Activating small molecules for catalysis using organometallic complexes.

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ABSTRACT

Ruthenium complexes are known to possess catalytic properties which are of great value in organic syntheses. This project is divided into two parts. First, the mechanism of Ru(CO)₃(PPh₃)₂ and Ru(CO)H₂(CO(PPh₃)₃ towards aromatic C-H addition onto olefins was investigated, using acetophenone and styrene. FTIR studies revealed that the initial step of the reaction with Ru(CO)H₂(CO(PPh₃)₃ does not involve acetophenone. These studies also show that the complex formed from the reaction of Ru(CO)₃(PPh₃)₂ in acetophenone could be a cyclometallated ruthenium intermediate in the reaction pathway. Second, the catalytic properties of other ruthenium complexes were looked into. Experiments involving ruthenium-thiol complex led to the discovery of catalytic hydrocarboxylation. Selectivity of the products observed provides some information on the reaction mechanism.

INTRODUCTION

Ruthenium complexes are known to possess catalytic properties which are of great value in organic syntheses. One example is the regiospecific ortho substitution of olefins on aromatic ketones using carbonyl(dihydrido)tris(triphenylphosphine) ruthenium (II), as reported by Murai et. al.º Two studies were carried out throughout this project. The first study was focused on the mechanism of catalytic addition from aryl C-H bond onto olefins using tricarbonylbis(triphenylphosphine) ruthenium(0), which was reported as one of the effective catalyst by Murai. Styrene and acetophenone were used as reactants. The key intermediate of the reaction was found to be a cyclometallated complex. This was supported by FTIR and computational studies. Murai’s proposed mechanism for the reaction involving Ru(CO)H₂(CO(PPh₃)₃ were supported by our FTIR studies. It is shown that this complex reacts with styrene but not with acetophenone in the initial step of its catalytic cycle.

The existence of sulphur-containing active sites of biological enzymes led to interest in the use of transition metal-sulphur complexes as model compounds.¹ This work encompasses the use of thiol as ligands in ruthenium compounds, which leads to the formation of a thiol-bridged ruthenium oligomer. The complex was first demonstrated to be capable of hydrocarboxylation to form acylated enol esters, which are of medicinal importance as prodrugs.³ Acetate derivatives and phenols were also employed to further investigate its catalytic properties.

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MATERIALS AND METHODS

IR spectra were measured using Shimazdu Prestige-21 FTIR Spectrometer. CDCl₃ was used as solvent for NMR measurements and NMR data were recorded using Bruker Avance 300 at 300 Mhz. Photolysis was carried out using Blak-Ray Longwave UV lamp. All chemicals and solvents used were purchased from Sigma Aldrich Co.

Synthesis of Ru(CO)₃(PPh₃)₂

Ru₃(CO)₁₂ and hex-1-ene were mixed and sealed in vacuum and left under UV lamp with stirring for 4 hours at room temperature. Next, 1 mol equivalent of PPh₃ to Ru₃(CO)₁₂ was added into the flask and left under UV lamp with stirring for 2 hours, after which 1.2 mol equivalent of PPh₃ was added and photolysed for 1 hour. Reaction mixture was filtered and pale yellow residue obtained was washed with hexane.

Synthesis of Ruthenium-thiol species

Ru₃(CO)₁₂ and 4-methylbenzene thiol (4-MBT) was reflux with toluene with stirring in a sealed test tube for 24 hours. Dark orange solution was concentrated using rotary evaporator and eluted with hexane, followed by dichloromethane using flash column chromatography. Dark orange amorphous solid was obtained on standing.

Mechanistic studies using Ru(CO)₃(PPh₃)₂ and Ru(CO)H₂(PPh₃)₃

Mechanistic experiments were done under nitrogen atmosphere containing the ruthenium complex and the reactant of interest (acetophenone and styrene). A sample was extracted periodically via syringe for IR measurements.

Catalysis using Ruthenium-thiol complex

The complex, phenylacetylene and glacial acetic acid (or other reactants in their corresponding stoichiometric proportion of 1:1) were dissolve in toluene. Reaction mixture was stirred at 90°C for 12 hours. Thereafter, benzaldehyde was introduced as an internal standard and toluene was added to fill up to the mark of the test tube and send for NMR analysis.
RESULTS AND DISCUSSION

Ru(CO)₃(PPh₃)₂ in acetophenone

Fig. 1: IR spectrum obtained from reaction of Ru(CO)₃(PPh₃)₂ and acetophenone showing spectra obtained at 0, 15, 30, 60, 90, and 150 min. IR ν (CO) (from right) = 1893 (catalyst), 1933, 1947, 1976, 1994, 2021 cm⁻¹. Reaction conditions were identical to the catalytic reaction condition.

Spectrum shows blue-shifted peaks in the CO stretching region. 15 mins into the reaction, new peaks appeared at IR bands at 1933, 1947, 1976, 1994 and 2021 cm⁻¹. Acetophenone could act as a two electron donor either via the lone pair of electrons on oxygen or the pi-bond of the carbonyl. Ligand substitution reaction is likely to occur due to high concentration of acetophenone. These IR peaks at 1933, 1947 and 2021 cm⁻¹ could correspond to the same intermediate formed in the reaction, since they show a proportional increase in intensity. On this note, this reaction does not seem to involve a simple two step equilibria involving the first substitution of triphenylphosphine, followed by a second substitution. The structure of this intermediate (Fig. 2) corresponding to the three IR peaks might be a mer-cyclometallated hydrido compound formed via the oxidative addition of acetophenone onto the catalyst. Computational calculations using Gaussian 03 produced an IR spectrum whose intensity and signal pattern matches that of CO bands of the three IR peaks.

Reactions involving the use of ruthenium-thiol complex

Table 1 summarizes the carboxylic acid derivatives and phenols used. Yield was calculated using the NMR data collected.

<table>
<thead>
<tr>
<th>No.</th>
<th>Reactants</th>
<th>Product</th>
<th>Yield</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Acetic acid</td>
<td>Styryl acetate</td>
<td>58.7 %</td>
</tr>
<tr>
<td>2</td>
<td>Trimethylacetic acid</td>
<td>Styryl trimethylacetate</td>
<td>86.5 %</td>
</tr>
<tr>
<td>3</td>
<td>Trifluoroacetic acid</td>
<td>Phenylacetylene</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>Phenol</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>2,4 dinitrophenol</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Table 2. Product Selectivity ratio

<table>
<thead>
<tr>
<th>No.</th>
<th>Product</th>
<th>E/Z isomer</th>
<th>β/α products</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Styryl acetate</td>
<td>3.6 : 1</td>
<td>13.7 : 1</td>
</tr>
<tr>
<td>2</td>
<td>Styryl trimethylacetate</td>
<td>3.6 : 1</td>
<td>23 : 1</td>
</tr>
</tbody>
</table>

Reactions 1 and 2 affords both anti-markonikov and markonikov products, whose NMR data are in good agreement with literature.6,7 Higher yield reported in 2 could suggest that the sterically bulky trimethyl substituent being more able to stabilize the transition state to favour the anti-markonikov (β) products than the methyl substituent in the catalytic reaction. Interestingly, the E/Z ratio for 1 and 2 is similar. It implies that the increase of steric bulk from a methyl to a tert-butyl group does not destabilize the Z isomer enough for the reaction to produce more of the thermodynamically stable E isomer.

Vinylic protons were not detected when phenylacetylene was reacted with trifluoroacetic acid and the phenols. This could imply that the hydrocarboxylation reaction pathway require a carbonyl group which has to be sufficiently nucleophilic for binding onto the catalyst. The pi bond of the carbonyl group might be coordinated to the ruthenium metal center. Electron-withdrawing substituent reduces this electron density to prevent stable binding, while phenols do not have a carbonyl necessary for this coordination to happen.

Conclusion

It was concluded from FTIR studies that the first step in the reaction pathway of Ru(CO)H₂(PPh₃)₃ does not involve acetophenone. The investigation of the catalytic pathway involving Ru(CO)₃(PPh₃)₂ in acetophenone revealed that a cyclometallated compound is likely to be the intermediate formed, while the reaction in styrene shows the possibility of ligand substitution reaction. Future work for this part of the project will include the Isolation of this intermediate and in-situ NMR studies for reaction pathway of Ru(CO)₃(PPh₃)₂. For the reactions of the ruthenium-thiol complex, it was found that its catalytic pathway could involve a carbonyl group for binding onto the ruthenium metal as a key step in the formation of the product. Further work will include the use of other derivatives of the reactants and in-situ FTIR studies.

References