Novel Propargylic Substitution Reactions Catalyzed by Thiolate-Bridged Diruthenium Complexes via Allenylidene Intermediates

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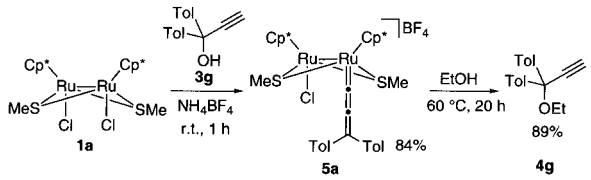
We have long been interested in development of homogeneous catalysis of polynuclear transition metal complexes since direct and indirect cooperation of plural transition metals can be expected for the activation of substrates to provide novel transformations that are not attainable at conventional monometallic centers. Toward this end, our studies have been focused on the synthesis and reactivities of polynuclear noble metal complexes with bridging sulfur ligands.[1] In the course of our investigation, we have synthesized a series of thiolate-bridged diruthenium complexes such as [Cp*RuCl(μ_2-SR)$_2$RuCp*Cl] (Cp* = η^5-C$_5$Me$_5$; R = Me (**1a**), Et (**1b**), ^{n}Pr (**1c**), ^{i}Pr (**1d**)), [Cp*RuCl(μ_2-S^{i}Pr)$_2$RuCp*(OH$_2$)]OTf (**1e**; OTf = OSO$_2$CF$_3$), and [Cp*Ru(μ_2-S^{i}Pr)$_3$RuCp*] (**2**) and revealed that these complexes provide unique reaction sites for various stoichiometric and catalytic transformations of terminal alkynes.[2]

Transition metal allenylidene (M=C=C=C<) complexes have attracted a great deal of attention in recent years as a new type of organometallic intermediate.[3] Theoretical studies indicate that the C$_\alpha$ and C$_\gamma$ carbon atoms of allenylidene ligands are electrophilic centers, while the C$_\beta$ carbon atom is nucleophilic.[4] In fact, *stoichiometric* reactions of allenylidene ruthenium complexes with a variety of nucleophiles have been reported, where nucleophiles attack either the C$_\alpha$ or C$_\gamma$ carbon atom in allenylidene ligands to afford Fischer-type carbenes or alkynyl complexes, respectively.[5] In sharp contrast, only a few examples of *catalytic* reactions via allenylidene intermediates have been reported until now.[6,7] As an extension of our study on reactivities of terminal alkynes at the thiolate-bridged diruthenium complexes,[2] we have now found propargylic substitution reactions of propargylic alcohols with a variety of nucleophiles catalyzed by **1**. This provides a new type of catalytic reaction via an allenylidene ruthenium complex as a key intermediate. Preliminary results on this catalytic reaction are described here.

Treatment of 1-phenyl-2-propyn-1-ol (**3a**) in EtOH in the presence of **1a** (5 mol %) and NH_4BF_4 (10 mol %) at 60 °C for 15 min afforded the corresponding ethyl ether (**4aa**) in 88% isolated (95% GLC) yield (Table 1; run 1).[8] Interestingly, the substitution occurred selectively at the propargylic *ipso*-carbon. Neither allenic byproduct nor other regioisomer of **4aa** was observed by GLC and ^{1}H NMR. The reaction at room temperature was completed within 1 h to give **4aa** in 90% GLC yield. Similar thiolate-bridged diruthenium(III,III) complexes (**1b**−**e**) were also effective in the reaction, however, a diruthenium(II,III) complex **2**[9] was ineffective. Noteworthy is that conventional monoruthenium complexes such as [CpRuCl(PPh$_3$)$_2$] (Cp = η^5-C$_5$H$_5$), [RuCl$_2$(dppe)$_2$] (dppe = 1,2-bis(diphenylphosphino)ethane), [RuCl$_2$(PPh$_3$)$_3$], and [RuCl$_2$(*p*-cymene)], which were known to react with propargylic alcohols to produce the corresponding allenylidene complexes (vide infra),[3b,c] did not work at all.[8] When MeOH and ^{i}PrOH were used in place of EtOH, the corresponding methyl and isopropyl ethers (**4ab** and **4ac**) were obtained in 84 and 91% yields, respectively (Table 1; runs 2 and 3).

Reactions of various propargylic alcohols catalyzed by **1a** have been investigated. Propargylic substitution reactions of 1-monoalkyl- and 1,1-dialkyl-substituted propargylic alcohols (**3c**−**e**) at 60 °C occurred rapidly to afford the corresponding ethers (**4c**−**e**) in high yields, respectively (Table 1; runs 5−7). In contrast, reactions of 1,1-diaryl-substituted propargylic alcohols (**3f** and **3g**) were sluggish under identical conditions, prolonged time being required to produce the diaryl-substituted ethers (**4f** and **4g**) in moderate yields (Table 1; runs 8 and 9). On the other hand, when the reactions of **3a** with 5 equiv of chiral alcohols were carried out in ClCH$_2$CH$_2$Cl at 60 °C for 1 h, a mixture of two diastereomeric isomers was obtained in moderate to high yields with the isomer ratio of ca. 1:1 (Table 1; runs 11−14).

To elucidate the mechanism of the propargylic *ipso*-substitution, the following stoichiometric and catalytic reactions were investigated. Reaction of **1a** with 1 equiv of **3g** in the presence of NH_4BF_4 in EtOH at room temperature for 1 h afforded the allenylidene complex [Cp*RuCl(μ_2-SMe)$_2$RuCp*(C=C=C(Tol-*p*)$_2$)]BF$_4$ (**5a**) in 84% yield, which was unambiguously characterized by X-ray crystallography (eq 1).[10] The structure of **5a** is



(1)

essentially the same as that of the previously reported allenylidene complex [Cp*RuCl(μ_2-S^{i}Pr)$_2$RuCp*(C=C=C(Tol-*p*)$_2$)]OTf[11] (**5b**), which is obtained from **1e** and **3g**. Treatment of **5a** in EtOH at 60 °C for 20 h gave rise to the formation of **4g** in 89% GLC yield. Furthermore, reaction of **3g** with EtOH in the presence of 5 mol % of **5a** at 60 °C for 20 h afforded **4g** in 69% GLC yield. These results indicate that the propargylic substitution reactions of propargylic alcohols with various alcohols proceed via allenylidene complexes such as **5a**.

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(10) Crystallographic data for **5a**·(EtOH)$_2$: C$_{43}$H$_{62}$BClF$_4$O$_2$Ru$_2$S$_2$, fw = 999.48, black, orthorhombic, *C222$_1$* (No. 20), *a* = 9.532(6) Å, *b* = 24.712(8) Å, *c* = 38.47(1) Å, *V* = 9062(7) Å^3, *Z* = 8, *R* = 0.069, R_w = 0.086, GOF = 2.43.

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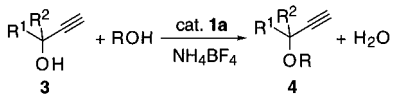
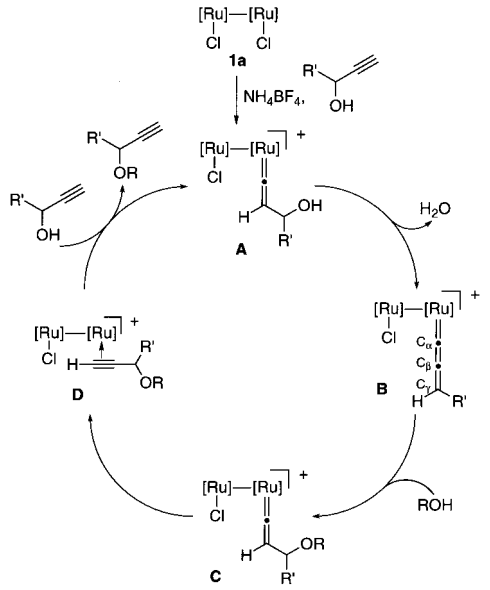
Table 1. Propargylic Substitution Reactions Catalyzed by [Cp*RuCl(μ_2-SMe)$_2$RuCp*Cl] (**1a**)[a]



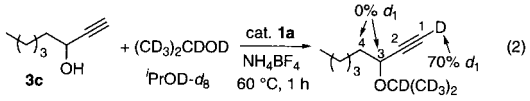
run		R^1, R^2	R	time	yield of **4**[b]	
1	**3a**	Ph, H	Et	15 min	**4aa**	88
2	**3a**	Ph, H	Me	15 min	**4ab**	84
3	**3a**	Ph, H	^{i}Pr	15 min	**4ac**	91
4	**3b**	Fc, H	Et	60 min	**4b**	88
5	**3c**	^{n}C$_5$H$_{11}$, H	^{i}Pr	15 min	**4c**	75
6[c]	**3d**	$-(CH_2)_5-$	Et	30 min	**4d**	57
7[c]	**3e**	$-(CH_2)_4-$	Et	30 min	**4e**	54
8	**3f**	Ph, Ph	Et	20 h	**4f**	62
9	**3g**	*p*-Tol, *p*-Tol	Et	20 h	**4g**	61
10[d]	**3a**	Ph, H	Ph	60 min	**4ad**	65
11[d]	**3a**	Ph, H	R*[1 e]	60 min	**4ae**	80
12[d]	**3a**	Ph, H	R*[2 f]	60 min	**4af**	92
13[d]	**3a**	Ph, H	R*[3 g]	60 min	**4ag**	69
14[d]	**3a**	Ph, H	R*[4 h]	60 min	**4ah**	43

[a] All the reactions of **3** (0.60 mmol) were carried out in the presence of **1a** (5 mol %) and NH_4BF_4 (10 mol %) in alcohol (15 mL) at 60 °C. [b] Isolated yield. [c] At room temperature. [d] Reactions were carried out with **3a** (0.60 mmol) and alcohol (3.0 mmol) in $ClCH_2CH_2Cl$ (15 mL). [e] R*[1] = (*S*)-$CH_2CH(Me)Et$. [f] R*[2] = (*S*)-$CH_2CH(Me)Ph$. [g] R*[3] = (*S*)-$CH(Me)Ph$. [h] R*[4] = (*S*)-$CH(Me)Et$.

Scheme 1

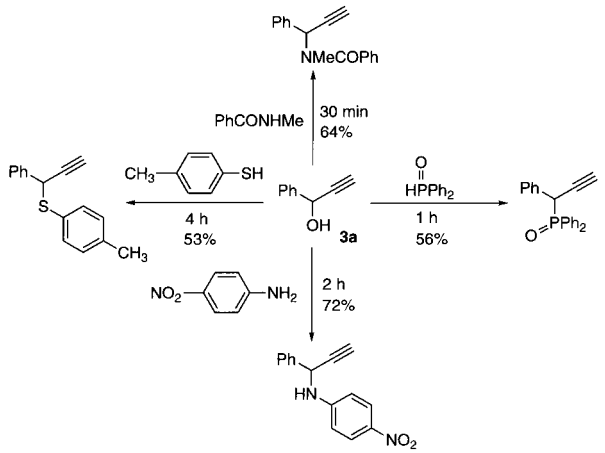


On the basis of these findings a mechanism for this novel catalytic reaction (Scheme 1) is proposed. The initial step is the formation of a vinylidene complex (**A**) from the reaction of **1a** with a propargylic alcohol in the presence of NH_4BF_4. This is followed by conversion of **A** into an allenylidene complex (**B**). Subsequent nucleophilic attack of an alcohol on the C_γ atom in the allenylidene ligand results in the formation of another vinylidene complex (**C**).[12] Complex **C** is then transformed into the η^2-coordinated propargylic ether tautomer (**D**), which liberates a propargylic ether by reaction with a propargylic alcohol to regenerate **A**.[13] The mechanism is strongly supported by the finding that isopropyl-d_7 propargylic ether was obtained in 63% yield with 70% deuterium incorporation at the C-1 position when **3c** was treated with 100 equiv of ^{i}PrOH-d_8 in the presence of **1a** (eq 2).[14,15]



(2)

Scheme 2[a]



[a] All the reactions were carried out with **3a** (0.60 mmol) and nucleophiles (3.0 mmol) in the presence of **1a** (5 mol %) and NH_4BF_4 (10 %mol) in $ClCH_2CH_2Cl$ (15 mL) at 60 °C.

We extended the propargylic substitution by employing other heteroatom-centered nucleophiles. Typical results are shown in Scheme 2. Amide, amine, thiol, and diphenylphosphine oxide reacted with **3a** in the presence of **1a** to give the corresponding propargylic derivatives in high yields with complete regioselectivities. Thus, propargylic amide, amine, thioether, and phosphine oxide derivatives were directly obtained from **3a**. These catalytic reactions have genuine potential for practical application in organic synthesis. In all cases, allenic byproducts, which were always produced by the classical propargylic substitutions,[16,17a] and other isomers were not observed at all. It is to be noted that nucleophiles are exclusively introduced at the propargylic carbon of **3a**. The Nicholas reaction is known to be effective for propargylic substitution; however, a stoichiometric amount of $Co_2(CO)_8$ is required.[17] Further, several steps are necessary to obtain propargylic derivatives from propargylic alcohols via cationic propargyl complexes $[(propargyl)Co_2(CO)_6]^+$.[17]

In summary, we have found ruthenium-catalyzed propargylic substitution reactions of propargylic alcohols with various nucleophiles to produce propargylic derivatives in high yields with complete regioselectivities. Further work is currently in progress aimed at the elucidating the detailed reaction mechanism, broadening the scope of the catalytic substitution, and developing an enantioselective version.

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Supporting Information Available: Experimental procedures and spectral data for all of the new compounds, and crystallographic data for **5a** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) The incorporation of deuterium was quantitatively analyzed by both ^{1}H and ^{2}H NMR. See Supporting Information for experimental details.

(15) No exchange of the terminal proton of **4c** with deuterium occurred in ^{i}PrOD-d_8 in the presence of **1a** and NH_4BF_4 under the same reaction conditions. This result indicates that propargylic alcohols do not exchange the terminal proton via a vinylidene intermediate in these reactions.

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