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Solvent effects in the liquid-phase hydrogenation of 4-phenyl-2-butanone over Pt / TiO_2

Part 2: A kinetic analysis methodology to elucidate the roles of metal, support and solvent

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Abstract (max 150)

In part I of this study, experimental data were presented for the hydrogenation of 4-phenyl-2-butanone with a 4% Pt/TiO_2 catalyst where the reaction rate and selectivity (ketone vs. aromatic ring) varied with solvent. In this paper, a rigorous kinetic model is presented utilising these data, incorporating statistical analysis methods to strengthen the foundations of mechanistically sound kinetic models.

A fundamental kinetic model for the system is presented and a 2-site model was determined to be most appropriate, describing aromatic hydrogenation (postulated to be over a platinum site) and ketone hydrogenation (at the platinum titania interface). Solvent choice has little impact on the ketone hydrogenation rate constant but strongly impacts aromatic hydrogenation due to solvent-catalyst interaction. Reaction selectivity is also correlated to a fitted product adsorption constant parameter. This kinetic analysis method is the first of its kind demonstrating the role of solvents in influencing reactant adsorption and reaction selectivity.

1. Introduction

Solvents are an indispensable presence in many catalytic liquid-phase reactions. The choice of solvent should not be arbitrary and is one which can be highly beneficial or detrimental to both activity and selectivity of catalytic reactions. Such a fact is well known, with observations of solvent effects originating in works such as those by Menshutkin, who in 1890 stated: *'By means of a proper choice of solvent, decisive acceleration or deceleration of a chemical reaction can be achieved'* [1].

Consequently, solvent effects have become very well documented in organic synthesis [2] and, in the past 50 years have been reported in heterogeneous catalysis [3]. Properties of the solvent such as dielectric constant and polarity play a role in determining the solubilities of gases (such as hydrogen), solvation of reactants and products as well as other mass transfer effects [4]. As well as influencing reactant and product behaviour, the solvent may also interact with the metal and/or support of the catalyst. A classic example of this is shown in the work by Boudart and co-workers [5-7] which explored the liquid phase hydrogenation of cyclohexene using a variety of silica (SiO_2) supported catalysts with a range of solvents. Therein, the turn-over frequency (TOF) for Pd/SiO_2 was found to be solvent insensitive whilst in contrast, when using a Ni/SiO_2 catalyst, the use of polar or oxygenated solvents resulted in a marked decrease in TOF and a strong adsorption of the solvent itself on the nickel metal.

Ultimately, numerous effects can arise between solvent, catalyst and substrate which result in catalytic reaction systems whose behaviour can be very difficult to predict. This presents a particular challenge to industry where the following problems can be manifested as a result of these difficulties:

- High E-factors (kg by-products/kg products), in particular for the pharmaceutical industry.
- 'Scale-up confidence' – prediction of plant scale reactor performance.
- Catalyst, feedstock and solvent choice constraints due to economic feasibility and environmental restrictions.

To understand and predict solvent effects, methodologies are needed that probe reaction behaviour from a fundamental physical and chemical standpoint but are also pragmatic in nature so that a broad spectrum of application is possible.

1.1 Kinetic modelling of solvent effects in literature

When modelling kinetics to describe solvent effects in catalytic liquid multi-phase reactions it is essential that proposed models have a fundamental mechanistic basis, together with estimated parameters that are physically meaningful in value and are statistically significant to justify their presence.

Table 1 provides a summary of rate models that have previously been used for this area of study. Bertero et al. [8] considered a wide range of Langmuir-Hinshelwood (LH) expressions to describe the hydrogenation of acetophenone. Quality of fit (R^2) for all models used in this work was very high (0.999) possibly because at least some were parametrically over-determined. Optimal model choice was, therefore, based on the physical meaning of measured parameters (such as discounting models with negative adsorption constants) and using model selection criteria based upon comparison of residuals and degrees of freedom in each final model. Mathew et al. [9] utilised a similar approach and also checked adsorption parameters for thermodynamic consistency.

Table 1: Rate model approaches previously employed to model kinetics of solvent effects within liquid phase hydrogenations in literature.

References	Rate Model	Mechanistic Basis
• Bertero et al. [8] • Mathew et al. [9]	$r = \frac{k_b \cdot K_a \cdot [R]}{\left(1 + K_a \cdot [R] + \sum K_d [I]\right)^n}$	• LH approach with competitive adsorption of organics. • Surface reaction rate determining step (r.d.s.)
• Mounzer et al. [10]	$r = \frac{k_b \cdot K_a \cdot [R]}{\left(1 + K_a \cdot [R] + \frac{[P]}{K_c}\right)^n}$	• LH approach with product desorption term. • Surface reaction r.d.s.
• Gamez et al. [11]	$r = \frac{K_{a,b,c} \cdot [R]}{\left(1 + K_{a,c}[R]\right)}$	• Michaelis-Menten approach.

- Kishida and Teranishi [12] - Lemcoff [13] - Mukherjee and Vannice [14]	$r = \frac{k_b \cdot K_a \cdot [R]}{\left(1 + K_a \cdot [R] + K_s [S]\right)^n}$	- LH approach with a competitive solvent adsorption term. - Assumes solvent interacts with catalyst surface. - Surface reaction r.d.s.

Symbols denote:

- r: rate of reaction (mol L^{-1} min^{-1}), k: rate constant (min^{-1} (for 1st order)), K: equilibrium constant (L mol^{-1} (for 1st order))
- [ ]: concentration (mol L^{-1}), R, P, I and S: reactant, product, inhibiting species and solvent respectively
- Subscripts a, b, c, d and s: reactant adsorption, surface reaction, product desorption, inhibition and solvent adsorption steps respectively.

Mounzer et al., [10] modelled the kinetics of 2-octanol oxidation performed using a variety of heptane/dioxane mixtures as solvents. A LH approach including a product ketone desorption parameter, which was experimentally measured, provided the best description. This model was found to be statistically significant via both the F- and T-test and showed an excellent correlation between solvent compositions, oxidation rate and the ketone desorption parameter.

Other approaches include the use of Michaelis-Menten-type expressions [11]. This method was shown to be pragmatic in describing solvent effects in ethyl pyruvate hydrogenation by discriminating a lumped reaction term from one relating to adsorption. The limited number of parameters in this model compromises quality of fit and, therefore, may be difficult to implement in multi-response systems.

A number of studies have attempted to include a competitive solvent adsorption term, K_S, in their models. Kishida and Teranishi, [12] developed a model for the hydrogenation of acetone using n-hexane as the solvent and, subsequently, fixed the rate constants in order to measure K_S for other solvents. The assumption that the solvent does not influence rate constants was not justified in the work and the study also did not consider the effect of hydrogen solubility as a function of solvent. In contrast, Lemcoff [13] developed models with thermodynamically sound adsorption parameters for a mixture of polar and apolar solvents, again for acetone hydrogenation and found the K_s term was only significant in the kinetic expressions for polar solvents such as water and 2-propanol. Recently, Mukherjee and Vannice [14] demonstrated a similar approach for citral hydrogenation. Their model was developed around citral conversion and validated against prediction of product formation. In this work, the assumption that the solvent competes for an active site is based around the fact that other possible solvent effects namely, mass transport limitations, liquid phase H_2 solubility and liquid-phase non-ideality were found to be insignificant in terms of influencing the large changes in rate behaviour observed between different solvents. In all cases, experimental validation for K_S was not undertaken which limits the physical meaning of this estimated parameter. The competitive adsorption of the solvent onto an active site, whilst possible with some solvent choices, is not necessarily a universal effect.

A key element which is missing from the aforementioned studies is a detailed statistical analysis which can ascertain the significance of parameters and the models developed. Such an approach could take model critique beyond R^2 and the removal of parameters due to lower or upper bound constraints. A possible approach is afforded by Quiney and Schuurman [15] who described the modelling of the water gas shift reaction kinetics under continuous flow and used a methodology which examined parameter sensitivities, parameter cross correlation and influence of parameter removal on R^2 values via use of the F-test.

1.2 Study of 4-phenyl-2-butanone hydrogenation over a Pt/TiO_2 catalyst

In this paper a detailed study of the hydrogenation of 4-phenyl-2-butanone (PBN) has been undertaken. This reaction has two distinctive routes to produce the fully hydrogenated product, 4-cyclohexyl-2-butanol (CBL). Intermediate compounds are 4-phenyl-2-butanol (PBL), produced by hydrogenation of the carbonyl C=O group and 4-cyclohexyl-2-butanone (CBN) by hydrogenation of the aromatic ring. The reaction scheme is shown in **Error! Reference source not found.** and features two reaction types, namely ketone (dashed arrow) or aromatic ring (solid arrow) hydrogenation.

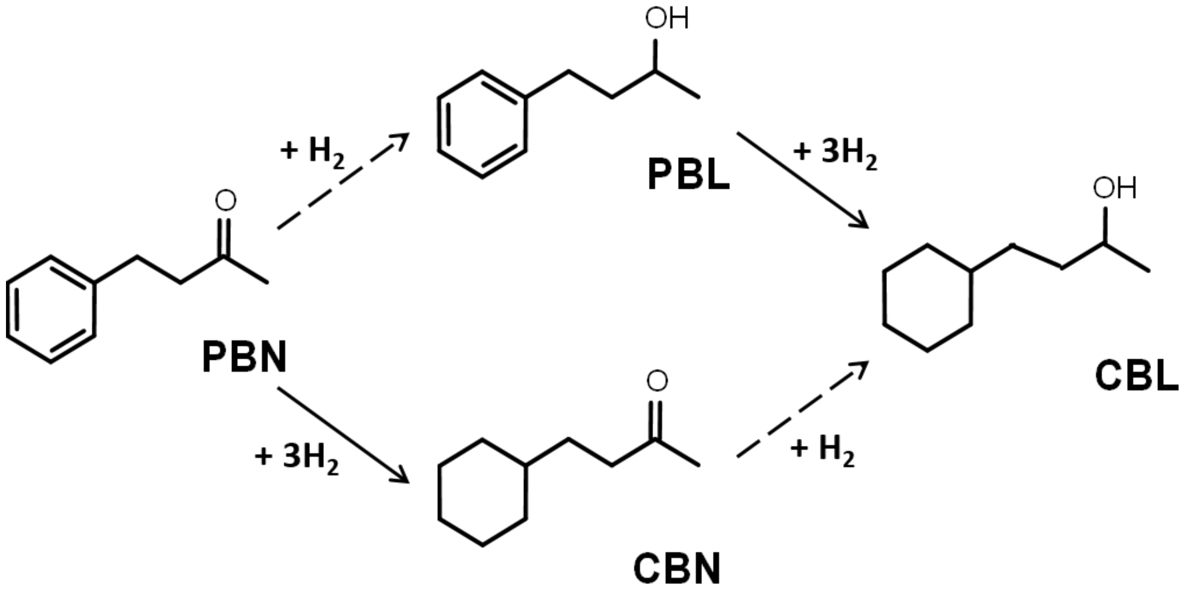

Figure 1: The hydrogenation pathway of 4-phenyl-2-butanone (PBN) to 4-phenyl-2-butanol (PBL), 4-cyclohexyl-2-butanone (CBN) and 4-cyclohexyl-2-butanol (CBL). Solid arrow indicates aromatic ring hydrogenation and dashed arrow indicates C=O group hydrogenation.

The reaction system was chosen as the selectivity of the two pathways from the original 4-phenyl-2-butanone reactant can be influenced by the choice of solvent [16]. At the time of writing no kinetic studies are reported in the literature for 4-phenyl-2-butanone hydrogenation, however, individual aromatic ring and C=O bond hydrogenations, described in section 1.1 are well studied reactions.

In Part I of the present study, experimental data were presented for 4-phenyl-2-butanone hydrogenation using a 4% Pt/TiO_2 catalyst [16]. The regime of operation was demonstrated to be free of internal and external mass transport limitations. In Part I, a variety of solvents were tested which were found to impact on the reaction pathway selectivity and TOF of the catalyst. In general, protic, polar solvents (primary and secondary alcohols) favoured selectivity towards ketone hydrogenation whilst apolar, aprotic solvents (alkanes) favoured the aromatic ring hydrogenation route. In terms of TOFs, those observed for alkanes and secondary alcohols were much greater than those for aromatic or primary alcohol solvents. A two site active site model was postulated whereby the aromatic ring hydrogenation was proposed to be occurring over the Pt with ketone hydrogenation occurring at the interface between the Pt and the titania support with activation of the C=O group through adsorption in the titania oxygen vacancies.

In this paper, a rigorous kinetic model is presented utilising these data. Statistical analysis methods, inspired by the work of Quiney and Schuurman [15], are used to strengthen the foundations of mechanistically sound kinetic models. A fundamental kinetic model for ketone and aromatic hydrogenation catalysis in this system is determined using an expansive dataset which employs n-hexane as the solvent. From this model, the effects of a wide range of solvents have been determined. This information provides a clear demonstration of not only the role of solvents in influencing reaction selectivity and reactant adsorption but also their interaction with metal and support of the catalyst during reaction.

2. Materials and methods

2.1 Experimental reaction studies

The experimental materials and methods are described in detail by [16], therefore, a brief recapitulation is given, herein.

The 4% Pt/TiO_2 catalyst was supplied by Johnson Matthey and was prepared by incipient wetness from $Pt(NO_3)_4$ (Johnson Matthey) as the precursor with titania as the support (P25, Degussa). The catalyst was dried for 12 h at 120 °C and then calcined at 500 °C for 6 h. The catalyst was ground using a mortar and pestle and sieved to $\leq$ 45 μm for all reactions. The BET surface area of the catalyst Pt/TiO_2 (P25) was 56.1 m^2 g^{-1} with a pore size of 2.2 nm. The titania had an anatase to rutile ratio of 3:1 as determined by XRD and TEM analysis showed a metal particle size of 4.7 nm with a dispersion of 33 %.

Reaction studies were carried out using a 100 cm^3 Hazard Evaluation Laboratory (HEL) autoclave pressure reactor. In all cases, 0.1 g catalyst and 30 cm^3 solvent were added to the autoclave and pre-reduced in situ under 1 bar H_2, 60 °C, stirrer speed 800 rpm for 1 h. Following reduction a solution of 4-phenyl-2-butanone in a further 20 cm^3 solvent were added to the reactor; reactions were carried out at 70 °C, 5 bar H_2 and 1400 rpm stirrer speed. Catalyst characterisation and demonstration that the reaction kinetics are intrinsic, not influenced by transport limitations, can be found in Part I of this study [16].

Table 2 summarises the three strategies of the experimental programme which have been taken in this work to build a mechanistically sound kinetic model that will link selectivity and adsorption constants to the choice of solvent. Series A utilises isothermal data with different starting concentrations of 4-phenyl-2-butanone. This dataset will allow the impact of concentration driving force on the kinetics to be explored. A number of Langmuir-Hinshelwood type models (varying in rate determining step and types of site) will be discriminated on the basis of parameter estimate quality and model response residuals.

The best candidate models will be taken forward to Series B, which incorporates multi-temperature data. Here activation energies will be estimated and the models further refined. Model fitting parameters will be strongly criticised from a statistical and physico-chemical perspective. This will further discriminate remaining models and potentially lead to additional fundamental understanding of the prevailing reaction mechanism.

The most suitable model will finally be tested against experiments using a range of solvents (Series C) with the purpose of demonstrating the link between solvent, selectivity and the dominant adsorption constant.

Table 2: Experimental data modelled in this study

Series	Variables	Constants
A	Effect of PBN concentration - 0.13 – 0.39 mol L^{-1} (5 points)	- hexane solvent - 70 °C operation
B	Effect of temperature 30 – 80 °C (6 points)	- hexane solvent - 0.26 mol L^{-1} starting PBN concentration
C	Effect of solvent - Alkanes - Aromatics - Primary alcohols - Secondary alcohols - Halogenates - Ethers	- 0.26 mol L^{-1} starting PBN concentration - 70 °C operation

2.2 Kinetic modelling procedure

Parameter estimation within the kinetic models was carried out using Athena Visual Studio v14.2© software [17]. The kinetic models tested within this work contain non-linear parameters (e.g. activation energies in the Arrhenius equation) and also include multiple concentration responses. To handle these challenges, two estimation methods were used in succession, namely, non-linear least squares and Bayesian estimation.

In general, the non-linear least squares method was used for first passes of kinetic models and initial discrimination. The objective function of this method is the total residual sum of squares for the entire model. Subsequently the Bayesian estimation method was used to fine tune the parameter estimation outputs. This method considers the error covariance matrix between responses and aligns the objective function accordingly. By this method, any prejudice towards the smaller magnitude responses in the dataset is largely eliminated enabling a sounder basis for multi-response estimation and a stronger critique of model performance [18].

All response variables in the 4-phenyl-2-butanone hydrogenation reaction network are dependent upon the multiple reactions shown in **Error! Reference source not found.**, so the models must be solved implicitly using a set of differential equations:

$$\frac{\mathrm{dy}}{\mathrm{dt}} = \mathrm{f}\left(\mathrm{y},\beta\right) \tag{1}$$

In Eq. (1), y denotes model responses, t denotes time and β denotes the model parameters. A direct decoupled method is used to estimate parametric sensitivities [19]:

$$\mathrm{B(t)} = \frac{\partial \mathrm{y(t)}}{\partial \beta} \tag{2a}$$

$$\frac{\delta}{\delta\beta}\left(\frac{\mathrm{dy}}{\mathrm{dt}}\right) = \frac{\mathrm{d}}{\mathrm{dt}}\mathrm{B(t)} = \frac{\delta \mathrm{f}}{\delta \mathrm{y}} \cdot \mathrm{B(t)} + \frac{\delta \mathrm{f}}{\delta\beta} \tag{2b}$$

In Eq. (2a), B(t) defines the sensitivity function for each model response with respect to the model parameters. In Eq. (2b) it can be seen that defining sensitivities as a function of time allows them to be solved alongside the main system differential equations, improving solver efficiency and performance.

To minimise cross-correlation between the energy (activation energy, E_a or equilibrium adsorption energy, ΔH_{ads}) and pre-exponential factor (A_i) parameters, a re-parameterised Arrhenius or Van't Hoff equation was used:

$$k_i = A_{i,343} \cdot \exp\left(\left(\frac{E_a}{T_{base} \cdot R}\right) \cdot \left(1 - \frac{T_{base}}{T}\right)\right) \tag{3a}$$

$$K_i = A_{i,343} \cdot \exp\left(\left(\frac{\Delta H_{ads}}{T_{base} \cdot R}\right) \cdot \left(1 - \frac{T_{base}}{T}\right)\right) \tag{3b}$$

Where base temperature, T_{base} = 343 K and $A_{i,343}$ is the value of the rate constant k_i or K_i at 343 K. 343 K is chosen as this temperature was used for the isothermal stage (Series A) of the parameter estimation process. Hence, this provides an accurate initial prediction for the A_i parameters during the multi-temperature data fitting stage, thus facilitating a more accurate estimation of E_a or ΔH_{ads} parameters.

The fitting process can be further improved by solving $A_{i,343}$ as an exponential term and lumping fitted value, E_a or ΔH_{ads} with constants T_{base} and ideal gas constant, R ($J\ K^{-1}\ mol^{-1}$) to give fitting parameter $E_{a,lump}$ or $\Delta H_{ads,lump}$. This typically brings the values of $A_{i,343}$ and $E_{a,lump}$ or $\Delta H_{ads,lump}$ into the same order of magnitude (typically ± 1 – 10) further reducing cross-correlation in this expression:

$$k_i = \exp\left(A_{i,343} + \left(E_{a,lump} \cdot \left(1 - \frac{T_{base}}{T}\right)\right)\right) \tag{3c}$$

$$K_i = \exp\left(A_{i,343} + \left(\Delta H_{ads,lump} \cdot \left(1 - \frac{T_{base}}{T}\right)\right)\right) \tag{3d}$$

3. Results and discussion

3.1 Kinetic modelling of the effect of initial 4-phenyl-2-butanone concentration in a hexane solvent

In Part I of this study, the reaction profiles as a function of time were shown to be very similar up to 60 min for all starting concentrations. Initial rates which are independent of initial organic reactant concentrations have been previously seen for acetophenone hydrogenation [20]. A zero order dependence of 4-phenyl-2-butanone concentration on reaction rate is unlikely as the individual concentration profiles show an apparent order dependence on 4-phenyl-2-butanone that is always greater than 1. These observations are therefore consistent with a reaction mechanism that may feature the following:

- Competition between organic reactants and hydrogen to adsorb onto surface sites.
- An influence of product adsorption effects, slowing the overall progress of 4-phenyl-2-butanone conversion over time.

In order to explore these effects the following generalised sequence of elementary steps was used as a basis for the kinetic models in this study in order to describe the dataset in Series A

$$R + *_i \underset{kA'}{\overset{kA}{\rightleftarrows}} R*_i \tag{4a}$$

$$R*_i \underset{kB'}{\overset{kB}{\rightleftarrows}} P*_i \tag{4b}$$

$$P*_i \underset{kC'}{\overset{kC}{\rightleftarrows}} P + *_i \tag{4c}$$

$$I + *_i \underset{kD'}{\overset{kD}{\rightleftarrows}} I*_i \tag{4d}$$

Where $*_i$ denotes a particular active site on the catalyst surface (where i = 1,2,…,n). In conjunction with this the following are noted:

- H_2 partial pressure was not varied during the study and therefore a distinct mechanistic step was not included for the adsorption of this reactant in the elementary steps. This does not discount the importance of the hydrogen driving force on the reaction but instead acknowledges that this parameter could be explored in a wider experimental programme.

- H_2 could compete for the same active site $*_i$ as the organic reactants or adsorb onto a separate site as part of the reaction mechanism. In the absence of explicit exploration of the impact of H_2, the site competition effect will still be explored by placing a square term on the denominator of the kinetic expressions.
- H_2 solubility into the liquid phase does change with both solvent choice and temperature. This was incorporated into the kinetic expressions [21].

Based on the elementary steps described in Eq. (4a-d), eight candidate models were derived which may be suitable for the 4-phenyl-2-butanone hydrogenation system (see Table 3). These models will systematically explore three key features of the reaction mechanism:

- Rate determining step of mechanism: either organics adsorption (Eq. 4a) or surface reaction (Eq. 4b).
- Competition between organics and hydrogen for a specific active site.
- The presence of different active sites for the ketone and aromatic ring hydrogenation reaction routes.

Table 3: Candidate rate models for describing reactions in the 4-phenyl-2-butanone hydrogenation network

Equation No.	Generalised Rate Model	Basis
(6a,b)	$r = \dfrac{k_b \cdot K_a \cdot [R] \cdot [H_2]}{\left(1 + K_a \cdot [R] + K_c [P] + \sum K_d [I]\right)^n}$	- Surface reaction (Eq. 4b) is the r.d.s. - Same site for ketone and aromatic ring hydrogenation. - n = 1 (6a)[1]; n = 2 (6b)[2]
(6c,d)	$r_{ket} = \dfrac{k_{b,ket} \cdot K_{a,ket} \cdot [R] \cdot [H_2]}{\left(1 + K_{a,ket} \cdot [R] + K_{c,ket} [P] + \sum K_{d,ket} [I]\right)^n}$	- Surface reaction (Eq. 4b) is the r.d.s. - Different site for ketone

	$r_{arom} = \frac{k_{b,arom} \cdot K_{a,arom} \cdot [R] \cdot [H_2]}{\left(1 + K_{a,arom} \cdot [R] + K_{c,arom}[P] + \sum K_{d,arom}[I]\right)^n}$	and aromatic ring hydrogenation. • n = 1 (6a)$^{1.}$; n = 2 (6b)$^{2.}$
(6e,f)	$r = \frac{k_a [R] \cdot [H_2]}{\left(1 + K_{b,c}[P] + \sum K_d [I]\right)^n}$	• Organic adsorption (Eq. 4a) is the r.d.s. • Same site for ketone and aromatic ring hydrogenation. • n = 1 (6a)$^{1.}$; n = 2 (6b)$^{2.}$
(6g,h)	$r_{ket} = \frac{k_{a,ket}[R] \cdot [H_2]}{\left(1 + K_{b,c,ket}[P] + \sum K_{d,ket}[I]\right)^n}$ $r_{arom} = \frac{k_{a,arom}[R] \cdot [H_2]}{\left(1 + K_{b,c,arom}[P] + \sum K_{d,arom}[I]\right)^n}$	• Organic adsorption (Eq. 4a) is the r.d.s. • Different site for ketone and aromatic ring hydrogenation. • n = 1 (6a)$^{1.}$; n = 2 (6b)$^{2.}$

1. n = 1 implies different adsorption site for organics and H_2
2. n = 2 implied same adsorption site for organics and H_2

The Series A dataset was fitted to all eight of the models described in Table 3. The dataset comprised 25 independent experimental observations (5 start concentrations x 5 batch-time sampling points), each containing concentration responses for 4-phenyl-2-butanone, 4-phenyl-2-butanol, 4-cyclohexyl-2-butanone and 4-cyclohexyl-2-butanol. Figure 2 shows the residuals for all concentration responses in the eight models when a first estimation pass was carried out using non-linear least squares:

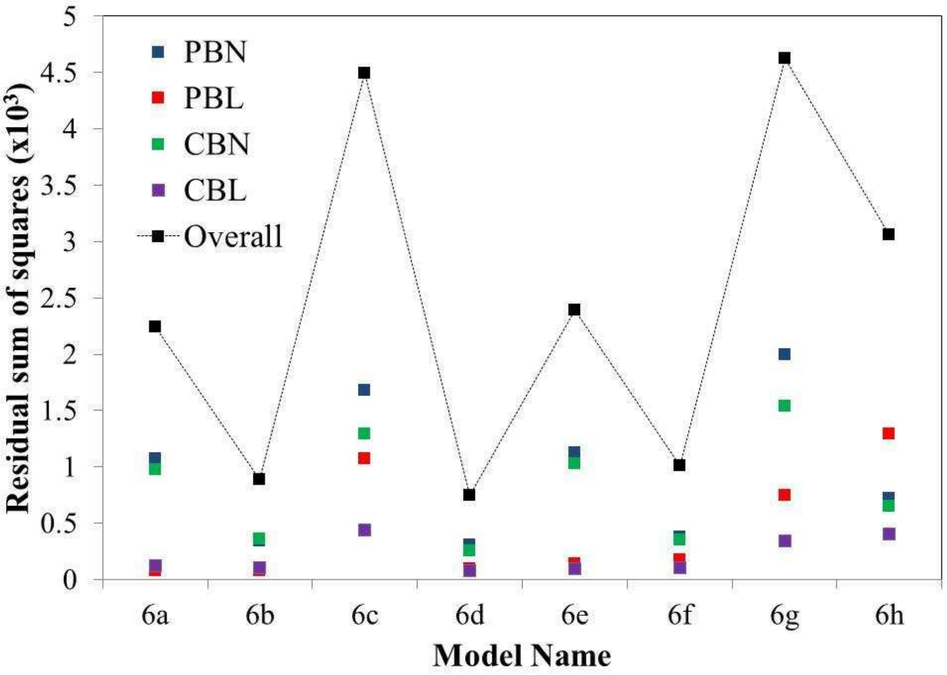

Figure 2: Residual sum of squares for individual and overall concentration responses for the Series A dataset when fitted to the eight candidate models in Table 3.

Inspection of Figure 2 affords some initial discrimination; models 6b, 6d and 6f systematically contain the lowest residuals for all responses, models 6a and 6e exhibit poorer residuals for the 4-phenyl-2-butanone and 4-cyclohexyl-2-butanone responses and models 6c, 6g and 6h are in general poorer in the prediction for all responses. Further inspection of the batch-time predictions of the latter three models showed the experimental trends were poorly captured. This was further confirmed by running the parameter estimation routine using the Bayesian approach.

Before selecting a smaller group of strong candidate models, quality of the parameter estimates was also investigated for the eight candidate models. As models 6a and 6e show a clear compromise in residuals for 4-phenyl-2-butanone and 4-cyclohexyl-2-butanone concentration responses, a further assessment can be made by looking at the quality of the parameter estimate for the rate constant of the 4-phenyl-2-butanone to 4-cyclohexyl-2-butanone aromatic ring hydrogenation reaction (PBN → CBN), as shown in Figure 3:

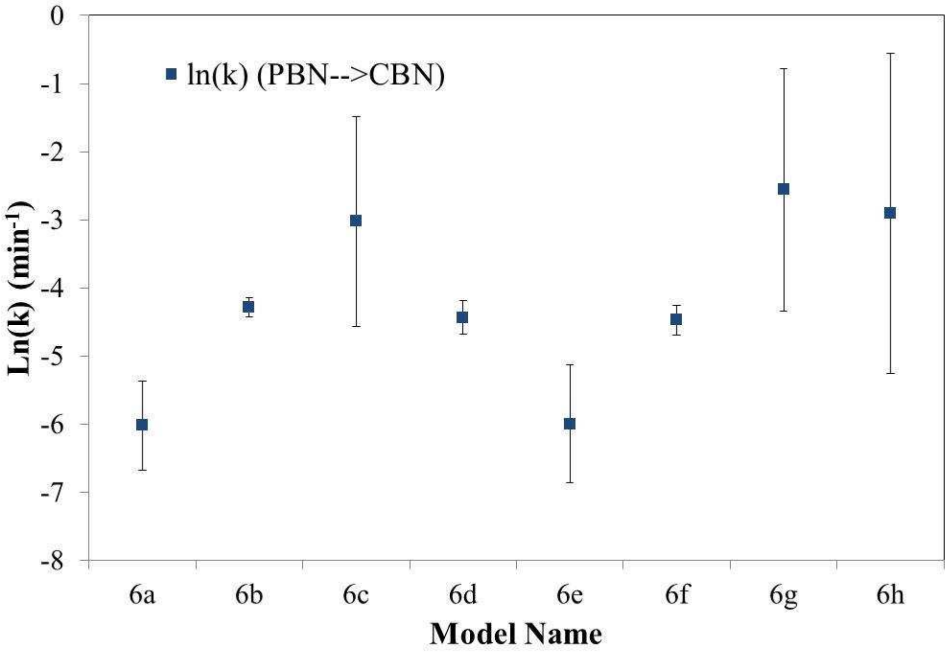

Figure 3: Estimated parameter values and 95% asymptotic confidence intervals for the ln(k) parameter for the 4-phenyl-2-butanone to 4-cyclohexyl-2-butanone (PBN → CBN) reaction using the non-linear least squares method.

Critically, Figure 3 shows that the confidence intervals for this reaction are much larger for 6a and 6e than the 6b, 6d and 6f models. Similar trends were seen for the parameters describing adsorption of 4-phenyl-2-butanone onto the surface. In line with this, models 6b, 6d and 6f were taken forward for further analysis as they provide the best fitted description of the data matched by the best parameter confidence intervals. All three models have site competition between organics and hydrogen in common, which is in line with observations discussed at the start of this section and in Part I of this study.

Models 6b, 6d and 6f were subsequently tested using the Bayesian estimation method for additional model refinement and identify parameters of importance in each model. The results are presented in Table 4:

Table 4: Final Bayesian estimation results for models 6b, 6d and 6f using the Series A dataset

	Model 6b	**Model 6d**	**Model 6f**
Number of Parameters	6	7	7
Bayesian Objective	-94.0	-94.9	-97.4

Function			
Residual Sum of Squares	9.35 * 10^{-4}	7.63 * 10^{-4}	6.86 * 10^{-4}
Ln(k) Rate Constants[1.] (min^{-1})			
PBN → PBL	-4.08 ± 0.17	-5.75 ± 0.34	-5.87 ± 0.21
PBN → CBN	-2.69 ± 0.13	-4.45 ± 0.29	-4.44 ± 0.20
PBL → CBL	-6.59 ± 0.20	-5.70 ± 0.32	-5.56 ± 0.23
CBN → CBL	-5.30 ± 0.27	Negligible	-6.76 ± 0.32
Ln(K) Equilibrium Constants[1.] (L mol^{-1})			
PBN	-0.16 ± 0.69	2.69 ± 0.35 (ketone site) 2.04 ± 0.20 (aromatic site)	2.03 ± 0.16
PBL	4.39 ± 0.16	4.38 ± 0.71	3.76 ± 0.56
CBN	Negligible	2.86 ± 0.23	2.20 ± 0.46

1. ± values are 95% higher probability density (HPD) intervals as determined by the Bayesian estimation method.

Each model is similar in overall performance (e.g. Bayesian objective function and residual sum of squares). For the rate constant (ln(k)) parameters, a key difference is seen with model 6d which suggests that the onward 4-cyclohexyl-2-butanone to 4-cylohexyl-2-butanol (CBN → CBL) reaction does not occur. For the adsorption (ln(K)) parameters there is a clear difference in the dominant product inhibition, in both magnitude and confidence interval. The introduction of temperature varied data is a necessary next step to understand the difference between these models and discriminate further.

3.2 Kinetic modelling of the effect of temperature in a hexane solvent

Figure 4 shows that in n-hexane, the selectivity is highest to the product 4-cyclohexyl-2-butanone at all temperatures, formed via hydrogenation of the aromatic ring in 4-phenyl-2-butanone. This selectivity significantly increases with temperature. Selectivity towards 4-phenyl-2-butanol (via ketone group hydrogenation) is considerably lower and decreases with temperature. These temperature dependent observations suggest that the activation energy for aromatic ring hydrogenation is higher than that for ketone group hydrogenation, which agrees with the literature [20]. Selectivity to the fully hydrogenated product 4-cyclohexyl-2-butanol, increases with both time and temperature. In Figure 4, after 120 min, the selectivity to 4-cyclohexyl-2-butanol appears to increase with temperature at the expense of 4-phenyl-2-butanol selectivity. 4-phenyl-2-butanol to 4-cyclohexyl-2-butanol (PBL → CBL) is an aromatic ring hydrogenation route, again demonstrating the prevalence of this reaction in n-hexane.

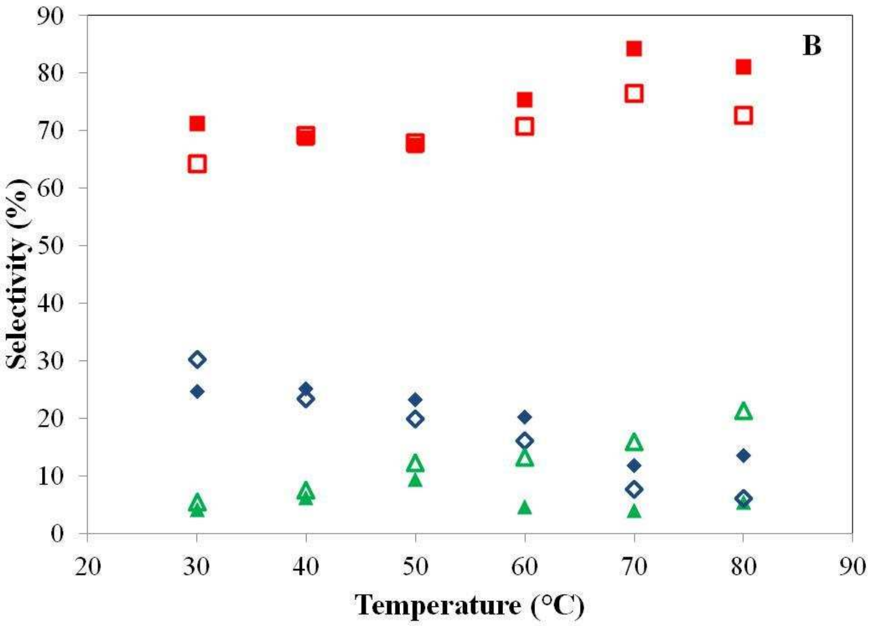

Figure 4: Selectivity of products at different temperatures after 10 min (closed symbols) and 120 min (open symbols) reaction. Symbols denote: (♦,◊) 4-phenyl-2-butanone, (■,□) 4-cyclohexyl-2-butanone, (▲,△) 4-cyclohexyl-2-butanol.

The Series B dataset was fitted to the three models taken forward from Section 3.1. The dataset comprised 30 independent experimental observations (6 reaction temperatures x 5 batch-time sampling points), each containing concentration responses for 4-phenyl-2-butanone, 4-phenyl-2-butanol, 4-cyclohexyl-2-butanone and 4-cyclohexyl-2-butanol. Here the rate and equilibrium constants fitted in Section 3.1 were expanded into full Arrhenius and Van't Hoff equation form, as described in Section 2.2.

Models 6b, 6d and 6f comprised 12, 14 and 14 fitting parameters respectively. The parameter values for the three isothermal models displayed in Table 4 were used as the initial predictions for the pre-exponential factors in the fitting in this section.

The first parameter estimation pass using Bayesian estimation revealed similar residuals and for all three models and a number of parameters with large 95% HPD intervals. This suggested that all three models were over-parameterised to describe the multi-temperature dataset. Statistical analysis was carried out on each model using a methodology based on Quiney and Schuurman, [15] in order to remove non-influential parameters from the fitting procedure. An example of this process, for a model based on Eq. (6d) is shown in the Supplementary Information.

Each time a parameter is removed from an overall set of rate expressions, an F-test is then invoked which addresses if the change in residuals of model responses in the *'n-1'* parameter model in comparison to the *'n'* parameter one is statistically significant. This is often defined as a 'nested model' problem and the F-statistic can be calculated as follows:

$$F = \frac{\left(\dfrac{\mathrm{RSS}_1 - \mathrm{RSS}_2}{\mathrm{par}_2 - \mathrm{par}_1}\right)}{\left(\dfrac{\mathrm{RSS}_2}{\mathrm{obs} - \mathrm{par}_2}\right)} \tag{7}$$

Where F is the F-statistic, RSS_1 and RSS_2 are the residual sum of squares in the nested and original model respective, par_1 and par_2 are number of parameters and obs is the total number of observations. The F statistic generated is compared with F_{crit} ($p = 0.05$) under these constraints. If the F statistic is smaller than F_{crit}, the removal, equating or fixing of a parameter is deemed acceptable as a statistically significant increase in residuals has not been induced.

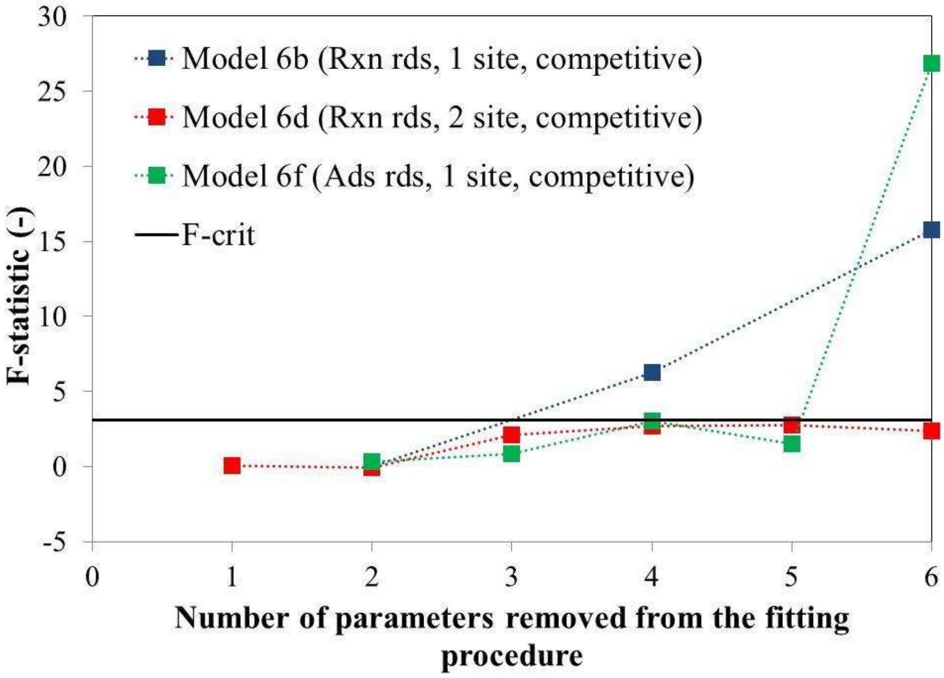

Figure 5: Calculated F-statistic for successive parameter removals across the entire system response for different models. N.B.: Lines are to guide the eye.

Figure 5 shows the successive F-statistic values obtained when parameters are removed from each of the model descriptions. Model 6b showed statistically significant changes to the residuals when more than 2 parameters are removed. Up to that point, the model also contained indeterminate parameters when solved. A similar outcome was seen for model 6f, albeit after the removal of a large number of parameters. These models were discarded due to both of these issues. Model 6d was the most successful and did not exceed F_{crit} during the removal of 6 parameters. At this point the model contained no indeterminate parameters or estimates with 95% HPD intervals greater than 100% of the estimated value.

A finding for all three model candidate models was that the parameter reduction procedure contained steps where two activation energies were equated with one another. In each case this involved 'pairing' of reaction pathways which have the same mechanism: ketone hydrogenation and aromatic ring hydrogenation.

For the most successful model, 6d, the adsorption parameter $K_{ket,PBL}$, featuring in the ketone hydrogenation routes, was found to be insignificant. Meanwhile $K_{arom,CBN}$ was found to be a highly significant parameter for the aromatic ring hydrogenation route. The removal of the $K_{arom,CBN}$ parameter was found to have a significant effect on the residuals.

The final parameter estimates for model 6d, the most appropriate model to describe the reaction kinetics of the system, is detailed in Table 5. Full details of the final statistical plots (parity, residual) for this model can be found in Supplementary Information. The final rate equations for the model are as follows:

$$r_{ket}(PBN \rightarrow PBL) = \frac{k_{1,ket} \cdot K_{ket,PBN} \cdot [PBN] \cdot [H_2]}{\left(1 + K_{ket,PBN} \cdot [PBN]\right)^2} \tag{8a}$$

$$r_{arom}(PBN \rightarrow CBN) = \frac{k_{1,arom} \cdot K_{arom,PBN} \cdot [PBN] \cdot [H_2]}{\left(1 + K_{arom,PBN} \cdot [PBN] + K_{arom,CBN}[CBN]\right)^2} \tag{8b}$$

$$r_{arom}(PBL \rightarrow CBL) = \frac{k_{2,arom} \cdot [PBL] \cdot [H_2]}{\left(1 + K_{arom,PBN} \cdot [PBN] + K_{arom,CBN}[CBN]\right)^2} \tag{8c}$$

Table 5: Parameter estimates and 95% HPD intervals for Model 6d using the Bayesian estimation method.

Parameter	Estimate	95% HPD Interval
$\mathrm{Ln}(A_{1,ket,343})$ (min^{-1}) **(PBN → PBL)**	-5.80	± 0.12
$\mathrm{Ln}(A_{1,arom,343})$ (min^{-1}) **(PBN → CBN)**	-4.47	± 0.05
$\mathrm{Ln}(A_{2,arom,343})$ (min^{-1}) **(PBL → CBL)**	-5.68	± 0.10
$E_{a,ket}$ (kJ mol^{-1})	27.9	± 3.47
$E_{a,arom}$ (kJ mol^{-1})	50.9	± 2.00
$\mathrm{Ln}(K_{ket,PBN})$ (L mol^{-1})	2.74	± 0.24
$\mathrm{Ln}(K_{arom,PBN})$ (L mol^{-1})	1.98	± 0.18
$\mathrm{Ln}(K_{arom,CBN})$ (L mol^{-1})	2.81	± 0.09

Examining the results summarised in Table 5, the E_a for the aromatic ring hydrogenation steps is higher than that for ketone hydrogenation, which was discussed following experimental observation in section 3.1. The E_a values estimated are in line with a surface reaction limited mechanism rather than an adsorption limited step. Previous work on a similar system, p-isobutyl acetophenone hydrogenation [9], estimated $E_{a,ket}$ and $E_{a,arom}$ to be 42 and 47 kJ mol^{-1}, respectively, whilst the heat of adsorption of the reactant was -5 kJ mol^{-1}. Similarly, in a kinetic study of ketone hydrogenation [21], heat of adsorption parameters were found to be in the range -5 to -15 kJ mol^{-1}. In the current study, the fitted heats of adsorption parameters were found to be indiscriminate from zero, which is feasible in line with the low value estimates from previous studies.

The presence of the parameter $K_{arom,CBN}$ in the final model has significant similarities with the study by Mounzer et al. [10]. This suggests that desorption of this intermediate, the selective product using n-hexane as the solvent, is a critical component of reaction progress and selectivity. In parallel to this, the final model found the subsequent ketone hydrogenation of 4-cyclohexyl-2-butanone to be a negligible parameter, owing to the fact that 4-cyclohexyl-2-butanone shows a preference to adsorb on the aromatic hydrogenation site rather than the ketone hydrogenation site.

The final model confirms that the organic reactants, for both reactions, compete with adsorbed hydrogen. Additionally, in part I of this study, it was postulated that two active sites were present, namely a Pt site which is largely selective to aromatic hydrogenation and a site at the interface between the platinum and titania support for ketone hydrogenation; C=O adsorption in an oxygen vacancy weakening the C=O bond for hydrogenation. In [16] it was discussed that the former site could be suppressed by use of certain solvents such as aromatics, which could strongly adsorb on the Pt. The success of the two site model gives credence to this postulation and will be further tested for a range of solvents in Section 3.3.

Qualitative discussion may be afforded around partition coefficients of the different reactants and products in this system (based on their relative distribution in octanol vs. water at equilibrium) which could explain the importance of $K_{arom,CBN}$ but not $K_{ket,PBL}$. An examination of logP values reveals only a small transition when 4-phenyl-2-butanone is converted to 4-phenyl-2-butanol (2.46 → 2.47) but it is significant when 4-phenyl-2-butanone is converted to 4-cyclohexyl-2-butanone (2.46 → 2.77). The strength of 4-

cyclohexyl-2-butanone adsorption appears to be a critical solvent parameter in this case and more hydrophobic solvents, such as the hexane examined, herein, may be critical to assisting this final stage of the aromatic hydrogenation reaction mechanism.

3.3 Kinetic modelling of 4-phenyl-2-butanone hydrogenation in a range of solvents

The kinetic model elucidated in sections 3.1 and 3.2 can now be applied to a range of solvent types (Series C in section 2.1). In all cases, individual solvent reaction data were fitted to a two site model with competition between hydrogen and the organics. The parameter reduction method of Quiney and Schuurman [15] used above was again applied to reduce the expression if necessary.

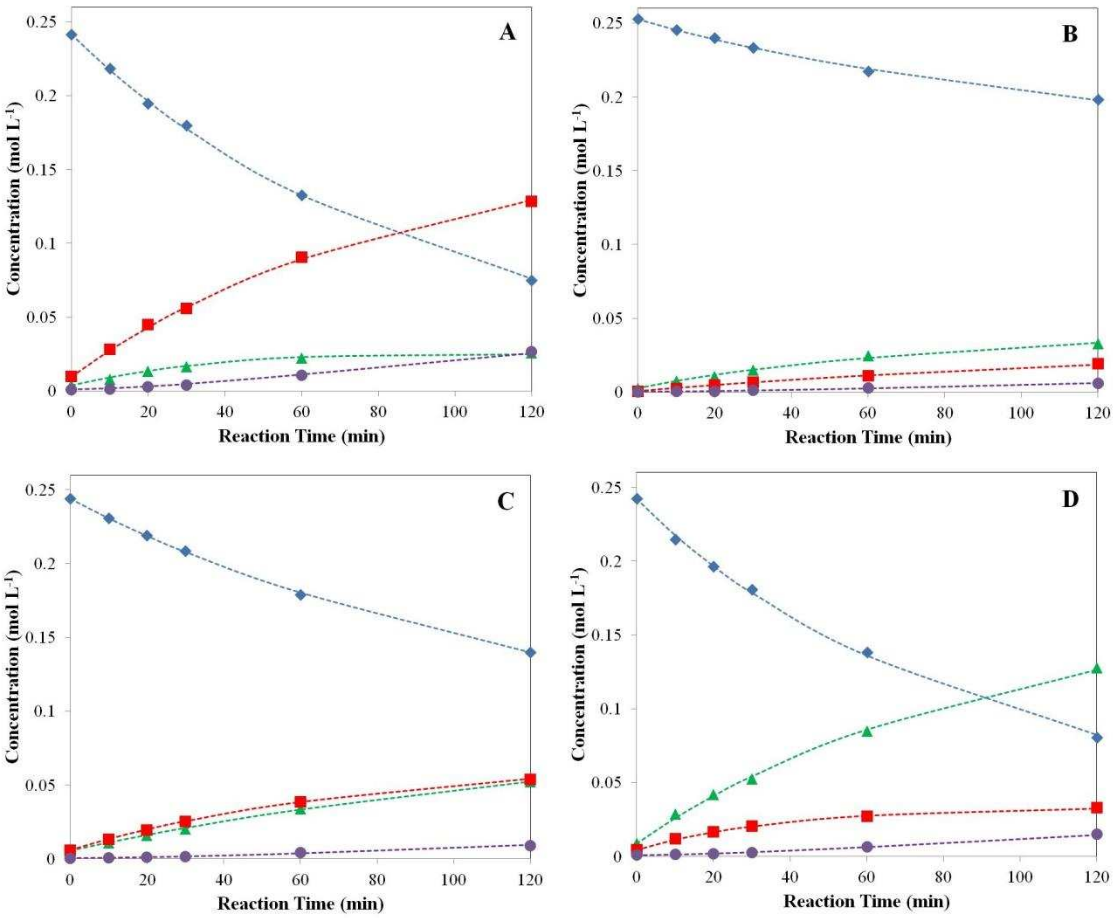

Figure 6: Batch concentration-reaction time plots for 4-phenyl-2-butanol hydrogenation in A) n-hexane, B) toluene, C) 1-propanol, D) 2-propanol at 70 °C conditions, 5 bar H_2 pressure and 0.26 mol L^{-1} [PBN]. Symbols denote experimental readings, lines denote model predictions: (♦) 4-phenyl-2-butanone, (▲) 4-phenyl-2-butanol, (■) 4-cyclohexyl-2-butanone, (●) 4-cyclohexyl-2-butanol.

As Figure 6 shows, the generalised model for 4-phenyl-2-butanone hydrogenation shows a good correlation when applied to a range of different solvents and gives good predictions. The next step is to assess the key parameters (k_{arom}, k_{ket} and $K_{arom,CBN}$) across the entire range of solvents.

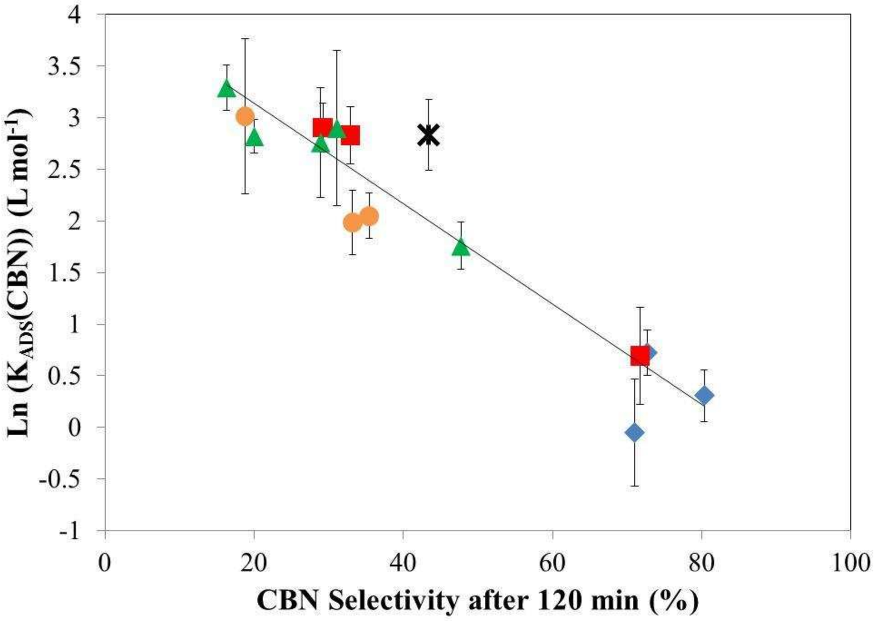

Figure 7: Fitted adsorption constant, $K_{arom,CBN}$ plotted against CBN selectivity after 120 min for a range of solvents tested. (♦) denotes alkane solvents, (■) aromatics, (▲) primary alcohols, (●) secondary alcohols, (*) ethers. N.B.: No significant adsorption constant was found for halogenates.

Figure 7 shows a log-linear plot of fitted adsorption constant, $K_{arom,CBN}$ against 4-cyclohexyl-2-butanone selectivity after 120 min. A good correlation is seen for the majority of the solvents, with acceptable 95% HPD intervals for the individual solvents in most cases. This correlation was also observed at all reaction times (see Supplementary Information, Figure S4 for an example after 10 min). This relationship suggests that desorption of the 4-cyclohexyl-2-butanone product is a key factor in determining the reaction selectivity in each of the solvents studied. For the alkanes examined, the adsorption constant is low and the 4-cyclohexyl-2-butanone product is easily desorbed into the liquid phase, giving rise to a high 4-cyclohexyl-2-butanone selectivity. In primary and secondary alcohol solvents, the adsorption constant is much higher and desorption of the 4-cyclohexyl-2-butanone product is much more difficult. This may be understood by the weaker solvation of the 4-cyclohexyl-2-butanone in the hydrophilic alcohol solvents compared with the alkanes which are likely to interact with the cyclohexyl group on the 4-cyclohexyl-2-butanone product resulting in a less favourable desorption process. A weaker trend is found for the aromatic solvents with toluene and p-xylene showing low 4-cyclohexyl-2-butanone selectivity and high $K_{arom,CBN}$ in contrast to t-butyl-toluene which features an alkyl group in its structure so may display aromatic-alkane hybrid behaviour.

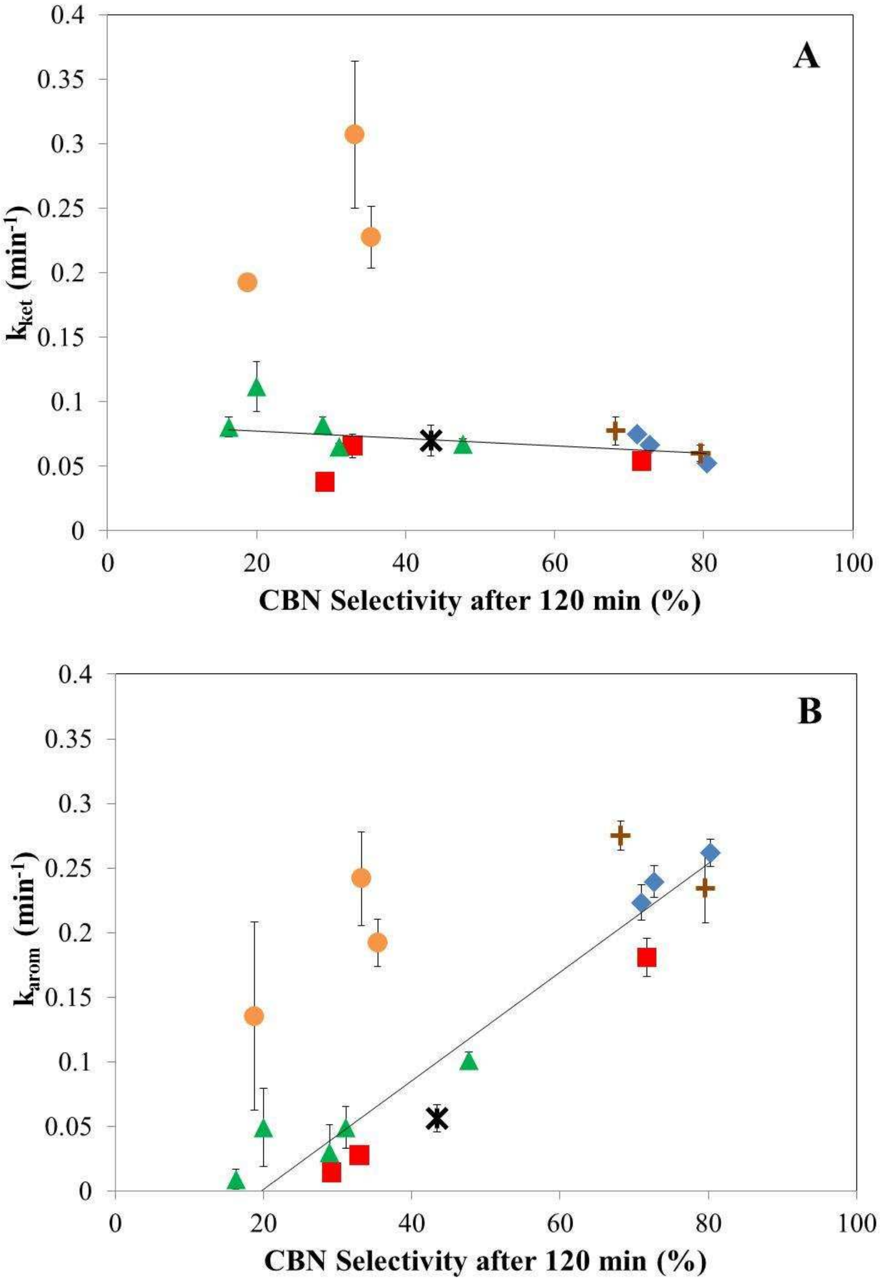

Figure 8: Fitted rate constant, A) k_{ket} and B) k_{arom} plotted against CBN selectivity after 120 min for a range of solvents tested. (♦) denotes alkane solvents, (■) aromatics, (▲) primary alcohols, (●) secondary alcohols, (*) ethers, (+) halogenates.

Figure 8 plots the rate constants for ketone and aromatic hydrogenation for the solvents examined. Whilst the rate of phenyl group hydrogenation (k_{arom}) is strongly dependent on choice of solvent, the ketone group hydrogenation rate (k_{ket}) is found to largely independent of the solvent used. The exceptions to this are the secondary alcohol solvents and these will be discussed later. The change in selectivity as a function of solvent is thus largely driven by its effect on the rate of phenyl group hydrogenation. This is consistent with the proposed dual site nature of the catalyst [16]. Again, the correlations shown in Figure 8 were observed at all different reaction times (see Supplementary Information, Figure S5 for an example after 10 min).

An important note is that the normalised cross correlation values between estimates of k_{arom} and $K_{arom,CBN}$ never reached significant values (>0.95) [22]. This statistical observation further shows that the key kinetic parameters used in fitting solvent data describe different effects, in this case availability of sites and/or TOF (k_{ket} and k_{arom}) and ease of desorption of CBN over Pt ($K_{arom,CBN}$). Full details of condition numbers for all solvents are given in Supplementary Information.

The aromatic hydrogenation route has been discussed to occur on the Pt sites of the catalyst surface [16]. Based on this, k_{arom} could be described as $k_{Pt}(1-\theta_{solv})$ which relates the number of vacant sites available as a function of solvent adsorption strength. The flatness of the $k_{1,ket}$ parameter across most solvents suggests that solvent inhibition is not a factor over this site. This site is postulated to be the interfacial site which hydrogenates the C=O bond, a functional group not present in any of the solvents used. Product inhibition over the ketone hydrogenation site was ultimately found to be a low sensitivity parameter in section 3.2.

The clear exception in Figure 8 are the secondary alcohols which show k_{arom} sites in comparable levels to an alkane solvent and a higher level of k_{ket} sites. In Figure 6B, the selectivity to 4-cyclohexyl-2-butanone is found to be low in secondary alcohols which would suggest that these solvents do not strongly adsorb on the Pt sites but still inhibit reactant adsorption mode via a different mechanism. An examination of dipolarity (π^{x}_{1}) in [23] shows that 1-propanol and 2-propanol have values of 0.52 and 0.48 respectively, whilst hexane has a value of -0.08. Hence the large difference in k_{arom} observed between primary and secondary alcohols suggest that electronic effects are an unlikely cause of this disparity. This indicates that the effect observed is likely to be steric in nature, owing to the difference in adsorption conformation of primary and secondary alcohols.

4-cyclohexyl-2-butanone selectivity is also low in secondary alcohols as this product does not desorb easily into the liquid phase due to hydrophobicity factors discussed earlier. The higher k_{ket} parameter for secondary alcohols may suggest this parameter may be coupled in this instance, i.e. ketone hydrogenation is occurring at both the interface sites (C=O activated by adsorption in the vacancies on TiO_2) and on Pt. In Part I of this study, ketone hydrogenation in 2-propanol was possible over a Pt/SiO_2 catalyst which lacks the vacancy sites found on a TiO_2 support.

Table 6: Parameter estimates and 95% HPD intervals for fits of experimental data using mixtures of hexane and toluene as solvent

Parameter	**Hexane solvent**		**Hexane solvent doped with 5.7 wt% toluene**		**Toluene solvent**	
	Estimate	**95% HPD Interval**	**Estimate**	**95% HPD Interval**	**Estimate**	**95% HPD Interval**
$\mathbf{k_{ket}}$	0.08	0.01	0.06	0.01	0.07	0.01
$\mathbf{k_{arom}}$	0.22	0.02	0.08	0.02	0.03	0.01
$\mathbf{K_{arom,CBN}}$	0.95	0.55	19.68	7.47	16.94	5.44

Examining the use of doped solvents in Table 6 depicts the separate parameters which impact selectivity and active site availability. k_{ket} is again largely unchanged across the results, whilst k_{arom} drops by ~60% when a small amount of toluene is added to the n-hexane and by ~85% when the solvent is completely switched to toluene. Overall, 4-phenyl-2-butanone conversion over 120 min follows a similar trend. Selectivity is tuned much more aggressively by the addition of toluene with a small amount influencing the $K_{arom,CBN}$ parameter.

3.4 Findings in context to previous solvent effects work

In section 1.1, it was stressed that the pursuit of elucidating solvent effects in liquid-phase reactions via kinetic modelling should incorporate a strong statistical and mechanistic basis. The approach demonstrated in this work is discussed in reference to these critical requirements.

The critical pre-determining step in any kinetic study is the number of proposed models to which data are subsequently fitted. Use of a range of models that include different rate determining steps in their mechanism [8.10,22], assumptions of non-competitive and competitive reactant adsorption [14,20], dissociative or associative molecular adsorption [9,20] and inhibition effects [10,14] all define this scope. At a maximum of these possibilities, model comparison without a systematic statistical analysis is likely to provide limited conclusions which have a physical meaning. In the current work, such a range of steps were condensed down into eight, ‘over-parameterised’, starting models with different rate determining steps and active site basis. From there, parameter reduction via sensitivity, condition number and F-test analysis takes each model to a defined stop point. In this case, the bi-directional problem of over-simplification/complication of kinetic models can be avoided.

In the work of Bergault et al. [20], the batch-time acetophenone hydrogenation behaviour draws comparison with the current study, particularly with initial rate behaviour at different acetophenone start concentrations. All possible adsorption effects (including inhibition) were considered and led to indeterminacy in their estimation when the data were fitted, as is seen in the current study. This was circumvented by normalising the adsorption constant values; however, therein the statistical significance of the newly estimated parameters is not discussed. Similarly, their proposed model does not link parameters in identical reaction pathways, of which the estimated parameters in the work would suggest to be a viable move. A similar process is found in the study by Mathew et al., [9]. In this work, two E_a values for aromatic ring hydrogenation are estimated at 47 and 44 kJ mol^{-1} but are left unpaired. A parameter pairing approach in the current work was found to have little impact on residuals and freed up extra degrees of freedom to aid in the parameter estimation process, building on these studies.

A parallel can be drawn between the current study and the mixed ketone hydrogenation study of Chang et al. [21]. The latter eliminated parameters based on insignificant t-values and wide 95% confidence intervals. A product desorption term was found to be a significant parameter for the dominant ketone hydrogenation pathway but not the other reaction pathways. Instead, this desorption term appears as an inhibition factor for the other pathways, again as reported in this study. The study also demonstrated that all ketone hydrogenation routes could be adequately lumped together into one expression, which is similar to the linking of the reaction pathways demonstrated in this work.

The importance of a product desorption term is also in line with the work of Mounzer et al. [10], whereby desorption of product P from active sites was driven by solvent composition. In the current work, the ring hydrogenated product, 4-cyclohexyl-2-butanone, exhibits greater hydrophobicity than that of the ketone hydrogenated product 4-phenyl-2-butanol. The former has a greater likelihood of removal from the catalyst surface by apolar aprotic solvents such as n-hexane compared with the alcohols. The correlation between solvent selectivity towards 4-cyclohexyl-2-butanone and $K_{arom,CBN}$ may be a reflection of this.

A further comparison can be made with previous works which have used K_S to describe the inhibition role of the solvent [12,13,24]. In the current work, the essence of this parameter is seen in the analysis of the full solvent range; values of k_{arom} are significantly reduced in primary alcohols and aromatic solvents hence providing a measure of inhibition to catalytically active sites compared to solvents which adsorb weakly (e.g. alkanes). As described earlier, solvent to substrate ratios are often high in batch-time kinetic studies and so the magnitude of the [S] variable can induce a bias towards K_S in the fitting procedure, swamping the importance of other variables in the regression. The methodology shown in the current work can also elucidate solvent inhibition with limited data; a wide range of solvents could be tested using a single isothermal experimental run protocol each time.

4. Conclusions

The role of the solvent can be critical in many catalytic liquid phase reactions; in particular influencing adsorption/desorption of reactants and products as well as influencing overall catalytic turnover rates and gas phase solubility. Modelling the role of the solvent as well as catalyst metal/support and reactants/products is a complex system. Data from an experimental study of 4-phenyl-2-butanone hydrogenation over a 4% Pt/TiO$_2$ catalyst have been used to develop a kinetic analysis methodology to elucidate solvent effects and unify solvation, dominant adsorption constant and product selectivity.

The methodology has successfully drawn upon previous mechanistic descriptions proposed in the literature [9,10,20]. The fitting of data to these models has been combined with a rigorous statistical analysis procedure to eliminate non-influential parameters in their descriptions [15]. During this procedure, the physical and chemical meaning of estimated parameters was considered and this led to pairing of similar reaction pathways (e.g. initial reactant and intermediate ketone hydrogenation). The final model assumed the surface reaction of the organic species with hydrogen to be the rate determining step and included a selective product, 4-cyclohexyl-2-butanone, desorption term. Desorption of this product was found to vary with solvent and was directly linked to the observed product selectivity.

The kinetic analysis methodology proposed can quickly elucidate a fundamentally and statistically sound kinetic model for a chosen system even with limited experimental data. This can subsequently be used to understand the link between solvent, dominant mode of adsorption and selectivity as well as predict catalytic turnover rates based on availabilities of different catalytically active sites in the presence of a range of solvents. In terms of 4-phenyl-2-butanone hydrogenation over 4% Pt/TiO$_2$, kinetic modelling has confirmed a number of the experimental findings in Part I of the study, chiefly the presence of two active sites, the impact of solvent on availability of Pt active sites and the role of the solvent in assisting desorption of intermediate 4-cyclohexyl-2-butanone.

5. Acknowledgments

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6. Appendices

6.1 Appendix A: Nomenclature and acronyms

Symbol	Description	SI Units

A	Pre-exponential factor	min^{-1} (for 1st order)
B(t)	Sensitivity function	-
$C(J_k)$	Cross correlation coefficient	-
D_{eff}	Effective diffusivity	cm^{2} g^{-1}
E_a	Activation energy	kJ mol^{-1}
F	F-value	-
I	Inhibiting organic species	mol L^{-1}
K	Rate constant	min^{-1} (for 1st order)
k_H	Henry’s constant	-
K	Equilibrium adsorption constant	L mol^{-1} (for 1st order)
L	Length	M
N	Reaction order	-
N	Stirred speed	min^{-1}
P	Product organic species	mol L^{-1}
par	Number of parameters	-
R	Rate of reaction	mol L^{-1} min^{-1} (for intrinsic rates unless noted)
r_p	Particle size radius	Cm
R	Reactant organic species	mol L^{-1}
R_g	Universal gas constant	J K^{-1} mol^{-1}
R^2	Sum of square of residuals	-
S	Solvent species	mol L^{-1}
S_k	Parameter sensitivity matrix	-
T	Reaction time	Min
T	Temperature	K
Y	Model response	-
[ ]	Of concentration	mol L^{-1}
*	Active site	-

Greek letters:		
α_1	Hydrogen bond donor parameter	-

α_2	Hydrogen bond acceptor parameter	-
B	Sensitivity	-
ΔH_{ads}	Heat of adsorption	kJ mol^{-1}
E	Dielectric constant	-
M	Dipole moment	-

Subscripts:	
A	Adsorption step
app	Apparent
arom	Aromatic
B	Reaction step
bas	Base temperature
C	Desorption step
crit	Critical
D	Inhibition step
I	Of reaction i
J	Of parameter j
K	Number of model responses
Ket	Ketone
L	Number of model parameters
lump	Lumped
M	Number of experiments
S	Solvent adsorption step
s,A	At particle surface
v,app	Apparent, volume-based
0	Initial

Acronym	**Description**
CBL	4-cyclohexyl-2-butanol
CBN	4-cyclohexyl-2-butanone
HPD	Higher probability density
LH	Langmuir-Hinshelwood

PBL	4-phenyl-2-butanol
PBN	4-phenyl-2-butanone
TOF	Turnover frequency

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