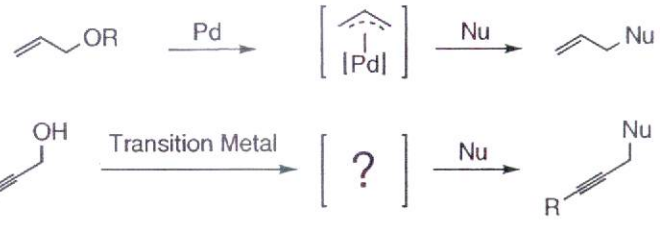
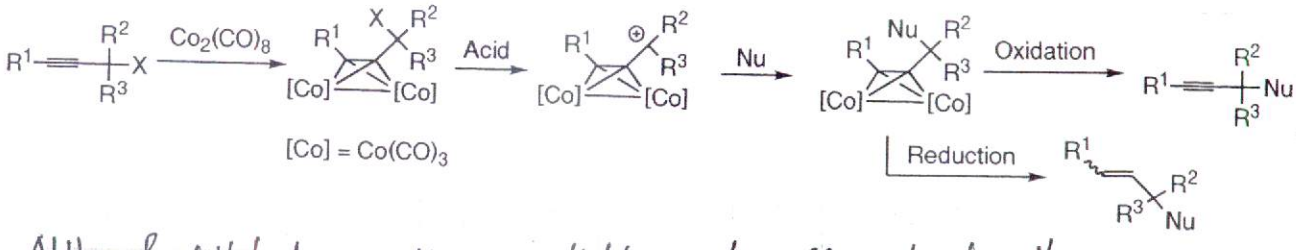
04/10/27 Y. Suto

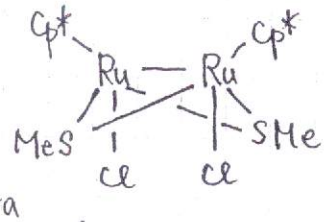
Catalytic Propargylic Alkylation



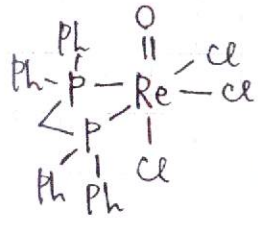
Both allylic substitution and propargylic substitution reactions are thought to be one of the most powerfull carbon-carbon formation reactions. The allylic substitution reactions has been explored extremely. In sharp contrast, much less attention has been paid to the catalytic propargylic substitution reactions. The Nicholas reaction has been known to be effective for propargylation by using stoichiometric amount of $Co_2(CO)_8$.



Although Nicholas reaction is reliable and well explored, there are several draw backs. Stoichiometric amount of $Co_2(CO)_8$ and several steps are required to obtain substituted product from simple propargyl alcohols or halides. Recently two kinds of catalytic propargyl substitution reactions have been reported, one is catalyzed by thiolate bridged diruthenium complex and the other by rhenium(V)-oxo complex.

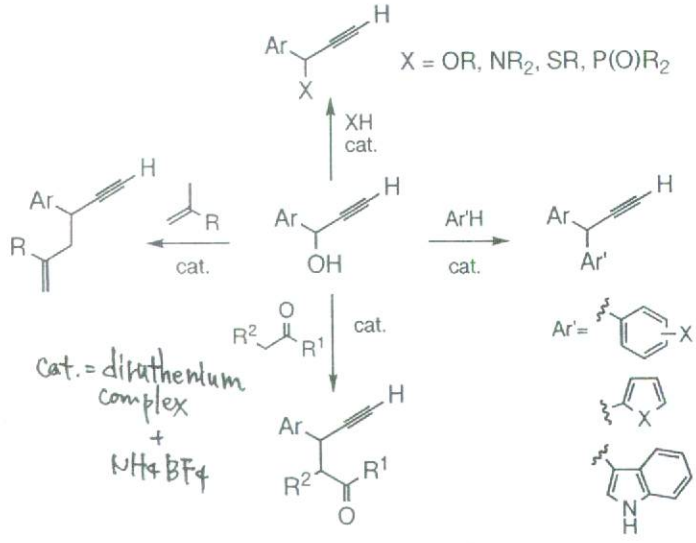


S. Uemura
M. Hidai et.al.



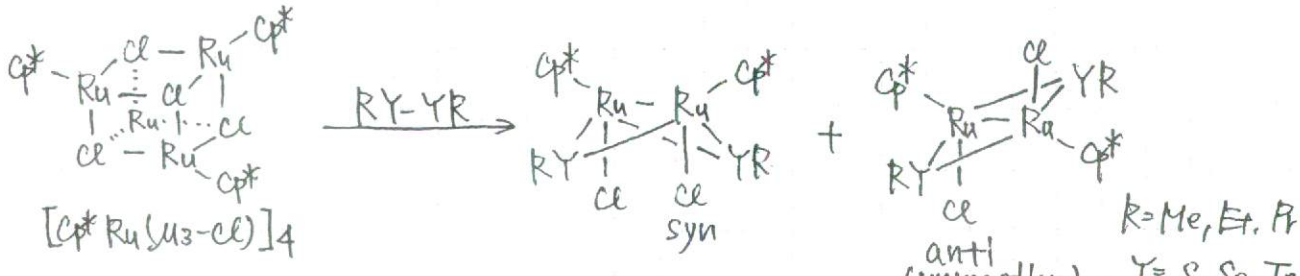
F.D. Toste et.al.

Thiolate-Brided Diruthenium complex



From 2000, ruthenium catalyzed propargylic substitution reactions has been reported by S. Uemura and M. Hidai et.al. These reactions proceed under mild conditions. (rt. ~ 60°c, slightly acidic)

Many kinds of nucleophiles can be used.



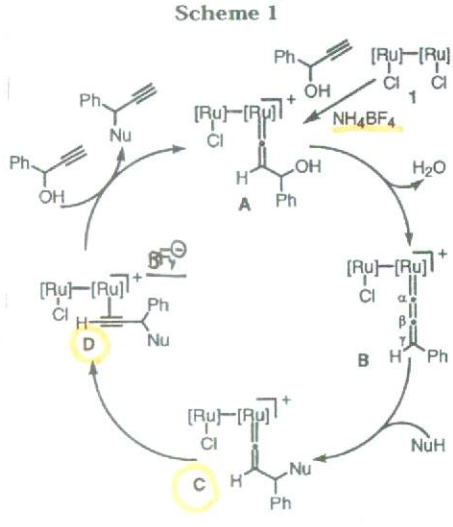
$[Cp^*Ru(\mu_3\text{-}Cl)]_4$

R = Me, Et, Pr

Y = S, Se, Te

The catalysts, diruthenium complexes can be easily prepared from $[Cp^*Ru(\mu_3\text{-}Cl)]_4$ in good to moderate yield.

Proposed mechanism



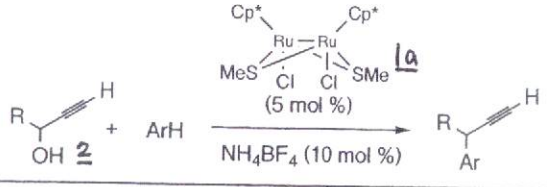
The catalytic cycle can be separated to 3 parts.

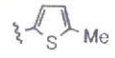
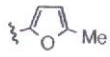
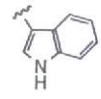
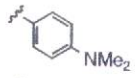
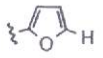
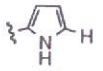
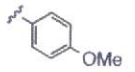
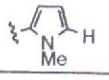
1) The formation of allenylidene complex (key intermediate) with dehydration.
2) Nucleophilic addition. The Cα and Cγ of C3 unit are electrophilic sites.
3) Isomerization from vinylidene complex to alkyne complex and ligand exchange. Usually vinylidene complexes are more stable than alkyne complexes. So this isomerization/ ligand exchange step is probably most problematic.

J. AM. CHEM. SOC. 2002, *124*, 11846−11847

Ruthenium-Catalyzed Propargylation of Aromatic Compounds with Propargylic Alcohols

Yoshiaki Nishibayashi,† Masato Yoshikawa,† Youichi Inada,† Masanobu Hidai,*,‡ and Sakae Uemura*,†



Entry	R	Ar	Yield (%)	Entry	R	Ar	Yield (%)
1	Ph		85	9	Ph		86
2	*p*-Me-C_6H_4		83				
3	*p*-F-C_6H_4		70	10	Ph		52
4	PhCH=CH_2		59				
5	Cyclohexyl		61	11	Ph		50
6	Ph		68				
7	Ph		67	12	Ph		38
8	Ph		94				

[a] All of the reactions of **2** (0.60 mmol) with heterocyclic compound (6.00 mmol) were carried out in the presence of **1a** (0.03 mmol) and NH_4BF_4 (0.06 mmol) in $ClCH_2CH_2Cl$ (15−30 mL) at 60 °C for 1 h. [b] Isolated yield. [c] GLC yield.

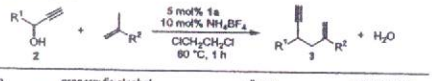
- The first example of the direct reaction of allenylidene ligand with aromatic compounds.
- The reaction occured selectively at γ-position of allenylidene complex.
- In entry 1 to 9 propargylation occurred selectively at the α-position of heterocyclic rings, and the reaction of indol with **2** afforded β-propargylated indole with complete selectivity.

J. AM. CHEM. SOC. 2003, *125*, 6060−6061

Ruthenium-Catalyzed Carbon−Carbon Bond Formation between Propargylic Alcohols and Alkenes via the Allenylidene-Ene Reaction

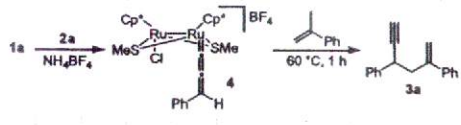
Yoshiaki Nishibayashi,† Youichi Inada,† Masanobu Hidai,*,‡ and Sakae Uemura*,†

Table 1. Reaction of Propargylic Alcohols (**2**) with Alkenes in the Presence of **1a**[a]



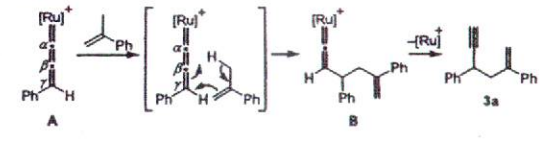
run	propargylic alcohol	alkene	yield of **3**, %[b]
1	**2a**, R^1 = Ph	R^2 = Ph	**3a**, 46 (34)[c]
2	**2b**, R^1 = *p*-MeC_6H_4	R^2 = Ph	**3b**, 56
3	**2c**, R^1 = *p*-$MeOC_6H_4$	R^2 = Ph	**3c**, 13
4	**2d**, R^1 = *p*-ClC_6H_4	R^2 = Ph	**3d**, 27
5	**2e**, R^1 = *p*-FC_6H_4	R^2 = Ph	**3e**, 42
6	**2a**, R^1 = Ph	R^2 = *p*-MeC_6H_4	**3f**, 50
7	**2b**, R^1 = *p*-MeC_6H_4	R^2 = *p*-MeC_6H_4	**3g**, 67
8	**2c**, R^1 = *p*-$MeOC_6H_4$	R^2 = *p*-MeC_6H_4	**3h**, 40
9	**2d**, R^1 = *p*-ClC_6H_4	R^2 = *p*-MeC_6H_4	**3i**, 35
10	**2e**, R^1 = *p*-FC_6H_4	R^2 = *p*-MeC_6H_4	**3j**, 60
11	**2a**, R^1 = Ph	R^2 = *p*-ClC_6H_4	**3k**, 30

[a] All the reactions of **2** (0.50 mmol) with α-methylstyrene (10 mmol) were carried out in the presence of **1a** (5 mol %) and NH_4BF_4 (10 mol %) in $ClCH_2CH_2Cl$ (12 mL) at 60 °C for 1 h. [b] Isolated yield. [c] At room temperature for 1 h.



The reaction of **2a** with α-methyl styrene in the presence of 5 mol% **4** afforded **3a** in 90% GLC yield. This result indicate the reaction should proceed via allenylidene intermediate.

Scheme 1



Scheme 2

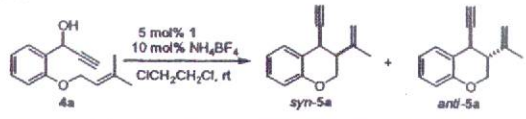
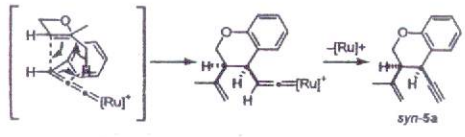


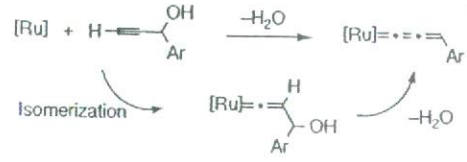
Chart 2

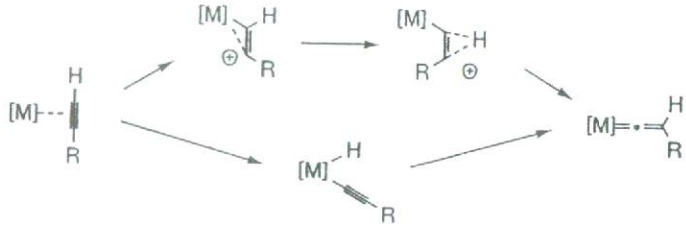


The use of complexes bearing sterically more demanding groups dramatically increased the diastereoselectivity.

Mechanism more detail

Formation of allenylidene complex.

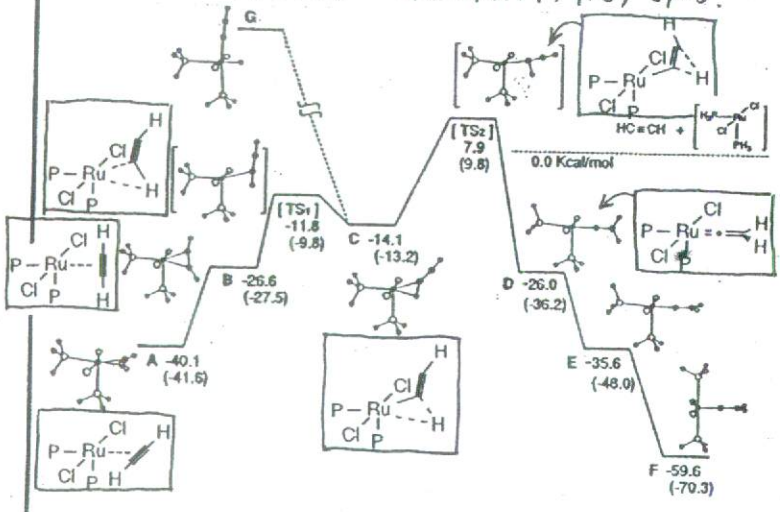




The isomerization of terminal alkynes to vinylidene complexes has been shwon to occur by two alternative pathways. Several groups have studied and reported about these two pathways.

Ab initio molecular orbital simulation about Ru(II) complex.

Y. Wakatsuki et.al. JACS, 1994, 116, 8105.



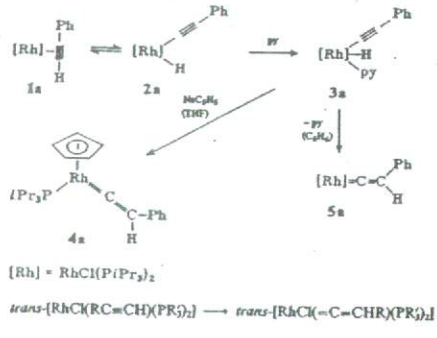
$RuCl_2(PH_3)_2 + H-C\equiv C-H \longrightarrow Cl_2Ru(PH_3)_2(=C=CH_2)$

In the case of Ru(II) complex, 1,2-migration seems more plausible.

To the formation of Ru(IV)(H)(C≡CH) high activation energy is required (C → G) and it is very unstable.

For Rh(I) and Ir(I) complexes, 1,3-hydrogen migration is more plausible.

H. Werner et.al. Angew. Chem. Int. Ed. 1985, 24, 406.

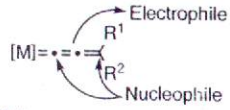


An equilibrium between the alkyne complex 1a and the alkynyl (hydrido) complex 2a exist in solution. On addition of pyridine this equilibrium is completely sifts to the right.

3a is rather labile in solution and react in benzene at rt by elimination of pyridine to produce 5a

Generally low oxidation state metal complexes such as Rh(I) and Ir(I) seem to isomerize via 1,3-migration. In the case of thiolate-bridged diruthenium complex, the oxidation state of Ru is 3, and usually Ru(II) or Ru(III) complexes are isolated. → 1,2-Migration is more plausible.

Reactivity and regioselectivity of allenylidene complexes



A series of theoritical calculations on allenylidene complexes involving several metallic fragments have now been reported.

While the allenylidene fragments are σ-donor-π-acceptor ligands, they are stronger π-acceptor than σ-donor, so that there is a net transfer of 0.4 ~ 0.5 e to them.

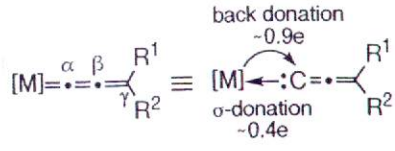


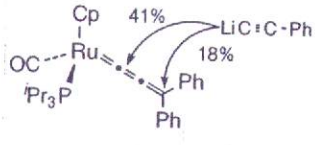
Table 1. LUMO and HOMO distribution and net charges of the allenylidene chain on half-sandwich Ru^{II} and Os^{II} complexes

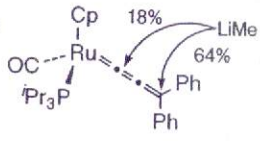
Model	HOMO (%) C_α	C_β	C_γ	LUMO (%) C_α	C_β	C_γ	Net charges C_α	C_β	C_γ
$[Ru(\eta^5\text{-}C_9H_7)(PH_3)_2]^+$	3	21	0	20	6	34	−0.352	−0.151	−0.048
$[Ru(\eta^5\text{-}C_9H_7)(CO)(PH_3)]^+$	4	21	0	24	4	37	−0.267	−0.118	0.033
$[Ru(\eta^5\text{-}1,2,3\text{-}Me_3C_9H_4)(CO)(PH_3)]^+$	4[a]	21[a]	0[a]	23	4	36	−0.281	−0.118	0.023
$[Ru(\eta^5\text{-}C_5H_5)(CO)(PH_3)]^+$	[b]	20	[b]	23	6	31	−0.36	−0.13	−0.05
$[OsCl(\eta^5\text{-}C_5H_5)(PH_3)]$	4	22	0	24	5	30	−0.46	−0.07	−0.17
$[Os(\eta^5\text{-}C_5H_5)(PH_3)_2]^+$	4	25	0	24	5	31	−0.41	−0.10	−0.15
$[Os(\eta^5\text{-}C_5H_5)(CO)(PH_3)]^+$	5	23	0	28	3	33	−0.33	−0.08	−0.09

[a] Next HOMO. – [b] $C_\alpha + C_\gamma = 6\%$.

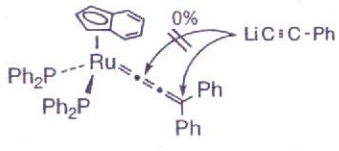
The C_β atom is Nucleophilic site

The LUMO distribution along the C_3 unit is similar, regardless of the nature of metal (Ru, Os) and the auxiliary ligands. (C_α, 20~30%, C_γ, 30~40%)
Electrophilic centers located at the C_α and C_γ.





The regioselectivity of nucleophilic additions seems to be controled by nucleophiles.



Also the regioselectivity of the nucleophilic additions being highly dependent on the steric property of the ancially ligands.

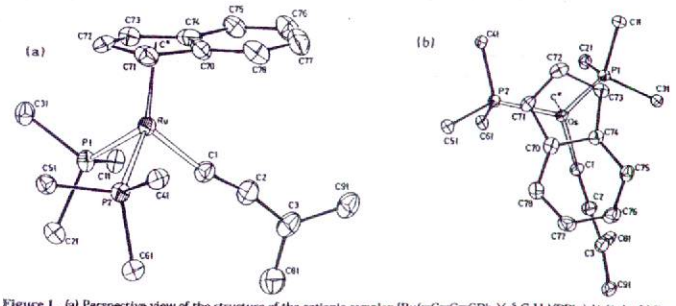
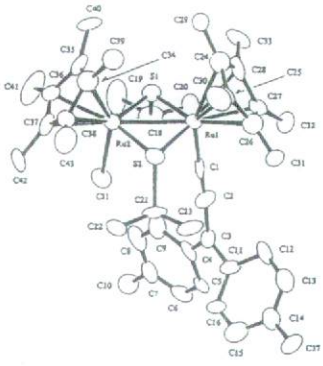
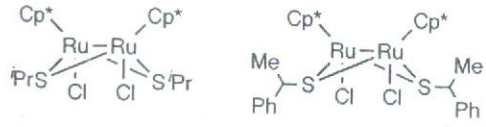
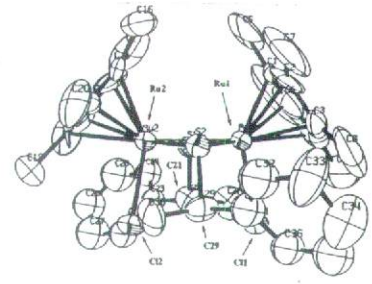


Figure 1. (a) Perspective view of the structure of the cationic complex $[Ru(=C=C=CPh_2)(\eta^5\text{-}C_9H_7)(PPh_3)_2]^+$ (1a). (b) Top view of the structure of the cationic complex $[Os(=C=C=CPh_2)(\eta^5\text{-}C_9H_7)(PPh_3)_2]^+$ (3). For clarity, aryl groups of the triphenylphosphine ligands are omitted (C* = centroid of the indenyl ring).







In the case of thiolate bridged diruthenium complexes nucleophilic additions were observed at only Cr position, probably due to steric hindrance around Cα.

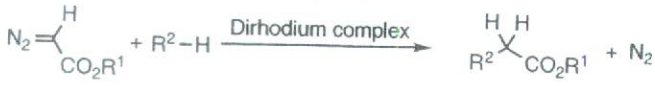
About Ru-Ru bond. Charge transfer from one Ru to the other.

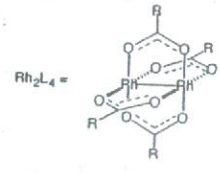
The ease of the charge transfer from one Ru atom to the other in the complexes may be one of the important factor in promoting a key ligand exchange step for these catalytic reactions.

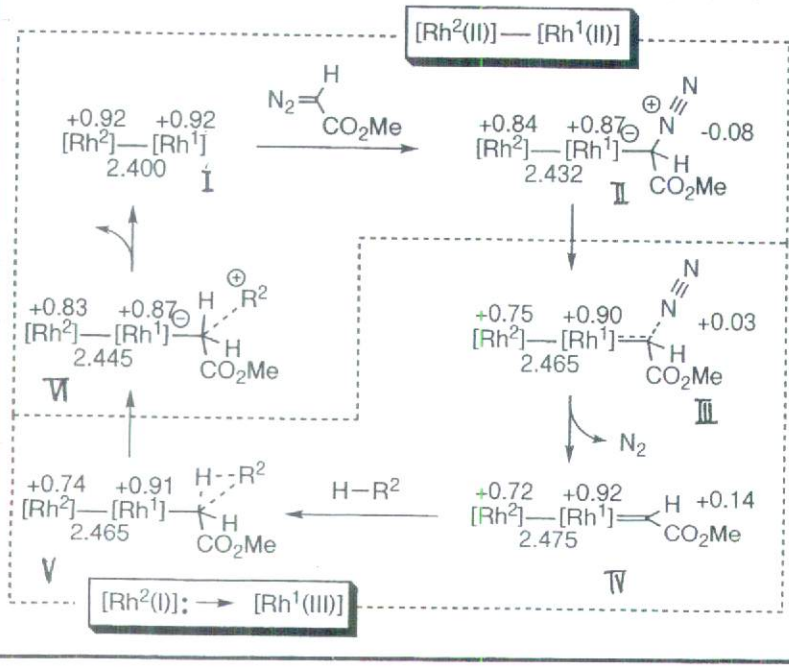
The example of the charge transfer in bimetal complex

E. Nakamura et.al. JACS, 2002, 124, 7181

Using computational method, they explained the mechanism of C-C-bond formation reaction between diazo compound and alkane catalyzed by dirhodium tetracarboxylate.





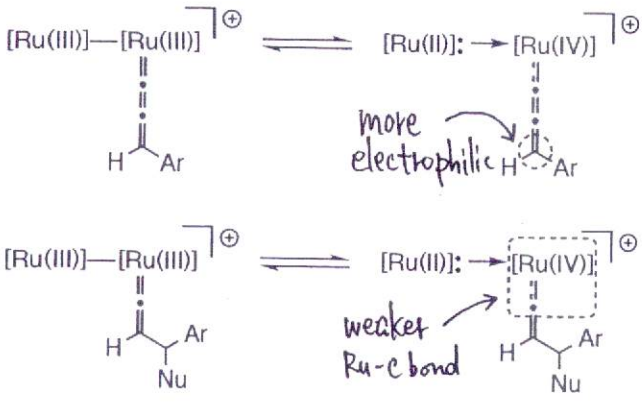


Ⅱ→Ⅲ Charge transfer from Rh¹ to Rh² occur. (due to interaction of electron pair of diazoester with σ*-orbital of Rh-Rh bond?)

Ⅲ→Ⅳ Rh¹ and carbene carbon have relatively high positive charge.

Ⅴ→Ⅵ The formation of C-C bond is enhanced by charge transfer from Rh² to Rh¹

In the case of diruthenium complexes. Organometallics, 2004, 23, 26.

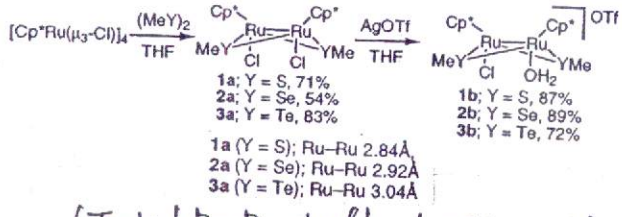


When the charge transfer from one Ru to the other occurs the back donation from Ru to the C3 unit decreases

⇨ The C3 unit in allenylidene complexes become more electrophilic.

⇨ The Ru-C bond in vinylidene complexes become weaker (double → singl), so the isomerization is facilitated.

Experimental data.

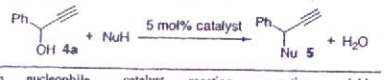


1a (Y = S); Ru–Ru 2.84Å
2a (Y = Se); Ru–Ru 2.92Å
3a (Y = Te); Ru–Ru 3.04Å

(Typical Ru-Ru singl bond : 2.71 ~ 3.02 Å)

The cyclic voltammogram of 1b and 2b revealed reversible waves at +0.58V and +0.53V respectively (Ru(III) → Ru(IV)). In contrast, the cyclic voltammogram of 3b exhibited one irreversible wave at 1.9 V.

Table 1. Propargylic Substitution Reactions of Propargylic Alcohol (4a) with Nucleophiles Using a Neutral Ru Complex as Catalyst[a]

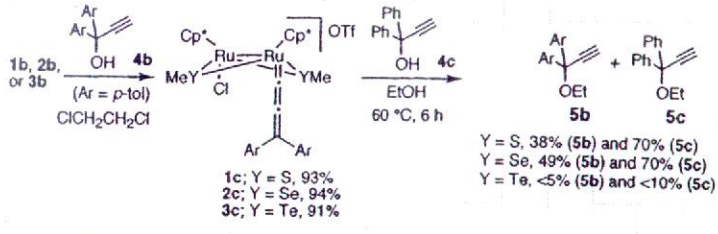


run	nucleophile	catalyst	reaction temp. (°C)	reaction time (h)	yield (%)[b]
1		1a	reflux[c]	3	88
2		2a	reflux[c]	3	95
3		3a	reflux[c]	3	0
4		1a	60[d]	1	81
5	EtOH	2a	60[d]	1	80
6		3a	60[d]	1	2
7		1a	60[f]	1	80
8	$PhNH_2$[e]	2a	60[f]	1	95
9		3a	60[f]	1	0
10		1a	60[f]	3	74
11		2a	60[f]	3	80
12		3a	60[f]	3	0
13		1a	60[f]	1	94
14		2a	60[f]	1	81
15		3a	60[f]	1	2

[a] All the reactions of 4a (0.60 mmol) with nucleophile were carried out in the presence of catalyst (5 mol %) and NH_4BF_4 (10 mol %). [b] Isolated yield. [c] Acetone was used as solvent. [d] Ethanol was used as solvent. [e] Aniline (5 equiv) was used as nucleophile. [f] $ClCH_2CH_2Cl$ was used as solvent. [g] 2-Pyrrolidinone (5 equiv) was used as nucleophile. [h] 2-Methylfuran (10 equiv) was used as nucleophile.

The propargyl substitution reactions were investigated using 1, 2 and 3

Although diruthenium complexes 1 and 2 showed catalytic activity, the reaction didn't proceed almost at all in the presence of 3a and 3b

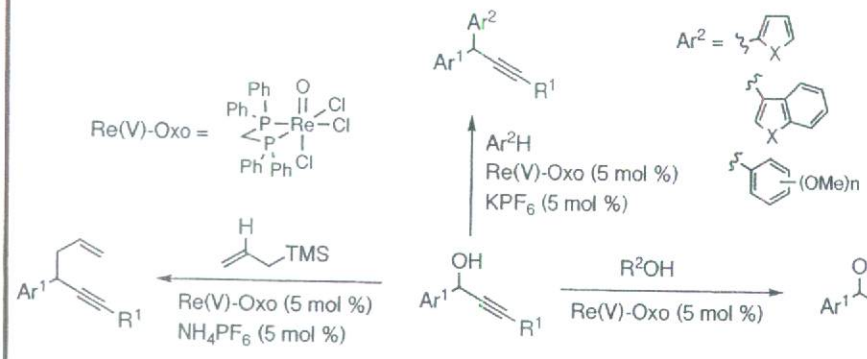


1c; Y = S, 93%
2c; Y = Se, 94%
3c; Y = Te, 91%

Y = S, 38% (5b) and 70% (5c)
Y = Se, 49% (5b) and 70% (5c)
Y = Te, <5% (5b) and <10% (5c)

Allenylidene complexes could be obtained from any thiolate-bridged diruthenium complexes.

Rhenium(V)-oxo complex catalyzed propargyl substitution reactions.



The reaction is tolerant of air and moisture, and in many cases requires only a slight excess of nucleophiles and gives water as the only by product

Proposed mechanism

Major by products when catalyst other than dppm ReO(O)Cl3 was used.

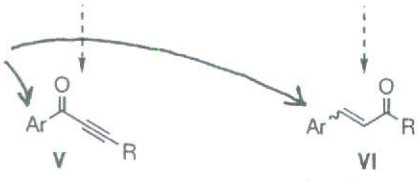
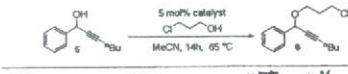


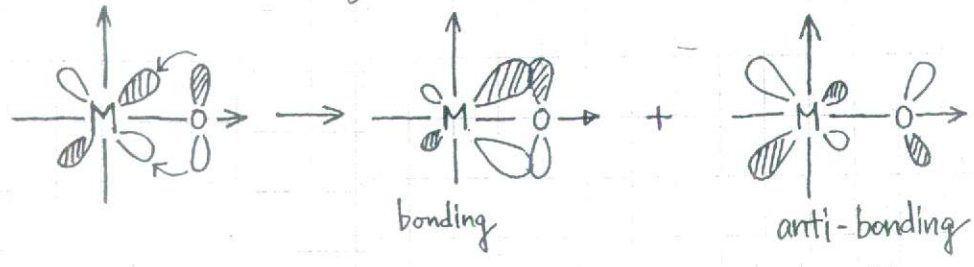
Table 1. Selectivity of Metal-Oxo Catalysts for Propargyl Etherification[a]



entry	catalyst	% VI	% V	% IV
1	$V(O)(acac)_2$	0	29	19
2	$[Mo_2O_2(BINOL)_2](NBu_4)_2$	0	10	15
3	$MoO_2(acac)_2$	20	trace	77
4	(catechol)$ReOCl_3$	75	0	25
5	(dppm)$ReOCl_3$	trace	trace	96

[a] Reaction conditions: 5 mol % catalyst, 3.0 equiv of alcohol, 1 M (substrate) in MeCN. Conversions were determined by ^1H NMR of the crude reaction mixture.

I → II The oxo ligand shows strong trans effect. The ligand exchange on the trans position of oxo ligand should occur smoothly.



The oxo ligand is σ-donor and π-donor ligand. The formation of M–O π bond decreases the electron density of the opposite site of M-O bond. Because of the formation of M-O π* bond the opposite site of M-O bond becomes electrophilic site.

II → III 1,3-transposition of propargylic (and allylic) alcohols are catalyzed by a variety of oxo metal complexes (V, Mo, W, Re)

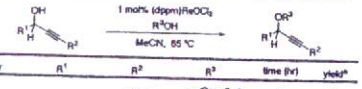
III → IV O=[Re]-O$^{\ominus}$ works as good leaving group.

J. AM. CHEM. SOC. 2003, 125, 6076−6077

A Mild C−O Bond Formation Catalyzed by a Rhenium-Oxo Complex

Benjamin D. Sherry, Alexander T. Radosevich, and F. Dean Toste*

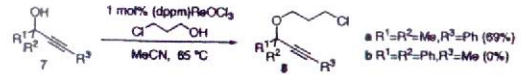
Table 2. Re-Oxo-Catalyzed Etherification of Propargyl Alcohols



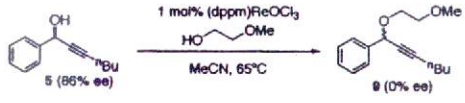
entry	R^1	R^2	R^3	time (hr)	yield[a]
1		*n*-Bu		6	78
2[b]		C_6H_5		14	78
3[b]		$SiMe_3$		6	74
4[b]		$SiMe_3$		8	86
5[c]		*n*-Bu		10	60[d]
6[e]		$-(CH_2)_3OH$	Me–	20	53
7		*n*-Bu		5	79[c]
8		Me		7	85[d]
9		Me		2	86
10		Me		2	89
11[e]		CO_2Et		10	89
12		Me	Me–	4	82
13[f]		Me	Me–	8	77
14		Me		5	79
15		Me		2	85
16		Me		7	78
17[e]		Me		10	80

[a] Reaction conditions: 1 M propargyl alchohol in MeCN, 3.0 equiv of R^3OH. Isolated yield after chromatography. [b] Carried out at 80 °C. [c] Obtained as a 1:1.6 mixture of diastereomers. [d] Obtained as a 1:1 mixture of diastereomers. [e] Run with 5 mol % catalyst. [f] Run with 0.1 mol % catalyst.

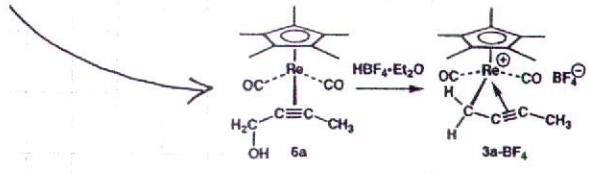
Substitution occured with a wide variety of propargyl alcohol substrates. Acid-labile groups such as acetals, ketals and t-butylcarbamates were not cleaved under the reaction conditions.



Tertiary alcohol 7a readily undergoes propargylic etherification to afford tertiary ether 8a in 69% yield.



Starting from enantiomerically enriched alcohol 5, the Re(V)-oxo catalyzed reaction afforded racemic ester 9. From this result, an alternative mechanism of ionization to produce an achiral propargyl cation can also be envisioned.

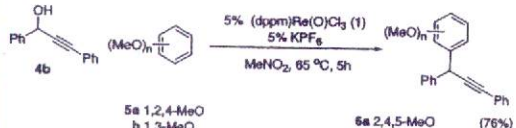


ORGANIC LETTERS
2004
Vol. 6, No. 8
1325−1327

Rhenium-Catalyzed Aromatic Propargylation

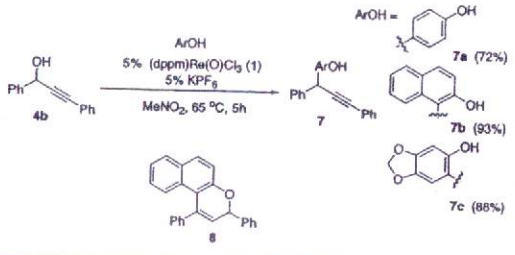
Joshua J. Kennedy-Smith, Lauren A. Young, and F. Dean Toste*

Scheme 2



Aromatic compounds that didn't participate in the ruthenium-catalyzed propargylation such as anisole and 1,3-dimethoxybenzene are excellent nucleophiles in this reaction.

Scheme 3



The propargylation of phenols, catalyzed by a ruthenium complex or protic acid, generally results in the formation of benzopyran (e.g. 8).

Scheme 4