**Supplementary information**

# Possibility of a non-amino acid pathway in the biosynthesis of marine-derived oxazoles

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## General Remarks

$^1$H and $^{13}$C NMR spectra were recorded on a JEOL JNM-EX270 or a JEOL JNM-A400 specrometer with $CDCl_3$ as a solvent.

## General synthetic procedures for oxazoles

1) 2-dimethoxymethyl-cyclododecanone **1**:

To a solution of cyclododecanone (5.00g, 27.4 mmol) and trimethylorthoformate (6.00 mL, 54.8 mmol) in dichloromethane (28 mL) was added slowly $BF_3$ etherate (7.00 mL, 55.2 mmol) at –78°C. The solution was stirred for 30 min. *N, N*-diisopropyl ethylamine (14.3 mL, 82.1 mmol) was added, and the reaction mixture was further stirred for 90 min at the same temperature. The reaction was quenched by addition of sat. $NH_4Cl$aq. (50 mL), and the resulting mixture was extracted with dichloromethane. The extract was washed with brine, dried, and concentrated to dryness. Chromatography of the residue (silicagel, hexane-ether) gave 2-dimethoxymethyl-cyclododecanone **1** (7.03 g, quant.) as a pale yellow oil.

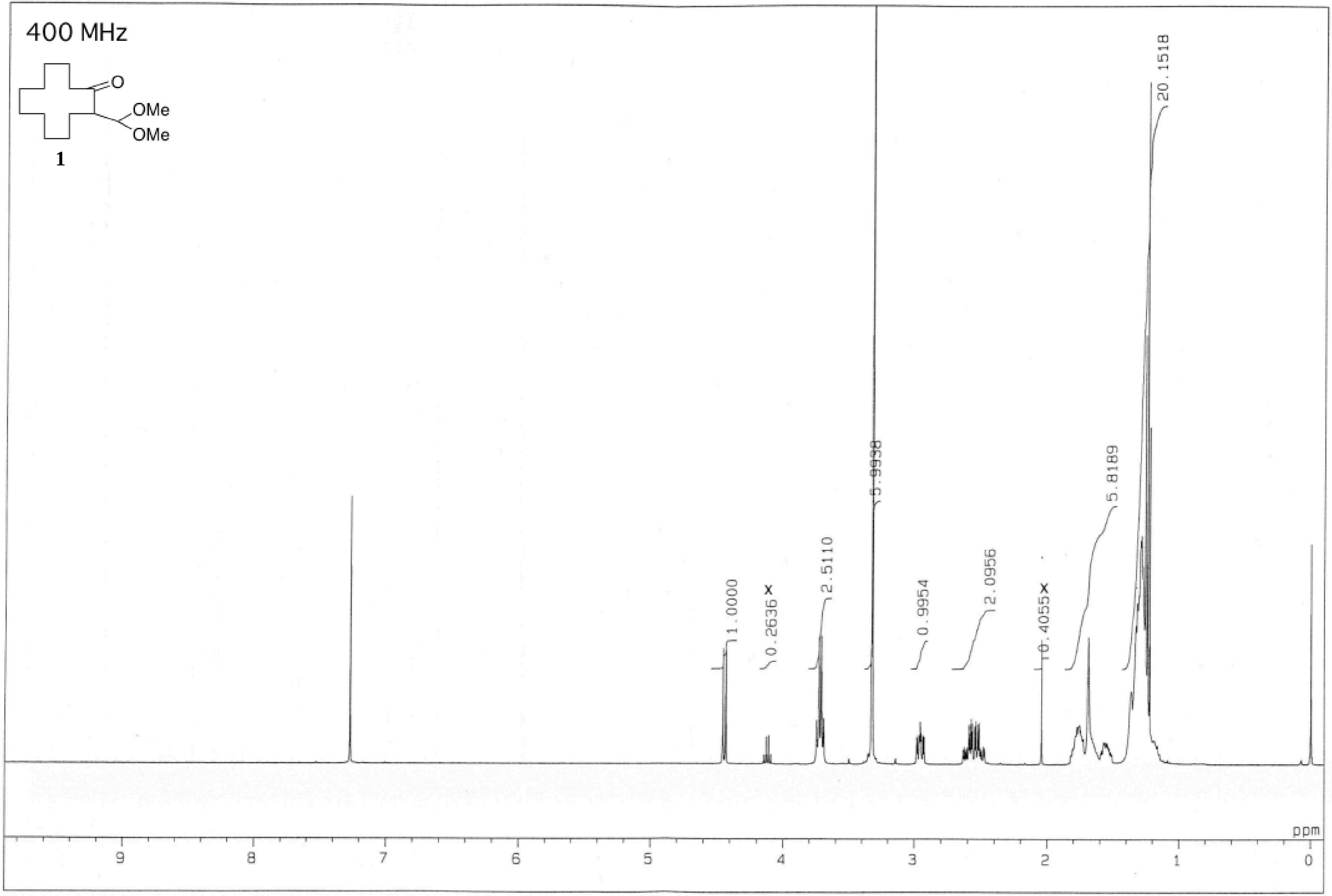
2) Oxime formation and subsequent Beckmann rearrangement to oxazole **3** (Method A)

A solution of **1** (130 mg, 507 μmol) and $HONH_2 \cdot HCl$ (70 mg, 1.01 mmol) in pyridine (1.0 mL, 12.4 mmol) was stirred at 50°C for 8 hr. The reaction mixture was diluted with ether (20 mL), and washed with the sat. $NH_4Cl$aq. (50 mL). The organic phase was washed with brine, dried, and concentrated to dryness. Chromatography of the residue (silicagel, hexane-ether) gave ketoxme **2** (112 mg, 81%) as a pale yellow solid.

A solution of ketoxime **2** (32.8 mg, 121 μmol) and polyphosphoric acid (100 mg) in toluene (3 mL) was heated under reflux conditions for 8 hr. The reaction was quenched by addition of sat. $NaHCO_3$aq. (10 mL), and the resulting mixture was extracted with ether (20 mL). The organic phase was washed with brine, dried, and concentrated to dryness. Chromatography of the residue (silicagel, hexane-ether) gave oxazole **3** (25.1 mg, quant.) as a pale yellow solid.

3) One-pot oxazole formation from ketone **1** (Method B)

A solution of 2-dimethoxymethyl-cyclododecanone (**1**, 100 mg, 390 μmol) and $HONH_2 \cdot HCl$ (54.0 mg, 777 μmol) in toluene (2 mL) was heated under reflux conditions for 24 hr. Polyphosphoric acid (100 mg) was then added to the reaction mixture, and stirred further at the same temperature for 4 hr. The reaction was quenched by addition of sat. $NaHCO_3$aq. (5 mL), and the resulting mixture was extracted with ether (5 mL). The organic phase was washed with brine, dried, and concentrated to dryness. Chromatography of the residue (silicagel, hexane-ether) gave oxazole **3** (37.1 mg,46%) as a pale yellow solid.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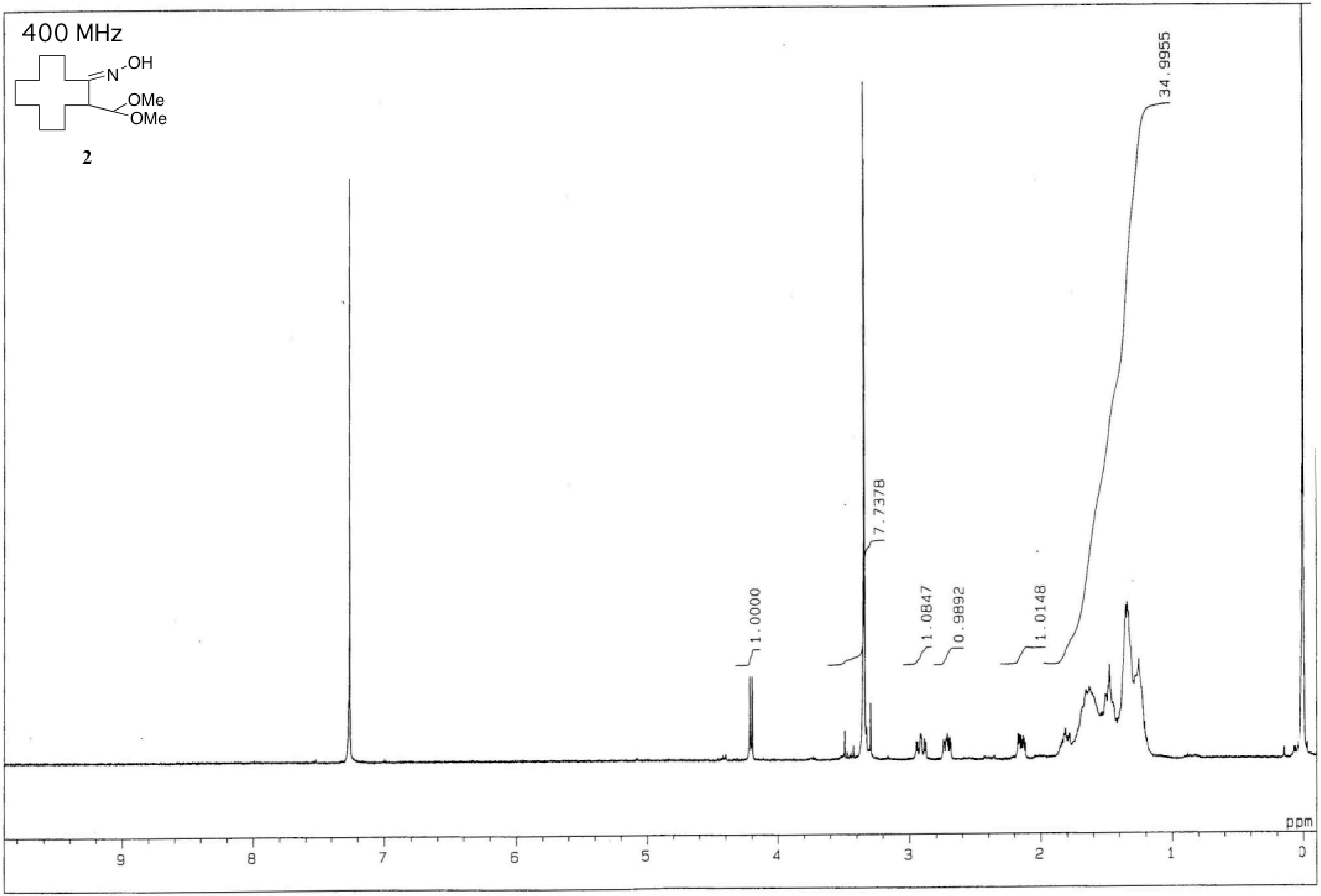
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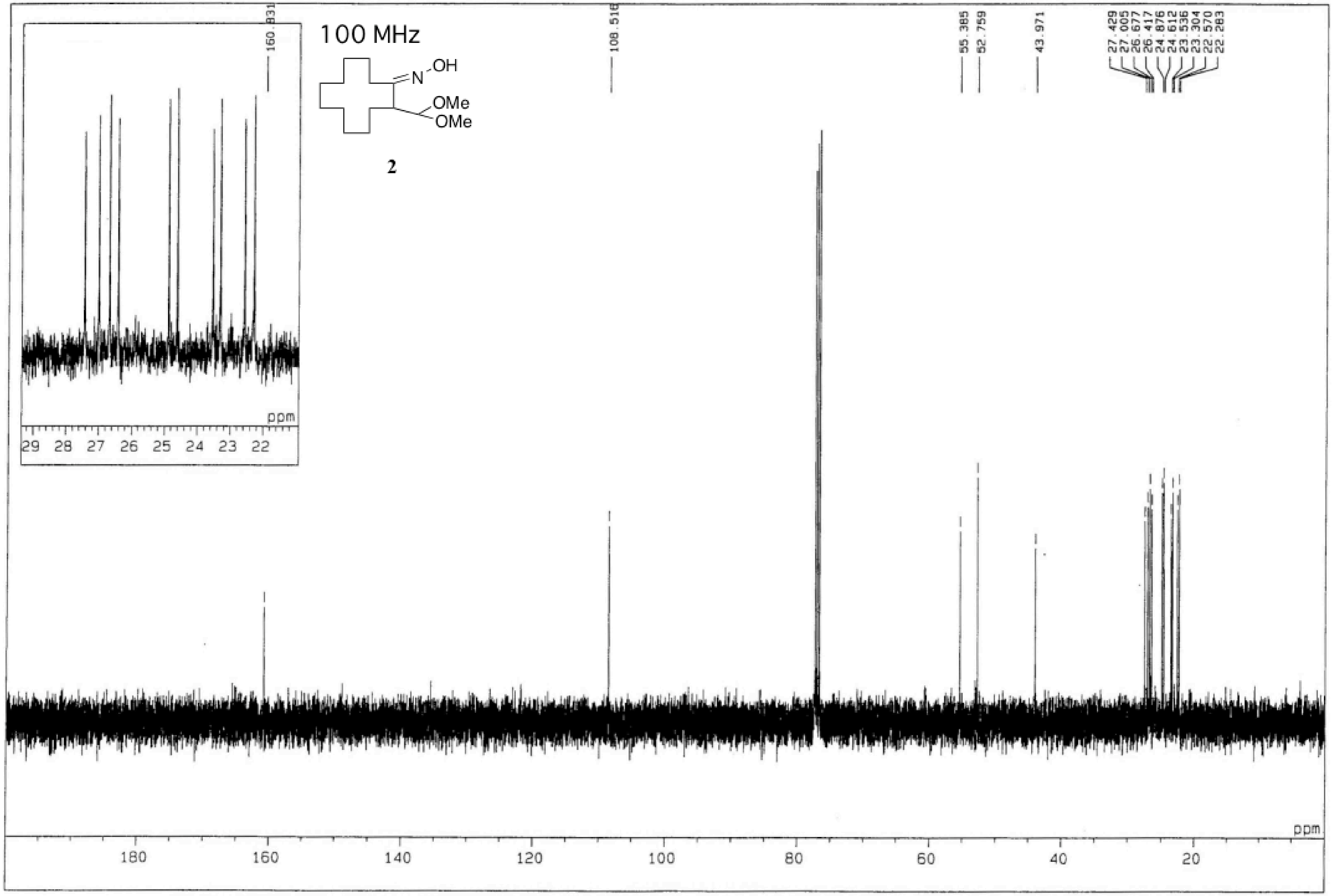
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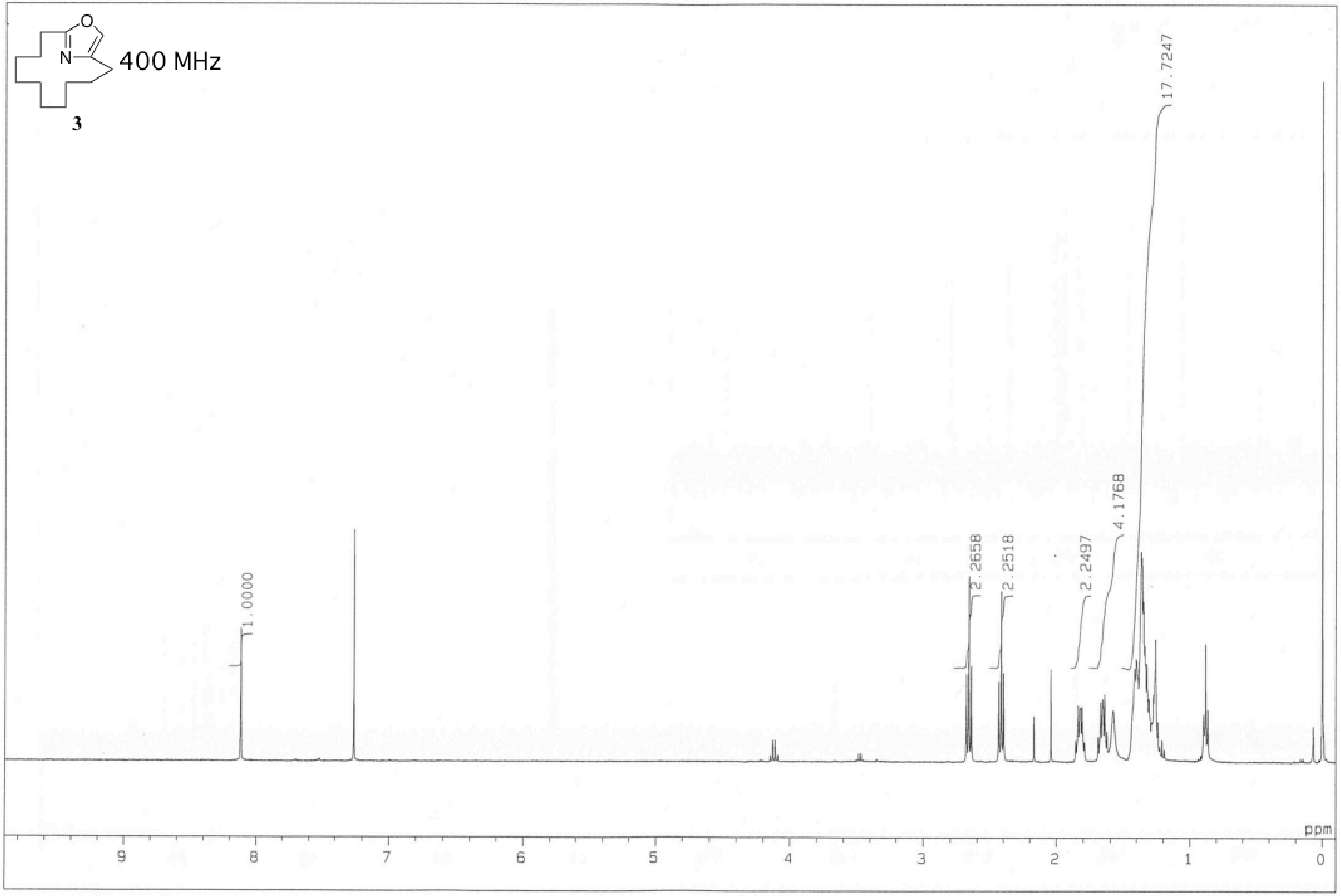
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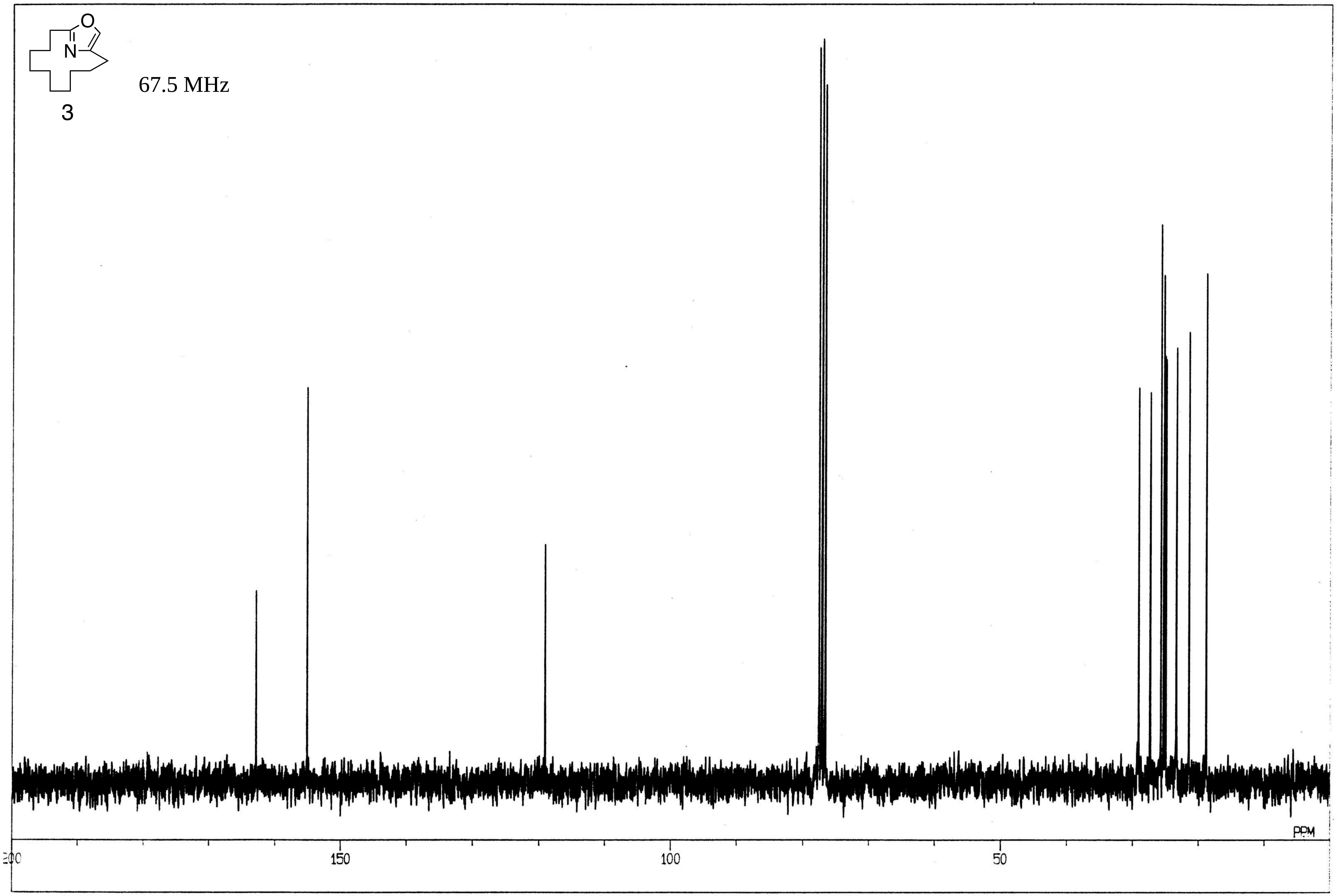
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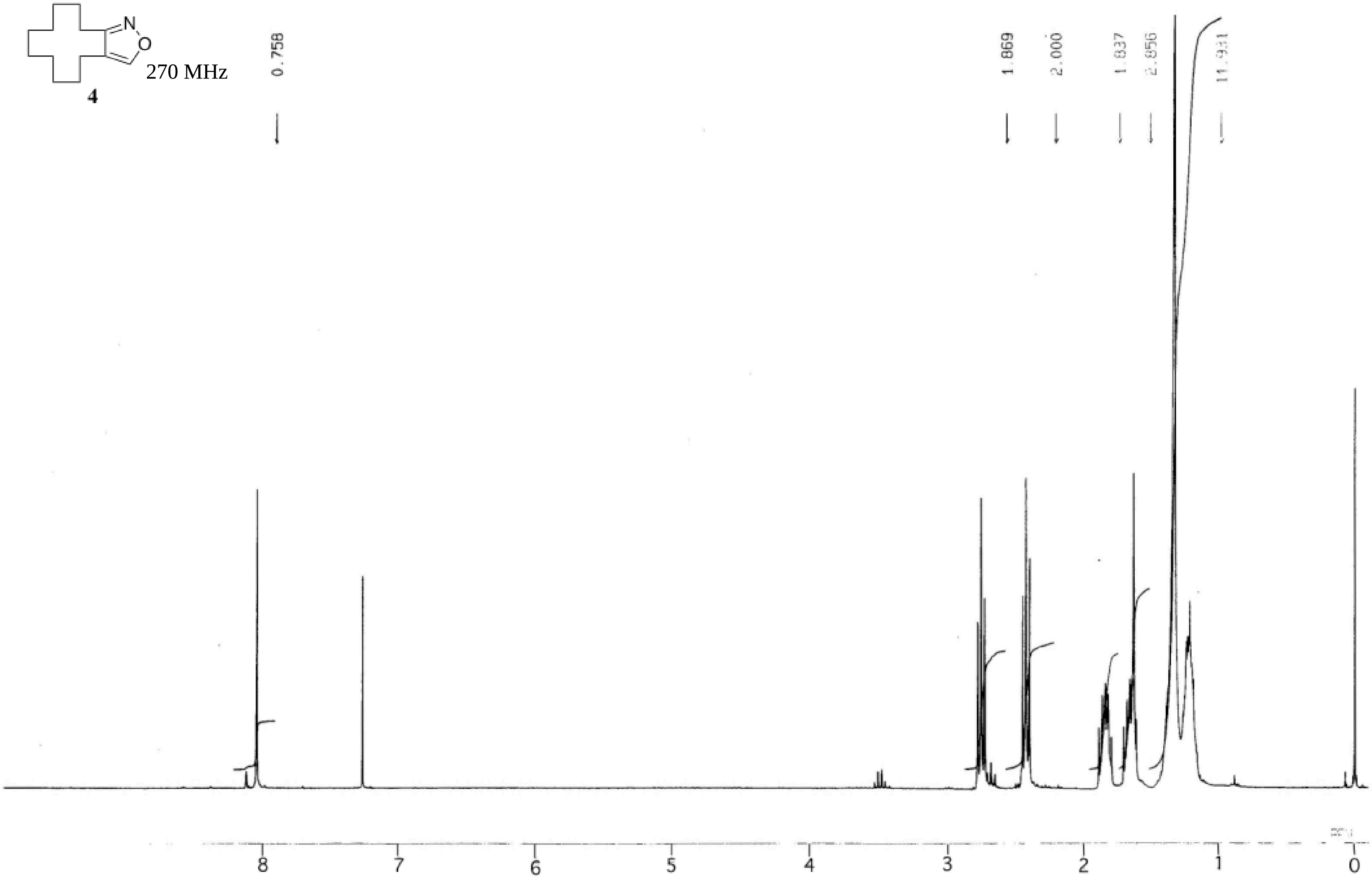
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