The Synthesis of Laurolactam from Cyclododecanone via a Beckmann Rearrangement

Article – "In the Laboratory: Green Chemistry"

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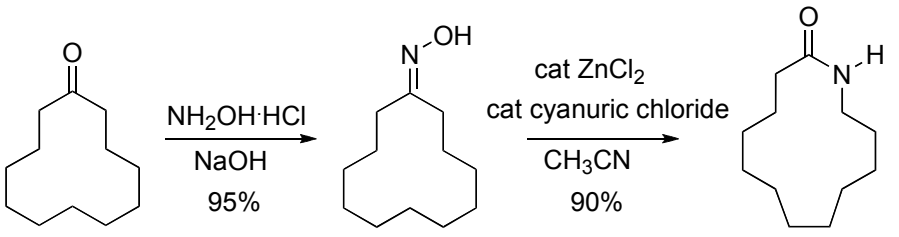
Douglass F. Taber* and Patrick J. Straney

Department of Chemistry and Biochemistry, University of Delaware, Newark, DE 19716

*taberdf@udel.edu; Fax: (302) 831-6335

Abstract:

A simple and green procedure for the production of laurolactam (cyclododecanone lactam) from cyclododecanone is described. This synthesis was designed for the undergraduate organic chemistry laboratory course.



1 **2** **3**

m.p. = 132-133 °C m.p. = 148-149 °C

Key Words: organic synthesis, mechanisms of reactions, and laboratory equipment/apparatus.

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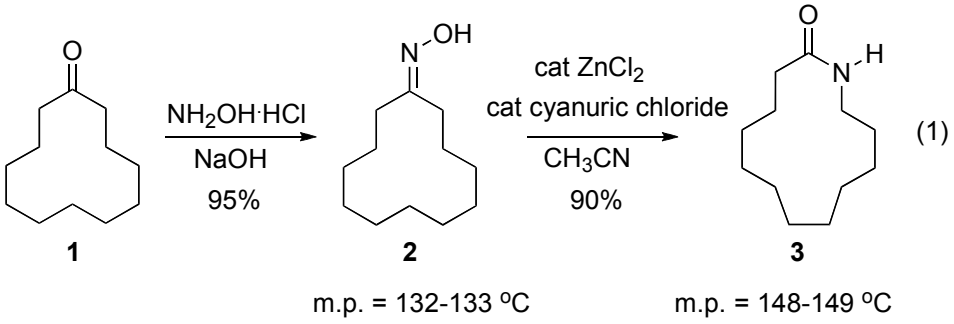
Lab Summary:

Although the Beckmann rearrangement, the conversion of a ketone via its oxime to the amide, is a widely practiced procedure, an efficient and simple procedure has yet to be reported in this journal. Recently, Yamamoto reported [1] an efficient protocol for the Beckmann rearrangement, using 0.5 mol. % of cyanuric chloride, supported by 1 mol. % of anhydrous zinc chloride. We have incorporated this inexpensive procedure into a new experiment for the undergraduate laboratory course.

We were led to cyclododecanone **1** (Eq. 1) as the starting material, as both the oxime **2** and the amide **3** are crystalline. Oxime formation from **1** is rapid and the crystalline product is easily separated [2]. The Beckmann rearrangement requires warming, but it too can be completed in less than one hour. Both the procedure for the synthesis of the oxime and the lactam had high yields (95% and 90%, respectively). Products **2** and **3** were identified by melting point and by ^{13}C and ^{1}H NMR.



This procedure is best suited for an undergraduate organic chemistry lab. Synthesis of laurolactam from cyclododecanone is expected to take approximately four hours. Students performing the procedure will learn about catalytic cycles and reaction mechanisms, as well as the Beckmann rearrangement, a classic reaction in organic chemistry. In recovering their reaction products, students will learn how to properly use separatory funnels, Buchner funnels, and the rotary evaporator. Additionally, the students will learn how to quickly purify and identify the products through recrystallization and melting point determination. As the procedure requires no unusual laboratory equipment or reaction conditions, the synthesis of laurolactam from cyclododecanone will be a simple yet instructional procedure for any undergraduate to perform.

Apart from laboratory techniques, students will also have the opportunity to further research several current and important topics in organic chemistry. The use of two catalytic reagents and the high reaction yields make this experiment an excellent example of green chemistry. As well, the product laurolactam is used on a commercial scale to prepare polyamide-12 (Nylon-12), in a reaction that proceeds at room temperature (*3*). This experiment can be used to illustrate topics such as polymerization, peptide bonds, thermoplastics, and the applications of synthetic materials.

Hazards:

When dealing with any of the solvents or reagents in this lab, standard laboratory safety precautions apply. Wearing protective gloves is advisable, as cyanuric chloride and hydroxylamine hydrochloride are known to cause skin irritation. As well, the cyanuric chloride reacts violently with water, so it must not be exposed to water. The ethanol and acetonitrile are highly flammable, and they must be kept away from open flames. As well, acetonitrile can be

absorbed by the skin, which further stresses the importance of wearing protective gloves. Avoid direct ingestion and inhalation of all solvents and reagents.

Supplemental Material

Instructions for the students and notes for the instructor are available in this issue of *JCE Online*.

Literature Cited

1. Furuya, Y.; Ishihara, K.; Yamamoto, H. *J. Am. Chem. Soc.* **2005**, *127*, 11240.
2. Shriner, R. L., R. C. Fuson, and D. Y. Curtin. *The Systematic Identification of Organic Compounds: A Laboratory Manual, Fifth Edition*; Wiley: New York, **1948**.
3. Kim, I.; White, J. L. *J. Appl. Polym. Sci.* **2003**, *90*, 3797.
4. Zakharkin, L.; Guseva, V. *Russ. Chem. Rev.* **1978**, *47*, 955.
5. Olah, G. A.; Fung, A. P. *Synthesis* **1979**, *7*, 538.

Lab Documentation

Instructions to Students

The Synthesis of Laurolactam from Cyclododecanone in a Two Step Conversion Process

Conversion to Cyclododecanone Oxime:

In a round bottom flask, dissolve 1.5 grams of cyclododecanone (99%+ pure) in about 8 mL of 95% ethanol. To this, add 0.6 grams of hydroxylamine hydrochloride (97% pure), along with 25 mL of deionized water. Lastly, add 15 mL of a 10% by weight aqueous solution of NaOH. Attach a reflux condenser, and heat the solution to reflux (100 °C) using a heating mantle. Stir the assembly periodically while heating. Completion of the reaction is marked by the formation of large crystals that float on the surface of the reaction mixture, which normally occurs about 35 minutes after initially heating. Chill the mixture in an ice/water bath, and then recover the crystals using a Buchner funnel. Allow the recovered crystals to dry on filter paper, and then obtain the mass and melting point of the product.

Crystallization of Oxime:

To further purify the product, place the crystals in a clean round bottom flask and dissolve them in 95% ethanol (10 mL ethanol per gram of crystals recovered). To obtain a clear solution, the flask must be heated until the crystals dissolve. Upon the addition of deionized water (15 mL water per gram of crude oxime crystals recovered) the product will immediately crystallize. Chill the mixture in an ice/water bath, and recover the recrystallized oxime product via filtration using a Buchner funnel. Allow the crystals to dry on filter paper, and mass once dry.

Identify the melting point of the product, and compare it to that of the reference value, 132 – 133 °C (*4*).

Conversion to Cyclododecanone Lactam (Laurolactam):

To a round bottom flask, add the recrystallized cyclododecanone oxime. To this, add 12 mL of the acetonitrile solution containing 8.0 mg of cyanuric chloride and 11.5 mg of anhydrous zinc chloride. Using the previous equipment setup, heat the solution to reflux (82 °C) for about 60 min. Monitor reaction completion by using thin-layer chromatography (TLC) plates and observing the disappearance of the oxime spot and the appearance of the more polar product spot. Elute the TLC plates in a 1:1 mixture of methyl tert-butyl ether and petroleum ether, and use an iodine chamber to visualize the spots. Remember to calculate the R_f value for each spot observed. After the reaction is complete (TLC), remove the flask from the heating mantle and immediately quench the reaction with 20 mL of a saturated aqueous solution of $NaHCO_3$. Quantitatively transfer the reaction mixture to a 100 mL separatory funnel, and extract the product using three 15 mL portions of ethyl acetate. For each separation, wash the reaction mixture with the ethyl acetate, shake, and allowed to separate. Collect the aqueous layer back into the 50 mL round bottom flask, and collect the organic layer in a 125 mL Erlenmeyer flask. After the separation, dry the ethyl acetate by adding 0.5 grams of anhydrous magnesium sulfate and stirring for about ten minutes. Once dried, filter the magnesium sulfate out of the solution using a Buchner funnel. Concentrate the solution under vacuum and mass the crude product.

Crystallization of Lactam:

Dissolve the crude lactam in one part of 95% ethanol (7 mL ethanol per gram of crude lactam crystals recovered). No heating is required. The product will crystallize upon the addition of two parts of deionized water. Filter the crystals with a Buchner funnel, dry on filter paper, and compare the melting point to the reference value of 148 – 149 °C (*5*).

Safety Notes:

When dealing with any of the solvents or reagents in this lab, standard laboratory safety precautions apply. Wearing protective gloves is advisable, as cyanuric chloride, hydroxylamine hydrochloride, and acetonitrile can cause skin irritation. The cyanuric chloride reacts violently with water, so be sure to store it in a dry location. Acetonitrile and ethanol are highly flammable and must be kept away from an open flame. Lastly, avoid direct ingestion and inhalation of all solvents and reagents.

Instructor Notes:

Note 1: The conversion of cyclododecanone oxime to cyclododecanone lactam is water sensitive; either fresh, anhydrous acetonitrile should be used, or else the acetonitrile should be freshly distilled each day. As well, the zinc chloride must be anhydrous.

Note 2: In order to shorten the amount of time it would take for the students to measure the indicated amounts of acetonitrile, zinc chloride, and cyanuric chloride, the instructor is advised to prepare a solution of acetonitrile that is 0.667 grams/L in cyanuric chloride (184.41 g/mol) and 0.96 grams/L in anhydrous zinc chloride (136.315 g/mol). This solution should be prepared fresh each day.

Note 3: The laboratory instructor should prepare the 10% by weight NaOH solution as well as the saturated $NaHCO_3$ solution prior to the experiment.

Note 4: To prepare the iodine chamber, place several crystals of I_2 and a piece of filter paper in a screw-top jar.

Amounts for 15 Students:

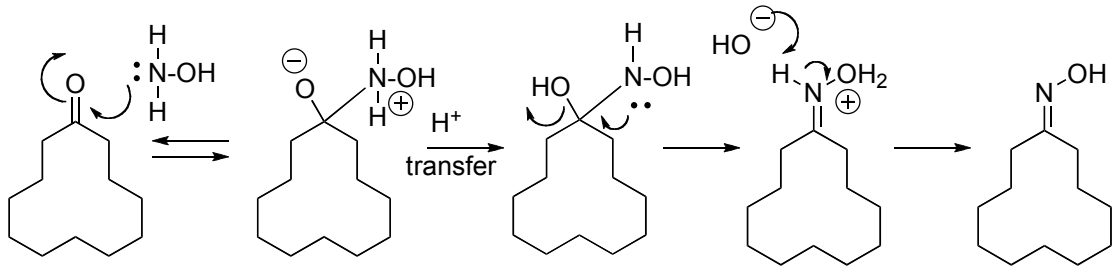
- Cyclododecanone: 22.5 g
- Hydroxylamine Hydrochloride: 9.0 g
- Deionized Water: 1600 mL (for recrystallization and solution preparation)
- 95% EtOH: 500 mL
- NaOH: 22.5 g (for 225 mL of a 10% by weight aqueous solution)
- Acetonitrile: 180 mL
- Cyanuric Chloride: 0.358 g (for 180 mL of a 10.8 mM solution of acetonitrile)
- $ZnCl_2$: 0.555 g (for 180 mL of a 10.8 mM solution of acetonitrile)
- Petroleum Ether (PE): 75 mL (assuming each student receives 10 mL of the 1:1 MTBE and PE solution)
- MTBE: 75 mL (assuming each student receives 10 mL of the 1:1 MTBE and PE solution)
- $MgSO_4$: 7.5 g
- $NaHCO_3$: about 24 g (for 300 mL of saturated aqueous solution)

Sample Pre-Lab Questions

1. Draw the arrow pushing mechanism for the conversion of cyclododecanone to cyclododecanone oxime.
2. Describe thin layer chromatography. What is the retention factor, R_f, and how is it calculated?
3. Why do different compounds have different R_f values? In your answer, please define the terms "mobile phase" and "stationary phase". Based on your answer, which compound should have a higher R_f, cyclododecanone oxime or laurolactam?
4. Diagram and label the apparatus used to heat the reaction mixture in both procedures. Hint—the apparatus consists of the round bottom flask, reflux condenser, and heating mantle. As well, diagram and label the proper use of a Buchner funnel.
5. The final product, laurolactam, is widely used to synthesize polyamide-12. What is the common name for polyamide-12 and what are some of its uses?

Answers to Sample Pre-Lab Questions

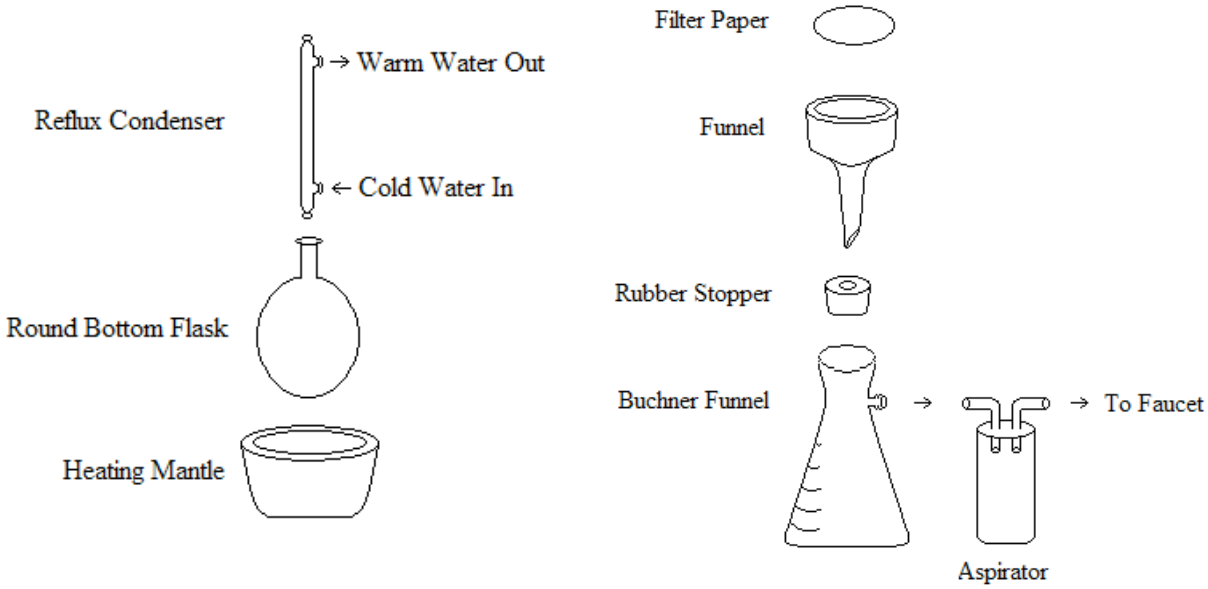
1.



2. In thin layer chromatography (TLC), a small amount of a mixture is "spotted" onto a baseline drawn on the chromatography plate. When the TLC plate is placed in the solvent, the solvent begins to travel up the length of the plate due to capillary motion. As the solvent travels, it carries along the material spotted on the baseline. The retention factor for each individual spot is calculated by dividing the distance traveled by the solvent by the distance traveled by the product spot.

3. The retention factor, R_f, is a measurement of the interactions of the component with the mobile phase (the solvent) and the stationary phase (the surface of the TLC plate). As the polarity of the component increases, so does the strength of the interaction between the component and the stationary phase. The strength of this interaction directly determines the distance the component moves. For example, a highly polar molecule will have a strong interaction with the stationary phase. As the mobile phase travels up the TLC plate, the strong interactions with the stationary phase prevent the component from moving along with the solvent. So, as the polarity of the component increases, the R_f value will decrease. As the lactam is more polar than the oxime, the lactam will have a smaller R_f value than the oxime.

4.



5. Polyamide-12 is more commonly referred to as Nylon-12. The term polyamide indicates that the compound is a polymer of molecules joined by peptide bonds, which is a bond formed by the condensation of a carbonyl group and an amino group. Nylons are used for a variety of applications, from clothing and ropes to screws and other mechanical parts.

CAS Registry Numbers: cyclododecanone, 830-13-7; hydroxylamine hydrochloride, 5470-11-1; ethanol, 64-17-5; sodium hydroxide, 1310-73-2; cyclododecanone oxime, 946-89-4; cyanuric chloride, 108-77-0; anhydrous zinc chloride, 7646-85-7; acetonitrile, 75-05-8; sodium bicarbonate, 144-55-8; ethyl acetate, 141-78-6; anhydrous magnesium sulfate, 7487-88-9; laurolactam, 947-04-6.

References:

1. Furuya, Y.; Ishihara, K.; Yamamoto, H. *J. Am. Chem. Soc.* **2005**, *127*, 11240.
2. Shriner, R. L., R. C. Fuson, and D. Y. Curtin. *The Systematic Identification of Organic Compounds: A Laboratory Manual, Fifth Edition*; Wiley: New York, **1948**.
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4. Zakharkin, L.; Guseva, V. *Russ. Chem. Rev.* **1978**, *47*, 955.
5. Olah, G. A.; Fung, A. P. *Synthesis* **1979**, *7*, 538.

Oxime
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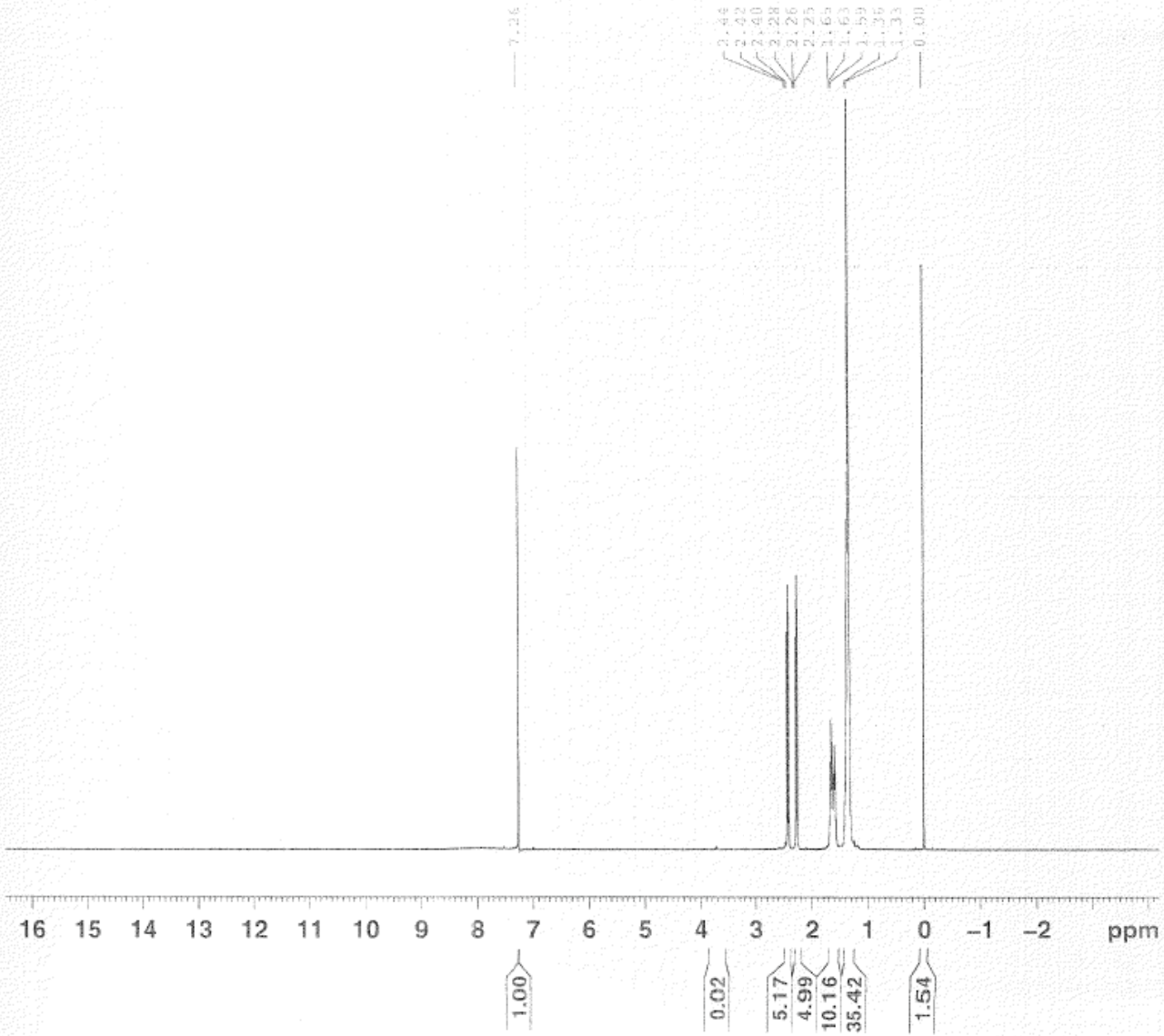

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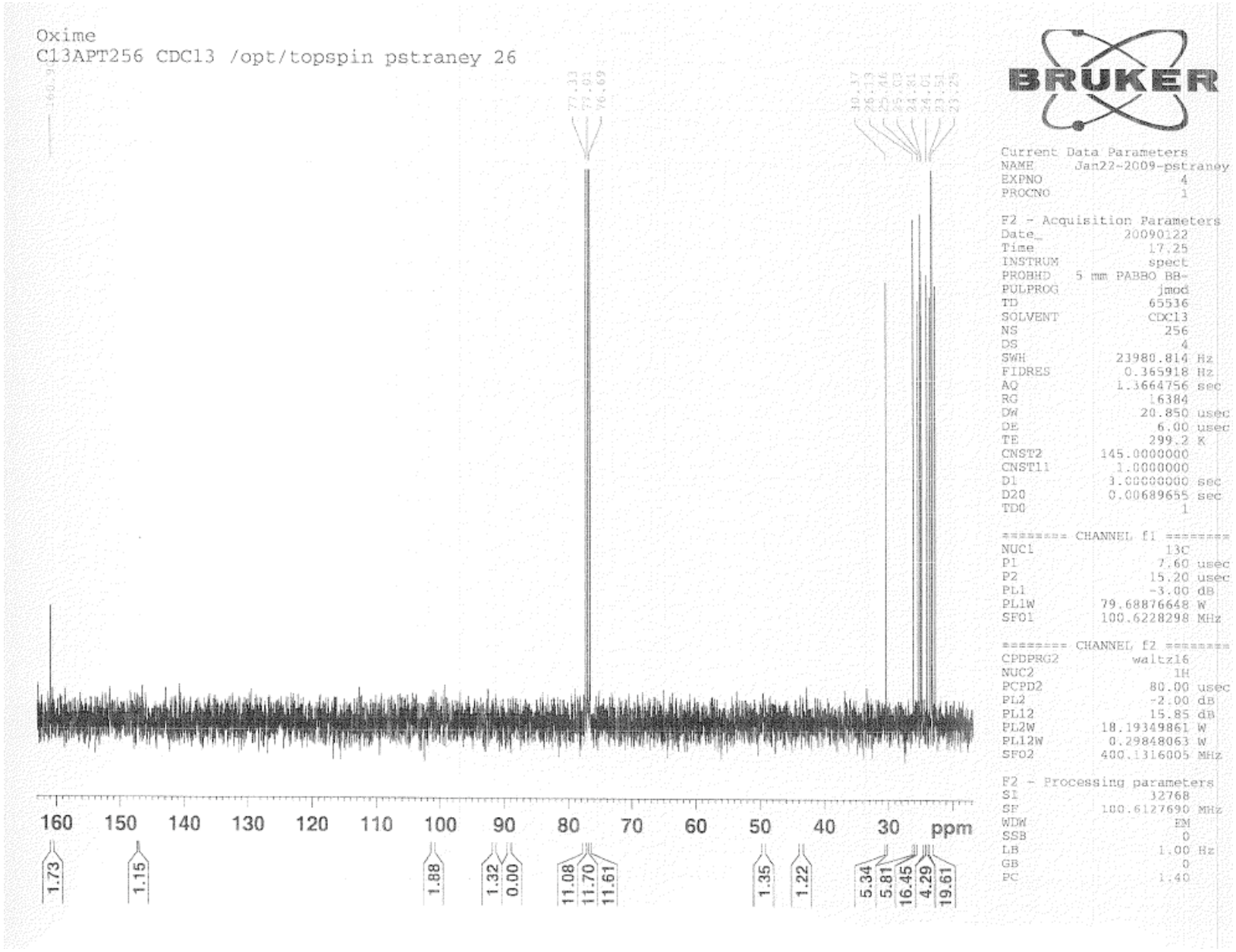
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Laurolactam
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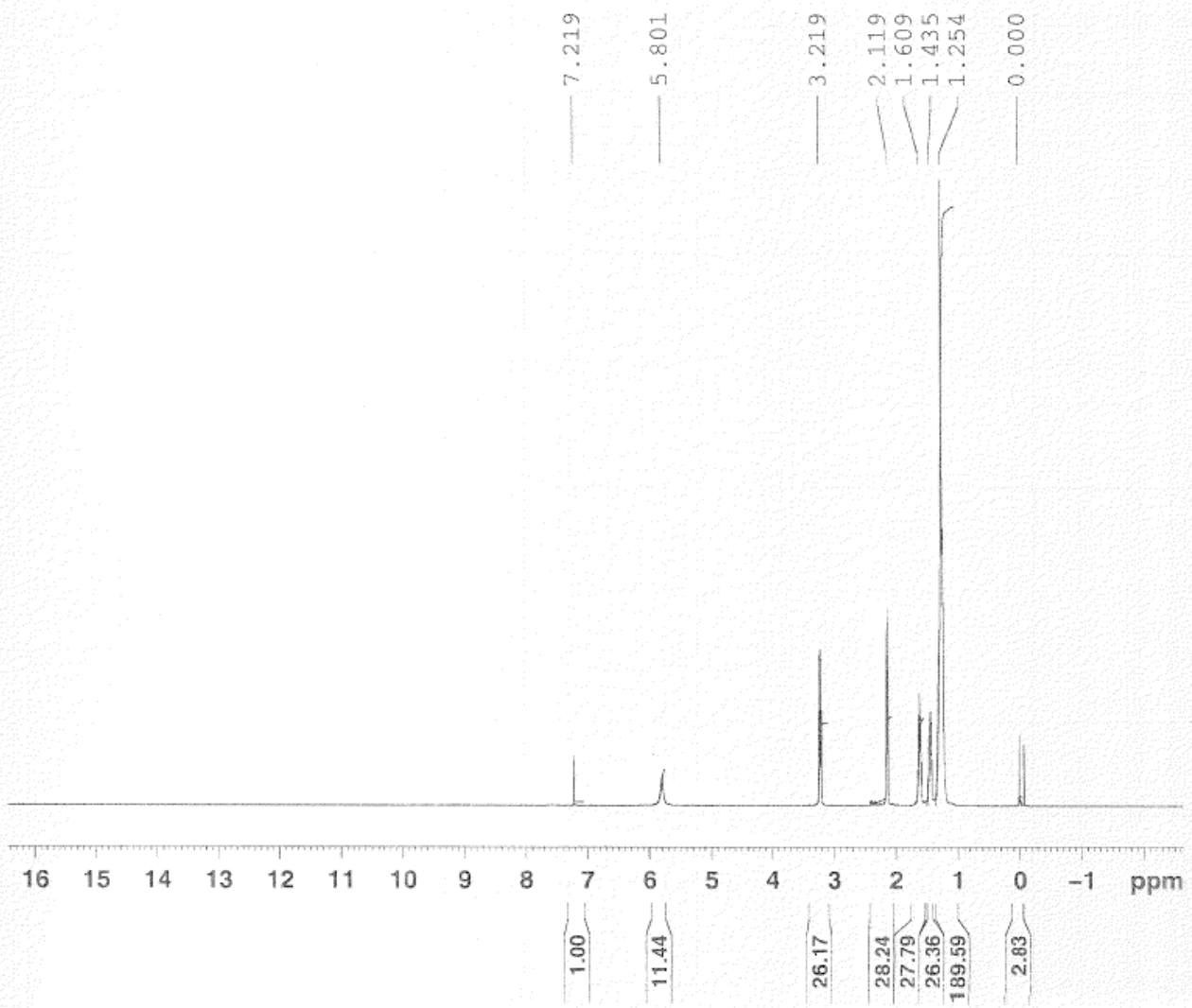

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Laurolactam
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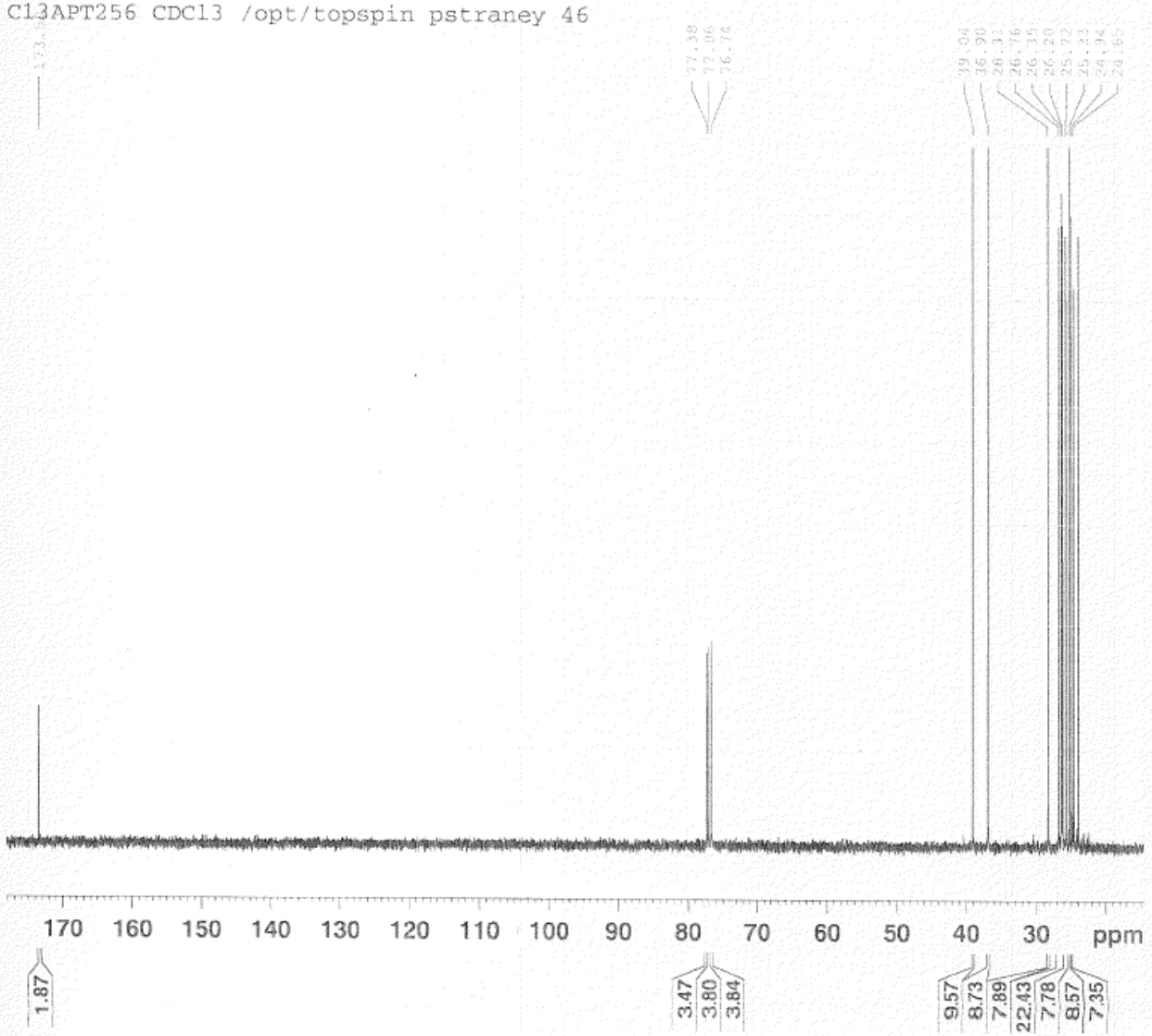

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