
m = mass
n= number of protons giving rise to a given NMR signal (The total number of protons is set to one because an average of all normalized integrals is carried out)

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MW_{Ec}=88.06	MW_2 = 392.63
M_{EC}= 4.5 mg	m_2= 20.8 mg
P_{EC} > 99 %	

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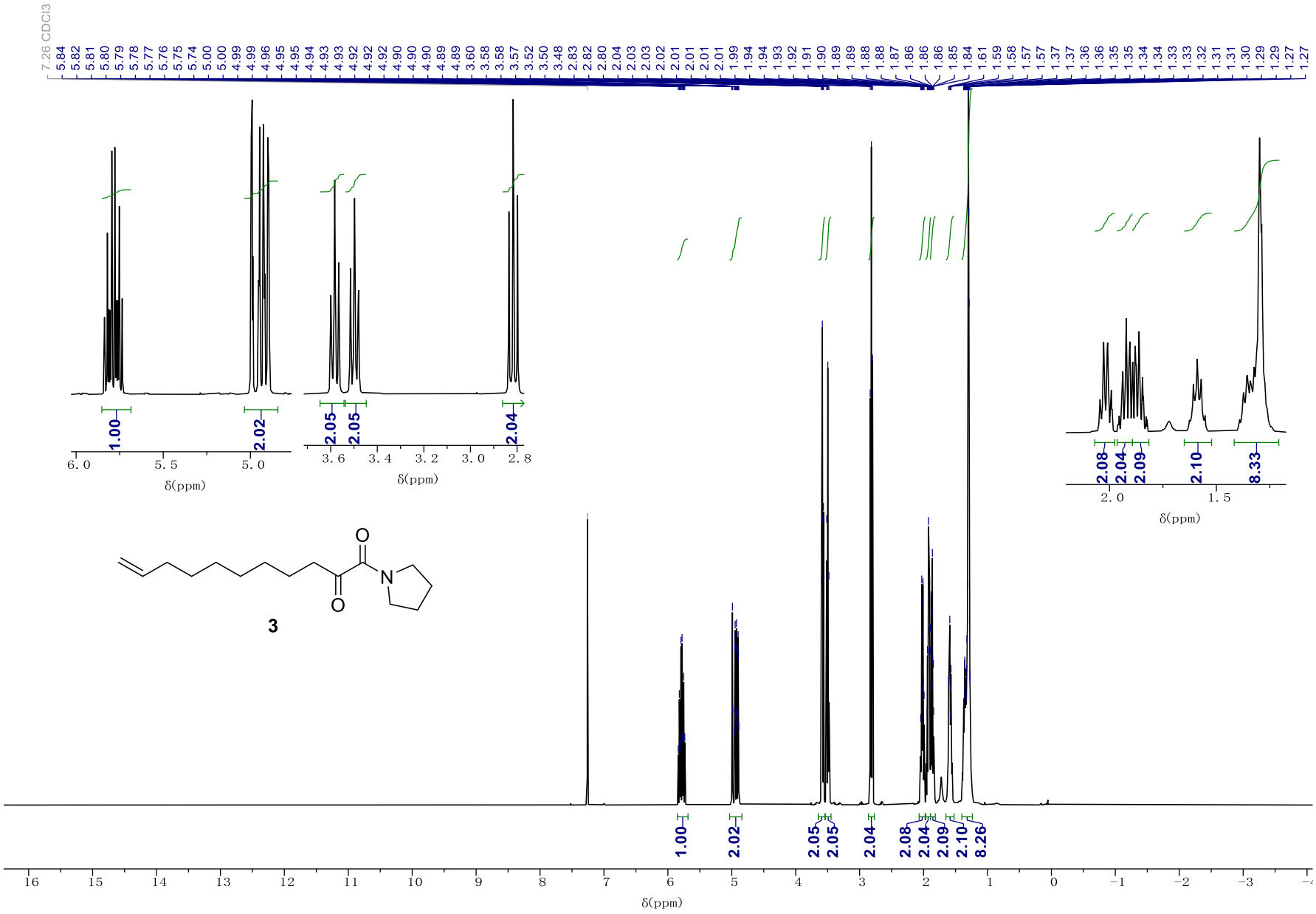
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N
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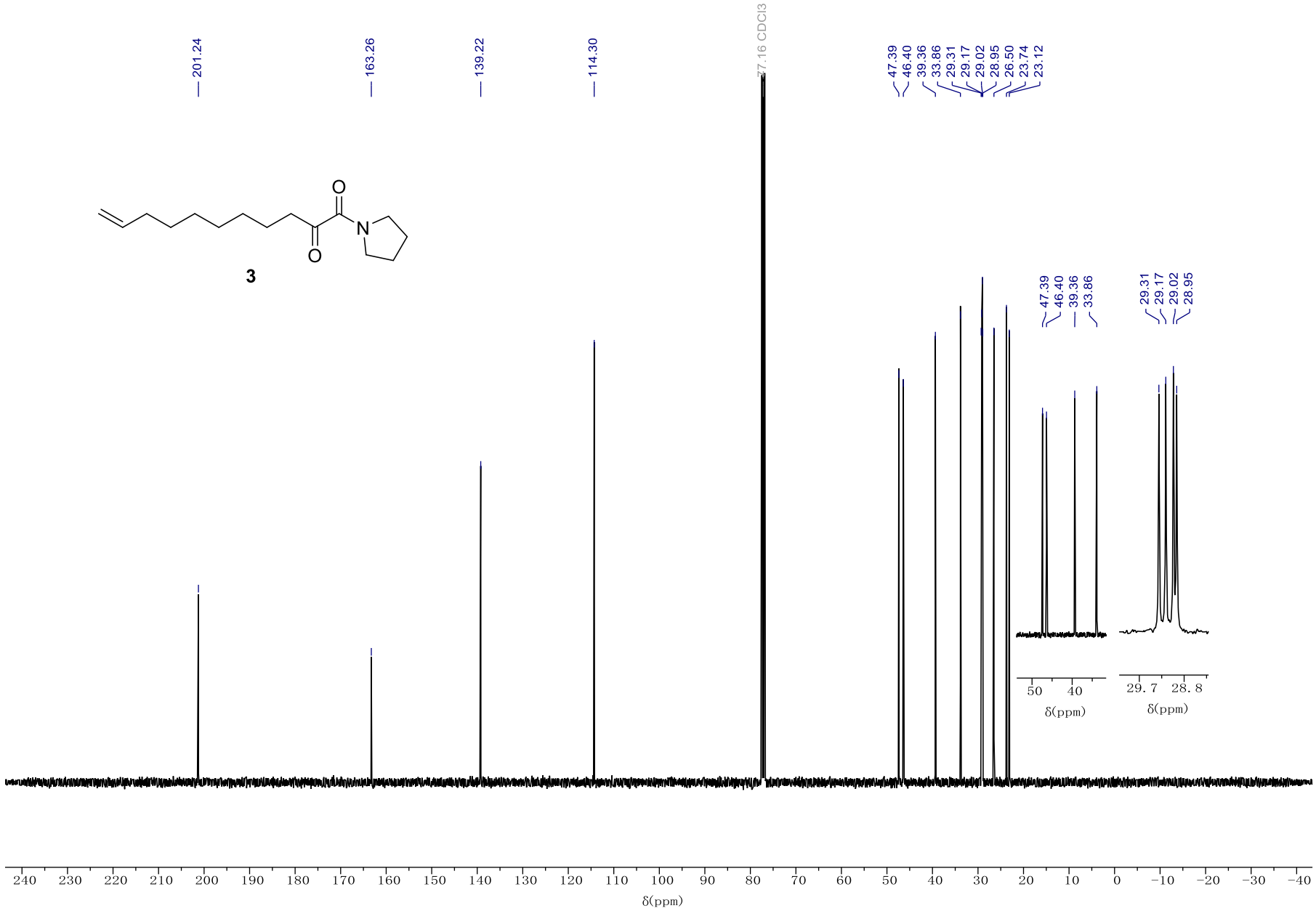
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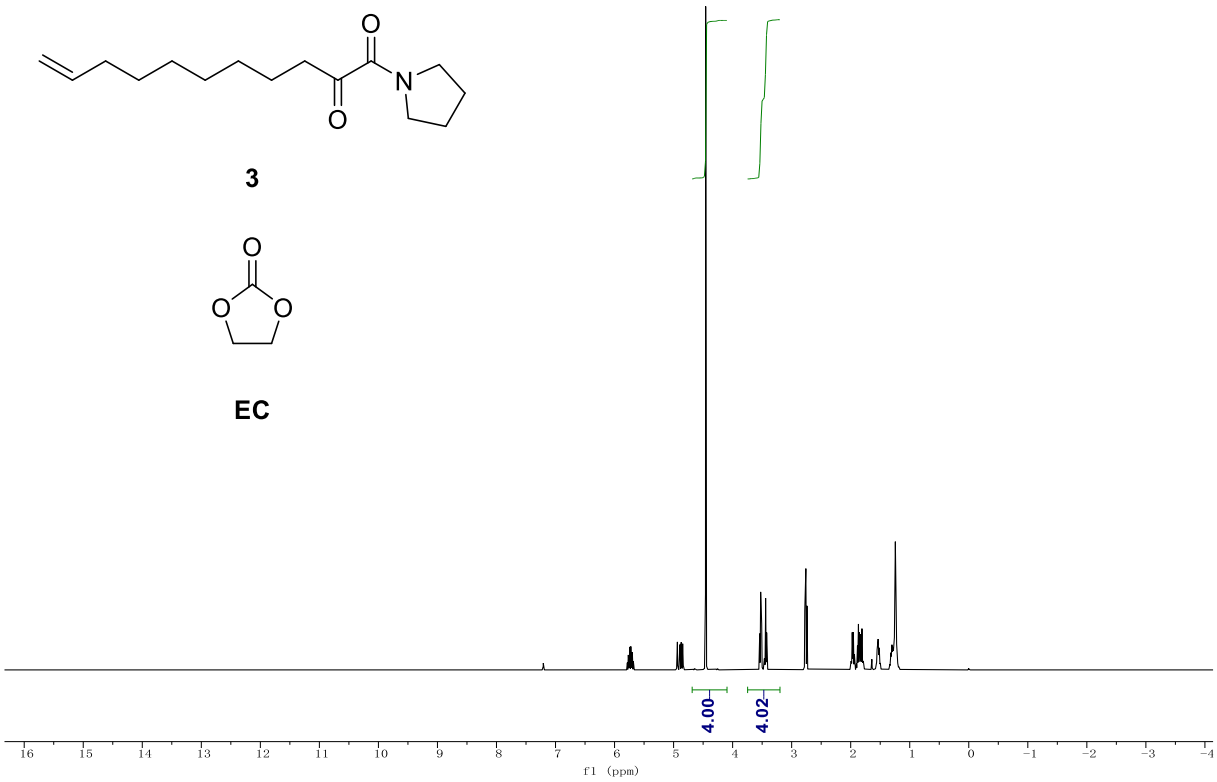

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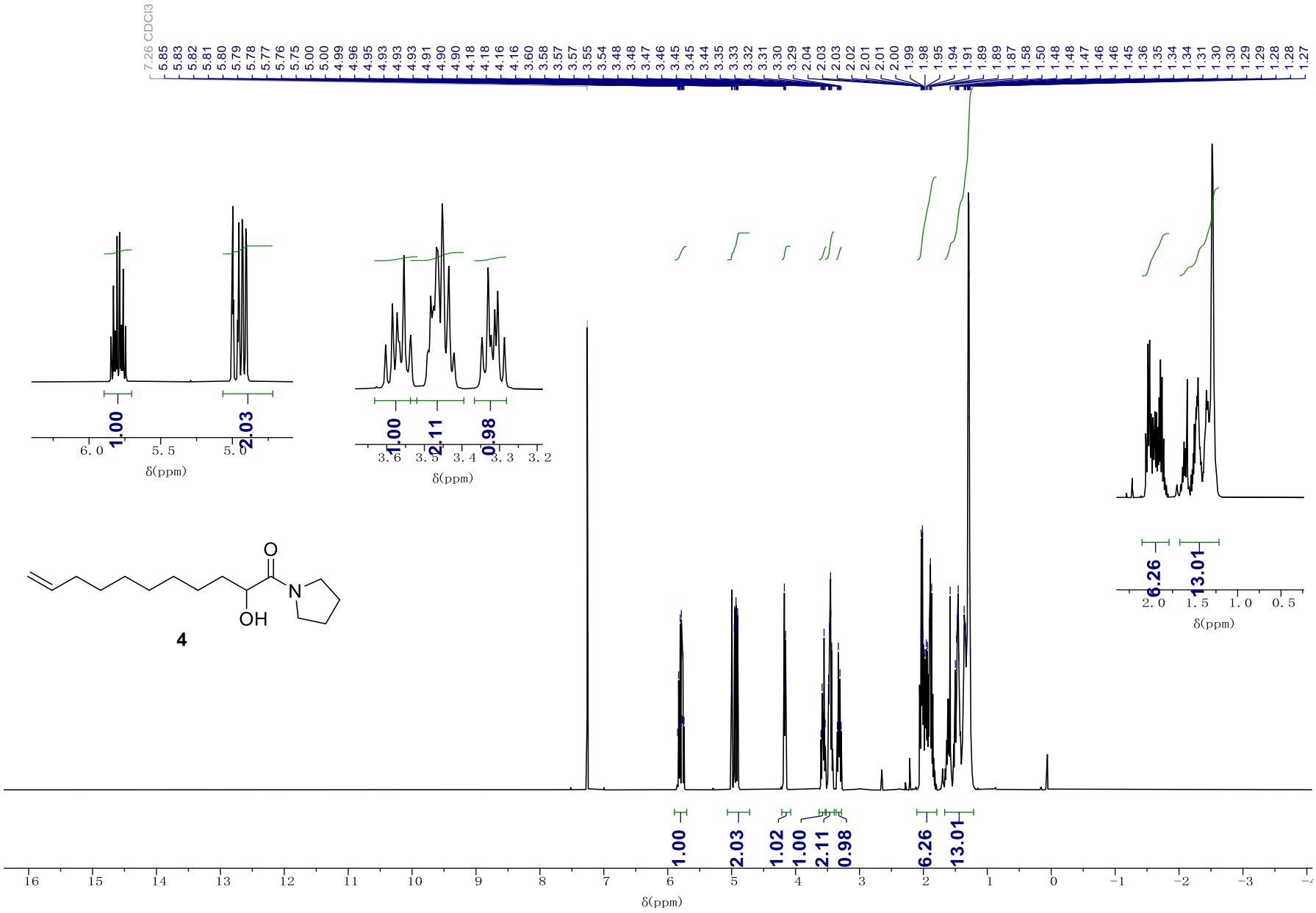
m = mass
n= number of protons giving rise to a given NMR signal (The total number of protons is set to one because an average of all normalized integrals is carried out)

$n_{EC} = 1$	$n_3 = 1$
$Int_{EC} = 1.00$	$Int_3 = 1.005$
$MW_{Ec} = 88.06$	$MW_3 = 251.37$
$M_{EC} = 4.7$ mg	$m_3 = 13.4$ mg
$P_{EC} > 99$ %	

$$P(\%) = \left(\frac{n_{EC} \cdot Int_3 \cdot MW_3 \cdot m_{EC}}{n_3 \cdot Int_{EC} \cdot MW_{EC} \cdot m_3}\right) \cdot P_{EC} = 99.6\%$$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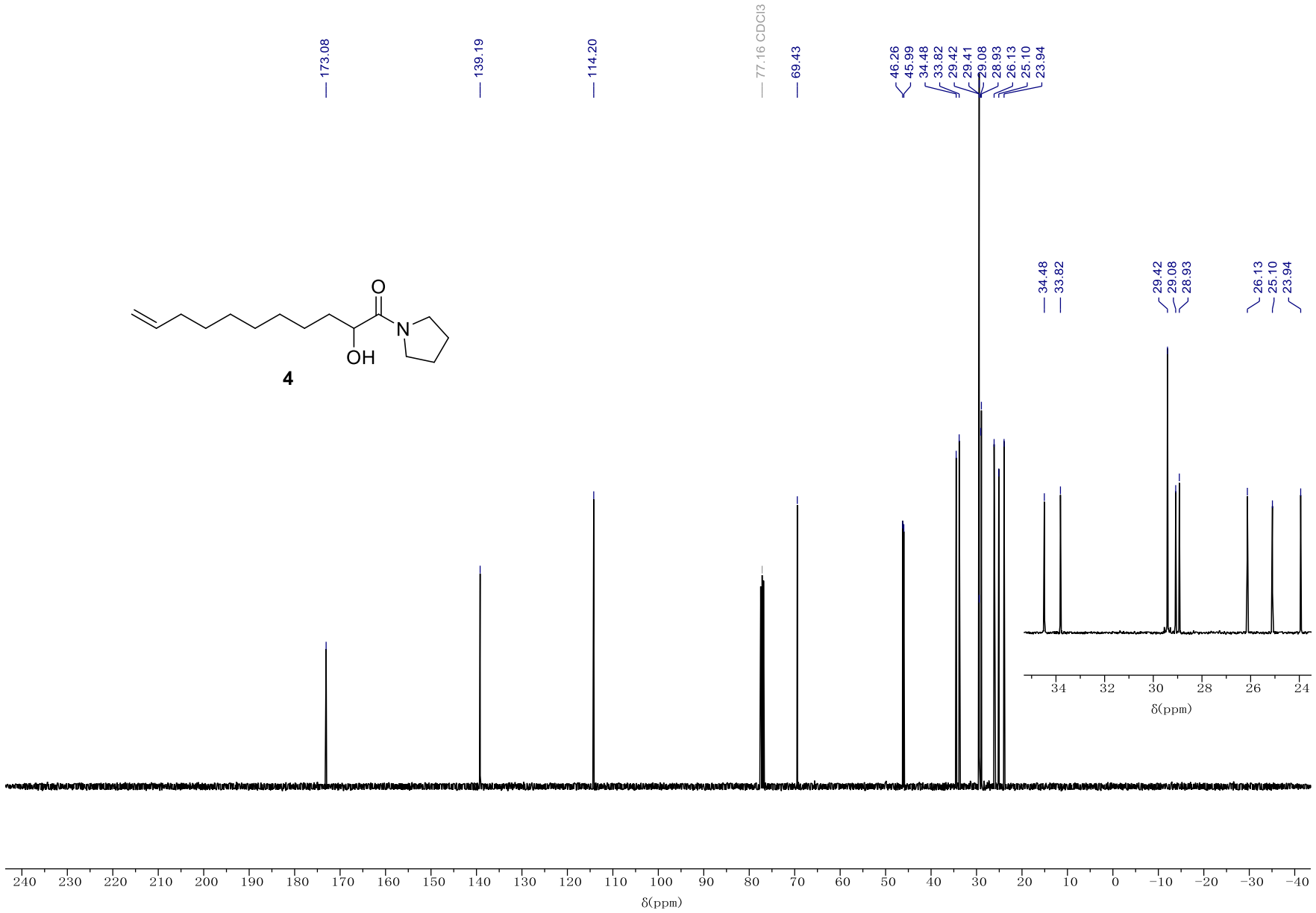
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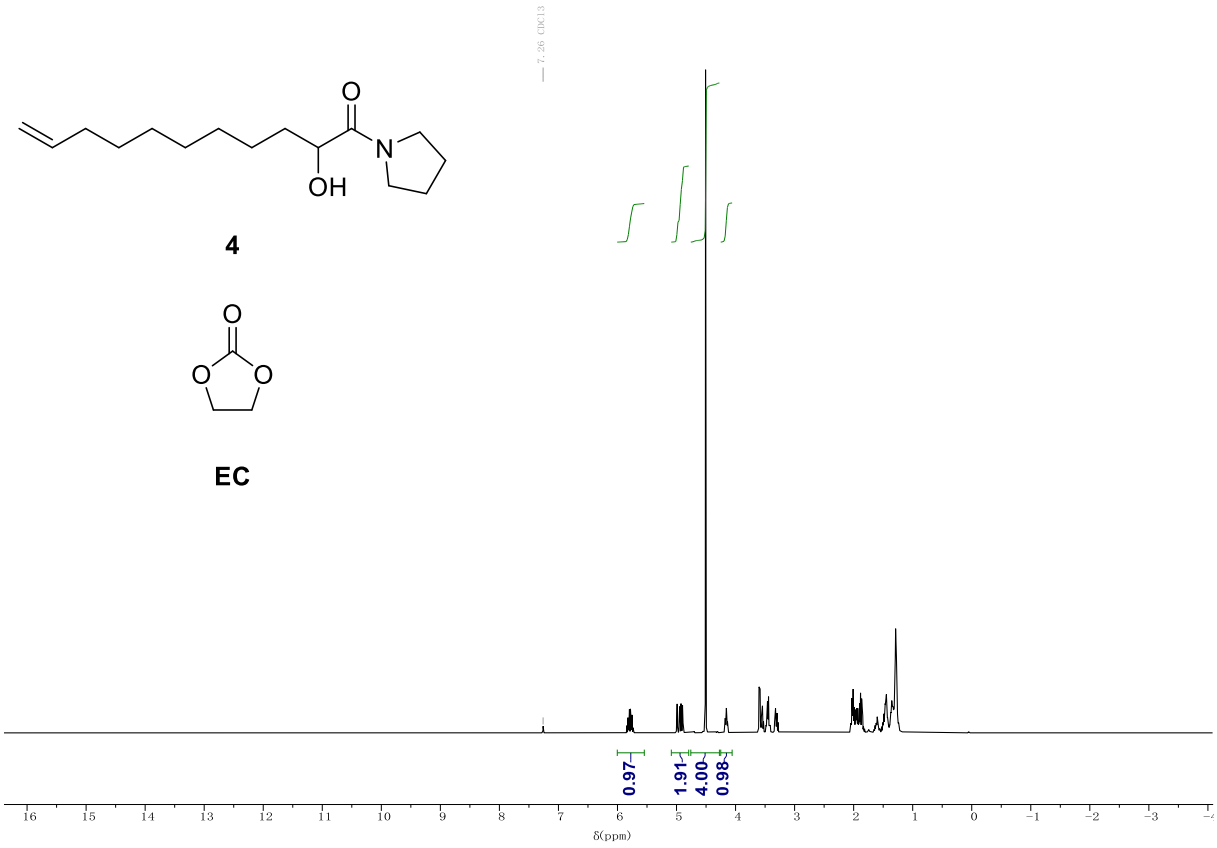

^{1}H NMR (400 MHz, $CDCl_3$) of compound 4 + EC as internal standard

Int= average of normalized integrals values
MW =molecular weight
P =Purity (as percent value)
m = mass
n= number of protons giving rise to a given NMR signal (The total number of protons is set to one because an average of all normalized integrals is carried out)

n_{EC} = 1	n_4= 1
Int_{EC}= 1.00	Int_4 = 0.965
MW_{Ec}=88.06	MW_4 = 253.39
M_{EC}= 4.77 mg	m_4= 13.13 mg
P_{EC} > 99 %	

$$P(\%)= \left(\frac{n_{EC}\cdot Int_4\cdot MW_4\cdot m_{EC}}{n_4\cdot Int_{EC}\cdot MW_{EC}\cdot m_4}\right)\cdot P_{EC} = 99.8\%$$