Organic Syntheses

Rhodium-Catalyzed Addition of Carboxylic Acids to Terminal Alkynes towards *Z*-Enol Esters

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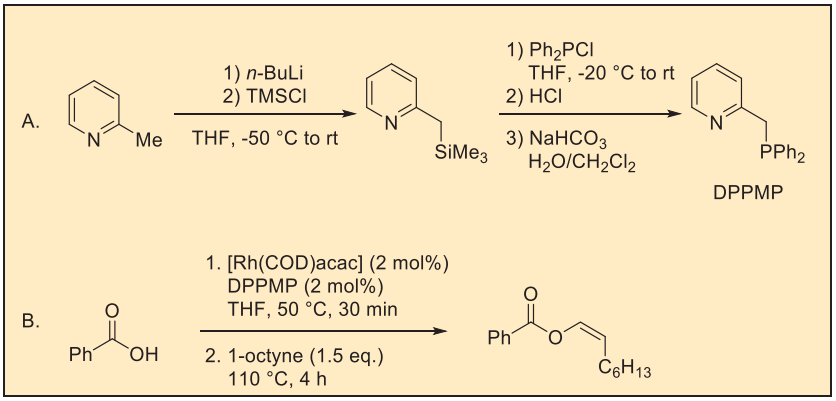

Procedure

Caution! A protection shield should be placed in front of the reaction set-up used for the preparation of (Z)-1-benzoyloxy)-1-octene.

A. 2-(Diphenylphosphino-methyl) pyridine (DPPMP). A dry argon-flushed (Notes 1 and 2) 250 mL round-bottomed Schlenk-flask (Note 3)

containing a magnetic stirring bar (oval, 30 x 16 mm) is charged with THF (75 mL) (Notes 4 and 5). 2-Picoline (7.40 mL, 6.98 g, 75.0 mmol) (Note 6) is added by syringe (Note 5) at rt. The solution is cooled to –50 °C (Note 7). Subsequently, a solution of ^{n}BuLi (30.0 mL, 2.5 M in hexane, 75.0 mmol, 1 equiv) (Note 8) is added dropwise by syringe over 1 h (Note 9). The reaction mixture is then stirred at –20 °C (Note 7) for 1.5 to 2 h. Meanwhile, a solution of TMSCl (9.50 mL, 8.13 g, 75.0 mmol, 1.0 equiv) (Note 10) in THF (10 mL) (Notes 4 and 5) is prepared in a dry argon-flushed (Notes 1 and 2) 250 mL round-bottomed Schlenk-flask (Note 3) containing a magnetic stirring bar (oval, 30 x 16 mm) and cooled to –20 °C (Note 7). The solution of deprotonated 2-picoline is then transferred *via* cannula (Note 11) to the TMSCl solution over a period of 2 h (Figure 1). After complete addition, the

Figure 1. The red solution of deprotonated 2-picoline (left) is transferred *via* cannula to the solution of TMSCl (right)

Figure 2. Reaction mixture after complete addition of deprotonated 2-picoline to TMSCl

flask of the 2-picoline solution is rinsed with THF (10 mL) (Notes 4 and 5) and this solution is also transferred by cannula. The reddish reaction mixture (Note 12) is allowed to warm to rt and stirred overnight (Figure 2). The reaction flask is equipped with a distillation apparatus (Note 13), and solvent and unreacted TMSCl are removed by distillation at ambient pressure. The residue is transferred by syringe to a 50 mL round-bottomed flask and fractionally distilled at 90 °C under reduced pressure of 20 mmHg (Note 14) (Figure 3) to afford 2-[(trimethylsilyl)methyl]pyridine as colorless oil (9.57 g, 57.9 mmol, 77%) (Note 15).

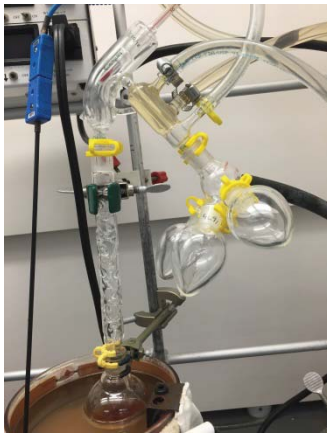

Figure 3. Distillation apparatus for the purification of 2-[(trimethylsilyl)methyl]pyridine

A dry argon-flushed (Notes 1 and 2) 250 mL round-bottomed Schlenk-flask (Note 3) containing a magnetic stirring bar (oval, 30 x 16 mm) is charged by syringe with 2-[(trimethylsilyl)methyl]pyridine (8.83 g, 53.4 mmol) and THF (45 mL) (Notes 4 and 5). The solution is cooled to –20 °C (Note 7) and PPh_2Cl (10.6 mL, 13.0 g, 58.8 mmol, 1.1 equiv) (Note 16) is added by syringe (Note 5) over 10 min. The reaction mixture is stirred at –20 °C for 1 h, allowed to warm to rt and stirred overnight. Then HCl (2.0 M in Et_2O, 30 mL, 60 mmol, 1.1 equiv) (Note 5) (Note 17) is added over 5 min at 0 °C (Note 18). The mixture is stirred for 1 h before the solvent is carefully removed while being connected to oil pump vacuum (0.15 mmHg). The residue is recrystallized (Note 19) (Figures 4, 5, and 6) from EtOH (Notes 20 and 21) and Et_2O (Note 21) to afford 2-((diphenylphosphino)-

methyl)pyridine hydrochloride (DPPMP•HCl) as acicular crystals (12.0 g, 38.2 mmol, 72%) (Note 22).

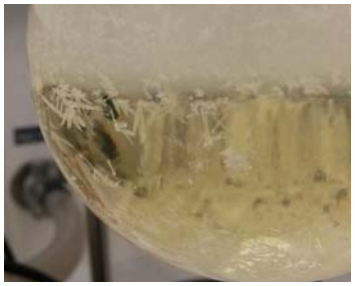

Figure 4. Crystal formation of DPPMP•HCl in EtOH overlaid by Et_2O

Figure 5. Crystals of DPPMP•HCl in EtOH/Et_2O

Figure 6. Crystals of DPPMP•HCl after removal of the solvents

A dry, argon-flushed (Notes 1 and 2) 50 mL round-bottomed Schlenk-flask (Note 3) containing a magnetic stirring bar (cylindric, 15 x 4.5 mm) is charged with $NaHCO_3$ (368 mg, 4.38 mmol, 2.2 equiv) (Note 23). Distilled water (25 mL) (Note 20) is added by syringe and the mixture stirred at rt until the salt is completely dissolved. Meanwhile, an argon-flushed 100 mL round-bottomed Schlenk-flask containing a magnetic stirring bar (cylindric,

20 x 6 mm) is charged with DPPMP•HCl (627 mg, 2.00 mmol) (Note 24). Dichloromethane (33 mL) (Note 25) is added by syringe to give a clear colorless solution. The aqueous solution of $NaHCO_3$ is added by syringe and the biphasic mixture is vigorously stirred for 30 min. The organic layer is transferred by syringe to an argon-flushed 50 mL round bottomed Schlenk-flask (Note 3). The organic layer is washed with distilled water (10 mL) (Note 21), carefully concentrated and dried under oil pump vacuum (0.15 mmHg). The free ligand 2-((diphenylphosphino)-methyl)pyridine is obtained as a colorless solid (546 mg, 1.97 mmol, 99%) (Notes 26 and 27).

B. *(Z)-1-(Benzoyloxy)-1-octene*. A dry argon-flushed (Notes 1 and 2) 120 mL Teflon screw cap pressure vessel (Note 28) containing a magnetic stirring bar (cylindric, 20 x 6.0 mm) is charged with [Rh(COD)acac] (248 mg, 0.800 mmol, 2.0 mol%) (Note 29), 2-(diphenylphosphino-methyl) pyridine (DPPMP, 222 mg, 0.8 mmol, 2.0 mol%) and benzoic acid (4.88 g, 40.0 mmol) (Note 30) in a glove box. Degassed anhydrous THF (62 mL) (Notes 4 and 5) is added, the flask sealed (Note 31), and immediately immersed in a pre-heated oil bath (bath temperature 50 °C) outside of the glove box. The yellow mixture (Figure 7) is stirred for 30 min and then allowed to cool down to rt (Note 32). 1-Octyne (8.85 mL, 6.61 g, 60.0 mmol,

Figure 7. Reaction mixture before addition of 1-octyne

1.5 equiv) (Note 33) is added in the glove box, the flask sealed (Note 31), and immediately immersed in a pre-heated oil bath (bath temperature 110 °C) outside of the glove box. The mixture turns orange (Figure 8) while

Figure 8. Reaction mixture after addition of 1-octyne and heating

being stirred for 4 h. After cooling to rt for 25 min, the mixture is filtered through a pad of silica gel (30 x 70 mm) (Note 34) and eluted with ethyl acetate (3 x 20 mL) (Note 35) to separate the catalyst. The solvent is removed under reduced pressure first on a rotary evaporator (225 mmHg down to 15 mmHg, bath temperature 40 °C), then under oil pump vacuum (0.2 mmHg, room temperature) and the crude product (Note 36) purified by column chromatography on silica gel (100 x 120 mm, eluent pentane : dichloromethane = 5:1, R_f = 0.3) (Note 37). The solvents are removed under reduced pressure first on a rotary evaporator (600 mmHg down to 15 mmHg, bath temperature 40 °C), then under oil pump vacuum (0.2 mmHg, room temperature) to furnish (*Z*)-1-(benzoyloxy)-1-octene (8.67 g, 37.3 mmol, 93%) (Note 38) as a light orange oil (Note 39).

Notes

1. Vessels are dried by heating with the heat gun for 2 minutes while connected to the oil pump vacuum (0.15 mmHg).
2. Argon 5.0 from Sauerstoffwerke Friedrichshafen.
3. Equipped with a rubber septum and connected to argon.
4. THF (anhydrous, >99.9%, inhibitor-free) was purchased from Sigma Aldrich.
5. A syringe purchased from Henke Sass Wolf is flushed with argon three times and used for the addition.

6. 2-Picoline (98% purity) was purchased from Aldrich and distilled at 75 °C under 150 mmHg. The freshly distilled colorless 2-picoline was removed under an Argon counter flow. A yellowish oil remained in the flask.
7. Cooling was performed using a dry ice/ethanol bath.
8. ^{n}BuLi (2.5 M in hexane) was purchased from Sigma Aldrich. The concentration was checked by titration using *N*-(*o*-tolyl)pivalamide (Suffert's reagent) prior to use.[2]
9. The previously colorless solution turns orange and finally ruby red.
10. Chlorotrimethylsilane (≥98.0%) was purchased from Sigma Aldrich and distilled at 57 °C under argon prior to use.
11. The picoline flask is attached to a continuous argon flow. A stainless steel cannula is used for the transfer.
12. The reaction mixture turns yellowish then reddish after complete addition of 2-picoline.
13. The distillation apparatus consists of a Claisen stillhead, a fused Liebig condenser (10 cm) and a fused vacuum connection. Solvent and TMSCl are distilled off at about 65 °C (oil bath temperature 85 °C) at ambient pressure. The distillates are collected in a 100 mL flask.
14. A Vigreux column (10 cm) is attached and 2-[(trimethylsilyl)methyl]-pyridine is distilled at 90 °C (oil bath temperature 150 °C) and 22 mmHg. The distillates are separated *via* a multi limb delivery adapter and collected in suitable flasks (Figure 3).
15. A second run on the same scale provided 9.74 g (79%) of the same material. 2-[(trimethylsilyl)methyl]pyridine exhibits the following spectroscopic properties: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.00 (s, 9H), 2.33 (s, 2H), 6.90–6.98 (m, 2H), 7.47 (dt, J = 7.6, 2.0 Hz, 1H), 8.41 (bd, J = 5.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: –1.70, 30.31, 119.10, 122.12, 135.78, 149.01, 161.35; ESI-HRMS (*m*/*z*) calcd. for $C_9H_{16}NSi$ $[M+H]^+$ 166.10465, found 166.1039.
16. Chlorodiphenylphosphine (96% purity) was purchased from Sigma Aldrich and distilled at 90 °C (oil bath temperature 150 °C) at 0.004 mmHg.
17. HCl (2.0 M in Et_2O) was purchased from Sigma Aldrich and used as received.
18. Cooling is performed using an ice-water bath.
19. The residue is dissolved in a minimum amount of EtOH (70 to 100 mL) and carefully overlaid with Et_2O (EtOH:Et_2O = 1:1) (Figure 4). After

crystallization overnight at rt (Figure 5), the mother liquor is transferred *via* cannula to another 250 mL round-bottomed Schlenk-flask and 2-((diphenylphosphino)methyl)-pyridine hydrochloride is afforded in acicular crystals (8.90 g, 28.4 mmol) (Figure 6). The mother liquor was concentrated under oil pump vacuum (0.15 mmHg) and the residue recrystallized overnight at rt from a minimum amount of EtOH (50 mL) and carefully overlaid with Et_2O (EtOH:Et_2O = 1:2) to give more DPPMP•HCl (2.30 g, 7.3 mmol).

20. Absolute anhydrous EtOH was purchased from Sigma Aldrich.
21. The solvent is degassed by bubbling argon through the solvent using a cannula for 30 min while being stirred.
22. 2-((Diphenylphosphino)methyl)pyridine hydrochloride exhibits the following spectroscopic and physical properties: NMR samples should be prepared in degassed solvents. The solvent (~3 mL) is degassed by bubbling argon through the solvent for 5-10 min. ^{1}H NMR (400 MHz, CD_2Cl_2) δ: 4.19 (s, 2H), 7.34–7.39 (m, 1H), 7.40–7.45 (m, 6H), 7.55–7.61 (m, 4H), 7.61–7.67 (m, 1H), 8.11 (dt, *J* = 8.0, 1.6 Hz, 1H), 8.51 (dd, *J* = 5.8, 1.0 Hz, 1H); ^{13}C NMR (101 MHz, CD_2Cl_2) δ: 33.3, 123.8, 127.2, 128.8, 129.7, 133.1, 135.3, 140.4, 144.4, 155.7; ^{31}P NMR (121 MHz, CD_2Cl_2) δ: –4.66; ESI-HRMS (*m*/*z*) calcd. for $C_{18}H_{17}NOP$ $[M\text{-}Cl+O+H]^+$ 294.10422, found 294.1036.
23. $NaHCO_3$ was purchased from Fisher Chemical and used as received.
24. After being charged with the DPPMP•HCl the flask is evacuated and filled with argon three times, equipped with a septum and an argon line.
25. Anhydrous dichloromethane from Sigma Aldrich and used as received after degassing by bubbling argon for 15 minutes.
26. 2-((Diphenylphosphino)methyl)pyridine exhibits the following spectroscopic and physical properties: mp 57–58 °C; ^{1}H NMR (400 MHz, CD_2Cl_2) δ: 3.54 (s, 2H), 6.89-6.99 (m, 2H), 7.21-7.26 (m, 6H), 7.31-7.42 (m, 5H), 8.33-8.38 (m, 1H); ^{13}C NMR (101 MHz, CD_2Cl_2) δ: 38.5, 120.9, 123.6, 128.4, 128.7, 132.8, 136.0, 138.3, 149.2, 158.2; ^{31}P NMR (121 MHz, CD_2Cl_2) δ: –11.12.; ESI-HRMS (*m*/*z*) calcd. for $C_{18}H_{17}NP$ $[M+H]^+$ 278.10931, found 278.1095.
27. The ligand DPPMP is sensitive to oxidation when being stored over a longer period of time. Therefore, the authors recommend releasing the required amount of free ligand from the HCl salt shortly before the catalysis. The pure ligand should be stored under argon. The oxide

may be separated by filtration over silica gel under inert atmosphere using degassed dichloromethane.

28. Pressure vessel was purchased from Chem Glass.
29. [Rh(COD)acac] (elemental Rh (ICP): 32.99%, $[Rh(COD)Cl]_2$ < 0.1%) was purchased from Alfa Aesar and used as received.
30. Benzoic acid (>99.5% purity) was purchased from Sigma Aldrich and used as received.
31. The cap was screwed back on tightly. A protection shield should be placed in front of the reaction apparatus.
32. The cooling required 15 minutes.
33. 1-Octyne (98% purity) was purchased from Alfa Aesar and filtered over a pad of basic alumina (30x 20 mm) prior to use. The basic alumina was purchased from Sigma Aldrich.
34. Silica gel 60, 230-400 mesh (Fisher Chemical) is used as stationary phase.
35. Ethyl acetate of technical grade is used after evaporation and recollection of the solvent in the receiving flask of a rotary evaporator (200 mmHg, bath temperature 50-60 °C).
36. The ratio *anti*-Markovnikov-*Z* (AM-*Z*):*anti*-Markovnikov-*E* (AM-*E*):Markovnikov (M) = 92:4:4 is determined by ^{1}H NMR analysis.[3] An enyne-byproduct from homocoupling of 1-octyne is observed.
37. The product is purified by flash chromatography through silica gel using a Teledyne Isco CombiFlash Rf (120 g column, from Silicycle) with hexane:dichloromethane = 5:1 as eluent. The product is typically found in fractions 11-39 *via* TLC analysis on silica gel (hexane:dichloromethane = 5:1, $R_f = 0.3$, visualization with $KMnO_4$ stain).
38. A second run on the same scale provided 8.49 g (91%) of the same products. The enyne-byproduct was separated and not observed in the ^{1}H NMR product spectrum after column chromatography. A ratio AM-*Z*:AM-*E*:M = 94:1:4 was determined by ^{1}H NMR analysis. Quantitative NMR (500 MHz, $CDCl_3$, 1,3,5-trimethoxybenzene (≥ 99% purity, Sigma Aldrich)) delivers a purity of >96 wt% with a ratio of AM-*Z*:AM-*E*:M = 95:1:4. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.84–0.91 (m, 3H), 1.26–1.40 (m, 6H), 1.40–1.49 (m, 2H), 2.29 (dq, *J* = 7.5, 1.5 Hz, 2H), 7.24–7.28 (m, 1H), 7.45–7.50 (m, 2H), 7.62–7.57 (m, 1H), 8.09–8.13 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.1, 22.6, 24.6, 28.9, 29.2, 31.7, 115.0,

128.5, 129.5, 129.9, 133.4, 134.2, 163.6; ESI-HRMS (*m*/*z*) calcd. for $C_{15}H_{24}NO_2$ $[M+NH_4]^+$ 250.18015, found 250.1798.

39. If product with higher purity is desired, the product (7.47 g) is distilled at 75 °C at 0.4 mmHg to provide a colorless oil (7.02 g, 94%). Quantitative NMR (500 MHz, $CDCl_3$, 1,3,5-trimethoxybenzene (≥ 99% purity, Sigma Aldrich)) delivers a purity of >96 wt% with a ratio of AM-*Z*:AM-*E*:M = 95:1:4. The distillation apparatus consists of a 25 mL round-bottomed flask connected to a Claisen stillhead, a fused Liebig condenser (5.5 cm) with fused vacuum adapter and a multi-limb delivery adapter with three 10 mL flasks (Figure 9).

Figure 9: Distillation apparatus for further purification of the product

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Discussion

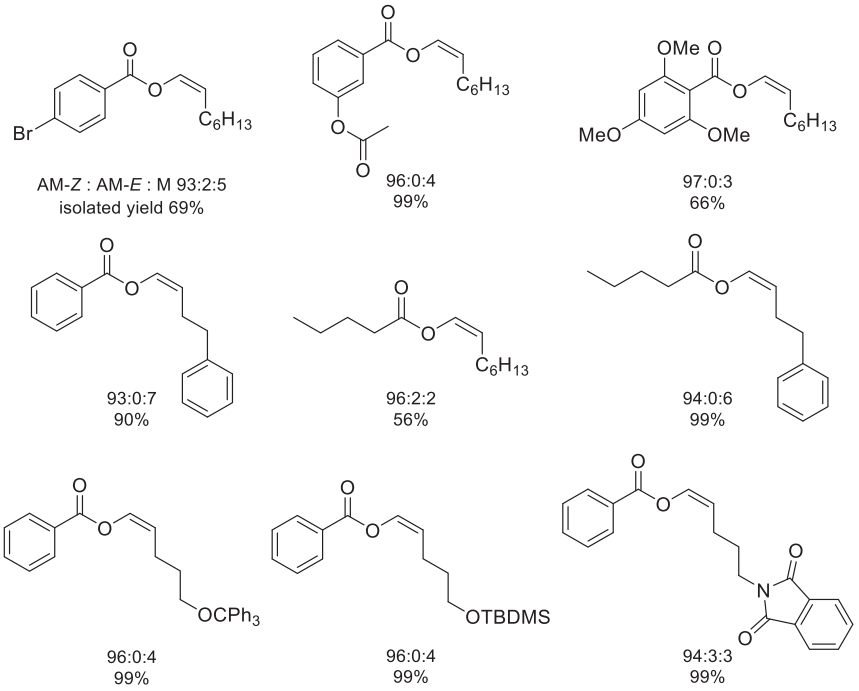
Enol esters are versatile building blocks in organic synthesis, finding application as substrates in a wide range of reactions such as acylations,[4] asymmetric epoxidations,[5] cyclopropanations[6] and hydroformylations[7] besides being important monomers for polymerisation.[8] Moreover, the enol ester motif is found in several biologically active natural products such as Phenochalasin B[9] and Grenadadiene.[10] Since the first report on a ruthenium-catalyzed addition of carboxylic acids to an alkyne by Shvo *et al.* in 1983,[11] several other intermolecular methodologies were developed employing iridium,[12] rhenium,[13] palladium,[14] gold[15] as well as an intramolecular rhodium-catalyzed synthesis of alkylidene lactones.[16]

While these mostly lead to Markovnikov (M) or *anti*-Markovnikov (AM-*E*) addition, our recently reported atom- and redox-economic rhodium-catalyzed hydro-oxycarbonylation[17] leads selectively to the *Z*-enol ester (AM-*Z*) in high yields in a reaction time of 16-24 hours. Recently, the methodology was successfully applied in natural product synthesis by Burke *et al.* in the total synthesis of Patulolide C.[18]

Following our first report employing the $[Rh(COD)Cl]_2$/DPPMP catalyst system, further investigations have led to a more active

Rh(COD)acac/DPPMP catalyst system, which furnishes the desired *Z*-enol esters in equally high yields and selectivities however with a reduced reaction time of only 4 hours.[19] Furthermore, this novel catalyst system employed in the herein reported protocol was found to be compatible with a wide range of functionalities (Table 1).

Table 1. Further Z-enol esters prepared using this protocol[20]



As a result of the milder reaction conditions, this improved methodology is highly suitable for the synthesis of *Z*-enol esters containing sensitive moieties such as the enol ester derived from *p*-bromo benzoic acid. In addition, the compatibility with commonly employed protecting groups such as trityl, TBDMS and *N*-phthalimide reinforces the applicability of our methodology in total synthesis.

In conclusion, the catalyst systems developed by us show complementary functional group compatibility, allowing for a broad application of the rhodium-catalyzed hydro-oxycarbonylation in organic synthesis.

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20. These results were obtained for reactions performed at a 0.45 mmol scale. For the full characterization data see: Wei, S.; Pedroni, J.; Meißler, A.; Lumbroso, A.; Drexler, H.-J.; Heller, D.; Breit, B. *Chem. Eur. J.* **2013**, *19*, 12067–12076.

Appendix
Chemical Abstracts Nomenclature (Registry Number)

Benzoic acid: (65-85-0)
1-Octyne: (629-05-0)
[Rh(COD)acac]: (Acetylacetonato)(1,5-cyclooctadiene) rhodium (I); (12245-39-5)
n-BuLi: *n*-Butyllithium; (109-72-8)
2-Picoline: (109-06-8)
TMSCl: Chlorotrimethylsilane; (75-77-4)
PPh_2Cl: Chlorodiphenylphosphine; (1079-66-9)
1,3,5-Trimethoxybenzene: (621-23-8)

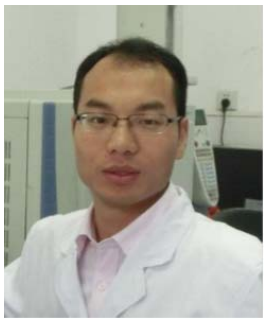
Stephanie Ganss studied chemistry in Darmstadt (Germany) and Lausanne (Switzerland) and received her diploma degree from the Technical University Darmstadt in 2010. She completed her diploma thesis in the group of Professor Waser at the EPF Lausanne (Switzerland) working on palladium catalyzed electrophilic acetylination of indoles using hypervalent iodine compounds. In 2016, she completed her Ph.D. under the supervision of Professor Breit at the Albert-Ludwigs University Freiburg (Germany). Her current research focuses on the application of rhodium catalyzed CH functionalization and the development of macrolactonization reactions.

Julia Pedroni was born in 1984 in Campinas, Brazil. During her undergraduate studies at the Albert-Ludwigs-Universität Freiburg she worked in the group of Professor Breit on Rh-catalysis. Since July 2013, she is working in the group of Professor Cramer at the EPF Lausanne as a Ph.D. student.

Alexandre Lumbroso studied chemistry at the University of Nantes (France). He completed his Ph.D. under the supervision of Professor Jean-Paul Quintard in 2009, working on the utilization of organostannanes for the stereoselective synthesis of imino sugar derivatives. His postdoctoral studies in the group of Prof. Dr. Bernhard Breit at the Albert-Ludwigs-University Freiburg (Germany) focused on the development of new atom-economic regio-and stereoselective reactions using homogeneous catalysis. He is now working as laboratory leader at Syngenta (Switzerland).

Günter Leonhardt-Lutterbeck successfully completed his apprenticeship for lab-technician at the Universtiy of Freiburg in 1986. He then joined the group of Professor Horst Prinzbach working on the synthesis of pagodan. Since 2001, he is part of the group of Professor Breit mainly focusing on ligand syntheses for hydroformylation.

Antje Meißner studied Biology and Chemistry at the University of Rostock (Germany) and received her degree in Chemistry in 2010. She is currently doing her doctorate under the supervision of Prof. Dr. Detlef Heller. Her present research focuses on the systematic investigations into the in situ synthesis of dinuclear rhodium diphosphine complexes and the implications of the results in homogeneous catalysis.



Siping Wei received a Ph.D. from the Sichuan University in 2011, and then worked as a post-doctoral fellow/research scientist at Leibniz-Institut für Katalyse e. V. at the University of Rostock (LIKAT Rostock, Germany). He has been an associate professor at Luzhou Medical College since 2014. His current research interest focuses on developing new NHC-Metal Complexes for homogeneous catalysis.

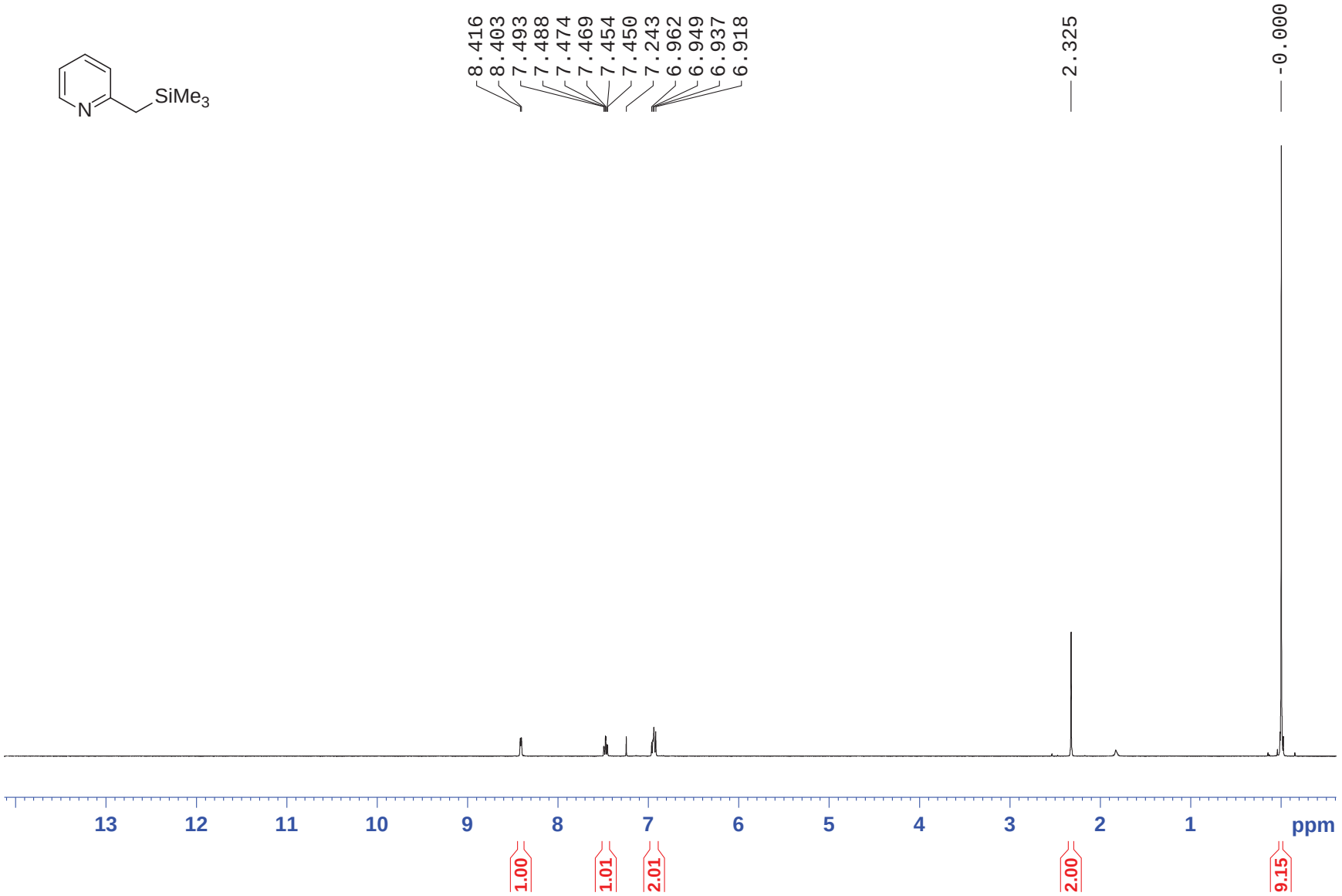
Hans-Joachim Drexler graduated in Chemistry at the University of Rostock (Germany) under the supervision of Prof. Hans-Jürgen Holdt in 1997. Since 1999 he is a scientific co-worker at the Leibniz-Institut für Katalyse e.V., Rostock. His research interests are in the fields of organometallic chemistry, asymmetric homogeneous catalysis and especially X-ray analysis. The successful cooperation with industrial partners is documented by several joint projects and patents.

Detlef Heller studied Chemistry at the University of Greifswald (Germany), where he also obtained his Ph.D. under the supervision of Prof. Kurt Madeja. Since 1987 he is a researcher at the Leibniz-Institut für Katalyse e.V., Rostock, since 1998 as group leader. In 1999 he completed his Habilitation in the field of physical chemistry. His research interests within organometallic chemistry deal with the kinetics, mechanisms and deactivation phenomena of homogeneous catalysis, with a special emphasis on rhodium complexes towards the design of efficient general in situ techniques for catalyst generation. Beside he is very fond of the history of Chemistry from a philatelic point of view.

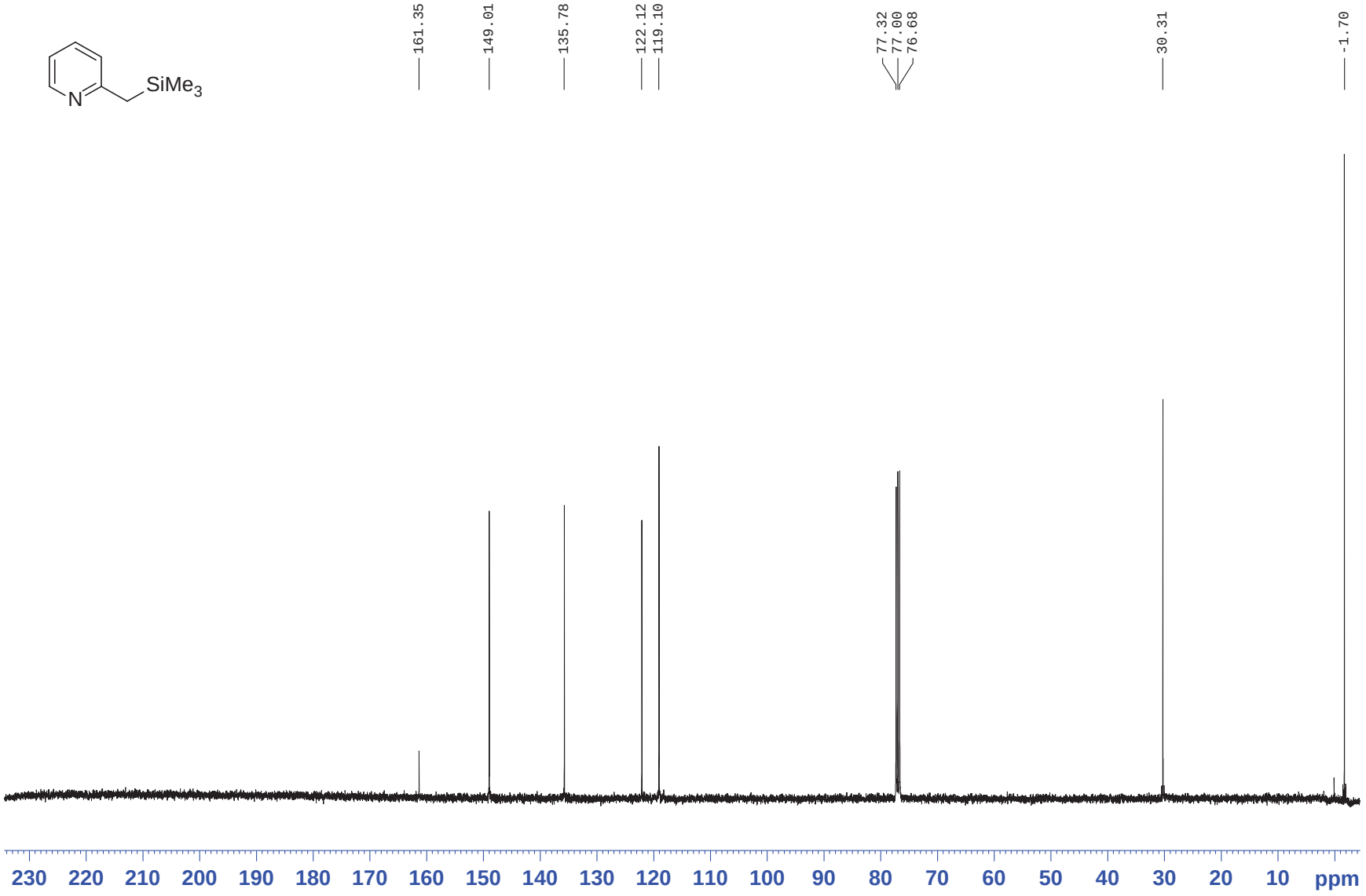
Bernhard Breit studied chemistry at the University of Kaiserslautern, Germany, where he obtained his doctorate in 1993 with Professor Regitz. After postdoctoral training with Professor Trost at Stanford University, he worked in Marburg, Germany, with Professor R. W. Hoffmann to obtain his habilitation in 1998. In 1999 he was appointed as an Associate Professor at the University of Heidelberg, Germany. Since 2001 he has been a Full Professor of Organic Chemistry at the Albert-Ludwigs-Universität Freiburg i. Brsg. His research interests focus on the exploration and development of catalytic methods for organic synthesis. He is author of 200 publications.

Sonia Rodriguez studied Chemical Sciences at the Universitat Autònoma de Barcelona, Spain, where she received her Ph.D. in Organic Chemistry in 2000 under the supervision of Profs. Pedro de March and Marta Figueredo. After industrial experience at Finnovequim and Deripol, she broadened her synthetic background during a postdoctoral appointment with Prof. Peter Wipf at the University of Pittsburgh from 2001 to 2003. Subsequently, she joined the department of Chemical Development at Boehringer Ingelheim Pharmaceuticals, Inc., where she has been a member of the Catalysis group since 2007. Her research interests include the development and application of catalytic asymmetric reactions in the development of new economical processes.

2-[(trimethylsilyl)methyl]pyridine, ^{1}H-NMR ($CDCl_3$, 400 MHz)



2-[(trimethylsilyl)methyl]pyridine, ^{13}C-NMR (CD_2Cl_2, 101 MHz)



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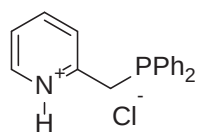
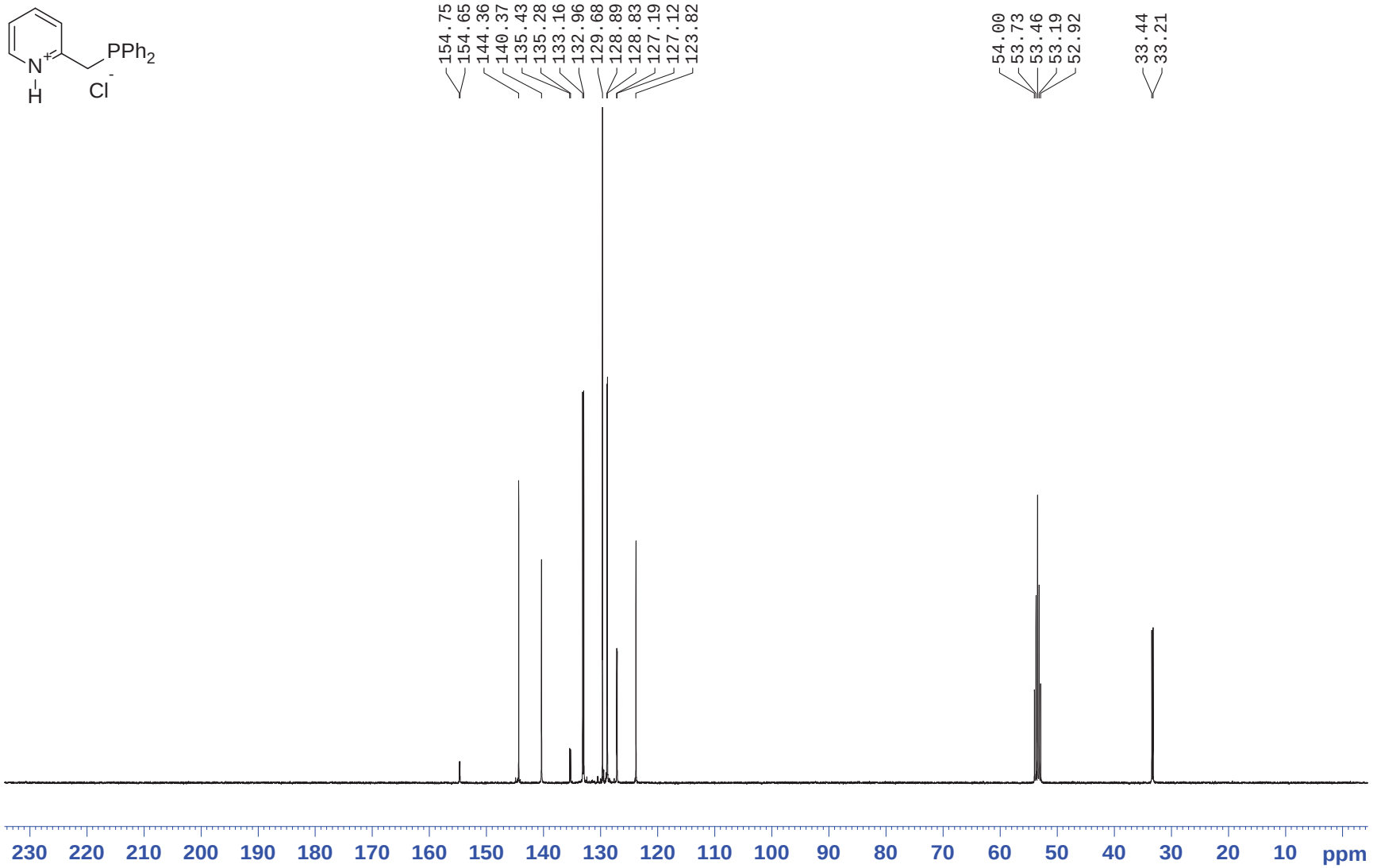
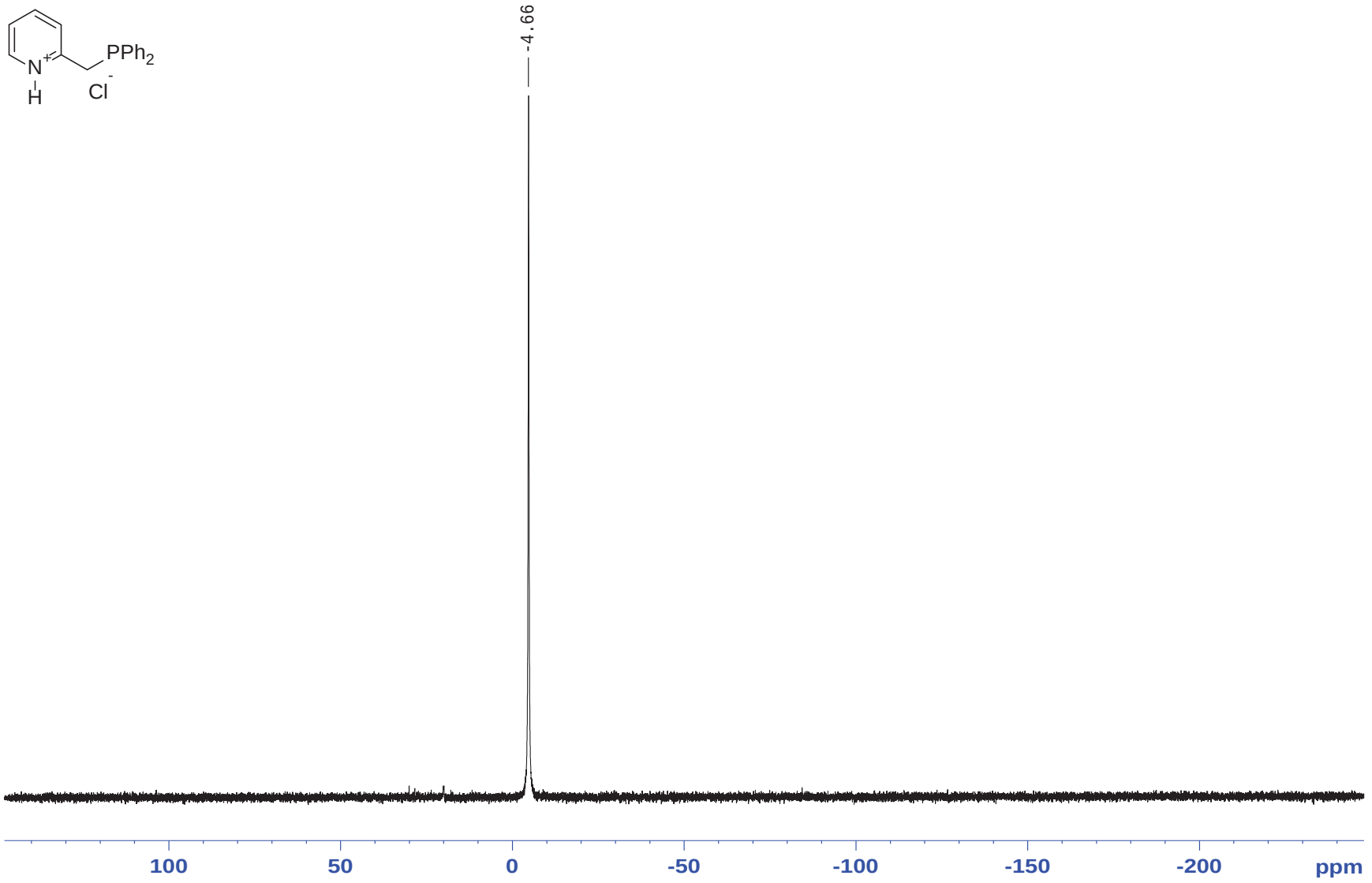


DPPMP.HCl, ^{13}C-NMR (CD_2Cl_2, 101 MHz)



DPPMP.HCl, ^{31}P-NMR (CD_2Cl_2, 121 MHz)



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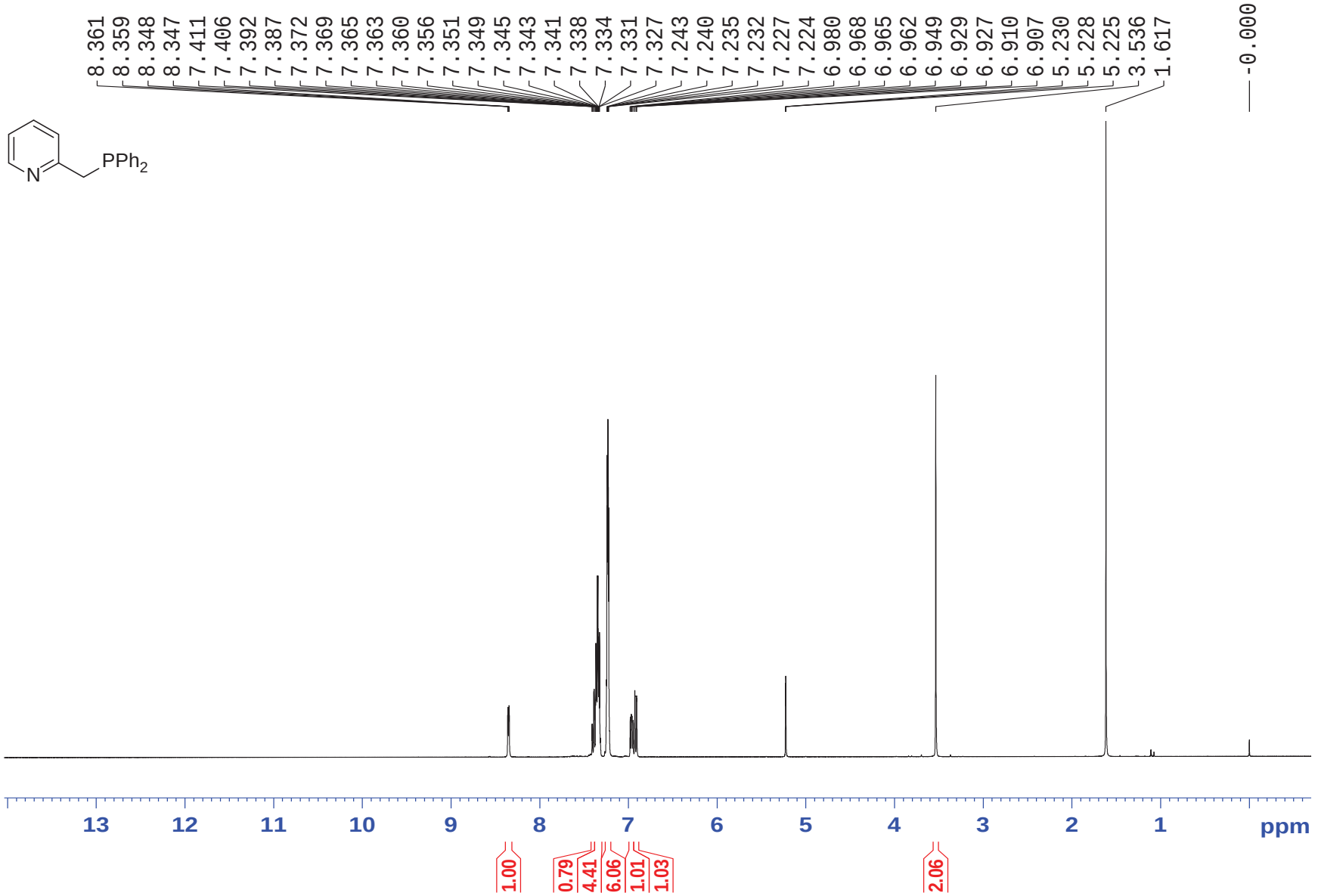

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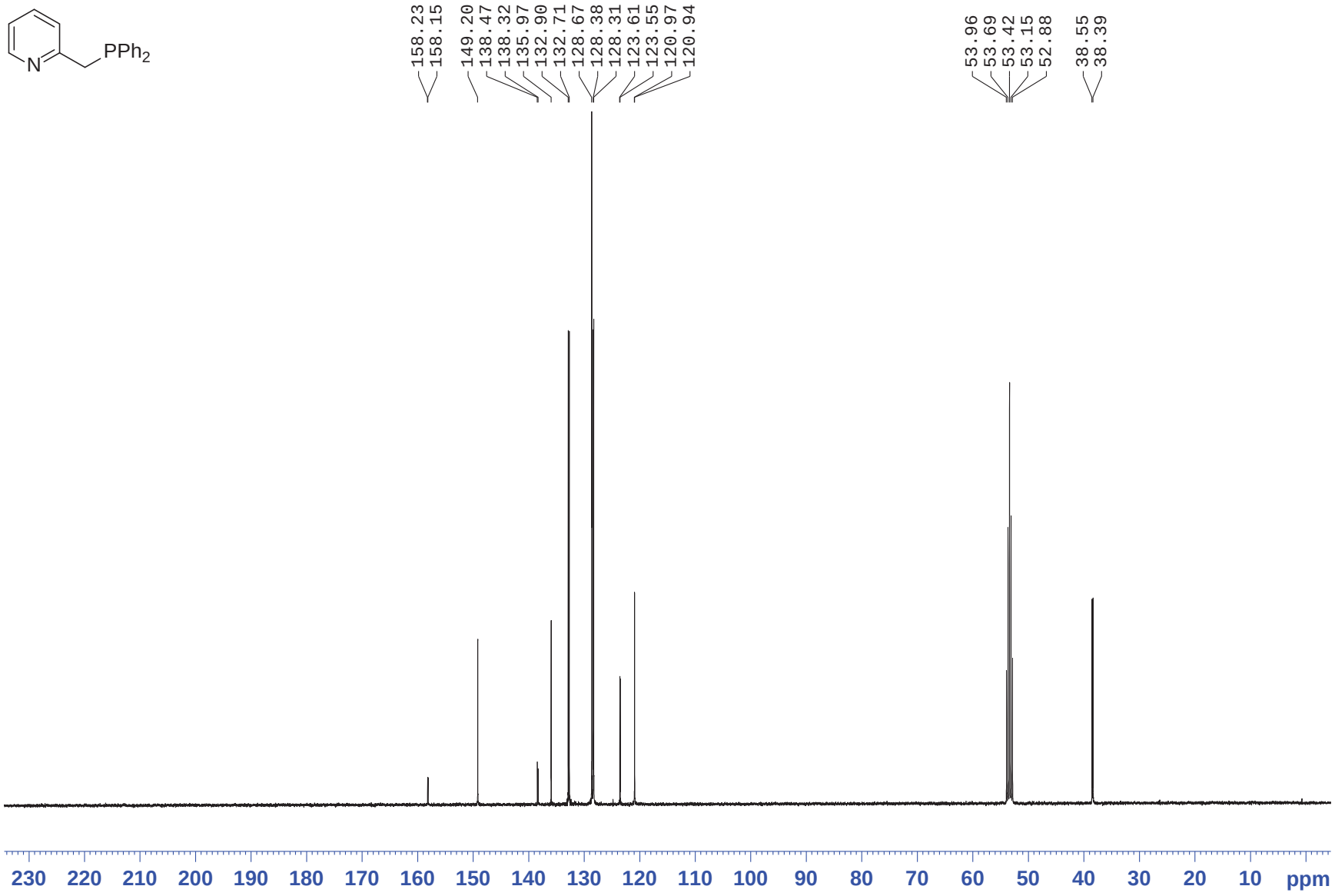
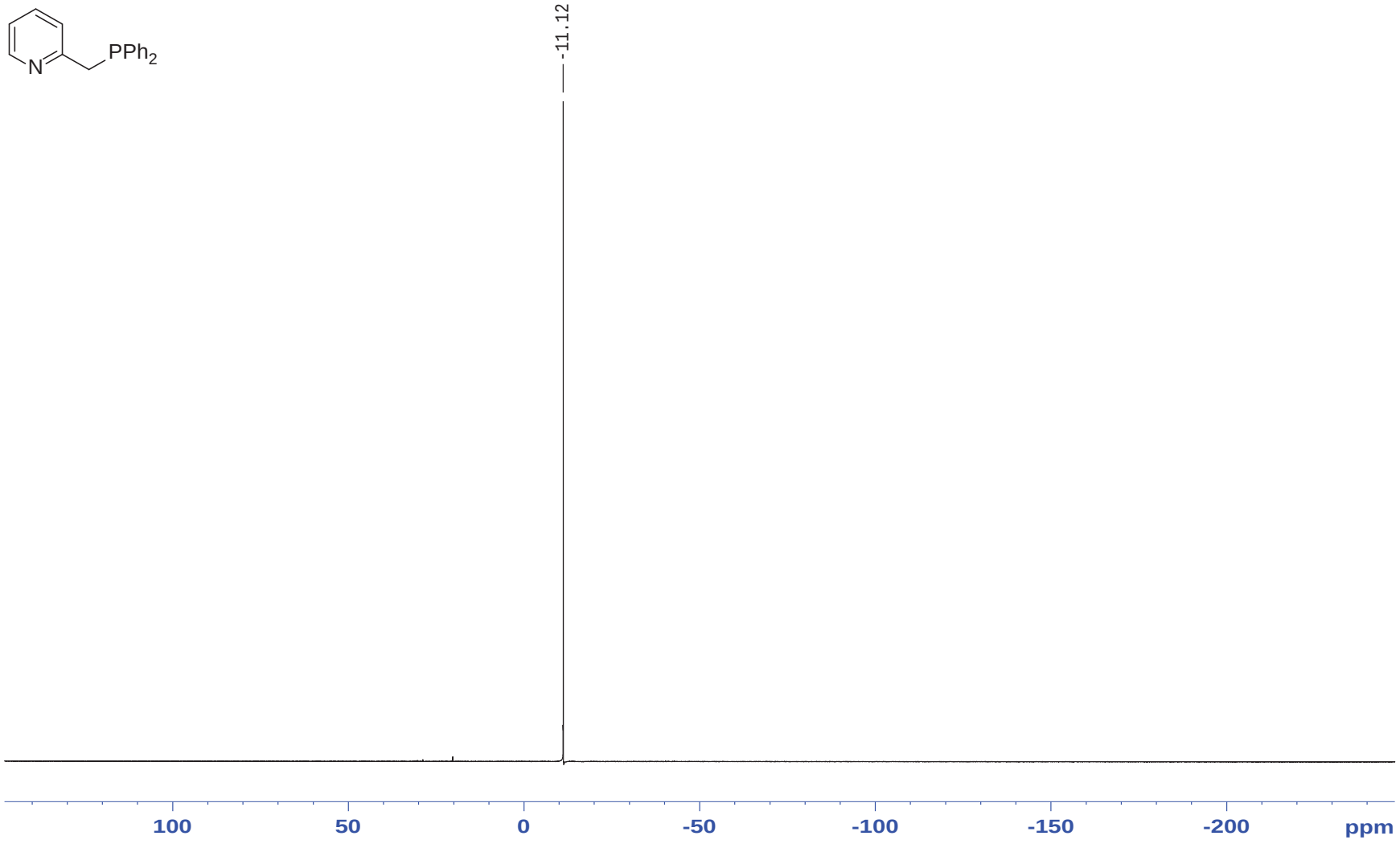
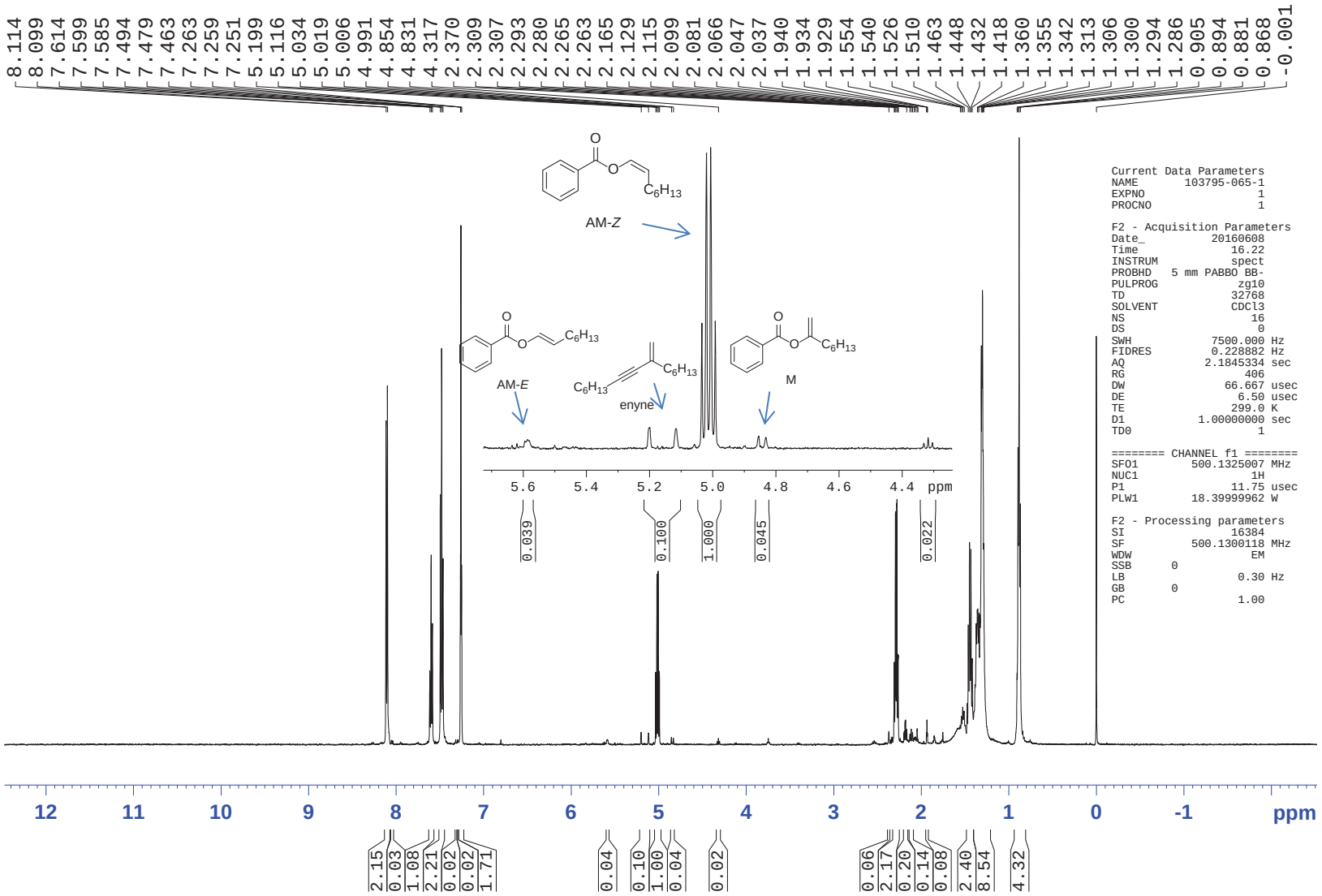


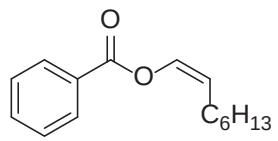
DPPMP, ^{31}P-NMR (CD_2Cl_2, 121 MHz)



^{1}H NMR (500 MHz, $CDCl_3$) spectrum of the crude product of the Rh-catalyzed addition of benzoic acid and 1-octyne with indication of the AM-*E* : enyne : AM-Z ratio in $CDCl_3$

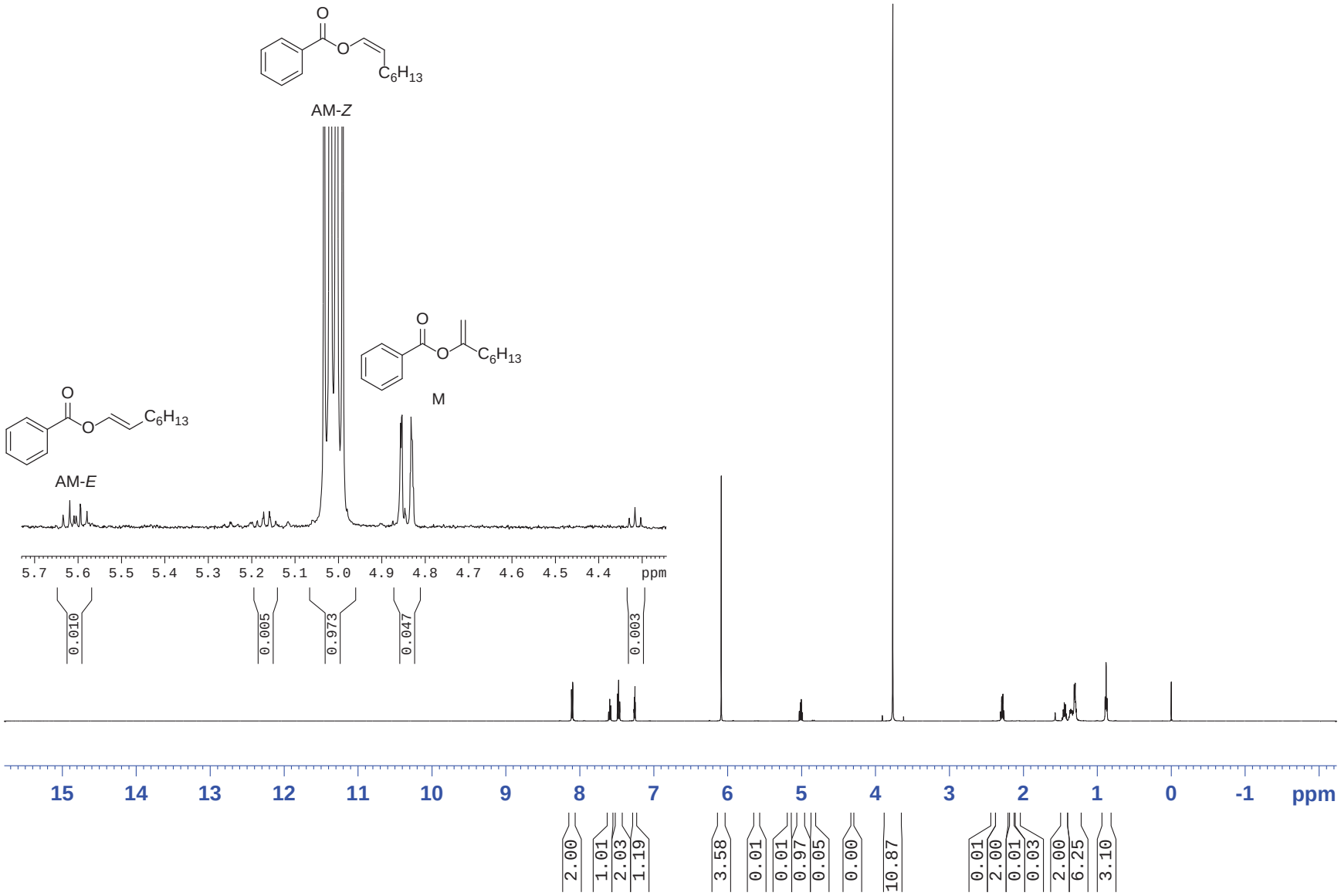


(*Z*)-1-(Benzoyloxy)-1-octene, ^{13}C NMR (125 MHz, $CDCl_3$)

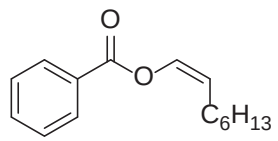


AM-*Z*

Quantitative ^{1}H NMR (500 MHz, $CDCl_3$) of (*Z*)-1-(benzoyloxy)-1-octene (AM-*Z*) using 1,3,5-trimethoxybenzene after purification via column chromatography (14.8 mg product + 12.3 mg 1,3,5-trimethoxybenzene)



(*Z*)-1-(Benzoyloxy)-1-octene, ^{13}C NMR (125 MHz, $CDCl_3$)



AM-*Z*

Quantitative ^{1}H NMR (500 MHz, $CDCl_3$) of (*Z*)-1-(benzoyloxy)-1-octene (AM-*Z*) after purification via distillation using 1,3,5-trimethoxybenzene (23.7 mg product + 20.9 mg 1,3,5-trimethoxybenzene)