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Supplementary Material

# Vortex Fluidic Ethenolysis, Integrating A Rapid Quench of Ruthenium Olefin Metathesis Catalysts

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## General Considerations

All solvents and reagents were used as received from commercial suppliers, with the exception of methyl oleate, which was synthesized from the method stated on page S5, and toluene, which was distilled prior to use.

Infrared (IR) spectra were recorded on a Perkin Elmer ATR Fourier Transform spectrometer as liquid films, or solid crystals. Absorption maxima ($\nu_{max}$) are reported in wavenumbers ($cm^{-1}$).

All NMR was performed on either 600 or 400 MHz Bruker advance spectrometers, using $CDCl_3$ or $D_2O$ as the solvent, as specified. Spectra were acquired using a relaxation delay-time of 4 seconds. All chemical shifts are presented in ppm, using residual solvent as the internal standard.

The vortex fluidic device (VFD)[1] shown in Figure S1 is modular in nature, allowing this device to have many configurations. Unless otherwise specified, throughout this report the following specifications were used. The tube used was a borosilicate glass, 19 cm long with a 20 mm outer diameter (OD). “Confined mode” refers to the mode of operation where a finite amount of reagent is reacted within the tube, “continuous flow” refers to mode of operation where reagents are delivered *via* stainless steel jet feeds (2 mm OD) to the base of the rotating tube, and the reaction mixture is collected after exiting the tube. Liquid reagents were delivered using syringe pumps, with a borosilicate glass syringe and plunger, and stainless steel 17 G needles. Rotating tube was always operated at a 45˚ tilt angle ($\theta$).

Thin layer chromatography (TLC) was carried out using aluminium backed sheets, coated with 60F254 silica gel. Visualization of the silica plates was achieved using a UV lamp ("max = 254 nm) and/or potassium permanganate (5% $KMnO_4$ in 1M NaOH with 5% potassium carbonate). Flash column chromatography was carried out using 40-60 mm silica gel, wet packed to a height of 15 cm in a 30 mm OD column.

1. J. Britton, K. A. Stubbs, G. A. Weiss and C. L. Raston, *Chem. - Eur. J.*, 2017, **23**, 13270-13278.

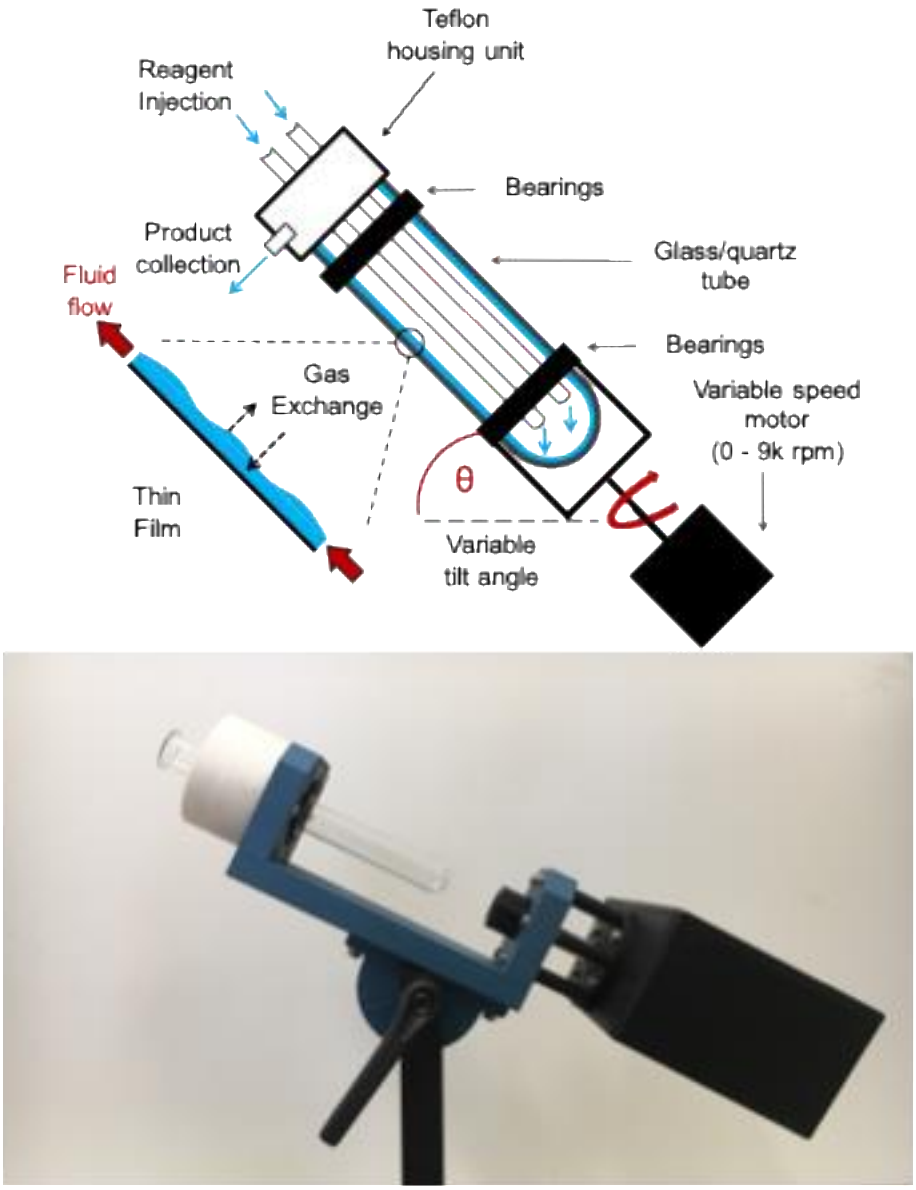
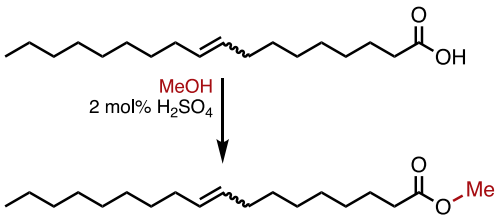



Figure S1. Schematic representation and photograph of the vortex fluidic device (VFD).

## Ethenolysis

Ethenolysis was performed to demonstrate a scalable application, made possible through the unique techniques explored in this study. This was achieved by performing a continuous flow reaction, generating value added chemicals from renewable sources. The renewable source was oleic acid. Oleic acid is commonly found in cooking oils such as olive or canola oil. To allow for high throughput characterisation *via* GCMS, the oleic acid was first converted to methyl oleate through a simple esterification with methanol. Methyl oleate is less volatile, allowing for GCMS analysis.

### Esterification of Oleic Acid




Oleic acid (9 mL, 28.5 mmol) was mixed with methanol (56 mL) and concentrated sulfuric acid (60 mg, 0.61 mmol) and stirred at 60 ˚C for 12 hours. Crude NMR at this point revealed a conversion from oleic acid to methyl oleate of 94%. The resulting solution was washed with a saturated aqueous solution of $NaHCO_3$ (2x15 mL), followed by washing with water (3x15 mL). Remaining solution was purified under reduced pressure. This resulted in a clear oil that freezes solid on a cool day. (8.41 mL, 87% yield). NMR, IR and MS data can be found below.

**$^1$H NMR (600 MHz, $CDCl_3$):** $\delta_H$ = 5.33 (2H, m, -HC=CH-), 3.65 (3H, s, -$COOCH_3$), 2.29 (2H, t, J=8 Hz, -$CH_2COOCH_3$), 2.00 (4H, m), 1.61 (2H, m), 1.26-12.9 (20H, m), 0.87 (3H, t, J = 7 Hz, -$CH_2CH_3$).

**$^{13}$C NMR (600 MHz, $CDCl_3$):** $\delta_C$ = 174.2 (C=O), 129.9 (HC=C'H), 129.9 ((HC=C'H), 51.4, 34.1, 31.9, 29.8, 29.7, 29.5, 29.3, 29.2, 29.15, 29.1, 27.23, 27.17, 24.9, 22.7, 14.1

**IR ($\upsilon_{max}$, liquid ATR):** 3010, 2925, 2855, 2877, 1745, 1465, 1435, 1360, 1240, 1200, 1170, 1010, 880, 860, 725, 590

**LR-MS:** 297 m/v $[M+H]^+$.

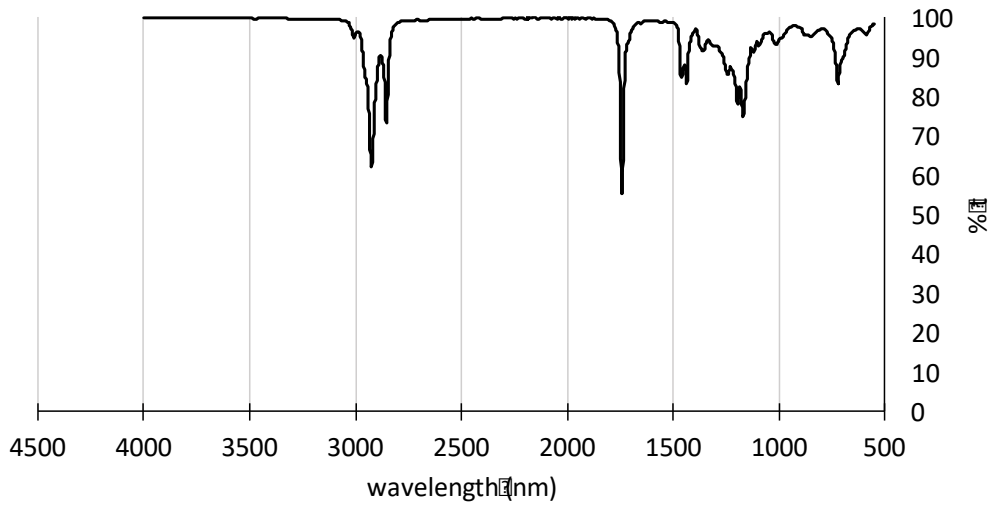



Figure S2. IR spectrum of methyl oleate

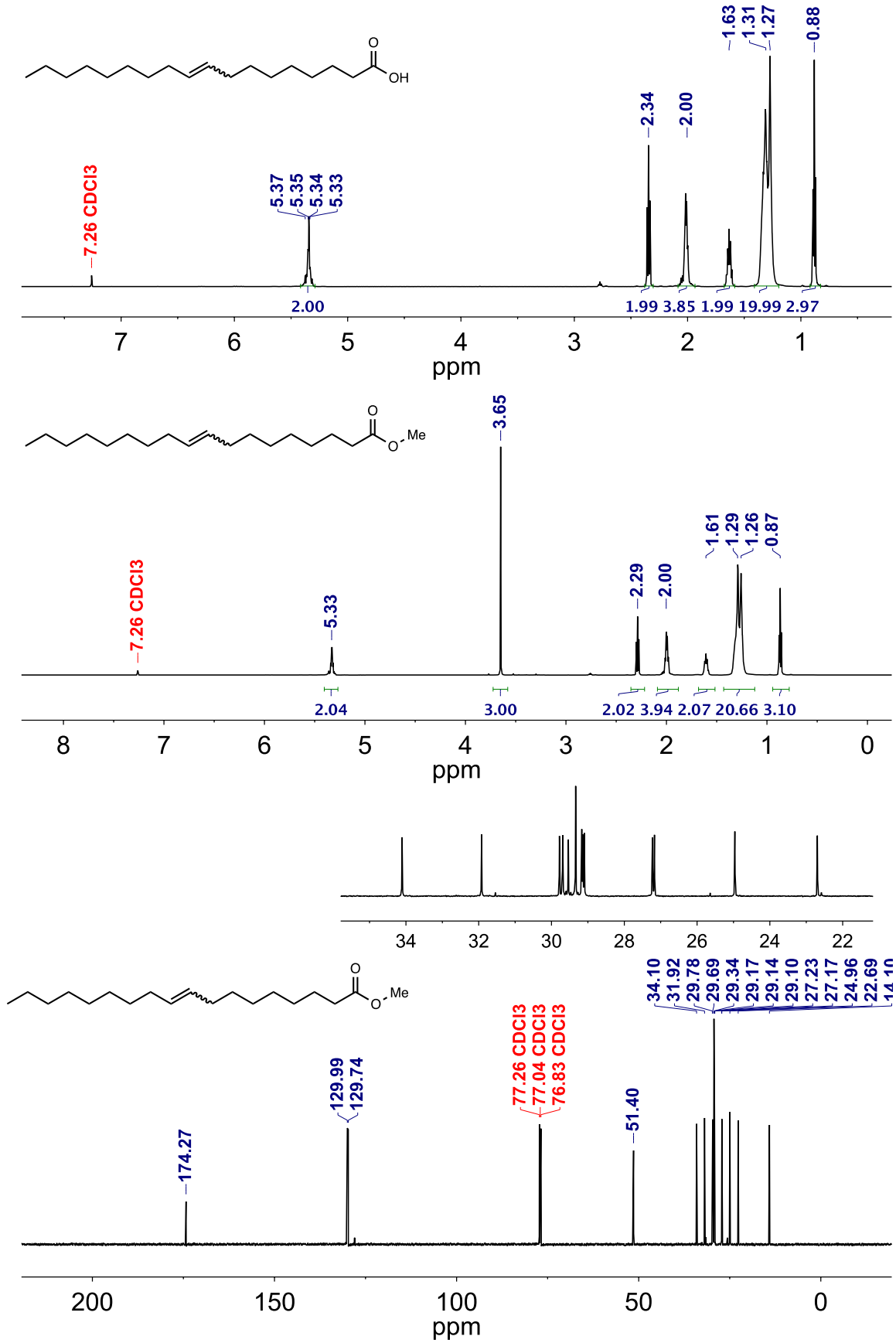
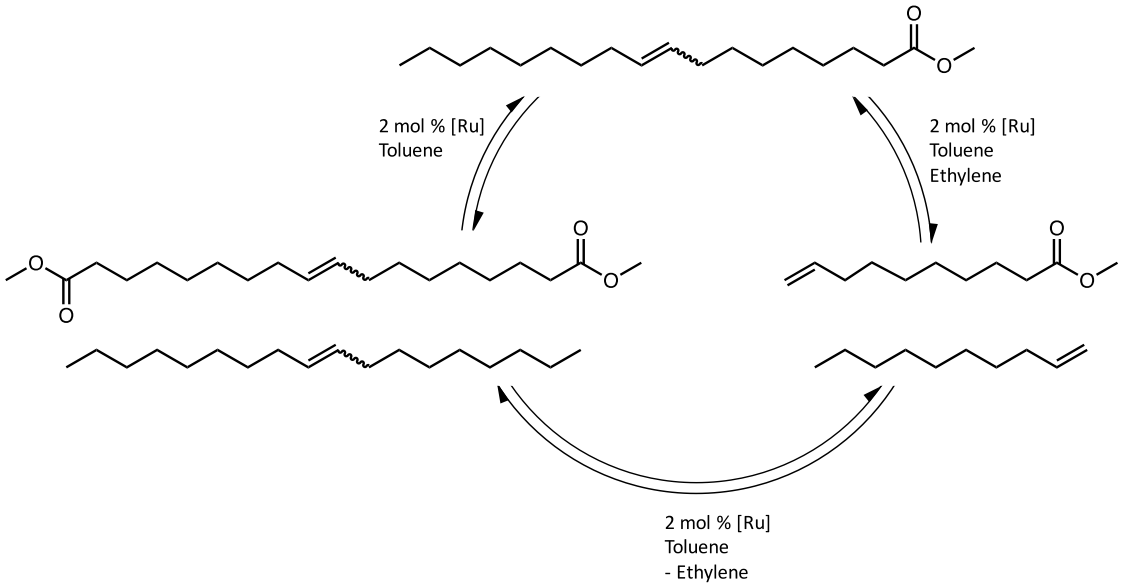



Figure S3. From top to bottom, 1H-NMR spectrum of oleic acid, 1H-NMR spectrum of methyl oleate 13C-NMR spectrum, with expansion between 20 – 40 ppm of methyl oleate.

## Ethenolysis of Methyl Oleate




## Confined Mode vs Batch Comparison

VFD experiments were performed first to establish optimal parameters before moving to continuous flow. The following procedure was employed. The atmosphere within two 20 mm (OD) VFD tubes was evacuated and then filled with ethene gas. The catalyst **GI** (4 mg, $4.86 \times 10^{-3}$ mM) was weighed into a vial, and dissolved in toluene (2 mL). In a separate vial, methyl oleate (73 mg, 0.24 mM) was diluted in toluene (2 mL). Half of each solution (1 mL each) was added to the each of the 2 VFD tubes, with the MO solution added first followed by the catalyst solution. During which time an ethene atmosphere was maintained *via* balloons filled with ethene. One tube was magnetically stirred at ≈300 rpm, and the other tube was operated in the VFD at 7 krpm. After 30 minutes of reaction time, a solution of N-acetyl-L-cysteine in MeCN (1 mL, 0.12 M) was added to quench each reaction. Following this, each reaction mixture was diluted in $CHCl_3$ for GCMS analysis. In the GC trace, all 5 compounds could be accounted for, confirmed by the MS which showed the corresponding m/z of the molecular ions. The integrations of the peaks in the GC trace were used to calculate the % conversions. A representative GCMS spectrum can be found below.

The method for the GCMS was as follows. Injection port temperature was set to 250˚C. The column oven was held at 100˚C for 2 minutes, before ramping to 200 ˚C at 10 ˚C/min,

then the temperature was ramped to 300 ˚C at 20 ˚C/min and held at 300 ˚C for 5 minutes. The MS operated with a mass detection range from 50 to 600 m/z.

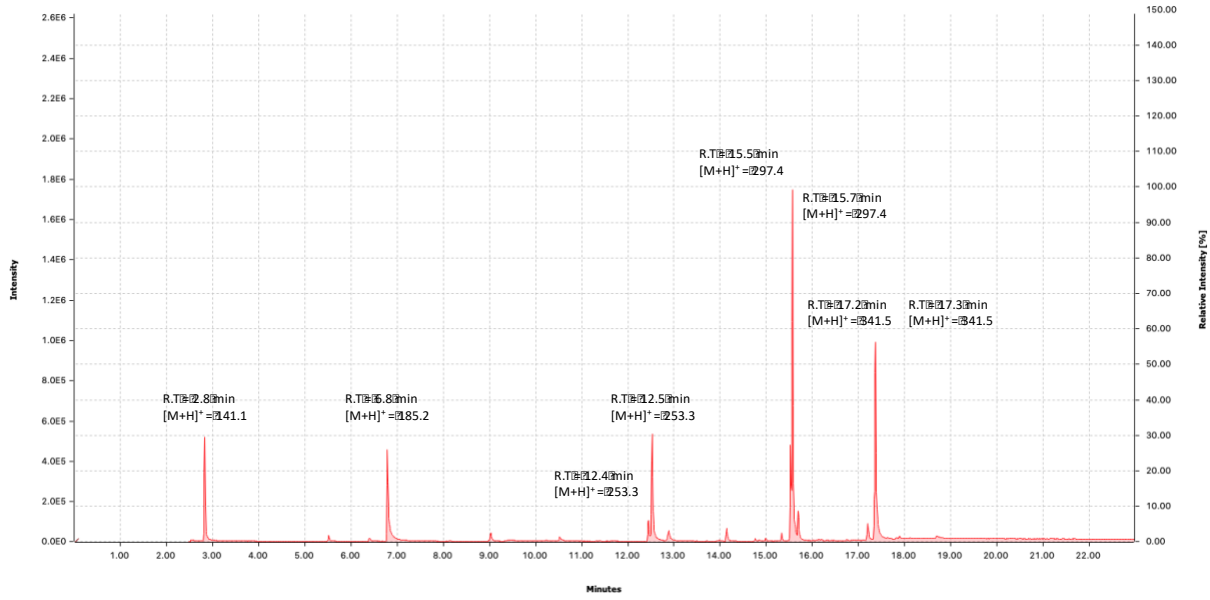



Figure S4. GC trace representing crude reaction mixture after the ethenolysis of methyl oleate with a Ru-grubbs type catalyst under an atmosphere of ethene.

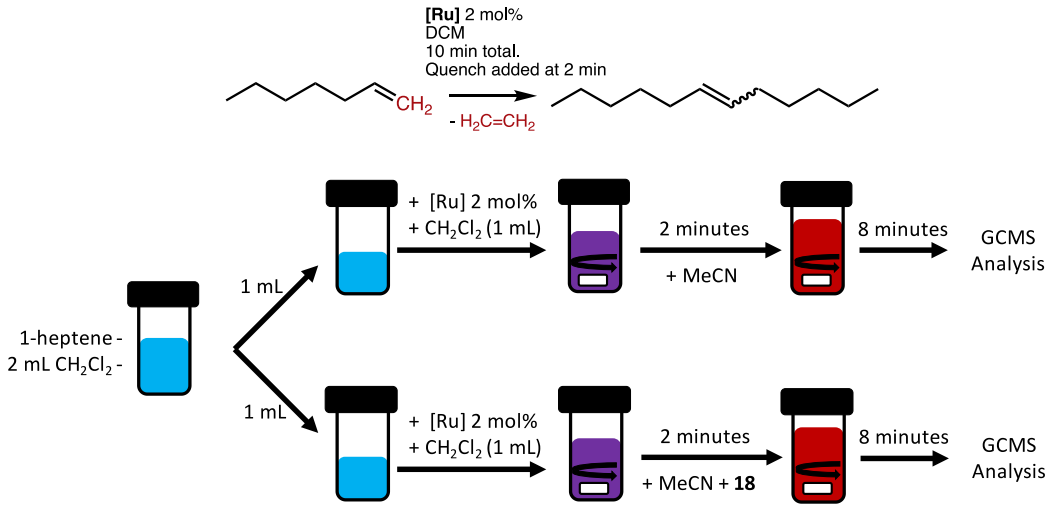
## Continuous Flow Ethenolysis

To demonstrate scalability, ethenolysis was performed in continuous flow mode of operation. The following method was employed. Two syringe pumps were set up to inject two separate solutions. In one syringe was a solution of catalyst **HGII** (9 mg, $1.44 \times 10^{-5}$ mol, 1.59 mM) in toluene (9 mL), and in the other syringe was a solution of methyl oleate (212 mg, $7.13 \times 10^{-4}$ mol, 79.2 mM) in toluene (9 mL). Each syringe was set to deliver their contents to the base of the rotating tube, each at a flow rate of 0.05 mL/min, giving a total flow of 0.1 mL/min. Simultaneously, ethene gas was flowed through a stainless-steel jet feed to base of the tube. This was delivered at ≈ 0.5 L/min for the duration of the experiment, maintaining an atmosphere of ethene at ≈1 atm. The product solution was collected into a pre-made quenching solution of AcCysOH in MeCN (10 mL, 0.12 M). During the course of the reaction, the collection vial was replaced every 30 minutes, resulting in 6 fractions being collected. These 6 fractions were then analysed *via* GCMS. The first fraction (collected in the first 30 minutes) was omitted, because a steady state of flow had not been reached. From the final 5 fractions, the integrations in the GCMS trace were used to determine the conversions.

## Quenching Catalysts With *N*-Acetyl-L-Cysteine

A protocol for the inhibiting the activity of the catalyst was necessary. This is the case because we were interested in the reactivity in the VFD, and aimed to isolate this reactivity from any further reactivity in the collection vessel. A novel method was sought-after, considering the toxicity and the cost of previously reported quenching agents for Grubbs-type OM catalysts. The process below describes a quench using N-acetyl-L-cysteine (AcCysOH) with acetonitrile as a co-solvent. This method has the added benefit of altering the polarity of the ruthenium complex, which can potentially aid in chromatographic catalyst removal methods.

### Quenching Various Grubbs-Type Catalysts




A solution of 1-heptene (50 eq. relative to catalyst (depending on Mw of catalysts)) was dissolved in $CH_2Cl_2$ (2 mL). Half (1 mL) of this solution was transferred into a new, separate vial, creating two separate *vial*s with identical contents. To each of these *vial*s, 1 mL of a $CH_2Cl_2$ solution of catalyst (2 mg/mL) was added. Both solutions were stirred at room temperature. After 2 minutes of reaction time, a solution of AcCysOH in MeCN (1 mg in 250 µL) was added to one vial, and MeCN (250 µL) was added to the other. Both solutions were stirred for a further 8 minutes. After this, small aliquots were taken and dissolved in chloroform for GCMS analysis. GCMS was then performed, and conversions were calculated from the ratios of the integrals of the starting material and the final product. Results, shown in figure below, show that MeCN has quenching properties, but when combined with AcCysOH is a more efficient quenching solution for Grubbs-type OM catalysts. GCMS method is detailed below, along with a representative GC trace.

For GCMS, injection port temperature was set to 250˚C. The column oven was held at 100˚C for 2 minutes, before ramping to 200 ˚C at 10 ˚C/min, then the temperature was ramped to 300 ˚C at 20 ˚C/min and held at 300 ˚C for 5 minutes. The MS operated with a mass detection range from 50 to 600 m/z.

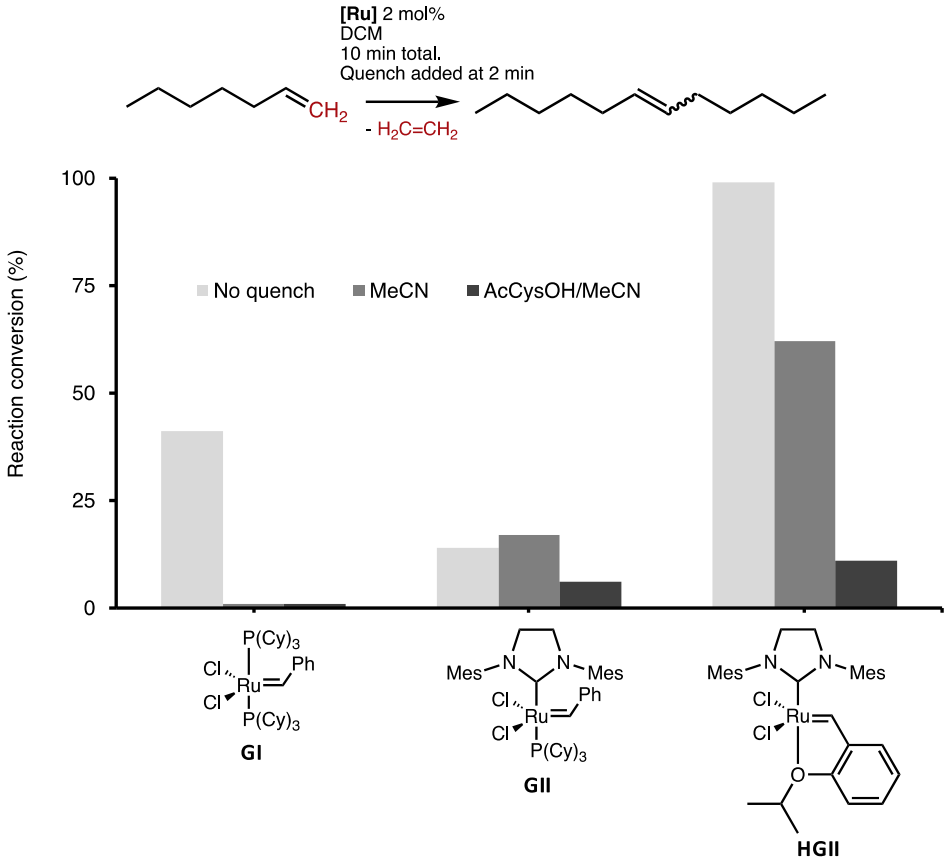



Figure S5. Quenching activity of both MeCN and a MeCN/AcCyst solution for three different Grubbs-type Ru-based OM catalysts

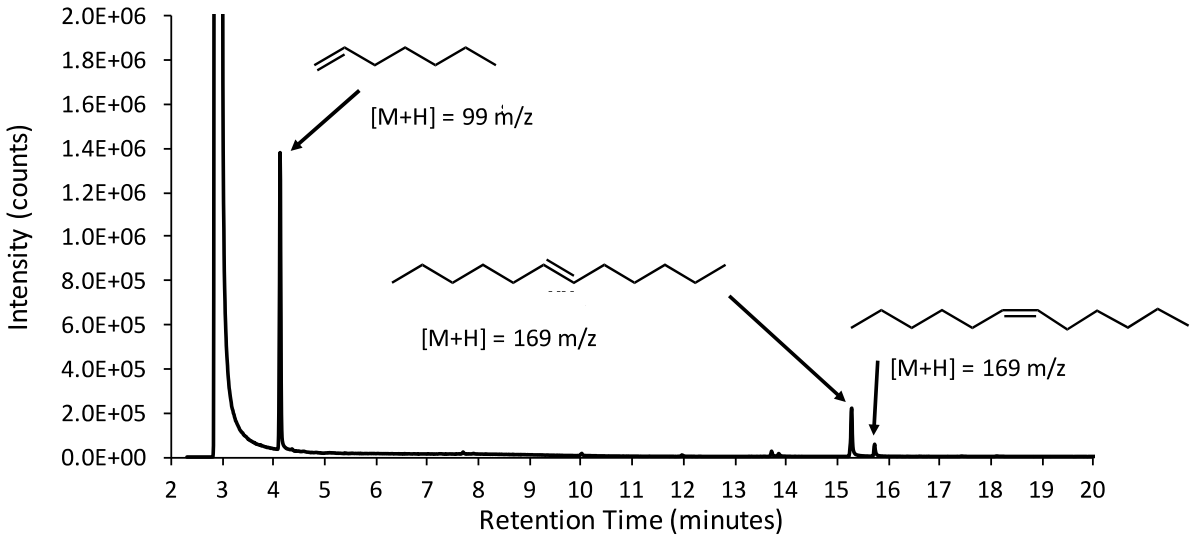
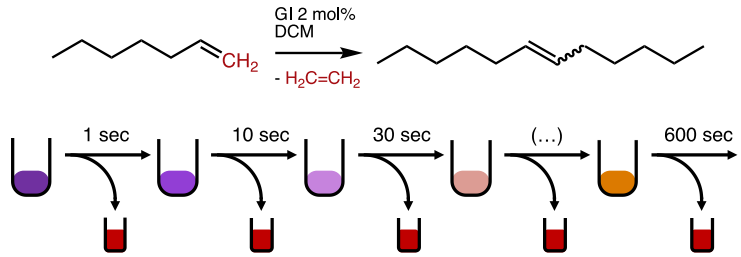



Figure S6. GC trace for a representative crude reaction mixture, after 10 minutes with quench added at the 2 minute mark

## Monitoring Reaction Progress in Batch. Quenched vs No Quench




The following experiment was performed to monitor the reaction of 1-heptene with the GI catalyst over time, and to monitor the quenching ability for the solution of AcCysOH in MeCN. Firstly, a quenching solution was prepared by dissolving AcCysOH (400 mg, 2.43 mmol) in MeCN (20 mL) creating a 20 mg/mL (0.122 M) solution. *NB* sonication was employed to aid in solvation. Secondly, a series of 24 GCMS vials were prepared with 1.25 mL of $CHCl_3$ and 100 µL of the quenching solution. For the reaction solution, the catalyst GI (10 mg, $1.22 \times 10^{-5}$ mol, 2 mol %) was weighed in a glass vial and dissolved in 10 mL of DCM. To this solution, 1-heptene (85 µL, 0.6 mmol) was added. A 250 µL aliquot of the reaction solution was taken and placed in one of the 24 pre-made quench solutions. At set time intervals of 1, 10, 20, 30, 45, 60, 90, 120 and then every 30 seconds until 600 seconds. GCMS was then performed on these samples, and conversions were calculated from comparing the integrations of the peaks corresponding to the two E & Z isomer products with the starting heptene.

## Interaction of Catalyst GI with *N*-acetyl-L-cysteine

In order to gain insight regarding the nature of the catalyst once quenched with the AcCysOH in MeCN solution, the following UV-vis, NMR and mass spectra were recorded. Attempts to grow crystals of the resulting compounds were unsuccessful, likely due to the existence of multiple product compounds.

### UV-Vis of GI/AcCysOH Interaction

The colour of the complexes was clearly affected from the addition of the quenching agents. Shown below are the UV-Vis spectra for the catalyst GI, the catalyst GI with MeCN and the catalyst GI with the solution of AcCysOH/MeCN (0.12 M).

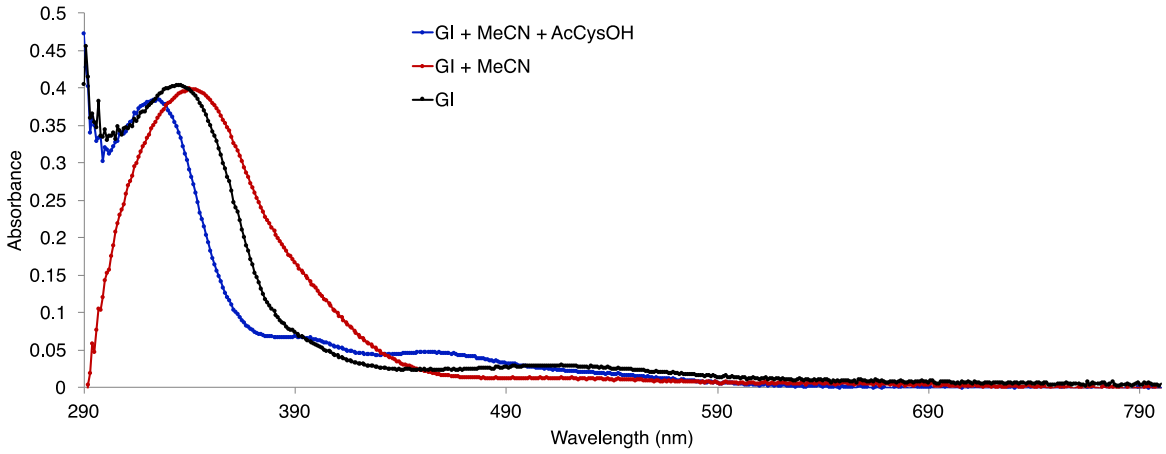



Figure S7. UV-Vis spectra in solutions of $CHCl_3$. Spectra for GI, GI with MeCN and finally the catalyst GI with the quenching solution of AcCysOH in MeCN (0.12 M).

Below are the photographs and associated UV-Vis spectra for the colours observed in the reaction mixtures of 1-heptene. This demonstrates the interaction with the active methylidene species.

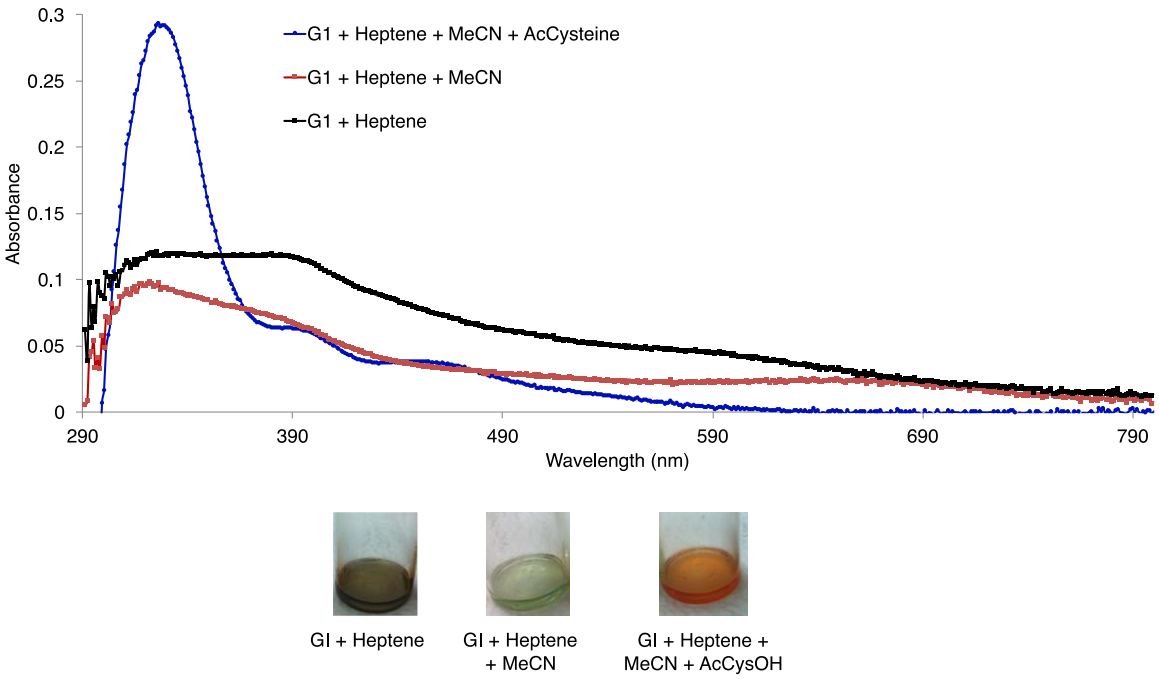



Figure S8. UV-Vis spectra and photographs of the 1-heptene/GI reaction in solution ($CHCl_3$), and also when quenched, both with MeCN and AcCysOH/MeCN

## NMR of GI/AcCysOH Interaction

In order to monitor the interaction of the catalyst with the quenching agent, a solution of GI (10 mg, 0.012 mmol) was titrated against a solution of AcCysOH in MeCN (20 mg/mL, 0.12 M). An internal standard of trimethoxybenzene (4 mg, 0.012 mmol) was used for qualitative analysis of peak integrals. A focus was placed on the alkylidene (Ru=CHPh) proton, and also on the 5 phenyl protons. Note the higher field scan range (between 25 – 5 ppm), necessary to observe the high field alkylidene. Spectra are shown below, qualitatively showing the consumption of GI (Figure S9) and the formation of a new compound (Figure S10). Peak integrals were used to quantify the degradation of GI (Figure S11) and the formation of the new compound (Figure S12). Note that the formation of the new alkylidene suggests only ≈15 % conversion (Figure S12), where as ≈96% of the original GI has been consumed. This suggests that other compounds are produced after reacting with the AcCysOH/MeCN solution.

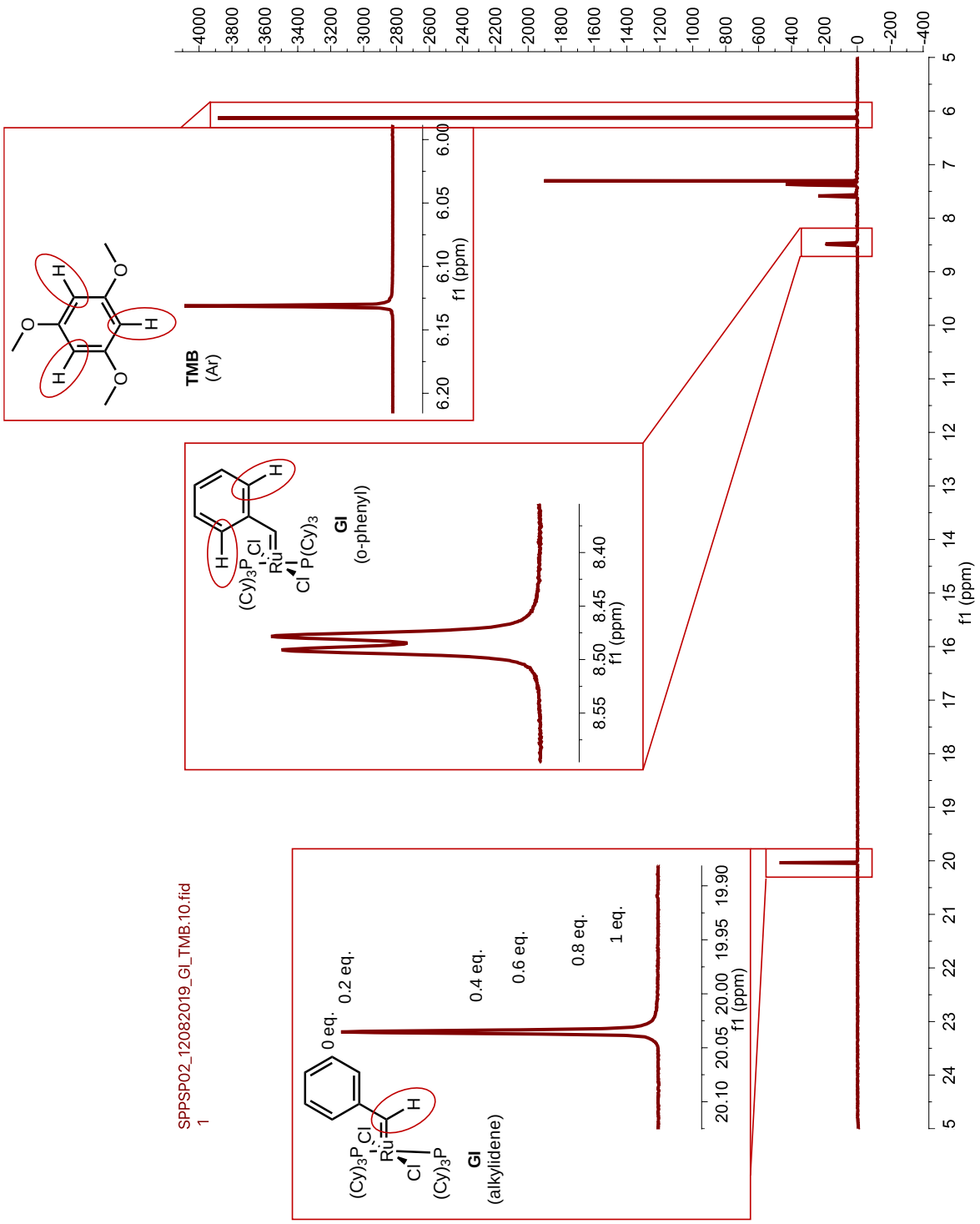



Figure S9. Super imposed $^{1}$H-NMR spectra of catalyst GI titrated against AcCysOH (20mg/mL in MeCN). Contains an internal standard of trimethoxybenzene (TMB, 1 eq. wrt. GI). Added at equivalents of, from left to right, 0 eq. (red), 0.2 eq. (yellow), 0.4 eq. (green), 0.6 eq. (cyan), 0.8 eq. (blue), 1 eq. (purple). Note the convenient down-field shift at each addition, likely due to the increasing concentration of MeCN. This allows visualization without shifting the spectra relative to each-other.

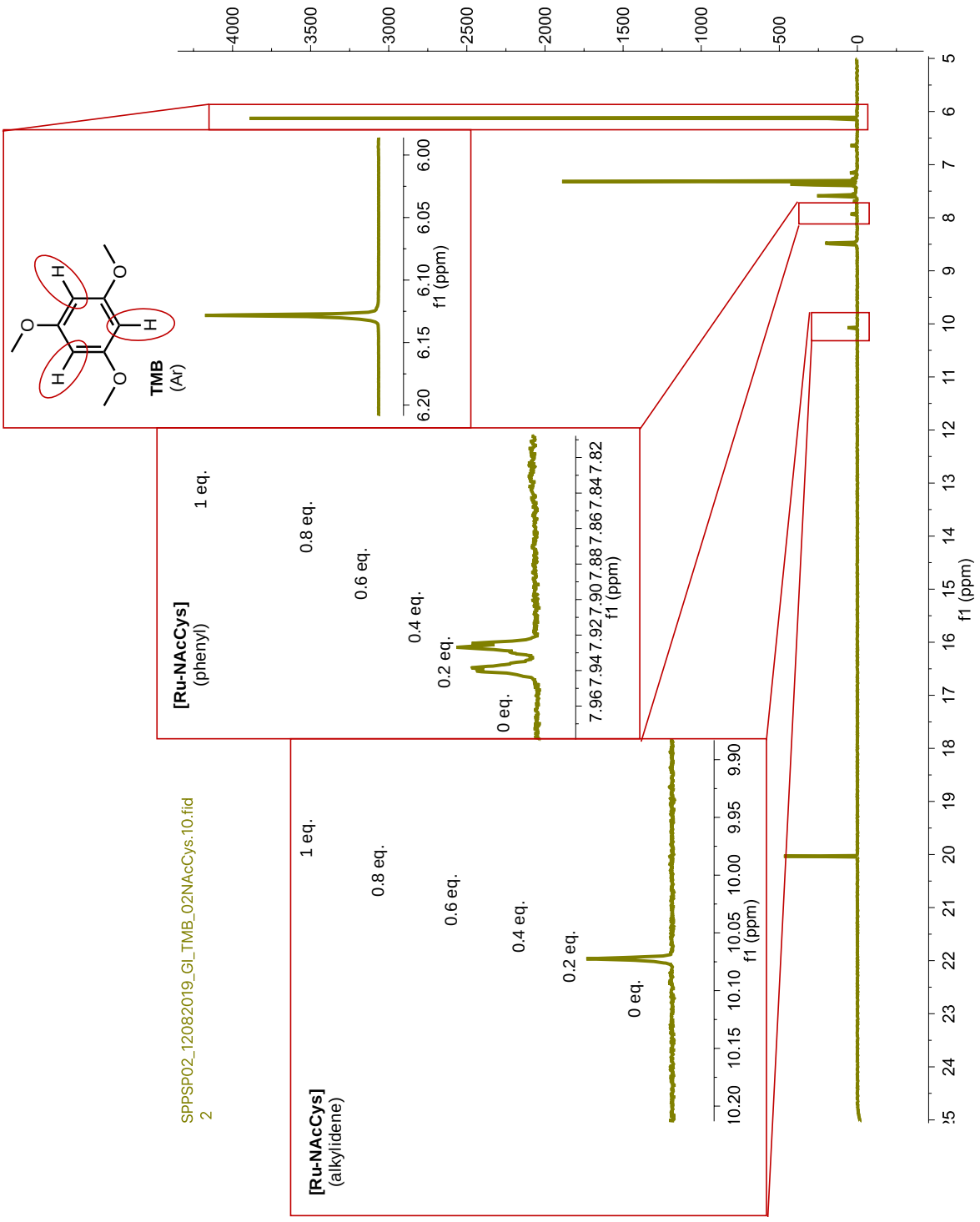



Figure S10. Super imposed $^{1}$H-NMR spectra of catalyst GI titrated against AcCysOH (20mg/mL in MeCN). Contains an internal standard of trimethoxybenzene (TMB, 1 eq. wrt. GI). Shown are the new peaks formed after addition of the AcCysOH solution. Added at equivalents of, from left to right, 0 eq. (red), 0.2 eq. (yellow), 0.4 eq. (green), 0.6 eq. (cyan), 0.8 eq. (blue), 1 eq. (purple).

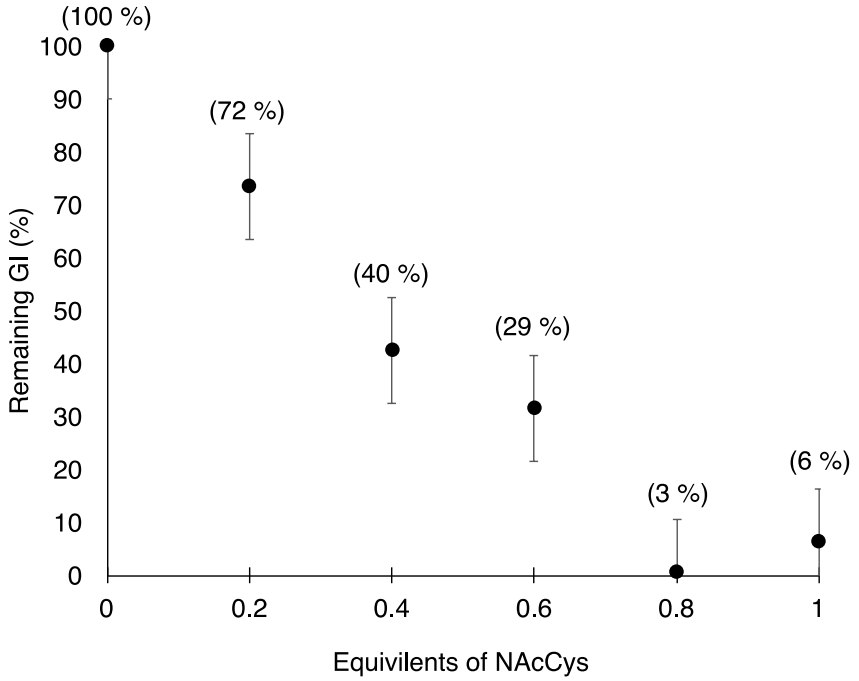



Figure S11. Consumption of GI after addition of AcCysOH solution (20 mg/mL in MeCN) to GI. Determined from the alkylidene $^{1}$H-NMR peak relative to internal standard (TMB).

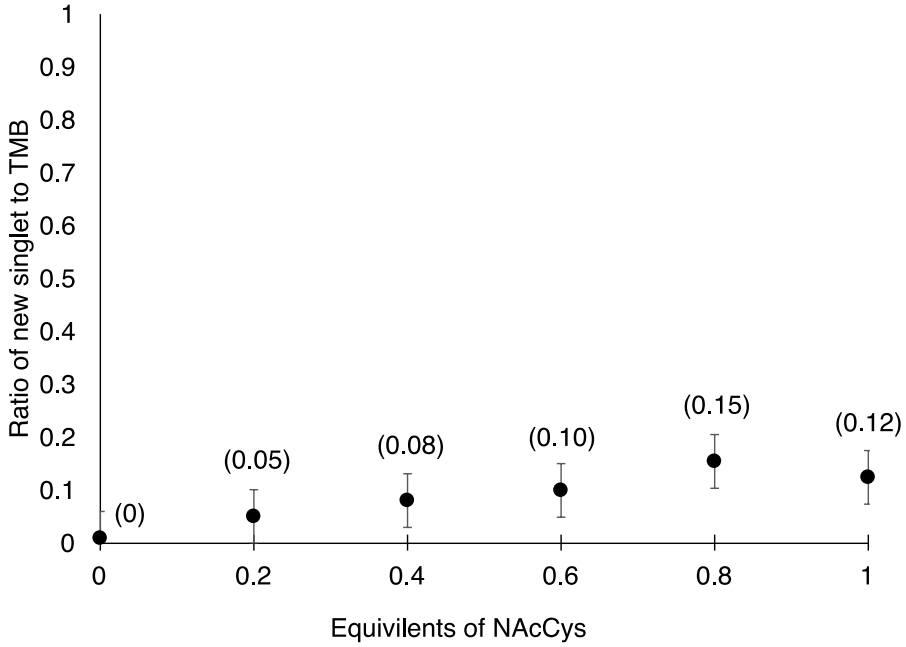



Figure S12. Formation of new singlet at 10.05 ppm after additions of AcCysOH solution (20 mg/mL in MeCN) to GI. Determined from the new $^{1}$H-NMR singlet at 10 ppm. Integral relative to internal standard (TMB). Note that the TMB integral is a result of three $^{1}$H nuclei and has been adjusted as such.

## MS of GI/AcCysOH Interaction

The following MS, although being inconclusive, shows that there is no simple ligand exchange occurring between GI and the AcCysOH + MeCN. Tables 1 & 2 show the possible masses that would result from ligand exchanges, and cannot be found in the MS.

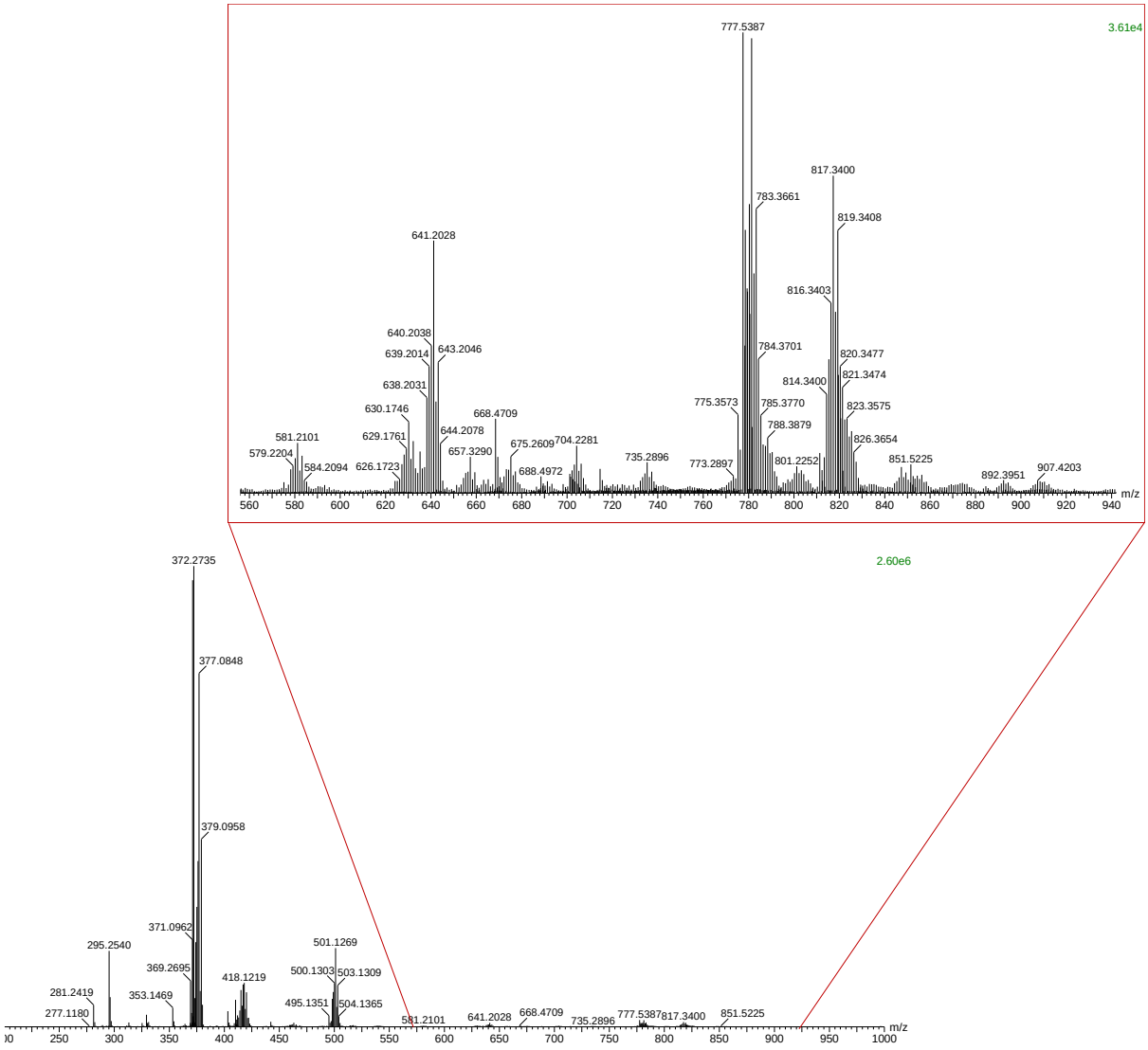



Figure S13. HRMS (+ve) of crude mixture after reacting GI with AcCysOH/MeCN solution (1 eq., 20 mg/mL).

Table 1. Possible molecular ions for ligand exchanges in (+ve) mode

| [M]+ | + none | + AcCysOH | + MeCN | + AcCysOH + MeCN |
|---|---|---|---|---|
| **- none** | 823.96 | 986.96 | 864.96 | 1027.96 |
| **- 1 Cl** | 788.51 | 951.51 | 829.51 | 992.51 |
| **- 2 Cl** | 753.06 | 916.06 | 794.06 | 957.06 |
| **- 1 P(Cy)3** | 543.73 | 706.73 | 584.73 | 747.73 |
| **- 2 P(Cy)3** | 263.5 | 426.5 | 304.5 | 467.5 |
| **- 1 Cl - 1 P(Cy)3** | 508.28 | 671.28 | 549.28 | 712.28 |
| **- 1 Cl - 2 P(Cy)3** | 228.05 | 391.05 | 269.05 | 432.05 |
| **- 2 Cl - 1 P(Cy)3** | 472.83 | 635.83 | 513.83 | 676.83 |
| **- 2 Cl - 2 P(Cy)3** | 192.6 | 355.6 | 233.6 | 396.6 |

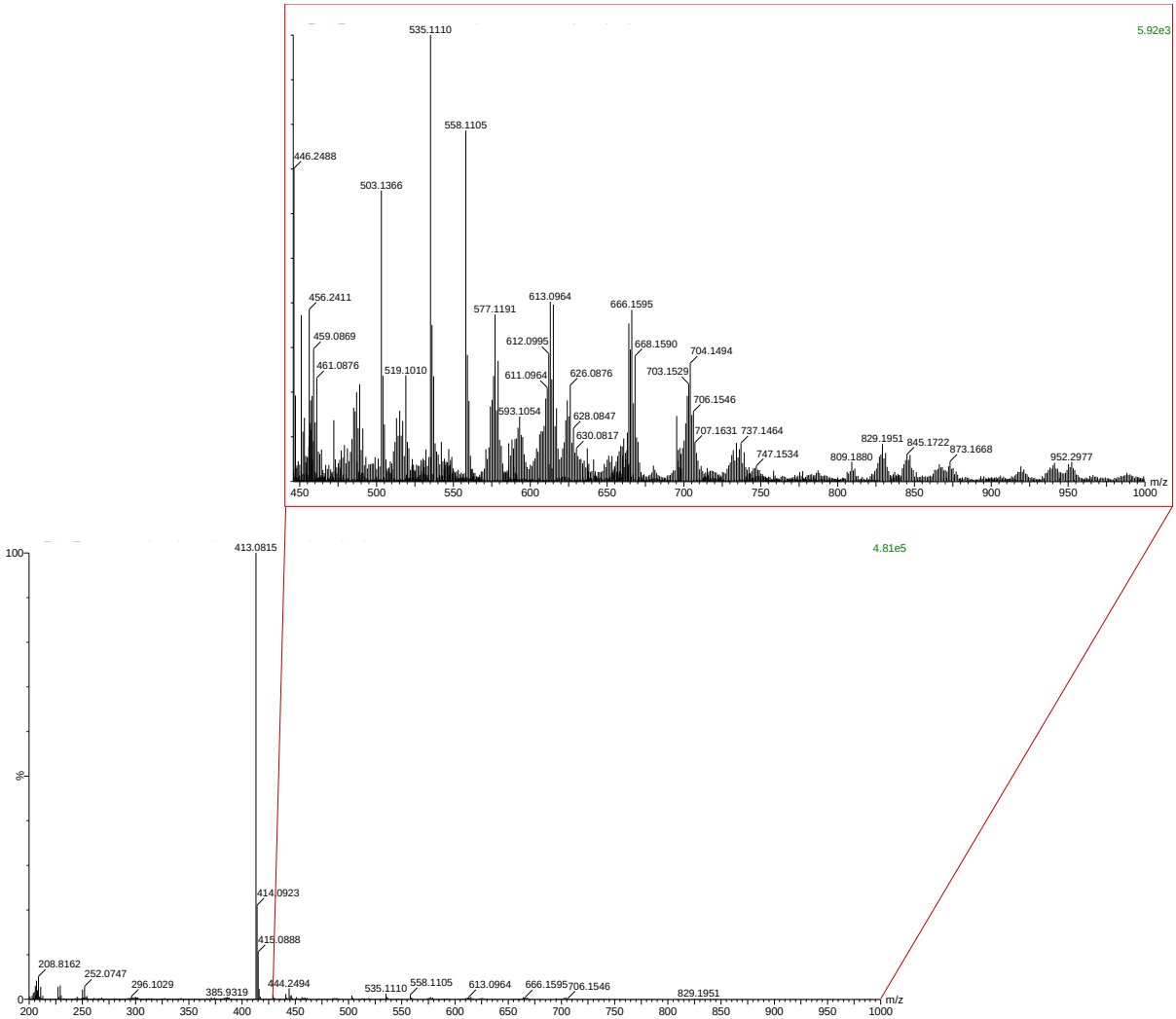


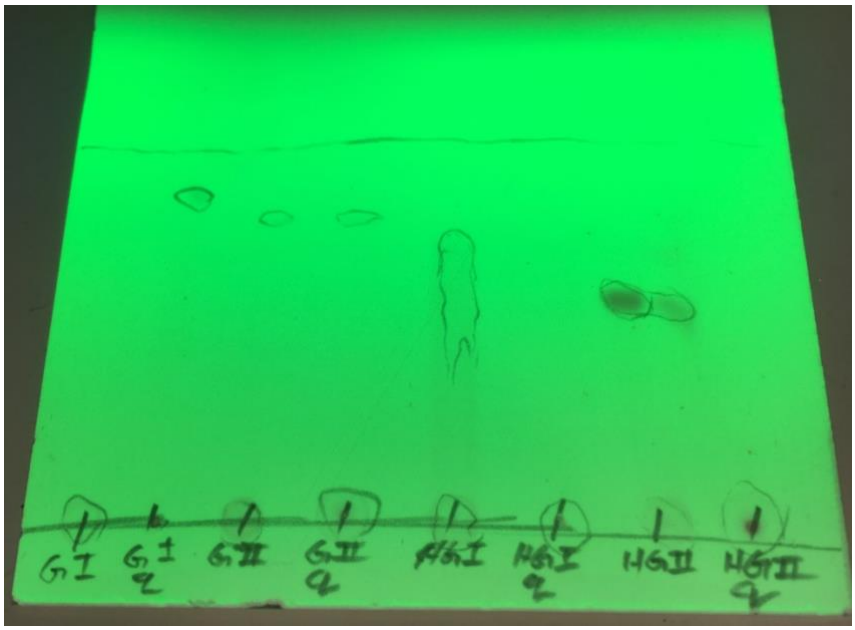

Figure S14. HRMS (-ve) of crude mixture after reacting GI with AcCysOH/MeCN solution (1 eq., 20 mg/mL).

Table 2. Possible molecular ions for ligand exchanges in (-ve) mode

| [M]- | + none | + AcCysOH | + MeCN | + AcCysOH + MeCN |
|---|---|---|---|---|
| **- none** | 821.96 | 984.96 | 862.96 | 1025.96 |
| **- 1 Cl** | 786.51 | 949.51 | 827.51 | 990.51 |
| **- 2 Cl** | 751.06 | 914.06 | 792.06 | 955.06 |
| **- 1 P(Cy)3** | 541.73 | 704.73 | 582.73 | 745.73 |
| **- 2 P(Cy)3** | 261.5 | 424.5 | 302.5 | 465.5 |
| **- 1 Cl - 1 P(Cy)3** | 506.28 | 669.28 | 547.28 | 710.28 |
| **- 1 Cl - 2 P(Cy)3** | 226.05 | 389.05 | 267.05 | 430.05 |
| **- 2 Cl - 1 P(Cy)3** | 470.83 | 633.83 | 511.83 | 674.83 |
| **- 2 Cl - 2 P(Cy)3** | 190.6 | 353.6 | 231.6 | 394.6 |

## Chromatographic Mobility

To observe the effect of the quenching method on the chromatographic mobility of the ruthenium complex, TLC was used. A mobile phase of 20 % EtOAc in hexane on a silica coated aluminium TLC plate. The spots were able to be visualised with UV light (256 nm). As seen in the photograph below, the catalyst bearing NHC ligands (GII & HGII) were not affected, but both GI and HGI had vast changes in the chromatographic retention factor.




| $R_F$ | GI | GII | HGI | HGII |
|---|---|---|---|---|
| $R_F$ Free | 0.0 | 0.7 | 0.6 | 0.5 |
| $R_F$ Quenched | 0.9 | 0.7 | 0.0 | 0.5 |

Figure S15. Chromatographic retention of the four different Ru-based OM catalysts, GI, GII, HGI and HGII. Mobile phase of 20% EtOAc in hexanes. Stationary phase of Silica coated aluminum plate. Visualized with UV light (256 nm). Table shows the retention factors ($R_F$) of each catalyst, quenched and un-quenched.

## Scope of Quenching Method

The following experiments were performed to demonstrate the validity of this quenching method with a variety of other OM conditions. A stock of the catalyst GI (10 mg, 0.012 mmol) was dissolved in 10 mL of $CH_2Cl_2$. To two separate vials, 1 mL of the catalyst stock was added to each. Allylphenyl sulphide (8.9 µL, 0.061 mmol) was added to both vials, and after 30 seconds had passed, one vial was quenched with the addition of AcCysOH in MeCN (20 mg/mL, 0.5 mL). This was repeated over 5 replicates. GCMS was perfomed on each sample 24 hours later to determine the ratio of starting material to products. This was then repeated for: the GII catalyzed CM of 1-heptene, the HGI RCM of diallyl diethylmalonate and the HGII RCM of N,N-diallyl-2,2,2-trifluoroacetamide.