Kinetics of Liquid-Phase Catalytic Hydrogenation of Benzophenone to Benzhydrol

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Abstract:

Catalytic hydrogenation of benzophenone to benzhydrol was carried out in 2-propanol using Raney nickel as a catalyst at hydrogen pressures in the range of 800-2200 kPa, reaction temperatures 323-343 K, catalyst loadings 4-20 g dm⁻³ and benzophenone concentrations 0.44-1.32 mol dm⁻³. Effects on the hydrogenation of benzophenone to benzhydrol of various catalysts (Pd/BaSO₄, Pd/C, Pt/C, Raney nickel, Pd/CaCO₃) and solvents (methanol, 2-propanol, xylene, toluene, hexane, dimethylformamide) have been reported. Speed of agitation beyond 17 rps had no effect on the progress of reaction. Benzophenone can be selectively hydrogenated to benzhydrol, and the initial rate of hydrogenations showed first-order dependence with respect to the hydrogen partial pressure and catalyst loading and zero-order dependence with respect to benzophenone concentration. The activation energy for the catalytic hydrogenation of benzophenone was found to be 56 kJ mol⁻¹. A Langmuir-Hinshelwood-type kinetic model with hydrogen from the liquid-phase attacking adsorbed benzophenone has been proposed.

Introduction

The hydrogenation of benzophenone is a well-known route to obtain benzhydrol that is widely used as an intermediate for the commercial production of pharmaceutical substances. The conventional reduction process using zinc and aqueous alkali is known to generate substantial waste. Reduction using stoichiometric but expensive sodium borohydride gives rise to similar problems.¹ The catalytic hydrogenation of benzophenone can be utilized as the simplest technical route for the synthesis of benzhydrol. It is usually carried out in alcoholic solvents in the presence of various metallic catalysts but produces diphenylmethane, an over-reduction product. Gosser obtained 97% yield of benzhydrol and 86% conversion of benzophenone in tertbutanol as a solvent with the use of Lindlar, lead-poisoned Pd/CaCO3 catalyst.1 Various methods have been reported for the synthesis of benzhydrol.^{2–7} Upadhya et al. have reported 91% yield of benzhydrol in the hydrogen-transfer process with 2-propanol and Ni-stabilized zirconia $(Zr_{0.8}Ni_{0.2}O_2)$

catalyst, and Andrews et al. obtained 80% yield using Raney nickel catalyst and 2-propanol.^{8–9} Kumbhar et al. studied the hydrogenation of benzophenone to benzhydrol over Ni and Ni-based bimetallic Ni–Cu and Ni–Fe catalysts. The hydrogenation was accompanied by the formation of ether and 1-methoxy-1,1-diphenylmethane in addition to the expected hydrogenation product, benzhydrol.¹⁰ Hideyuki et al. used homogeneous rhodium, ruthenium, iridium, and platinum catalysts for the hydrogenation of benzophenone to obtain benzhydrol in 90% yield.¹¹ Sajiki et al. have used 10% Pd/*C*-ethylenediamine complex as a catalyst to obtain 89% yield of benzhydrol.¹²

However, limited kinetic information concerning the catalytic hydrogenation of benzophenone to benzhydrol has been published. $^{10-12}$



Materials

Benzophenone, 2-propanol, methanol, toluene, xylene, hexane, and dimethylformamide used were of laboratory reagent grade and obtained from S.D. Fine Chemicals, Mumbai, India. Hydrogen (cylinder purity 99.98%) was obtained from India Oxygen Limited, Mumbai, India, and was used as such. Commercially prepared 5%Pd/C, 5%Pd/BaSO₄, 5%Pt/C, 5%Pd/CaCO₃ were obtained from Parekh Platinum Ltd, Mumbai, India, and Raney nickel was obtained from Monarch Chemicals, Mumbai, India.

Experimental Section

Experiments were carried out in an autoclave (diameter = 65 mm, capacity = 100 mL). The reactor had provisions for automatic temperature control, variable agitation speed (pitched blade turbine, diameter = 35 mm), a safety rupture disk, and the sampling of the liquid phase. The appropriate quantities of the benzophenone, the solvent, and the catalyst were added to the clean and dry autoclave. Before heating

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Figure 1. Hydrogenation of benzophenone to benzhydrol and its recovery.

the autoclave to the required temperature, it was repeatedly purged first with nitrogen and then with hydrogen at room temperature in the absence of agitation. Once the required temperature was reached, it was pressurized with hydrogen to obtain the desired partial pressure of hydrogen and stirring was started. As the reaction proceeded, the consumed hydrogen was replenished so as to maintain a constant pressure in the autoclave. Samples of 2 mL were withdrawn through the sample outlet at regular time intervals and analyzed using HPTLC. The conditions of analysis for the reaction mixture were as follows:

TLC plate type	200 mm \times 200 mm Al plate coated with silica gel 60 F_{254}
solvent system	toluene/hexane (1:1)
applicator used	Desaga applicator
densitometer used	CD60 densitometer

Results and Discussion

The main objective of the present work was to study the effect of various operating parameters on the catalytic hydrogenation of benzophenone to benzhydrol. Initial experiments on catalytic hydrogenation of benzophenone were carried out to establish the material balance of reactant consumed and product formed and the balance to the extent of minimum 98% as per the stoichiometry given by eq 1 was established for the organic reactants and products. After completion of the reaction, the catalyst was separated by filtration and washed with 2-propanol. The filtrate and the washings were mixed and distilled to separate 2-propanol and the product (Figure 1). The product thus obtained had a melting point of 64.6 °C. In a typical experiment, starting with 0.055 mol benzophenone and 100% conversion, the final product benzhydrol recovered by this process was 0.054 mol, amounting to 98% process recovery of the product.

For kinetic experiments, progress of the reaction was monitored by off-line analysis of the reaction mixture by HPTLC and the consequent estimation of the moles of the reactant consumed as a function of time in each run. On the basis of the amount of reactant consumed, the initial rates were calculated graphically using a third-order polynomial equation.

Table 1. Effect of various catalysts on the catalytic hydrogenation of benzophenone^{*a*}

			catalyst
temperature (k)	conversion (%)	yield of benzhydrol (%)	loading (g dm ⁻³)
	. ,		
343	100	44	1.6
353	100	49	1.6
343	100	77	1.6
323	93	100	1.6
343	52	82	1.6
343	no reaction	_	1.6
363	100	89	4
353	100	97	4
343	100	100	4
333	83	100	4
	temperature (k) 343 353 343 323 343 343 363 353 343 333	temperature (k) conversion (%) 343 100 353 100 343 100 323 93 343 52 343 no reaction 363 100 353 100 353 100 353 100 343 100 353 100 343 100 343 83	$\begin{array}{c cccc} temperature & conversion & yield of \\ benzhydrol (\%) & benzhydrol (\%) \\ \hline 343 & 100 & 44 \\ 353 & 100 & 49 \\ 343 & 100 & 77 \\ 323 & 93 & 100 \\ 343 & 52 & 82 \\ 343 & no reaction & - \\ 363 & 100 & 89 \\ 353 & 100 & 97 \\ 343 & 100 & 100 \\ 333 & 83 & 100 \\ \hline \end{array}$

^{*a*} Hydrogen partial pressure: 1500 kPa; agitation speed: 22 rps; benzophenone concentration: 0.88 mol dm⁻³; solvent (2-propanol): 0.05 dm³.



Figure 2. Influence of reaction time on the yields of benzhydrol and diphenylmethane. (Δ) Yield (%) of benzhydrol with Pd/C catalyst; (\bigcirc) yield (%) of benzhydrol with Pd/BaSO4 catalyst; (\square) yield (%) of diphenylmethane with Pd/C catalyst; (\bigcirc) yield (%) of diphenylmethane with Pd/BaSO4 catalyst. Reaction temperature: 343 K; hydrogen partial pressure: 1500 kPa; catalyst loading: 1.6 g dm⁻³; benzophenone concentration: 0.88 mol dm⁻³.

Effect of Various Catalysts. Use of metallic catalysts may lead to the formation of diphenylmethane along with the desired benzhydrol.^{8–12} The main objective of the present study was to provide a process which gave very high yield of benzhydrol.

The effect of several catalysts was investigated in the hydrogenation of benzophenone in the present study (Table 1). Pd/BaSO₄ catalyst gave low yield of benzhydrol after complete conversion of benzophenone, and reaction did not progress with Pd/CaCO₃ catalyst. At higher temperatures (>343 K) with Pd/C as a catalyst, diphenylmethane was also formed along with benzhydrol, and at lower temperatures (<333 K), no diphenylmethane was detected. At higher temperature as the reaction progresses, yield of benzhydrol decreases, and the variation of yields of benzhydrol and diphenylmethane with Pd/BaSO₄ and Pd/C as a catalyst with respect to time is shown in Figure 2. The reaction was very slow when Pt/C was used as a catalyst in the hydrogenation of benzophenone to benzhydrol, with 52% conversion of benzophenone with 83% yield of benzhydrol. When hydrogenation of benzophenone with Raney nickel as a catalyst

Table 2. Effect of various solvents on the catalytic hydrogenation of benzophenone^{*a*}

solvent	initial rate $\times 10^3 \text{ (mol dm}^{-3} \text{ s}^{-1}\text{)}$
2-propanol	17
xylene + methanol (9:1)	6
xylene + methanol (4:1)	11
xylene + methanol (1.5:1)	11
toluene + methanol (4:1)	9
hexane + methanol (4:1)	6

 a Reaction temperature: 343 K; hydrogen partial pressure: 1500 kPa; agitation speed: 22 rps; benzophenone concentration: 0.88 mol dm $^{-3}$; catalyst loading: 10 g dm $^{-3}$.

was carried out at high temperatures (>353 K), diphenylmethane was also formed along with benzhydrol; however, at lower temperature (<343 K), only benzhydrol was obtained, and no diphenylmethane was detected. Therefore, in the hydrogenation of benzophenone to benzhydrol optimal reaction conditions have to be maintained to obtain benzhydrol in high yields. Among the catalysts used, Raney nickel was found to be an effective and selective in hydrogenation of benzophenone to benzhydrol at lower temperatures; hence, in subsequent studies Raney nickel was used as a catalyst.

Effect of Solvent. Solvents are known to have a significant effect on the rate of catalytic hydrogenations. The effect of solvent is attributed to various factors, which include solubility of hydrogen, thermodynamic interaction of solvent with the reactants and products, agglomeration of catalysts in some solvent, competitive adsorption of solvent, etc.¹³ The solvents employed were methanol, 2-propanol, toluene, xylene, hexane, and dimethylformamide, and the effect of solvents on initial rate of reaction is shown in Table 2. The rate of reaction was very low in methanol. Hydrogenation of benzophenone to benzhydrol did not progress when dimethylformamide, toluene, hexane, and xylene were used as solvents and Raney nickel as a catalyst. Agglomeration of Raney nickel catalyst was observed in hexane, toluene, and xylene. To avoid this, some quantity of methanol was added to these solvents before starting the reaction, and the effect of various concentrations of methanol on the reaction was also studied. The initial rate of hydrogenation was found to increase when the methanol concentration increased from 10 to 20%. As the initial rate of hydrogenation of benzophenone was very low when methanol was used as solvent, increase in methanol concentration more than 20% caused the decrease in the rate of hydrogenation, indicating the dominant effect of methanol on the catalyst. The rate of hydrogenation of benzophenone was higher in 2-propanol; therefore, 2-propanol was used as a solvent for the hydrogenation of benzophenone to benzhydrol.

Effect of Speed of Agitation. The effect of impeller speed on the initial rate of catalytic hydrogenation of benzophenone to benzhydrol in the range 10–22 rps at reaction temperature 343 K was studied. The initial rate was found to increase when the speed increased from 10 to 17 rps. This indicates that gas-to-liquid or liquid-to-solid mass-transfer resistance



Figure 3. Effect of catalyst loading on the initial rate of catalytic hydrogenation of benzophenone. Reaction temperature: 343K; hydrogen partial pressure: 1500 kPa; agitation speed: 22 rps; benzophenone concentration: 0.88 mol dm⁻³.



Figure 4. Effect of hydrogen partial pressure on the initial rate of catalytic hydrogenation of benzophenone. Reaction temperature: 343 K catalyst loading: 10 g dm⁻³; agitation speed: 22 rps; benzophenone concentration: 0.88 mol dm⁻³.

was significant between 10 and 17 rps. The impeller speed had no effect on the initial rate after 17 rps, indicating the absence of any external mass-transfer limitation. The external mass-transfer resistances can be eliminated by operating at a high speed of agitation.

Effect of Catalyst Loading. The effect of catalyst loading on the initial rate of catalytic hydrogenation of benzophenone is shown in Figure 3. The catalyst loading was varied between 4 and 20 g dm⁻³ for the catalytic hydrogenation of benzophenone. The initial rate of reaction was found to increase linearly with the catalyst loading.

Effect of Hydrogen Partial Pressure. The effect of hydrogen partial pressure was studied in the range 800–2200 kPa. The effect of hydrogen partial pressure on the initial rate of reaction is shown in Figure 4. The rate was found to increase linearly with the hydrogen partial pressure. The result indicates first-order dependence of the initial rate of reaction on the hydrogen partial pressure. The solubility

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Figure 5. Effect of benzophenone concentration on the initial rate of catalytic hydrogenation of benzophenone. Reaction temperature: 343 K; hydrogen partial pressure: 1500 kPa; agitation speed: 22 rps; catalyst loading: 10 g dm⁻³.

of hydrogen in 2-propanol was estimated from the correlation given by Shaw¹⁵ and the predicted values at 343 K were found to obey the relationship p = 16000S, where p is the hydrogen partial pressure (kPa) and S is the hydrogen solubility in 2-propanol (mol dm³).

Effect of Benzophenone Concentration. Benzophenone concentration was varied from 0.44 to 1.32 mol dm⁻³ for the catalytic hydrogenation of benzophenone. Figure 5 shows the effect of reactant concentration on the initial rate of catalytic hydrogenation. It was found that reactant concentration did not have any effect on the initial rate of reaction, indicating a zero-order dependence on the reactant concentration.

Zero-order dependence of rate with respect to benzophenone was observed by Ustinov, V. A. et al. in the hydrogenation of benzophenone using Pd/Al₂O₃ catalyst and ethanol as a solvent.14

Effect of Temperature. The reactions were carried out at different temperatures in the range 323-343 K. The initial rate of catalytic hydrogenation increased with increasing the reaction temperature.

Kinetic Model. All the experiments were carried out to eliminate the external mass-transfer resistances by operating at high speed of agitation (22 rps). It was found that reaction temperature had a strong effect on the initial rate of the reaction, and the rate of reaction is first-order with respect to hydrogen pressure and zero-order with respect to benzophenone.

A Langmuir-Hinshelwood (L-H)-type model has been proposed to describe the hydrogenation of benzophenone to benzhydrol.¹⁶ Several variations of the L-H model (Table 3) were evaluated, including those with molecular adsorption of all the reactants and dissociative hydrogen adsorption. These models are based on the assumption that one of the

Table 3. L	–H models for the diff	erent controlling
mechanism	n for the hydrogenation	of benzophenone ¹⁶
Model No	Controlling Mechanism	Rate Model

Single site-All the reaction species adsorbed molecularly

I	Adsorption of A controlling	$r_{O} = \frac{k_{1}C_{AO}}{1 + K_{H_{2}}C_{H_{2}}}$
II	Adsorption of H ₂ controlling	$r_{O} = \frac{k_2 C_{H_2}}{1 + K_A C_{AO}}$
ш	Surface reaction controlling	$r_{O} = \frac{k_{3}K_{A}K_{H_{2}}C_{Ao}C_{H_{2}}}{1 + K_{A}C_{Ao} + K_{H_{2}}C_{H_{2}}}$
	Single site-Molecularly adsorbed A and atom	ically adsorbed H ₂
IV	Adsorption of A controlling	$r_{\rm o} = \frac{k_4 C_{Ao}}{k_4 C_{Ao}}$

 $1 + \sqrt{K_{II}C_{II}}$

 $r_{O} = \frac{k_{5}C_{H_{H}}}{(1 + K_{4}C_{4})^{2}}$ Adsorption of H2 controlling

v

 $\frac{k_6 K_A K_H C_{Ao} C_{H_2}}{(1 + K_A C_{Ao} + \sqrt{K_H C_{H_2}})^3}$ VI Surface reaction controlling

Single site-Molecularly adsorbed A and H₂ in the liquid phase

VII $r_{O} = k_{7}C_{AO}$ Adsorption of A controlling $r_{O} = \frac{k_{8}K_{A}C_{AO}C_{H_{2}}}{1 + K_{A}C_{AO}}$ VIII Surface reaction controlling





three elementary steps (adsorption of benzophenone, adsorption of hydrogen, surface reaction between adsorbed benzophenone and hydrogen) is rate controlling. To select the correct rate equation, a nonlinear least-squares regression analysis was used for each rate equation to obtain the best values of the parameters using "polymath software". Models with molecular adsorption of all the reactants and dissociative hydrogen adsorption gave negative rates or adsorption constants, high residual sum of squares (RSS), and variance (σ^2) , and hence were rejected. Only for the model VIII, involving reaction between adsorbed benzophenone and hydrogen in the liquid phase, all kinetics and adsorption constants were positive for all temperatures. Therefore, model

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Table 4. Parameters for the L-H model (model VIII)

temperature (K)	k_{8} (s ⁻¹)	K_A (dm ³ mol ⁻¹)	RSS	σ^2
323	5.41	47.07	$\begin{array}{c} 1.32 \times 10^{-4} \\ 1.09 \times 10^{-3} \\ 6.17 \times 10^{-3} \end{array}$	3.12×10^{-6}
333	11.14	34.16		3.45×10^{-6}
343	18.82	25.40		3.46×10^{-6}

VIII was considered the best model for representing the kinetics of hydrogenation of benzophenone to benzhydrol.

From the values of the parameters of model VIII, it is observed that $K_A C_{AO} \gg 1$, and the model VIII reduces to the following equation:

$$r_{\rm O} = k_8 C_{\rm H2}$$

which shows that the rate of reaction is zero order with respect to A and first order with respect to H₂, as is experimentally observed.

The comparison of the experimental and predicted initial rates of hydrogenation shows good agreement between the model predictions and the observed values (Figure 6). The adsorption coefficients obtained for the above model followed the expected trend of decrease in the values of adsorption coefficients with temperature (Table 4). The heat of adsorption calculated from the plot of $\ln K_A$ vs 1/T was found to be 28 kJ//mol.

Arrhenius plot (Figure 7) of $\ln k_8$ vs 1/T gave activation energy 56 kJ mol⁻¹ for catalytic hydrogenation of benzophenone. This high value of activation energy also indicates that the reaction is kinetically controlled.

Conclusions

Benzophenone can be selectively hydrogenated to benzhydrol using Raney nickel as a catalyst and 2-propanol as a solvent. The initial rate of hydrogenation had first-order dependence with respect to the hydrogen partial pressure, and the catalyst loading and zero-order dependence with respect to reactant concentration. A Langmuir-Hinshelwoodtype model was proposed. The model predictions were in good agreement with experimental data. The activation



Figure 7. Arrhenius plot. Benzophenone concentration: 0.88 mol dm⁻³; agitation speed: 22 rps; catalyst loading: 10 g dm⁻³; hydrogen partial pressure: 1500 kPa.

energy for the catalytic hydrogenation of benzophenone was found to be 56 kJ mol⁻¹.

Nomenclature

Variables

$C_{ m AO}$	initial concentration of A (mol dm ⁻³)
$C_{ m H2}$	concentration of H_2 (mol dm ⁻³)
r _o	Initial rate of reaction (mol dm ⁻³ s ⁻¹)
$K_{\rm A}, K_{\rm B}, K_{\rm H}, K_{\rm H2}$	adsorption equilibrium constant
k_8	surface reaction rate constant for the hydrogenation of A (s^{-1})
Subscripts	
٨	hanzonhanana

А	benzophenone
H_2	hydrogen
В	benzhydrol

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