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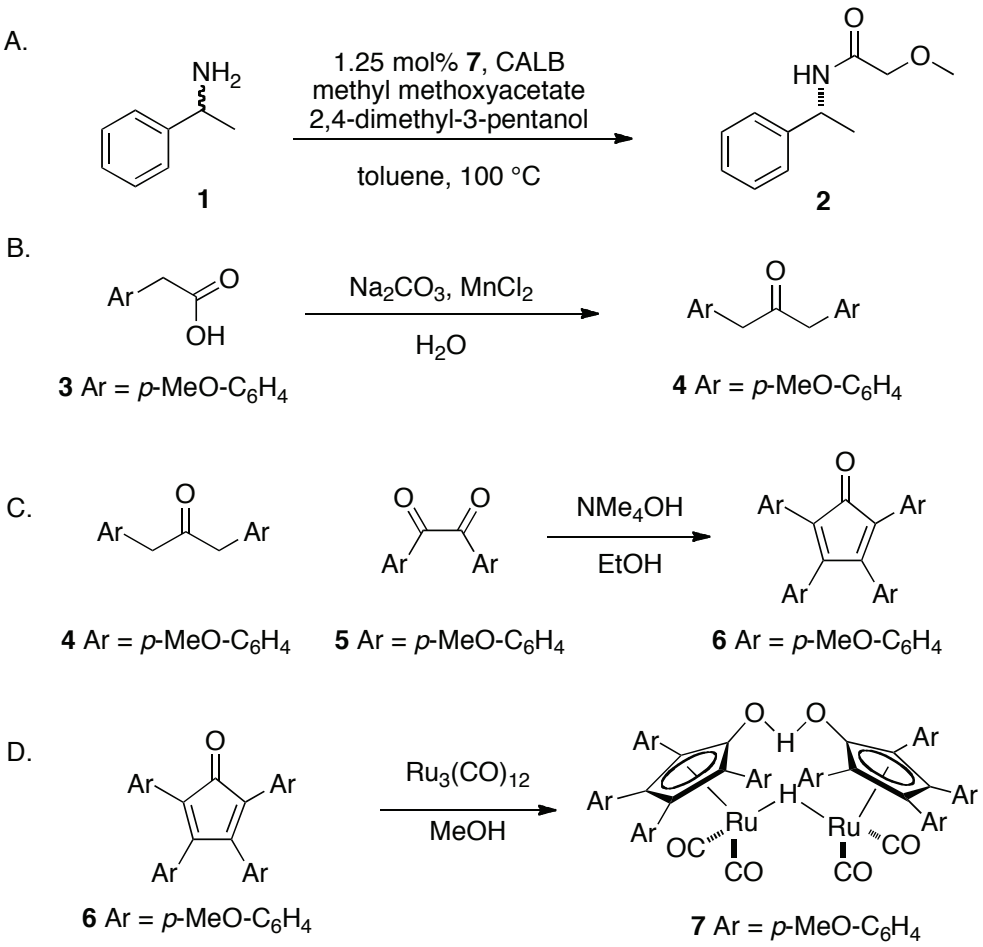
September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.089.0255

Synthesis of (*R*)-2-Methoxy-*N*-(1-Phenylethyl)Acetamide via Dynamic Kinetic Resolution



Submitted by Lisa Kanupp Thalén, Christine Rösch, and Jan-Erling Bäckvall.[1]
Checked by Marc-André Müller and Andreas Pfaltz.

1. Procedure

A. (R)-2-Methoxy-N-(1-phenylethyl)acetamide (**2**). A flame-dried, 1-L two-necked round-bottomed flask is equipped with a two-tap Schlenk adapter connected to a bubbler and an argon/vacuum manifold (Note 1) in the middle neck. The flask is equipped with a stir bar (4.0 cm) and is charged with Novozym 435 (340 mg) (Note 2), Na_2CO_3 (900 mg, 8.49 mmol, 0.19 equiv) (Note 3), and Ru-complex **7** (745 mg, 0.56 mmol, 1.25 mol%) under a constant flow of argon. The other neck is equipped

with a rubber septum and the vessel is evacuated and refilled with argon three times. Under an argon atmosphere, anhydrous toluene (225 mL) (Note 4) is added via syringe to afford a brown solution. (±)-1-Phenylethylamine (**1**, 5.80 mL, 5.45 g, 45.0 mmol, 1.00 equiv) (Note 5), 2,4-dimethyl-3-pentanol (8.00 mL, 6.63 g, 57.1 mmol, 1.27 equiv) (Note 6) and methyl methoxyacetate (3.40 mL, 3.57 g, 33.8 mmol, 0.75 equiv) (Note 7) are subsequently added via syringe. The septum is then changed to a glass stopper equipped with a teflon ring (Note 8) under constant argon flow. The glass stopper is secured with a metal clamp, the reaction mixture is stirred vigorously and the reaction mixture is heated to 100 °C. After the reaction mixture reaches 100 °C the two taps are closed (Notes 9 and 10). After 24 h the tap connected to the bubble counter is opened to release pressure. The second tap connected to the argon inlet is subsequently opened and the reaction vessel is allowed to cool for 10 min at rt. The adapter is then opened under argon flow, the glass stopper is exchanged for a rubber septa, and methyl methoxyacetate (1.60 mL, 1.68 g, 15.8 mmol, 0.35 equiv) (Note 7) is added via syringe. The septum is removed under an argon flow and Novozym 435 (110 mg) (Note 1) is quickly added. The flask is subsequently closed with a glass stopper secured with a metal clamp. The reaction mixture is heated up to 100 °C and the two taps are closed after reaching 100 °C. After a reaction time of 72 h, the reaction is cooled to rt, the solids are removed by filtration through a sintered glass funnel (poor size 3) (Note 11) and are subsequently washed with dichloromethane (4 × 10 mL) (Note 12). Half of the combined filtrate is transferred to a 250-mL round-bottomed flask and concentrated by rotary evaporation (40 °C, 20 mmHg). The remaining filtrate is also transferred to the same 250-mL round-bottomed flask and concentrated by rotary evaporation (40 °C, 20 mmHg). The crude material is further vacuum dried at rt (10 mmHg) until a solid is obtained (24 h). Purification by Kugelrohr distillation (Note 13) yields (*R*)-2-methoxy-N-(1-phenylethyl)acetamide (**2**) as a colorless solid (6.72–6.89 g, 34.8–35.7 mmol, 77–79%, 97–98% *ee*) (Note 14). Recrystallization from pentane yields (*R*)-2-methoxy-*N*-(1-phenylethyl)acetamide (**2**) as colorless crystals (6.03–6.18 g, 31.2–32.0 mmol, 69–71%, >99% *ee*) (Note 15).

B. 1,3-Bis(4-methoxyphenyl)propan-2-one (**4**).[2] A 250-mL one-necked, round-bottomed flask equipped with a cross-shaped magnetic stir bar (2.5 cm) is charged with 2-(4-methoxyphenyl)acetic acid (8.30 g, 50.0 mmol, 1.00 equiv) (Note 16). The flask is not equipped with a stopper.

Upon addition of water (50 mL) a colorless suspension is obtained. Na_2CO_3 (5.30 g, 50.0 mmol, 1.00 equiv) (Note 17) is added in portions over a period of 5 min while the mixture is stirred vigorously to obtain a colorless solution. After the evolution of gas ceases , a solution of $MnCl_2$ (10.0 g, 50.0 mmol, 1.00 equiv) (Note 18) in water (15 mL) is slowly added over a period of 20 min. A white foam forms during the addition. Subsequently water (50 mL) is added resulting in the formation of a homogenous, white suspension. The reaction mixture is stirred vigorously for 3 h and subsequently filtered through a Büchner funnel. The resulting colorless solid is divided into three portions of an approximately equal amount and each portion is dried at 160 °C under reduced pressure (0.3 mmHg) for 1 h. The brown solid is finely ground using a mortar and pestle. Kugelrohr distillation (225 °C, 0.06 mmHg) affords 1,3-bis(4-methoxyphenyl)propan-2-one as light yellow solid (2.97–3.17 g, 11.0–11.7 mmol, 44–47%) (Note 19).

C. 2,3,4,5-Tetrakis(4-methoxyphenyl)cyclopenta-2,4-dienone (**6**). A 250-mL, one-necked, round-bottomed flask equipped with an oval shaped magnetic stir bar (2.5 cm) is charged with 1,3-bis(4-methoxyphenyl)propan-2-one (2.00 g, 7.40 mmol, 1.00 equiv), 4,4-dimethoxybenzil (2.00 g, 7.40 mmol, 1.00 equiv) (Note 20) and tetramethylammonium hydroxide pentahydrate (4.00 g, 22.1 mmol, 1.00 equiv) (Note 21) is added. Upon addition of ethanol (100 mL) a yellow suspension is obtained. Subsequently, the flask is equipped with a reflux condenser and the mixture is refluxed for 3 h, during which time the suspension's color gradually changes from yellow to orange to black. The black mixture is allowed to cool to rt and is filtered through a sintered glass funnel (pore size 3) The resulting black powder is washed with ethanol until the washing solvent remains colorless (Note 22). Subsequently the solid is washed with pentane (3 × 10 mL). The black solid is dried under reduced pressure (10 mmHg) at rt to afford 2,3,4,5-tetrakis(4-methoxyphenyl)cyclopenta-2,4-dienone as black powder (2.85–3.06 g, 5.62–6.06 mmol, 76–82%) (Note 23).

D. Ruthenium complex {{[2,3,4,5(4-OMe-C_6H_4)$_4$](η^5-C_4CO)}$_2$H}-$Ru_2(CO)_4(\mu$-H) (**7**). A 250-mL oven-dried, two-necked, round-bottomed flask is equipped with a magnetic stir bar (2.5 cm), reflux condenser, a two-tap Schlenk adapter connected to a bubbler and an argon/vacuum manifold (Note 1) in the middle neck, and a rubber septum in the other neck. The apparatus is evacuated and refilled with argon three times. The flask is charged with 2,3,4,5-tetrakis(4-methoxyphenyl)cyclopenta-2,4-dienone (**6**, 1.00 g, 1.98 mmol, 1.00 equiv) and $Ru_3(CO)_{12}$ (428 mg, 0.67 mmol,

0.34 equiv) (Note 24) under a constant argon flow. Methanol (100 mL) (Note 25) is added. Argon is bubbled through the mixture for 5 min via a needle inserted through the septum. The septum is replaced with a glass stopper under a constant flow of argon. The mixture is heated to reflux (Note 26) for 24 h. During this time the color changes from black to mustard yellow. The mixture is cooled to rt and the precipitate is removed by filtration through a sintered glass funnel (pore size 3) with a filter paper. The collected solid is washed with pentane (3 × 10 mL) and subsequently dried under reduced pressure (10 mmHg) at rt to provide ruthenium complex $\{\{[2,3,4,5(4\text{-OMe-}C_6H_4)_4](\eta^5\text{-}C_4CO)\}_2H\}Ru_2(CO)_4(\mu\text{-H})$ (**7**) as a yellow powder (0.77–0.80 g, 581–603 μmol, 59–61%) (Note 27 and 28).

2. Notes

1. A two-tap Schlenk adapter connected to a bubbler and an argon/vacuum manifold is illustrated in Yu, J.; Truc, V.; Riebel, P.; Hierl, E.; Mudryk, B. *Org. Synth.* **2008**, *85*, 64–71.

2. *Candida antarctica* lipase B (CALB) was purchased from Sigma-Aldrich Chemicals Co., Inc. and was used as immobilized and thermostable Novozym 435.

3. Na_2CO_3 (anhydrous, extra pure) was purchased from Acros Organics and dried under reduced pressure (0.06 mmHg) at 120 ºC for 1 h.

4. Toluene absolute, over molecular sieves (H_2O ≤0.005%), ≥99.7% (GC) was obtained from Sigma-Aldrich Chemicals Co., Inc. and used as obtained.

5. (±)-1-Phenylethylamine (99%) was obtained from Sigma-Aldrich Chemicals Co., Inc. and distilled before use.

6. 2,4-Dimethyl-3-pentanol (99%) was obtained from Sigma-Aldrich Chemicals Co., Inc. and was stored over 3 Å molecular sieves. The alcohol is added as a hydrogen donor in the racemization process.[4]

7. Methyl methoxyacetate (99%) was obtained from Sigma-Aldrich Chemicals Co., Inc. and was stored over 3 Å molecular sieves.

8. The submitters used a greased glass stopper.

9. Upon heating the reaction mixture slowly changed from light brown to light yellow.

10. The reaction was stirred with a Heidolph MR 3001 K stirrer at 800 rpm.

11. The reaction vessel is washed with toluene (3 × 20 mL) to remove all of the residual solids.

12. In the submitter's protocol, prior to filtration, the grease is removed from the ground glass joint by wiping the joint with a tissue dampened with pentane.

13. The brown crude residue is then purified by Kugelrohr distillation (0.05 mmHg). Two bulbs are used for collection: one in the oven and one cooled with dry ice. The oven is heated to 40 ºC and after 0.5 h, the bulb cooled with dry ice is exchanged for a clean bulb. The oven is then heated to 135 ºC for 1 h. A white solid is collected in the dry ice cooled bulb. The solid is dissolved with DCM (10 mL) and concentrated under reduced pressure (40 °C, 530 mmHg) to afford (*R*)-2-methoxy-N-(1-phenylethyl)acetamide (**2**).

14. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.54 (d, *J* = 6.9 Hz, 3 H), 3.42 (s, 3 H), 3.89 (d, *J* = 15.0 Hz, 1 H), 3.95 (d, *J* = 15.0 Hz, 1 H), 5.17–5.24 (m, 1 H), 6.77 (br s, 1 H), 7.26–7.31 (m, 1 H), 7.34–7.39 (m, 4 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 22.1, 48.2, 59.3, 72.2, 126.3, 127.6, 143.2, 168.7; IR (ATR, cm^{-1}) 3324, 2975, 1643, 1521, 1448, 1197, 1110, 689; HRMS (ESI-MS) calc. (*m/z*) for $C_{11}H_{16}NO_2$ [M+H$^+$] 194.1176 found 194.1174; Chiral GC-analysis (CP-Chirasil-DEX CB column (25 m Ø x 0.25 mm)): Injector 250 °C; 60 kPa H_2, Program: 100 °C/ 5 min/ 3 °C × min^{-1}/ 155 °C/ 5 min/ 180 °C/ 10 min. t_S = 25.5 min, t_R = 26.3 min.

15. (*R*)-2-Methoxy-*N*-(1-phenylethyl)acetamide (**2**) was added to a round bottomed flask equipped with a stirring bar and pentane (75 mL/ 1.00 g compound) was added. A reflux condenser was connected and the suspension was stirred under reflux until a solution was obtained. Stirring was stopped and the oil bath was removed. The solution was allowed to cool to room temperature and allowed to stand for 14 h. Recrystallization is completed by storage in the freezer (– 25 °C) for 6 h. The crystals were collected by filtration and washed with cold pentane (3 × 10 mL) to afford (*R*)-2-methoxy-N-(1-phenylethyl)acetamide (**2**) as colorless crystals (90% recovery, >99% *ee*). mp 57–58 °C; $[\alpha]^{23}_D$ = +102.4 (c = 1.00, $CHCl_3$).

16. 2-(4-Methoxyphenyl)acetic acid (99%) was obtained from Sigma-Aldrich Chemicals Co., Inc. and used as received.

17. Na_2CO_3 (anhydrous, extra pure) was obtained from Acros Organics and used as received.

18. $MnCl_2$ (tetrahydrate, extra pure) was obtained from Sigma-Aldrich Chemicals Co., Inc. and used as received.

19. mp 83–85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.66 (s, 4 H), 3.80 (s, 6 H), 6.87 (d, *J* = 8.5 Hz, 4 H), 7.08 (d, *J* = 8.4 Hz, 4 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 48.2, 114.4, 126.3, 130.6, 158.8, 206.6; IR (ART): $\tilde{\nu}$/cm^{-1} = 3013, 2974, 2934, 2901, 2841, 2043, 1904, 1699, 1663, 1607, 1580, 1508, 1470, 1456, 1445, 1433, 1319, 1305, 1279, 1242, 1180, 1153, 1107, 1063, 1024, 966, 945, 932, 910, 878,789, 735, 716, 698, 669, 635; HRMS (ESI-MS) calc. (*m/z*) for $C_{17}H_{19}O_3$ [M+H$^+$] 271.1329; found 271.1324.

20. 4,4-Dimethoxybenzil (99%) was obtained from Acros Organics and used as received.

21. Tetramethylammonium hydroxide pentahydrate (97%) was obtained from Sigma-Aldrich Chemicals Co., Inc. and used as received.

22. The solid was rinsed in 10 mL aliquots of EtOH until the wash was colorless.

23. mp 257–260 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.79 (s, 12 H), 6.72 (d, *J* = 8.8 Hz, 4 H), 6.79 (d, *J* = 8.9 Hz, 4 H), 6.86 (d, *J* = 8.8 Hz, 4 H), 7.19 (d, *J* = 8.9 Hz, 4 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 55.4, 113.6, 113.8, 123.9, 124.1, 125.9, 131.3, 131.6, 153.0, 159.0, 159.8, 201.5; IR (ART): $\tilde{\nu}$/cm^{-1} = 3005, 2991, 2961, 2840, 1705, 1599, 1570, 1564, 1502, 1466, 1456, 1443, 1418, 1319, 1285, 1240, 1175, 1153, 1109, 1024, 1009, 960, 839, 810, 773, 694, 636; HRMS (ESI-MS) calc. (*m/z*) for $C_{33}H_{28}O_5$ [M$^+$] 504.1931; found 504.1917.

24. $Ru_3(CO)_{12}$ (99%) was obtained from Strem Chemicals Inc. and used as received.

25. Methanol (99.8%) was obtained from Sigma-Aldrich Chemicals Co., Inc.and used as received.

26. The oil bath is heated to 90 °C.

27. ^{1}H NMR (400 MHz, $CDCl_3$) δ: ¯18.5 (s, 1 H), 3.69 (s, 12 H), 3.78 (s, 12 H), 6.54 (d, *J* = 8.8 Hz, 8 H), 6.57 (d, *J* = 8.8 Hz, 8 H), 6.93 (d, *J* = 8.8 Hz, 8 H), 7.05 (d, *J* = 8.8 Hz, 8 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 55.2, 55.3, 87.7, 102.3, 113.2, 113.2, 122.8, 123.1, 132.5, 133.5, 153.9, 158.4, 201.5, ; IR (ATR, cm^{-1}) = 2958, 2933, 2904, 2832, 2028, 2004,1985, 1961, 1607, 1514, 1291, 1244, 1174, 1028, 824, 808; HRMS (ESI-MS) calc. (*m/z*) for $C_{70}H_{59}O_{14}Ru_2$ [M+H$^+$] 1327.1986; found 1327.1999.

28. The solid was stored in a desiccator under air.

Safety and Waste Disposal Information

All hazardous materials should be handled and disposed of in accordance with "Prudent Practices in the Laboratory"; National Academies Press; Washington, DC, 2011.

3. Discussion

Dynamic kinetic resolution (DKR) of primary amines has sparked a growing amount of interest over the past decade. DKR is an attractive method for the synthesis of chiral amines and combines the well-established and commonly used method of kinetic resolution (KR) with *in situ* racemization of the non-converted substrate. Thus the main drawback of KR (a theoretical maximum of 50% yield) is eliminated.

The first example of DKR of benzylic amines using a transition metal racemization catalyst and a lipase was demonstrated by the Reetz group in 1996.[3] The drawback of this method was the long reaction time of 8 days and the moderate yield.

In 2002, our group reported {{[2,3,4,5(C_6H_4)$_4$](η^5-C_4CO)}$_2$H}-$Ru_2(CO)_4$(μ-H) (**8**) as a highly efficient amine racemization catalyst.[4] This catalyst was reported by Shvo and co-workers[5,6] in 1985 and has since been used in the hydrogenation of unsaturated substrates,[5] transfer hydrogenation of ketones and imines,[7] Oppenauer-type oxidations of alcohols[8,9] and amines,[10-12] and the racemization of alcohols[13,14] and amines.[4] A modified procedure for the synthesis of a tolyl-substituted analogue of **8** ({{[2,5-(C_6H_4)$_2$-3,4-(4-CH_3-C_6H_4)$_2$](η^5-C_4CO)}$_2$H}$Ru_2(CO)_4$(μ-H)) was reported by Casey et. al.[15] In 2005, our group reported **7** (anisyl-substituted analogue of **8**) as a highly selective amine racemization catalyst.[16] Catalyst **7** was combined with *Candida antarctica* lipase B (CALB) and applied in the DKR of benzylic and aliphatic amines to obtain the corresponding amides in high yield and excellent ee.[16-18]

Independent work by the Jacobs-De Vos group identified Pd on alkaline earth supports as a viable racemization catalyst for use in chemoenzymatic DKR.[19,20] They observed that byproduct formation could be minimized by using Pd on alkaline supports instead of Pd/C. The group of Kim and Park later reported the DKR of primary amines combining a Pd nanocatalyst and CALB.[21] However, in both cases the substrate scope is

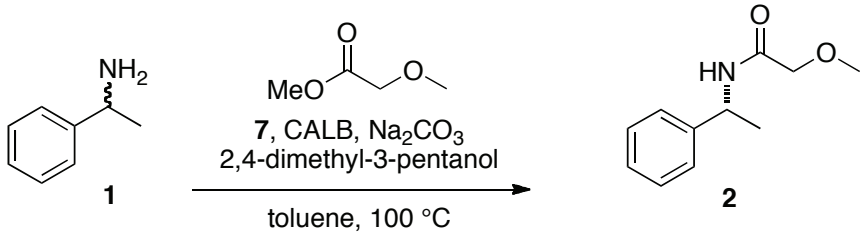
limited to amines that are not susceptible to reduction under hydrogenation conditions.

Additional methods that combine racemization with enzymatic KR in the DKR of amines have been developed.[22-26]

The DKR protocol originally reported by our group utilizes 4 mol% **7**, 40 mg CALB per mmol amine substrate, and isopropyl acetate as the acyl donor.[16] A large excess of isopropyl acetate was used and upon concentrating the reaction mixture during the development of a large scale procedure, it was found that isopropyl acetate was not a suitable acyl donor under the desired conditions.[27] As isopropyl acetate became the primary solvent, a drop in enantiomeric excess was observed. Upon reducing the excess of isopropyl acetate to 1–3 equiv the reaction became sluggish. Therefore, an alternative acyl donor was desirable. Methyl methoxyacteate was chosen as the acyl donor and was added portion wise to avoid uncatalyzed chemical acylation of the substrate that occurs at elevated temperatures when using acyl donors of this type in the DKR of primary amines.[26,27]

For application on gram scale, the catalyst loadings were reduced to 1.25 mol% **7** and 10 mg CALB per mmol amine substrate. As seen in Table 1, a two-portion addition of CALB concurrent with a two-portion addition of methyl methoxyacteate provided amide **2** in the highest yield (83%, Table 1, entry 3).

Table 1. Dynamic kinetic resolution.



Entry	**1** (mmol)	Acyl donor (equiv) 0 h	24 h	48 h	Toluene (mL)	ee (%)	Yield (%)[b]
1	10	0.75	0.35	-	50	98	74
2[c]	45	0.4	0.35	0.35	225	98	68
3[d]	45	0.75	0.35	-	225	98	83

[a] Conditions: **1**, 1.25 mol% of **4**, 100 mg of CALB, 200 mg of Na_2CO_3, acyl donor, 1.25 equiv 2,4-dimethyl-3-pentanol, 100 °C, 72 h; [b] isolated yield; [c] 225 mg of CALB, addition of 113 mg of CALB after 24 and 48 h; [d] 340 mg of CALB, addition of 110 mg of CALB after 24 h.

1. Stockholm University, Department of Organic Chemistry, Arrhenius Laboratory, SE-106 91, Stockholm, Sweden, jeb@organ.su.se. This work was funded by the European Union (EU-project "INTENANT, Integrated Synthesis and Purification of Enantiomers"; NMP2-SL-2008-214129).

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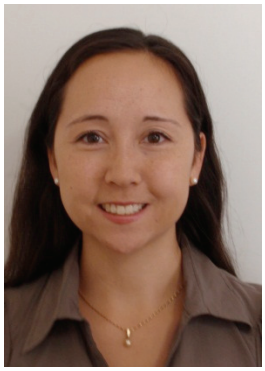
Appendix
Chemical Abstracts Nomenclature; (Registry Number)

Novozym 435, Lipase acrylic resin from *Candida antárctica*; (9001-62-1)
Sodium carbonate; (497-19-8)
(±)- α -Methylbenzylamine; (618-36-0)
2,4-Dimethyl-3-pentanol; (600-36-2)
Methyl methoxyacetate; (6290-49-9)
4-Methoxyphenylacetic acid; (104-01-8)
Manganese(II) chloride tetrahydrate; (13446-34-9)
4,4'-Dimethoxybenzil; (1226-42-2)
Tetramethylammonium hydroxide pentahydrate; (10424-65-4)
(*R*)-2-Methoxy-*N*-(1-phenylethyl)acetamide; (162929-44-4)
Ruthenium carbonyl; (15243-33-1)
1,3-Bis(4-methoxyphenyl)propan-2-one; (29903-09-1)
2,3,4,5-Tetrakis(4-methoxyphenyl)cyclopenta-2,4-dienone; (49764-93-4)
Ruthenium complex {{[2,3,4,5(4-OMe-$C_6H_4)_4$](η^5-C_4CO)}$_2$H}-$Ru_2(CO)_4$(μ -H) **; (**873815-22-6)

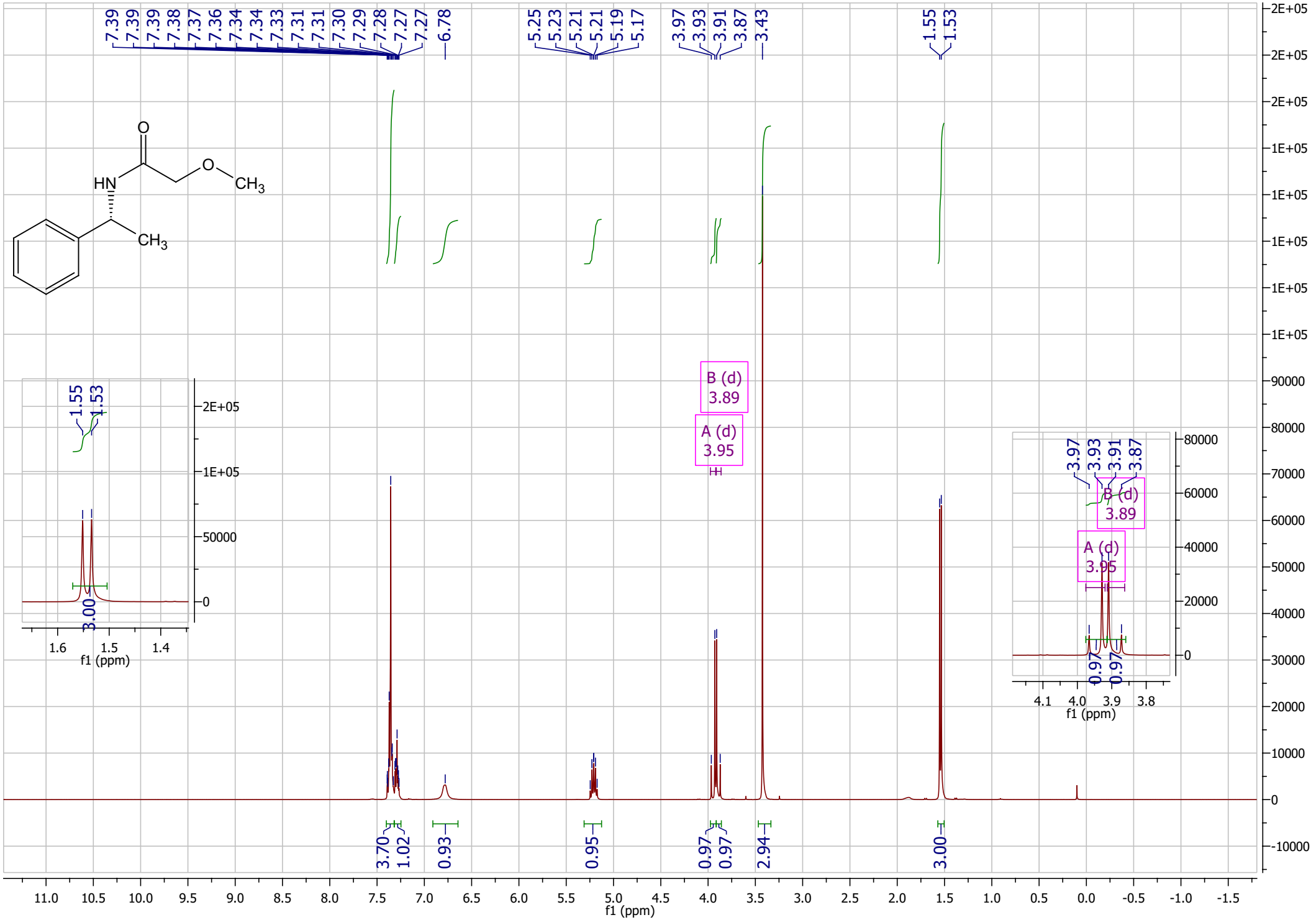
Jan-Erling Bäckvall was born in Malung, Sweden, in 1947. He received his Ph.D. from the Royal Institute of Technology, Stockholm, in 1975 under the guidance of Prof. B. Åkermark. After postdoctoral work (1975-76) with Prof. K. B. Sharpless at Massachusetts Institute of Technology he joined the faculty at the Royal Institute of Technology. He was appointed Professor of Organic Chemistry at Uppsala University in 1986. In 1997 he moved to Stockholm University where he is currently Professor of Organic Chemistry. He is a member of the Royal Swedish Academy of Sciences and the Finnish Academy of Science and Letters. He is also a member of the Nobel Committee for Chemistry. His current research interests include transition metal-catalyzed organic transformations, biomimetic oxidations, and enzyme chemistry.

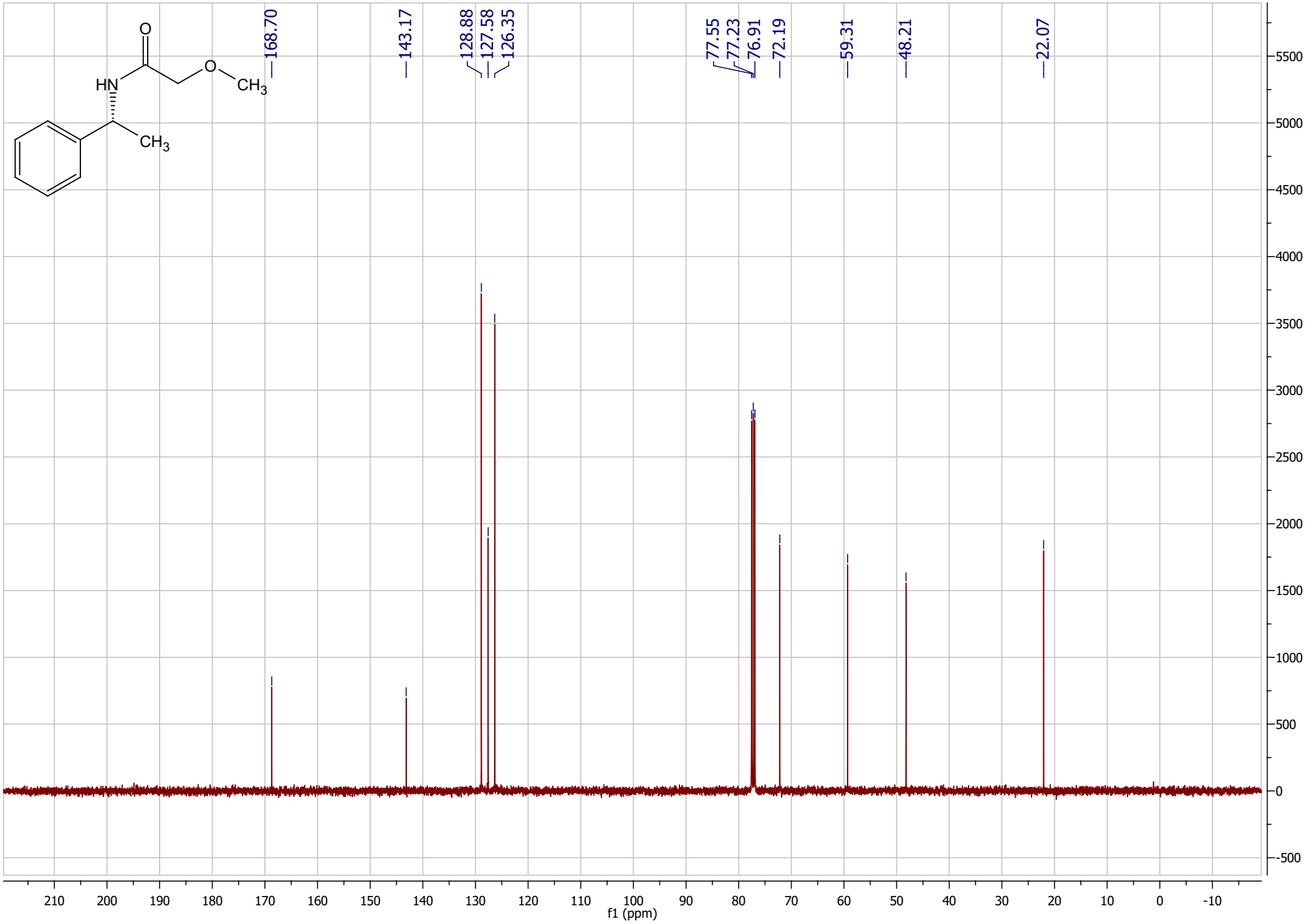


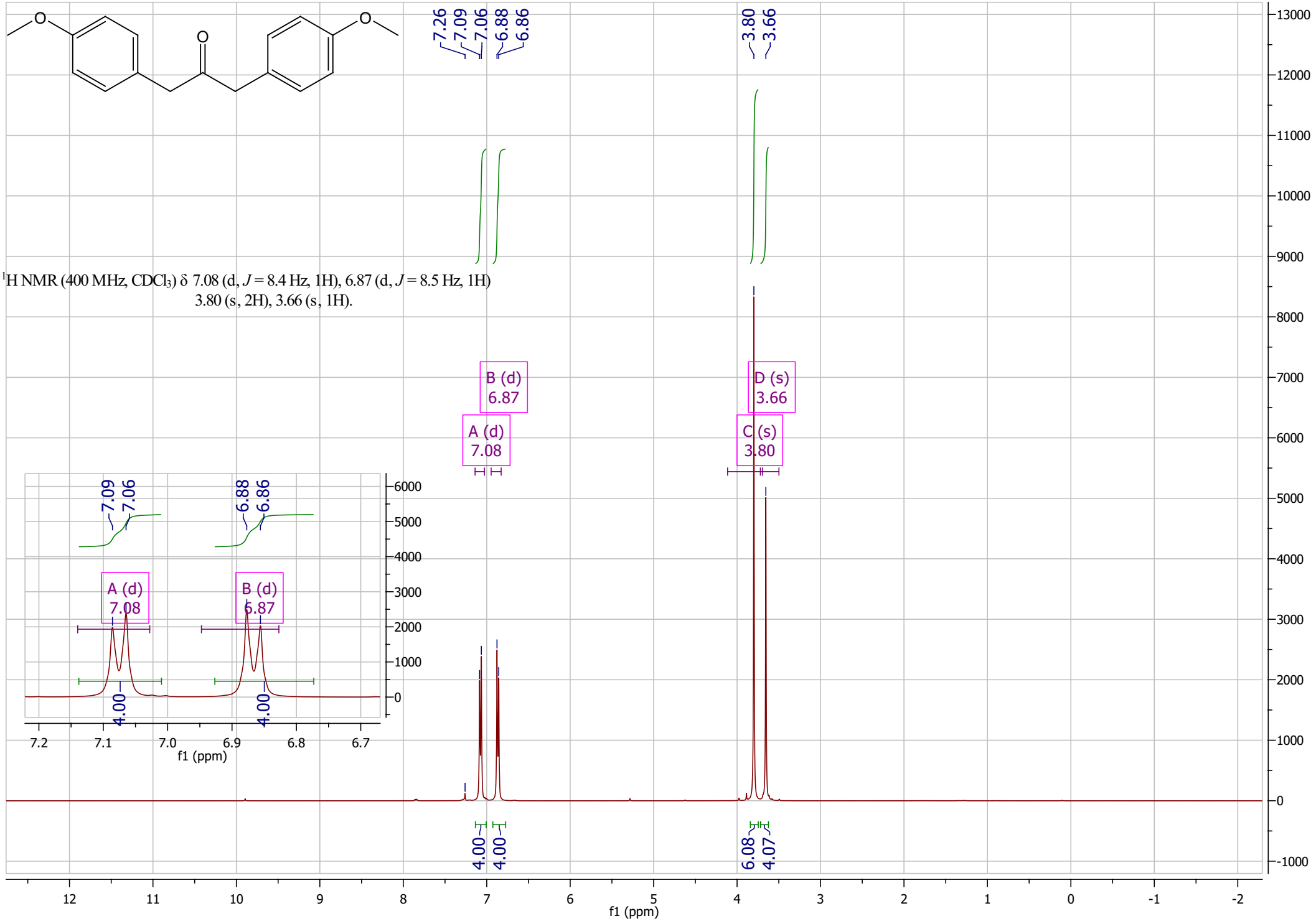
Lisa Kanupp Thalén was born in Asheville, NC, in 1980. She received a B.Sc. from East Carolina University in 2002 and completed a research project in the group of Assoc. Prof. William E. Allen. She then received a M.Sc. from Uppsala University in 2005 while working in the group of Prof. Per I. Arvidsson. After completing her master's degree studies, she joined the group of Prof. Jan-Erling Bäckvall at Stockholm University and completed her doctoral studies in 2010. Her research focused on dynamic kinetic resolution and its application in the synthesis of biologically active small molecules.

Christine Rösch (née Hoben) was born in 1978 in Mainz, Germany. She joined the group of Prof. H. Kunz at Johannes Gutenberg-Universität Mainz in 2002 and obtained her Ph.D. in 2006 while working on carbohydrate-based catalysts for the asymmetric Strecker-reaction. Afterwards she was a postdoctoral scholar in the group of Prof. J.-E. Bäckvall at the University of Stockholm, Sweden and worked on the dynamic kinetic resolution of amines. Since 2007 she has worked for BASF SE in Ludwigshafen, Germany.

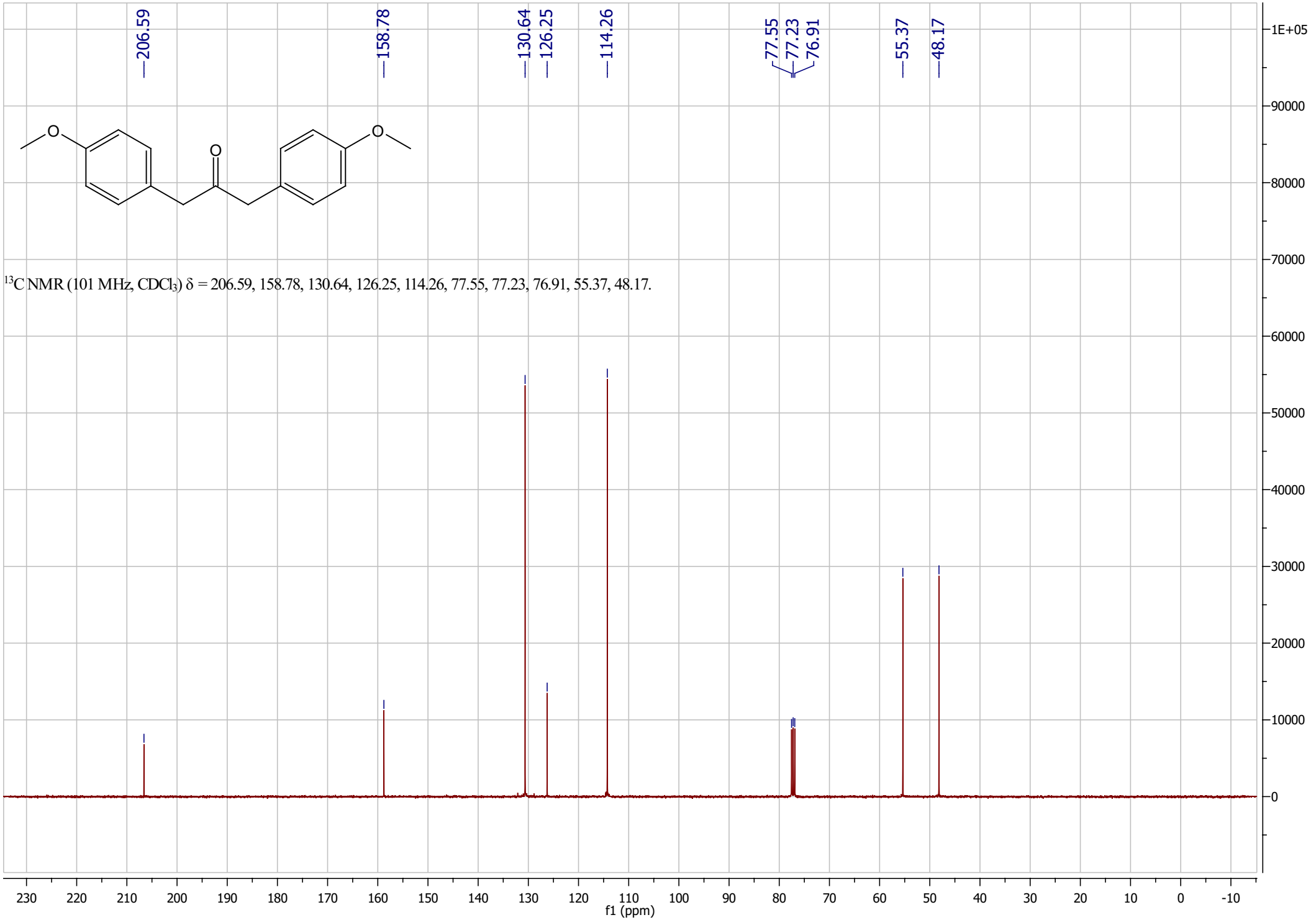
Marc-André Müller was born in Bad Säckingen (Germany) in 1985 and did his chemistry studies at the University of Basel where he obtained his M. Sc. degree in 2010 under the supervision of Prof. Andreas Pfaltz. He began his Ph.D. work in May 2010 in the same group, where he is currently working in the field of Ir-catalyzed enantioselective hydrogenation of unfunctionalized olefins.


7.39 7.39 7.39 7.38 7.37 7.36 7.34 7.34 7.33 7.31 7.31 7.30 7.29 7.28 7.27 7.27 6.78
5.25 5.23 5.21 5.21 5.19 5.17
3.97 3.93 3.91 3.87 3.43
1.55 1.53
O
HN
O
CH3
CH3
B (d)
3.89
A (d)
3.95
3.70 1.02 0.93 0.95 0.97 0.97 2.94 3.00
f1 (ppm)


O
HN
O
CH3
CH3
168.70
143.17
128.88
127.58
126.35
77.55
77.23
76.91
72.19
59.31
48.21
22.07
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

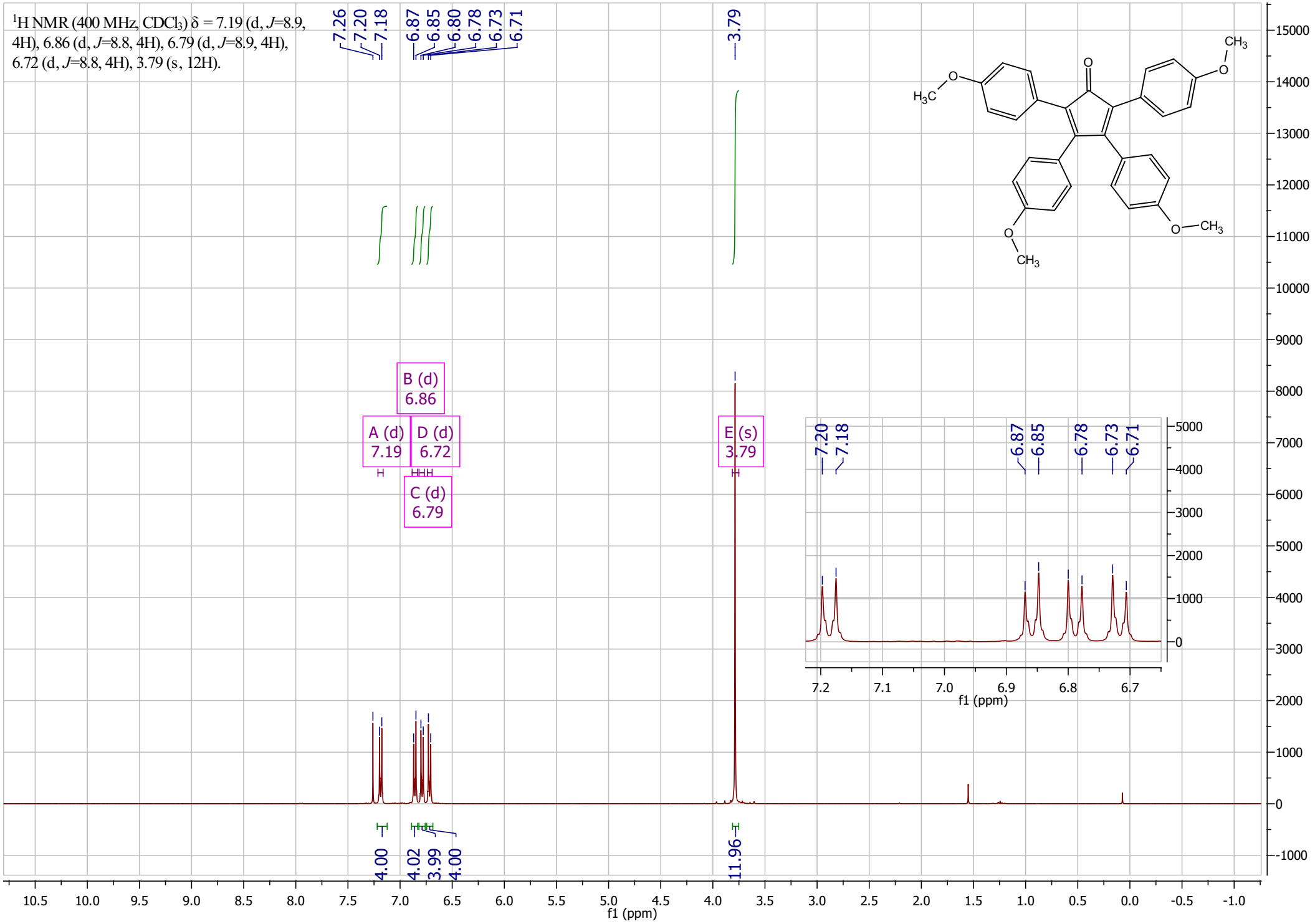


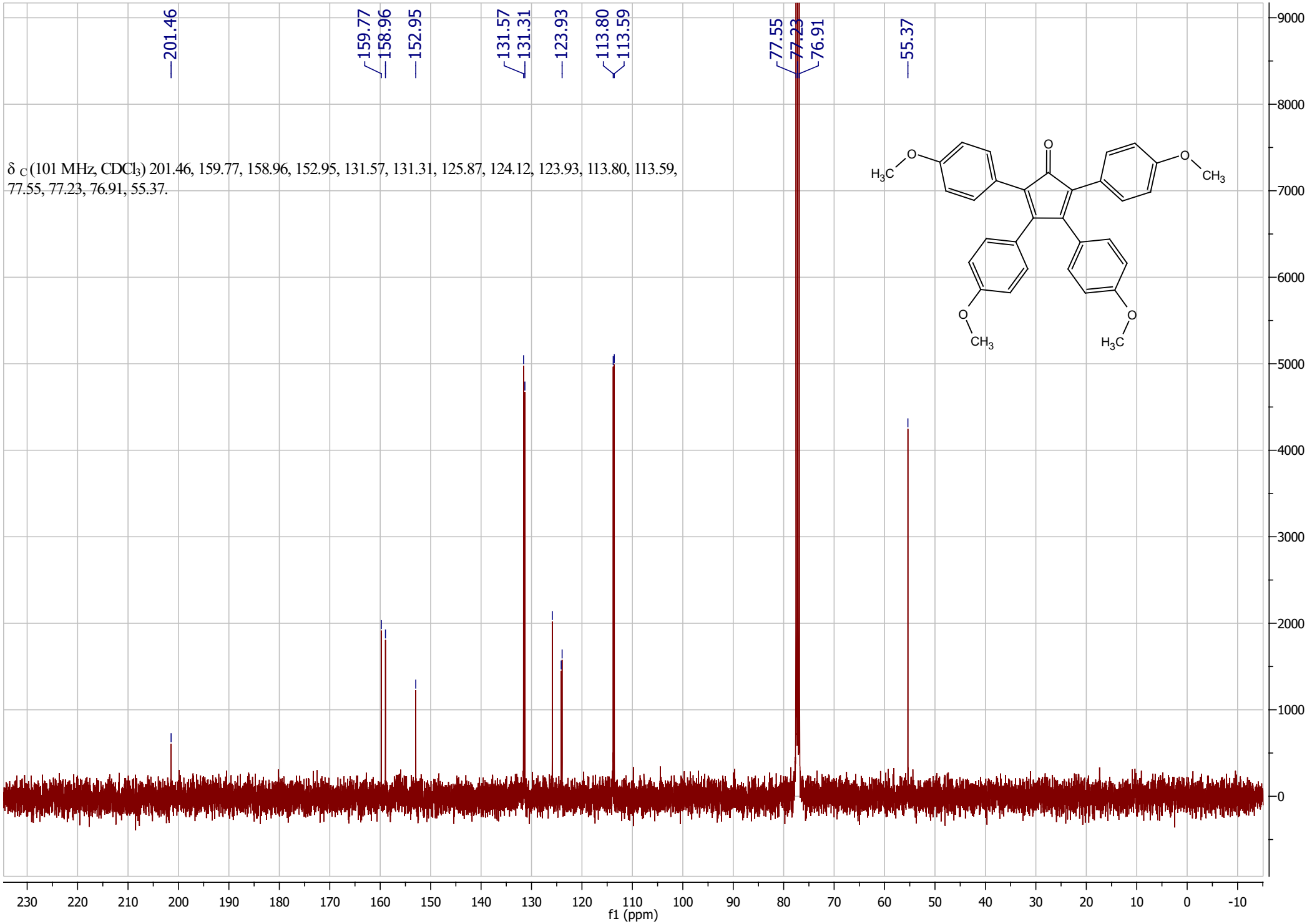
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (d, J = 8.4 Hz, 1H), 6.87 (d, J = 8.5 Hz, 1H) 3.80 (s, 2H), 3.66 (s, 1H).

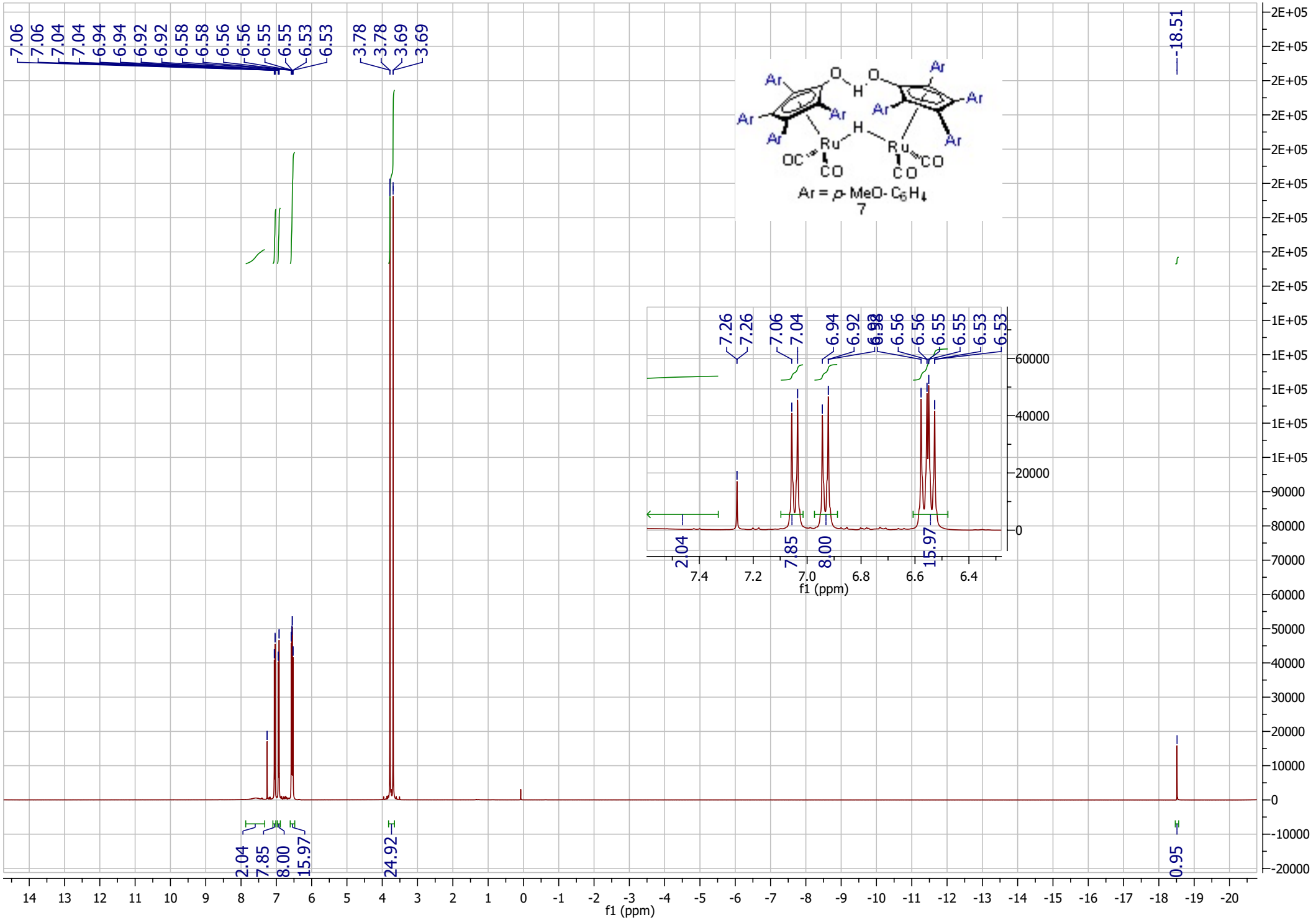


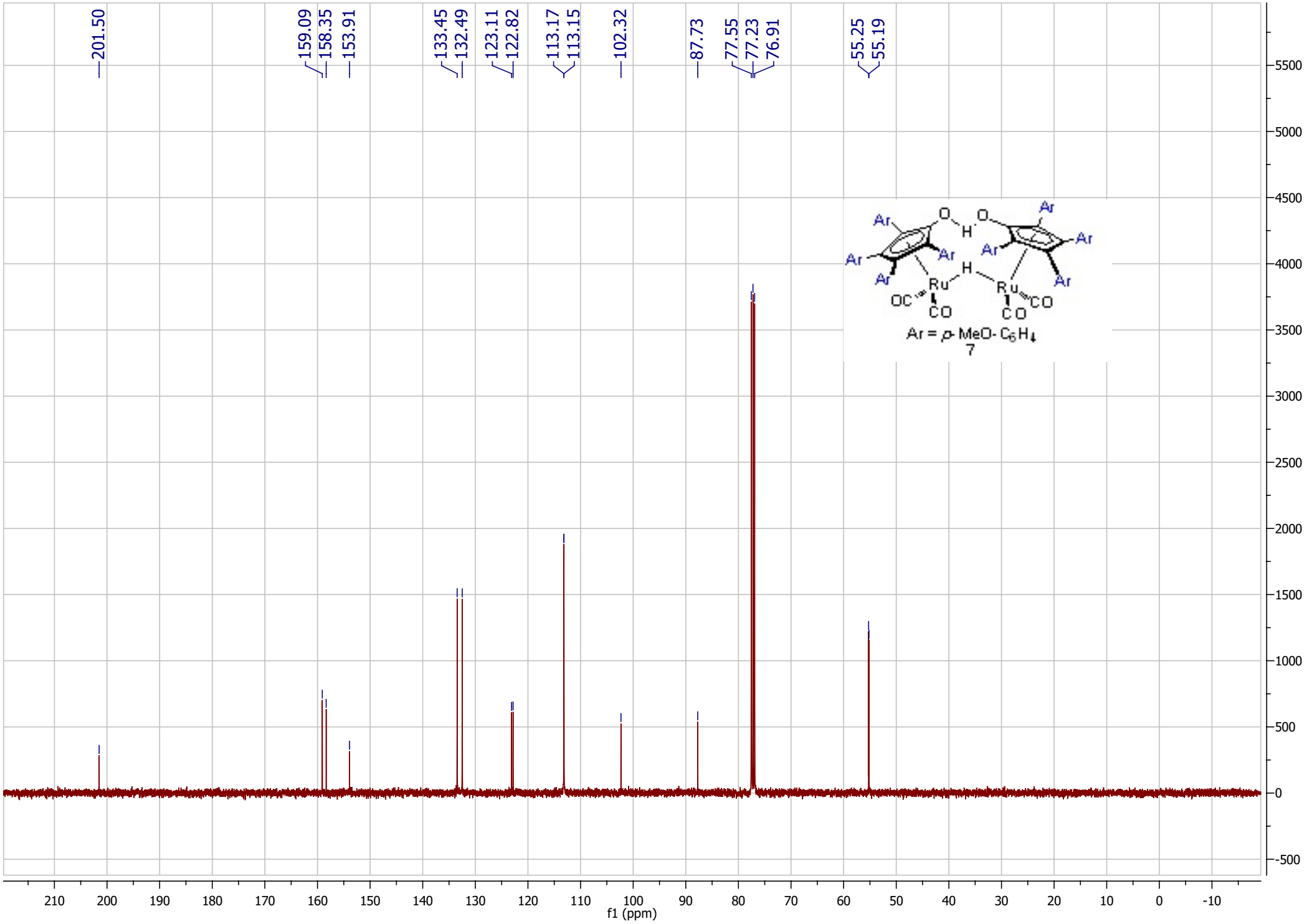
^{13}C NMR (101 MHz, $CDCl_3$) δ = 206.59, 158.78, 130.64, 126.25, 114.26, 77.55, 77.23, 76.91, 55.37, 48.17.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.19 (d, *J*=8.9, 4H), 6.86 (d, *J*=8.8, 4H), 6.79 (d, *J*=8.9, 4H), 6.72 (d, *J*=8.8, 4H), 3.79 (s, 12H).




201.46
159.77
158.96
152.95
131.57
131.31
123.93
113.80
113.59
77.55
77.23
76.91
55.37
δ C (101 MHz, CDCl3) 201.46, 159.77, 158.96, 152.95, 131.57, 131.31, 125.87, 124.12, 123.93, 113.80, 113.59, 77.55, 77.23, 76.91, 55.37.
f1 (ppm)


7.06
7.06
7.04
7.04
6.94
6.94
6.92
6.92
6.58
6.58
6.56
6.56
6.55
6.55
6.53
6.53
3.78
3.78
3.69
3.69
18.51
Ar = p-MeO-C6H4
7
2.04
7.85
8.00
15.97
24.92
0.95
f1 (ppm)


201.50
159.09
158.35
153.91
133.45
132.49
123.11
122.82
113.17
113.15
102.32
87.73
77.55
77.23
76.91
55.25
55.19
Ar = p-MeO-C6H4
7
f1 (ppm)