Aliphatic Carbon−Carbon Bond Activation of Nitriles by Rhodium(II) Porphyrin

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Summary: The aliphatic C(α)−C(β) bonds of a series of nitriles were activated by Rh(tmp) using Ph₃P as the promoting ligand from 100 to 130 °C. Kinetic studies at 130 °C revealed the rate law, rate = k'K₁[Rh(tmp)][Ph₃P]ⁿ + k₃K₂(K₁[Ph₃P])/ (1 + K₁[Ph₃P])[Rh(tmp)][ᵗBuCN] and suggested the carbon− carbon bond activation occurred at the coordinated ᵗBuCN with Rh(tmp) in a 1:1 ratio in the transition state.

Carbon−carbon bond activation (CCA) by a transition-metal complex is an active and challenging research area.[1] Selective aliphatic CCA is difficult and is often associated with competitive carbon−hydrogen bond activation (CHA).[1] The activation of the C(α)−CN bond in alkyl or aryl nitriles is of great interest, because the alkyl or aryl metal cyanides formed have been proposed as intermediates in a number of important catalytic processes such as cyanation of aryl halides,[2] utilization of aryl cyanides for cross-coupling,[3] arylcyanation of alkynes,[4] and methylation using acetonitrile.[5] Most reports of CCA of nitriles by transition-metal complexes show that it occurs at the C(α)− CN bonds[6] rather than at the aliphatic C(α)−C(β) bonds. The more facile C(α)−CN activation may likely be steric in origin, since the bond energies of C(α)−CN (103−125 kcal mol⁻¹) are higher than those of C(α)−C(β) bonds (60−83 kcal mol⁻¹).[7] The formation of a strong metal cyanide may also contribute to the driving force of the activation.

We have reported that rhodium(II) *meso*-tetramesitylporphyrin (**1**; Rh(tmp)[8]) activates the aliphatic carbon−carbon bonds in nitroxides[9] and ketones.[10] In expanding the scope of the aliphatic
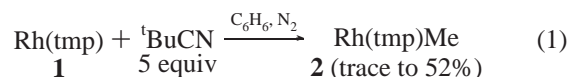
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Table 1. Optimization of CCA Conditions

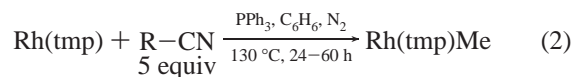| entry	amt of PPh₃ (equiv)	temp (°C)	reaction time (h)	product (yield[a] (%))
1	0	130	120	Rh(tmp)Me (trace)
2	1	110	60	Rh(tmp)Me (20)
3	1	130	60	Rh(tmp)Me (52)
4	1	150	48	Rh(tmp)Me (30) Rh(tmp)Et (16)

[a] Average yield of at least two runs.

CCA, we have investigated the reactions of Rh(tmp) with alkyl nitriles. Herein, we report the discovery of the selective and ligand-enhanced aliphatic CCA at the C(α)−C(β) positions of nitriles as well as results of mechanistic studies.

When the prototypical substrate of *tert*-butyl cyanide was reacted with Rh(tmp) in benzene at 70 °C for 2 days, no reaction was observed. When the reaction temperature was increased to 130 °C, a trace of Rh(tmp)Me was detected (Table 1, entry 1 and eq 1). Further optimization of CCA was achieved by the

$$\text{Rh(tmp)} + {}^{t}\text{BuCN} \xrightarrow{\text{C}_6\text{H}_6, \text{N}_2} \text{Rh(tmp)Me} \quad (1)$$
$$\mathbf{1} \qquad\quad \text{5 equiv} \qquad\qquad \mathbf{2} \text{ (trace to 52\%)}$$

addition of Ph₃P to form a more electron-rich and reactive Rh(tmp)Ph₃P.[10,11] At 110 °C, when 1 equiv of Ph₃P was used, 20% of Rh(tmp)Me was obtained in 120 h. At 130 °C, a higher yield (52%) of Rh(tmp)Me was isolated in 60 h. However, at 150 °C, the reaction gave a mixture of Rh(tmp)Me (30%) and Rh(tmp)Et (16%). The formation of Rh(tmp)Et was rationalized from the reaction of Rh(tmp)Me with Rh(tmp) to give Rh(tmp)- CH₂, which further reacted with Rh(tmp)Me to give Rh(tmp)- Et. Indeed, Rh(tmp) reacted with Rh(tmp)Me at 150 °C in 60 h to give 26% Rh(tmp)Et and recovered Rh(tmp)Me in 43%. Therefore, the CCA of *ter*t-butyl cyanide appears to have a narrow temperature range from about 110 to 130 °C.

The optimized reaction conditions were then applied to a series of nitriles (eq 2), and Table 2 gives the results. Except in

$$\text{Rh(tmp)} + \text{R−CN} \xrightarrow[130\,°\text{C}, 24−60\,\text{h}]{\text{PPh}_3, \text{C}_6\text{H}_6, \text{N}_2} \text{Rh(tmp)Me} \quad (2)$$
$$\text{5 equiv}$$

CH₃CN, which underwent C(α)−CN activation to give a low yield of Rh(tmp)Me (Table 2, entry 1), all of the other nitriles showed selective aliphatic C(α)−C(β) CCA. The yields and rates of reactions increased with decreasing C(α)−C(β-Me)

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Table 2. CCA of Nitriles with Rh(tmp)

entry	nitriles	$C(\alpha)-C(\beta)$ BDE[7] (kcal mol^{-1})	time (h)	yield[a] (%)
1	MeCN		60	10
2	EtCN	83.2	48	38
3	Me_2CHCN	79.5	48	41
4	Me_3CCN	74.7	24	52
5	$Me_2C(CN)_2$	76	48	47
6	PhMeCHCN	63	36	48
7	$PhMe_2CCN$	59.9	24	61
8	Ph_2MeCCN		36	38
9	$4\text{-}MeC_6H_4CMe_2CN$		24	57
10	$4\text{-}CF_3C_6H_4CMe_2CN$		24	65

[a] Average isolated yield of at least two runs.

bond dissociation energy (BDE).[7] The absence of Rh(tmp)Ph suggests that the reaction goes through a radical[12] rather than a concerted oxidative addition process via an elusive Rh(IV).[13,14] The slight decrease in reactivity in Ph_2MeCCN as compared to that in $PhMe_2CCN$ (Table 2, entry 8 vs 7) can be accounted for by an increase in large steric hindrance caused by the phenyl group. The electron-withdrawing CF_3 appeared to increase the yield of Rh(tmp)Me slightly to 65% in comparison to the more electron rich Me-substituted species (Table 2, entries 9 and 10 vs 7).

Competitive carbon−hydrogen bond activation at the benzylic or aliphatic hydrogens did not likely occur to give Rh(tmp)H.[15] If there were any Rh(tmp)H formed, $PhMe_2CCH=NH[Rh(tmp)]$ would have been observed, as Rh(tmp)H was found to react with $PhMe_2CCN$ to give $PhMe_2CCH=NH[Rh(tmp)]$ in 27% yield at 130 °C in 24 h. The absence of other tertiary Rh alkyls is likely due to the instability of the tertiary rhodium macrocycle caused by steric hindrance.[16]

Kinetic studies were carried out to gain further mechanistic insight into the CCA. First, the stoichiometry and binding constants of Ph_3P with Rh(tmp) were measured spectrally at 522 nm from 20 to 50 °C (Table S1 and Figure S1, Supporting Information) and analyses of the data confirmed the formation of 1:1 complex and yielded $K_{1,130\ °C}$(extrapolated) = 10.7 M^{-1} ($=k_1/k_{-1}$), $\Delta H_1 = -12 \pm 1$ kcal mol^{-1}, and $\Delta S_1 = -26 \pm 2$ cal mol^{-1} K^{-1} (Figure S2, Supporting Information).

Kinetic measurements of the reaction of Rh(tmp) and ^tBuCN with excess Ph_3P carried out spectrally at 522 nm under the conditions 130 °C and initial concentrations $(5.55-16.65) \times 10^{-5}$ M Rh(tmp), $(2.97-8.90) \times 10^{-3}$ M ^tBuCN, and 1.10×10^{-3} M Ph_3P for at least 4 half-lives yielded the rate law shown in eq 3.
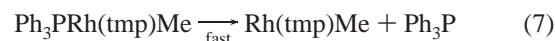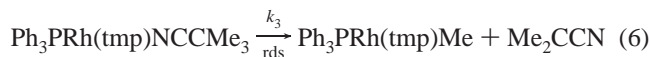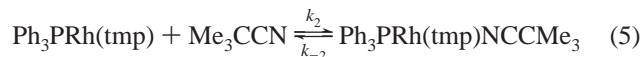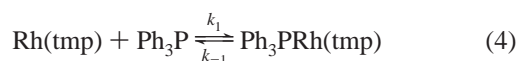
$$-d[\text{Rh(tmp)}]/dt = k'K_1[\text{Rh(tmp)}]_0[\text{Ph}_3\text{P}]^n + k_3K_2(K_1[\text{Ph}_3\text{P}])/$$

$$(1 + K_1[\text{Ph}_3\text{P}])[\text{Rh(tmp)}]_0[^t\text{BuCN}] \quad (3)$$

The rate is composed of two parallel processes, with the first process being ^tBuCN independent and the second one ^tBuCN dependent (Figures S3−5 and Table S2, Supporting Informa-

tion). Since Rh(tmp) was stable in benzene at 130 °C for 2 days (Figure S6, Supporting Information), the ^tBuCN-independent reaction was found to be dependent on Ph_3P, as evidenced by the spectral change of $Ph_3Rh(tmp)$ at 130 °C (Figure S7, Supporting Information). We rationalized that $Ph_3PRh(tmp)$ undergoes disproportionation (k') to $Rh^I(tmp)^-$ and $(Ph_3P)_2Rh^{III}\text{-}(tmp)^+$ at high temperature.[11,17,18] For the ^tBuCN-dependent process relevant to aliphatic CCA, the rate was found to be first order in both Rh(tmp) and ^tBuCN and exhibited saturation kinetics in excess Ph_3P.[14]

A proposed mechanism for CCA conforming to the kinetic evidence is depicted in Scheme 1. Initially, facile coordination of Ph_3P with Rh(tmp) occurs to give $Ph_3PRh(tmp)$ (k_1), which is then complexed by ^tBuCN to give $Ph_3PRh(tmp)^tBuCN$ (k_2). The mode of nitrile coordination is likely N-bound rather than side-bound, to minimize steric hindrance. Subsequently, Rh abstracts the methyl group of loosely bound ^tBuCN to yield $Ph_3PRh(tmp)Me$ in the transition state in the rate-determining step (k_3), which is in contrast with the termolecular transition state in the activation of methane by Rh(tmp).[8,15] The fate of the nitrile-containing fragment, presumably a carbon-centered radical, remains unclear. We were not able to detect any coupling product of $(NCMe_2C)_2$ in the reaction mixture of Rh(tmp) with ^tBuCN by GC-MS. Presumably, $NCMe_2C$ readily abstracts a hydrogen atom rather than coupling with either itself or Rh(tmp).[19,20]

Scheme 1

$$\text{Rh(tmp)} + \text{Ph}_3\text{P} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{Ph}_3\text{PRh(tmp)} \quad (4)$$

$$\text{Ph}_3\text{PRh(tmp)} + \text{Me}_3\text{CCN} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \text{Ph}_3\text{PRh(tmp)NCCMe}_3 \quad (5)$$

$$\text{Ph}_3\text{PRh(tmp)NCCMe}_3 \underset{\text{rds}}{\overset{k_3}{\longrightarrow}} \text{Ph}_3\text{PRh(tmp)Me} + \text{Me}_2\text{CCN} \quad (6)$$

$$\text{Ph}_3\text{PRh(tmp)Me} \underset{\text{fast}}{\longrightarrow} \text{Rh(tmp)Me} + \text{Ph}_3\text{P} \quad (7)$$

In summary, the selective aliphatic $C(\alpha)-C(\beta)$ bonds of a series of nitriles have been activated by Rh(tmp) using PPh_3 as the promoting ligand. The CCA was affected by bond energy, steric hindrance, and the small electronic effect of aryl aceto-nitriles. No $C(\text{aryl})-C(\alpha)$ bond nor CH activation was observed. Further studies of bond activation are ongoing.

Supporting Information Available: Text, tables, and figures giving experimental details and kinetic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) The kinetic order of Rh(tmp) was preliminarily estimated from the first-order fit of the absorbance change. We did not investigate the kinetic order of Ph_3P: i.e., n in eq 3.

(19) No $^tBuRh(tmp)$ was observed in the reaction of ^tBuNC with Rh(tmp).[11a] The formation of $Rh(tmp)CMe_2CN$ is likely sterically hindered.

(20) Reaction of $BrCMe_2CN$ with Rh(tmp) gave Rh(tmp)Br but no $Rh(tmp)CMe_2CN$. However, the sterically less hindered $BrCH_2CN$ reacted with Rh(tmp) at room temperature in 1 h to give Rh(tmp)Br and Rh(tmp)-CH_2CN in 38 and 47%, yields, respectively. These reactions demonstrated the importance of steric effects in coupling.