A kinetic analysis methodology to elucidate the roles of metal, support and solvent for the hydrogenation of 4-phenyl-2-butanone over Pt/TiO$_2$

S.K. Wilkinson [a,b,*], I. McManus [a], H. Daly [a], J.M. Thompson [a], C. Hardacre [c,*], N. Sedaie Bonab [b], J. ten Dam [c], M.J.H. Simmons [a,*], C. D'Agostino [d], J. McGregor [d,1], L.F. Gladden [d,*], E.H. Stitt [c]

[a] School of Chemical Engineering, University of Birmingham, Birmingham B15 2TT, UK
[b] Johnson Matthey Technology Centre, P.O. Box 1, Belasis Avenue, Billingham TS23 1LB, UK
[c] School of Chemistry and Chemical Engineering, Queen's University, Belfast BT9 5AG, UK
[d] Department of Chemical Engineering and Biotechnology, University of Cambridge, Cambridge CB2 3RA, UK

ARTICLE INFO

ABSTRACT

The rate and, more importantly, selectivity (ketone vs aromatic ring) of the hydrogenation of 4-phenyl-2-butanone over a Pt/TiO$_2$ catalyst have been shown to vary with solvent. In this study, a fundamental kinetic model for this multi-phase reaction has been developed incorporating statistical analysis methods to strengthen the foundations of mechanistically sound kinetic models.

A 2-site model was determined to be most appropriate, describing aromatic hydrogenation (postulated to be over a platinum site) and ketone hydrogenation (postulated to be 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. The kinetic analysis method shown has demonstrated 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, over 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 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 [8,9].
- '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

Nomenclature

Symbol	Description
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 ($mol\,dm^{-3}$)
k	rate constant (min^{-1} (for 1st order))
k_H	Henry's constant (–)
K	equilibrium adsorption constant ($dm^3\,mol^{-1}$ (for 1st order))
L	length (m)
n	reaction order (–)
N	stirred speed (min^{-1})
P	product organic species ($mol\,dm^{-3}$)
Par	number of parameters (–)
R	rate of reaction ($mol\,dm^{-3}\,min^{-1}$ (for intrinsic rates unless noted))
r_p	particle size radius (cm)
R	reactant organic species ($mol\,dm^{-3}$)
R_g	universal gas constant ($J\,K^{-1}\,mol^{-1}$)
R^2	sum of square of residuals (–)
S	solvent species ($mol\,dm^{-3}$)
S_k	parameter sensitivity matrix (–)
T	reaction time (min)
T	temperature (K)
Y	model response (–)
$[\ ]$	of concentration ($mol\,dm^{-3}$)
$*$	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
$Base$	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

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 the 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. [10] 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. [11] utilised a similar approach and also checked adsorption parameters for thermodynamic consistency.

Mounzer et al. [12] modelled the kinetics of 2-octanol oxidation performed using a variety of n-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-tests 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 [13]. 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 [14] 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 [15] 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 [16] 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

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

Ref.	Rate model	Mechanistic basis
• Bertero et al. [10] • Mathew et al. [11] • Mounzer et al. [12]	$r = \dfrac{k_b \cdot K_a \cdot [R]}{\left(1 + K_a \cdot [R] + \sum K_d[I]\right)^n}$ $r = \dfrac{k_b \cdot K_a \cdot [R]}{\left(1 + K_a \cdot [R] + \frac{[P]}{K_C}\right)^n}$	• LH approach with competitive adsorption of organics • Surface reaction rate determining step (r.d.s.) • LH approach with product desorption term • Surface reaction r.d.s.
• Gamez et al. [13]	$r = \dfrac{K_{a,b,c} \cdot [R]}{(1 + K_{a,c}[R])}$	• Michaelis–Menten approach
• Kishida and Teranishi [14] • Lemcoff [15] • Mukherjee and Vannice [16]	$r = \dfrac{k_b \cdot K_a \cdot [R]}{\left(1 + K_a \cdot [R] + K_s[S]\right)^n}$	• LH approach with a competitive solvent adsorption term • Assumes solvent interacts with catalyst surface • Surface reaction r.d.s.

Symbols denote the following:
- r: rate of reaction (mol dm^{-3} min^{-1}), k: rate constant (min^{-1} (for 1st order)), K: equilibrium constant (L mol^{-1} (for 1st order)).
- [ ]: concentration (mol dm^{-3}), 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.

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 each of the parameters in 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 [17] 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 group and 4-cyclohexyl-2-butanone (CBN), by hydrogenation of the aromatic ring. The reaction scheme is shown in Fig. 1 and features two reaction types, namely ketone (dashed arrows) or aromatic ring (solid arrows) 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 as shown by McManus et al.

[18]. Therein, a variety of solvents were tested which were found to impact on the reaction pathway selectivity and rate of reaction. 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 the rates, 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 TiO$_2$ support with activation of the C=O group through adsorption in the titania oxygen vacancies.

In this paper, a kinetic model is presented utilising these data. In this work, an aim is to stress the importance of using established statistical analysis methods in the development of mechanistically based kinetic models, with application in this case to liquid phase hydrogenations and solvent effects. The approach, inspired by the work of Quiney and Schuurman [17], is used to strengthen the foundations of these 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 the 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 in the study by McManus et al. [18]; therefore, only 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 ⩽45 μm for all reactions. The BET surface area of the catalyst Pt/TiO$_2$ (P25) was 56 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 2.2 nm with a dispersion of 33%.

Reaction studies were carried out using a 100 ml Hazard Evaluation Laboratory (HEL) autoclave pressure reactor. In all cases, 0.1 g catalyst and 30 ml solvent were added to the autoclave and pre-reduced *in situ* under 1 bar H$_2$ pressure, 60 °C, stirrer speed
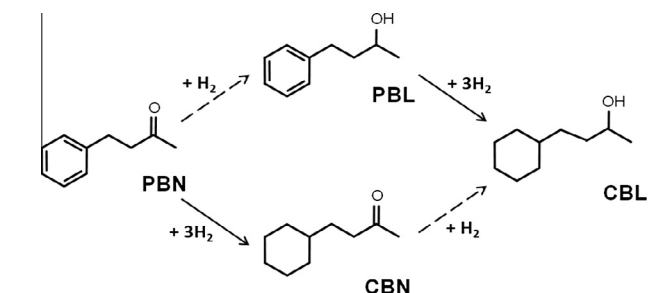

Fig. 1. Hydrogenation pathway of 4-phenyl-2-butanone (PBN) to 4-phenyl-2-butanol (PBL), 4-cyclohexyl-2-butanone (CBN) and 4-cyclohexyl-2-butanol (CBL). Solid arrows indicate aromatic ring hydrogenation and dashed arrows indicate C=O group hydrogenation.

Table 2
Experimental data modelled in this study.

Series	Variables	Constants
A	Effect of PBN concentration – 0.13–0.39 mol d m^{-3} (5 points)	– n-Hexane solvent – 70 °C operation
B	Effect of temperature 30–80 °C (6 points)	– n-Hexane solvent – 0.26 mol dm^{-3} starting PBN concentration
C	Effect of solvent – Alkanes – Aromatics – Primary alcohols – Secondary alcohols – Halogenates – Ethers	– 0.26 mol dm^{-3} starting PBN concentration – 70 °C operation

800 rpm for 1 h. Following reduction, a solution of 4-phenyl-2-butanone in a further 20 ml solvent was added to the reactor; reactions were carried out at 70 °C, 5 bar H_2 and 1400 rpm stirrer speed. The reaction kinetics are intrinsic and not from transport limitations [18].

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, the 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.

2.2. Kinetic modelling procedure

Parameter estimation within the kinetic models was carried out using Athena Visual Studio v14.2© software [19]. 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 initial discrimination of each of the kinetic models. 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 [20,21].

All response variables in the 4-phenyl-2-butanone hydrogenation reaction network are dependent upon the multiple reactions shown in Fig. 1, so the models must be solved implicitly using a set of differential equations:

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

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 [21,25]:

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

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

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 the 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:

$$k_i = \exp\left(Ln(A_{i,343}) + \left(E_{a,lump} \cdot \left(1 - \frac{T_{base}}{T}\right)\right)\right) \tag{4a}$$

$$K_i = \exp\left(Ln(A_{i,343}) + \left(\Delta H_{ads,lump} \cdot \left(1 - \frac{T_{base}}{T}\right)\right)\right) \tag{4b}$$
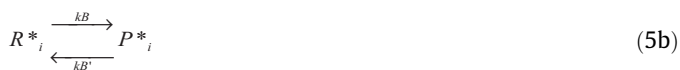
3. Results and discussion

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

In the study by McManus et al. the reaction profiles as a function of time were shown to be very similar up to 60 min for all starting concentrations [18]. Initial rates which are independent of initial organic reactant concentrations have also been previously seen for acetophenone hydrogenation [22]. This has been described as an *apparent* zero order observation as it is relevant to the initial stage of the reaction. Mechanistically, this observation suggests that adsorption of 4-phenyl-2-butanone is strong on the catalyst surface and may dominate in terms of surface coverage. Therefore, it is important to incorporate 4-phenyl-2-butanone

adsorption within mechanistic descriptions of the kinetics. In all individual experiments however, 4-phenyl-2-butanone shows an apparent order dependence of greater than one with reaction time, irrespective of starting 4-phenyl-2-butanone concentration. These observations are, therefore, consistent with a reaction mechanism that may feature the following:

- An adsorption term for the reactant 4-phenyl-2-butanone, as apparent zero order observations in the work of McManus et al. suggest a strong interaction of this species on the catalyst surface.
- 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 to describe the dataset in Series A:

$$R + *_i \underset{kA'}{\overset{kA}{\rightleftharpoons}} R*_i \tag{5a}$$

$$R*_i \underset{kB'}{\overset{kB}{\rightleftharpoons}} P*_i \tag{5b}$$

$$P*_i \underset{kC'}{\overset{kC}{\rightleftharpoons}} P + *_i \tag{5c}$$

$$I + *_i \underset{kD'}{\overset{kD}{\rightleftharpoons}} I*_i \tag{5d}$$

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

- The rate of hydrogenation of 4-phenyl-2-butanone was found to be apparent first order in H_2 in the study of McManus et al. In the proposed models (Table 3), the hydrogen driving force is always taken as first order. The H_2 pressure varied data in McManus et al. were explored at one starting 4-phenyl-2-butanone concentration (0.26 mol dm^{-3}). The need for an additional H_2 adsorption (and/or dissociation) equilibrium constant term was found to be negligible across these data. This suggests either H_2 does not adsorb onto the surface (i.e. plays an Eley–Rideal type role) or its adsorption is significantly weaker than the organics in competing for the same site.
- In order to explore the above possibilities, an 'apparent' site competition effect will be explored by placing a square term on the denominator of the kinetic expressions, and for the

Eley–Rideal-type mechanism the denominator will remain first-order.
- The first order in H_2 behaviour in the paper of McManus et al. would suggest that H_2 behaves in an associative rather than dissociative manner in the reaction mechanisms. In the latter, an apparent order closer to 0.5 would be expected.
- H_2 solubility into the liquid phase does change with either solvent choice or temperature. This was incorporated into the kinetic expressions [23].

Based on the elementary steps described in Eqs. (5a-5d), 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: organic adsorption (Eq. (5a)) or surface reaction/hydrogen adsorption (Eq. (5b)); the latter two steps cannot be decoupled in the dataset utilised.
- Apparent competition between organics and hydrogen for a specific active site, or an Eley–Rideal type mechanism with H_2 playing a gas-phase role only.
- The presence of different active sites for the ketone and aromatic ring hydrogenation reaction routes.

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 × 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. Fig. 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.

Inspection of Fig. 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 results 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, the 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

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

Equation no.	Generalised rate model	Basis
(6a and 6b)	$r = \dfrac{k_b \cdot K_a \cdot [R] \cdot [H_2]}{\left(1 + K_a \cdot [R] + K_c [P] + \sum K_d [I]\right)^n}$	• Surface reaction or H_2 ads. (Eq. (5b)) is the r.d.s. • Same site for ketone and aromatic ring hydrogenation • $n = 1$ (6a)[a]; $n = 2$ (6b)[b]
(6c and 6d)	$r_{ket} = \dfrac{k_{b,ket} \cdot K_{a,ket} \cdot [R] \cdot [H_2]}{\left(1 + K_{a,ket} \cdot [R] + c_{c,ket} [P] + \sum K_{d,ket} [I]\right)^n}$ $r_{arom} = \dfrac{k_{b,arom} \cdot K_{a,arom} \cdot [R] \cdot [H_2]}{\left(1 + K_{a,arom} \cdot [R] + K_{c,arom} [P] + \sum K_{d,arom} [I]\right)^n}$	• Surface reaction or H_2 ads. (Eq. (5b)) is the r.d.s. • Different site for ketone and aromatic ring hydrogenation • $n = 1$ (6c)[a]; $n = 2$ (6d)[b]
(6e and 6f)	$r = \dfrac{k_a [R] \cdot [H_2]}{\left(1 + K_{b,c} [P] + \sum K_d [I]\right)^n}$	• Organic adsorption (Eq. (5a)) is the r.d.s. • Same site for ketone and aromatic ring hydrogenation. • $n = 1$ (6e)[a]; $n = 2$ (6f)[b]
(6g and 6h)	$r_{ket} = \dfrac{k_{a,ket} [R] \cdot [H_2]}{\left(1 + K_{b,c,ket} [P] + \sum K_{d,ket} [I]\right)^n}$ $r_{arom} = \dfrac{k_{a,arom} [R] \cdot [H_2]}{\left(1 + K_{b,c,arom} [P] + \sum K_{d,arom} [I]\right)^n}$	• Organic adsorption (Eq. (5a)) is the r.d.s. • Different site for ketone and aromatic ring hydrogenation • $n = 1$ (6g)[a]; $n = 2$ (6h)[b]

[a] $n = 1$ implies different adsorption site for organics and H_2.
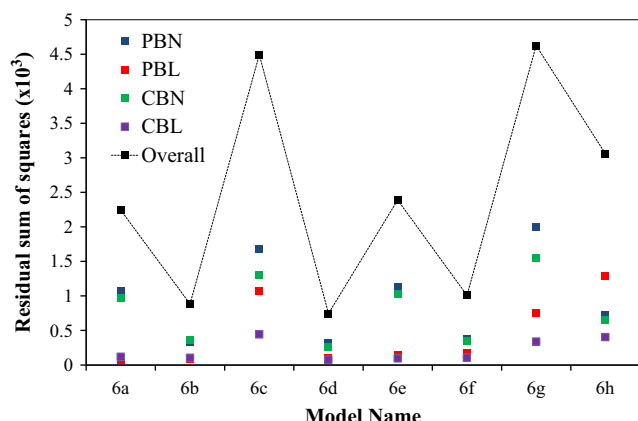[b] $n = 2$ implies same adsorption site for organics and H_2.

Fig. 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.

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 Fig. 3.

Critically, Fig. 3 shows that the confidence intervals for this reaction are much larger for 6a and 6e than for 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
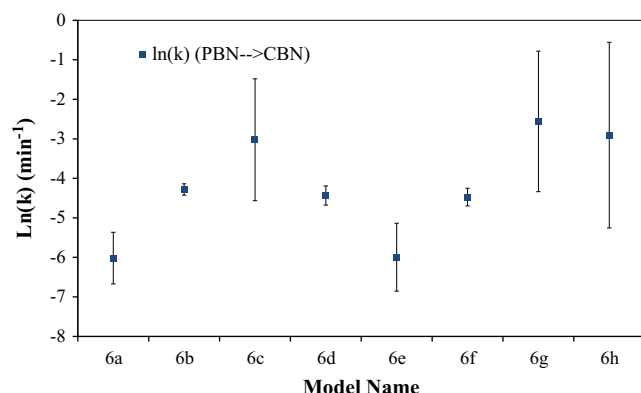
as they provide the best fitted description of the data matched by the best parameter confidence intervals. All three models have apparent site competition between organics and hydrogen in common, which is in line with observations discussed at the start of this section.

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

Each model is similar in overall performance, irrespective of the objective function approach (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 n-hexane solvent

Fig. 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
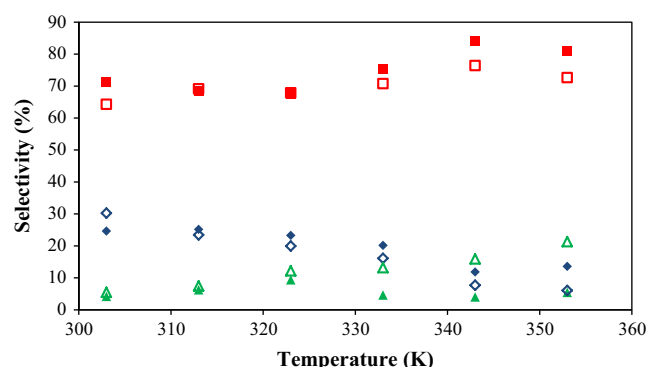

Fig. 3. Estimated parameter values and 95% asymptotic confidence intervals for the $ln(k)$ parameter for the 4-phenyl-2-butanone to 4-cyclohexyl-2-butanone (PBN → CBN) reaction using the non-linear least squares method.

Fig. 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.

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 function	−94.0	−94.9	−97.4
Residual sum of squares	$9.35 * 10^{-4}$	$7.63 * 10^{-4}$	$6.86 * 10^{-4}$
Ln(k) rate constants (min^{-1})[a]			
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 (dm^3 mol^{-1})[a]			
PBN	−0.16 ± 0.69	2.69 ± 0.35 (ketone site)	2.03 ± 0.16
		2.04 ± 0.20 (aromatic site)	
PBL	4.39 ± 0.16	4.38 ± 0.71	3.76 ± 0.56
CBN	Negligible	2.86 ± 0.23	±0.46

[a] ± Values are 95% higher probability density (HPD) intervals as determined by the Bayesian estimation method.

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 [22]. Selectivity to the fully hydrogenated product 4-cyclohexyl-2-butanol, increases with both time and temperature. In Fig. 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.

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 × 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 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, [17] 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 whether the change in residuals of model responses in the '*n* − 1' parameter model in comparison with 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:

$$F = \frac{\left(\frac{RSS_1 - RSS_2}{par_2 - par_1}\right)}{\left(\frac{RSS_2}{obs - par_2}\right)} \qquad (7)$$

where *F* is the *F*-statistic, RSS_1 and RSS_2 are the residual sum of squares in the nested and original model respectively, 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.

Fig. 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 candidate models was that the parameter reduction procedure contained steps where two activation energies
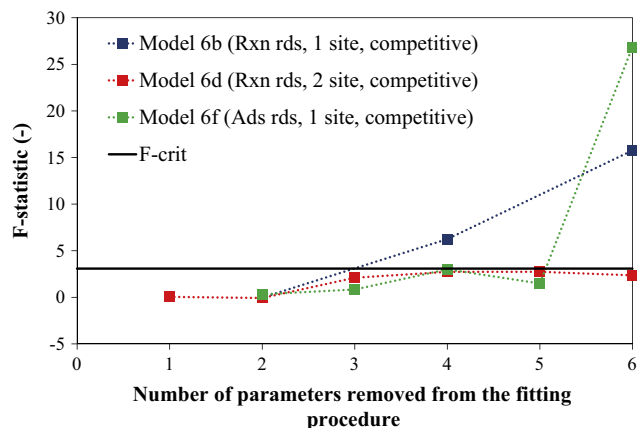

Fig. 5. Calculated *F*-statistic for successive parameter removals across the entire system response for different models. N.B.: Lines are to guide the eye.

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

Parameter	Estimate	95% HPD interval
$Ln\ (A_{1,ket,343})\ (\mathrm{min^{-1}})$ (PBN → PBL)	−5.80	±0.12
$Ln\ (A_{1,arom,343})\ (\mathrm{min^{-1}})$ (PBN → CBN)	−4.47	±0.05
$Ln\ (A_{2,arom,343})\ (\mathrm{min^{-1}})$ (PBL → CBL)	−5.68	±0.10
$E_{a,ket}\ (\mathrm{kJ\ mol^{-1}})$	27.9	±3.47
$E_{a,arom}\ (\mathrm{kJ\ mol^{-1}})$	50.9	±2.00
$Ln\ (K_{ket,PBN})\ (\mathrm{dm^3\ mol^{-1}})$	2.74	±0.24
$Ln\ (K_{arom,PBN})\ (\mathrm{dm^3\ mol^{-1}})$	1.98	±0.18
$Ln\ (K_{arom,CBN})\ (\mathrm{dm^3\ mol^{-1}})$	2.81	±0.09

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, are 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:

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

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

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

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 3.2. The E_a values estimated are in line with a surface reaction limited mechanism rather than an organic adsorption limited step. Previous work on a similar system, *p*-isobutyl acetophenone hydrogenation [11] 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 [23], heat of adsorption parameters was 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 removal of these heats of adsorption parameters for model 6d is demonstrated in Table S3 of Supplementary Information.

The presence of the parameter $K_{arom,CBN}$ in the final model has significant similarities with the study by Mounzer et al. [12]. 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. In the study by McManus et al. 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 this study it was discussed that the former site could be suppressed by the 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 log P 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 n-hexane examined, herein, may be critical to assisting this

final stage of the aromatic hydrogenation reaction mechanism. This suggests that in developing kinetics of solvent effects through Langmuir–Hinshelwood descriptions, solvation and adsorption of reactants and products may be coupled in many systems and care must be taken in the interpretation.

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 [17] used above was again applied to reduce the expression if necessary.

As Fig. 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.

Fig. 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, Fig. 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 back into the solvent is much more difficult. This may be understood by the weaker solvation of the 4-cyclohexyl-2-butanone in the hydrophilic alcohol solvents due to its greater hydrophobicity. The result, when using these solvents, is a less favourable desorption process for the 4-cyclohexyl-2-butanone
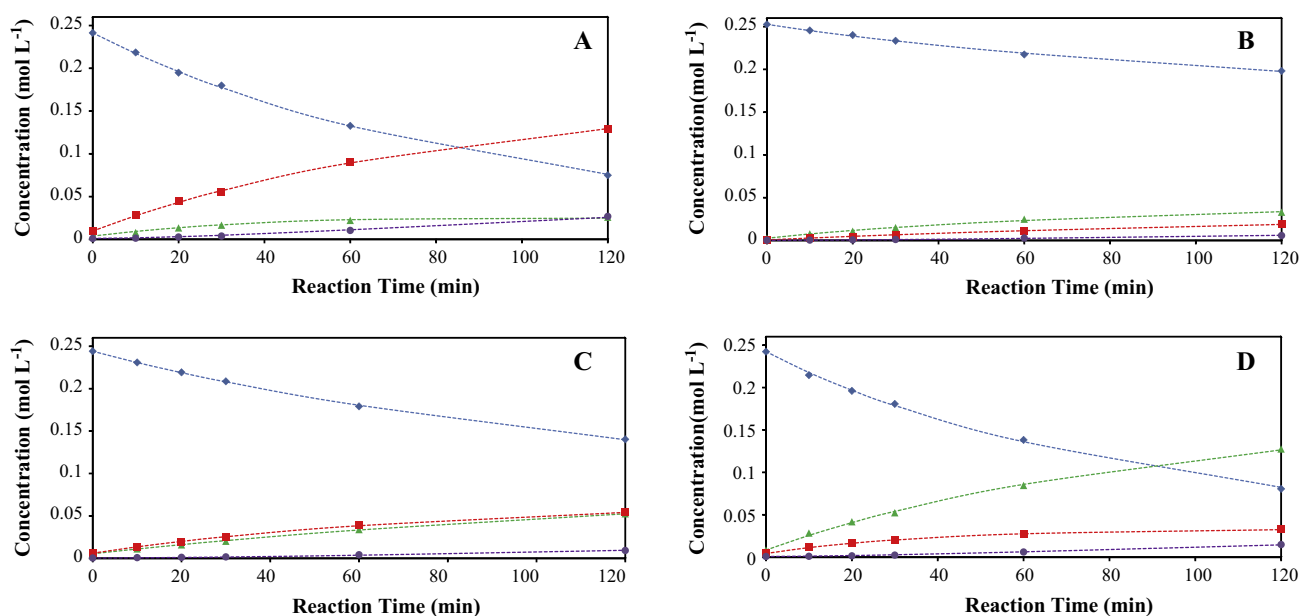

Fig. 6. Batch concentration-reaction time plots for 4-phenyl-2-butanol hydrogenation in (A) n-hexane, (B) toluene, (C) 1-propanol, (D) 2-propanol at 70 °C, 5 bar H$_2$ pressure and 0.26 mol dm^{-3} [PBN]. Symbols denote experimental readings, lines denote model predictions: (◆) 4-phenyl-2-butanone, (△) 4-phenyl-2-butanol, (■) 4-cyclohexyl-2-butanone, (●) 4-cyclohexyl-2-butanol.
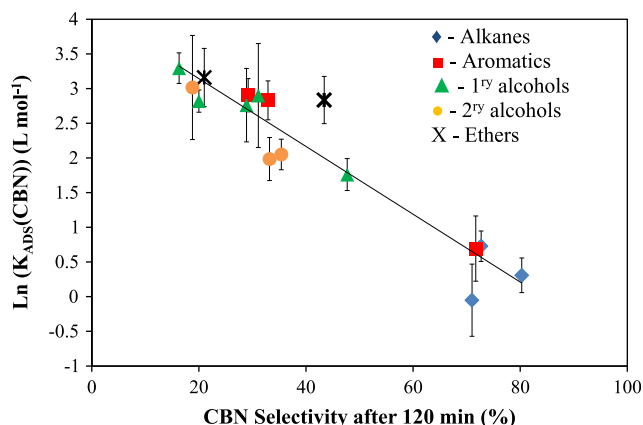
Fig. 7. Fitted adsorption constant, $K_{arom,CBN}$ plotted against 4-cyclohexyl-2-butanone %selectivity after 120 min for a range of solvents tested. (◆) denotes alkane solvents, (■) aromatics, (▲) primary alcohols, (●) secondary alcohols, (*) ethers. N.B.: No significant adsorption constant was found for halogenates.

product. 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 tert-butyl-toluene which features an alkyl group in its structure so may display aromatic-alkane hybrid behaviour.

Fig. 8 shows the ratio of the rate constants for the two pathways (k_{arom}/k_{ket}) with solvent. There is a clear connection between the ratios of the rate constants (reflecting selectivity to 4-cyclohexyl-2-butanone) with solvent type: with high values found for solvents with little interaction with the catalyst and low values (⩽1) for solvents which strongly interact with the
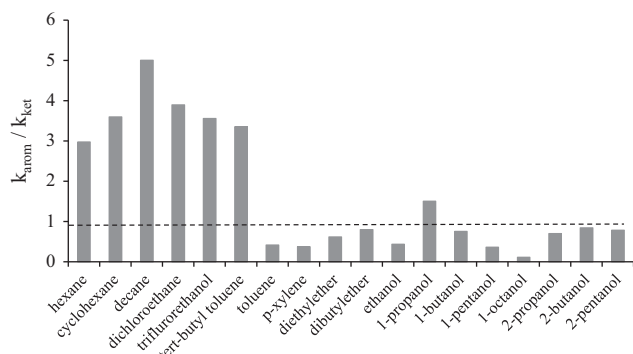

Fig. 8. Calculated k_{arom}/k_{ket} ratios for the hydrogenation of 4-phenyl-2-butanone in all solvents. The dotted line indicates a k_{arom}/k_{ket} ratio of 1 where there is no preference for either pathway.
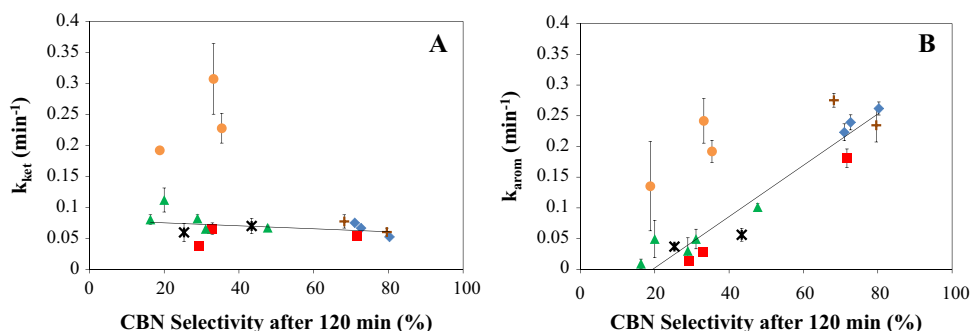
catalyst. In Fig. 9, the rate constants for ketone and aromatic hydrogenation for the solvents are examined. Whilst the rate of phenyl group hydrogenation (k_{arom}) is strongly dependent on choice of solvent, the ketone group hydrogenation rate (k_{ket}) is found to largely independent of the solvent used. The exception to this is 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 [18]. Again, the correlations shown in Fig. 9 were observed at all different reaction times (see Supplementary Information, Fig. 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) [24]. 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 rate (k_{ket} and k_{arom-}) as well as the 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 [18]. Based upon this, k_{arom} could be described as $k_{Pt}(1 − θ_{solv})$ 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 Fig. 9 is the secondary alcohols which show k_{arom} sites in comparable levels to an alkane solvent and a higher level of k_{ket} sites. In Fig. 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 [26] shows that 1-propanol and 2-propanol have values of 0.52 and 0.48 respectively, whilst n-hexane has a value of −0.08. Hence, the large difference in k_{arom} observed between primary and secondary alcohols suggests 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

Fig. 9. Fitted rate constant, (A) k_{ket} and (B) k_{arom} plotted against 4-cyclohexyl-2-butanone % selectivity after 120 min for a range of solvents tested. (◆) denotes alkane solvents, (■) aromatics, (▲) primary alcohols, (●) secondary alcohols, (*) ethers, (+) halogenates.

occurring both at the interface sites (C═O activated by adsorption in the vacancies on TiO_2) and on Pt. In the study by McManus et al. ketone hydrogenation in 2-propanol was possible over a Pt/SiO_2 catalyst which lacks the vacancy sites found on a TiO_2 support showing the reaction can be facilitated by Pt.

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.

In Table 6, a comparison is made with parameter estimation results estimated using the competitive solvent adsorption approach described in Table 1, with the aim of comparing the current method with a previous literature approach using concentration varied data. In this model, 5 adsorption parameters are fitted, namely, $K_{arom,CBN}$, $K_{arom,hexane}$, $K_{arom,toluene}$, $K_{ket,hexane}$, and $K_{ket,toluene}$. The hexane solvent adsorption terms were found to be insignificant on both sites, as was the adsorption of toluene on the ketone hydrogenation site. A strong adsorption of toluene was estimated, as postulated, and smaller but still significant adsorption strength of 4-cyclohexyl-2-butanone was seen. The $K_{arom,CBN}$ parameter returned a large 95% HPD interval but the removal of this parameter showed a significant drop in model quality as ascertained by the F-test. To further examine this result this parameter was reinstated and the predictions using this model were examined (Fig. 10).

The solvent adsorption parameter model provides a reasonable prediction of 4-phenyl-2-butanone consumption across the three datasets but there are discrepancies in the selectivity prediction of PBL and CBN, chiefly at high toluene concentrations. This is matched by the high uncertainty but remaining importance of the $K_{arom,CBN}$ parameter which suggests that this is changing as a function of solvent concentration. This suggests the observations cannot be related to adsorption strength of the catalyst surface alone and factors such as solubility of the reactants and products in the solvent, as discussed, must play a role in the overall observed kinetics in this system.

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 [10,12,24], assumptions of non-competitive and competitive reactant adsorption [16,22], dissociative or associative molecular adsorption [11,22] and inhibition effects [12,16] all defines 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. [22], 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. [11]. 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. [24]. 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. [12], 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,

Table 6
Parameter estimates and 95% HPD intervals for fits of experimental data using mixtures of n-hexane and toluene as solvent. Comparison with results when fitting all experiments at once using solvent adsorption approach.

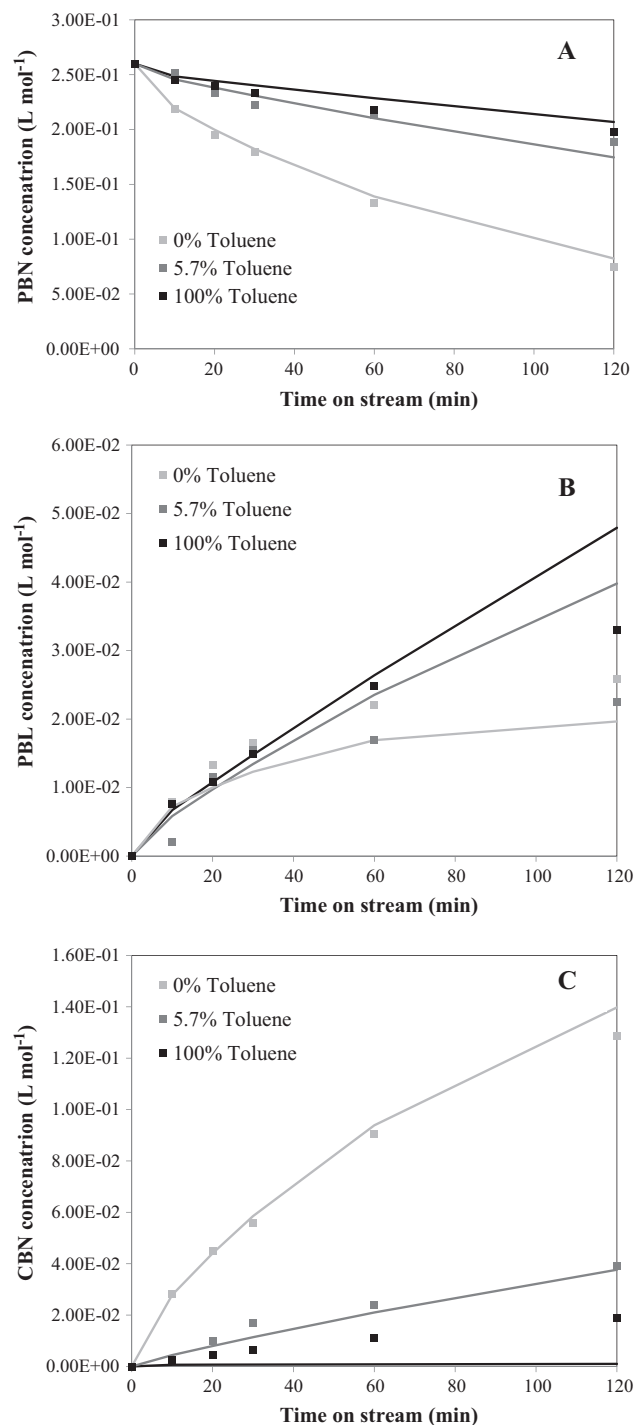| Parameter	n-Hexane solvent		n-Hexane solvent doped with 5.7 wt% toluene		Toluene solvent	
	Estimate	95% HPD interval	Estimate	95% HPD interval	Estimate	95% HPD interval
k_{ket}	0.08	0.01	0.06	0.01	0.07	0.01
k_{arom}	0.22	0.02	0.08	0.02	0.03	0.01
$K_{arom,CBN}$	0.95	0.55	19.68	7.47	16.94	5.44
			Estimate			95% HPD Interval
All three experiments fitted at once						
k_{ket}			0.002			0.0002
k_{arom}			0.008			0.0001
$K_{arom,CBN}$			0.55			2.02
$K_{arom,Toluene}$			2.92			1.11

Fig. 10. Experimental (squares) against model predictions (lines) for (A) 4-phenyl-2-butanone (PBN), (B) 4-phenyl-2-butanol (PBL) and (C) 4-cyclohexyl-2-butanone (CBN) for the approach incorporating a solvent adsorption parameter for three experiments varying hexane to toluene solvent concentration.

A further comparison can be made with previous works which have used K_S to describe the inhibition role of the solvent [14,15,27]. 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.

In the current work, the use of the K_s fitting approach was explored over three datasets where hexane and toluene solvent concentrations were varied. Whilst this approach clearly highlighted the strong adsorption of toluene over the sites for aromatic ring hydrogenation, it was unable to achieve an encompassing description across the dataset. This was attributed to the changing $K_{arom,CBN}$-parameter as a function of solvent choice which the authors believe to be linked to ease of product desorption back into the solvent. It is therefore recommended that care is taken when considering the K_s parameter in the analysis and a prudent first step is to analyse individual experimental runs without it.

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. Development of a physically sound model of this role, as well as catalyst metal/support and reactants/products is very complex due to the influence and interdependencies between each of the model parameters. Data from an experimental study of 4-phenyl-2-butanone hydrogenation over a 4% Pt/TiO₂ 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 [11,12,22]. The fitting of data to these models has been combined with a rigorous statistical analysis procedure to eliminate non-influential parameters in their descriptions [17]. 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/TiO₂, kinetic modelling has confirmed 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 [18].

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. It is suggested that for future study, this selective adsorption effect could be explored computationally via the use of density functional theory (DFT), such as the approach used in the work explored in [4].

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jcat.2015.06.007.

References

[1] N. Menshutkin, Z. Phys. Chem. 6 (1890) 589.
[2] F.A. Carey, R.J. Sundberg, Advanced Organic Chemistry, Plenum Press, New York, 1990.
[3] U.K. Singh, M.A. Vannice, Appl. Catal. A 213 (2001) 1.
[4] B.S. Akpa, C. D'Agostino, L.F. Gladden, H. Hindle, H. Manyar, J. McGregor, R. Li, M. Neurock, N. Sinha, E.H. Stitt, D. Weber, J.A. Zeitler, D.W. Rooney, J. Catal. 289 (2012) 30.
[5] R.J. Madon, J.P. O'Connell, M. Boudart, AIChE J. 24 (1978) 904.
[6] E.E. Gonzo, M. Boudart, J. Catal. 52 (1978) 462.
[7] M. Boudart, W.-C. Cheng, J. Catal. 106 (1987) 134.
[8] R.A. Sheldon, Green Chem. 9 (2007) 1273.
[9] R.A. Sheldon, Chem. Commun. (2008) 3352.
[10] N.M. Bertero, C.R. Apesteguia, A.J. Marchi, Appl. Catal. A 349 (2008) 100.
[11] S.P. Mathew, M.V. Rajesekharam, R.V. Chaudhari, Catal. Today 49 (1999) 49.
[12] H.N. Mounzer, J. Wood, E.H. Stitt, Chem. Eng. Sci. 65 (2010) 179.
[13] A. Gamez, J. Köhler, J. Bradley, Catal. Lett. 55 (1998) 73.
[14] S. Kishida, S. Teranishi, J. Catal. 12 (1968) 90.
[15] N.O. Lemcoff, J. Catal. 46 (1977) 356.
[16] S. Mukherjee, M.A. Vannice, J. Catal. 243 (2006) 131.
[17] A.S. Quiney, Y. Schuurman, Chem. Eng. Sci. 62 (2007) 5026.
[18] I. McManus, H. Daly, J.M. Thompson, E. Conor, C. Hardacre, S.K. Wilkinson, N. Sedaie Bonab, J. ten Dam, M.J.H. Simmons, E.H. Stitt, C. D'Agostino, J. McGregor, L.F. Gladden, J. Catal., submitted for publication.
[19] Athena Visual Workbench 14.2, Stewart & Associates Engineering Software Inc.
[20] W.E. Stewart, M. Caracotsios, Computer-aided Modelling of Reactive Systems, 2008.
[21] M. Caracotsios, W.A.E. Stewart, Comp. Chem. Eng. 94 (1985) 359.
[22] I. Bergault, P. Fouilloux, C. Joly-Vuillemin, H. Delmas, J. Catal. 175 (1998) 328.
[23] T. Katayama, T. Nitta, J. Chem. Eng. Data 21 (1976) 194.
[24] N.-S. Chang, S. Aldrett, M.T. Holtzapple, R.R. Davison, Chem. Eng. Sci. 53 (2000) 5721.
[25] Y. Bard, Nonlinear Parameter Estimation, fourth ed., Acad. Press, 1974.
[26] M.H. Abraham, P.L. Grellier, J-L.M. Abboud, R.M. Doherty, R.W. Taft, Can. J. Chem. 66 (1988) 2673.
[27] S. Mukherjee, M.A. Vannice, J. Catal. 243 (2006) 108.