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O-Methylation of Dihydroxybenzenes with Methanol in the Vapour Phase over Alkali-Loaded SiO_2 Catalysts: A Kinetic Analysis

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Abstract:

The vapour-phase *O*-methylation of the dihydroxybenzenes (DHBs; *o*-dihydroxybenzene (catechol), *m*-dihydroxybenzene (resorcinol), and *p*-dihydroxybenzene (hydroquinone)) with excess methanol has been investigated over alkali (Li, Na, K, and Cs) oxide loaded-SiO_2 as catalysts. The reaction takes place in two consecutive steps, the formation of the monomethoxyphenol in the first step (rate constant, k_1) and the dimethoxybenzene in the second step (rate constant, k_2). The two steps have been assumed to follow a pseudo-first-order kinetics with respect to the substrates (DHB in the first step and the monomethoxy phenol in the second step) and the kinetic parameters, k_1, k_2, t_{max}, and R_{max} have been calculated. The trends in the values of the above kinetic parameters have been explained on the basis of the reactivity and electronic properties of the three DHBs, the surface basicity of the catalysts, and the mode of adsorption of the molecules on the support.

Introduction

O-Methylated dihydroxybenzenes are important synthetic intermediates in the production of fine chemicals and pharmaceuticals.[1] They are conventionally synthesized by methylation with dimethylsulphate[2] or with methyl halide in the presence of sodium hydride.[3] These methylating agents are corrosive and toxic. The greater desire for environmentally safer processes have, in recent times, led to the development of processes based on solid catalysts and vapour-phase reactions in fixed-bed reactors. Vapour-phase methylation of aromatic hydroxy compounds with methanol over heterogeneous catalysts such as metal oxides, sulphates, phosphates, and zeolites has been attempted.[4−9] Fu et al.[10−12] reported the vapour-phase *O*-methylation of catechol with dichloromethane (DCM) over supported alumina catalysts.

Table 1. **Composition and physicochemical properties of alkali-loaded silica samples**

catalyst[a]	metal loading as oxide (wt %)	S area[b] (m^2/g)	TPD of CO_2 (mmol/g)[c]
SiO_2	–	166	–
Li(1.5)SiO_2	2.25	104	0.062
Na(1.5)SiO_2	4.65	99	0.071
K(1.5)SiO_2	7.05	91	0.078
Cs(1.5)SiO_2	21.1	70	0.079

[a] The number in parentheses denotes the mmol of alkali metal loaded per g of SiO_2. [b] Measured by N_2 adsorption (BET method). [c] mmol of CO_2 desorbed/g of catalyst.

We have reported the selective vapour-phase *O*-methylation of the dihydroxybenzenes, catechol, resorcinol, and hydroquinone with methanol over alkali (Li, Na, K, and Cs)-loaded silica catalysts.[13] We found that alkaline silica catalysts produced *O*-alkylated products with high selectivity. We now present a kinetic analysis of the *O*-methylation of dihydroxybenzenes over alkali metal oxides supported on SiO_2 to facilitate a better appreciation of the methylation reaction. Methylation occurs in two steps, first the monomethoxy product formation and then the dimethoxy product formation. The two consecutive methylation reactions are analyzed by assuming them to be two independent first-order reactions. The kinetic analysis presented should assist in identifying the optimal conditions for the production of the various methylated compounds.

Experimental Section

Materials and Methods. Fumed silica (Cab-osil, Fluka) was used as the support for the alkali metal oxides. The alkali metals were loaded (1.5 mmol/g) onto the support by an impregnation procedure (incipient wetness method) using a minimum amount of aqueous metal hydroxide/acetate (Li, Na, K, and Cs).[13] They were dried at 373 K for 6 h and calcined at 773 K for 6 h in air. Granular catalysts (10−22 mesh) were prepared by pelletting the powder and crushing to the desired size.

All the reactions were carried out in a vertical down-flow glass reactor (15 mm i.d.) using 2 g of the catalyst. The zone above the catalyst bed (∼15 cm long) was packed with ceramic beads and served as a preheater. The reactor was placed inside a temperature-controlled furnace (Geomecanique, France). The reaction temperature was measured with a thermocouple placed at the center of the catalyst bed. The catalyst was activated in situ in flowing air (20 mL/min) at 773 K for 3 h and flushed with nitrogen, and the temperature was adjusted to the desired reaction temperature (673 K).

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Table 2. **Activities of different catalysts in the methylation of dihydroxybenzenes**[a]

	o-dihydroxybenzene				*m*-dihydroxybenzene				*p*-dihydroxybenzene			
		sel. (wt %)				sel. (wt %)				sel. (wt %)		
catalyst[b]	conv. (wt %)	mono-[c]	di-[d]	others[i]	conv. (wt %)	mono-[e]	di-[f]	others[i]	conv. (wt %)	mono-[g]	di-[h]	others[i]
SiO_2	3.5	–	–	100	4.2	–	–	100	4.8	–	–	100
$Li(1.5)SiO_2$	5.2	75.1	15.7	9.2	30.9	36.9	44.3	18.8	27.1	59.1	14.0	26.9
$Na(1.5)SiO_2$	10.3	71.3	22.5	6.2	45.3	33.8	52.1	14.1	44.2	47.7	31.0	21.3
$K(1.5)SiO_2$	17.3	63.3	31.5	5.2	65.7	22.6	64.7	12.7	49.1	45.8	41.0	13.2
$Cs(1.5)SiO_2$	57.2	47.0	53.0	0	87.4	10.7	89.3	0	87.9	24.8	75.2	0

[a] Conditions: temperature: 673 K; TOS: 1 h; contact time: 0.376 h; N_2 flow: 18 mL/min. [b] The number in the bracket denotes the mmol/g of alkali metal loaded on SiO_2. [c] 2-methoxy phenol. [d] 1,2-dimethoxy benzene. [e] 3-methoxy phenol. [f] 1,3-dimethoxy benzene. [g] 4-methoxy phenol. [h] 1,4-dimethoxy benzene [i] Mostly *C*-alkylated products.

Table 3. **Comparison of the kinetic parameters in the methylation of dihydroxybenzenes over different alkali metal catalysts**[a]

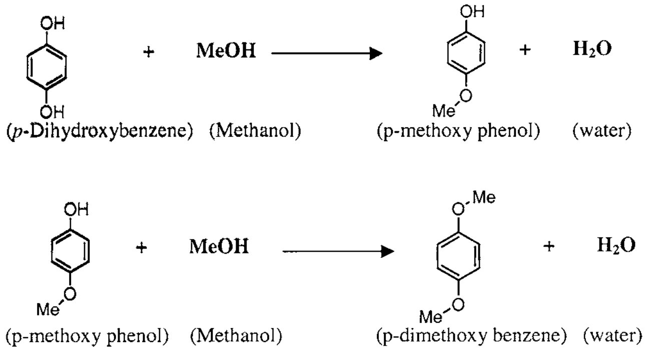
catalyst	hydrocarbon	k_1 (h^{-1})	k_2 (h^{-1})	t_{max} (h)	R_{max}	k_2/k_1	di/total
Li(1.5)SiO2	*o*-dihydroxybenzene	0.008	0.029	62.20	0.17	3.6	0.17
	m-dihydroxybenzene	0.186	2.018	1.292	0.07	10.6	0.55
	p-dihydroxybenzene	0.131	1.179	2.095	0.08	9.1	0.19
Na(1.5)SiO2	*o*-dihydroxybenzene	0.0295	0.212	10.811	0.10	7.1	0.23
	m-dihydroxybenzene	0.286	5.313	0.579	0.05	18.3	0.61
	p-dihydroxybenzene	0.903	10.180	0.261	0.07	11.3	0.39
K(1.5)SiO2	*o*-dihydroxybenzene	0.065	0.478	4.696	0.10	7.4	0.33
	m-dihydroxybenzene	1.602	30.89	0.101	0.04	19.3	0.74
	p-dihydroxybenzene	1.230	18.98	0.154	0.05	15.8	0.47
Cs(1.5)SiO2	*o*-dihydroxybenzene	0.952	10.268	0.255	0.07	10.8	0.53
	m-dihydroxybenzene	3.978	84.3	0.038	0.04	21.1	0.89
	p-dihydroxybenzene	3.445	85.2	0.039	0.04	24.7	0.75

[a] Conditions: temperature: 673 K; TOS: 1 h; substrate:methanol (mol ratio) = 1:5, $R_{max} = C_{rmax}/C_{a_0}$; t_{max} = time at which R_{max} is observed.

The feed (a mixture of the substrate and methanol, mole ratio: 1:5) was passed into the reactor using a syringe pump (Braun, Germany) along with nitrogen gas (18 mL/min). Catechol, resorcinol, and hydroquinone were used as the substrate. The product was cooled in a water-cooled condenser, collected in a receiver and analyzed using a gas chromatograph (HP 5880 A; capillary column HP1, 50 m × 0.2 mm; FID detector). Product identification was done by GC−IR, GC−MS, and NMR. Carbon mass balances were carried out for many of the experiments and were found to be 95 ± 5%. Experiments were carried out at 673 K for different residence times (0.018−0.75 h). A time-on-stream (TOS) of 1 h was used for the collection of data.

Kinetic Analysis. Dihydroxybenzenes (DHBs) react with methanol in two steps. In the first step, the substrate reacts to form the monomethoxy phenol and water. The monomethoxy phenol further reacts with methanol to yield the dimethoxy phenol and an equivalent amount of water.

Example:



This can be represented by the following general equations

$$A + B \rightarrow R + D \tag{1}$$

and

$$R + B \rightarrow S + D \tag{2}$$

where A is the DHB, B is methanol, D is water; R and S are the corresponding monomethoxy phenol and dihydroxybenzene, respectively. Since excess of methanol is used in the experiments, the reaction can be simplified as two pseudo-first-order reactions in series,

$$A \xrightarrow{k_1} R \xrightarrow{k_2} S \tag{3}$$

with k_1 as the rate constant for step 1 and k_2 the rate constant for step 2.

The value of k_1 was estimated from the standard first-order expression,

$$C_a/C_{a_0} = e^{(-k_1 t)} \tag{4}$$

where C_a and C_{a_0} are the molar concentrations of the hydrocarbon A at time *t* and at the start of the reaction, respectively.

The rate constant for the second step k_2 was estimated from the concentrations of R and S (C_r, C_s) using the expression,

$$d(C_s/C_{a_0})/dt = k_2 C_r/C_{a_0} \tag{5}$$

During the initial period when the change in concentration of S with time is small or when the overall conversion is

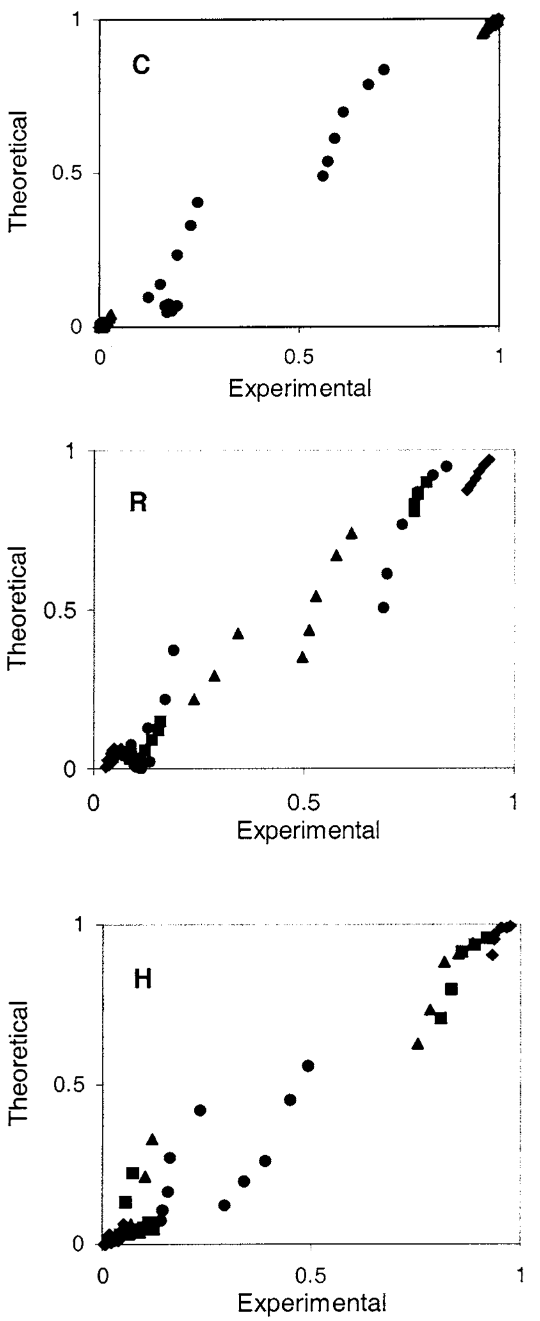


Figure 1. **Comparison of theoretical and experimental concentrations in the methylation of catechol (C), resorcinol (R), and hydroquinone (H) with methanol at 673 K, using different catalysts. The symbols ■, ●, ▲ represent (C/C_{a_0}) for the reactant, monomethyl, and dimethyl products, respectively, obtained from different experiments (substrate:methanol mol ratio = 1:5; time: 0.018−0.75 h)**

low, the above equation can be approximated to

$$C_s/(C_{a_0}t) = k_2 C_r/C_{a_0} \qquad (6)$$

k_2 was estimated from the slope of the linear plot of $C_s/(C_{a_0}t)$ versus C_r/C_{a_0}.

The maximum concentration of the intermediate R (monomethoxy product) and the time at which this occurs were determined using the following expressions:

$$C_{r,\max}/C_{a_0} = (k_1/k_2)^{(k_2/(k_2-k_1))} \qquad (7)$$

and

$$t_{\max} = (\ln (k_2/k_1))/(k_2 - k_1) \qquad (8)$$

Results and Discussion

The three substrates used in this study are isomeric dihydroxybenzenes. The electronic influence of one −OH group on the reactivity of the other depends on the relative location of the two groups (ortho-, meta-, or para-positions). In addition, the adsorption of these molecules on the catalyst surface will also be influenced by the electronic properties and stereochemistry of the −OH groups and the acid−base property of the catalyst surface. These aspects are now examined in the methylation of dihydroxybenzenes with methanol. A series of SiO_2-supported alkali oxide catalysts (Table 1) possessing different acid−base characteristics are used in these studies. The results of the methylation of the three dihydroxybenzenes (catechol, *o*-isomer; resorcinol, *m*-isomer; and hydroquinone, *p*-isomer) with methanol at 673 K are presented in Table 2.

The composition (metal oxide loading) and the surface areas of the samples are presented in Table 1. The basicities of the samples as characterized by the amount of CO_2 desorbed during the temperature-programmed desorption (TPD) of adsorbed CO_2 are also presented in Table 1. It was found during the TPD experiments that CO_2 was weakly adsorbed on to the samples and all the adsorbed CO_2 was desorbed in the temperature range 375−400 K. The amount of CO_2 desorbed (adsorbed) increases from Li to Cs suggesting an increase in the basicity of the sample. The expected order of the basicity of the samples based on the electronegativity of the alkali metals is in the same order as the amount of CO_2 desorbed during the TPD experiments.

The results of Table 2 reveal that the activity is in the order of the basicity of the samples: $Li-SiO_2 < Na-SiO_2 < K-SiO_2 < Cs-SiO_2$. The selectivity for the *O*-methylated products is very high over all the catalysts and increases in the same order as activity, the selectivity being 100% in the case of $Cs-SiO_2$. It is also noticed that the order of reactivity of the three dihydroxy benzenes is: resorcinol > hydroquinone > catechol. Another observation that can be made from the table is that the ratio of the dihydroxy benzene to monohydroxy phenol (di-/mono-) increases with the basicity/activity of the catalyst (Table 3). The reaction can be modeled as already described, to consist of two first order reaction steps. As up to about 25% of other products (side products: mostly *C*-methylated derivatives) are formed in the case of less active and less basic catalysts especially $Li-SiO_2$, only the *O*-methylated products are being considered for the kinetic analysis. To enable a kinetic analysis of the consecutive reaction, experiments were carried out at different contact times (0.018−0.75 h) using a mixture of phenol and methanol (1:5 mol ratio) at 673 K.

The concentration profiles of the reactions over a larger time interval were generated with the k_1 and k_2 values estimated using eqs 4 and 6 from data obtained in a limited time interval (0.018−0.75 h). Comparison of theoretical and experimental concentrations (C/C_{a_0}) for the reactions over

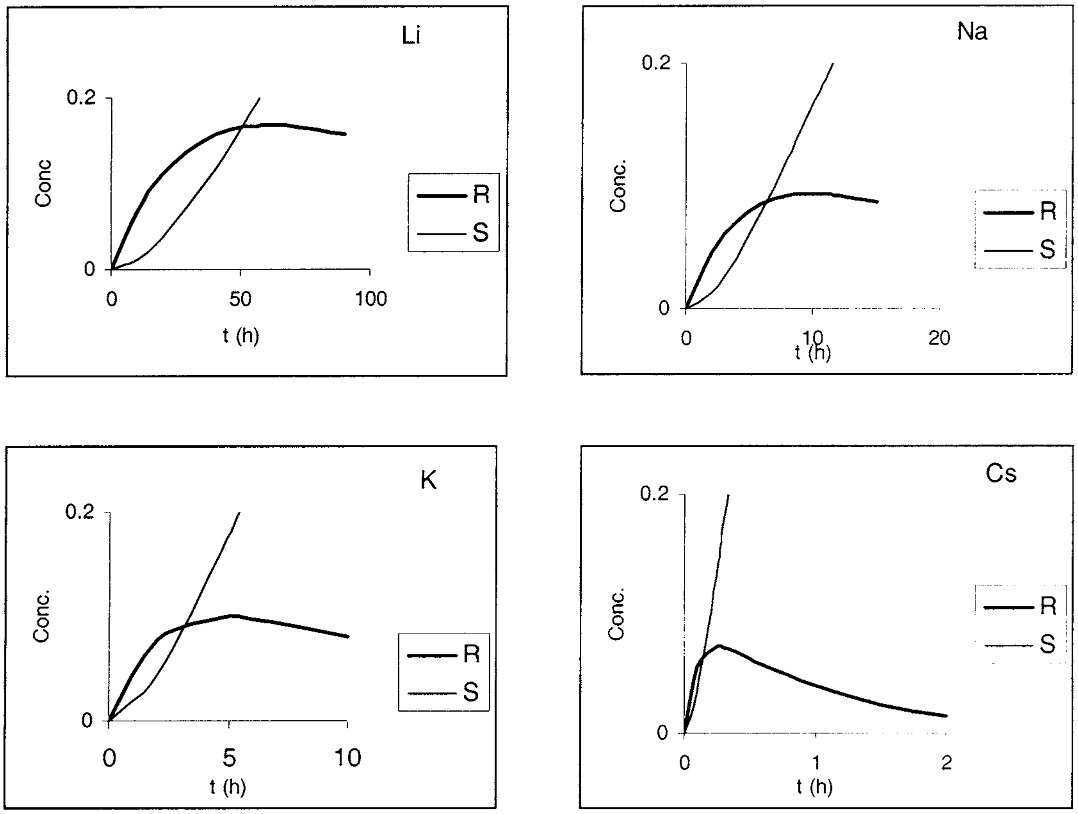


Figure 2. **Comparison of concentration profiles in the methylation of catechol over different alkali metal catalysts at 673 K (catechol: methanol mol ratio = 1:5; R: monomethyl catechol; S: dimethyl catechol).**

different catalysts (Li-, Na-, K-, Cs-SiO_2) is presented in Figure 1.

The plots reveal some scatter, specifically at the central region and for the hydroquinone−methanol alkylation. The assumed pseudo-first-order equations are truly valid only at small conversions and reaction times. Cs−SiO_2 catalyst is highly active, and the hydroquinone−methanol reaction is comparatively fast. Hence, the figure shows some scatter for these cases. The standard deviations of most of the data lie between 0 and 0.05 although larger deviations (up to 0.12) were observed in the case of Cs-loaded catalysts. Although the use of a greater MeOH content might have better justified the assumption of a pseudo-first-order reaction, a larger ratio would have been less acceptable from a practical (commercial application) viewpoint. However, the reasonable fit between the calculated and measured values (Figure 1) does validate our assumptions.

The concentration profiles with time for the intermediate R (monomethoxy compound) and the final product S (dimethoxy compound) in the methylation of catechol are presented in Figure 2. The profiles are those expected for consecutive reactions. The nature of the profile especially that for R, depends on the relative rates (k_1 and k_2) of the two consecutive reactions. Both the maximum value of R (R_{max}) and the time (t_{max}) at which R_{max} occurs depend on the relative values of k_1 and k_2 and the magnitude of k_1. The value of k_1 determines the rate of disappearance of the reactant (conversion) into the *O*-methylated product. Examining the Figure, it is apparent that Li−SiO_2 and Na−SiO_2 are less active catalysts because of the longer time taken for the attainment of maximum value for the intermediate R. This is especially obvious for the less reactive catechol.

The values for k_1, k_2, t_{max}, and R_{max} for the methylation of the three DHBs are presented in Table 3. The following observations are based on the data reported in Table 3.

(i) For any given substrate, k_1 and k_2 increase with increasing basicity of the catalyst, k_2 increases faster than k_1, and the ratio k_2/k_1 also increases with the basicity of the catalyst as: Cs−SiO_2 > K−SiO_2 > Li−SiO_2.

(ii) t_{max} decreases with the basicity of the catalyst (Li−SiO_2 > Na−SiO_2 > K−SiO_2 > Cs−SiO_2) and the reactivity of the DHB (*o*-dihydroxybenzene > *p*-dihydroxybenzene > *m*-dihydroxybenzene).

On the basis of the kinetic analysis of a consecutive reaction, one would expect the ratio k_2/k_1 to reflect the dimethoxybenzene/total *O*-methoxy product (di-/total) ratio in the product. In fact, a plot of k_2/k_1 versus di-/total ratio (Table 3) produces a straight line (Figure 3), suggesting the kinetic analysis to be a realistic one.

This increase in activity and *O*-alkylation selectivity of the catalysts on going from Li− SiO_2 to Cs−SiO_2 is a result of increasing basicity of the catalyst. As the basicity increases, the *C*-alkylation reaction which generally involves the attack of a carbenium ion at a carbon atom on the electron-rich benzene ring is suppressed due to the absence of acid sites responsible for the creation of carbenium ion moieties. This therefore results in an increase in the *O*-selectivity of the catalyst with basicity. The basic sites are the O^{2-} ions associated with the alkali metal cations. As the

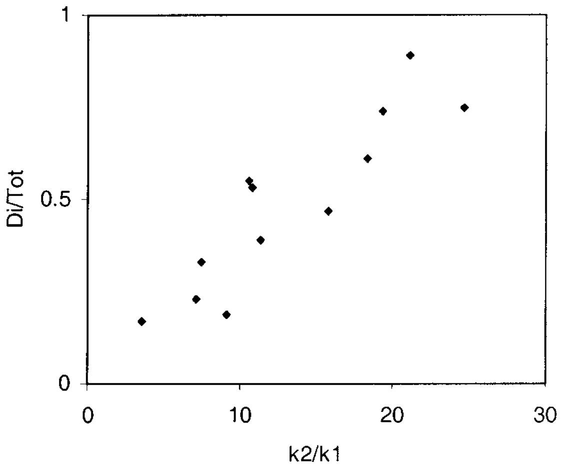
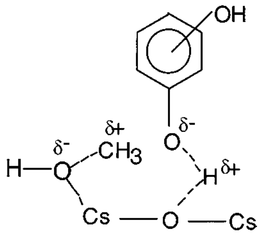


Figure 3. **Selectivity for the dimethylated product as a function of the ratio of the reaction rate constants in the methylation of dihydroxybenzenes over different alkali metal catalysts at 673 K.**

Scheme 1. **Probable mode of adsorption of the reactants**



size and electropositive nature of the cation increases (Li to Cs) the charge on the O^{2-} ions increases as the cation is not able to fully balance the O^{2-} charge, thus making the catalyst more basic, that is, increasing its ability to attract a positively charged species. Dihydroxy benzenes are expected to adsorb on the basic sites in our catalysts by the −OH group as shown in Scheme 1. These adsorbed species will be stabilized better over basic catalysts thereby increasing their concentration at the surface and the *O*-alkylation rate.

In the case of a less basic catalyst (e.g., $Li-SiO_2$), one would expect adsorption also by the ring π-electron leading (additionally) to *C*-alkylation products (Table 2).

The reactivity of the DHBs increases in the order, *o*-dihydroxybenzene < *p*-dihydroxybenzene < *m*-dihydroxybenzene. The reason for this reactivity trend is the difference in the acidity of the three compounds and ease of formation of the above-surface transition state. The reactivity trend matches the acidity of the three DHBs (*o*-dihydroxybenzene < *p*-dihydroxybenzene < *m*-dihydroxybenzene) and the electron density trends at the ortho-, meta-, and para-positions of phenol. The +M effect of the −OH group tends to cause a lower electron density at the meta-position in the case of *m*-dihydroxybenzene and favours the formation of the $[HO-C_6H_5-O^{\delta-}]$ adsorbed species (Scheme 1). On the other hand, the larger electron densities at the ortho- and para-positions in the case of *o*-dihydroxybenzene and *p*-dihydroxybenzene will destabilize the above transition state. In addition, steric effects may also be responsible for the lower reactivity of *o*-dihydroxybenzene.

Conclusions

Conversion and *O*-methylation selectivity in the vapour-phase alkylation of dihydroxybenzenes with excess methanol over different alkali-loaded SiO_2 catalysts increases with the basicity of the catalyst. The order of reactivity of the three dihydroxybenzenes is *m*-dihydroxybenzene > *p*-dihydroxybenzene > *o*-dihydroxybenzene. Kinetic modeling of the methylation reaction by assuming pseudo-first-order kinetics has been used to quantify the relative activities of the catalysts and the relative reactivities of the substrates through the two rate constants, k_1 and k_2 and the parameter t_{max}, the time at which the concentration of the intermediate (monomethoxy phenol) attains a maximum value. The ratio of the two rate constants (k_1/k_2) is found to predict the ratio of the dimethoxy product to the total amount of methoxy products.

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