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Ab initio study of the selective alkylation of m-cresol with tert-butanol catalyzed by SO_3H-functionalized ionic liquids

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ABSTRACT

Our previous work showed that for catalytic alkylation of m-cresol with tert-butanol (TBA) SO_3H-functionalized ionic liquids exhibited several characteristic advantages over conventional catalysts. This work investigated the reaction mechanism of the alkylation of m-cresol with tert-butanol catalyzed by the SO_3H-functionalized ionic liquid (IL) through quantum chemical calculation in combination with the experimental studies. The experimental results showed that 2-tert-butyl-5-methyl phenol (2-TBC), 4-tert-butyl-3-methyl phenol (4-TBC) and tert-butyl-m-cresol ether (TBMCE) products were all primary products, while 2,6-di-tert-butyl-3-methyl phenol (2,6-DTBC) was a secondary product. The calculation results indicated that the selectivities of the products depended on the fundamental natures of the reactive sites, including the orbital overlap, the Coulomb and the steric effect in the interaction between the tert-butyl ion ($[t\text{-}C_4H_9]^+$) and the m-cresol; the TBMCE was dynamically favored but not thermodynamically stable, while the C-alkylated products, especially 2-TBC, were the thermodynamically preferred products; the IL played an important role in generating the $[t\text{-}C_4H_9]^+$ from the TBA and the final products from the intermediates.

1. Introduction

2-Tert-butyl-5-methyl phenol (2-TBC) is a precursor for a number of commercially important antioxidants and a light protection agent for bisphenols and thiobisphenols. 2-TBC is also used to prepare important UV absorber and musk ambrette, which is a perfume fixation agent [1]. Many kinds of acid catalysts have been used for the synthesis of tert-butylated m-cresol, such as H_2SO_4 [2], Al-MCM-41 [3] and mesoporous solid superacids UDCaT [4]. However, these catalysts bear some disadvantages. The liquid acid catalysts may cause equipment corrosion and environmental pollution, and the solid acids usually deactivate rapidly due to coke formation at high reaction temperature. Recently, functionalized ionic liquids, known as environmentally benign catalysts, have been investigated extensively [5–8]. In our laboratory, we have studied the alkylation of m-cresol with TBA using SO_3H-functionalized ionic liquids as catalysts, and they have exhibited several characteristic advantages over conventional catalysts [9]. The ionic liquids can be recycled after the reaction. No significant deterioration of their catalytic performance, including their activity and selectivity, was observed. When compared with those solid acid catalysts, the tert-butylation of m-cresol over the ionic liquid catalysts can be conducted at lower reaction temperature. The reaction results showed that the alkylation of m-cresol with tert-butanol in ionic liquids produced mixed products, including the isomers of tert-butylated phenols in terms of the type of alkyls and the position of alkyl substitute: mono C-alkylated products, dialkylated products and tert-butyl-m-cresol ether (TBMCE). With increasing reaction time the selectivity to 2-TBC increased rapidly and reached the highest equilibrium level, while a significant decrease of the selectivity to TBMCE and finally disappearance of TBMCE in the products were observed.

The goal of this work was to investigate this reaction mechanism involving the fundamental nature of the ionic liquid with computational chemistry in combination with the experimental study. The frontier orbital theory based on the quantum chemical calculations has been applied to investigate the key steps of the reaction pathway of the alkylation of m-cresol with TBA in the acidic catalyst system at a molecular and atomic level, especially those critical factors that determine the selectivities.

2. Experimental

2.1. Preparation of ionic liquids

The SO_3H-functionalized ionic liquid (cation = $(C_2H_5)_3$–N–$(CH_2)_4$–SO_3H; anion = HSO_4) was synthesized according to the

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literature [5–7]. Triethylamine and 1,4-butanesultone were mixed by stirring for 12–24 h at 313–353 K. After the mixture solidified, the solid (zwitterion) was washed three times with ethyl ether and then dried under vacuum (393 K, 0.01 Torr). A stoichiometric amount of sulphuric acid was added to the zwitterions precursor. The mixture was stirred at 353 K for 8 h to form the ionic liquid. The product was washed repeatedly with cyclohexane and ethyl ether to remove residues, and dried under vacuum (393 K, 0.01 Torr); the ionic liquid (IL) is a viscous liquid at room temperature.

2.2. Catalyst testing

The tert-butylation of m-cresol with TBA was carried out in a glass reactor at 343 K. The typical loading amounts of reactants, catalyst and solvent were m-cresol 6.0 mmol, TBA 6.0 mmol, ionic liquid 1.0 mmol, cyclohexane 12 ml (m-cresol:TBA:IL = 6:6:1), respectively. The mixture was stirred at the reaction temperature for 1 h. Identification of the products was conducted on a HP6890/5973 GC/MS with a HP-5MS column; quantitative analysis was carried out on a 7890 GC (Shanghai Tianmei Co.) equipped with a SE-30 column (30 m × 0.25 mm).

3. Computational methods

3.1. Molecular cluster selections

Selecting a finite structure that not only represents the real state perfectly but also saves computational cost is very important [10–12]. For the reaction studied here, the key step might be the electrophilic substitution reaction of tert-butyl ion (termed as $[t\text{-}C_4H_9]^+$) with the H^+ on the aromatic ring or the hydroxyl group of m-cresol. The reaction could produce many kinds of products theoretically, but our experiments showed that the main product was 2-TBC, followed by 4-TBC. TBMCE was a special product which was first formed in a significant amount and then disappeared gradually. The selectivity of the alkylation is mainly dependent on the natures of the active sites of m-cresol. Considering the computational economy as well as essential structural and chemical information of the system studied in this work, our calculation was focused on the interaction between $[t\text{-}C_4H_9]^+$ and m-cresol, assuming that the $[t\text{-}C_4H_9]^+$ attacked the O1 atom, C2 atom and C4 atom of m-cresol (see Fig. 1) to form three intermediates (intermediates A–C) and then the final products (TBMCE, 2-TBC and 4-TBC), respectively.

In this reaction, it is believed the IL plays an important role both in the generation of the $[t\text{-}C_4H_9]^+$ through the elimination of the hydroxyl group from the TBA and in the formation of the final products by removal of the H^+ from the Intermediates. So the catalytic effect of the ionic liquid is also studied in this computational work. First the structures of the cation and the anion of the IL were optimized and analyzed, and then the possible interacting structures between the IL and the TBA or the intermediates were constructed, optimized and analyzed.

3.2. Computational method

The Møller–Plesset perturbation theory (MP2) at the 3-21G level was selected for the geometry optimization, the frequency calculation and the atomic charge analysis of the reactants, the intermediates and the final products. The geometries were calculated with a complete structural optimization. And then, the optimized structures were used for the energy calculation and the frontier orbital analysis at the MP2/6-311++G** level; the zero-point-vibration-energy (ZPE) corrections were done on the base of the MP2/3-21g frequency results. All these calculations were performed using the Gaussian 03 program supplied by Gaussian, Inc [13].

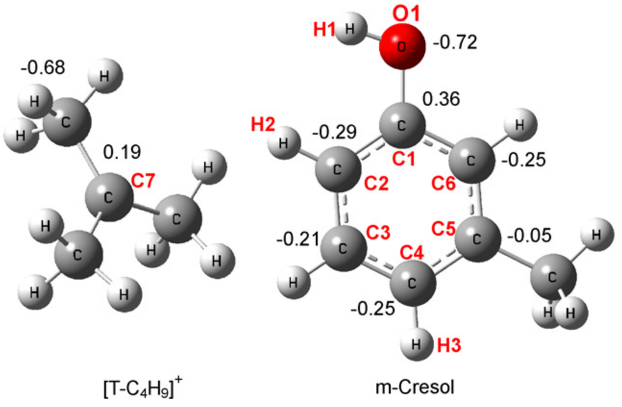


Fig. 1. Optimized geometries and the atomic charges of the $[t\text{-}C_4H_9]^+$ and m-cresol.

The binding energy discharged by the interaction between the m-cresol and the $[t\text{-}C_4H_9]^+$ were calculated according to the following equation [14]:

$$\Delta E = E_{A-B} - (E_A + E_B) \tag{1}$$

where ΔE is the binding energy, E_A and E_B are the individual energies of the m-cresol and the $[t\text{-}C_4H_9]^+$ before bonding, respectively, and E_{A-B} is the energy of the corresponding intermediate product.

4. Results and discussion

4.1. Experimental result

Fig. 2 shows the results of the selectivities as a function of the conversion. When the conversion was near zero, all the three products, 2-TBC, 4-TBC and TBMCE, were detected. With increase in the conversion of m-cresol, the selectivity to 2-TBC increased rapidly and the selectivity to 4-TBC rose slightly, while the selectivity to TBMCE dropped rapidly and eventually disappeared. Therefore, it was believed that 2-TBC, 4-TBC and TBMCE products were the primary products, while 2,6-DTBC was a secondary product. The product distribution of this electrophilic substitution reaction is mainly related to the active sites of m-cresol which have their characteristics in terms of the Coulomb force, the frontier

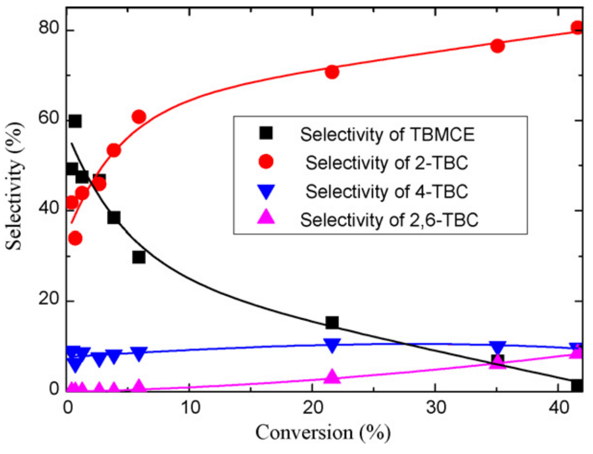


Fig. 2. Product distribution at different conversions. Reaction conditions: m-cresol (20 mmol):TBA:IL3 (6:6:1) molar ratio; 343 K; cyclohexane: 12 ml.

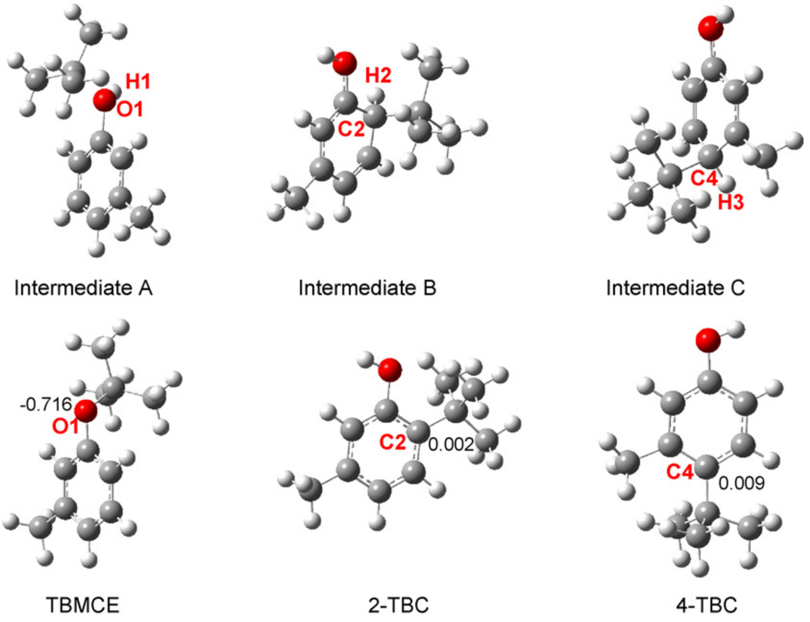


Fig. 3. Optimized geometries of the intermediates and the final products.

orbital distribution and the stereo-hindrance effect. These aspects will be discussed thoroughly according to the computational results.

4.2. The Coulomb force discussion

The optimized molecular geometries of $[t\text{-}C_4H_9]^+$ and m-cresol are shown in Fig. 1, and the optimized structures of the intermediates (A–C) and final products (TBMCE, 2-TBC and 4-TBC) are shown in Fig. 3. $[t\text{-}C_4H_9]^+$ has an approbatory plane structure, in which the central carbon atom takes on positive charge while the other three carbon atoms show negative charges. Therefore, the central carbon (C7) of $[t\text{-}C_4H_9]^+$ is the active site in the electrophilic substitution. M-cresol shows an aromatic structure, in which the atomic net charges of O1, C2, C3 and C4 sites are −0.72, −0.29, −0.21 and −0.25, respectively. The O1 site shows a high negative charge, so it can be postulated that the $[t\text{-}C_4H_9]^+$ is more prone to interacting with the O1 atom via an electrophilic effect. This would result in a fast formation of the intermediate A, and then the product TBMCE, which is in agreement with the experimental observation. The charges of the carbon atom in the aromatic ring are not identical. Among C2, C3 and C4, C2 takes on the highest amount of negative charge, followed by C4 and C3. This means that among those three active sites, C2 has the highest superiority in Coulomb attraction.

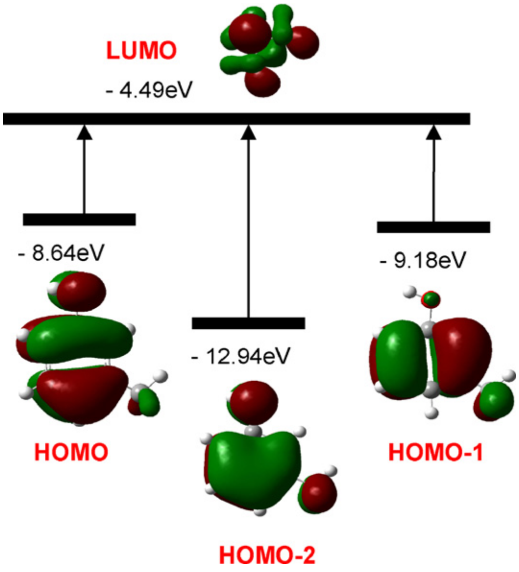


Fig. 4. LUMO of the $[t\text{-}C_4H_9]^+$ and frontal occupied molecular orbitals of m-cresol.

4.3. The orbital distribution discussion

Besides the electrostatic interactions, the effect of orbital overlap may also play a role in the reaction between m-cresol (an electron donor) and $[t\text{-}C_4H_9]^+$ (an electron acceptor) according to the frontier molecular orbital theory. The typical phase of LUMO of $[t\text{-}C_4H_9]^+$ primarily embodies an unoccupied P_i orbital of the central carbon atom, as shown in Fig. 4. The HOMO, the orbital next to the HOMO (termed as HOMO-1) and the orbital next to the HOMO-1 (termed as HOMO-2) of m-cresol (shown in Fig. 4) are mostly composed of multitudinous P_i orbital of C atoms and little P_i orbital of O1 atom. It is believed that the orbital overlap effect between the symmetry-allowed occupied and unoccupied orbitals mainly depends on two sides: one is the orbital coefficient, and the other is the orbital energy gap. The orbital coefficient influences the magnitude of electron density in each localized site, and the active site of the m-cresol with a larger orbital coefficient can donote more electrons to the LUMO of the $[t\text{-}C_4H_9]^+$, forming a stronger conjugation. On the other hand, the symmetry-allowed orbitals might overlap with each other to a considerable extent only if they are of comparable energy. So using the super-delocalizability parameter (S_r) [15,16] to evaluate the orbital overlap effect is preferred as it considers both the orbital coefficient and the orbital energy. S_r is a reactivity index of aromatic hydrocarbons (AH), proposed by Fukui as the following formula:

$$S_r = 2\sum_{j=1}^{m}\left(\frac{c_{jr}^2}{e_j}\right)$$

Here the term S_r is the superdelocalizability at position r, e_j is the bonding energy coefficient in the jth molecular orbital (eigenvalue), c is the molecular orbital coefficient at position r in the HOMO

Table 1
The total energies of the intermediates and products (A.U.).

	Intermediate A	Intermediate B	Intermediate C	TBMCE	2-TBC	4-TBC
Energy	−502.7255049	−502.7314033	−502.7297011	−502.4040175	−502.4181119	−502.4111086

and *m* is the index of the HOMO. This descriptor can be used to predict the relative reactivity of the atoms in aromatic hydrocarbons. For the alkylation in this study, a site with a relatively larger S_r will result in a stronger orbital overlap, and then form a more stable covalent bond between the $[t\text{-}C_4H_9]^+$ and m-cresol.

The S_r values of m-cresol on the O1 and C atoms are shown in Fig. 5. Among the C2, C4 and O1 sites, the S_r of C2 is the largest, followed by C4 and O1. According to S_r, it can be deduced that a stable covalent bond between the $[t\text{-}C_4H_9]^+$ and m-cresol can be formed in C2 site, followed by that in C4, and the new bond formed in the O1 site cannot be as strong as that in C2 or C4 site. This conclusion is in agreement with the stabilities of the intermediate products and the final products. Through comparison of the total energies of the optimized structures (see Table 1), it was found that the total energies of the intermediate B and the intermediate C were 15.5 kJ/mol and 11.0 kJ/mol lower than that of the intermediate A, respectively, and the total energy of 2-TBC and 4-TBC were 37.0 kJ/mol and 18.6 kJ/mol lower than that of TBMCE, respectively. This means the stability orders among these species were intermediate B > intermediate C > intermediate A and 2-TBC > 4-TBC > TBMCE.The stereo-hindrance effect discussionAnother factor that might affect the product selectivity is the stereo-hindrance effect on the different active sites of m-cresol. The O1 site stands out of the aromatic ring and is not hindered by any other functional groups, while the C2 and C4 sites are influenced by the hydroxyl and the methyl, respectively. So it can be deduced that the stereo-hindrance effects on these sites are: C4 site > C2 site > O1 site.

4.5. *Mechanism discussion*

From the analysis above, it is clear that each active site on m-cresol has its particularity in the fundamental natures of the Coulomb force, the orbital distribution and the stereo-hindrance effect. Considering the higher negative charge and the weaker stereo-hindrance effect on the O1 site, it is postulated that the $[t\text{-}C_4H_9]^+$ is more prone to interacting with the O1 atom in m-cresol via an electrophilic effect, forming intermediate A and then the product TBMCE quickly. This is in agreement with the experimental result that a large amount of TBMCE was formed at the early stage of the reaction. However, intermediate A is not very stable due to the weak orbital overlap effect in O1 site in spite of its easy formation. Moreover, the O1 atom in TBMCE still takes a high negative charge (−0.716) and is prone to being attracted by a positive group, such as H^+. This would result in a reversible reaction between intermediate A and TBMCE. The geometry-optimization results show that when a H^+ approaches the O1 of TBMCE, the distance between the O1 and the butyl-C of the $[t\text{-}C_4H_9]^+$ increases from 1.511 Å to 1.614 Å. This means that the $[t\text{-}C_4H_9]^+$ tends to leave and may rearrange to form intermediate B and intermediate C. But the reverse reactions of the intermediates to produce 2-TBC and 4-TBC are very difficult as the atomic net charges of the C2 and C4 atoms are too low to interact with H^+ ions.

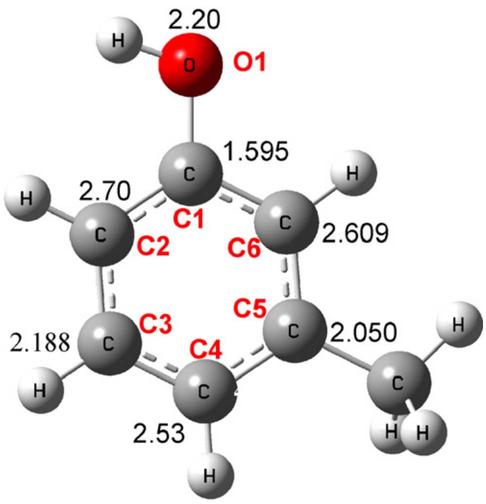
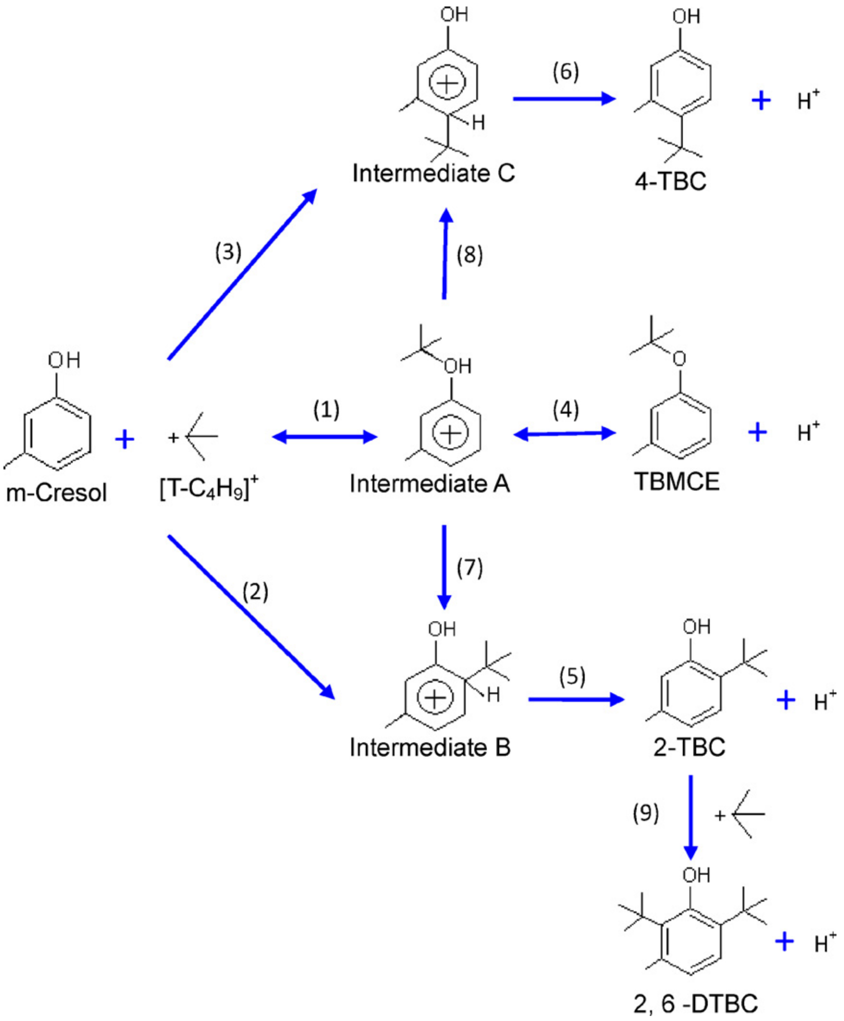


Fig. 5. The S_r values of m-cresol on the O1 and C atoms.

According to the experimental and computational results above, a mechanism for the selective alkylation of m-cresol with tert-butanol can be proposed, as shown in Scheme 1. The electrophilic interaction of the $[t\text{-}C_4H_9]^+$ with the hydroxyl group or the C2 and C4 atoms of m-cresol results in the formation of the products TBMCE, 2-TBC and 4-TBC through intermediates A, B and C, respectively. However, due to the higher electron density and the less stereo-hindrance effect on the O1 atom, the formations of intermediate A and the final product TBMCE are easy and fast, but they are not stable. There is a reversible reaction between intermediate A and TBMCE, so the TBMCE can reverse to intermediate A and that can rearrange to intermediate B or C with B preferred due to its good stability and short distance between O1 and C2 sites. With increasing reaction time intermediates B and C are consumed gradually by further reactions, and they will mainly be complemented by the rearrangement of intermediate A formed by the recombination of TBMCE and H^+. This reaction chain will speed up the reverse reaction from TBMCE to intermediate A. As a result, the kinetically preferred O-alkylated product (TBMCE) disappears gradually. Among those products, 2-TBC, 4-TBC and TBMCE products are all primary products, and 2,6-DTBC product is a second product which is derived from 2-TBC. Between the two C-alkylated products, 2-TBC is the thermodynamically preferred product at the end. Because of the stronger orbital conjugation and the Coulombic interaction and the weaker stereo-hindrance effect of the $[t\text{-}C_4H_9]^+$ with m-cresol on the C2 site than on the C4 site.

4.6. *The catalytic function of the ionic liquid*

For this reaction, besides the key steps of the $[t\text{-}C_4H_9]^+$ electrophilically adsorbing on the O1, C2 and C4 sites of m-cresol and the formation the intermediates, other steps, such as the departure of the hydroxyl group ($-OH^-$) from TBA to form the $[t\text{-}C_4H_9]^+$, or the removal of H^+ from the intermediates and then the generation of the final products, are also critical. The IL plays an important role in these important steps. The optimized geometries and the atomic charges of the cation and the anion of IL are shown in Fig. 6. The O atoms take on negative charges and the S and H (H4, H5) bear positive charges. In order to break the C7–O5 bond (see Fig. 7) in TBA, it is helpful to have an electrophilic group to bond with the O5 atom so that it can attract the electron and weaken the C7–O5 bond. We have tried to conjugate H4 (in cation), H5 and S1 (in anion) with O5 (in TBA) in the initial-structure hypothesizers, but the optimized structures shows that only the H4–O5



Scheme 1. Proposed reaction network for alkylation of m-cresol.

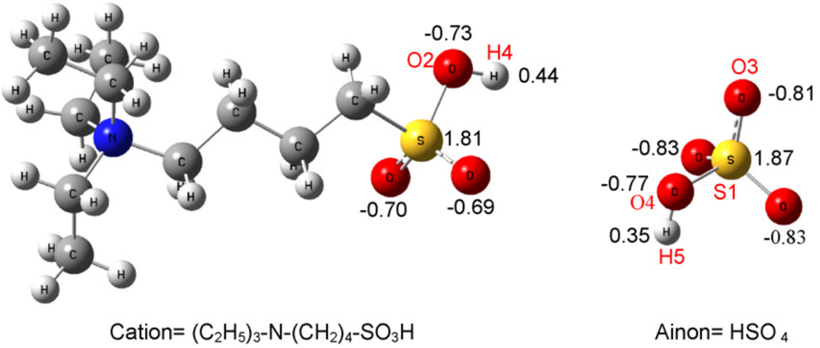


Fig. 6. Optimized geometries and the atomic charges of cation and anion of IL.

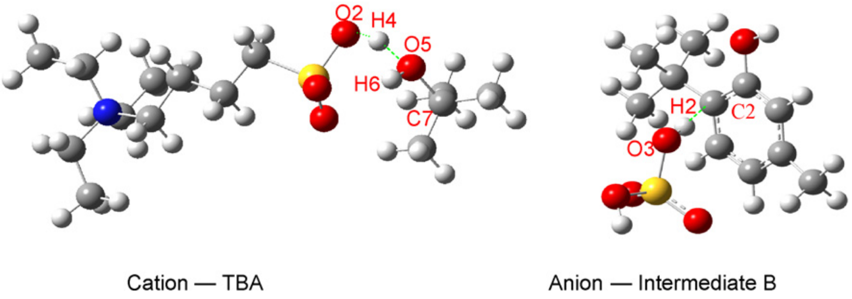


Fig. 7. Optimized geometry of cation with TBA and anion with intermediate B.

conjugation structure (see Fig. 7 "cation–TBA") could exist by forming a strong hydrogen bond between H4 and O5, and this hydrogen bond weakens the C7–O5 bond significantly since the length of the C7–O5 bond increases from 1.451 Å to 1.514 Å after cation–TBA interaction. It is possible that both the C7–O5 bond and the O2–H4 bond break and a H_2O molecule is formed in the further reaction of this step. The initial structures of the O2 in TBA conjugating with H5 or S1 in anion after optimization take on a hydrogen bond between the H5 in TBA and the O atom in anion (except for O4), and this hydrogen bond has little contribution to the C7–O2 bond breaking. Removing of H^+ from the intermediates is possible with an O atom in cation or anion to attract the H^+. For example, when the O3 in anion approaches the H2 in intermediate B, the optimized structure (see Fig. 7 "anion–intermediate B") shows that the H2 atom nearly departs from the C2 atom in intermediate B since the distance of H2–C2 in "anion–intermediate B" structure is 2.107 Å. And the anion in combination with the H^+ will form a H_2SO_4 molecule. The new formed H_2SO_4 might give a H^+ to the cation who has lost the H^+. This H^+ transfer is possible since the IL is generated by the zwitterions precursor acquiring the H^+ from the sulphuric acid. By then a catalysis cycle is completed.

5. Conclusions

In this study, the quantum chemical calculation in combination with experimental studies were used to investigate the fundamental natures of the alkylation of m-cresol with tert-butanol. Among those products, 2-TBC, 4-TBC and TBMCE products are all primary products, while 2,6-DTBC is a secondary product. The selectivities of the products mainly depend on the fundamental natures of the reaction active sites of m-cresol, such as the natures of the orbital overlap, the Coulomb and the steric effect presented in the interaction between the $[t\text{-}C_4H_9]^+$ and the O1, C2 and C4 sites of m-cresol. The intermediate A and TBMCE are dynamically favored but not thermodynamically stable, while the C-alkylated products, especially 2-TBC, are the thermodynamically preferred products. The IL plays an important catalytic role in generating the $[t\text{-}C_4H_9]^+$ from TBA and the final products from the intermediates.

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