

## REDUCTION OF CONJUGATED AND NON-CONJUGATED C=O/C=C SYSTEMS VIA TRANSFER HYDROGENATION

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### Abstract

The non-conjugated alkene/ketone compound 5-hexen-2-one was successfully reduced to 2-hexanol via transfer hydrogenation using Wilkinson's catalyst and isopropanol as the hydrogen-transfer agent (H-TA). Employing palladium on carbon as the catalyst and 1,3-cyclohexadiene as the H-TA leads to the selective reduction of 5-hexen-2-one, yielding 2-hexanol as the product. Chalcones are a set of compounds that contain a conjugated C=O/C=C system. A series of chalcones were successfully reduced to their tetrahydrochalcone derivatives using the Wilkinson catalyst/isopropanol transfer hydrogenation system. Reductions of chalcones with the Pd on C/1,3-cyclohexadiene system were inconclusive.

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Keywords: Transfer hydrogenation, Wilkinson's catalyst, reduction, isopropanol, chalcones

### Introduction

Organic compounds containing C=C and C=O bonds can be traditionally reduced using hydrogen gas and a transition metal catalyst (1,2). In transfer-hydrogenation (3-6), the unsaturated organic compound can be reduced without using an external source of H<sub>2</sub> gas. Hydrogen transfer agents (H-TA) are molecules that can act as a source of hydrogen, with the transition metal catalyst essentially removing hydrogen from one reagent and transferring it to another. Each H-TA agent produces a stable product on removal of hydrogen, which acts as a driving force for the reaction. Although each transfer hydrogenation reaction is potentially reversible, using an excess of donor agent appears to prevent this (7). In previous publications from our group (8,9), we described how Wilkinson's catalyst [RhCl(PPh<sub>3</sub>)<sub>3</sub>] was successfully used as a hydrogen-transfer catalyst along with isopropanol as the hydrogen-transfer agent to reduce a series of organic compounds containing C=C and C=O bonds. KOH is also used in this system as the initiator. In this method, the formation of acetone, which is produced when hydrogen was removed from the isopropanol hydrogen-transfer agent, can be monitored using infrared spectroscopy. Chalcones are a series of compounds that contain an α,β-unsaturated C=O/C=C system, prepared via an aldol condensation between an aldehyde and ketone (10). Previous publications have described a variety of reduction methods of chalcones (11-17), of which some describe selective reduction of either the C=O (18) or C=C (19-21) bonds. One of the goals of this paper was to see if our method could be extended to successfully reduce chalcones.

An experiment in the undergraduate organic chemistry laboratory can also be used to illustrate the concepts of transfer hydrogenation. A palladium on carbon heterogeneous catalyst can be used in collaboration with cyclohexene as the hydrogen donor agent to partially hydrogenate olive oil (22). 1,3-cyclohexadiene can be similarly employed to perform reductions of this type (3) and both systems yield benzene as evidence of transfer hydrogenation.

### Experimental

#### Materials and Instrumentation

All chemicals, apart from the starting chalcones, were obtained from Sigma-Aldrich or Strem and used without further purification. The chalcones were prepared via a solvent-free aldol

condensation (10). All reactions were performed under an inert atmosphere of nitrogen, and the isopropanol solvent degassed under nitrogen prior to use. Infrared (IR) spectra were recorded on a Thermo Scientific Nicolet 6700 FT-IR Spectrometer. Analysis of reaction products via G.C. were performed on a GOW-MAC Gas Chromatograph using a 4' x 1/4' 20% DC 200 on Chrom.-P 80/100 Mesh column. Runs were carried out at an isotherm of either 120°C or 150°C with a helium carrier gas pressure of 40 psi (specific temperature is noted in the relevant experimental). Reaction yields for the liquid products were calculated via GC based on area under peak integration calculations as compared to standards. Proton NMR spectra were recorded on a Varian EM360A NMR spectrometer with Anasazi Eft-60.

#### Synthesis of 2-hexanol from 5-hexen-2-one

RhCl(PPh<sub>3</sub>)<sub>3</sub> (50mg, 0.05mmol) was placed in a 25ml Schlenk tube, and the tube evacuated and refilled with nitrogen several times. Nitrogen purged isopropanol (5ml) was added, followed by 5-hexen-2-one (0.2ml, 1.7mmol) and KOH (1.5ml, 0.1M sol<sup>n</sup> in isopropanol). The reaction was stirred overnight at room temperature under nitrogen and the catalyst allowed to settle. The infrared spectrum of the reaction liquor was taken to confirm that the starting 5-hexen-2-one had completely reacted and acetone had been produced. FT-IR of reaction mixture (iPrOH): peaks due to 5-hexen-2-one at 1712 cm<sup>-1</sup> (C=O) and 1643 cm<sup>-1</sup> (C=C) go down, peak at 1710 cm<sup>-1</sup> (C=O of acetone) produced. G.C (150°C): RT of 2-hexanol produced (44 sec) versus 2-hexanol standard (43 sec). Yield 56 %.

#### Synthesis of hexane from 1-hexene

Pd/C (5%) was placed in a 25ml Schlenk tube, and the tube evacuated and refilled with nitrogen several times. Nitrogen purged cyclohexadiene (5ml) was added, followed by 1-hexene (0.2ml, 1.6mmol). The reaction was heated under reflux for 5hrs and the catalyst allowed to settle. The infrared spectrum of the reaction liquor was taken to confirm that the starting 1-hexene had completely reacted and benzene had been produced. FT-IR of reaction mixture (C<sub>6</sub>H<sub>8</sub>): Peak due to 1-hexene 1641 cm<sup>-1</sup> (C=C) goes down, peaks at 1956, 1811, 1527, 1480 cm<sup>-1</sup> (benzene) produced.

#### Synthesis of 2-hexanone from 5-hexen-2-one

Pd/C (5%) was placed in a 25ml Schlenk tube, and the tube evacuated and refilled with nitrogen several times. Nitrogen

purged cyclohexadiene (5ml) was added, followed by 5-hexen-2-one (0.2ml, 1.7mmol). The reaction was heated under reflux for 5hrs and the catalyst allowed to settle. The infrared spectrum of the reaction liquor was taken to confirm that the starting 5-hexen-2-one had completely reacted and benzene had been produced. FT-IR of reaction mixture ( $C_6H_8$ ): Peak due to 5-hexen-2-one at  $1642\text{ cm}^{-1}$  ( $C=C$ ) goes down, ( $C=O$  peak at  $1720\text{ cm}^{-1}$  unchanged), peaks at  $1956, 1811, 1527, 1480\text{ cm}^{-1}$  (benzene) produced. (Fig1). G.C. ( $150^\circ$ ): RT of generated 2-hexanone (1.08 min, Fig. 2a) versus 2-hexanone standard (1.07 min, Fig. 2b), compared to starting 5-hexen-2-one standard (1.20 min, Fig. 2c). Yield ~68 %.

#### Synthesis of 1,3-Diphenyl-1-propanol from simple chalcone

$RhCl(PPh_3)_3$  (50mg, 0.05mmol) and simple chalcone (0.2g, 0.9mmol) were placed in a 25ml Schlenk tube, and the tube evacuated and refilled with nitrogen several times. Nitrogen purged isopropanol (5ml) was added, followed by KOH (1.5ml, 0.1M sol<sup>n</sup> in isopropanol). The reaction was stirred overnight at room temperature under nitrogen and the catalyst allowed to settle. The infrared spectrum of the reaction liquor was taken to confirm that the starting chalcone had completely reacted and acetone had been produced. FT-IR of reaction mixture (iPrOH): peaks due to simple chalcone at  $1662\text{ cm}^{-1}$  ( $C=O$ ) and  $1605\text{ cm}^{-1}$  ( $C=C$ ) go down, peak at  $1711\text{ cm}^{-1}$  ( $C=O$  of acetone) produced. The liquor was removed and the solvent removed via rotary evaporator. The residue was extracted into diethyl ether and filtered through a celite pad. The ether was then removed under vacuum and the product isolated. Yield approx. 65 %.  $^1H$  NMR (60 Mhz): d 7.2 (m, 10H), d 4.7 (t, 1H), d 2.8 (m, 2H), d 2.1 (m, 2H).

#### Synthesis of 3-(4-methylphenyl)-1-phenyl-1-propanol from 4-methylchalcone

The above procedure was repeated using 4-methylchalcone (0.2g, 0.85mmol) in place of simple chalcone. Yield~70%. FT-IR of reaction (iPrOH): peaks due to 4-methylchalcone at  $1658\text{ cm}^{-1}$  ( $C=O$ ) and  $1602\text{ cm}^{-1}$  ( $C=C$ ) go down, peak at  $1711\text{ cm}^{-1}$  ( $C=O$  of acetone) produced. (Fig.3).  $^1H$  NMR (60 Mhz): d 7.3 (m, 9H), d 4.7 (t, 1H), d 2.6 (m, 2H), d 2.3 (s, 3H), d 2.1 (m, 2H).

#### Synthesis of 3-(4-chlorophenyl)-1-phenyl-1-propanol from 4-chlorochalcone

The above procedure was repeated using 4-chlorochalcone (0.2g, 0.8mmol) in place of simple chalcone. Yield~70%. FT-IR of reaction (iPrOH): peaks due to 4-chlorochalcone at  $1661\text{ cm}^{-1}$  ( $C=O$ ) and  $1608\text{ cm}^{-1}$  ( $C=C$ ) go down, peak at  $1711\text{ cm}^{-1}$  ( $C=O$  of acetone) produced.  $^1H$  NMR (60 Mhz): d 7.2 (m, 9H), d 4.6 (t, 1H), d 2.6 (m, 2H), d 2.0 (m, 2H). (Fig. 4b)

## Results and Discussion

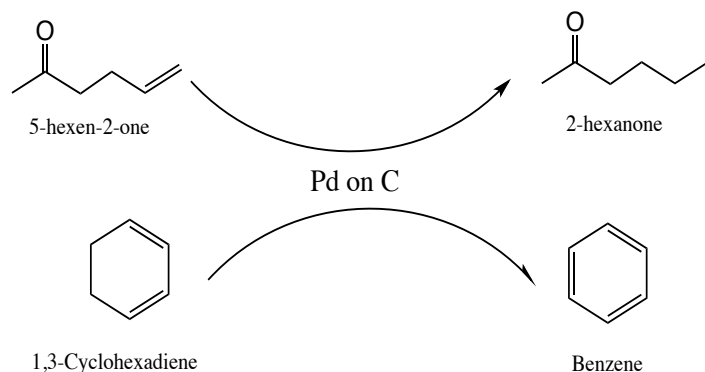
Transfer-hydrogenation involves hydrogen being removed from one species (the hydrogen-transfer agent, H-TA) and being donated to the organic substrate that is being reduced. When isopropanol is used as the donor agent, it is converted to acetone. Therefore observing the formation of acetone in the infrared spectra of the reaction mixtures serves as the first evidence that hydrogen transfer has occurred. Acetone has a characteristic  $C=O$  stretch at  $1711\text{ cm}^{-1}$ , and its formation can be clearly followed. In addition, as the unsaturated organic substrate adds the transferred hydrogen, any IR stretches that are due to the starting material, such as  $C=O$  or  $C=C$  bonds, would be expected to go down in the

IR of the product.

In previous publications from our research group (8,9) we described the reduction of a series of unsaturated organic substrates using isopropanol as the H-TA agent and Wilkinson's catalyst. One of these substrates was 5-hexen-2-one, containing both  $C=O$  and  $C=C$  bonds, which was reduced to 2-hexanol. As the reaction proceeds, it could be clearly observed in the infrared spectra that the  $C=C$  peak at  $1643\text{ cm}^{-1}$  was removed and that the double bond had been saturated. Confirmation that the ketone group was also reduced was less conclusive in the IR, as the  $C=O$  stretch of the starting substrate ( $1712\text{ cm}^{-1}$ ) coincides with that of the acetone produced in the reaction ( $1711\text{ cm}^{-1}$ ). However this peak was clearly observed to have increased significantly in size. G.C analysis of the product of the reaction against a standard sample of 2-hexanol in isopropanol confirmed that the product of the reaction was indeed 2-hexanol. The yield was approximately 60 % as determined by a peak area calculation.

There was interest in our group to look at other catalyst/H-TA systems that could perform similar reductions of  $C=O$  and  $C=C$  bonds. We next investigated a palladium on carbon heterogeneous catalyst with cyclohexene as the H-TA agent. In this system, cyclohexene would theoretically produce benzene upon giving up its hydrogens as the byproduct of hydrogen transfer. After attempting several reductions with simple alkene and ketone substrates, no reaction was observed at either room temperature or under refluxing conditions. The H-TA agent was then changed from cyclohexene to 1,3-cyclohexadiene, which is nearer to the 'electron sink' benzene final product. Reducing 1-hexene with Pd on C/1,3-cyclohexadiene did not give any reaction at room temperature, however upon reflux a reaction was clearly observed. Recording the infrared spectra of the reaction mixture shows that the  $C=C$  stretch of the starting 1-hexene at  $1641\text{ cm}^{-1}$  has been removed. In addition, the generation of benzene can be clearly observed from the presence of the characteristic aromatic overtone peaks at  $1956, 1811\text{ cm}^{-1}$ , along with additional peaks at  $1527$  and  $1480\text{ cm}^{-1}$ . Also of interest was the generation of a small amount of cyclohexene in the reaction mixture, as noted by a new peak at  $1653\text{ cm}^{-1}$ . Attempts at extending this method to reduce a ketone were unsuccessful, as no comparable reduction was observed with 2-hexanone. That led us to believe that this system should therefore be able to selectively reduce 5-hexen-2-one to 2-hexanone, instead of the 2-hexanol produced via the Wilkinson's catalyst/isopropanol system. This could indeed be observed upon reacting 5-hexen-2-one with Pd on C/1,3-cyclohexadiene, as outlined in scheme 1.

**Scheme 1:** Outline of the transfer-hydrogenation of 5-hexen-2-one using Palladium on Carbon and 1,3-Cyclohexadiene



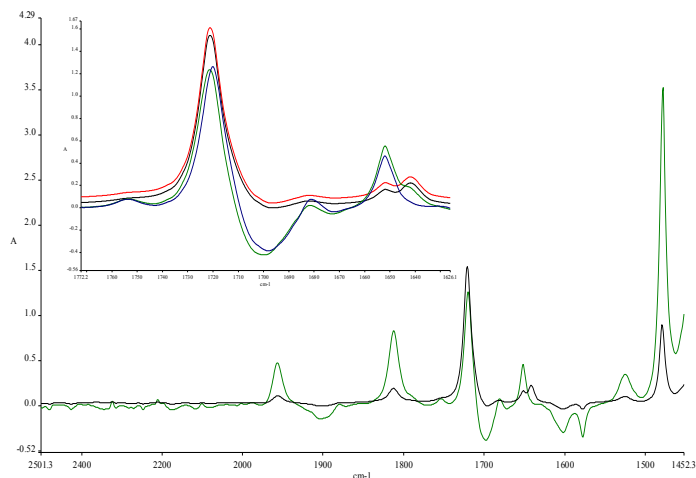


Figure 1: FT-IR of 5-hexen-2-one reduction mixture.

After heating under reflux for 5 hrs, the infrared spectrum of the reaction mixture shows that the C=C stretch at  $1642\text{ cm}^{-1}$  has been removed, but the C=O peak at  $1721\text{ cm}^{-1}$  is still present. This can be observed in Fig. 1, which shows the infrared spectrum in Absorbance, which is the norm in these types of reactions, as it is easier to observe peaks being formed and removed as the reaction proceeds. The main spectrum shows the product of the reaction (green) overlaid over the starting material (black). The C=O/C=C region has also been expanded and appears in the top left corner. This includes four overlaid spectrum, obtained from monitoring the reaction over the duration of the reflux. In the expanded spectrum, it can be clearly observed that the C=C peak at  $1642\text{ cm}^{-1}$  has been removed but that the C=O peak at  $1721\text{ cm}^{-1}$  remains. In addition, the formation of the benzene byproduct can also be observed from

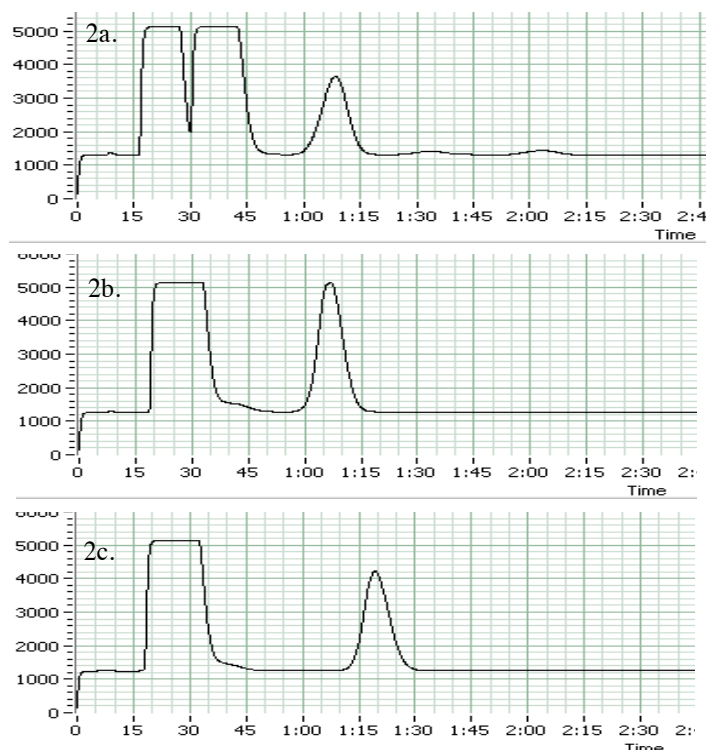
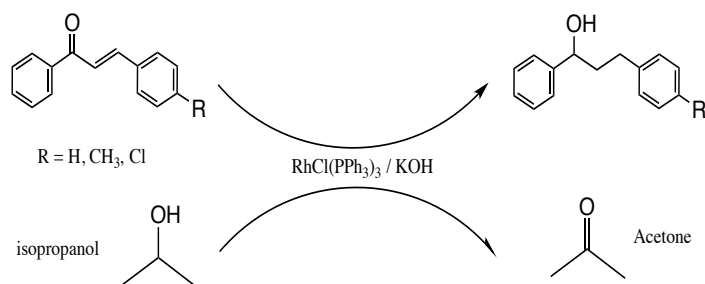


Fig. 2a. G.C. of 2-hexanone produced via transfer hydrogenation. (Top)  
 Fig. 2b. G.C. of 2-hexanone standard. (Middle)  
 Fig. 2c. G.C. of 5-hexen-2-one standard. (Bottom)

the generated stretches at  $1957$ ,  $1814$ ,  $1625$  and  $1480\text{ cm}^{-1}$  in the main spectrum. The additional peak at  $1652\text{ cm}^{-1}$  corresponds to cyclohexene.

Product formation was confirmed by G.C analysis, as can be observed in Fig.2. The generated product of the reaction is seen in Fig. 2a (RT 1.08) and compared to a 2-hexanone standard (Fig. 2b, RT 1.07) and the 5-hexen-2-one starting material (Fig. 2c, RT 1.20). The yield of the reaction is approximately 68 % based on the area under the peak integration calculations.

Based on the success of our previous reductions of alkenes and



Scheme 2: Outline of the transfer-hydrogenation of chalcones using Wilkinson's catalyst and isopropanol.

ketones using the Wilkinson's catalyst/isopropanol conditions, we next wished to investigate whether this method could be extended to include molecules that contained a conjugated set of C=C/C=O bonds. In the conversion of 5-hexen-2-one substrate to 2-hexanol, both unsaturated bonds were reduced. In this molecule, the C=O and C=C bonds are not conjugated and are separated by two  $sp^3$  carbons. It was assumed that the reactivity of the unsaturated bonds would be different in an  $\alpha,\beta$ -conjugated ketone system. A series of Chalcones were selected as the compounds to investigate due to their ease of synthesis and potential chemical importance (10). The outline of the reaction can be seen in scheme 2.

Four different chalcones were investigated; 'simple chalcone' (R=H), 4-methylchalcone, 4-chlorochalcone and 4-nitrochalcone. As before, the reductions can be monitored via infra-red

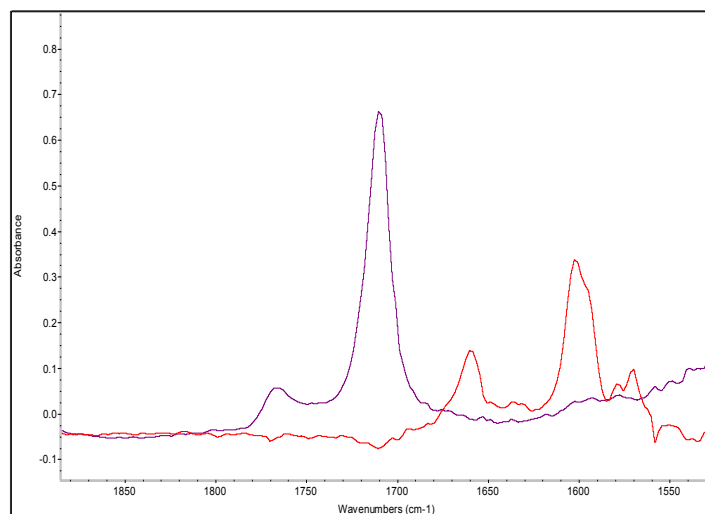


Figure 3: FT-IR of 4-chlorochalcone reduction reaction mixture

spectroscopy as they proceed. Fig. 3 shows the reaction mixture of the transfer-hydrogenation of 4-methylchalcone. The initial spectra (red) shows the stretches for the C=O (1658  $\text{cm}^{-1}$ ) and C=C (1602  $\text{cm}^{-1}$ ) of the  $\alpha,\beta$ -unsaturated ketone starting material. As the reaction proceeds, it can be clearly observed that these peaks disappear and that a new peak is seen at 1711  $\text{cm}^{-1}$ , which corresponds to the generated acetone (purple). Similar conversions can be observed in the IR for the simple chalcone and 4-chlorochalcone. However, no reaction was observed for 4-nitrochalcone. This may have been due to the electron withdrawing nature of the nitro group reducing reactivity or due to the fact that the 4-nitrochalcone was considerably less soluble in the isopropanol solvent.

The  $^1\text{H}$  NMR spectra of the final tetrahydrochalcones were recorded in  $\text{CDCl}_3$  and compared to the starting chalcone in each case. Fig. 4a. shows the proton NMR of 4-Chlorochalcone, and Fig. 4b. the isolated 3-(4-chlorophenyl)-1-phenyl-1-propanol. The olefin (=CH) protons of the starting material can be observed in Fig. 4a at  $\delta$  8.0 ppm. In the reduced product, this signal is no longer present, as expected. The existence of the added protons can be confirmed by the presence of new signals at  $\delta$  4.6 ppm, ( $\text{CHOH}$ ) and  $\delta$  2.6, 2.0 ppm, ( $\text{CH}_2$ ).

The Wilkinson Catalyst/isopropanol system was able to reduce both the C=C and C=O bonds of 5-hexen-2-one, whereas the Pd on C/1,3-cyclohexadiene system selectively reduces only the C=C bond. Therefore there was an interest in seeing whether a similar selectivity would be observed with the  $\alpha,\beta$ -unsaturated chalcones. Several attempts were made at reducing

simple chalcone with Pd on C/1,3-cyclohexadiene, but the results obtained were inconclusive. Heating the system under reflux for several hours does show the generation of benzene in the infrared spectra of the products. However, the C=O and C=C stretches of the reactants do not appear to go down in the IR spectra and a clean NMR spectrum of the products could not be obtained. Further work needs to be investigated on this.

## Conclusion

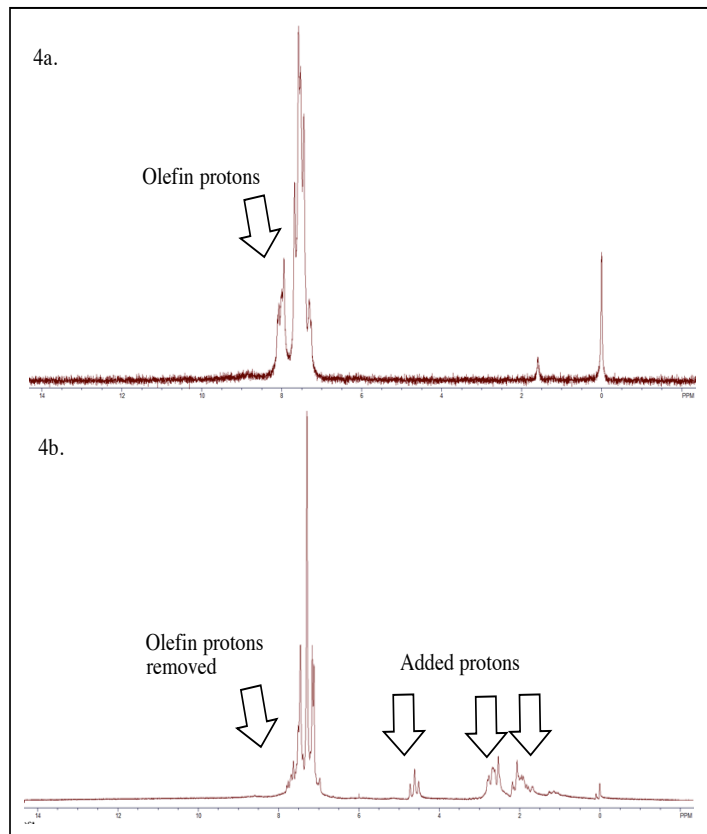
Based on the results of this study, the reactions described in this paper provide an effective and efficient method of reducing non-conjugated and  $\alpha,\beta$ -conjugated unsaturated organic substrates via hydrogen transfer employing isopropanol as the hydrogen-transfer agent and  $\text{RhCl}(\text{PPh}_3)_3$  as the catalyst. Using Pd on Carbon with 1,3-cyclohexadiene leads to the selective reduction of the non-conjugated alkene/ketone compounds.

## Acknowledgements

The Ramapo College TAS Research Honors Program for providing funds for consumables. Mrs. Carol Ichinco, the chemistry lab coordinator, for her help with the instrumentation and equipment.

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**Figure 4a.**  $^1\text{H}$  NMR of 4-chlorochalcone (Starting Material)

**Figure 4b.**  $^1\text{H}$  NMR of 3-(4-methylphenyl)-1-phenyl-1-propanol (product)