Reaction Mechanisms

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Functionalization of Alkynes by a (Salen)ruthenium(VI) Nitrido Complex**

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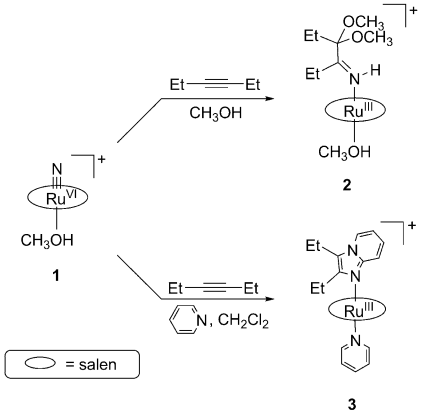
Abstract: *Exploring new reactivity of metal nitrides is of great interest because it can give insights to N_2 fixation chemistry and provide new methods for nitrogenation of organic substrates. In this work, reaction of a (salen)ruthenium(VI) nitrido complex with various alkynes results in the formation of novel (salen)ruthenium(III) imine complexes. Kinetic and computational studies suggest that the reactions go through an initial ruthenium(IV) aziro intermediate, followed by addition of nucleophiles to give the (salen)ruthenium(III) imine complexes. These unprecedented reactions provide a new pathway for nitrogenation of alkynes based on a metal nitride.*

Exploring new reactivity of metal nitrides continues to be of great interest to chemists. Apart from their important roles in N_2 fixation, metal nitrides are also potentially useful reagents for nitrogenation of various substrates.[1–3] In the last two decades, novel N–C, N–N, N–P, and N–E (E = O, S, Se) bond-formation reactions between various nucleophiles and electrophilic polypyridylosmium(VI) nitrides have been reported.[4–6] We have also demonstrated that the highly electrophilic (salen)ruthenium(VI) nitrido complex $[Ru^{VI}(N)(L)(CH_3OH)]^+$ (**1**) (L = *N*,*N*′-bis(salicylidene)-*o*-cyclohexyldiamine dianion)[7] is capable of reacting with various organic substrates at ambient conditions.[8] Notably, **1** readily undergoes aziridination of alkenes[9] and C–H activation of alkanes.[10] It is therefore anticipated that **1** should also be able to functionalize alkynes.

Complexes with metal–ligand multiple bonds have been used in alkyne functionalization. For example, the oxidation of alkynes by a number of oxo complexes (M=O) of ruthenium,[11] chromium,[12] zirconium,[13] and osmium[14] have been reported. There are also a few reports on nitrogenation of alkynes by metal-imido (M=NR) or metal-nitrido (M≡N) complexes. Treatment of the (imido)titanium(IV) complex $[Cp^*_2Ti{=}NPh]$ with a terminal alkyne (RC≡CH) affords either an azametallacyclic, $[Cp^*_2TiN(Ph)CH_2{=}CH_2]$ (R = H), or anilido-acetylide species, $[Cp^*_2TiN(H)Ph(C{\equiv}CR)]$ (R = Ph or $SiMe_3$).[15] A molecular Ti-Zn nitride reacts with terminal alkynes to give alkynylimido complexes.[16] Metal nitrides have also been used as catalysts for alkyne–nitrile cross-metathesis.[17,18] Herein we report novel alkyne functionalization reactions by a (salen)ruthenium(VI) nitride (**1**; Scheme 1).



Scheme 1. Synthesis of ruthenium(III) imine complexes **2** and **3**.

Reaction of **1**$[PF_6]$ with excess EtC≡CEt in CH_3OH at ambient conditions afforded **2**$[PF_6]$ as a green solid. Its X-ray crystal structure (see Figure 1 and Tables S1 and S2 in the Supporting Information) shows that the ruthenium center adopts a distorted octahedral geometry with a salen ligand, a methanol, and a 4,4-dimethoxy-3-hexanimine ligand which is formally derived from the addition of one EtC≡CEt and two methanol molecules to the nitrido ligand. The Ru1–N3 distance of 2.050(2) Å suggests that it is a single bond, while

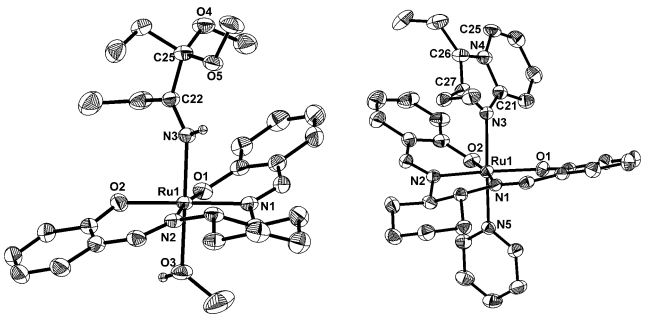


Figure 1. Molecular structures of **2** (left) and **3** (right). Thermal ellipsoids are drawn at 50% probability. CH hydrogen atoms are omitted for clarity.

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the N3–C22 distance of 1.278(3) Å is consistent with an imine function.

The electrospray ionization mass spectrum (ESI-MS) of **2**[PF_6] (see Figure S1) exhibits peaks at *m*/*z* 613 and 581, which are assigned to [**2**]$^+$ and [**2**-CH_3OH]$^+$, respectively. The cyclic voltammogram (CV) of **2**[PF_6] in CH_3CN (see Figure S2) exhibits two well-separated reversible waves at +0.66 and −0.67 V (vs $Cp_2Fe^{+/0}$), which are assigned to $Ru^{IV/III}$ and $Ru^{III/II}$ couples, respectively. The IR spectrum shows a sharp ν(N-H) stretch at 3236 cm^{-1}. Similar (salen)ruthenium(III) dimethoxyalkylimine products were also observed in the reaction of **1** with other alkynes, such as MeC≡CMe and PrC≡CH, as monitored by ESI-MS (see Figures S3 and S4).

Since the reactivity of **1** can be greatly enhanced by pyridine,[9,10] we also investigated the pyridine-assisted reaction of **1** with alkynes. Reaction of **1**[ClO_4] with EtC≡CEt in the presence of pyridine, followed by chromatography, afforded the complex **3**. The X-ray structure of **3** (see Figure 1 and Tables S1 and S3) shows that the ruthenium atom adopts a distorted octahedral geometry with a planar salen ligand, a pyridine, and an N-coordinated 2,3-diethylimidazo[1,2-*a*]pyridine, which is formally derived from the addition of a EtC≡CEt and a pyridine molecule to the nitrido ligand. The bicyclic ligand is planar with average C–N and C–C bond distances of (1.379 ± 0.014) and (1.382 ± 0.029) Å, respectively. The Ru–N3 distance of 2.108(3) Å is slightly longer than the Ru–N(imine) distance of **2** [2.050(2) Å]. Reaction of **1** with EtC≡CEt in the presence of other donor ligands, such as 4-substituted pyridine (4-X-py, where X = Me, OMe, or *t*Bu) or pyrazine, also gave similar products, as revealed by ESI-MS (see Figure S5).

Kinetic studies on the reaction of **1** with EtC≡CEt in CH_3OH has been carried out by UV/Vis spectrophotometric methods. The spectral changes in CH_3OH reveal that this reaction consists of two steps (Figure 2), and well-defined isosbestic points (λ = 254, 328, 418 and 474 nm) are found for the first step (spectrum **a** to **b**). In the presence of excess alkyne, pseudo-first-order kinetics were observed for both steps. The pseudo-first-order rate constant, k_{obs}, for the first step is independent of [**1**], but depends linearly on [EtC≡CEt] (Figure 2, inset), with a second-order rate constant, k_2, of $(3.35 \pm 0.08) \times 10^{-3}\,M^{-1}s^{-1}$ at 298.0 K. The second step (spectrum b to c) is independent of both [**1**] (5.00–10.0 × 10^{-5} M) and [EtC≡CEt] (0.05–0.40 M), with a first-order rate constant of $k = (6.60 \pm 0.60) \times 10^{-5}\,s^{-1}$ (see Figure S6). The final spectrum is similar to that of an equimolar mixture of **2** and [Ru^{III}(L)-$(MeOH)_2$]$^+$ (see Figures S7–S9). This mixture is also supported by ESI-MS which shows peaks arising from **2** and [Ru(L)$(MeOH)_2$]$^+$ (see Figure S10). The effects of temperature on the rate constants for the first step have also been studied from 288.0 to 318.0 K (see Figure S11). $\Delta H^{\neq}$ and $\Delta S^{\neq}$ were found to be (15.5 ± 0.5) kcal mol^{-1} and (−18 ± 1) cal $mol^{-1}K^{-1}$, respectively.

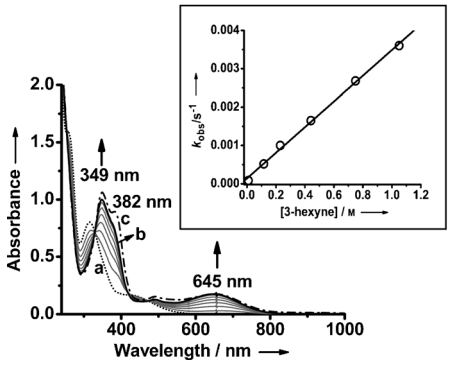
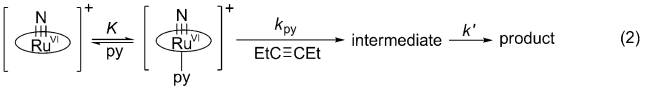


Figure 2. UV/Vis spectral changes for the reaction of **1** (7.18×10^{-5} M) with EtC≡CEt (0.20 M) in CH_3OH at 298.0 K. a) Before mixing (dot line), b) after 2100 s (solid line), c) after ca. 23 h (dash line). Inset shows the plot of k_{obs} versus [EtC≡CEt] for the first step: slope = $(3.35 \pm 0.08) \times 10^{-3}\,M^{-1}s^{-1}$, *y*-intercept = $(1.39 \pm 0.47) \times 10^{-4}$, $r^2 = 0.997$.

Similar kinetic behavior was observed for the reaction of various substituted phenylacetylenes with **1** (see Figure S12 and S13). A fairly linear Hammett correlation between $\log(k_2^X/k_2^H)$ and σ^+ was obtained (see Figure S14), with the reaction constant $\rho^+ = -(1.2 \pm 0.1)$. The small negative ρ^+ value suggests nucleophilic attack of X-PhC≡CH at the nitrido ligand of **1**, with a weakly polar transition state.

The kinetics of the reaction of **1** with EtC≡CEt in the presence of pyridine (py) were also investigated in 1,2-dichloroethane (see Figure S15). The UV/Vis spectral changes show that this reaction also consists of two steps. The first step follows clean pseudo-first-order kinetics for over three half-lives. The pseudo-first-order rate constant, k_{obs}, is independent of [**1**], depends linearly on [EtC≡CEt], but exhibits saturation behavior with respect to [py] (see Figure S16). The rate law is shown in Equation (1). This kinetic behavior is consistent with initial equilibrium binding of py to Ru≡N, followed by reaction with EtC≡CEt, as shown in Equation (2).

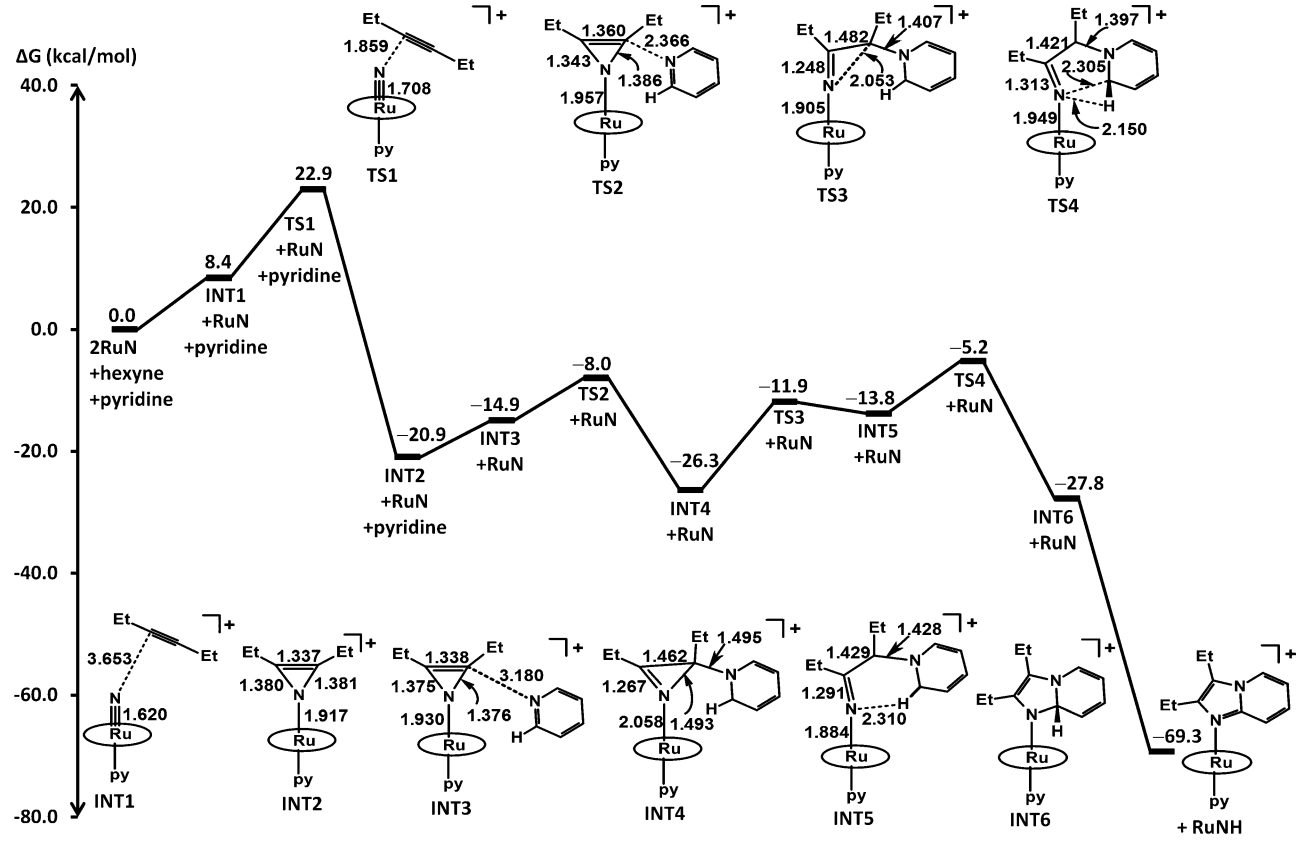
$$\frac{-d[Ru^{VI}(N)]}{dt} = k_{py}[Ru^{VI}(N)][EtC{\equiv}CEt]\left(\frac{K[py]}{1 + K[py]}\right) \quad (1)$$



(2)

The equilibrium constant, *K*, for the reversible binding of py to **1** was found to be $(16.0 \pm 1.1)\,M^{-1}$, and is in agreement with the values of $(15.6 \pm 1.1)\,M^{-1}$ and $(16.6 \pm 1.4)\,M^{-1}$ previously obtained for the py-assisted alkene aziridination and C–H activation of cyclohexane, respectively, by **1**.[9,10] The second-order rate constant (k_{py}) was found to be $(4.94 \pm 0.16) \times 10^{-3}\,M^{-1}s^{-1}$ at 298.0 K. The second step is independent of [**1**], [EtC≡CEt], and [py], and the first-order rate constant *k*′ was found to be $(1.5 \times 10^{-5})\,s^{-1}$ (see Figure S17). Product analysis by ESI-MS indicates the presence of **3** (*m*/*z* 675) and [Ru(L)$(py)_2$]$^+$ (*m*/*z* 580) (see Figure S18).

Similar kinetic behavior was observed for the py-assisted oxidation of various substituted phenylacetylenes by **1** in $(CH_2Cl)_2$. A fairly linear Hammett correlation between $\log(k_2^X/k_2^H)$ and σ^+ was also observed with a ρ^+ value of −1.1 ± 0.1 (see Figure S19). No kinetic isotopic effect was

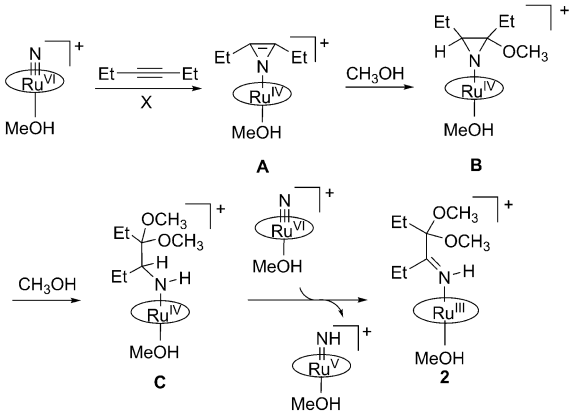


Scheme 2. Potential-energy surface for reaction of **1** with pyridine at the B3LYP level of theory using the LanL2DZ basis set (Ru) and 6-311G(d,p) basis set (nonmetals). Relative 298 K Gibbs free energies in $(CH_2Cl)_2$ are given in kcal mol^{-1} and selected bond lengths are in Å.

observed when PhC≡CD was used instead of PhC≡CH (see Figure S20).

Based on the experimental results and DFT calculations (see Scheme 2 and Table S4), a mechanism for the reaction of **1**/py with EtC≡CEt was proposed. The initial step involves nucleophilic attack of EtC≡CEt at the nitride to generate a ruthenium(IV) aziro (deprotonated azirine) intermediate (**INT2**). Reaction of [Cp*Zr=NPh] with acetylene is reported to give a azametallacyclobutene.[15] However, for the present system, DFT calculations show that the azametallacyclobutene is 12 kcal mol^{-1} higher in energy than the aziro complex (see Table S5), because of the repulsion between the cyclobutene ring and the planar salen ligand. **INT2** is readily attacked by another pyridine molecule, thus resulting in ring opening to generate **INT5**. Ring closure of **INT5** gives **INT6**, which then undergoes hydrogen-atom transfer (HAT) to another [Ru^{VI}≡N] to afford **3**. Intramolecular hydrogen-atom abstraction followed by N rebound of **INT5** has also been considered (see Scheme S1; blue line). However, the transition state (TS) is 11.6 kcal mol^{-1} higher and it also results in dissociation of the bicyclic imine ligand.

In CH_3OH (Scheme 3), the ruthenium(IV) aziro intermediate **A** is proposed to first add a CH_3OH molecule to give the intermediate **B**, which then undergoes ring opening and addition of another CH_3OH molecule to give **C**. The intermediate **C** then undergoes HAT to another Ru^{VI}≡N to give the complex **2**. In both cases, the [Ru^{V}(NH)] formed from



Scheme 3. Proposed mechanism for the reaction of **1** with EtC≡CEt in CH_3OH.

HAT is proposed to undergo rapid bimolecular N···N coupling[7,10] followed by air oxidation to give $[Ru(L)(X)_2]^+$ (X = CH_3OH or py), which has been observed by ESI-MS, CV, and UV/Vis spectroscopy.

In conclusion, we have reported the novel reactivity of **1** with various alkynes at ambient conditions. These unprecedented reactions provide a new alkyne nitrogenation pathway based on a ruthenium nitride. In particular, it is

potentially a useful method for the synthesis of new imidazo[1,2-*a*]pyridines. Imidazo[1,2-*a*]pyridine has been identified as the core structure in various natural products with significant biological and pharmaceutical activities.[19,20]

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