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Communications

Base-Promoted Selective Activation of Benzylic Carbon–Hydrogen Bonds of Toluenes by Rhodium(III) Porphyrins

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Summary: Toluenes underwent selective benzylic carbon–hydrogen bond activation with rhodium porphyrin chlorides. Both the rates and functional group compatibility were enhanced in the presence of K_2CO_3 .

Selective intermolecular carbon–hydrogen bond activation (CHA) by transition-metal complexes is an important area of research in organometallic chemistry for the controlled activation and functionalization of hydrocarbons.¹ Toluene is a unique hydrocarbon substrate, as three types of aromatic CHA and benzylic CHA are possible. The preferences for selective activation in toluene are not very well understood and are often case-^{2,3} and mechanism-dependent.^{4–6} Aromatic CHA (ArCHA) generally shows preference over the benzylic CHA (BnCHA)

and has been previously interpreted to be favored on both thermodynamic and kinetic grounds.³ Sterically hindered ligands of metal complexes can direct the benzylic CHA to be more selective, presumably due to kinetically less hindered approach at the metal center.⁴ However, the benzylic CHA has also been recently observed to be the thermodynamic pathway by Bercaw and others in Pt complexes in which reversible aromatic CHA allows shifting the equilibrium to the formation of benzyl complex via additional stabilization by arene coordination.³ The interplay of steric and electronic factors is of interest in the control and understanding of the selective activation of toluenes.

Rhodium(III) porphyrins (por) have been reported to undergo CHA. Rh(oep)Cl (oep = octaethylporphyrinate) in the presence of $AgClO_4$ reacts with arenes via aromatic CHA to give para-substituted arylrhodium porphyrins.⁸ On the basis of the para-substituted pattern of products and Hammett studies, an electrophilic aromatic mechanism was proposed. We have reported earlier the selective meta-aromatic CHA of benzeni-

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Scheme 1. Mechanism of CHA

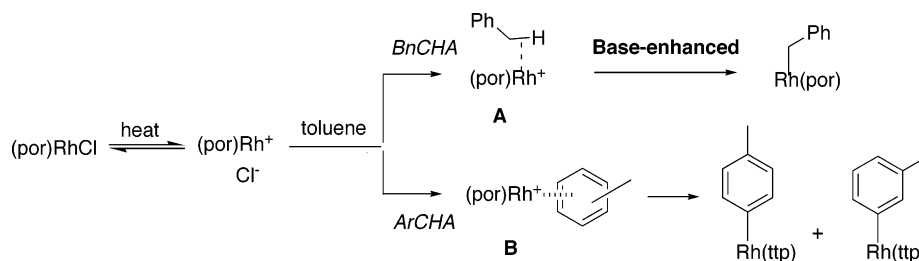


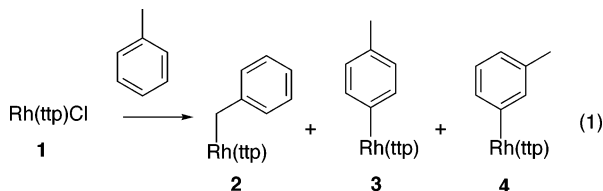
Table 1. Temperature Effect on CHA Reaction

entry	temp/°C	time/days	yield/% ^a		
			2	3	4
1	120	3	26	26	13
2	120	7	28	14	14
3	200	1	65		

^a Estimated from the integration of the mixture after chromatography by ¹H NMR.

trile.⁹ Selective aldehydic CHA of benzaldehydes¹⁰ without any aromatic CHA with rhodium(III) porphyrin complexes also occurs. In exploring the CHA with rhodium(III) porphyrins, we have successfully identified the base-promoted, selective benzylic CHA of functionalized toluenes by rhodium(III) tetrakis(4-tolylporphyrin) chloride (Rh(tpp)Cl).

Initially, toluene reacted with Rh(tpp)Cl at 120 °C in 3 days to give a mixture of 3-tolyl and 4-tolyl as well as benzylic rhodium porphyrin complexes (Table 1, eq 1). The absence of



Rh(tpp)(2-tolyl) is likely due to steric hindrance. Nonselective CHA had occurred. Prolonged heating of the reaction mixture for 7 days resulted in similar yields of products. However, at 200 °C after 1 day, only Rh(tpp)Bn was formed in 65% yield. High temperature favored the selective formation of the apparently less stable Rh(tpp)Bn, as RhAr has a stronger Rh–alkyl bond.¹¹ Both Rh(tpp)(4-tolyl) and Rh(tpp)Bn were stable toward toluene at an elevated temperature of 200 °C for 2 days without any interconversion; therefore, the benzylic CHA occurred in a parallel pathway with the aromatic CHA.

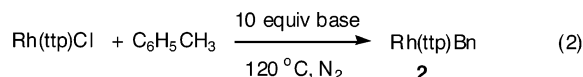
In view of the reported base-promoted aromatic CHA by transition-metal complexes,^{12,13} we had examined the effect of added ligands and bases. Coordinating ligands such as Ph₃P and pyridine were not effective, as they likely formed only coordination complexes with Rh(tpp)Cl without any CHA occurring. The noncoordinating base 2,6-di-*tert*-butylpyridine (30 equiv) proved to be encouraging, as Rh(tpp)Bn and Rh-

Table 2. Base Effect in CHA

entry	base	time/min	yield/%
1	NaOH	45	94
2	KOH	60	94
3	K ₂ CO ₃	30	97
4	KHCO ₃	600	94

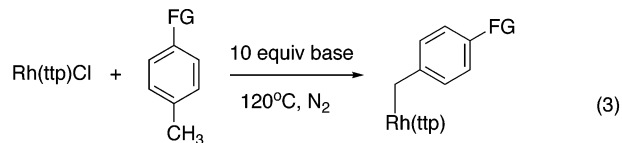
(tpp)(4-tolyl) were obtained in 46 and 18% yields, respectively, after 3 days at 120 °C.

Further improvements in selectivity, rate enhancement, and yields were discovered with other inorganic bases (Table 2, eq 2). When 10 equiv of K₂CO₃ was added, Rh(tpp)Bn was



selectively formed and isolated in 97% yield after 30 min (Table 2, entry 3). A lower loading of K₂CO₃ gave a slower reaction with a lower yield, and a higher loading (up to 100 equiv) resulted in little improved reaction efficiency. Other bases such as NaOH, KOH, and KHCO₃ were also effective but required longer reaction times.

When the optimized base-promoted reaction conditions were applied to various 4-substituted toluenes, high yields of rhodium porphyrin benzyls were obtained (Table 3, eq 3). With added



K₂CO₃, most reaction times were shortened to 30 min from 2–3 days and product yields were in general higher. The basic reaction conditions were more functional group compatible. No Me–O activation occurred in anisole (Table 2, entry 1).¹⁰ Even CN- and NO₂-substituted toluenes (Table 3, entries 7 and 8) reacted successfully, in contrast to no reaction or decomposition observed in the absence of base. The reactions were also successful with 10 equiv of toluene used in benzene solvent, though with slightly lower efficiency. Rh(tpp)Bn was obtained in a lower yield, 75%, after 1.5 h at 120 °C.

The observed isotope effects (k_H/k_D)_{obs} for the reactions of toluene with Rh(tpp)Cl at 120 °C were measured by competition experiments with an equimolar mixture of toluene and toluene-*d*₈. Without any base, (k_H/k_D)_{obs} values were measured to be 6.6 for aromatic CHA (indistinguishable of para and meta) and 4.0 for benzylic CHA. With K₂CO₃ added, (k_H/k_D)_{obs} was found to be 3.95. No benzyl exchange occurred under the same basic conditions, as Rh(tpp)Bn did not react with toluene-*d*₈ to give any Rh(tpp)Bn-*d*₇. These values suggested that the CHA steps were involved in or prior to the rate-determining step in the reactions.

Scheme 1 illustrates the proposed mechanism. Initially, Rh(tpp)Cl dissociates into a Rh(tpp) cation.^{8,10} In the absence of

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Table 3. Benzylic CHA of Toluenes

entry	FG	entry A (K ₂ CO ₃)		entry B (no K ₂ CO ₃)	
		time/min	product (yield/%)	time/days	product (yield/%)
1	OMe	30	2a (92)	2	2a (78)
2	^t Bu	45	2b (98)	2	2b (84)
3	Me	45	2c (90)		
4	3,5-Me ₂	45	2d (45)	3	2d (35)
5	H	30	2 (97)	3	2 (26)
6	F	240	2e (64)	3	2e (72)
7	CN	60	2f (83)	3	no reactn
8	NO ₂	30	2g (98)	1	no pdt

base, toluene can coordinate to the Rh(tpp) cation to form the (arene)Rh complex **B**, which then gives (aryl)Rh(tpp) in the ArCHA pathway. Alternatively, the benzylic C–H bond can coordinate to the Rh(tpp) cation to yield the benzylic C–H/Rh complex **A**, which then gives Rh(tpp)Bn in the BnCHA pathway. In the presence of base, the benzylic C–H/Rh(tpp) complex likely undergoes more facile deprotonation, due to the more acidic benzylic proton and sterically more favored coordination. An alternate mechanism involving Rh(tpp)OH formed by ligand substitution of Rh(tpp)Cl with hydroxide remains plausible. Rh(tpp)OH reacts with the benzylic CH bond to give Rh(tpp)Bn and water. A rhodium porphyrin hydroxide is known.¹⁴ IrOMe¹⁵ and RuOH¹⁶ complexes are known to undergo CHA. We currently favor the former mechanism involving a CH complex, in view of the similar observed kinetic isotope effects for benzylic CHA with and without base of 3.95 and 4.0, respectively. It remains hard to reconcile the lack of an anion effect on the magnitude of the kinetic isotope effect for the reactions with Rh(tpp)Cl and Rh(tpp)OH.

The base-promoted BnCHA did not follow a simple electronic effect. Competitive experiments were carried out with an equimolar mixture of 4-substituted (FG) toluene and toluene in reacting with Rh(tpp)Cl using K₂CO₃ (10 equiv) at 120 °C in 1 h in

benzene solvent. The ratios of Rh(tpp)(4-FG-benzyl) to Rh(tpp)-Bn were measured to be 3.95 (MeO), 0.28 (^tBu), 2.48 (F), 4.59 (CHO), 6.45 (CN), and 7.45 (NO₂). The ratios were kinetic ones, as no **2e** formed when Rh(tpp)Bn (**2**) was reacted with 4-fluorotoluene in benzene with 10 equiv of K₂CO₃ at 120 °C for 1 h. We rationalize the rates of forming the benzylic C–H complex or its stability and cleaving the C–H bonds are dependent on the electronic effects of substituents in an opposing manner.¹⁷ An electron-donating MeO substituent likely favors the formation of a C–H complex but disfavors the cleavage, due to its less acidic proton in comparison with a more electron withdrawing group.

In summary, we have discovered a base-promoted, selective, and functional group compatible benzylic CHA of toluenes with Rh(tpp)Cl. Further studies are ongoing.

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Supporting Information Available: Text giving experimental details and spectroscopic data for products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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