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Metalloradical-Catalyzed Aliphatic Carbon−Carbon Activation of Cyclooctane

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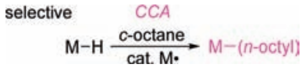
Alkane functionalization in a homogeneous medium is an important and challenging process which involves either carbon−hydrogen activation (CHA)[1] or carbon−carbon activation (CCA)[2] with organic, inorganic and organometallics reagents. Although aliphatic C−C bonds are weaker than aliphatic C−H bonds, CCA of alkanes is much less reported due to the steric hindrance of the C−C bond by the attack of a transition metal complex.[3]

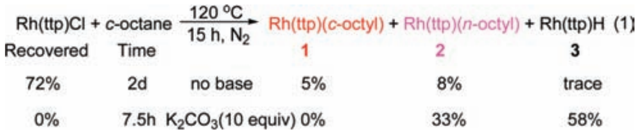
Cyclooctane (*c*-octane) is a relatively unstrained cycloalkane and therefore serves as a commonly investigated substrate in alkane functionalization, mostly involving CHA. Some examples of CHA of *c*-octane are the iridium(I) pincer dihydride-catalyzed dehydrogenation to *c*-octene,[4a] the $FeCl_3$-catalyzed aerobic oxidation to *c*-octanol and *c*-octanone,[4b] and the MnO_2-catalyzed bromination to *c*-octyl bromide.[4c] Examples of CCA of *c*-octane are rarely reported. A CCA of *c*-octane in a heterogeneous medium requires a very high reaction temperature of 530 °C and consequently results in both CHA and CCA.[3a] An oxidative CCA of *c*-octane catalyzed by *N*-hydroxyphthalides/Co(II)/Mn(II) at 100 °C in 14 h gives α,ω-dicarboxylic acids in 2% yield only.[3b]

We have recently discovered the base-promoted CHA of alkane with Rh(III) porphyrin[5] as well as the aliphatic CCA of nitroxides by Rh(II) porphyrin.[6] We now report the selective aliphatic CCA of *c*-octane by rhodium(III) porphyrin hydride to give a high yield of rhodium porphyrin *n*-octyl under mild reaction conditions and the mechanistic studies identifying the unique catalytic role of Rh(II) porphyrin (Scheme 1).

Scheme 1. CCA of *c*-Octane with MH



Initially, *c*-octane was found to react poorly with Rh(ttp)Cl (ttp =5,10,15,20-tetratolylporphyrinato dianion) to give Rh(ttp)(*c*-octyl) **1** and Rh(ttp)(*n*-octyl) **2** in 5% and 8% yields, respectively (eq 1). A 72% yield of Rh(ttp)Cl was recovered, and a trace amount of Rh(ttp)H **3** was observed. Both CHA and CCA products formed, but the reaction was inefficient. When K_2CO_3 (10 equiv) was added,[7] Rh(ttp)Cl was consumed in 7.5 h and Rh(ttp)(*n*-octyl) **2** and Rh(ttp)H **3** were obtained in 33% and 58% yields, respectively. The CCA product **2** is the formal 1,2-addition product of Rh(ttp)H into *c*-octane. The structures of **1** and **2** were confirmed by independent syntheses.[8] **2** was further characterized by X-ray crystallography (Figure 1).



To investigate whether the CHA product is an intermediate for CCA,[9] Rh(ttp)(*c*-octyl) **1** was heated in benzene-d_6 in both neutral and basic conditions separately. Without K_2CO_3, Rh(ttp)(*c*-octyl) **1** gave Rh(ttp)(*n*-octyl) **2**, Rh(ttp)H **3**, and *c*-octene **4** in 10%, 76%, and 36% yields, respectively after 21 h (eq 2, Figure S1, Table S1). In the presence of K_2CO_3 (10 equiv), Rh(ttp)(*n*-octyl) **2** was isolated in a higher yield of 21% in 16 h (eq 3, Figure S2, Table S2). However, both reactions were low yielding and incomplete. Therefore, the CHA product is not a major intermediate leading to the CCA product.

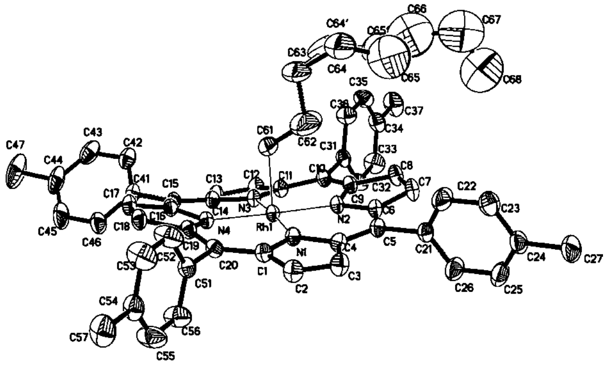
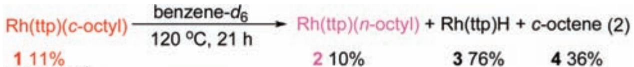
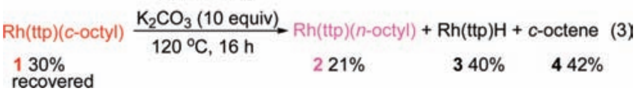


Figure 1. ORTEP presentation of Rh(ttp)(*n*-octyl) **2** (30% probability displacement ellipsoids). $Rh-C = 2.03$ Å, $R = 0.0522$.





To enhance the CCA reaction of Rh(ttp)Cl with *c*-octane based on mechanistic understandings, the reaction was monitored by ^1H NMR spectroscopy in a sealed NMR tube (eq 4, Figure S3, Table S3). Initially, Rh(ttp)Cl was first converted to $Rh_2(ttp)_2$ **5**.[5] **5** then slowly and completely reacted with the gradual formation of Rh(ttp)H **3**. Finally, Rh(ttp)(*n*-octyl) was generated in prolonged heating and still, Rh(ttp)H was consumed slowly and mostly remained unreacted. Therefore, both $Rh_2(ttp)_2$ and Rh(ttp)H are possible intermediates. The observed ^1H NMR upfield signals at $\delta = -5$ to 1 ppm (Figure S4) were assigned to Rh(ttp)-incorporated *c*-octene oligomers (about 15% NMR yield), which indicate the occurrence of Rh^{II}(ttp)-initiated oligomerization of *c*-octene.[10]

To investigate the intermediacy of Rh(ttp)H and $Rh_2(ttp)_2$, Rh(ttp)H **3** and $Rh_2(ttp)_2$ **5** were then separately reacted with *c*-octane. Rh(ttp)H **3** indeed reacted with *c*-octane at 120 °C in

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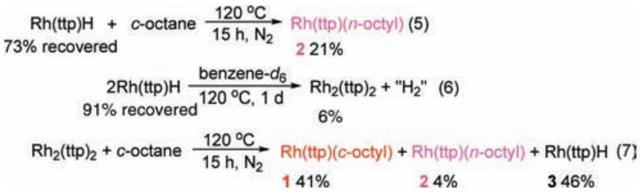
15 h to give Rh(ttp)(*n*-octyl) **2** selectively, though in only 21% yield, and was also recovered in 73% yield (eq 5). As Rh(ttp)H underwent slow dehydrogenative dimerization to give 6% yield of $\mathrm{Rh_2(ttp)_2}$ at 120 °C in 1 day, similar to the report by Wayland and co-workers (eq 6),[11] the small amount of $\mathrm{Rh_2(ttp)_2}$ formed in eq 5 likely facilitates the 1,2-addition of Rh(ttp)H into *c*-octane.[12] The other possible intermediate $\mathrm{Rh_2(ttp)_2}$ **5** was also reacted with *c*-octane. Rh(ttp)(*c*-octyl) **1**, Rh(ttp)(*n*-octyl) **2**, and Rh(ttp)H **3** were formed in 41%, 4%, and 46% yields, respectively (eq 7) with a very low yield of CCA product. Therefore, both Rh(ttp)H **3** and $\mathrm{Rh_2(ttp)_2}$ **5** gave low yielding reactions and are likely only minor reaction intermediates by themselves.



Based on the mechanism of the $\mathrm{Rh^{II}}$-catalyzed insertion of Rh(oep)H (oep = octylethylporphyrin dianion) into styrene reported by Halpern et al.,[12] we proposed that the CCA, being a 1,2-addition reaction, is catalyzed by $\mathrm{Rh^{II}}$ (Scheme 2). $\mathrm{Rh_2(ttp)_2}$ **5** formed from thermolysis of Rh(ttp)H initially undergoes homolysis to give $\mathrm{Rh^{II}}$(ttp) (eqs 8 and 9).[11] $\mathrm{Rh^{II}}$(ttp) then reacts with *c*-octane in parallel CHA (pathway iii, eq 10) and CCA (pathway iv, eq 11). $\mathrm{Rh^{II}}$(por) (por = porphyrinato dianion) has been shown to undergo CHA with alkane to give Rh(por)R and Rh(por)H.[5,13] For the CCA pathway, $\mathrm{Rh^{II}}$(ttp) can cleave the C−C bond of *c*-octane to generate the alkyl radical **6** (pathway iv, eq 11) which can also reverse back rapidly.[14] **6** can then abstract a hydrogen atom from the weak (ttp)Rh−H bond[15a] to form a strong alkyl C−H bond,[15b] providing the driving force of the reaction (pathway v). The proposed mechanism can be validated qualitatively by increasing the ratio of Rh(ttp)H/$\mathrm{Rh_2(ttp)_2}$ for more efficient trapping of **6** to **2** (Table 1, eq 12).

Indeed, mixtures of Rh(ttp)H and $\mathrm{Rh_2(ttp)_2}$ were more efficient reagents and enhanced the total yields up to 79% (Table 1, entries 2−4 vs 1). The selectivity toward CCA was further enhanced by an increase of the Rh(ttp)H:$\mathrm{Rh_2(ttp)_2}$ ratio. The CCA of *c*-octane with the mixture of Rh(ttp)H/$\mathrm{Rh_2(ttp)_2}$ in a 2:1 ratio gave Rh(ttp)(*c*-octyl) and Rh(ttp)(*n*-octyl) in 60% and 18% yields, respectively (Table 1, entry 2). When the Rh(ttp)H/$\mathrm{Rh_2(ttp)_2}$ ratio increased to 5:1, the yield of Rh(ttp)(*n*-octyl) increased to 26% yield but that of Rh(ttp)(*c*-octyl) decreased to 53% yield (entry 3). Rh(ttp)(*n*-octyl) was selectively obtained in 73% yield from the reaction with the 10:1 ratio of Rh(ttp)H/$\mathrm{Rh_2(ttp)_2}$ (entry 4). The aliphatic CCA of *c*-octane was thus achieved successfully with the $\mathrm{Rh^{II}}$-catalyzed 1,2-addition of Rh(ttp)H.

Scheme 2. Proposed Mechanism of $\mathrm{Rh^{II}}$-Catalyzed 1,2-Addition of *c*-Octane with RhH

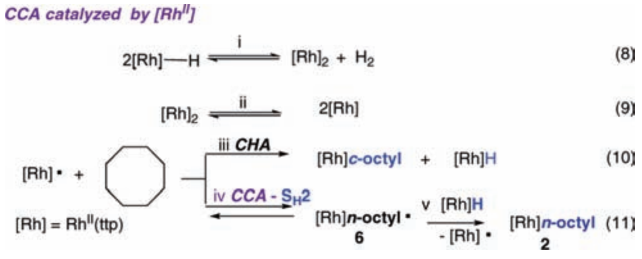
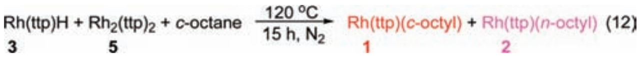


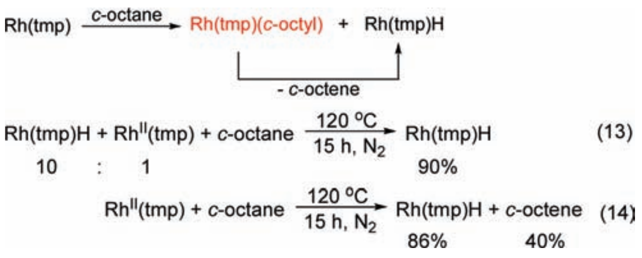
Table 1. $\mathrm{Rh^{II}}$(ttp)-Catalyzed CCA of *c*-Octane wih Rh(ttp)H



Entry[a]	3:5	Yield **1** (%)	Yield **2** (%)	Total yield (%)
1[b]	1:0	0	21	21
2	2:1	60	18	78
3	5:1	53	26	79
4	10:1	0	73	73

[a] The results are the average of at least duplicate. [b] 73% Rh(ttp)H recovered.

Scheme 3. Formation of Rh(tmp)H from CHA of $\mathrm{Rh^{II}}$(tmp) and *c*-Octane



The sterically more hindered Rh(tmp) was not effective for CCA (tmp = 5,10,15,20-tetramesitylporphyrinato dianion). When the mixture of Rh(tmp)H and $\mathrm{Rh^{II}}$(tmp) (10:1) was reacted with *c*-octane at 120 °C for 15 h, no reaction occurred and 90% yield of Rh(tmp)H was recovered (eq 13). $\mathrm{Rh^{II}}$(tmp) only underwent CHA with *c*-octane to give Rh(tmp)H and *c*-octene in 86% and 40% yields, respectively (eq 14). The formation of *c*-octene likely results from the CHA product Rh(tmp)(*c*-octyl) which rapidly undergoes facile *β*-hydride elimination to give *c*-octene and Rh(tmp)H (Scheme 3). Indeed, the attempted synthesis of Rh(tmp)(*c*-octyl) by reductive alkylation ($\mathrm{NaBH_4}$/*c*-octyl bromide) gave Rh(tmp)H and *c*-octene in 89% and 77% yields, respectively.

In conclusion, we have discovered the mild, selective $\mathrm{Rh^{II}}$-catalyzed 1,2-addition of Rh(ttp)H to *c*-octane via an aliphatic CCA. Further studies are ongoing.

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Supporting Information Available: Detailed experimental section, ^{1}H and ^{13}C NMR data of **1** and **2**, reaction time profiles of eqs 2−4, and details of crystallographic studies of **2** (including CIF file). This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) Rh(ttp)Cl reacted with alkane in basic medium to give $\mathrm{Rh_2(ttp)_2}$ and Rh(ttp)H as intermediates. See ref 5.

(8) **1** and **2** were fully characterized. The chemical shifts of ^{13}C NMR of Rh—C of **1** and **2** were $\delta = 40.62$ (d, $^{1}J_{\mathrm{Rh-C}} = 26.4$ Hz) and 15.69 (d, $^{1}J_{\mathrm{Rh-C}} = 26.8$ Hz), respectively.

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(15) (a) The estimated bond dissociation energy (BDE) of (ttp)Rh—H is ~60 kcal mol^{-1}. See ref 14b. (b) The BDE of *n*-octyl—H is ~100 kcal mol^{-1}; see: Luo, Y. R. *Handbook of Bond Dissociation Energies in Organic Compounds*; CRC Press: Boca Raton, FL, 2003.

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