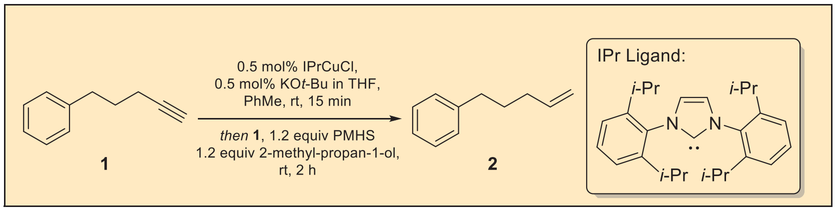
Copper-Catalyzed Semi-Reduction of Alkynes

Nick Cox,[1] Hester Dang,[2] Aaron M. Whittaker,[3] and Gojko Lalic[4]*

Department of Chemistry, University of Washington, Seattle, Washington 98195, United States

Checked by Miyu Furuta and John L. Wood



Procedure

4-Penten-1-ylbenzene (**2**). A 500 mL round-bottomed Airfree reaction flask with a 24/40 jointed neck and side-arm equipped with valve (Flask A) is charged with 20.6 g of 3 Å molecular sieves and sealed with a silicone-greased 24/40 glass stopper (Figure 1), then flame-dried under vacuum for approximately 10 min (Note 1). Flask A is then refilled with dry nitrogen, the glass stopper is replaced with a rubber septum, and Flask A is allowed to cool to room temperature. To Flask A is added a Teflon-coated magnetic stir bar (5 cm × 8 mm). Anhydrous toluene (PhMe) (128 mL) (Note 2), 4-pentyn-1-ylbenzene (**1**) (6.83 mL, 45.0 mmol, 1.00 equiv) (Note 3) and polymethylhydrosiloxane (PMHS) (3.25 mL, 54.0 mmol, 1.20 equiv of hydride) (Note 4) are added sequentially by syringe, followed by isobutanol (5.00 mL, 54.0 mmol, 1.20 equiv), also by syringe (Note 5). The contents of Flask A are stirred at 500 rpm at ambient temperature for approximately 40 min. While the solution in Flask A is stirring, a second 500 mL round-bottomed Airfree reaction flask with a 24/40 jointed neck and side-arm equipped with valve (Flask B) is charged with a Teflon-coated magnetic stir

DOI: 10.15227/orgsyn.093.0385
Published on the Web 11/9/2016

Figure 1. Apparatus Assembly for Flask A

bar (5 cm × 8 mm) and sealed with a silicone-greased 24/40 glass stopper, then flame-dried under vacuum. Flask B is then refilled with dry nitrogen, the glass stopper is replaced with a rubber septum, and Flask B is allowed to cool to room temperature. To Flask B is added chloro[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]-copper(I) (IPrCuCl) (109 mg, 0.22 mmol, 0.0050 equiv). Anhydrous PhMe (16 mL) and potassium *tert*-butoxide (KO*t*-Bu) (as 1 M solution in THF, 230 µL, 0.23 mmol, 0.0050 equiv) are added sequentially by syringe (Note 6). The contents of Flask B are stirred at 300 rpm at ambient temperature for 5 min, at which point the solution transitions from a slightly cloudy suspension to a clear, colorless solution (Figure 2). Additional anhydrous PhMe (16 mL) is added by syringe, and the contents of Flask B are allowed to stir for an additional 15 min. At this point, the stir rate of flask B is increased to 500 rpm, and the solution from Flask A is transferred over 10 min via cannula to Flask B. The resultant mixture undergoes a small amount of foaming and changes from a yellow to an ash color (Figure 3). The sieves that remain in Flask A are then rinsed several times with anhydrous PhMe (4 x 16 mL), transferring the solvent to Flask B by cannula after each rinse. The stir rate is increased to 700 rpm, and the contents of Flask B are allowed to stir at ambient temperature for 70 min, at which point the alkyne (**1**) is completely consumed based on GC analysis (Note 7).

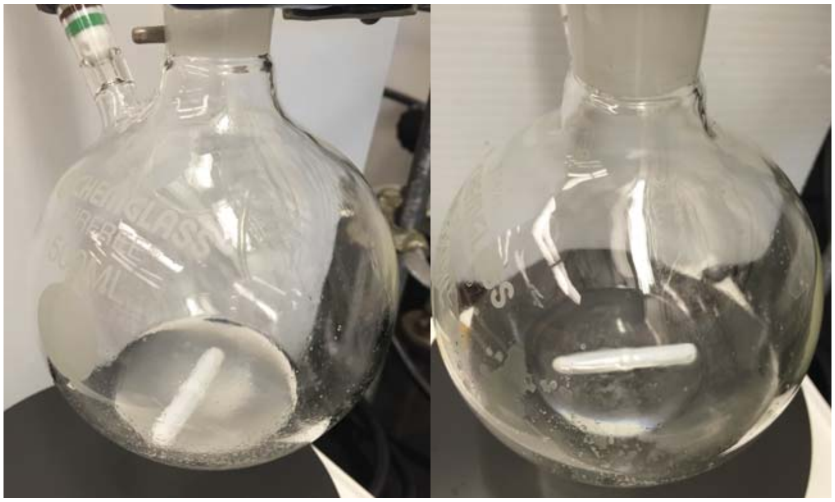


Figure 2. Color Transition Observed in Flask B

Figure 3. Addition of the solution of Flask A to Flask B

Filtration through silica gel is used to remove copper salts from the crude reaction products. A 60 mL Büchner filter funnel with a coarse frit is placed atop a 500 mL round-bottomed flask and packed with celite (1 cm) and then 30 g of silica gel (Note 8). The contents of Flask B are vacuum-filtered through the silica gel plug, which is then rinsed with 200 mL of hexanes. The flask is charged with a Teflon-coated magnetic stir bar (5 cm × 8 mm), and connected to a distillation head equipped with a 6 cm Vigreux column and a 1 L round-bottomed collection flask (Figure 4). The filtrate is concentrated to a volume of approximately 15 mL (Note 9 and 10).


Figure 4. Concentration of the filtrate

The remaining residue is transferred to a 25 mL round-bottomed flask via pipette and the flask was rinsed with hexanes (2 x 3 mL). The 25 mL flask containing the product is equipped with a Teflon-coated magnetic stir bar (2.5 cm × 1 cm), a short path distillation apparatus and a 10 mL pear-shaped collection flask (Figure 5). Distillation (Note 11) is carried out under reduced pressure (20 mmHg) to afford compound (**2**) (5.60 g, 85%) (Note 12) as a clear, colorless liquid (Note 13 and 14).

Figure 5. Distillation apparatus and pure final products

Notes

1. The submitters note that gently agitating the sieves by manually swirling the flask over the flame facilitates the removal of residual moisture. Heating was continued until the pressure in the vacuum line dropped below 0.05 mmHg.
2. The Submitters purchased anhydrous toluene (99.8%) in a Sure/Seal™ bottle from Sigma-Aldrich and used it as received. The Checkers used toluene (99.9%), purchased from EMD Millipore and passed it through a purification column (Glass Contour Solvent Systems by SG Water, USA) immediately prior to use.
3. 4-Pentyn-1-ylbenzene (98%) was purchased from GFS Chemicals and used as received.
4. PMHS was purchased from Acros Organics and used as received. The yellow color observed after addition of PMHS results from the formation of copper hydride. The Submitters found foaming is likely due to the formation of hydrogen gas, which can result from a reaction between copper hydride and residual moisture present in the reaction mixture.
5. Isobutanol, anhydrous (99.5%), was purchased from Sigma-Aldrich and used as received.

6. IPrCuCl (98%) was purchased from Strem Chemicals and used as received. The Submitters found this complex can be stored on the bench at ambient temperature and can be handled in air. KO*t*-Bu (1.0 M solution in THF) was purchased from Sigma-Aldrich and used as received.
7. GC analysis: The Submitters performed this analysis on a Shimadzu GC-2010 with a flame ionization detector and a SHRXI-5MS column (15 m x 0.25 mm x 0.25 μm). Temperature program: 60 °C hold 2 min, ramp to 160 °C at 13 °C/min, ramp to 250 °C at 30 °C/min, hold 5.50 min; $t_R(\mathbf{1})$ = 5.71 min, $t_R(\mathbf{2})$ = 5.40 min. The Checkers used an Agilent Technologies 7820A with flame ionization detector and an Agilent HP-5MS column (30 m x 0.25 mm x 0.25 μm). Temperature program: 60 °C hold 2 min, ramp to 160 °C at 13 °C/min, ramp to 250 °C at 30 °C/min, hold 5.50 min; $t_R(\mathbf{1})$ = 8.00 min, $t_R(\mathbf{2})$ = 7.69 min.
8. The Submitters purchased Celite 545 from J.T. Baker and used it as received. Silica gel (60 Å pore size, 230-400 mesh) was purchased from Agela Technologies and used as received. The Checkers purchased Celite 545 from Sigma-Aldrich and used it as received. Silica gel (60 Å pore size, 230-400 mesh) was purchased from SiliCycle and used as received.
9. The distillation is carried out under reduced pressure (61 °C/200 mmHg) with a bath temperature of 100 °C.
10. The Submitters note, at this stage, the major impurity consists of PMHS reaction byproducts, which are removed by a second silica gel filtration. The Submitters concentrated the filtrate using rotary evaporation (28 °C, 300 mmHg ramped down to 35 mmHg) to remove as much PhMe as possible. The Submitters found that for the isolation of non-polar compounds that are more mobile on silica gel than the PMHS-derived byproducts, it is essential to remove as much PhMe as possible prior to the next step of the purification sequence. The Submitters report that complete removal of PhMe can be acheived by re-suspending the crude reaction concentrate in 500 mL of hexanes and repeating the concentration using rotary evaporation (repeat if necessary). In attempting this procedure the checkers noted the loss of some product and thus employed distillation.
11. The distillation was performed as follows. Stirring was started and the pressure was gradually reduced to 20 mmHg. After vigorous bubbling due to loss of hexanes subsided, the distillation pot was heated to 105–125 °C. Two fractions were collected. The first fraction was of material

distilling from 62– 82 °C (5.16 g, 97.0% pure by QNMR). After removal of the vacuum and replacing the receiving flask, a 2nd fraction of material distilling from 82–83 °C at 20 mmHg was collected (0.44 g, 99.4% pure by QNMR) for a combined yield of 85% yield.

12. In a subsequent run it was found that collecting a single fraction distilling from 65–86 °C at 20 mmHg (bath temp. 100– 125 °C) furnished 5.56 g (84%) of product that was 97.3% pure by QNMR.
13. The Submitters performed the purification as follows: The desired alkene product (**2**) can be isolated by filtration through silica gel. A 350 mL Buchner filter funnel with a coarse frit is packed with celite (1 cm) followed by 180 g of silica gel, and then a layer of sand (1 cm). The crude reaction products are then dissolved in 33 mL of hexanes and loaded evenly over the top of the sand layer. An additional 33 mL of hexanes is used to recover remaining material from the flask, which is then poured evenly over the top of the sand layer. The silica gel plug is then washed with 1,200 mL of hexanes. The filtrate is collected in two 1 L round-bottomed flasks and concentrated using rotary evaporation (28 °C, 300 mmHg ramped down to 35 mmHg) to afford a clear, colorless liquid. Compound (**2**) is obtained in 87–92% yield (5.70–6.04 g) as a clear, colorless liquid. The purity is >99%(GC).
14. 4-Penten-1-ylbenzene (**2**) has the following properties: ^{1}H NMR (400 MHz, CD_2Cl_2) δ: 1.70 (tt, *J* = 7.7, 6.8 Hz, 2H). 2.09 (dtt, *J* = 7.7, 6.8, 1.5 Hz, 2H), 2.62 (t, *J* = 7.7 Hz, 2H), 4.97 (ddt, *J* = 10.4, 2.1, 1.5 Hz, 1H), 5.03 (ddt, *J* = 17.2, 2.1, 1.5 Hz, 1H), 5.85 (ddt, *J* = 17.2, 10.4, 6.8 Hz, 1H), 7.25–7.29 (m, 2H), 7.14-7.20 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.8, 33.4, 35.5, 114.8, 125.8, 128.4, 128.6, 138.8, 142.6. IR (neat, cm^{-1}): 3064, 3027, 2930, 2857, 1640, 1603, 1496, 1453, 1030, 991, 908, 741, 634. Elemental Analysis calculated for $C_{11}H_{14}$: C, 90.35; H, 9.65, Found: C, 90.16; H, 9.67. ESI-MS calculated for [M+H]+ 147.1168, found 147.1167. The purity was determined to be >97.0% by quantitative NMR spectroscopy with ethylene carbonate as the internal standard.

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

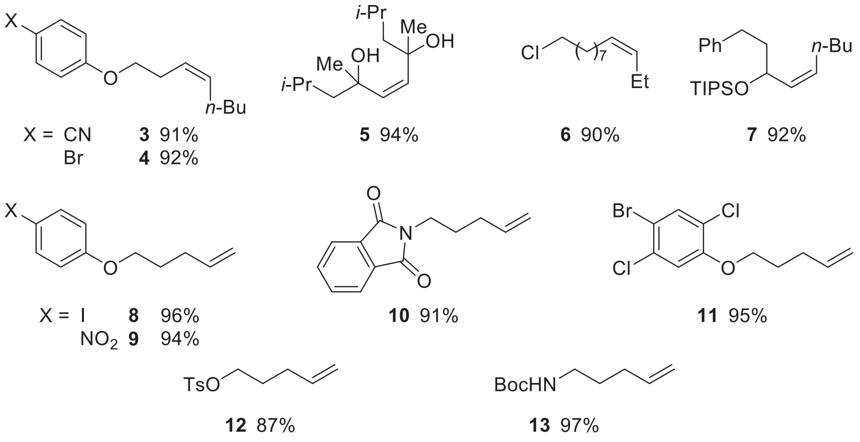
Discussion

The semi-reduction of alkynes to form alkenes is one of the most important reactions in organic chemistry. Traditional methods for achieving this transformation, such as Lindlar[5] or P-2 Nickel catalysts,[6] are complicated by a variety of factors including the E/Z isomerization of the alkene products[7] and over-reduction of the desired alkene to form alkanes.[8] These difficulties limit the practical use of these catalysts, as reactions must be carefully monitored to maximize conversion while minimizing over-reduction and isomerization. Furthermore, because the unreacted starting materials, alkene isomers, and over-reduced alkanes have very similar physical properties, purification of the desired alkene can be challenging.

Because of these complications, much effort has been devoted to the development of more selective techniques for alkyne semi-reduction. Several attempts have been made to modulate the reactivity of solid-state catalysts by using various poisons or by modifying the catalyst surface.[9] Other approaches using homogeneous catalysts have demonstrated improved selectivity using a variety of palladium,[8, 10] and copper[11] complexes in the reduction of arylacetylenes. Although significant progress has been made, these methods still suffer from one or more problems associated with isomerization, over-reduction, poor reactivity, limited functional group tolerance, the need for activating functional groups, high temperatures, or high pressures of molecular hydrogen. As a consequence, the Lindlar catalyst is still the preferred method for alkyne semi-reduction despite its drawbacks. The limitations of these methods provide motivation for the development of a convenient technique for the selective semi-reduction of alkynes that displays broad functional group compatibility with no over-reduction or isomerization.

The copper-catalyzed technique described here is an extension of previous work developed in our laboratory[12] and that of Tsuji.[11] This work is based on an earlier report by Sadighi,[13] who described the transfer of hydride from silicon to copper, and subsequent hydrocupration of an alkyne by copper hydride in a series of stoichiometric experiments. We showed that the resulting alkenyl copper species underwent protonation in the presence of a proton source to form an alkene and copper alkoxide complex. These observations led to our development of a copper-catalyzed semi-reduction of alkynes that is highly functional-group-tolerant, suffers from no over-reduction or isomerization of the alkene, and in the case of internal alkynes, is completely selective for the formation of the *Z* stereoisomer.[12a] As shown in Table 1, this approach can be used to selectively reduce both internal and terminal alkynes to the corresponding alkene in the presence of diverse functional groups, such as nitro, cyano, imide, carbamate, sulfonate, ester, silyl ether, hydroxyl, aryl iodide, aryl bromide, and alkyl and aryl chlorides. Importantly, there is no need for the alkyne to be adjacent to an activating group, no over-reduction to the alkane is detected, and the reduction of internal alkynes affords only the *Z* alkene.

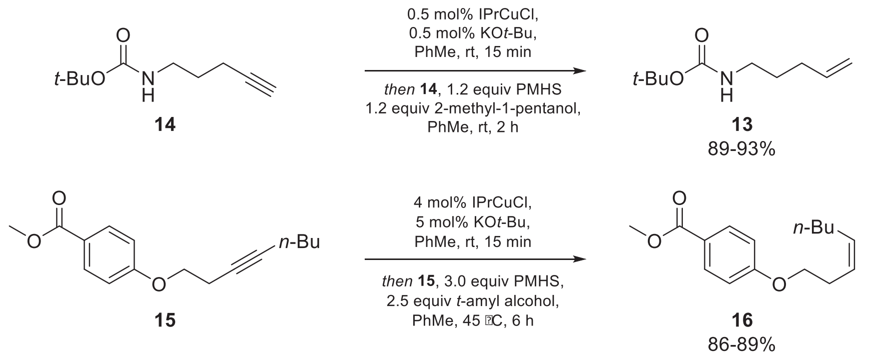
Table 1. Representative alkenes obtained from the copper-catalyzed semi-reduction of internal and terminal alkynes (previous work).



Previous conditions[12a] for internal alkyne reduction: 2.0 mol% IPrCuO*t*-Bu, 2.0 equiv PMHS, 2.5 equiv *t*-BuOH, toluene, 45 °C, 8 h. Previous conditions[12a] for terminal alkyne reduction: 0.5 mol% IPrCuO*t*-Bu, 1.2 equiv PMHS, 1.2 equiv *i*-BuOH, toluene, rt, 1 h.

Following our initial report,[12a] several additional developments have been made using NHC-Cu catalysts in the semi-reduction of alkynes. A variation using a $Cu(OAc)_2$•H_2O pre-catalyst and IPr•HCl salt was provided by Zhong,[14] which avoids the need to prepare the air-unstable IPrCuO*t*-Bu catalyst. An alkoxide-tethered NHC-Cu catalyst was developed by Teichert,[15] which enabled the efficient semihydrogenation of arylacetylenes using H_2 as the terminal reducing agent. Using a similar approach, Sawamura[16] recently described a procedure for alkyne semihydrogenation using H_2, the SIPrCuO*t*-Bu catalyst, and a NaO*t*-Bu additive. Other recent examples of alkyne semi-reduction have been reported using palladium,[17] nickel,[18] and gold[19] catalysts. A transition-metal free approach to the *E*-selective semi-reduction of diarylalkynes using Na_2S•H_2O has also been reported.[20]

Based on our initial report,[12a] we developed a more practical procedure[12b] that allows the reaction to be carried out with a commercially available pre-catalyst, without the need for an inert-atmosphere glovebox, and with an improved purification scheme that in most cases allows the desired alkenes to be isolated with two simple filtration steps (Scheme 1). IPrCuO*t*-Bu is air-sensitive and is not commercially available; this challenge has prompted study of suitable pre-catalysts in our laboratory and by Zhong.[14] We found that the active catalyst can be efficiently generated *in situ* using the commercially available IPrCuCl complex and potassium *tert*-butoxide. Although the reaction is sensitive to the presence of moisture, briefly exposing the starting materials to molecular sieves and using standard air-free techniques offers a convenient alternative to rigorously drying each reagent or using a moisture and air-free glovebox.



Scheme 1. Modified procedures for the glovebox-free semi-reduction of terminal and internal alkynes

The optimal reaction and purification conditions depend upon two factors: (1) the degree of substitution of the alkyne, and (2) the polarity of the alkene products. For the reduction of terminal alkynes, primary alcohols, such as isobutanol or 2-methyl-1-pentanol, should be used as the proton source (Scheme 1, top). For the reduction of internal alkynes, best results are achieved by increasing the catalyst loading to 4%, raising the temperature to 45 °C, and when using tertiary alcohols, such as *tert*-butanol or *tert*-amyl alcohol as the proton source (Scheme 1, bottom). With both terminal and internal alkynes, the choice of the alcohol depends on the polarity of the substrate and the purification procedure that will be used (see below).

The optimized purification scheme allows isolation the desired alkene products by two simple filtration steps in most cases. First, filtering the reaction mixture through a short plug of silica gel facilitates the removal of copper salts. After concentrating to remove toluene, filtration through a second plug of either silica gel or alumina allows for clean separation of

PMHS-derived polymer byproducts. For the semi-reduction of hydrophobic alkynes (Rf ≥ 0.3 in hexanes), more polar alcohols should be used as the proton source in the reaction: isobutanol for the reduction of terminal alkynes, and *tert*-butanol for the reduction of internal alkynes. Additionally, the second filtration step should be carried out using silica gel, as described in the Procedure section above. It should be noted that discretion should be applied in the amount of solvent used for the second filtration, as the polymer byproducts will elute following the desired alkenes.

Table 2. Summary of differences in procedure for the semi-reduction of alkynes based on substitution and polarity.

	Rf ≥ 0.3 in hexanes	Rf < 0.3 in hexanes
terminal alkyne	• 0.5 mol% catalyst • room temperature • isobutanol • 2nd filtration on silica gel	• 0.5 mol% catalyst • rt • 2-methyl-1-pentanol • 2nd filtration on alumina
internal alkyne	• 4 mol% catalyst • 45 °C • *tert*-butanol • 2nd filtration on silica gel	• 4 mol% catalyst • 45 °C • *tert*-amyl alcohol • 2nd filtration on alumina

For the semi-reduction of alkynes bearing polar functional groups (Rf < 0.3 in hexanes), less polar alcohols should be used as the proton source in the reaction: 2-methyl-1-pentanol for terminal alkynes, and *tert*-amyl alcohol for the reduction of internal alkynes. Additionally, the second filtration should be performed using alumina. We speculate that under these conditions, the resulting PMHS-derived byproducts are significantly more mobile on alumina than the desired alkene products, allowing for improved separation. Although slightly different protocols are used depending upon substitution and polarity of the alkyne, these adjustments do not significantly affect the procedure for reaction setup or purification. For clarity, these differences are summarized in Table 2.

In summary, these procedures offer a convenient and inexpensive method for the semi-reduction of alkynes to alkenes that is compatible with a wide variety of functional groups. These reactions reach full conversion without any over-reduction of the alkene to the alkane, avoiding the need for careful monitoring of reaction progress. In the case of internal alkynes, the semi-reduction is completely *Z*-selective and no isomerization is detected. Finally, this transformation can be achieved using commercially available reagents without the need for a glovebox, and the products can be easily isolated by filtration through silica or alumina.

References

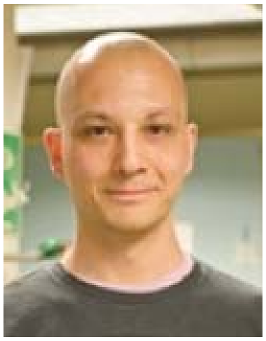
1. Stanford ChEM-H, Stanford University, Stanford, California 94305, United States.
2. Department of Chemistry, Yale University, New Haven, Connecticut, 06520, United States.
3. Department of Process Chemistry, Merck & Co. Inc, Rahway, New Jersey 07065, United States.
4. Department of Chemistry, University of Washington, Seattle, Washington, 98195, United States. Email: lalic@chem.washington.edu, Phone (206) 616-8493. Funding by NSF is gratefully acknowledged (CAREER Award #1254636).
5. (a) Lindlar, H. *Helv. Chim. Acta* **1952,** *35*, 446–450; (b) Lindlar, H.; Dubuis, R. *Org. Synth. Coll.* **1973,** *5*, 880.
6. (a) Brown, C. A. *Chem. Commun.* **1970**, 139–140; (b) Brown, C. A.; Ahuja, V. K. *J. Org. Chem.* **1973,** *38* (12), 2226–2230.
7. (a) Ulan, J. G.; Maier, W. F.; Smith, D. A., *J. Org. Chem.* **1987,** *52* (14), 3132–3142; (b) Molnár, Á.; Sárkány, A.; Varga, M. *J. Mol. Catal. A: Chem.* **2001,** *173* (1–2), 185–221; (c) Oger, C.; Balas, L.; Durand, T.; Galano, J.-M. *Chem. Rev.* **2013,** *113* (3), 1313–1350.
8. (a) van Laren, M. W.; Elsevier, C. J. *Angew. Chem. Int. Ed.* **1999,** *38* (24), 3715–3717; (b) Kluwer, A. M.; Koblenz, T. S.; Jonischkeit, T.; Woelk, K.; Elsevier, C. J. *J. Am. Chem. Soc.* **2005,** *127* (44), 15470–15480.
9. (a) Nishio, R.; Sugiura, M.; Kobayashi, S. *Org. Biomol. Chem.* **2006,** *4* (6), 992–995; (b) Panpranot, J.; Phandinthong, K.; Sirikajorn, T.; Arai, M.; Praserthdam, P. *J. Mol. Catal. A: Chem.* **2007,** *261* (1), 29–35; (c) Dominguez-Dominguez, S.; Berenguer-Murcia, A.; Pradhan, B. K.; Linares-Solano, A.; Cazorla-Amoros, D. *J. Phys. Chem. C* **2008,** *112* (10), 3827–3834; (d) Hori, J.; Murata, K.; Sugai, T.; Shinohara, H.; Noyori, R.; Arai, N.; Kurono, N.; Ohkuma, T. *Adv. Synth. Catal.* **2009,** *351* (18), 3143–3149; (e) Weerachawanasak, P.; Mekasuwandumrong, O.; Arai, M.; Fujita, S.-I.; Praserthdam, P.; Panpranot, J. *J. Catal.* **2009,** *262* (2), 199–205;

(f) Armbrüster, M.; Kovnir, K.; Behrens, M.; Teschner, D.; Grin, Y.; Schlögl, R. *J. Amer. Chem. Soc.* **2010,** *132* (42), 14745–14747; (g) Yabe, Y.; Yamada, T.; Nagata, S.; Sawama, Y.; Monguchi, Y.; Sajiki, H. *Adv. Synth. Catal.* **2012,** *354* (7), 1264–1268.

10. (a) Hauwert, P.; Maestri, G.; Sprengers, J. W.; Catellani, M.; Elsevier, C. J. *Angew. Chem. Int. Ed.* **2008,** *47* (17), 3223–3226; (b) Drost, R. M.; Bouwens, T.; van Leest, N. P.; de Bruin, B.; Elsevier, C. J. *ACS Catalysis* **2014,** *4* (5), 1349–1357.
11. Semba, K.; Fujihara, T.; Xu, T.; Terao, J.; Tsuji, Y. *Adv. Synth. Catal.* **2012,** *354* (8), 1542–1550.
12. (a) Whittaker, A. M.; Lalic, G. *Org. Lett.* **2013,** *15* (5), 1112–1115; (b) Cox, N.; Dang, H.; Whittaker, A. M.; Lalic, G. *Tetrahedron* **2014,** *70* (27–28), 4219–4231.
13. Mankad, N. P.; Laitar, D. S.; Sadighi, J. P. *Organometallics* **2004,** *23* (14), 3369–3371.
14. Wang, G.-H.; Bin, H.-Y.; Sun, M.; Chen, S.-W.; Liu, J.-H.; Zhong, C.-M. *Tetrahedron* **2014,** *70* (12), 2175–2179.
15. Pape, F.; Thiel, N. O.; Teichert, J. F. *Chem. Eur. J.* **2015,** *21* (45), 15934–15938.
16. Wakamatsu, T.; Nagao, K.; Ohmiya, H.; Sawamura, M. *Organometallics* **2016,** *35* (10), 1354–1357.
17. (a) Planellas, M.; Guo, W.; Alonso, F.; Yus, M.; Shafir, A.; Pleixats, R.; Parella, T. *Adv. Synth. Catal.* **2014,** *356* (1), 179–188; (b) Slack, E. D.; Gabriel, C. M.; Lipshutz, B. H. *Angew. Chem. Int. Ed.* **2014,** *53* (51), 14051–14054; (c) Verho, O.; Zheng, H.; Gustafson, K. P. J.; Nagendiran, A.; Zou, X.; Bäckvall, J. E. *Chem. Cat. Chem.* **2016,** *8* (4), 773–778; (d) Zhong, J.-J.; Liu, Q.; Wu, C.-J.; Meng, Q.-Y.; Gao, X.-W.; Li, Z.-J.; Chen, B.; Tung, C.-H.; Wu, L.-Z. *Chem. Commun.* **2016,** *52* (9), 1800–1803.
18. Richmond, E.; Moran, J. *J. Org. Chem.* **2015,** *80* (13), 6922–6929.
19. (a) Vasilikogiannaki, E.; Titilas, I.; Vassilikogiannakis, G.; Stratakis, M. *Chem. Commun.* **2015,** *51* (12), 2384–2387; (b) Wagh, Y. S.; Asao, N. *J. Org. Chem.* **2015,** *80* (2), 847–851; (c) Liang, S.; Hammond, G. B.; Xu, B. *Chem. Commun.* **2016,** *52* (35), 6013–6016.
20. Chen, Z.; Luo, M.; Wen, Y.; Luo, G.; Liu, L. *Org. Lett.* **2014,** *16* (11), 3020–3023.

Appendix
Chemical Abstracts Nomenclature (Registry Number)

Chloro[1,3-bis(2,6-di-i-propylphenyl)imidazol-2-ylidene]copper(I);
(578743-87-0)
Isobutanol (2-methyl-1-propanol); (78-83-1)
4-Pentyn-1-ylbenzene (1823-14-9)
Potassium *tert*-butoxide; (865-47-4)
Polymethylhydrosiloxane; (9004-73-3)



Gojko Lalic grew up in Belgrade, Serbia where he completed his B.Sc. in chemistry. After he obtained a Ph.D. from Harvard University under the mentorship of Prof. Matthew Shair, he completed a postdoctoral fellowship with Prof. Robert Bergman at UC Berkeley. After another postdoctoral fellowship with Prof. E. J. Corey, he joined the faculty at the University of Washington as an assistant professor in fall 2008.

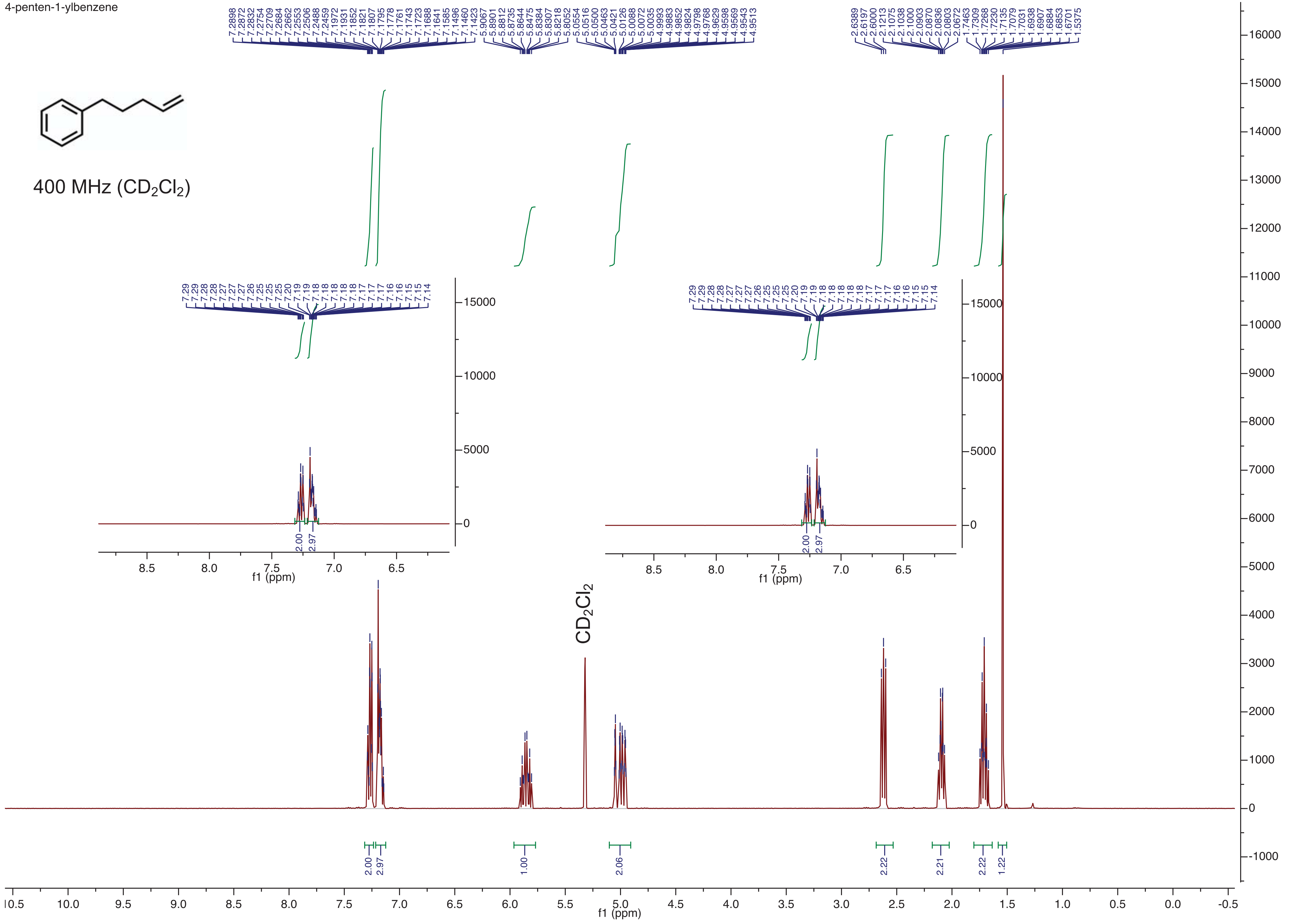
Nick Cox received his B.S. in Chemical Engineering from the University of Washington in 2007. After spending a year in industry, he returned to the University of Washington, where he completed his Ph.D. in Chemistry in 2013 under the mentorship of Professor Gojko Lalic. Nick is currently working as a postdoctoral scholar in medicinal chemistry at Stanford ChEM-H under the supervision of Professor Chaitan Khosla.

Hester Dang received her B.S. in Chemistry from Syracuse University in 2009. In 2010, she joined the University of Washington to pursue her Ph.D. in chemistry. As a member of Professor Gojko Lalic's group, she developed and investigated metal-catalyzed reactions. In the summer of 2016, Hester received her Ph.D. and has joined Seth Herzon's group as postdoctoral fellow at Yale University.

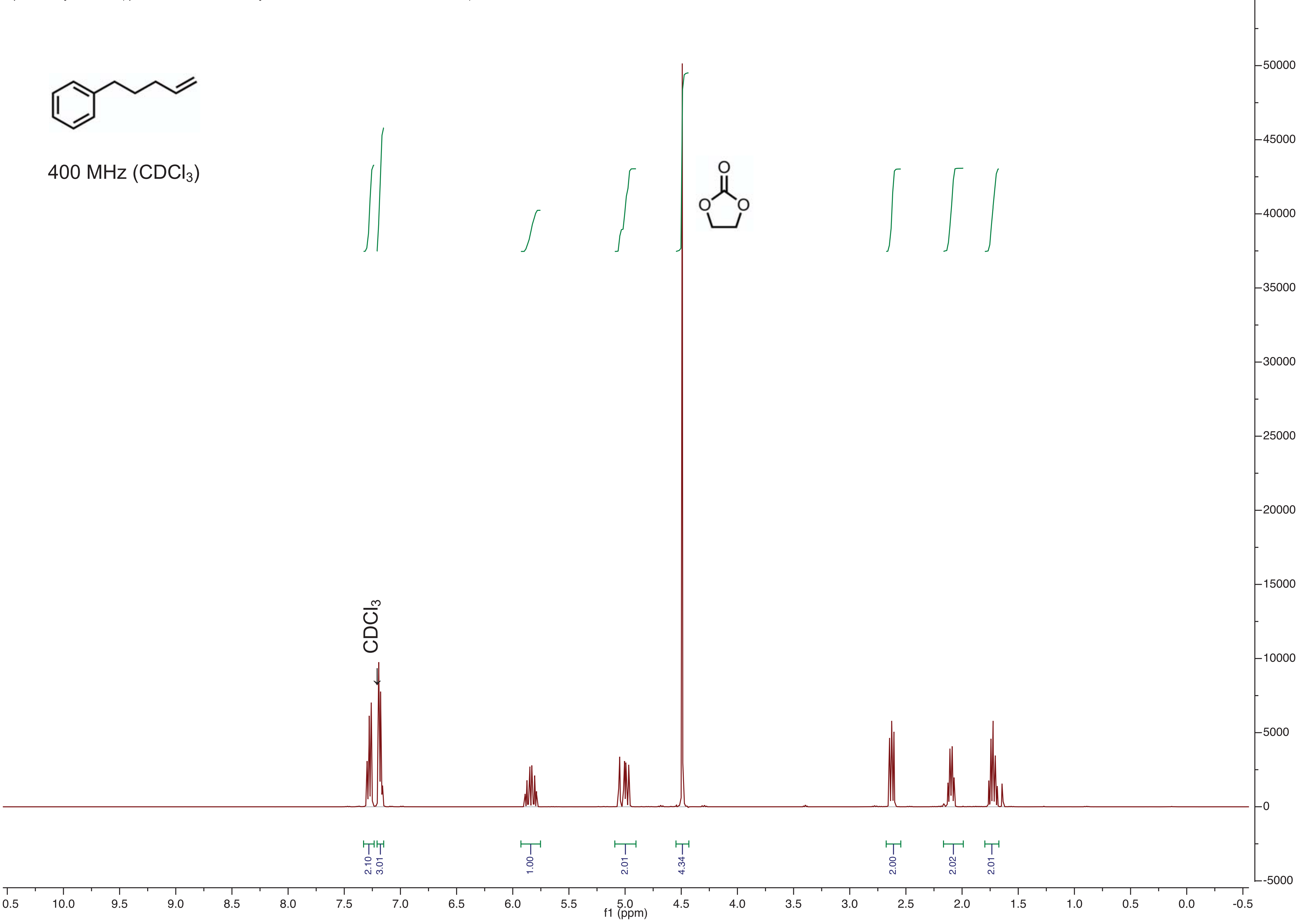
Aaron Whittaker received his B.S. from Northern Arizona University in 2008 where he studied the toxicity of depleted uranium under the supervision of Prof. Diane Stearns. He then moved to the University of Washington to develop copper-catalyzed transformations with Prof. Gojko Lalic where he received his Ph.D. in 2013. Aaron then did postdoctoral research on nickel catalyzed transfer hydrogenations with Prof. Vy Dong. He is currently a Senior Scientist in the Process Chemistry department at Merck Research Laboratories.

Miyu Furuta received her B.S. degree (2012) and her Ph.D. degree (2016) from Keio University under the direction of Professor Takeshi Sugai. She is a JSPS research fellow from 2015 and currently a post-doctoral fellow in the laboratory of Professor John L. Wood at Baylor University.

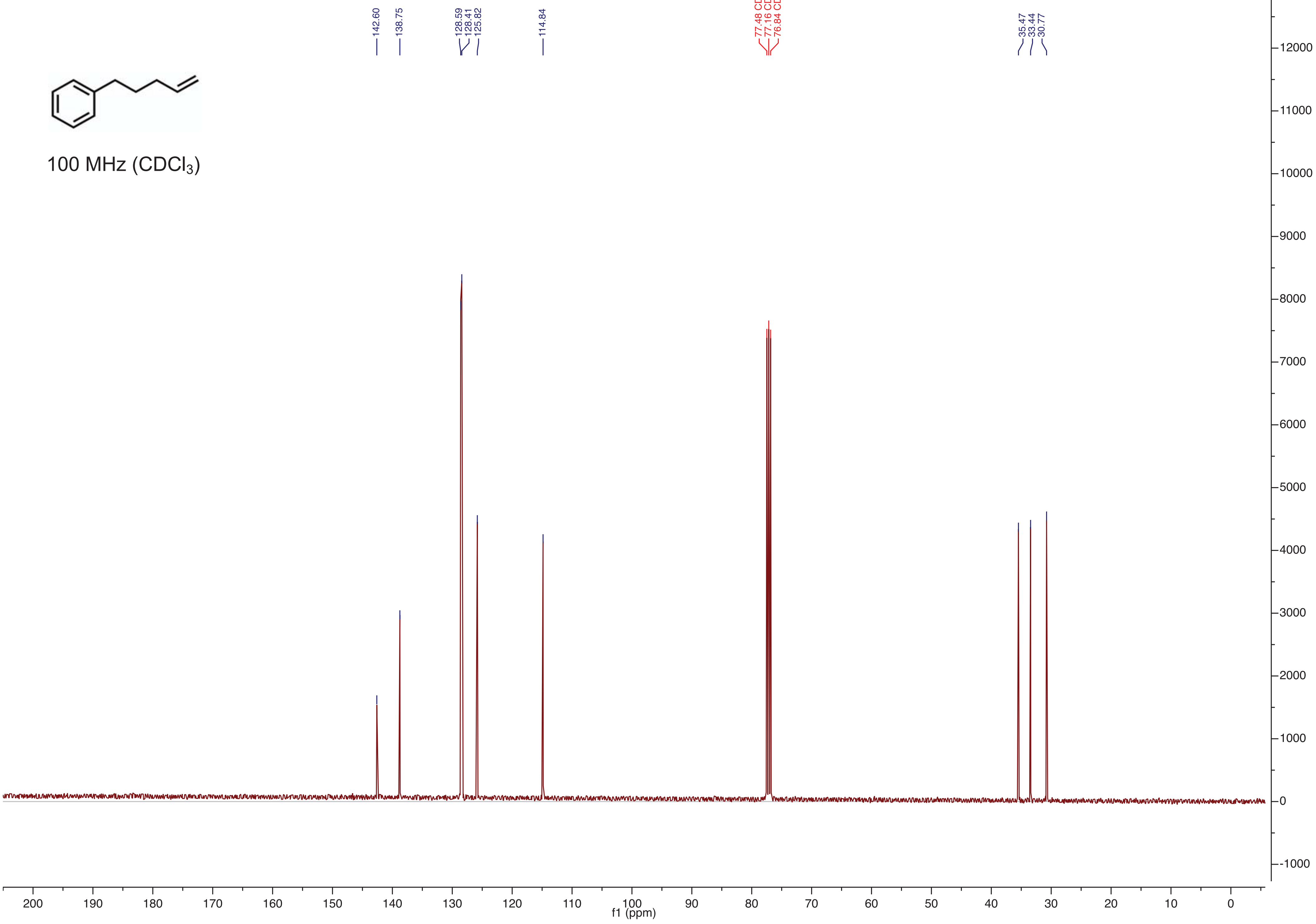
4-penten-1-ylbenzene



4-penten-1-ylbenzene (quantitative NMR with ethylene carbonate as the internal standard)



4-penten-1-ylbenzene



100 MHz (CDCl$_3$)