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Journal of Molecular Catalysis A: Chemical



journal homepage: www.elsevier.com/locate/molcata

Experimental and theoretical investigation of the oxidative carbonylation of toluene to toluic acid catalyzed by palladium(II) in the presence of vanadium and molecular oxygen

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ARTICLE INFO

Article history: Received 22 September 2011 Received in revised form 27 April 2012 Accepted 5 May 2012 Available online 11 May 2012

Keywords: Toluene Toluic acid Oxidative carbonylation Palladium Vanadium

ABSTRACT

The mechanism and kinetics of the liquid-phase, oxidative carbonylation of toluene to toluic acid over Pd(II) in the presence of trifluoroacetic acid (TFAH), trifluoroacetic anhydride (TFAA), and molecular oxygen were investigated through a combination of experimental and theoretical approaches. The experimental results are consistent with the previously proposed mechanism for the oxidative carbonylation of arenes. The reaction is initiated by coordination of toluene to the Pd(II) complex and activation of a C—H bond in the benzene ring. This initial step becomes rate limiting when a sufficiently high (NH₄VO₃)/Pd ratio is used for the reoxidation of Pd(0) to Pd(II). Both processes are found to be dependent on the electron withdrawing and donating capability of the anionic ligands. Overall catalyst activity peaks for ligands of intermediate basicity, and diminishes for both more and less basic ligands. Theoretical analysis of the coordination of toluene but have the opposite effect on the activation of the C—H bond. The tradeoff in these two effects leads to a maximum in the apparent rate coefficient with pK_a of the conjugate acid of the anionic ligands. The absence of significant product stereoselectivity is due to a lack of steric hindrance in the binding of toluene to the Pd(II) complex.

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1. Introduction

Palladium acetate has been shown to be an active catalyst for a number of reactions involving arene C—H bond activation [1–16]. We note, in particular, that the oxidative carbonylation of arenes to the corresponding aryl carboxylic acid can be catalyzed by Pd(II) in the presence of acetic acid and CO [1–10]. Early studies of this reaction revealed that in the course of this reaction, Pd(II) is reduced to Pd(0) and hence, in the absence of an oxidizing agent, the yield of products is stoichiometric in the initial concentration of Pd(II) [1]. The oxidative carbonylation of arenes can be made catalytic by adding an oxidant to convert Pd(0) to Pd(II) [2]. If BuOOH or K₂S₂O₈ is used as an oxidant, this component is consumed in the course of the reaction [2,3,8]. Molecular oxygen can also be used as the oxidant provided a co-catalysts include Cu(acetate)₂ [4], MnO₂ [6] and NH₄VO₃ [10].

A reaction mechanism has been proposed to rationalize the oxidative carbonylation of toluene to toluic acid [5]. It involves coordination of toluene to the Pd(II) center, activation of a C-H bond in the coordinated toluene at the para, meta, or ortho position of the benzene ring, electrophilic activation of the arene C-H bond, and subsequent insertion of CO into the Pd–C bond of the Pd-toluyl species formed in the preceding step. The resulting acyl species is envisioned to undergo reductive elimination to form a mixed anhydride of the desired aryl acid and the acid that was used in the reaction system to provide anionic ligands (e.g., trifluoroacetic acid). Pd(0) formed in this latter process is then re-oxidized to close the catalytic cycle. The observation that formation of toluic acid is faster when trifluoroacetic acid is used in place of acetic acid suggests that the activation of the arene C–H bond occurs via an electrophilic mechanism [9]. While the proposed mechanism is plausible, definitive evidence for electrostatic activation of the C-H bond of toluene is very limited as are the effects of changing the electrophilicity of the anionic ligand. Recent theoretical work by Davies et al. on model C-H bond activation systems indicates that the nature of such activation is specific to the metal and ligand environment, which has implications regarding transition state stabilization such as through

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^{1381-1169/\$ -} see front matter © 2012 Elsevier B.V. All rights reserved. http://dx.doi.org/10.1016/j.molcata.2012.05.006

the presence or absence of agostic H-metal interactions [12,13]. Understanding the nature of the ligand and metal interactions in the aforementioned Pd-catalyzed toluene activation is therefore important to developing improved arene oxidative carbonylation catalysts.

In recent studies of the oxidative carbonylation of toluene catalyzed by Rh(III) complexes involving acetate ligands, it was demonstrated that the activity of the catalyst can be tuned through a maximum by substitution of the H atoms of the methyl group in the acetate ligands by Cl or F, or combinations of the elements [17–19]. Experimental studies of the reaction have demonstrated that under conditions where most of the Rh is present as Rh(III), the rate-limiting step is the electrophilic activation of the C-H bond on the benzene ring of coordinated toluene. Theoretical analysis of the process shows that coordination of toluene is a reversible process that is sensitive to the composition of the acetate ligand, as is the activation of the C-H of the benzene ring. In the present study we show that the oxidative carbonylation of toluene to toluic acid catalyzed by Pd(II) also proceeds via electrophilic activation and that the catalyst activity is affected by the composition of the acetate ligand. Theoretical analysis of the coordination of toluene to Pd(II) and the activation of the benzene C-H bond explains why Pd(II) complexes are more active than Rh(III) complexes but less stereoselective toward the formation of p-toluic acid.

2. Experimental

Reactions were conducted in a stirred, 50 mL Parr autoclave made of Hastelloy C. Between experiments, the reactor was washed thoroughly with water and acetone and then dried in a vacuum oven overnight to avoid contamination. The reaction temperature was monitored using a thermocouple located inside a Hastelloy C thermowell. During a typical reaction, 3.46 g of anhydrous toluene (99.8%, Aldrich), 1.48 g of CF₃COOH (99%, Aldrich), 0.8 g of $(CF_3CO)_2O$ (\geq 99%, Aldrich), 0.0016 g of Pd(TFA)₂ (Aldrich) and 0.0604 g of NH₄VO₃ (99+%, Aldrich) were placed into the autoclave, which was then sealed and purged four times with nitrogen or helium. For the kinetic isotope experiment, a similar procedure was performed as described above except that toluene was substituted with 3.76 g d₈-toluene (99.6 atom% D, Aldrich). After purging, the reactor was pressurized at 293 K with 0.345 MPa O₂ (99.993%, Praxair) and 0.345 MPa CO (99.5%, Praxair). The reactor was then heated to 353 K in approximately 10 min and then held at this temperature for 4h. Upon the completion of the reaction, the reactor was quenched with ice water to 308 K and vented.

The contents of the reactor were emptied into a vial and weighed, after which approximately 12 g of deionized H_2O was added to the organic phase in order to extract the trifluoroacetic acid from it. The vial was inverted 20 times and the aqueous and organic phases were allowed to separate completely. After inverting the vial containing the mixture of aqueous and organic phases 20 times, the two phases were allowed to separate and the aqueous phase was discarded. Solids produced by the reaction were separated from the organic phase by centrifugation and dried overnight in a vacuum oven at 313 K.

The concentration of toluic acid in the organic phase was determined by gas chromatography using an Agilent Technologies 6890N gas chromatograph equipped with an HP-1 capillary column coated with crosslinked methyl siloxane and an FID detector. After washing with H₂O and drying, the product solids were dissolved in toluene and similarly analyzed by gas chromatography. The solid lines shown in all figures represent the average over all replicas.

3. Theoretical methods

Molecular structures, energies, vibrational modes, and rotational constants were calculated with Density Functional Theory [20] in Q-Chem [21]. Geometry optimization of minimum energy structures and vibrational analysis were performed with the B3LYP density functional [22–25] and the 6-31G* basis set. Electronic structure energies of the optimized molecular structures were also computed with the B3LYP density functional, and then refined at the 6-311++G** level. For all calculations, the core basis functions for palladium were replaced with the LANL2DZ effective-core potential [26]. Geometry optimization and single point energy calculations performed with larger basis sets did not significantly change the structure shapes or energies, indicating that the chosen basis sets were sufficient. Estimates of transition state structures were obtained with the Growing String Method [27] and refined within the normal geometry optimization functionality of Q-Chem.

All calculations were performed in the gas phase. No meaningful model of the solvent mixture of toluene and acetic acids was found to be practical, so solvent effects were ignored. Thermochemical calculations were performed at the experimental reaction temperature of 353 K, and invoked the rigid-rotor—harmonic oscillator approximation. The energetics of toluene binding were basis set superposition-error corrected using the counterpoise method. Equilibrium constants were calculated at a standard state of 1 bar and adjusted to molar concentration units according to Eq. (1):

$$K = \left(\frac{RTc^{o}}{P^{o}}\right)^{-\Delta \nu} \exp\left(\frac{-\Delta G^{o}}{RT}\right)$$
(1)

where *K* is the equilibrium constant, *R* is the gas constant, *T* is the absolute temperature, c^{0} is the standard-state concentration in the liquid phase (1 mol/L), P^{0} is the standard-state pressure (1 bar), $\Delta \nu$ is the difference between the sums of the stoichiometric coefficients of the products and reactants, and ΔG^{0} is the Gibbs free energy of reaction at the reaction temperature. Rate constants were computed from transition state theory, Eq. (2):

$$k = \frac{k_B T}{h} \exp\left(\frac{\Delta S^{\ddagger}}{R}\right) \exp\left(\frac{-\Delta H^{\ddagger}}{RT}\right)$$
(2)

4. Results and discussion

A proposed mechanism for the oxidative carbonylation of toluene to toluic acid is shown in Scheme 1. This scheme is very similar to that suggested in earlier work by [4,5,7,10]. The main catalytic cycle is initiated by the electrophilic reaction of toluene with Pd(TFA)₂ to form a methyl aryl complex, Pd(TFA)(C₆H₄CH₃) and TFAH, where TFA is trifluoroacetate. A CO molecule from the reaction mixture then binds to the complex and undergoes a migratory insertion to form $Pd(TFA)_2(COC_6H_4CH_3)$. This species then reacts via reductive elimination to produce Pd(0) and a mixed anhydride. The mixed anhydride then either hydrolyzes to give TFAH and toluic acid, or exchanges a proton with TFAH to produce trifluoroacetic anhydride and the toluic acid. Only the former version is shown in Scheme 1. The reduced Pd catalyst is re-oxidized with NH_4VO_3/O_2 [28] via a sequence of steps, which are taken to be identical to those established for the oxidation of Rh(I) to Rh(III) during the oxidative carbonylation of toluene catalyzed by Rh(III) acetate complexes [17 - 19].

Scheme 1 suggests that the reaction of $Pd(TFA)_2$ with toluene will become the rate-limiting step provided that the rate of reoxidation of Pd(0) to Pd(II) and the rates of carbonylation and mixed anhydride formation are rapid and, hence, kinetically insignificant. To test whether the rate of Pd(0) oxidation could be made to satisfy this criterion, experiments were carried out in which the amount of NH_4VO_3 was varied while keeping the quantity of Pd present in



Scheme 1. Proposed mechanism for Pd-catalyzed toluene oxidative carbonylation.

the reactor constant at 10 μ mol. Fig. 1 shows that in the absence of NH₄VO₃, ~10 turnovers of Pd were observed. This result suggests that O₂ alone can carry out a slow oxidation of Pd(0) but at a rate insufficient to maintain the catalytic activity of Pd. This conclusion is further supported by observation of Pd black deposition on the walls of the reactor under these conditions. The number of Pd turnovers increased linearly with the amount of NH₄VO₃ charged to the reactor up to the level of 0.516 mmol of vanadium,



Fig. 1. Palladium turnover number vs μ mol V. Reaction conditions: 37.5 mmol toluene (3.46 g); 13.0 mmol CF₃COOH (1.48 g); 3.8 mmol (CF₃CO)₂O (0.80 g); 10 μ mol Pd(TFA)₂ (0.0032 g); P_{CO} = 0.345 MPa; P_{O_7} = 0.345 MPa; T = 353 K; t = 4 h.

at which point ~1000 Pd turnovers were achieved in 4 h. No additional toluic acid was formed when the charge of NH_4VO_3 was increased above 0.516 mmol, as shown in Fig. 1. The linear relationship between NH_4VO_3 concentration and Pd turnovers shows that Pd(II) is reduced during the reaction cycle, and that a sufficient V/Pd ratio is necessary to prevent re-oxidation from becoming the rate-limiting step.

Strong evidence that the oxidative carbonylation of arenes by Pd(II) proceeds via an electrophilic mechanism is the sensitivity of the apparent rate constant for this reaction on the composition of the substituent present on the benzene ring. Fig. 2 shows a Hammett plot for the oxidative carbonylation of arenes by Pd(II) complexes in the presence of NH₄VO₃/O₂. The slope of this line ($\rho = -1.53$) indicates that the reaction proceeds through a mechanism that slightly favors an electron-donating substituent [30]. This result suggests that the oxidative carbonylation of the arene to the Pd(II) complex followed by activation of the C–H bond.

Further support for this interpretation comes from an examination of the effect of ligand composition on the activity of Pd(II) for the oxidative carbonylation of toluene. Fig. 3 illustrates the effect of the pK_a of the acid, from which the anionic ligands for Pd are derived, on the number of turnovers obtained after 4 h of reaction. Values of the pK_a were taken from reference [31]. Only acids with a pK_a near zero are effective in producing toluic acid, and optimal activity is observed for CF₃COOH. The order of activity observed in Fig. 3 can be attributed to two opposing factors—the electron withdrawing nature of the ligands, which makes the metal center more electropositive and thus more capable of toluene coordination, and the ability of the ligand to abstract a proton. While more electron withdrawing ligands facilitate the coordination of toluene to the metal, they are less able to abstract a proton from the coordinated



Fig.2. Hammett plot for Pd-catalyzed arene oxidative carbonylation in the presence of NH₄VO₃/O₂. Values of σ are taken from reference [29] and correspond to *para* substitution.

toluene to form the aryl–palladium complex. The optimal activity is observed for the ligand that best balances these opposing factors, which in the case of Pd is CF₃COOH. Fig. 4 shows the effects of ligand composition on the distribution of *para*, *meta* and *ortho* toluic acid products. For all but one ligand (CClH₂COO⁻), the *ortho* isomer is more abundant than the *para* and *meta* isomers and the *meta* isomer is always the least abundant.

Under conditions of high V/Pd ratio in the reaction mixture, Pd(II) becomes the most abundant form of Pd and the rate of toluic acid formation is then limited by the coordination and activation of toluene. This step may be broken into two substeps, as depicted in Fig. 5. The first is the coordination of toluene to Pd(TFA)₂, characterized by the free energy change ΔG^{0}_{coord} whereas the second step is the activation of a C–H bond on coordinated toluene, characterized by the free energy barrier, ΔG^{1}_{act} . ΔG^{0}_{coord} can be used to compute the equilibrium constant for toluene binding, K_{coord} , (Eq. (1)), while ΔG^{1}_{act} can be used to calculate k_{act} (Eq. (2)). In the limit



Fig. 3. Pd catalyzed oxidative carbonylation of toluene to toluic acid vs pKa of designated acid. Reaction conditions: 37.5 mmol toluene (3.46 g); 13.0 mmol designated acid; 3.8 mmol corresponding anhydride; 5 μ mol Pd(TFA)₂ (0.0016 g), 0.516 mmol NH₄VO₃ (0.0604 g); P_{C0} = 0.345 MPa; P_{0_2} = 0.345 MPa; T = 353 K; t = 4 h.



Fig. 4. Normalized distribution of *para*, *meta*, and *ortho* toluic acid products formed vs pK_a of the ligand conjugate acids. Data reported is based on a standard 4 h batch reaction.

that most of the Pd in solution is present as $Pd(TFA)_2$, the overall rate of toluic acid production, k_{app} , is described by Eq. (3).

$$k_{\rm app} = K_{\rm coord} k_{\rm act} \tag{3}$$

Eq. (3) suggests that k_{app} can be described by a single parameter, the total change in free energy, which is defined as $\Delta G_{app} = \Delta G_{coord}^{o} + \Delta G_{act}^{\dagger}$. This expression indicates that any changes in catalyst composition would be expected to affect the rate of reaction through the strength of toluene coordination and/or the rate of C–H activation.

To further understand the effect of ligand composition on the coordination and activation of toluene by Pd(II) complexes, values of ΔG_{app} were determined theoretically. Fig. 6 shows the calculated values of ΔG_{app} , assuming that toluene coordination occurs in the *para*, *meta*, and *ortho* positions. The values of ΔG_{app} for all three coordination positions decrease as the anionic ligand is changed from the comparatively strongly basic CH₃COO⁻ anions to the relatively less basic CF₃CF₂COO⁻ anions, and rise again for the very weakly basic CH₃SO₃⁻ anions. Fig. 7 shows the computed values of k_{app} determined from Eqs. (1) to (3) for the oxidative carbonylation of toluene at the para, meta, and ortho positions. The numerical values are also presented in Table 1. For short reactions times, the logarithm of k_{app} is proportional to the cumulative turnover number (TON), and thus the activity of a particular catalyst can be evaluated solely through k_{app} . Pd(II) ligated with CF₃CF₂COO⁻ anions is predicted to be the complex with the highest activity. The activity of the Pd complexes is predicted to decrease for anions that are either more or less basic than CF₃CF₂COO⁻. This pattern is roughly the same as that seen experimentally, but with the peak predicted activity occurring for a slightly more basic ligand, CF₃COO⁻. These theoretical predictions do not match exactly with experiment due to the sensitivity of k_{app} to the exact value of ΔG_{app} , which contains an inherent error from the inexact nature of DFT calculations.

Further insight regarding toluene coordination and C–H activaction can be obtained by substituting toluene with d_8 -toluene and comparing the relative toluic acid formation rates from these two substrates. A $k_{\rm H}/k_{\rm D}$ value of 1.04 was observed experimentally, which can be rationalized by considering two opposing factors that arise during Pd coordination to toluene and C–H activation. A change in hybridization of C in the arene from sp² to sp³ caused by Pd coordination to C in the arene alters the out-of-plane force constants, which kinetically favors deuterium substitution ($k_{\rm H}/k_{\rm D}$ < 1);



Fig. 5. Reaction schematic for the rate-limiting step of toluene coordination and C—H bond activation at the Pd(CF₃COO)₂ catalyst. Para coordination of toluene is illustrated although both meta and ortho coordination also occur.

Table 1

Computed values of ΔG_{app} and k_{app} for coordination in the *para*, *meta* and *ortho* positions, and the cumulative value of $k_{app} = k_{app}^{para} + 2(k_{app}^{meta} + k_{app}^{ortho})$ to account for the symmetry of toluene.

Ligand	pK _a	ΔG_{app}^{o} (kcal/mol)			Individual k_{app} ((mol s) ⁻¹)			Total k _{app}
		Para	Meta	Ortho	Para	Meta	Ortho	
CH ₃ SO ₃ -	-2.0	29.95	31.32	30.02	2.02E-04	2.99E-05	1.83E-04	6.28E-04
CF ₃ CF ₂ COO ⁻	-0.25	18.48	20.97	20.84	1.64E+03	5.20E+01	6.18E+01	1.87E+03
CF ₃ COO ⁻	0.0	21.47	21.34	20.19	2.58E+01	3.09E+01	1.52E+02	3.92E+02
CCIF ₂ COO ⁻	0.35	19.92	21.81	20.20	2.22E+02	1.62E+01	1.51E+02	5.56E+02
CCl ₃ COO ⁻	0.63	23.42	23.69	24.18	1.74E+00	1.18E+00	6.05E-01	5.31E+00
CCl ₂ HCOO ⁻	1.35	23.03	25.13	24.08	2.96E+00	1.61E-01	6.96E-01	4.67E+00
CCIH ₂ COO ⁻	2.86	24.79	25.63	25.72	2.58E-01	8.08E-02	7.16E-02	5.63E-01
CH_3COO^-	4.76	27.00	28.32	28.25	1.21E-02	1.94E-03	2.12E-03	2.02E-02

however, hyperconjugative stabilization of the positive charge in the intermediate favors hydrogen $(k_H/k_D > 1)$ [32]. Indeed, in the case of electrophilic aromatic substitution mechanisms, secondary kinetic isotope effects both larger and smaller than unity have been observed, and these effects may even cancel [32]. This result provides additional evidence that Pd-catalyzed reaction proceeds through an electrophilic mechanism.

The results presented in Fig. 4 show that the formation of *para*and *ortho*-toluic acid is preferred over the formation of *meta*-toluic acid independent of ligand composition; however, the selectivity differences among the three steroisomers are not large. This pattern suggests that product stereoselectivity is driven primarily by the free energy for toluene coordination, $\Delta G_{\text{coord}}^{0}$ ($\Delta G_{\text{act}}^{1}$ values for the different isomers are relatively constant, thus any difference in ΔG_{app} is attributable to coordination), and not by effects of steric hinderance, as was observed for the case of toluene coordination with Rh(III) complexes [19], since the *para* and *ortho* carbons of toluene are more negatively charged than the *meta* carbon. The lack of steric hindrance is apparent in the computed values of ΔG^{o}_{coord} for coordination of toluene. When coordinated with Pd(II), toluene interacts through an η^{2} bond. Fig. 8 illustrates the computed values of ΔG^{o}_{coord} for coordination to four of the six possible η^{2} configurations. The η^{2} configurations involving the primary carbon of the phenyl ring were ignored. The values presented show only a small difference between the various coordination sites, indicating a lack of steric hindrance. While small differences in the values of ΔG^{o}_{coord} are observed for different forms of toluene coordination and different ligands, the accuracy of the calculations are insufficient to reproduce the selectivity patterns seen in Fig. 4.

It is useful to compare and contrast the findings of this study with those reported recently for the oxidative carbonylation of toluene by Rh(III) complexes containing ligands identical to those investigated here [19]. In that work, it was demonstrated that the oxidative carbonylation of toluene catalyzed by Rh(III) complexes also proceeds by way of an electrophilic mechanism, in



Fig. 6. Plot of calculated ΔG_{app} vs pK_a of the conjugate acid of the catalyst ligand for *para*, *meta*, and, *ortho* activation.



Fig. 7. Plot of calculated k_{app} vs pK_a of the conjugate acid of the catalyst ligand. The values plotted are for the cumulative rate of all 3 toluic acid isomers.



Fig. 8. Computed values of ΔG_{coord}^{o} for toluene binding in various η^{2} configurations, and model toluene structure to indicate positions of the different carbons.

which the rate limiting step involves toluene coordination and C–H activation. A similar volcano plot of overall activity vs pK_a was found; however, the highest activity in this case was for CClF₂COO– anions. Theoretical analysis of that system revealed a minimum in the computed ΔG_{app} vs pK_a for CClF₂COO– anions, with a value of 26.9 kcal/mol. The experimentally observed p/m ratios ranged between 1.75 and 3.75, with the higher values occurring for ligands with a conjugate acid pK_a near zero. The production of *o*-toluic acid was minimal.

Under analogous reaction conditions, the activity of the Pd(II) complexes reported here is significantly higher than those for the Rh(III) complexes reported earlier [18]. The peak in TON (1740) for Pd(II) occurs for a less basic ligand, CF₃COO⁻, and is more than three times that (560) for Rh(III) with the optimal ligand, CCIF₂COO⁻. The calculated values of ΔG_{app} determined for Pd(II) and Rh(III) complexes are consistent with both the higher activity of Pd(II) relative to Rh(III) and the shift in the basicity of the optimal ligand. For Pd(II), the lowest value of ΔG_{app} for *para* activation of toluene is 18.5 kcal/mol with CF₃CP₂COO⁻ ligands. This value is nearly 10 kcal/mol lower than that for the minimum value of ΔG_{app} (26.9 kcal/mol) found for Rh(III) with CCIF₂COO⁻ ligands, consistent with experiment. Finally, the predicted selectivity for the Pd catalysts is low, given the relatively similar values of ΔG_{app} for *para*, *meta*, and *ortho* activation.

This result is likely due to the lack of steric hindrance toward toluene binding in the present square planar Pd(II) complex. The analogous Rh(III) system is octahedral and has ligands positioned to interfere with the methyl group of toluene and drive selectivity toward the *para* position.

5. Conclusions

The results of this study indicate that Pd(II) in the presence of CO, O₂, TFAH, and NH₄VO₃ is effective at promoting the oxidative carbonylation of toluene to toluic acid.

The reaction mechanism proceeds via coordination of toluene to the Pd(II) complex followed by activation of one of the C–H bonds on the benzene ring. This step is followed by the migratory insertion of CO into the Pd–C bond of the toluyl species and subsequent reductive elimination of a mixed anhydride of toluic acid and trifluroacetic acid. The second of these two steps also results in the reduction of Pd(II) to Pd(0). The mixed anhydride then undergoes hydrolysis to produce toluic acid. The reoxidation of Pd(0) to Pd(II) occurs via a separate catalytic cycle, in which $[VO_2(TFA)]_2$ is the oxidant. The VO(TFA)₂ produced as a product of the oxidation process is then reoxidized by O₂ to reform $[VO_2(TFA)]_2$. For sufficiently high V/Pd ratios, most of the Pd is in the form of Pd(TFA)₂, and the rate of toluic acid formation becomes limited by the reversible coordination of toluene and the activation of a C-H bond on the benzene ring. The overall rate of toluic acid formation is very sensitive to the basicity of the anionic ligand and passes through an optimum as the pK_a of the conjugate acid of the anionic ligand is varied from -1 to 5. This trend is explained by a theoretical analysis of the effects of ligand composition on the equilibrium constant for toluene coordination and the rate coefficient for activation of a C-H bond on the benzene ring. Consistent with experimental observation, the predicted apparent first-order rate coefficient passes through a well-defined maximum vs conjugate acid pK_a 's. Only minor numerical differences are seen in $\Delta G_{\text{coord}}^{0}$ and $\Delta G_{\text{act}}^{\ddagger}$ for toluene coordinated in the para, meta, and ortho positions, in agreement with the experimentally observed lack of selectivity for any specific isomer of toluic acid. Finally, when compared against previous studies of the analogous Rh(III) system, the present computations predict a higher activity for Pd(II) complexes relative to Rh(III) complexes, and a shift in the peak activity away from $CClF_2COO^-$ (the optimal ligand for Rh(III)) toward less basic ligands. The calculated curves for ΔG_{app} vs p K_a of the conjugate acids of the anionic ligand for activation in the para, meta, and ortho positions are more similar for Pd than for the Rh-based system in agreement with the observed low selectivity of Pd(II) complexes relative to the high selectivity to *para*-toluic acid seen for comparable Rh(III) complexes.

Acknowledgments

This work was supported by the Methane Conversion Cooperative funded by BP. Calculations were performed on a cluster provided to the University of California Berkeley, College of Chemistry through grant: NSF CHE-0840505.

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