

Supplementary Information for:

Ethylene-promoted vs. ethylene-free enyne metathesis

*Anne G. D. Grotevendt, Justin A. M. Lummiss, Melanie L. Mastronardi, Deryn E. Fogg**

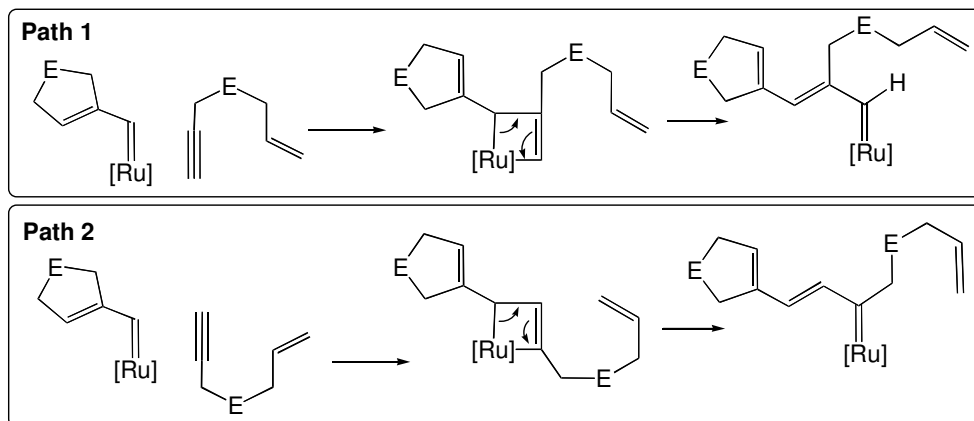
Center for Catalysis Research & Innovation, and Department of Chemistry, University of
Ottawa, Ottawa ON, Canada K1N 6N5

Table of Contents:

- 1a.** Possible isomers of **Ru-B**.
- 1b.** Atom-economy in enyne metathesis via the yne-first mechanism.
- 2.** Rate profiles for RCEYM reactions.
- 3.** General experimental procedures.
- 4.** Synthesis and characterization data for new compounds.
- 5.** ^1H and ^{13}C NMR spectra.
- 6.** References.

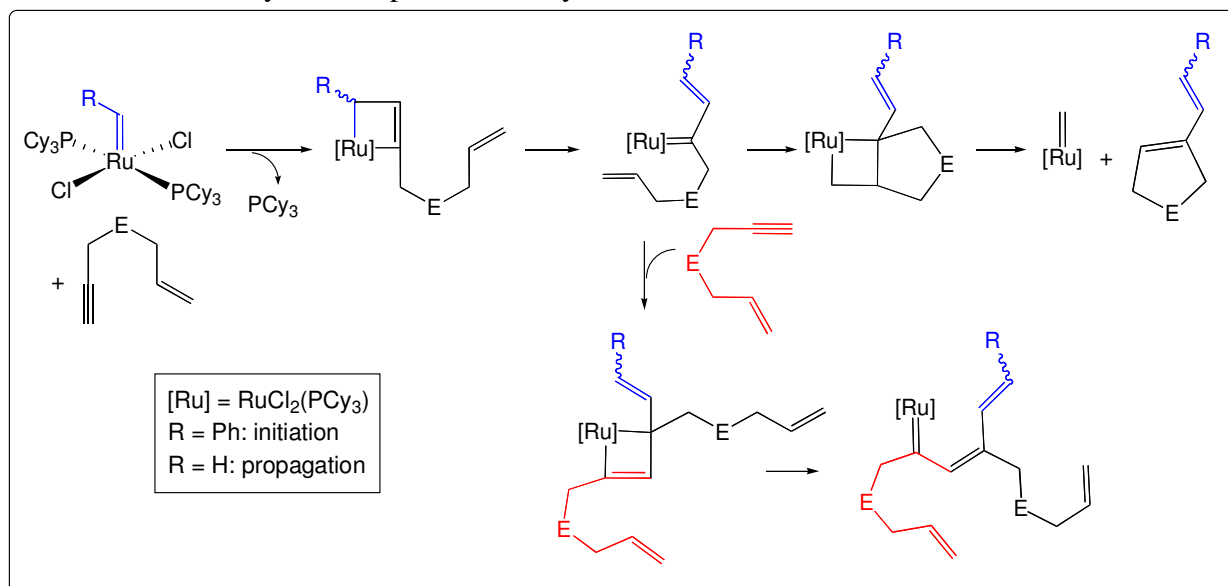
1a) Possible isomers of Ru-B. Two isomers can be anticipated for the intermediate **Ru-B** shown in Scheme 2a of the paper, depending on the orientation by which incoming alkyne approaches the metal centre for 2+2 cycloaddition. As shown in **Scheme S1** below, these result in positioning of the acetylenic end of the alkyne α (Path 1) or β (Path 2) to Ru in the metallacyclobutene intermediate. We chose to depict the latter in Scheme 2a, given the absence of new alkylidene signals in the ^1H NMR spectrum at early stages of reaction of **1a**.

Scheme S1. Orientation of incoming alkyne in cycloaddition via the ene-first mechanism.



1b) Atom-economy in enyne metathesis via the yne-first mechanism. Scheme 2b in the paper depicted an abbreviated version of the initiation step in RCEYM via the yne-first mechanism. This is expanded in **Scheme S1** below, which explicitly shows the atom-efficiency of initiation via this mechanism. This contrasts with the loss of ethylene required for the ene-first mechanism (shown in Scheme 2a of the paper).

Scheme S2. Expanded representation of catalyst initiation via the yne-first mechanism, showing full atom economy with respect to the enyne substrate.^a



^aNote that in the first cycle of catalysis, the benzylidene phenyl group of the Ru precatalyst is lost as a substituent on the pendant olefin of the 1,3-diene product.

2. Rate profiles for RCEYM reactions. Representative RCEYM rate profiles are shown for reactions under N₂. The single time-point data presented in Table 1 of the paper ($\pm 2.5\%$ in replicate runs) match the independently-generated rate profiles depicted below.

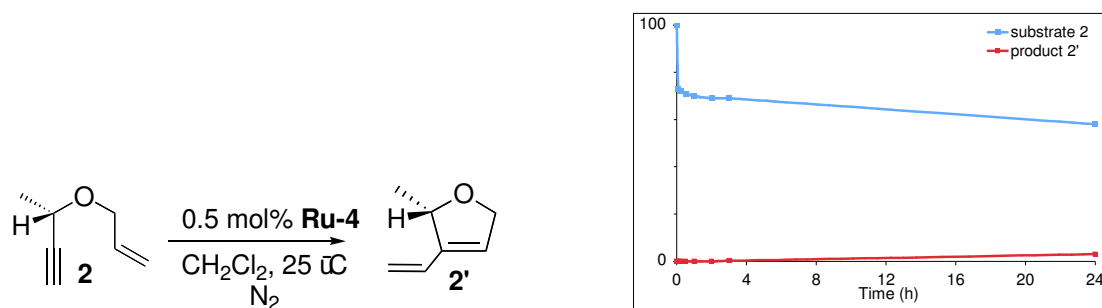


Figure S1. Rate profile for the RCEYM of substrate **2** with **Ru-4**.

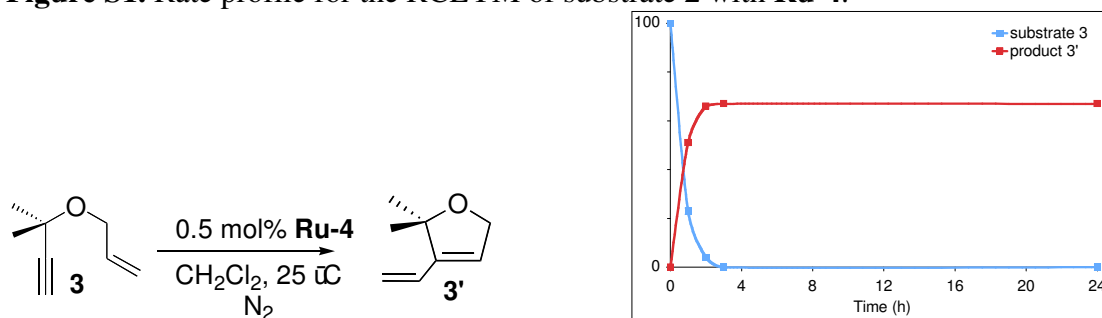


Figure S2. Rate profile for the RCEYM of substrate **3** with **Ru-4**.

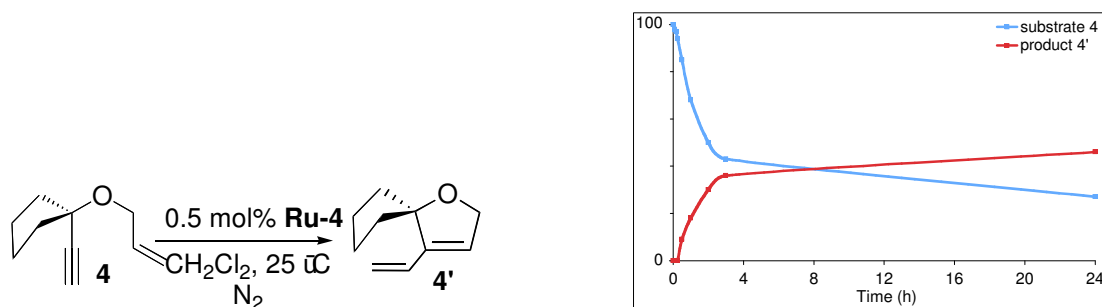


Figure S3. Rate profile for the RCEYM of substrate **4** with **Ru-4**.

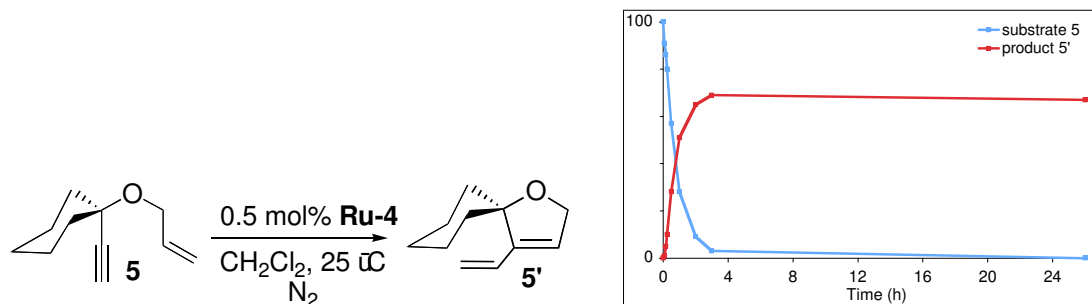


Figure S4. Rate profile for the RCEYM of substrate **5** with **Ru-4**.

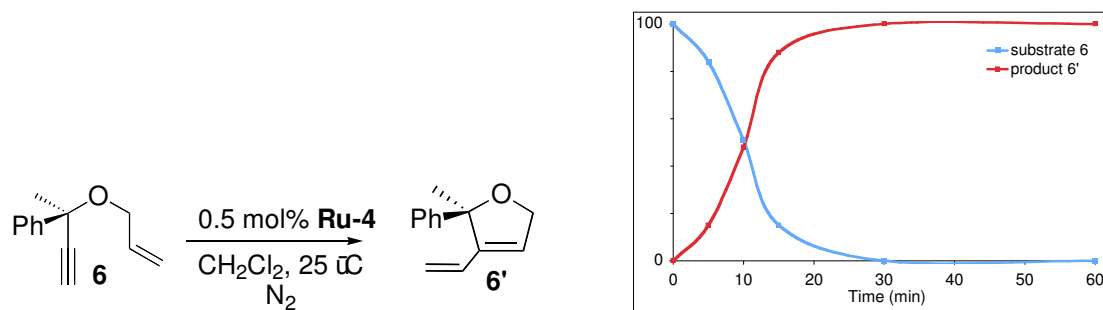


Figure S5. Rate profile for the RCEYM of substrate **6** with **Ru-4**.

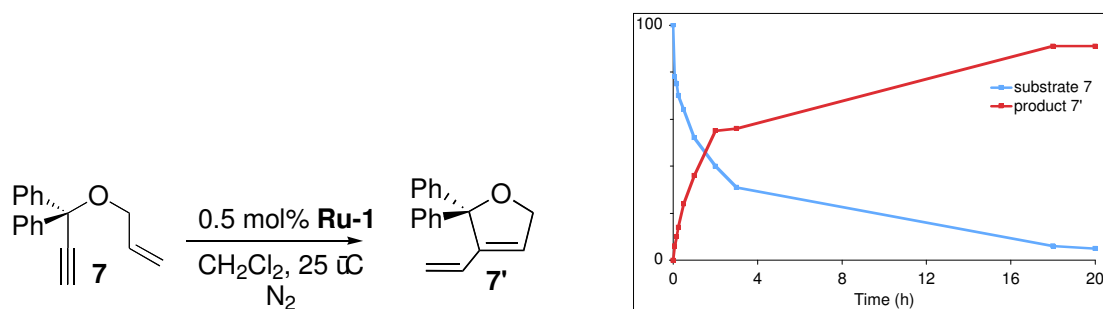


Figure S6. Rate profile for the RCEYM of substrate **7** with **Ru-1**.

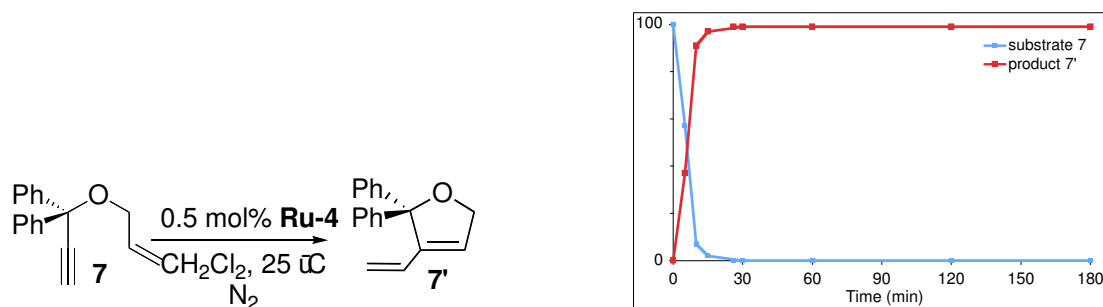


Figure S7. Rate profile for the RCEYM of substrate **7** with **Ru-4**.

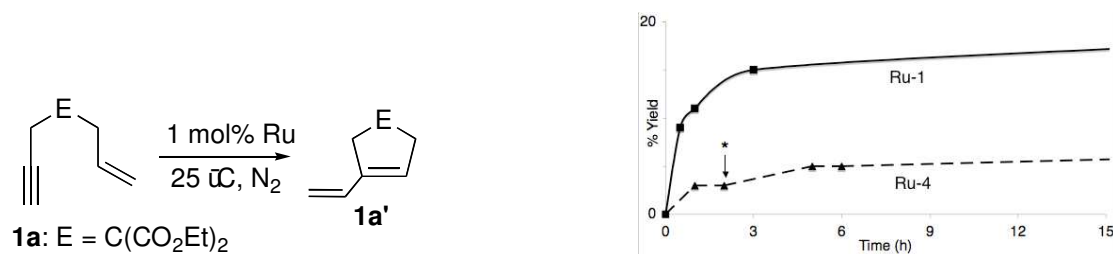


Figure S8. Rate profiles for RCEYM of **1** with **Ru-1** (CH_2Cl_2) and **Ru-4** (C_6H_6). At 2 h, the reaction of **Ru-4** had plateaued; it was re-initiated by adding a further 1 mol % **Ru-4**.

3. General Experimental Procedures. Substrate syntheses were carried out under N₂ using standard Schlenk techniques. RCEYM reactions were carried out at ambient temperature in a glovebox, in sealed Schlenk tubes under C₂H₄ or N₂, in solutions pre-saturated with the headspace gas. Dry, oxygen-free solvents were obtained using a Glass Contour solvent purification system, and stored over Linde 4Å molecular sieves. CDCl₃ was distilled over CaH₂ and stored over activated sieves (Linde 4Å). Linde Grade 3 ethylene (>99.9% purity) was used as received. Pyrene (99%), decane (anhydrous, ≥99%), chloroform-d (99.8%), and acetone-d₆ (99.9%) were purchased from Aldrich and used as received. Literature methods were used to prepare catalysts **Ru-1**¹ and **Ru-4**,² and enynes **1a**,^{3,4} **1b**,^{5,6} **1c**,^{7,8} and **5-7**.⁹ Enynes **2-4** and **8** were prepared following the general procedure used for **1c**.^{7,9}

NMR spectra were recorded on Bruker Avance 300, 400, and 500 spectrometers, at 296 K unless otherwise specified. Chemical shifts are reported relative to TMS (¹³C, ¹H) at 0 ppm, and were referenced to the carbon or residual proton signal of the deuterated solvent. Microanalyses were carried out by Guelph Chemical Laboratories (Guelph, ON). Charge-transfer MALDI-TOF mass spectra were collected using a Bruker Daltonics Omniflex mass spectrometer interfaced to an MBraun glovebox.¹⁰ Spectra were measured in positive reflectron mode, with the accelerating voltage held at 20 kV and laser power at the minimum level required to observe a signal. Matrix (pyrene) and analyte solutions were prepared in CH₂Cl₂ as previously described,¹⁰ at concentrations of 20 mg/mL and 1 mg/mL, respectively. Samples were mixed in CH₂Cl₂ with a matrix:analyte ratio of 8:1 by volume, and immediately spotted (1-3 µL) on the target plate using the dried-droplet method. Spectra were obtained within <5 minutes of removing the reaction aliquots. The mass spectrometer was calibrated externally before each use with *trans*-RuCl₂(dppe)₂ (calculated M⁺ *m/z* 968.11 and [M-Cl]⁺ *m/z* 933.14), using the linear fit method.

GC-FID analysis were performed on an Agilent 7890A Series GC-FID equipped with an Agilent 7683B Series autosampler and an Agilent HP-5 polysiloxane column (30 m length, 320 µm diameter), using an inlet split ration of 10:1, an inlet temperature of 250 °C, and helium (UHP grade) as the carrier gas to maintain column pressure at 11.512 psi. The FID response was maintained between 50-2000 pA, using analyte concentrations of ca. 5 mM. Retention times for enynes and diene products were confirmed with samples authenticated by GC-MS and NMR analysis. GC-FID quantification was established by constructing calibration curves of peak area vs. concentration in the relevant concentration regime, to account for the dependence on detector response for substrates, products and decane (internal standard in catalytic runs). Yields in

catalytic runs were determined from the integrated peak areas, referenced against decane and compared to the initial substrate : decane integration ratio. Low-resolution MS data, used to confirm identity of organic compounds, were collected using an Agilent 6890 Series GC equipped with an Agilent G6501-CTC autosampler, an Agilent 5975B inert XL EI/CI MSD detector, and an Agilent HP-5 column as above.

4. Synthesis and characterization data for new compounds.

Representative procedures for RCEYM. To a 25 mL Schlenk flask equipped with a magnetic stirbar was added 0.200 g of **1a** (0.84 mmol), 0.500 mL decane (internal standard) and 8.05 mL CH₂Cl₂. To this was added 3.45 mL of a stock solution of **Ru-1** (10.0 mg in 5.00 mL CH₂Cl₂) to give a final substrate concentration of 0.1 M and a catalyst loading of 1 mol %. The progress of the reaction was monitored by periodic removal of aliquots for GC-FID and/or MALDI-MS. MALDI-MS samples were analyzed immediately; GC-FID samples were immediately quenched by adding excess potassium tris(1-pyrazolyl)borohydride (>10 equiv. vs. Ru).¹¹ After 20-24 h the reaction was stopped and a final GC sample was taken. In some cases, diene products were isolated by removing the solvent and purifying by either column chromatography or distillation. Reactions under ethylene were treated similarly, but were sparged initially with C₂H₄ using a medium-frit gas dispersion tube in a septum-sealed Schlenk flask.

Representative synthesis of enynes: To a dry three-necked round bottom flask equipped with a magnetic stir bar, reflux condenser, and thermometer under N₂ was added 2.61 g of 3-butyne-2-ol (3.72 mmol) and the minimum volume of anhydrous *N,N*-dimethylformamide (DMF) required to dissolve the reagent. To a separate Schlenk tube charged with 1.00 g of sodium hydride (4.16 mmol) at -78 °C, anhydrous DMF (150 mL) was slowly added by cannula to generate a slurry. The 3-butyne-2-ol solution was likewise cooled to -78 °C, and to it was slowly added (cannula) the sodium hydride slurry. The reaction was stirred at -78 °C for ca. 90 min until gas evolution ceased, after which 4.50 g of allyl bromide (3.72 mmol) was added by syringe. The mixture was allowed to warm to room temperature, then heated to 60 °C and stirred overnight. The reaction was quenched with brine (50 mL) once complete. The product was extracted with ether, washed with brine, and dried over sodium sulfate. Removing the solvent afforded the crude product, which was purified by distillation.

2: Yield 1.30 g (32%), colorless liquid.

^1H NMR spectrum (400 MHz, CDCl_3): δ 5.91 (dddd, ^1H , $J = 17.3$ Hz, $J = 10.4$ Hz, $J = 6.3$ Hz, $J = 5.2$ Hz), 5.33-5.27 (m, ^1H , $J = 17.3$ Hz), 5.21-5.17 (m, ^1H , $J = 10.3$ Hz), 4.27-4.22 (m, ^1H), 4.19 (dq, ^1H , $J = 6.6$ Hz, $J = 2.1$ Hz), 3.99-3.93 (m, ^1H), 2.41 (d, ^1H , $J = 2.1$ Hz), 1.45 (d, 3H, $J = 6.7$ Hz). $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, CDCl_3): δ 134.5, 117.7, 83.9, 73.1, 69.8, 64.5, 22.2 (CH₃). GC-MS (EI, 70 eV): m/z 109 [M]⁺ (5), 95 (22), 79 (15), 67 (48), 53 (100).

3: Yield 0.55 g (12%), colorless liquid.

^1H NMR spectrum (300 MHz, CDCl_3): δ 5.95 (ddt, ^1H , $J = 17.2$ Hz, $J = 10.4$ Hz, $J = 5.6$ Hz), 5.33-5.26 (m, ^1H), 5.15 (ddt, ^1H , $J = 10.3$ Hz, $J = 1.8$ Hz, $J = 1.3$ Hz), 4.12-4.09 (m, 2H), 2.42 (s, ^1H), 1.49 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, CDCl_3): δ 135.5 (=CH), 116.6 (=CH₂), 86.2, 72.2, 70.3, 65.7, 28.9 (CH₃). GC-MS (EI, 70 eV): m/z 123 [M]⁺ (<1), 109 (35), 67 (100), 51 (11).

4: Yield 3.75 g (66%), colorless liquid.

^1H NMR spectrum (300 MHz, CDCl_3): δ 5.89 (ddt, ^1H , $J = 17.2$ Hz, $J = 10.5$ Hz, $J = 5.5$ Hz), 5.27-5.19 (m, ^1H), 5.11-5.06 (m, ^1H), 4.02 (ddd, 2H, $J = 5.5$ Hz, $J = 1.5$ Hz, $J = 1.5$ Hz), 2.41 (s, ^1H), 2.02-1.62 (m, 8H). $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (75 MHz, CDCl_3): δ 135.5, 116.5, 85.6, 80.3, 72.9, 66.2, 39.7, 39.7, 23.5, 23.5. GC-MS (EI, 70 eV): m/z 149 [M]⁺ (4), 135 (39), 121 (24), 107 (41), 91 (62), 79 (100), 65 (21), 53 (74).

8: Yield 0.47 g (16%) using 1-ethynyl-1-cyclohexanol and allyl bromide. Use of 1-vinyl cyclohexanol and propargyl bromide according to the same general procedure and workup gave 2.11 g (61%) of the product as a colorless liquid.

^1H NMR spectrum (400 MHz, CDCl_3): δ 5.72 (dd, ^1H , $J = 17.7$ Hz, $J = 11.0$ Hz), 5.24-5.21 (m, ^1H , $J = 11.1$ Hz), 5.21-5.17 (m, ^1H , $J = 17.7$ Hz), 3.96 (d, 2H, $J = 2.4$ Hz), 2.37 (t, ^1H , $J = 2.4$ Hz), 1.79-1.42 (m, 8H), 1.32-1.23 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, CDCl_3): δ 142.4, 115.9, 81.7, 77.5, 73.1, 50.4, 34.4 (2 x C), 25.8, 22.0 (2 x C).

Characterization of RCEYM products. Product identities were verified against literature NMR data for **1a**,¹² **1b**,¹³ **5**,⁹ **6**,¹⁴ and **7**.¹⁵ Data for others are provided below.

1c': Yield: ^1H NMR spectrum (300 MHz, CDCl_3): δ 6.58-6.48 (m, ^1H), 5.84-5.82 (m, ^1H), 5.19-5.15 (m, ^1H), 5.02-4.95 (m, ^1H), 4.77-4.69 (m, 4H). $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, CDCl_3): δ 138.5, 129.4, 124.9, 116.1, 76.0, 74.1. GC-MS (EI, 70 eV): m/z 96 $[\text{M}]^+$ (26), 67 (100), 53 (34).

2': ^1H NMR spectrum (400 MHz, CDCl_3): δ 6.48-6.39 (m, ^1H , $J = 17.9$ Hz, $J = 11.1$ Hz), 5.80-5.78 (m, ^1H), 5.18-5.14 (m, ^1H , $J = 11.1$ Hz), 5.14-5.09 (m, ^1H , $J = 17.8$ Hz), 5.09-5.03 (m, ^1H), 4.74-4.68 (m, ^1H), 4.62-4.56 (m, ^1H), 1.35 (d, 3H, $J = 6.3$ Hz). $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, CDCl_3): δ 142.8, 129.7, 124.9, 116.1, 80.9, 73.9, 21.2. GC-MS (EI, 70 eV): m/z 110 $[\text{M}]^+$ (28), 95 (32), 82 (64), 67 (100), 53 (24).

3': ^1H NMR spectrum (400 MHz, CDCl_3): δ 6.28-6.20 (m, ^1H , $J = 17.9$ Hz, $J = 11.4$ Hz), 5.30-5.25 (m, ^1H , $J = 17.8$ Hz), 5.13-5.10 (m, ^1H , $J = 11.3$ Hz), 4.55-4.53 (m, 2H), 1.94-1.64 (m, 8H). $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, CDCl_3): δ 142.6, 129.3, 124.6, 115.6, 97.6, 72.1, 37.5 (2 x C), 25.4 (2 x C). GC-MS (EI, 70 eV): m/z 150 $[\text{M}]^+$ (59), 135 (11), 121 (100), 107 (34), 91 (42), 79 (63), 66 (21), 55 (27).

4': ^1H NMR spectrum (400 MHz, CDCl_3): δ 6.29-6.21 (m, ^1H , $J = 17.9$ Hz, $J = 11.3$ Hz), 5.76 (bs, ^1H), 5.36-5.31 (m, ^1H , $J = 17.9$ Hz), 5.14-5.11 (m, ^1H , $J = 11.3$ Hz), 4.59-4.57 (m, 2H), 1.39 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, CDCl_3): δ 145.4, 129.2, 123.8, 115.6, 87.2, 72.0, 27.1 (2 x C). GC-MS (EI, 70 eV): m/z 124 $[\text{M}]^+$ (26), 109 (100), 96 (28), 81 (70), 67 (31), 55 (20).

5. ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra for Part 4.

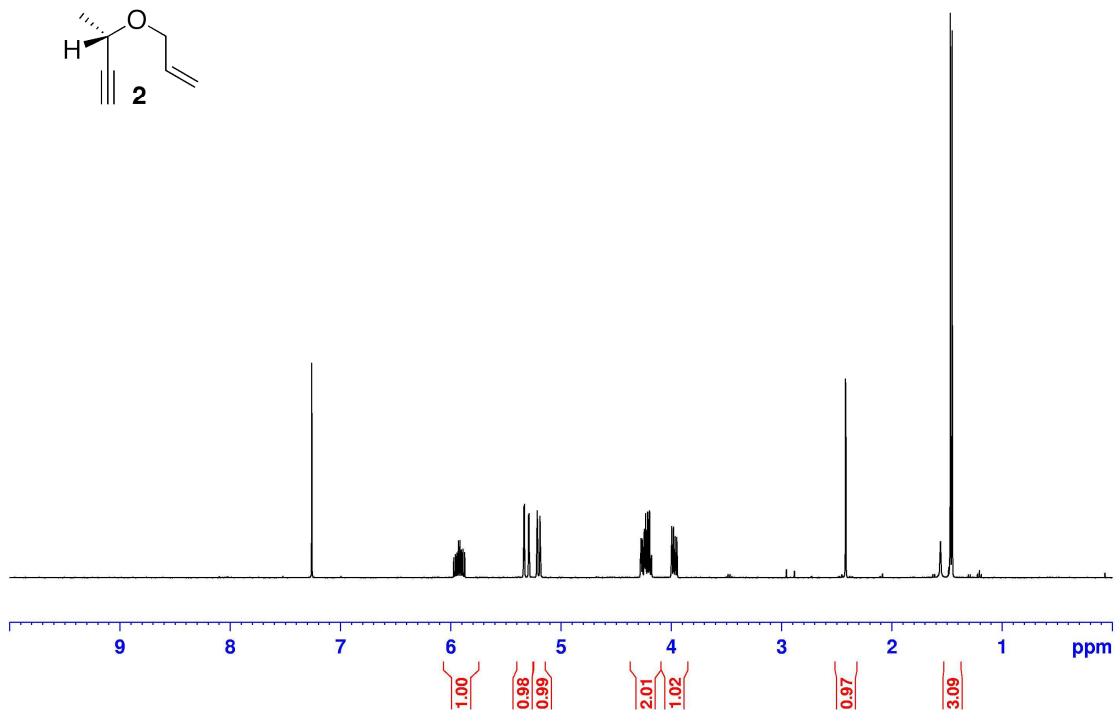


Figure S9. ^1H NMR spectrum (400 MHz, CDCl_3) for enyne **2**.

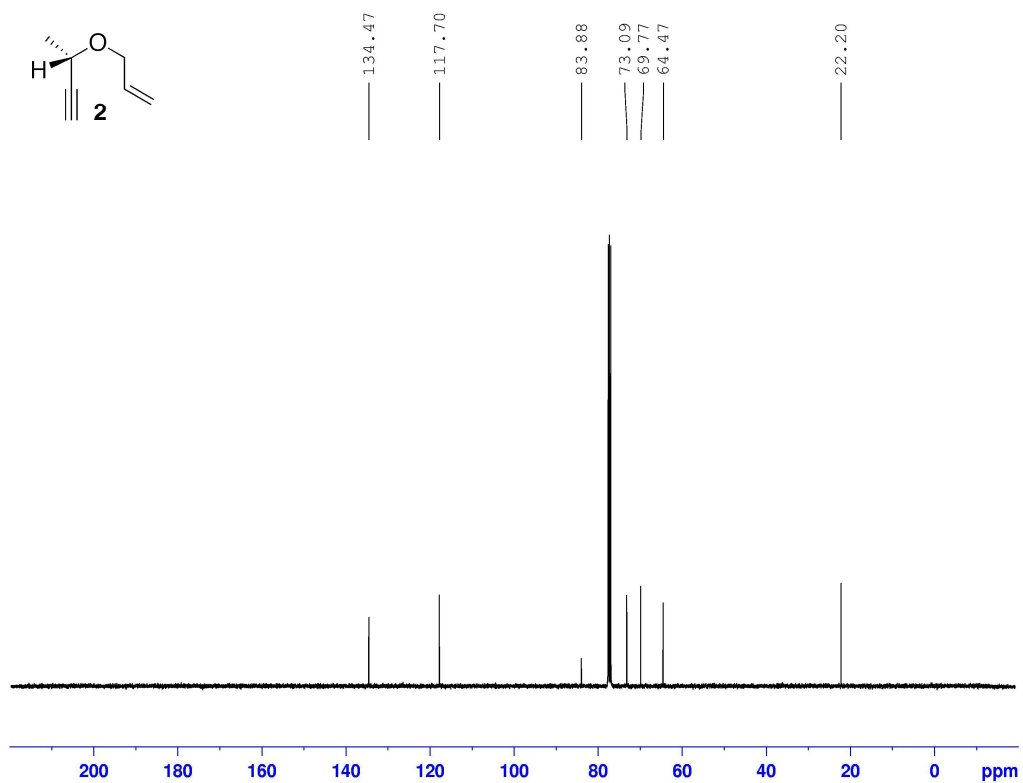


Figure S10. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, CDCl_3) for enyne **2**.

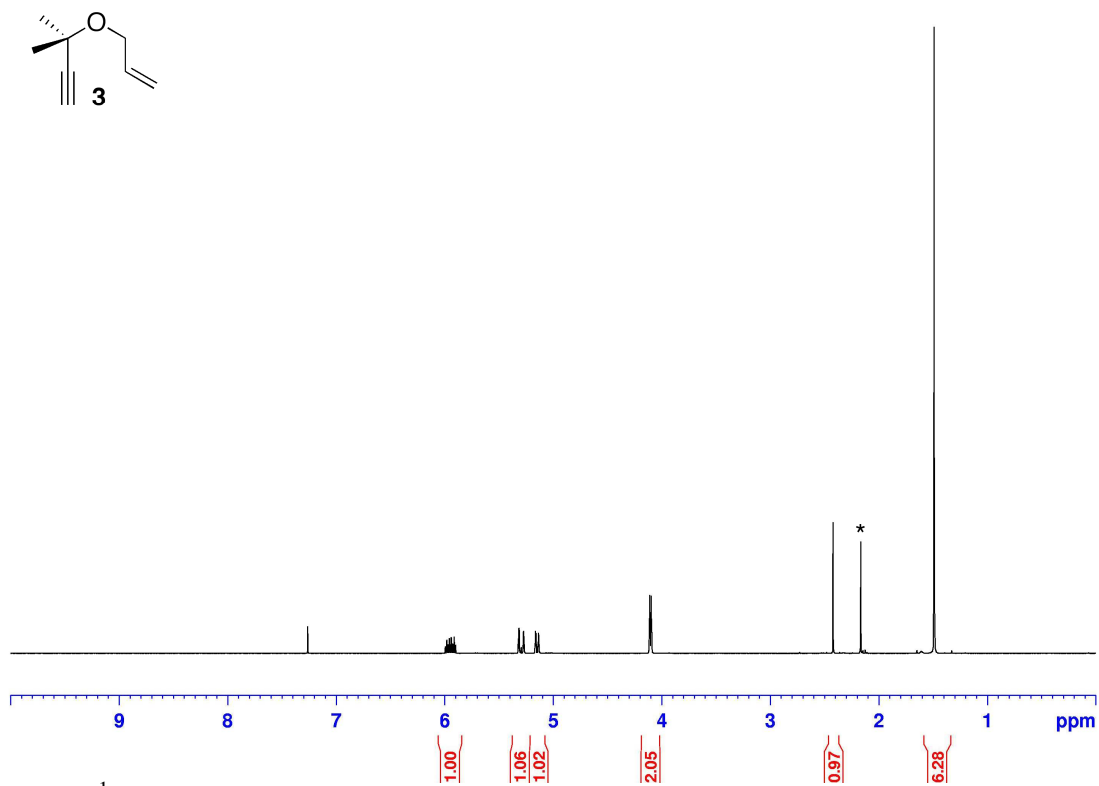


Figure S11. ¹H NMR spectrum (300 MHz, CDCl₃) for enyne **3**. Trace acetone is designated by (*).

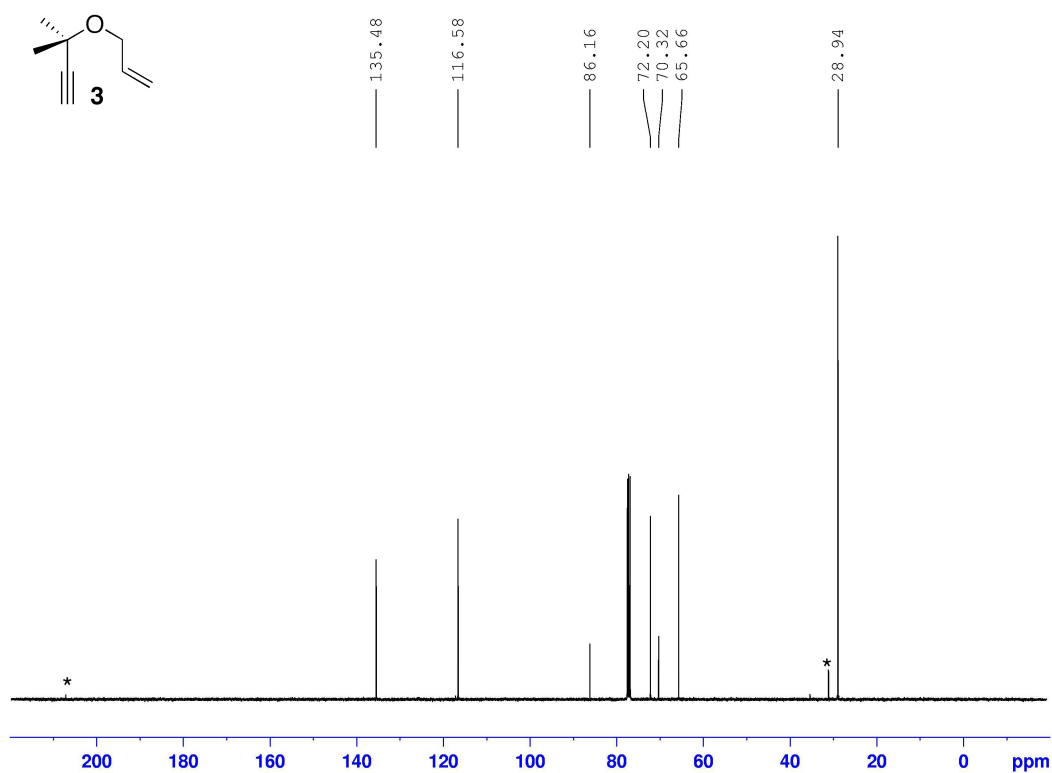


Figure S12. ¹³C{¹H} NMR spectrum (101 MHz, CDCl₃) for enyne **3**. Trace acetone is designated by (*).

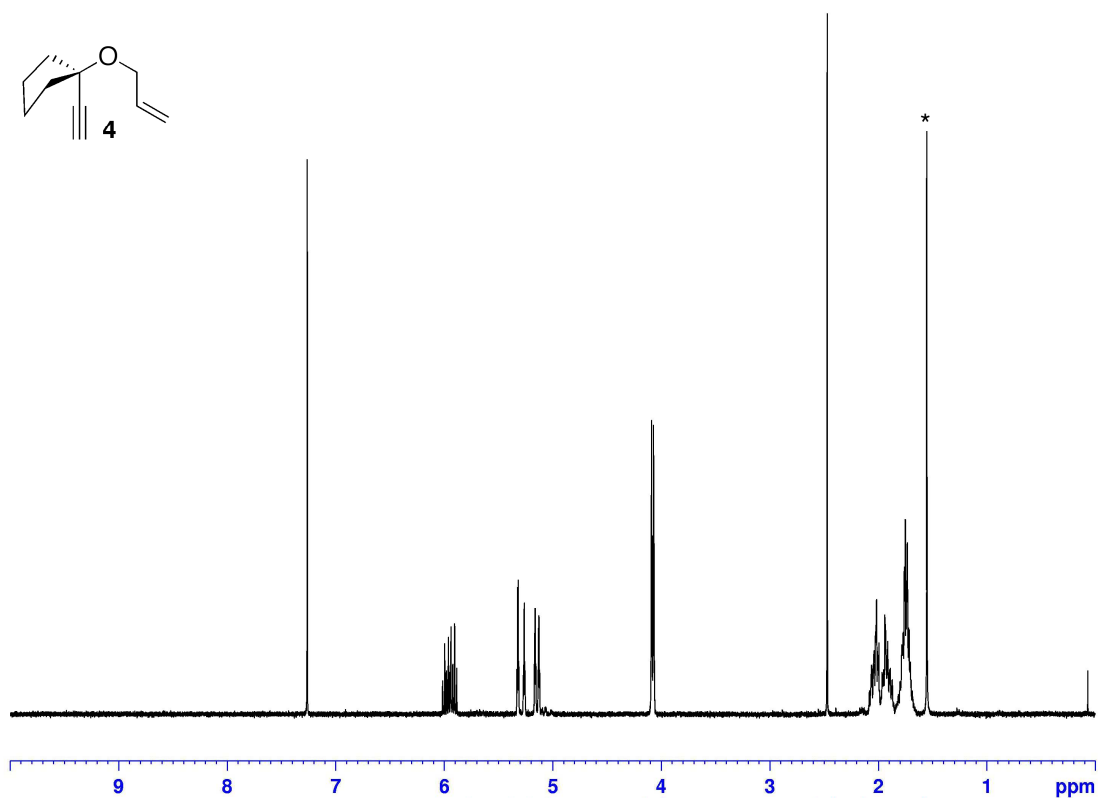


Figure S13. ^1H NMR spectrum (300 MHz, CDCl_3) for enyne **4**. Trace H_2O is designated by (*).

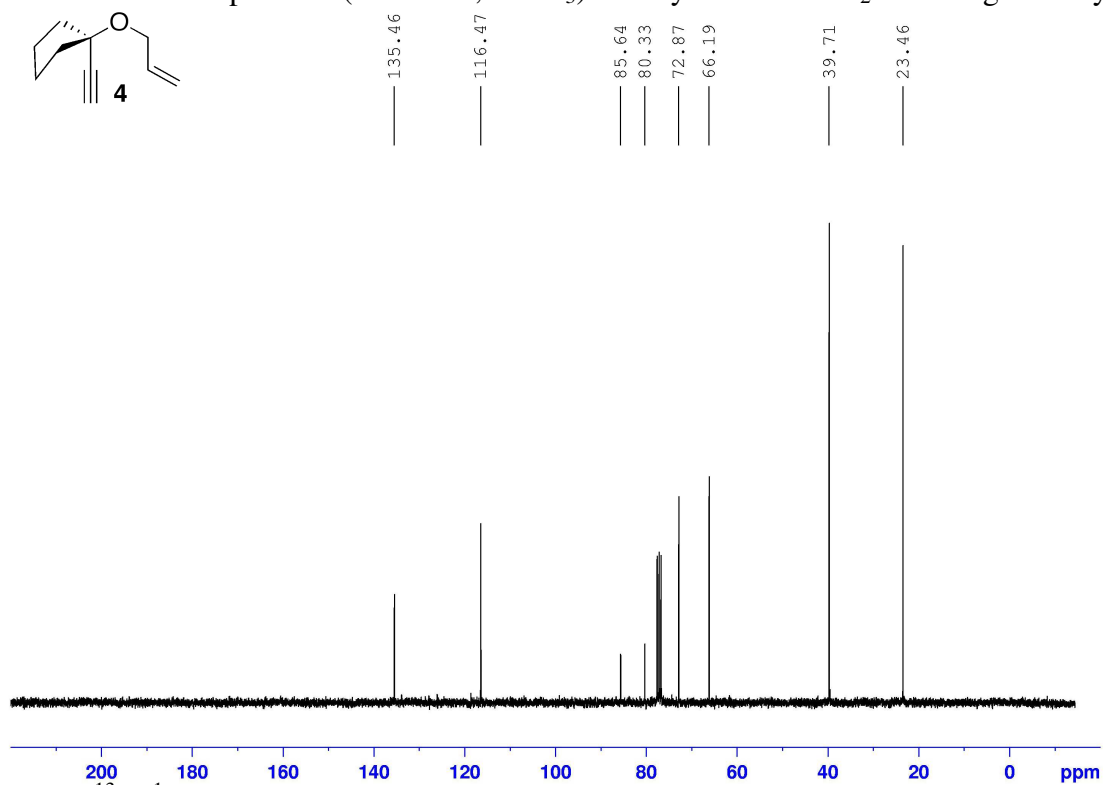


Figure S14. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (75 MHz, CDCl_3) for enyne **4**.

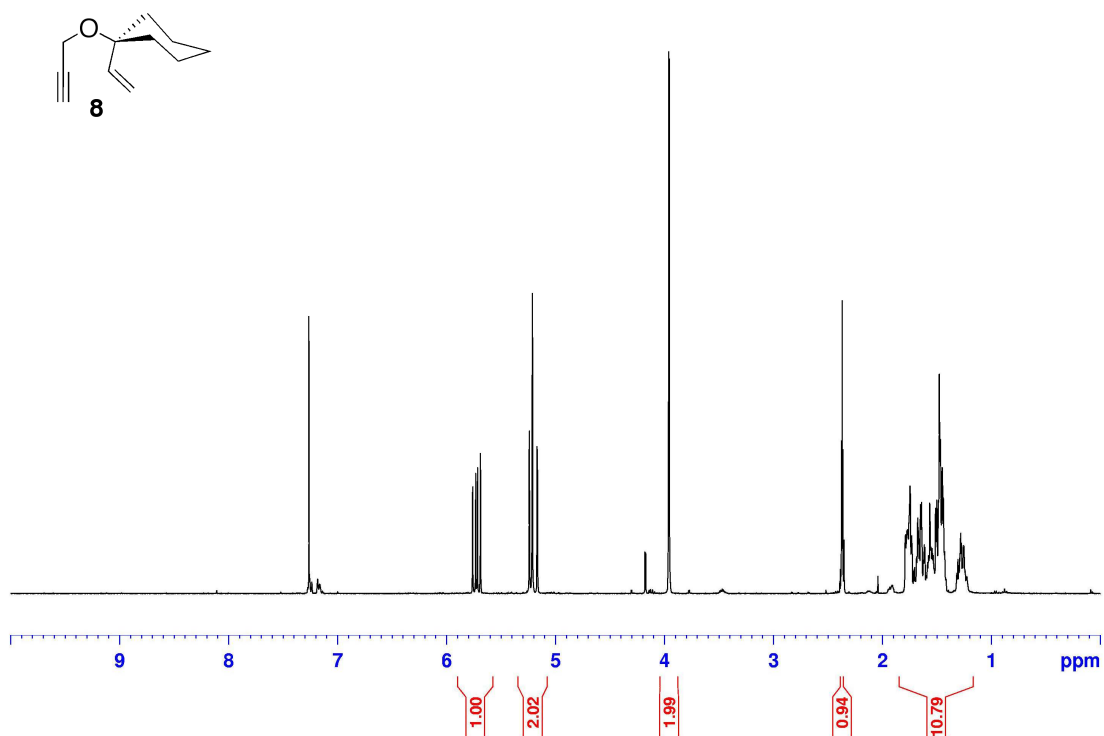


Figure S15. ¹H NMR spectrum (400 MHz, CDCl₃) for enyne **8**.

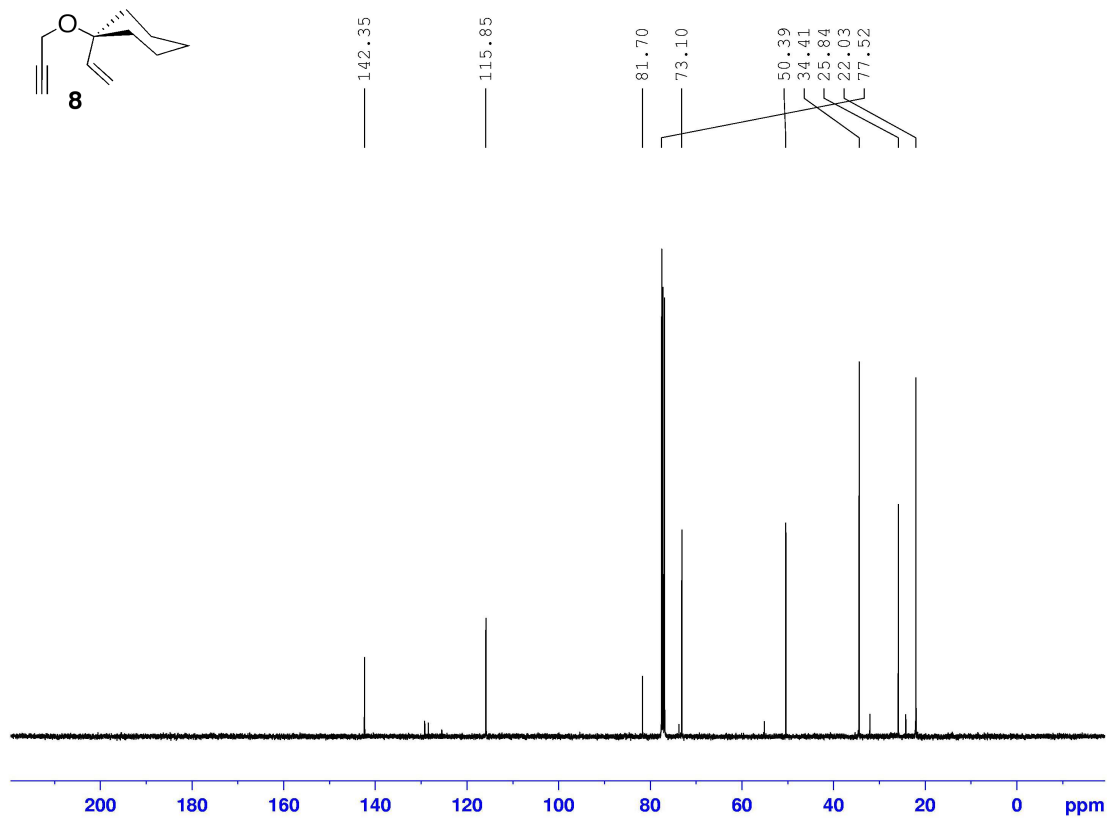


Figure S16. ¹³C{¹H} NMR spectrum (101 MHz, CDCl₃) for enyne **8**.

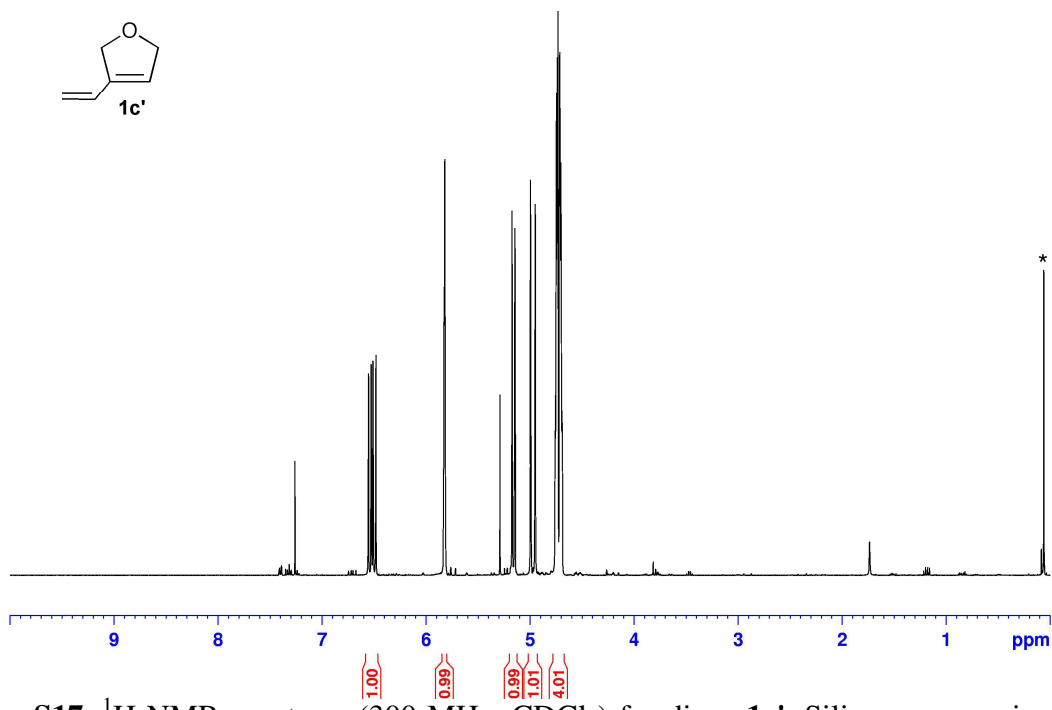


Figure S17. ¹H NMR spectrum (300 MHz, CDCl₃) for diene **1c'**. Silicone grease is designated by (*).

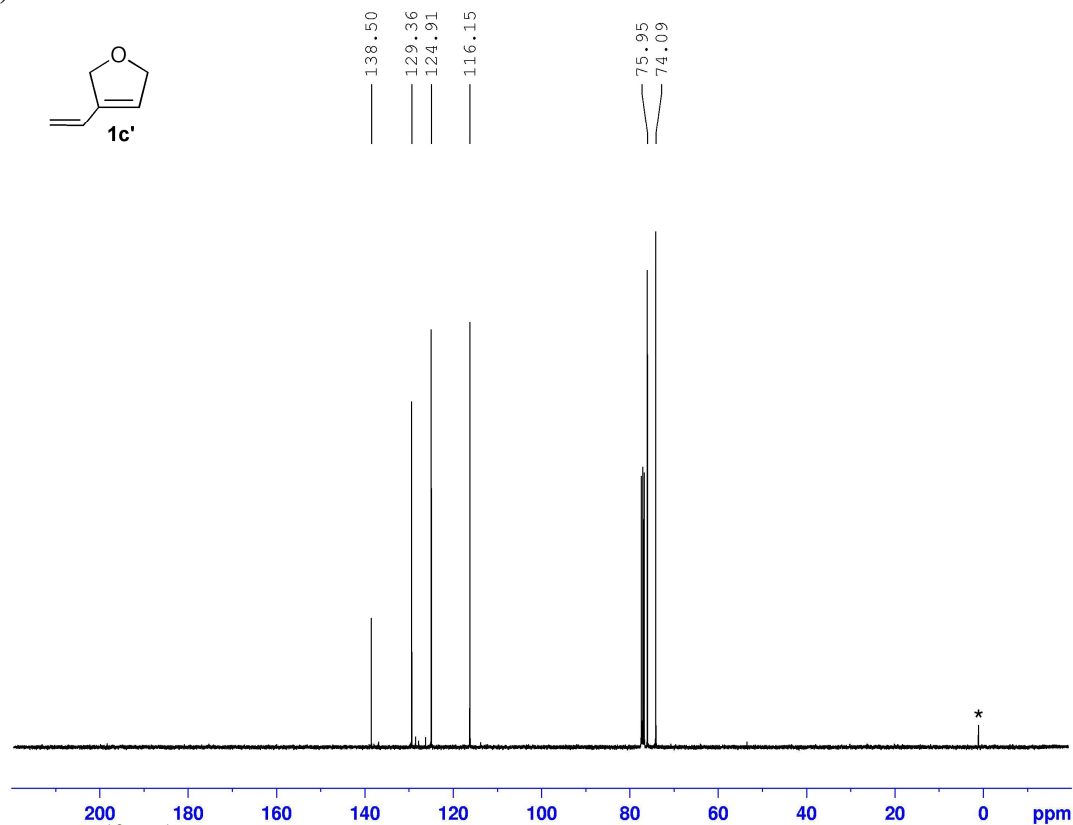


Figure S18. ¹³C{¹H} NMR spectrum (101 MHz, CDCl₃) for diene **1c'**. Trace silicone grease is designated by (*).

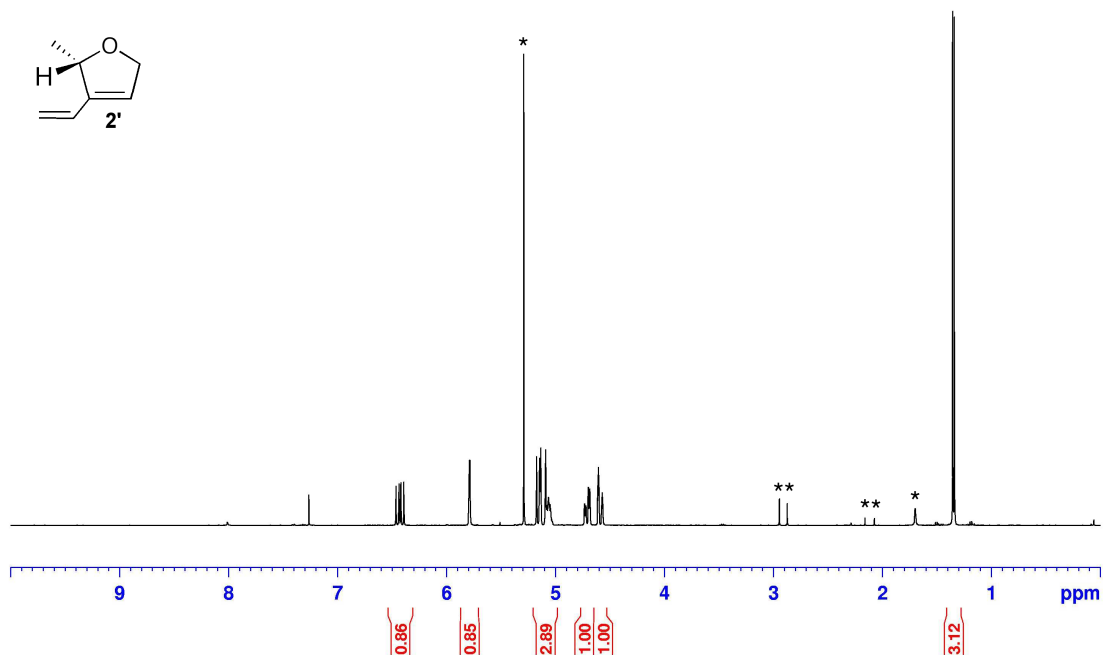


Figure S19. ¹H NMR spectrum (400 MHz, CDCl₃) for diene **2'**. Residual solvent is designated by (*).

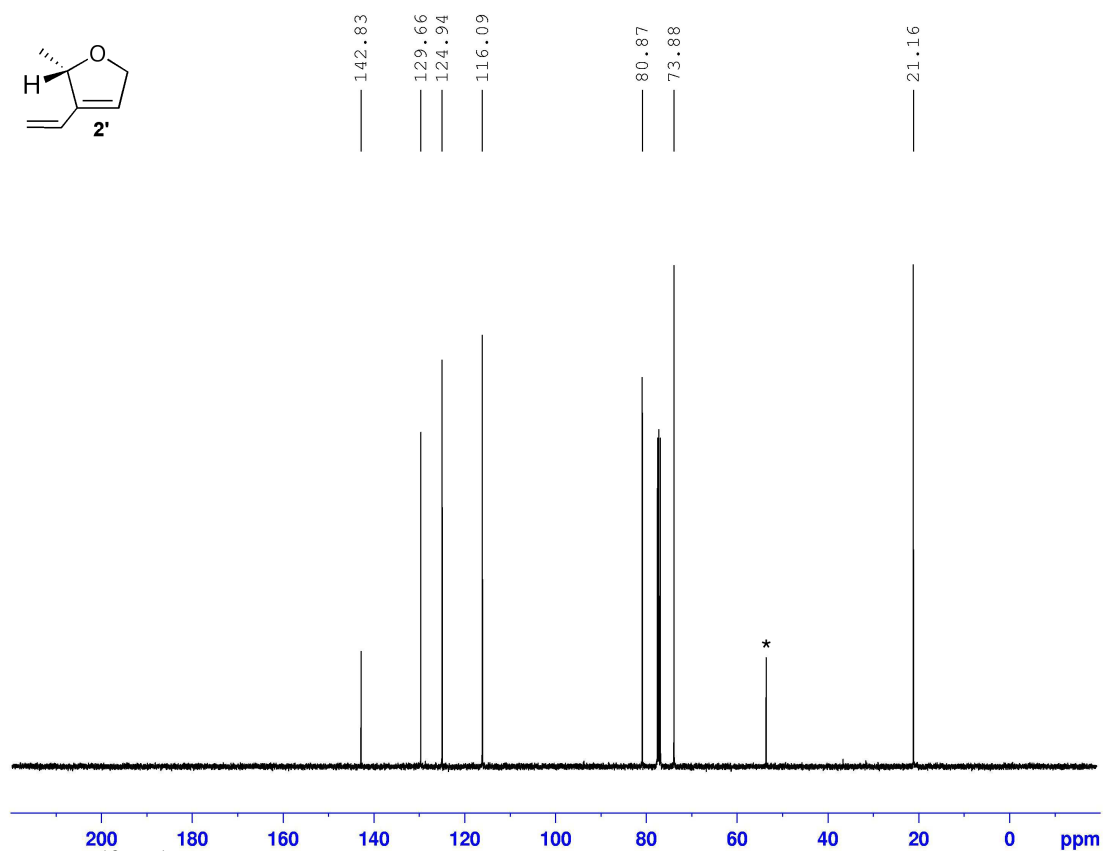


Figure S20. ¹³C{¹H} NMR spectrum (101 MHz, CDCl₃) for diene **2'**. Trace dichloromethane is designated by (*).

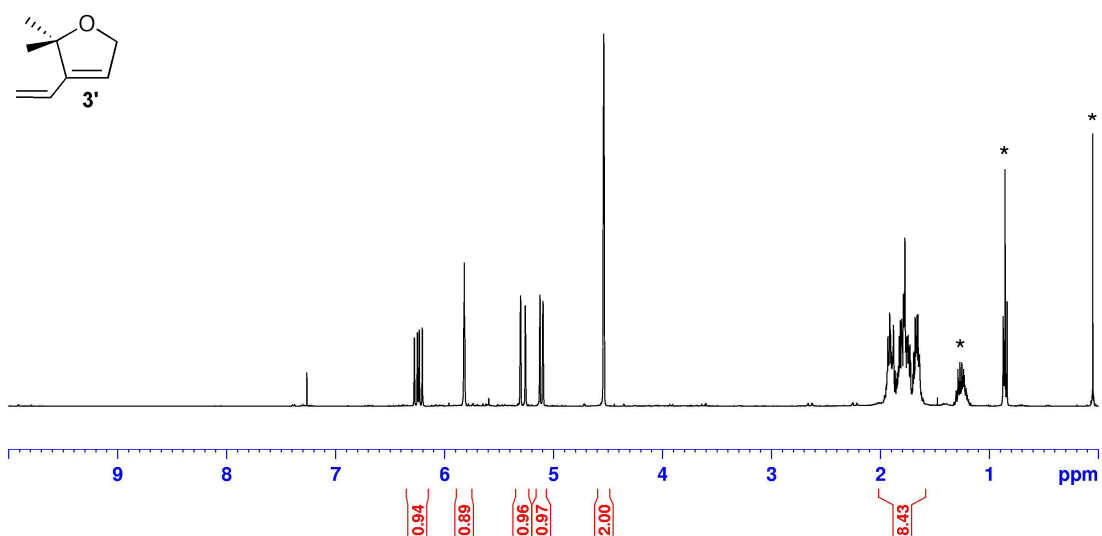


Figure S21. ¹H NMR spectrum (400 MHz, CDCl₃) for diene **3'**. Traces of pentane and silicone grease are designated by (*).

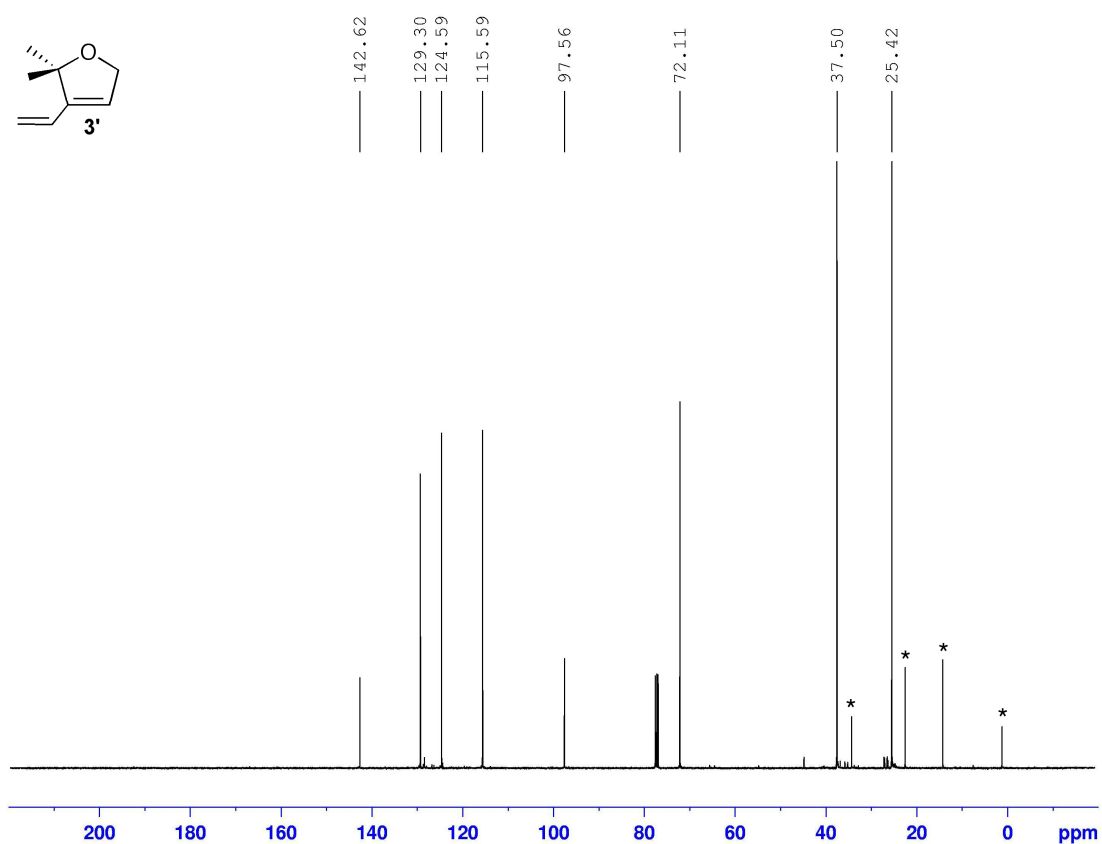


Figure S22. ¹³C{¹H} NMR spectrum (101 MHz, CDCl₃) for diene **3'**. Traces of pentane and silicone grease are designated by (*).

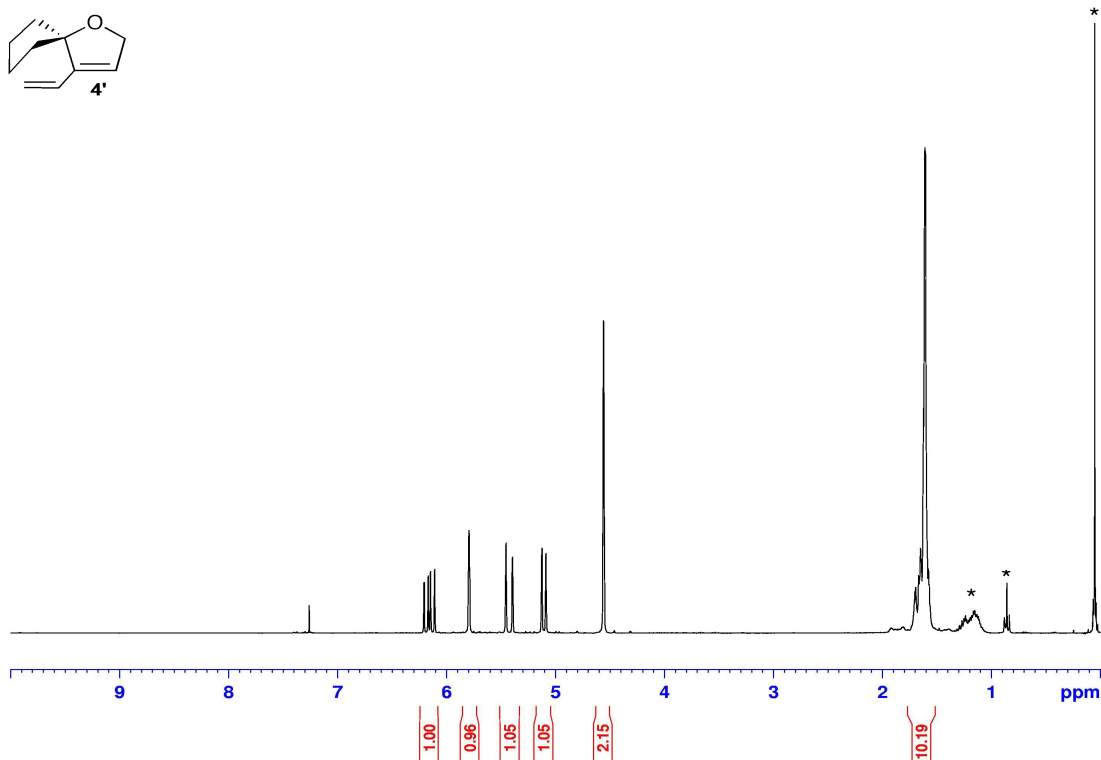


Figure S23. ¹H NMR spectrum (400 MHz, CDCl₃) for diene **4'**. Pentane and silicone grease are designated by (*).

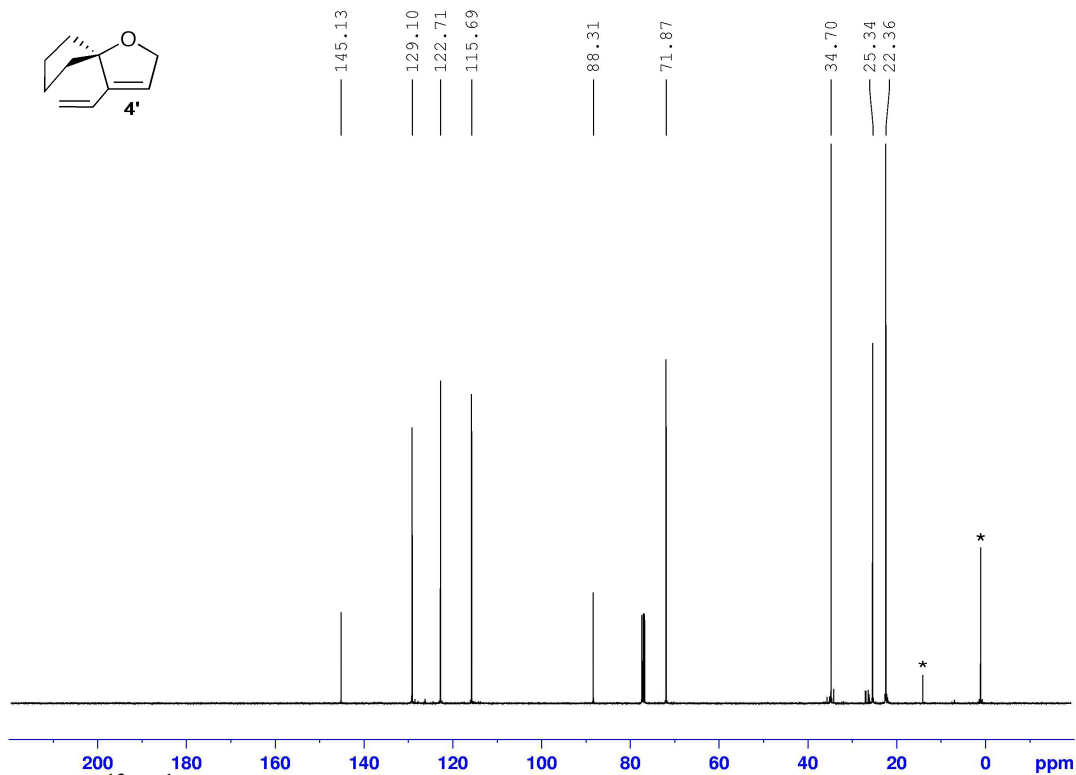


Figure S24. ¹³C{¹H} NMR spectrum (101 MHz, CDCl₃) for diene **4'**. Traces of pentane and silicone grease are designated by (*).

6. References.

- (1) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100-110.
- (2) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953-956.
- (3) Genin, E.; Toullec, P. Y.; Marie, P.; Antonietti, S.; Brancour, C.; Genet, J.-P.; Michelet, V. *ARKIVOC* **2007**, 67-78.
- (4) Kobayashi, T.; Koga, Y.; Narasaka, K. *J. Organomet. Chem.* **2001**, *624*, 73-87.
- (5) Dai, L.-Z.; Qi, M.-J.; Shi, Y.-L.; Liu, X.-G.; Shi, M. *Org. Lett.* **2007**, *9*, 3191-3194.
- (6) Gibson, S. E.; Hardick, D. J.; Haycock, P. R.; Kaufmann, K. A. C.; Miyazaki, A.; Tozer, M. J.; White, A. J. P. *Chem. Eur. J.* **2007**, *13*, 7099-7109.
- (7) Piquet, M.; Bruneau, C.; Dixneuf, P. H. *Chem. Commun.* **1998**, 2249-2250.
- (8) Gao, G.-L.; Niu, Y.-N.; Yan, Z.-Y.; Wang, H.-L.; Wang, G.-W.; Shaukat, A.; Liang, Y.-M. *J. Org. Chem.* **2010**, *75*, 1305-1308.
- (9) Clavier, H.; Nolan, S. P. *Chem. Eur. J.* **2007**, *13*, 8029-8036.
- (10) Eelman, M. D.; Blacquiere, J. M.; Moriarty, M. M.; Fogg, D. E. *Angew. Chem., Int. Ed.* **2008**, *47*, 303-306.
- (11) Blacquiere, J. M.; Jurca, T.; Weiss, J.; Fogg, D. E. *Adv. Synth. Catal.* **2008**, *350*, 2849-2855.
- (12) Lee, Y.-J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 10652-10661.
- (13) Furstner, A.; Stelzer, F.; Szillat, H. *J. Am. Chem. Soc.* **2001**, *123*, 11863-11869.
- (14) Boeda, F.; Clavier, H.; Jordaan, M.; Meyer, W. H.; Nolan, S. P. *J. Org. Chem.* **2008**, *73*, 259-263.
- (15) Michrowska, A.; Mennecke, K.; Kunz, U.; Kirschning, A.; Grela, K. *J. Am. Chem. Soc.* **2006**, *128*, 13261-13267.