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Homogeneous $RuCl_2(PPh_3)_3$-Catalyzed Regioselective Liquid-Phase Transfer Hydrogenation of Carbon−Carbon Double Bond in Chlorobenzylidene Ketones with Ethylene Glycol as Hydrogen Donor

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Abstract:

The regioselective transfer hydrogenation of a carbon−carbon double bond of different chlorobenzylidene ketones is effectuated in ethylene glycol with a very high selectivity in the presence of homogeneous, tris(triphenylphosphine)ruthenium(II) chloride catalyst. Different important process parameters such as temperature, catalyst loading, and reaction period are studied. The reaction follows a first-order kinetics, and the energy of activation was found to be 52 kJ/mol.

Introduction

Chemoselective hydrogenations of carbon−carbon double bond in α,β-unsaturated carbonyl compounds are always a challenge to the process chemists. Thus, different catalyst systems[1−10] have been investigated by several workers for the reduction of either the double bond or the carbonyl group. Pd is the preferred industrial catalyst as it can be recycled without altering the selectivity and reaction rate. Hydrogen gas or hydrogen transfer agents such as alcohols,[11] limonene,[12] ethylene glycol[13,14] have also been successfully employed for these type of reactions.

The heterogeneous Pd and hydrogen combination is always preferred for easy bulk management, minimal effluents, facile product separation, and longer catalyst life, and thus it is invariably used in large-scale industrial applications. Despite of these facts, there are limitations of this combination especially in the presence of a halo substituents. Pd is a known hydrodehalogenation[15,16] catalyst and thus could not be used for the selective double bond hydrogenation of halo-substituted α,β-unsaturated ketones. Thus, efforts have been made to use Rh catalyst[17,18] for the hydrogenation of double bonds in chlorobenzylidene ketones but that with some unavoidable dechlorinated product and the reaction ceased at around 50% conversion level, thus makes the product separation more tedious. Raney nickel[19] can be used selectively for this purpose, but very high hydrogen pressure requirements and the presence of an organic sulphur compound make the process somewhat complicated.

We have previously shown the possibility of selective transfer hydrogenation[20] of a carbon−carbon double bond with complete conversion of the starting chalcones. We now present the results of kinetic investigation and process parameter studies of highly selective transfer hydrogenation of double bonds in halo-substituted benzylidene ketones, catalyzed by homogeneous $RuCl_2(PPh_3)_3$ with ethylene glycol as the hydrogen donor.

Results and Discussion

In a typical reaction (Scheme 1), 2.5 g (10 mmol) of $4\text{-ClC}_6H_4CH{=}CHCOC_6H_5$ (**1a**), 0.15 g (0.156 mmol) of $RuCl_2(PPh_3)_3$, and ethylene glycol (total reaction volume, 25 mL) were charged to a glass reactor fitted with a condenser and a six-bladed turbine stirrer. The reaction mixture was heated for 4 h at 150 °C.

After the stipulated time, depending on reaction conditions, $4\text{-ClC}_6H_4CH_2CH_2COC_6H_5$ was found to be the sole product. The reaction profile is given in Figure 1.

Excellent selectivity to the double bond transfer hydrogenation was obtained using various substrates, as shown in Table 1. No hydro-dehalogenated products were observed throughout the reaction period with any of those different starting materials except **1c** and **1d**. In the case of **1c**, 30% hydro-dechlorination and 17% alcohol were obtained as byproducts, whereas for **1d**, only 18% debrominated product has been found.

After the reaction time, water was added to the reaction mixture, and the compound was extracted in dichloromethane. The organic layer was passed through a silica gel column to remove the catalyst, and then the desired product was isolated by simply evaporating the organic solvent.

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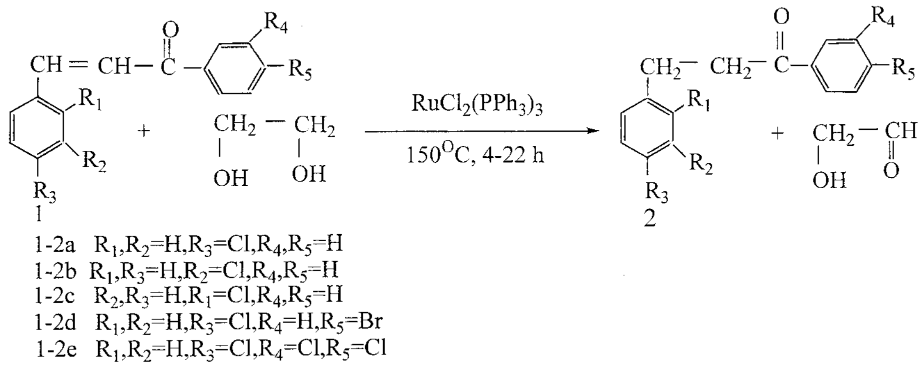
Scheme 1. **Transfer hydrogenation reaction using ethylene glycol**



Scheme 2. **Intermediate ketal formation and subsequent breaking to product**

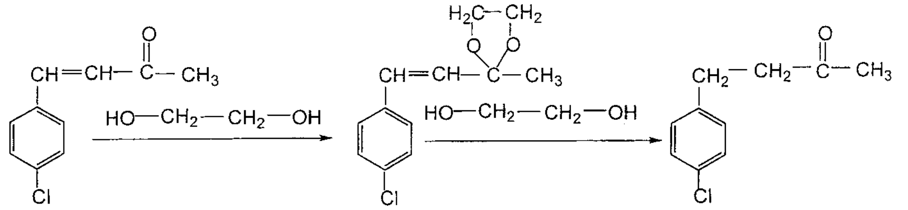


Table 1. [a]

entry	starting material	*t*/h	major product	conversion	selectivity
1	**1a**	4	**2a**	100	100
2	**1b**	6	**2b**	100	97
3	**1c**	8	**2c**	100	53
4	**1d**	5	**2d**	100	82
5	**1e**	7	**2e**	100	99

[a] Reaction conditions: starting ketone, 10 mmol, $RuCl_2(PPh_3)_3$ catalyst, 0.156 mmol, ethyleneglycol, 25 mL, temperature, 150 °C, 900 rpm stirring speed

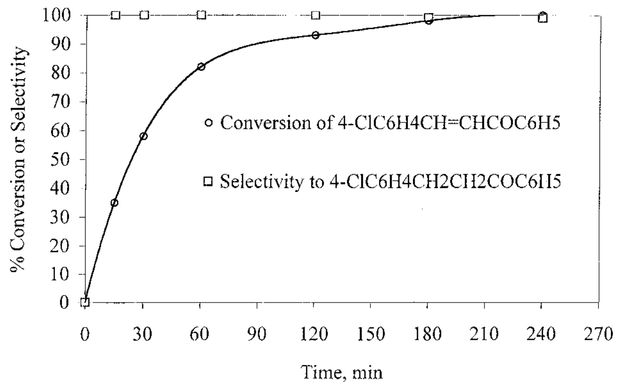


Figure 1. **Reaction profile for the transfer hydrogenation of $4\text{-}ClC_6H_4CH{=}CHCOC_6H_5$. Reaction conditions: substrate, 10 mmol; catalyst, 0.156 mmol; temperature, 150 °C; ethylene glycol (total reaction volume), 25 mL.**

An entirely different profile was obtained when the starting material was $4\text{-}ClC_6H_4CH{=}CHCOCH_3$. The reaction then proceeds via an intermediate ketal (Scheme 2). To our surprise it transformed with time to the desired product with 98% selectivity. The concentration profile is shown in Figure 2.

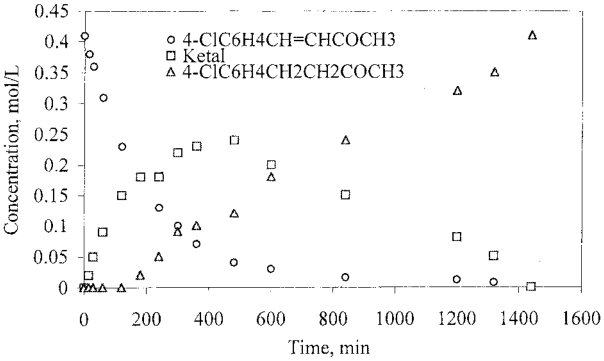


Figure 2. **Concentration profile for the transfer hydrogenation of $4\text{-}ClC_6H_4CH{=}CHCOCH_3$. Reaction conditions: substrate, 10 mmol; catalyst, 0.156 mmol; temperature, 150 °C; ethylene glycol (total reaction volume), 25 mL.**

$4\text{-}ClC_6H_4CH{=}CHCOC_6H_5$ (**1a**) was chosen as a model substrate for the kinetics and different process parameter studies. The reaction rate was found to be a function of the concentration of starting ketone and catalyst. A pseudo-first-order rate law was observed for fixed catalyst loading. The rate law can be expressed as follows:

$$-\mathrm{d}C_A/\mathrm{d}t = kC_{\text{ketone}}C_{\text{cat}}$$

$$-\mathrm{d}C_A/\mathrm{d}t = k_{\text{obs}}C_{\text{ketone}}, \quad \text{where} \quad k_{\text{obs}} = kC_{\text{cat}}$$

or

$$-\ln(1 - X_A) = k_{\text{obs}}t$$

where X_A is the fractional conversion of **1a**. The average k_{obs} value was 2.25×10^{-2} min^{-1} (see also Experimental Section), and the energy of activation, E_{act} was found to be 52 kJ/mol.

Temperature was found to influence both substrate conversion and product selectivity. Performing the reaction at higher temperatures led to a faster rate of reaction, as expected. However, the selectivity decreased marginally with temperature (Figure 3). This is due to the other hydrogen transfer reactions at different functional groups under the reaction conditions, leading to some dehalogenation and alcohol formation.

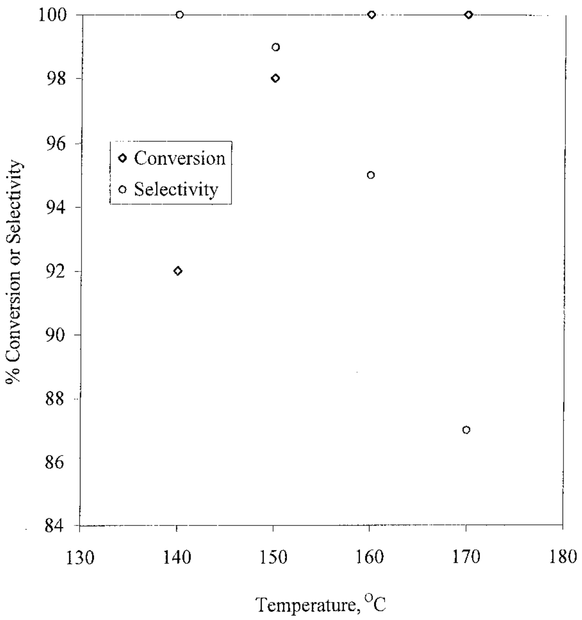


Figure 3. **Effect of temperature on conversion and selectivity. Reaction conditions: substrate, 10 mmol; catalyst, 0.156 mmol; temperature, 150 °C; time, 4 h; ethylene glycol (total reaciton volume), 25 mL.**

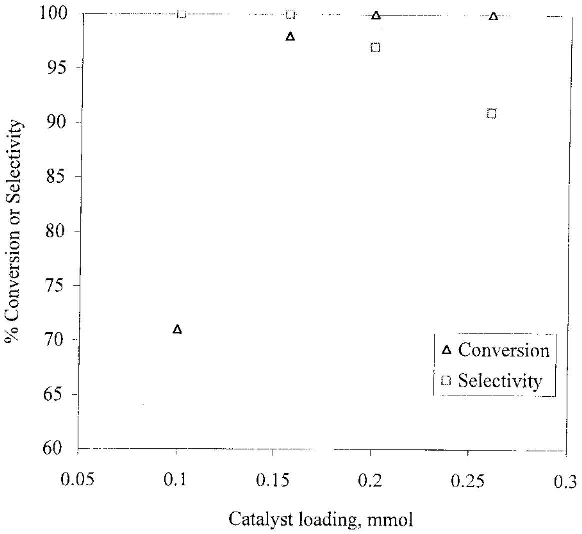


Figure 4. **Effect of catalyst loading on the rate and selectivity; reaction conditions: substrate, 10 mmol; temperature, 150 °C; time, 4 h; ethylene glycol (total reaction volume), 25 mL.**

Conversely, increasing the catalyst loading increased the rate of reaction, but the selectivity towards the desired product decreased after a specific catalyst loading (Figure 4). Optimum selectivity was obtained when catalyst loading was between 0.156 and 0.2 mmol.

Performing the reaction with homogeneous bis(triphenylphosphine) palladium(II) chloride (0.11 g, 0.156 mmol) catalyst led to only 18% selectivity to the desired saturated ketone. The major product was hydro-dehalogenated product. Use of other hydrogenating agents such as hydrogen gas even at room temperature, formate at 100 °C, with the same catalyst but instead of ethylene glycol, did not give any encouraging results. When the reaction was performed with propan-2-ol at 150 °C, only 41% selectivity to the desired product was achieved in 4 h, and the rest was hydro-dechlorination.

The formation of ketal under the reaction conditions when there is a methyl group adjacent to the carbonyl functional group could be supported by our previous work reported elsewhere.[21] The fact that there was no ketal formation, when the phenyl group was adjacent to the carbonyl group instead of the methyl group, might be explained by the steric hindrance decreasing the probability for ethylene glycol to access the carbonyl function.

Conclusions

Ethylene glycol can be directly utilized as a hydrogen-transfer agent for the regio-specific double bond hydrogenation of chlorobenzylidene ketones in the presence of $RuCl_2(PPh_3)_3$ catalyst at 150 °C with a very high selectivity. The separation process becomes much easier and convenient due to high selectivity and complete conversions unlike reported processes.

Experimental Section

Materials and Instrumentation. GC and GC−MS analyses were performed using a HP-5890 gas chromatography with a 50% diphenyl−50% dimethylpolysiloxane packed column (25 m/0.53 mm). Starting ketones[22] and the catalyst[23] were synthesized at laboratory without any difficulties. Other chemicals were purchased from commercial firms (>99% pure) and used without further purification. Starting material and products were characterized by MS data.

General Procedure for Transfer Hydrogenation. In a 100 mL glass reactor were charged 2.5 g (10 mmol) of $4\text{-}ClC_6H_4CH{=}CHCOC_6H_5$ (**1a**), 0.15 g (0.156 mmol) of tris-(triphenylphosphine) ruthenium(II) chloride catalyst, and ethylene glycol (total reaction volume 25 mL). The reactor was heated to 150 °C, and the mixture was stirred (900 rpm) at 150 °C for 4 h. Reaction progress was monitored by GC. After the stipulated time the mixture was cooled, and 50 mL of water was added to it. The product was then extracted with 40 mL of CH_2Cl_2. Solvent evaporation afforded 2.2 g of double bond hydrogenated product. In a view to do some scale up works, the same reaction was performed in a 10 times batch with substrate **1a**, and a substrate-to-catalyst ratio of 1:100 at 150 °C for 6 h. A 98% selectivity to the desired product has been achieved.

Experimental Procedure for Kinetic Studies. To a glass reactor fitted with a condenser and six-bladed turbine stirrer were charged 2.5 g (10 mmol) of $4\text{-}ClC_6H_4CH{=}CHCOC_6H_5$ (**1a**), 0.15 g (0.156 mmol) of $RuCl_2(PPh_3)_3$, and ethylene glycol (total reaction volume 25 mL). The reaction mixture was heated at 150 °C. Reaction progress was monitored by GC. The following parameters were studied: (i) initial substrate concentration, (three experiments at 10%w/v, $k_{obs} = 2.24 \times 10^{-2}$ min^{-1}, $r^2 = 0.97$ for 5 observations; 20%w/v, $k_{obs} = 2.77 \times 10^{-2}$ min^{-1}, $r^2 = 0.99$ for five observations; and 30%w/v, $k_{obs} = 2.83 \times 10^{-2}$ min^{-1}, $r^2 = 0.98$ for five observations); (ii) catalyst loading (four experiments using

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0.4% w/v $RuCl_2$ $(PPh_3)_3$, $k_{obs} = 0.8 \times 10^{-2}$ min^{-1}, $r^2 = 0.9838$ for nine observations; 0.6% w/v $RuCl_2$ $(PPh_3)_3$, $k_{obs} = 2.25 \times 10^{-2}$ min^{-1}, $r^2 = 0.982$ for six observations; 0.8% w/v mol % $RuCl_2(PPh_3)_3$, $k_{obs} = 3.08 \times 10^{-2}$ min^{-1}, $r^2 = 0.98$ for five observations; and 1.0% w/v $RuCl_2(PPh_3)_3$, $k_{obs} = 3.88 \times 10^{-2}$ min^{-1}, $r^2 = 0.998$ for four observations); (iii) reaction temperature (four experiments at 140 °C, $k_{obs} = 1.53 \times 10^{-2}$ min^{-1}, $r^2 = 0.996$ for eight observations; 150 °C, $k_{obs} = 2.25 \times 10^{-2}$ min^{-1}, $r^2 = 0.97$ for six observations; 160 °C, $k_{obs} = 3.5 \times 10^{-2}$ min^{-1}, $r^2 = 0.97$ for five observations; and 170 °C, $k_{obs} = 4.2 \times 10^{-2}$ min^{-1}, $r^2 = 0.94$ for five observations).

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