

Microwave Assisted Paal-Knorr Reaction. A Rapid Approach to Substituted Pyrroles and Furans

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Supplementary material.

Pag	2	General procedures for compounds 4 , 14 and 10
	3	¹ H NMR 4
	4	¹ H NMR 14
	5	¹³ C NMR 14
	6	¹ H NMR 18
	7	¹ H NMR 19
	8	¹³ C NMR 19
	9	¹ H NMR 20
	10	¹ H NMR 21
	11	¹³ C NMR 21
	12	¹ H NMR 22
	13	¹ H NMR 10

Methyl 2-(1-oxo-1-phenyl-methyl)-5,5-dimethyl-4-oxo-hexanoate (4). General procedure.

Diethyl zinc (30 mL of a 1.0 M solution in hexane, 30 mmol) was dissolved into dry dichloromethane (60 mL) under nitrogen and the mixture cooled to 0°C. Diiodo methane (2,4 mL, 30 mmol) was slowly added and the mixture stirred for 10 min. After the formation of a white precipitate, methyl 4,4 dimethyl-3-oxopentanoate **1** (1,2 mL, 7.3 mmol) was added and the reaction was stirred for 30 min. Benzaldehyde (previously distilled under vacuum and collected over molecular sieves) (0.78 mL, 7,68 mmol) was added and the mixture stirred at 0°C for 1 h. Silica gel (20.0 g) was added and the mixture stirred at room temperature for additional 30 min. The mixture was filtered under vacuum and the solvent evaporated. The crude (2.26 g) was dissolved in dry dichloromethane, PCC (3.3 g, 15.3 mmol) was added and the mixture stirred at room temperature until TLC analysis (eluent hexane: AcOEt 5: 1) showed disappearance of the starting material. Eventually, additional PCC could be added. The mixture was passed through a short path of silica gel and eluted with dichloromethane. The solvent was collected and evaporated under vacuum to give product **4** (1,9 g, 90% yield). ¹H NMR spectrum enclosed.

Methyl 1-benzyl-5-tert-butyl-2-phenyl-1H-pyrrole-3-carboxylate. 14.

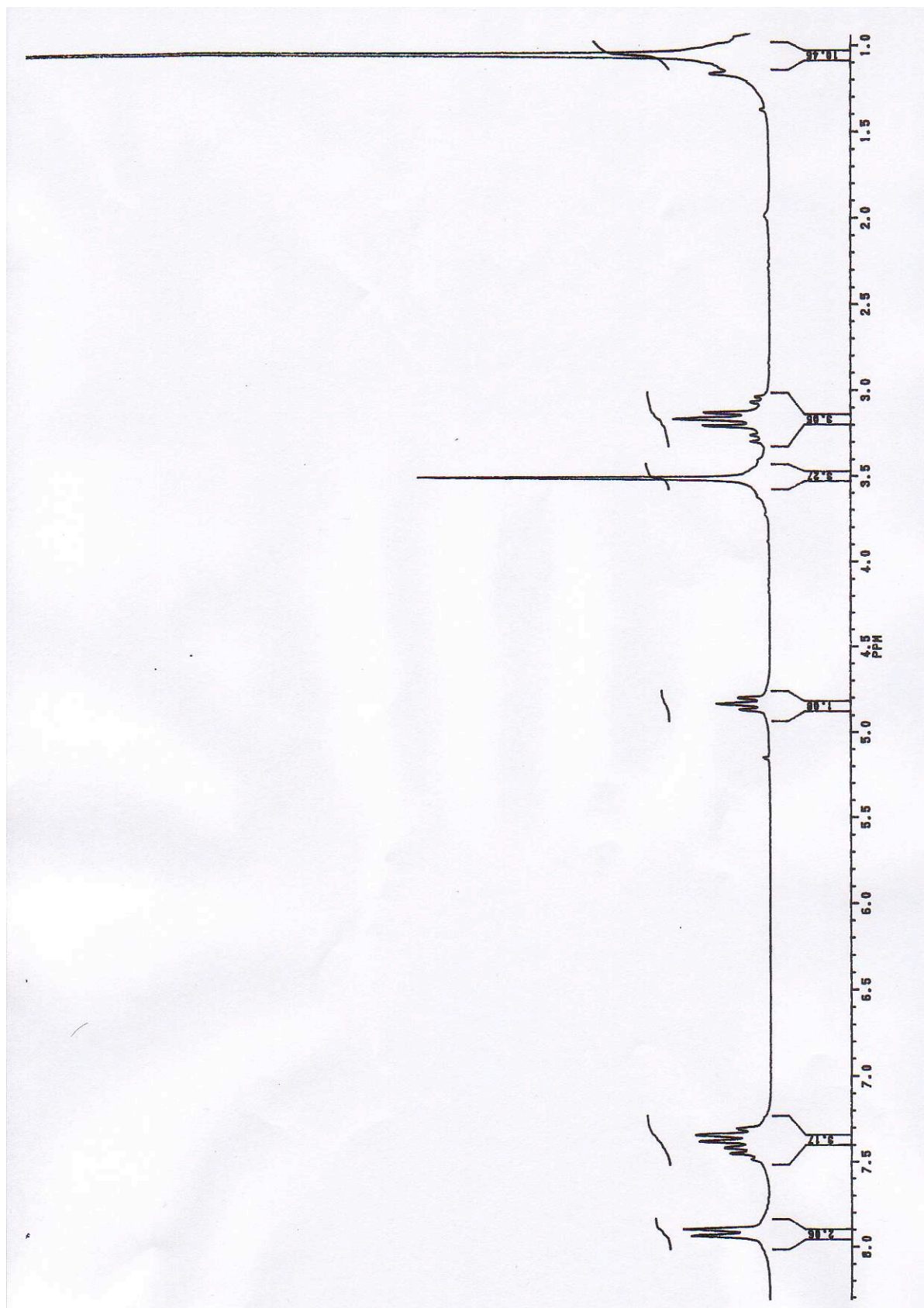
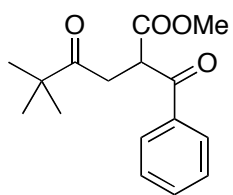
Product **4** (1g, 3,44 mmol) was dissolved into acetic acid (3 mL) into a 50 mL round-bottom flask equipped with a stir bar and a reflux condenser. Benzyl amine (1.84 g, 17.2 mmol) was added and the flask inserted into the cavity of a Discovery Microwave System apparatus (from CEM) and heated at 150 W for 12 min (internal temperature 170°C).

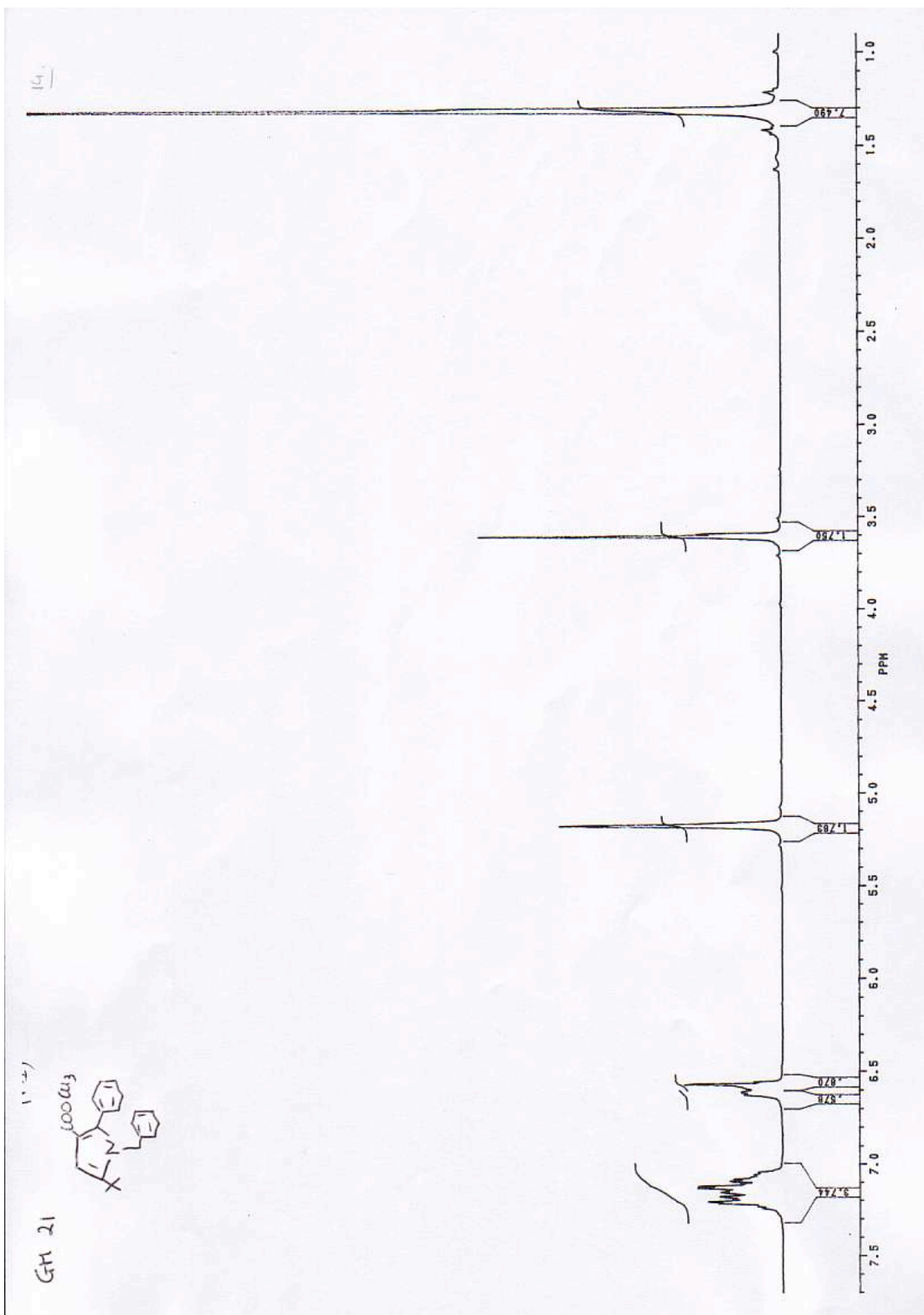
The mixture was diluted with AcOEt and the solvent washed several times with a saturated solution of NaHCO₃. The organic layer was dried over anhydrous Na₂SO₄ and the solvent evaporated. The ¹H NMR spectrum of the crude showed the presence of compound **14** together with benzylamine acetate. The required pyrrole was purified by flash chromatography (eluent Hexane: AcOEt 8: 1, R_f = 0.37) that gave product **14** (0.87 g, 70% yield). ¹H and ¹³C NMR spectra are enclosed.

Methyl 5-tert-butyl-2-(2-phenylethyl)furan-3-carboxylate. 12

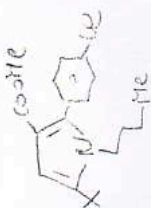
Product **5** (0.5 g, 1,64 mmol) was dissolved into EtOH (2 mL) into a 50 mL round-bottom flask equipped with a stir bar and a reflux condenser. HCl 0.1 mL of a 37% solution) was added and the flask inserted into the cavity of a Discovery Microwave System apparatus (from CEM) and heated at 150 W for 4 min (internal temperature 100°C).

The mixture was diluted with AcOEt and the solvent washed several times with a saturated solution of NaHCO₃. The organic layer was dried over anhydrous Na₂SO₄ and the solvent evaporated. The ¹H NMR spectrum of the crude showed the presence of pure furan **10** that could be eventually additionally purified by flash chromatography (eluent Hexane: AcOEt 8: 1, R_f = 0.75). Obtained 0.49 g, 95% yield. ¹H NMR spectrum enclosed.

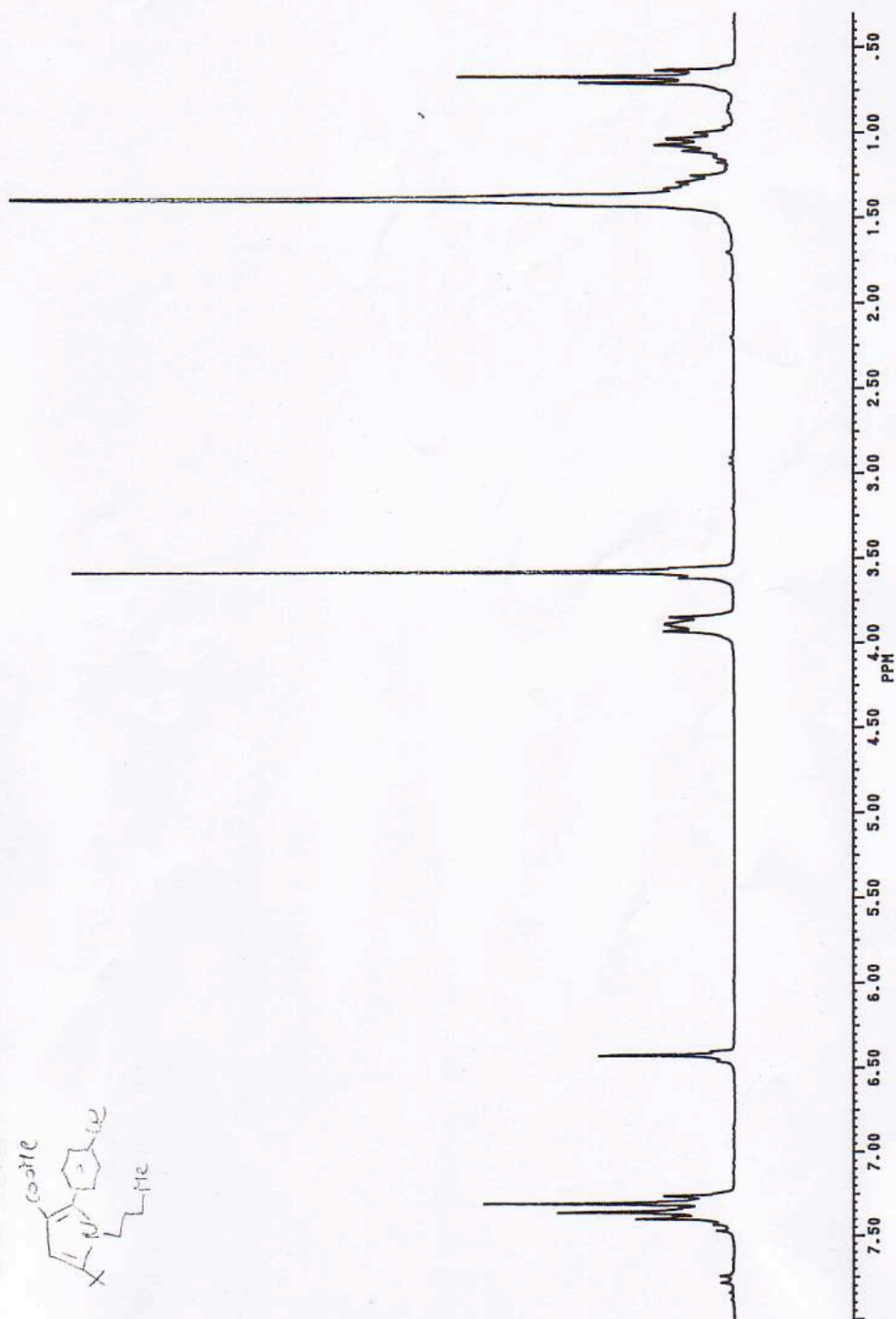


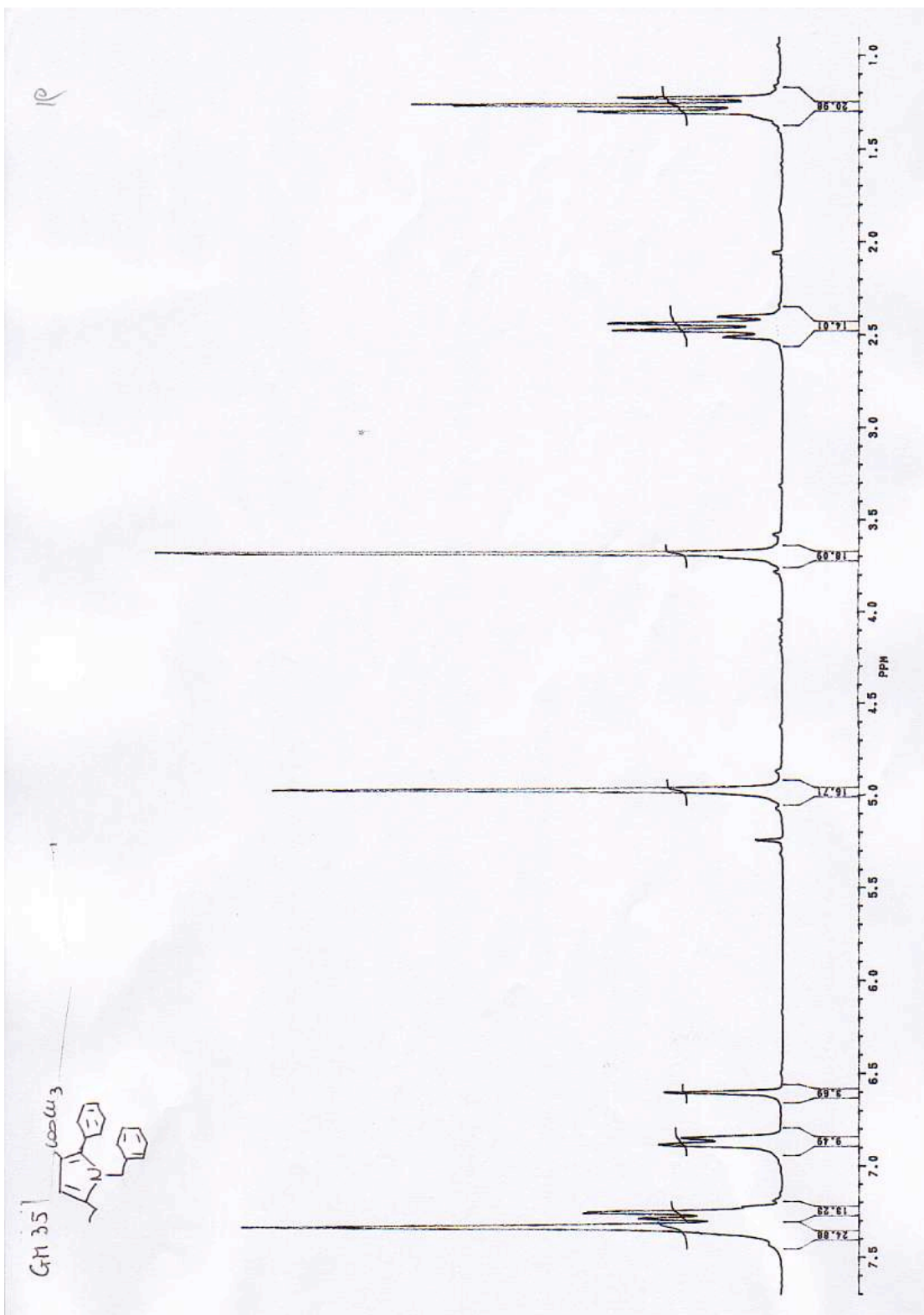


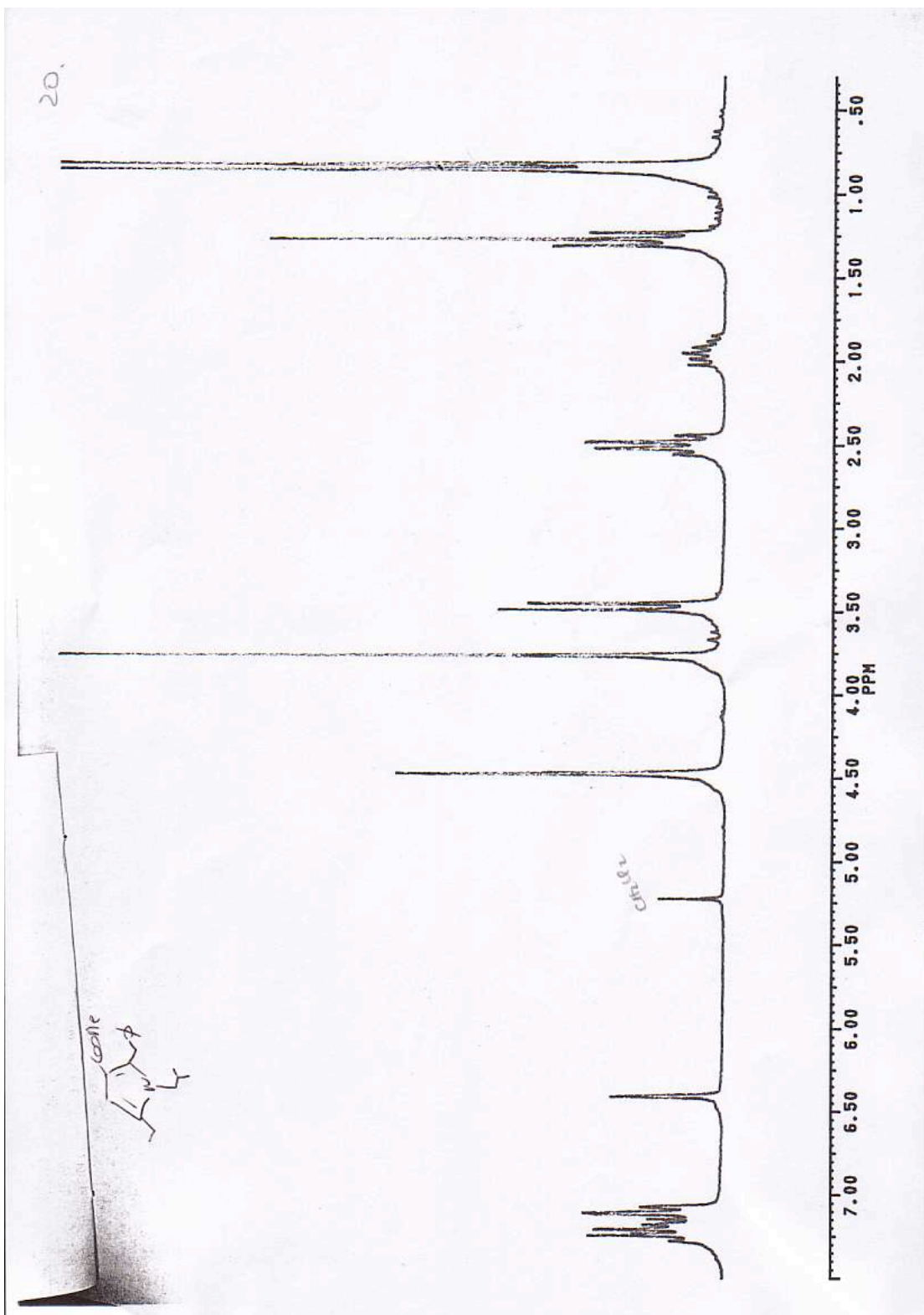
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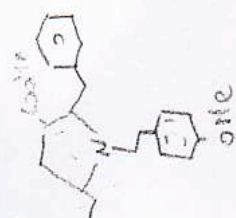
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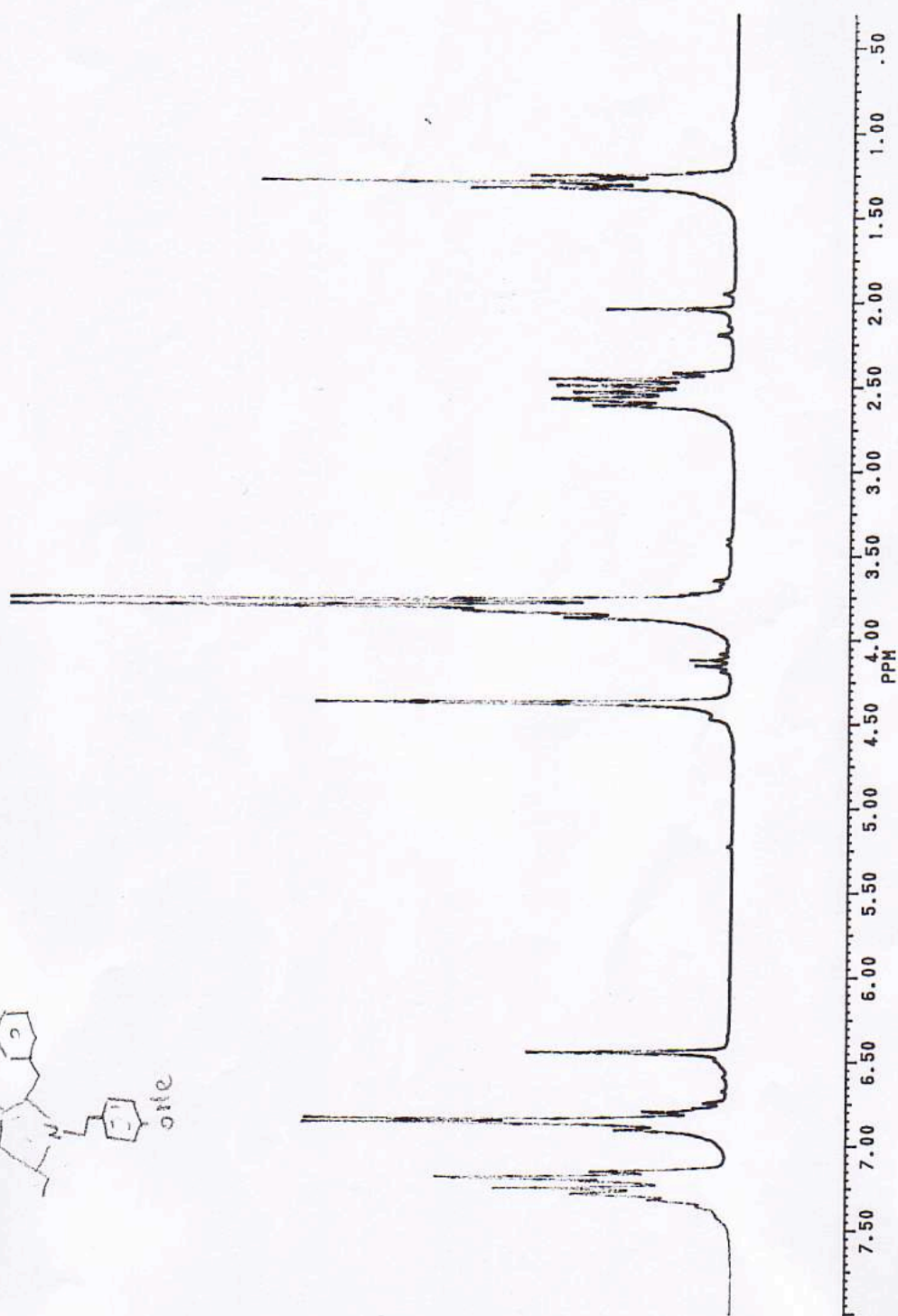


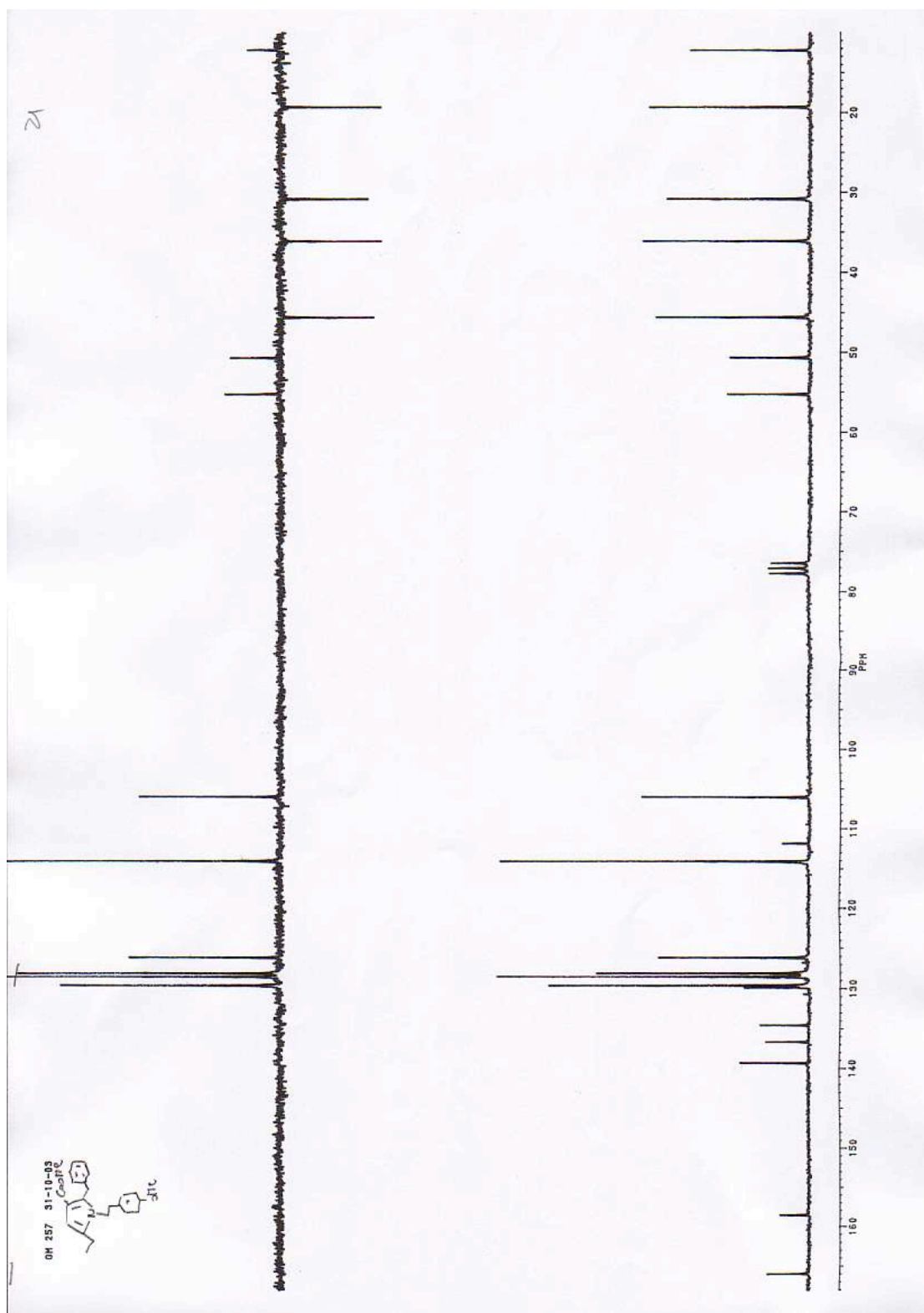


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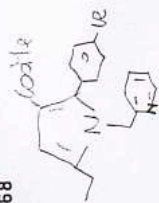


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