

# A Most Convenient and Atom-Economic Preparation of a Highly Active Ring-Closing Metathesis Catalyst

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## Supporting Information

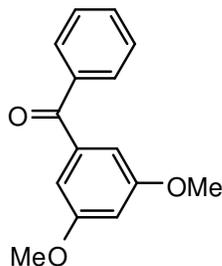
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## GENERAL INFORMATION

NMR spectra were recorded on a Bruker 400 MHz NMR spectrometer running Xwin-NMR software. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane (TMS) with reference to internal solvent for  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra. Chemical shifts are reported in parts per million (ppm) downfield from  $\text{H}_3\text{PO}_4$  for  $^{31}\text{P}$  NMR spectra. All glassware was oven dried and reactions were done under an atmosphere of argon unless otherwise noted. All organic solvents were dried by passage through solvent purification columns containing activated molecular sieves. All other commercial chemicals were used as obtained. Diethyl diallylmalonate was obtained from Sigma-Aldrich.  $\text{RuCl}_2(p\text{-cymene})(\text{PCy}_3)_2$ ,<sup>i</sup> (N,N-diallyl-4-methylbenzenesulfonamide,<sup>ii</sup> N-allyl-N-(but-3-enyl)-4-methylbenzenesulfonamide,<sup>iii</sup> and N-allyl-4-methyl-N-(pent-4-enyl)benzene-sulfonamide<sup>iii</sup> were prepared according to literature procedures. N-allyl-N-(hex-5-enyl)-4-methylbenzenesulfonamide<sup>iii</sup> was prepared from N-allyl-N-hex-5-enylamine<sup>iv</sup> following a procedure identical to the synthesis of N,N-diallyl-4-methylbenzenesulfonamide.

## SYNTHESIS OF THE ORGANIC PRECURSOR (5).

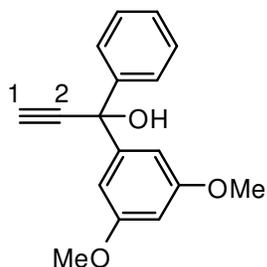
### Synthesis of 3,5-dimethoxybenzophenone.



This compound was previously prepared by a two-step process.<sup>v</sup> However, we prepared it by a one-step method adapted from another literature procedure.<sup>vi</sup> Neat 3,5-dimethoxybenzocnitrile (16.0 g, 98.1 mmol) was added to a 2.0 M solution of phenylmagnesium chloride in THF (98.0 mL, 196.1 mmol). The reaction mixture was refluxed for 24 hours at 70 °C. The solution was then transferred into a mixture of concentrated aqueous HCl (100 mL) and ice (300 g). The mixture was allowed to warm up to room temperature and stirred for 24 hours. The product was extracted with ether (3 x 300 mL) and the combined organic layers were washed with brine (200 mL) and water

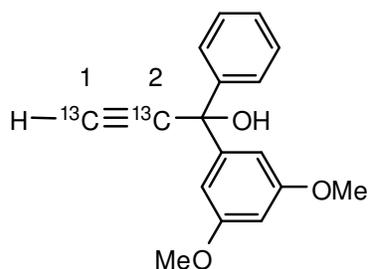
(150 mL) before being dried with anhydrous magnesium sulfate. The filtrate was dried *in vacuo* to afford 3,5-dimethoxybenzophenone as a yellow solid in 75 % yield.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  7.84 (d,  $^3J_{\text{H-H}} = 7.2$  Hz, 1H), 7.61 (t,  $^3J_{\text{H-H}} = 7.6$  Hz, 2H), 7.50 (t,  $^3J_{\text{H-H}} = 7.6$  Hz, 2H), 6.95 (d,  $^3J_{\text{H-H}} = 2.4$  Hz, 1H), 6.70 (t,  $^3J_{\text{H-H}} = 2.4$  Hz, 2H), 3.85 (s, 6H).

#### Synthesis of 1-(3,5-dimethoxyphenyl)-1-phenylprop-2-yn-1-ol (5).



The following method was adapted from a literature procedure.<sup>vii</sup> Anhydrous THF (50 mL) was cooled to  $-78$  °C. Purified acetylene gas was gently bubbled through the THF for 1 hour. A 2.5 M solution of n-butyllithium in THF (8.2 mL, 20.5 mmol) was then added drop-wise and the mixture was stirred vigorously for 20 minutes. 3,5-Dimethoxybenzophenone (5.0 g, 20.5 mmol) was dissolved in 10 mL of anhydrous THF and the solution was slowly dropped into the reaction flask. The mixture was stirred vigorously for 20 minutes at  $-78$  °C before being allowed to slowly warm to room temperature. A 5 % aqueous solution of  $\text{NH}_4\text{Cl}$  (60 mL) was added and the mixture stirred for 30 minutes. The product was extracted with ether (3 x 100 mL) and the combined organic layers were washed with brine (100 mL) and water (75 mL) before being dried with anhydrous magnesium sulfate. The filtrate was dried *in vacuo* to afford 1-(3,5-dimethoxyphenyl)-1-phenylprop-2-yn-1-ol (5) as a yellow oil in 95 % yield.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  7.60 (d,  $^3J_{\text{H-H}} = 7.2$  Hz, 2H), 7.31 (t,  $^3J_{\text{H-H}} = 6.4$  Hz, 2H), 7.27 (d,  $^3J_{\text{H-H}} = 7.2$  Hz, 1H), 6.77 (d,  $^3J_{\text{H-H}} = 2.4$  Hz, 2H), 6.35 (t,  $^3J_{\text{H-H}} = 2.4$  Hz, 2H), 3.74 (s, 6H), 2.93 (s, 1H), 2.84 (s, 1H).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  160.68, 146.99, 144.35, 128.39, 127.99, 126.03, 104.61, 99.84, 86.45 ( $\text{C}_2$ ), 75.56 ( $\text{C}_1$ ), 74.33, 55.46. HR-MS (FAB<sup>+</sup>) Calculated for  $\text{C}_{17}\text{H}_{17}\text{O}_3$ , 269.1172; found, 269.1178.

## SYNTHESIS OF THE $^{13}\text{C}$ -LABELED ORGANIC PRECURSOR ( $^{13}\text{C}_2$ -5).



A dry 100 mL reaction flask equipped with a stir bar was charged with anhydrous THF (20 mL) inside the glove box, capped with a septum, and taken out of the glove box. The THF was then frozen in a liquid  $\text{N}_2$  bath and evacuated before doubly labeled acetylene  $^{13}\text{C}_2\text{H}_2$  (0.5 L, 20.4 mmoles) was transferred into the reaction flask via the vacuum line. The flask was filled with Ar and warmed to  $-78\text{ }^\circ\text{C}$  in an acetone/dry ice bath. A 2.5 M solution of n-butyl lithium in hexanes (4.1 mL, 10.2 mmoles) was added dropwise under stirring and the reaction mixture was stirred for 20 minutes at  $-78\text{ }^\circ\text{C}$ . A suspension of 3,5-dimethoxybenzophenone (2.49 g, 10.2 mmol) in 5 mL of anhydrous THF was added dropwise and the reaction mixture was stirred at  $-78\text{ }^\circ\text{C}$  for 30 minutes. The solution was then allowed to slowly warm up to room temperature and the reaction was worked up in a manner analogous to the procedure for the preparation of **5**.  $^{13}\text{C}_2$ -**5** was obtained as a faint-yellow crystalline material in 89 % yield.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  7.61 (d,  $^3J_{\text{H-H}} = 7.2$  Hz, 2H), 7.31 (t,  $^3J_{\text{H-H}} = 6.4$  Hz, 2H), 7.26 (d,  $^3J_{\text{H-H}} = 7.2$  Hz, 1H), 6.78 (d,  $^3J_{\text{H-H}} = 2.4$  Hz, 2H), 6.36 (t,  $^3J_{\text{H-H}} = 2.4$  Hz, 2H), 3.74 (s, 6H), 2.84 (dd,  $^1J_{\text{C}_1\text{-H}} = 250.4$  Hz,  $^2J_{\text{C}_2\text{-H}} = 50.0$  Hz, 1H), protons from OH group not observed.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  160.79, 128.44, 128.04, 126.11, 104.62, 99.84, 86.58 (d,  $^1J_{\text{C-C}} = 171$  Hz,  $\text{C}_2$ ), 75.38 (d,  $^1J_{\text{C-C}} = 172$  Hz,  $\text{C}_1$ ), 55.53.

## PREPARATION OF THE OLEFIN METATHESIS CATALYST SOLUTIONS USING **5**

**Method 1:** A small conical vial equipped with a spin vane was charged with  $\text{RuCl}_2(p\text{-cymene})(\text{PCy}_3)$  (50 mg, 0.085 mmol) and 1-(3,5-dimethoxyphenyl)-1-phenylprop-2-yn-1-ol (**5**) (25 mg, 0.094 mmol, 1.1 equiv). THF was added to reach a total volume of 1.0 mL of dark orange solution. The vial was sealed, removed from the glove box, and heated at  $70\text{ }^\circ\text{C}$  under stirring for 16 hours. The dark brown solution was used as is to catalyze ring-closing metathesis (RCM) reactions (see below). The dark

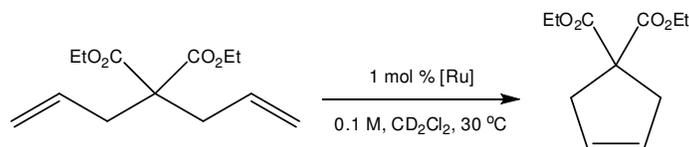
brown solution features two main phosphorus-containing species in a ~5/1 ratio according to  $^{31}\text{P}$  NMR spectroscopy. Major species:  $^{31}\text{P}\{^1\text{H}\}$  NMR (THF- $d_8$ ):  $\delta$  48.6 (s). Minor species:  $^{31}\text{P}\{^1\text{H}\}$  NMR (THF- $d_8$ ):  $\delta$  68.1 (s).

**Method 2:** A small conical vial equipped with a spin vane was charged with  $[\text{RuCl}_2(p\text{-cymene})]_2$  (52 mg, 0.085 mmol), 1-(3,5-dimethoxyphenyl)-1-phenylprop-2-yn-1-ol (**5**) (55 mg, 0.206 mmol, 1.2 equiv/Ru), and tricyclohexylphosphine (48 mg, 0.17 mmol, 1.0 equiv/Ru). THF was added to reach a total volume of 2.0 mL of dark orange suspension. The vial was sealed, removed from the glove box, and heated at 70 °C under stirring for 16 hours. The dark brown solution was used as is to catalyze RCM reactions (see below).  $^{31}\text{P}$  NMR spectroscopy reveals that this solution contains the same species in the same ratio as what was obtained with method 1.

#### PREPARATION OF THE OLEFIN METATHESIS CATALYST SOLUTION USING $^{13}\text{C}_2\text{-5}$

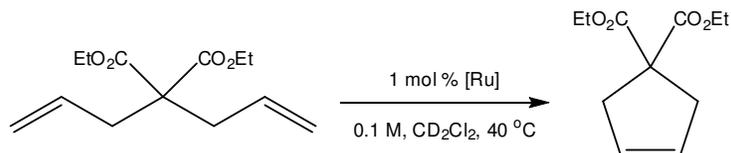
A solution of  $^{13}\text{C}$ -labeled catalyst was prepared by method 1 (see above) using the  $^{13}\text{C}$ -labelled organic precursor ( $^{13}\text{C}_2\text{-5}$ ). This solution contains the same major and minor species as described above according to  $^{31}\text{P}$  NMR spectroscopy. Furthermore, the  $^{13}\text{C}$  and  $^{31}\text{P}$  NMR data are consistent with a mono-phosphine ruthenium indenylidene structure (**6**) for the major species. Indeed, the shifts in the  $^{13}\text{C}$  NMR spectrum for the  $\text{C}_\alpha$  and the  $\text{C}_\beta$  are consistent with an indenylidene fragment as opposed to an allenylidene one.<sup>viii</sup> Additionally, the splitting (doublet of doublet) of the resonance corresponding to the  $\text{C}_\alpha$  of the major species indicates that only one phosphine ligand is attached to the ruthenium. Major species:  $^{13}\text{C}\{^1\text{H}\}$  NMR (THF- $d_8$ ):  $\delta$  287.0 ppm (dd,  $^2\text{J}_{\text{C}_\alpha\text{-P}} = 11$  Hz,  $^1\text{J}_{\text{C}_\alpha\text{-C}_\beta} = 49$  Hz,  $\text{C}_\alpha$ ), 129.2 ppm (d,  $^1\text{J}_{\text{C}_\alpha\text{-C}_\beta} = 51$  Hz,  $\text{C}_\beta$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR (THF- $d_8$ ):  $\delta$  48.6 (d,  $^2\text{J}_{\text{P-C}_\alpha} = 11$  Hz). Minor species:  $^{13}\text{C}\{^1\text{H}\}$  NMR (THF- $d_8$ ):  $\delta$  256.2 ppm (dd,  $^2\text{J}_{\text{C}_\alpha\text{-P}} = 15$  Hz,  $^1\text{J}_{\text{C}_\alpha\text{-C}_\beta} = 48$  Hz,  $\text{C}_\alpha$ ), 138.2 ppm (d,  $^1\text{J}_{\text{C}_\alpha\text{-C}_\beta} = 49$  Hz,  $\text{C}_\beta$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR (THF- $d_8$ ):  $\delta$  68.1 (d,  $^2\text{J}_{\text{P-C}_\alpha} = 15$  Hz).

**PROCEDURE FOR ACTIVITY PLOTS OF THE RCM OF DIETHYL DIALLYLMALONATE AT 30 °C<sup>ix</sup>**



A solution of the olefin metathesis catalyst – prepared by method 1 or method 2 as described above – (0.085 M, 6  $\mu$ L, 0.51  $\mu$ mol) and CD<sub>2</sub>Cl<sub>2</sub> (480  $\mu$ L) were transferred to an NMR tube equipped with a screw-cap septum top. The sample was equilibrated at 30 °C in the NMR probe before diethyl diallylmalonate (12  $\mu$ L, 12 mg, 50  $\mu$ mol, 0.1 M) was added via syringe. Data points were collected over a period of 1 hour. The conversion to the RCM product was determined by comparing the ratio of the integrals of the methylene protons in the substrate material,  $\delta$  2.61 (dt), with those in the product,  $\delta$  2.98 (s).

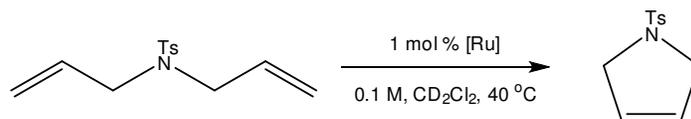
**PROCEDURE FOR THE RCM OF DIETHYL DIALLYLMALONATE CONDUCTED AT 40 °C**



A 0.1 M stock solution of diethyl diallylmalonate in CD<sub>2</sub>Cl<sub>2</sub> was prepared by dissolving diethyl diallylmalonate (60 mg, 0.25 mmol) in 2.44 mL of CD<sub>2</sub>Cl<sub>2</sub>. A portion of this stock solution (0.5 mL, 50  $\mu$ mol of diethyl diallylmalonate) was transferred to an NMR tube equipped with a screw-cap septum top. A solution of the olefin metathesis catalyst – prepared by method 1 or method 2 as described above – (0.085 M, 6  $\mu$ L, 0.51  $\mu$ mol, 1.0 mol %) was added to the diethyl diallylmalonate solution via syringe. The NMR tube was then capped and placed in an oil bath regulated at 40 °C and the reaction mixture was analyzed by <sup>1</sup>H NMR spectroscopy after a period of time. The extent of conversion of

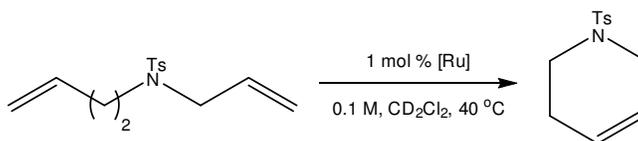
the RCM was determined by comparing the ratio of the integrals of the methylene protons in the substrate,  $\delta$  2.61 (dt), with those in the product,  $\delta$  2.98 (s).

#### PROCEDURE FOR THE RCM OF N,N-DIALLYL-4-METHYLBENZENESULFONAMIDE



A 0.1 M solution of N,N-diallyl-4-methylbenzenesulfonamide in  $\text{CD}_2\text{Cl}_2$  was prepared by dissolving N,N-diallyl-4-methylbenzenesulfonamide (12.5 mg, 50  $\mu\text{mol}$ ) in 480  $\mu\text{L}$  of  $\text{CD}_2\text{Cl}_2$ . A solution of the olefin metathesis catalyst – prepared by method 2 as described above – (0.085 M, 6  $\mu\text{L}$ , 0.51  $\mu\text{mol}$ , 1.0 mol %) was added to the N,N-diallyl-4-methylbenzenesulfonamide solution via syringe. The solution was transferred to an NMR tube equipped with a screw-cap septum top. The NMR tube was then capped and placed in an oil bath regulated at 40  $^\circ\text{C}$ . After 1 hour, the reaction mixture was analyzed by  $^1\text{H}$  NMR spectroscopy to reveal full conversion to the RCM product (no substrate and no side-product detected).

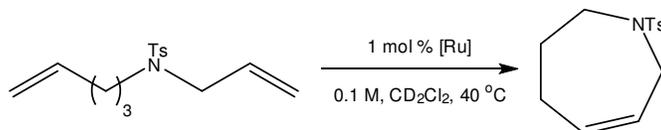
#### PROCEDURE FOR THE RCM OF N-ALLYL-N-(BUT-3-ENYL)-4-METHYLBENZENESULFONAMIDE



A 0.1 M solution of N-allyl-N-(but-3-enyl)-4-methylbenzenesulfonamide in  $\text{CD}_2\text{Cl}_2$  was prepared by dissolving N-allyl-N-(but-3-enyl)-4-methylbenzenesulfonamide (13.3 mg, 50  $\mu\text{mol}$ ) in 480  $\mu\text{L}$  of  $\text{CD}_2\text{Cl}_2$ . A solution of the olefin metathesis catalyst – prepared by method 2 as described above – (0.085 M, 6  $\mu\text{L}$ , 0.51  $\mu\text{mol}$ , 1.0 mol %) was added to the N-allyl-N-(but-3-enyl)-4-methylbenzenesulfonamide solution via syringe. The solution was transferred to an NMR tube equipped with a screw-cap septum top. The NMR tube

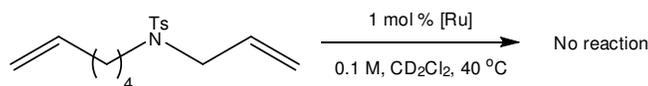
was then placed in an oil bath regulated at 40 °C. After 1 hour, the reaction mixture was analyzed by <sup>1</sup>H NMR spectroscopy to reveal full conversion to the RCM product (no substrate and no side-product detected).

**PROCEDURE FOR THE RCM OF N-ALLYL-N-(PENT-4-ENYL)-4-METHYLBENZENESULFONAMIDE**



A 0.1 M solution of N-allyl-N-(pent-4-enyl)-4-methylbenzenesulfonamide in CD<sub>2</sub>Cl<sub>2</sub> was prepared by dissolving N-allyl-N-(pent-4-enyl)-4-methylbenzenesulfonamide (14.0 mg, 50 μmol) in 480 μL of CD<sub>2</sub>Cl<sub>2</sub>. A solution of the olefin metathesis catalyst – prepared by method 2 as described above – (0.085 M, 6 μL, 0.51 μmol, 1.0 mol %) was added to the N-allyl-N-(pent-4-enyl)-4-methylbenzenesulfonamide solution via syringe. The solution was transferred to an NMR tube equipped with a screw-cap septum top. The NMR tube was then placed in an oil bath regulated at 40 °C. After 1 hour, the reaction mixture was analyzed by <sup>1</sup>H NMR spectroscopy to reveal full conversion to the RCM product (no substrate and no side-product detected).

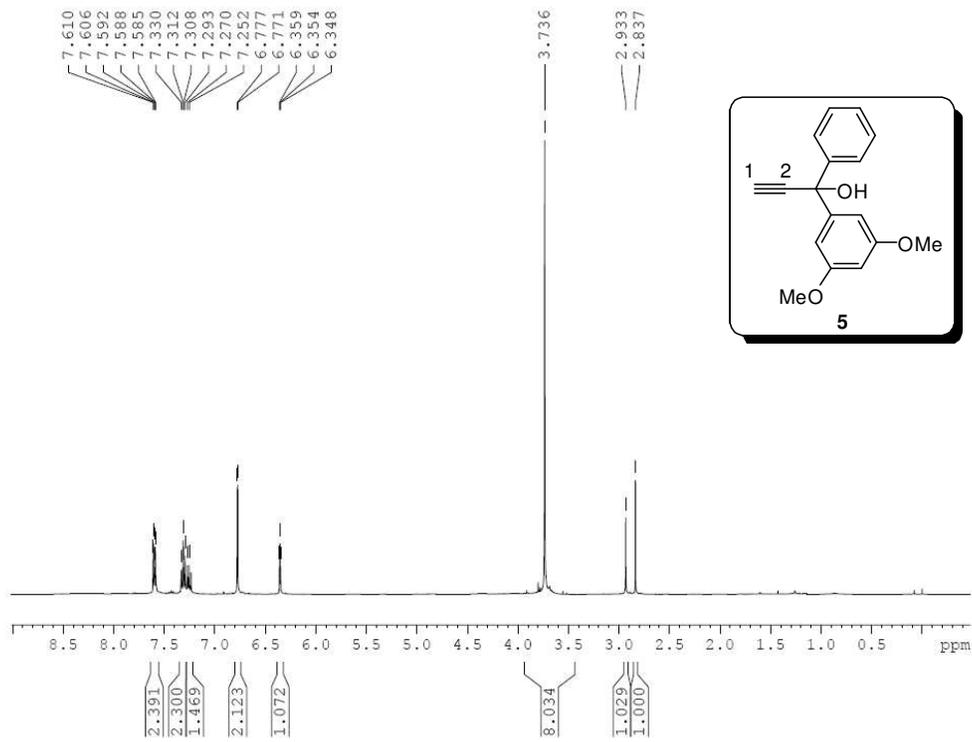
**PROCEDURE FOR THE RCM OF N-ALLYL-N-(HEX-5-ENYL)-4-METHYLBENZENESULFONAMIDE**



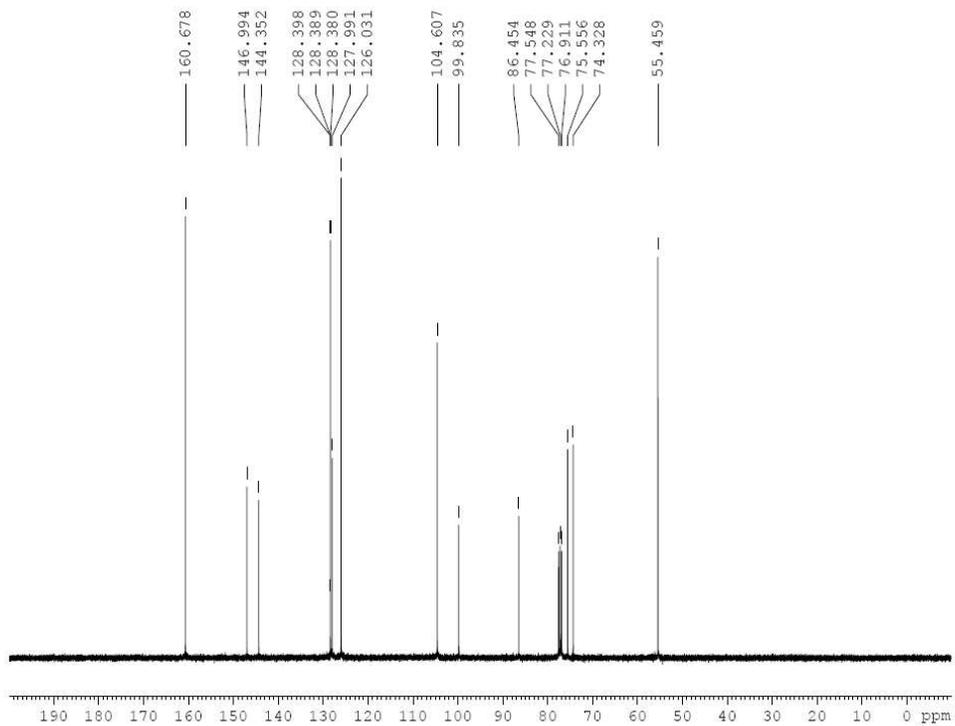
A 0.1 M solution of N-allyl-N-(hex-5-enyl)-4-methylbenzenesulfonamide in CD<sub>2</sub>Cl<sub>2</sub> was prepared by dissolving N-allyl-N-(hex-5-enyl)-4-methylbenzenesulfonamide (14.7 mg, 50 μmol) in 480 μL of CD<sub>2</sub>Cl<sub>2</sub>. A solution of the olefin metathesis catalyst – prepared by method 2 as described above – (0.085 M, 6 μL, 0.51 μmol, 1.0 mol %) was added to the N-allyl-N-(hex-5-enyl)-4-methylbenzenesulfonamide solution via syringe. The solution

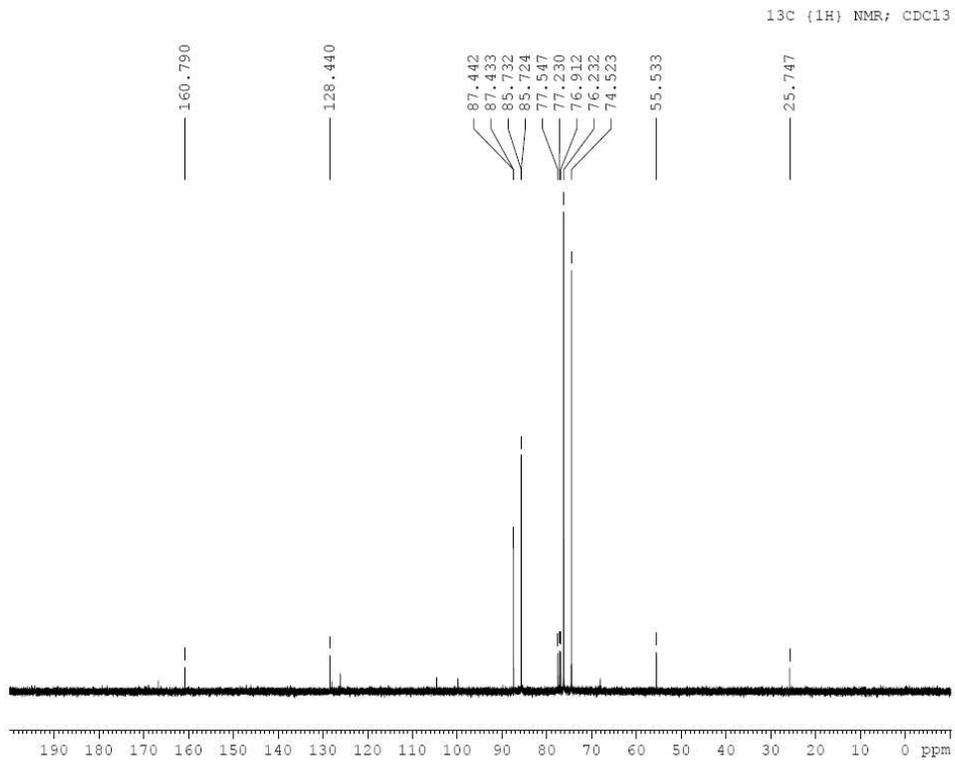
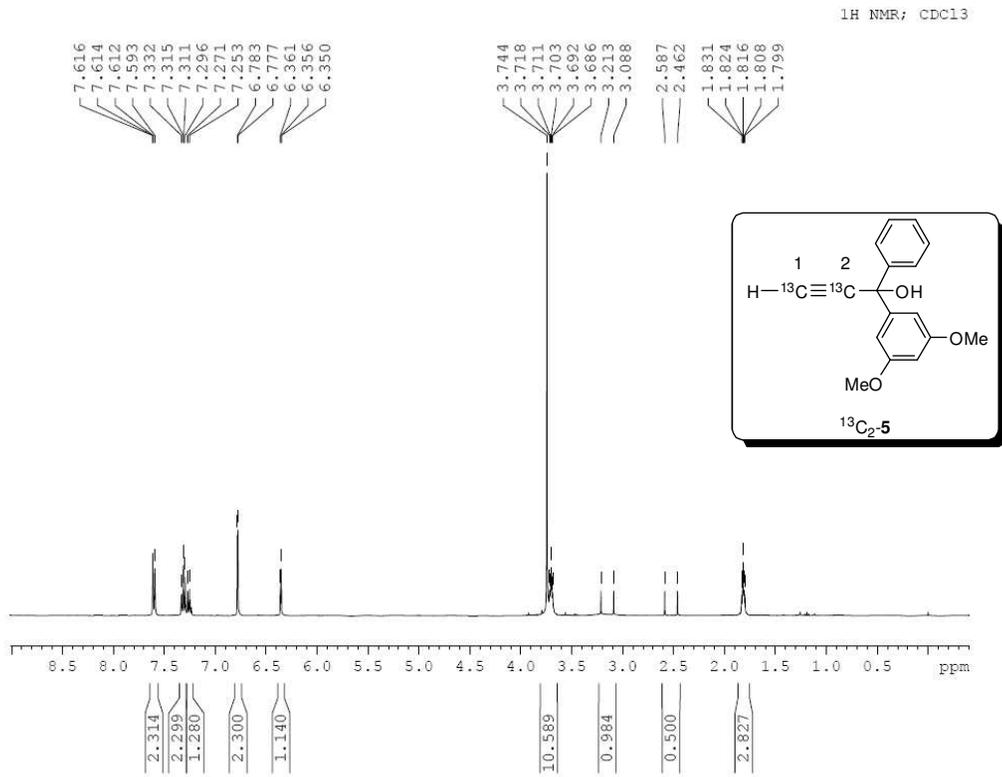
was transferred to an NMR tube equipped with a screw-cap septum top. The NMR tube was then placed in an oil bath regulated at 40 °C. After 2.5 hours, the reaction mixture was analyzed by  $^1\text{H}$  NMR spectroscopy to reveal that no RCM took place (no product detected).

<sup>1</sup>H NMR; CDCl<sub>3</sub>

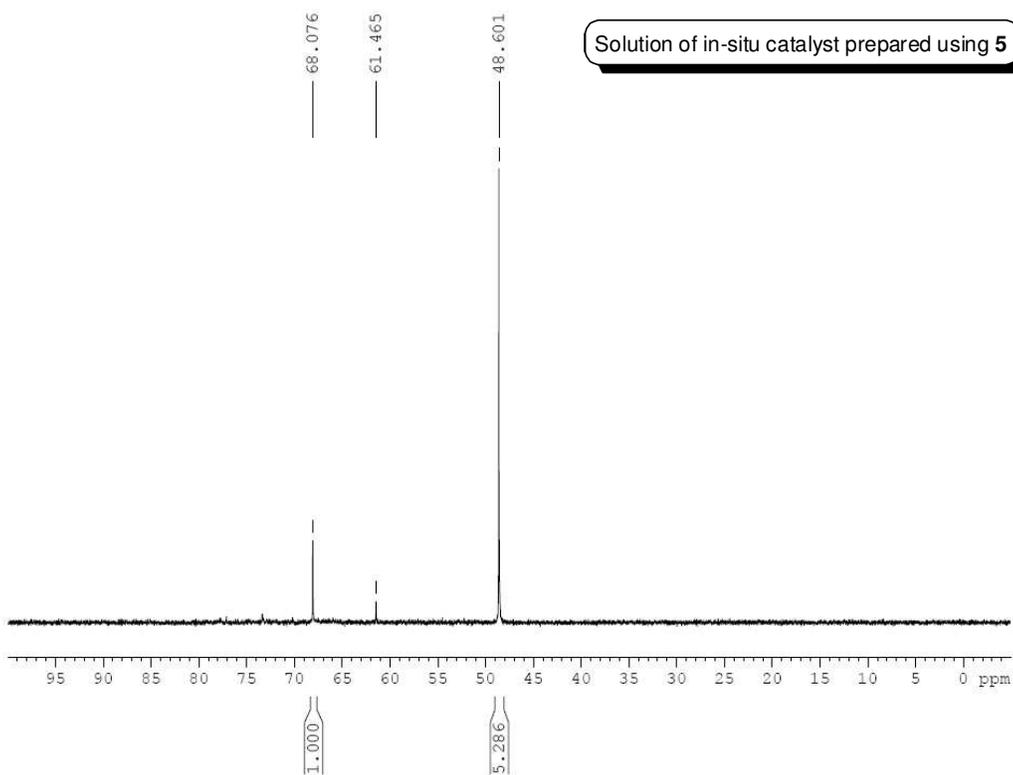


<sup>13</sup>C {<sup>1</sup>H} NMR; CDCl<sub>3</sub>

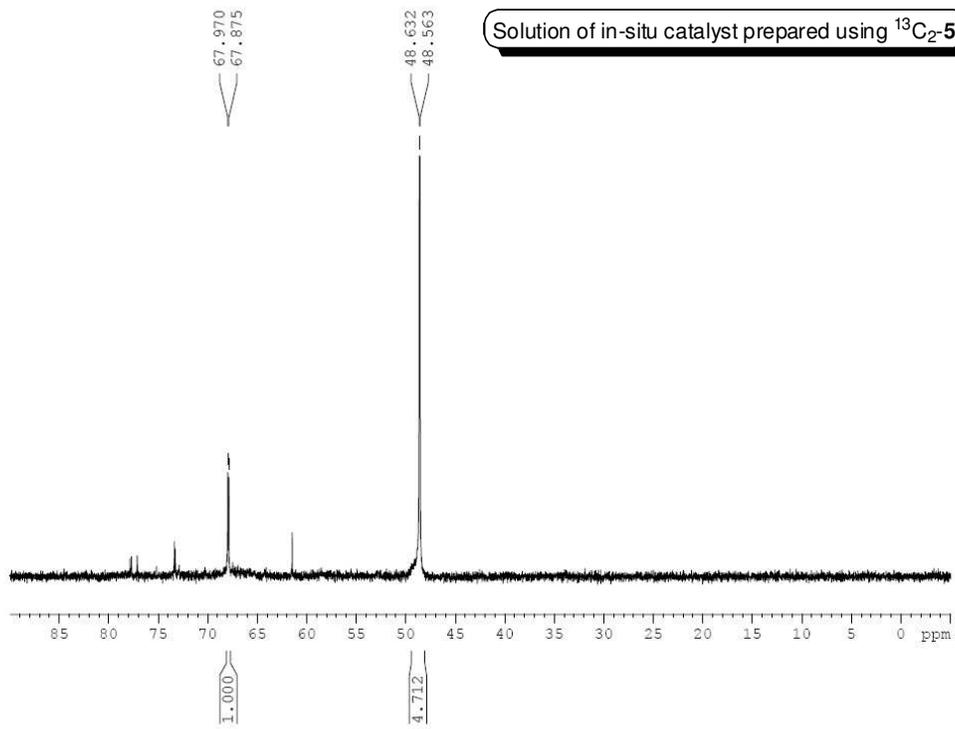




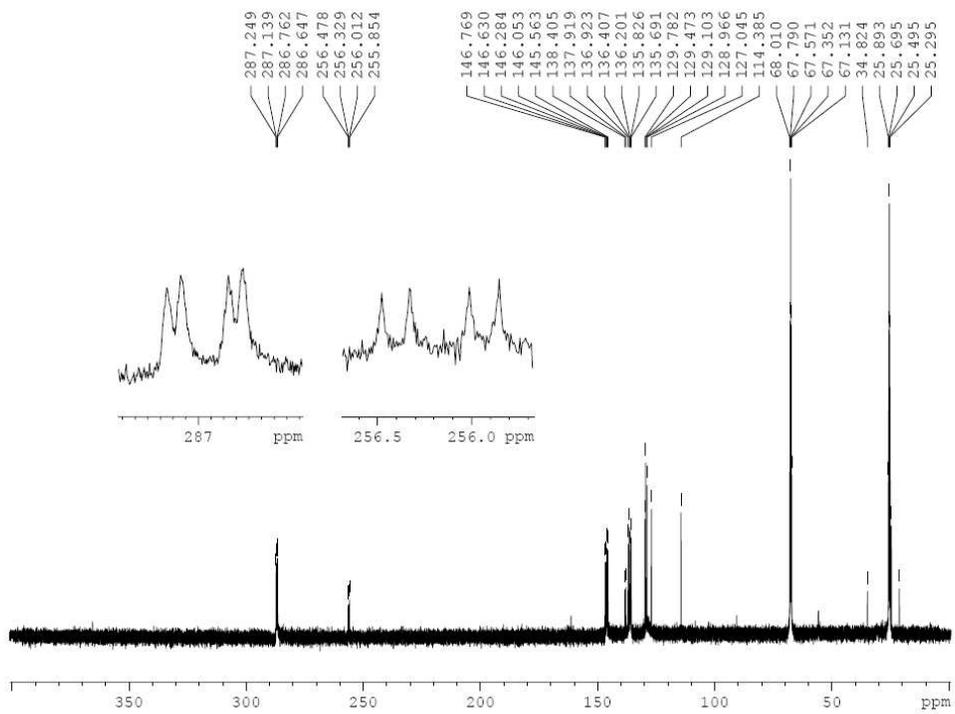
Solution of in-situ catalyst prepared using 5



31P {1H} NMR; THF-d8



$^{13}\text{C}$  {1H} NMR; THF-d8



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