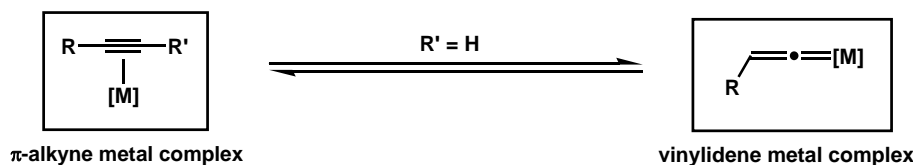


π -alkyne metal complex and vinylidene metal complex in organic synthesis

0. Introduction



Recently, electrophilic activation of alkynes through π -alkyne complex formation has been studied extensively.

ex. Au(I), Au(III), Pt(II), Ru(II), and so on.

More recently, there has been a large number of reactions involving metal vinylidenes as catalytic species.

ex. Cr⁰, Mn⁰, W⁰, Ru(II), Rh(I), Fe(II), and so on.

In this literature seminar, mainly three reports will be introduced in full detail.

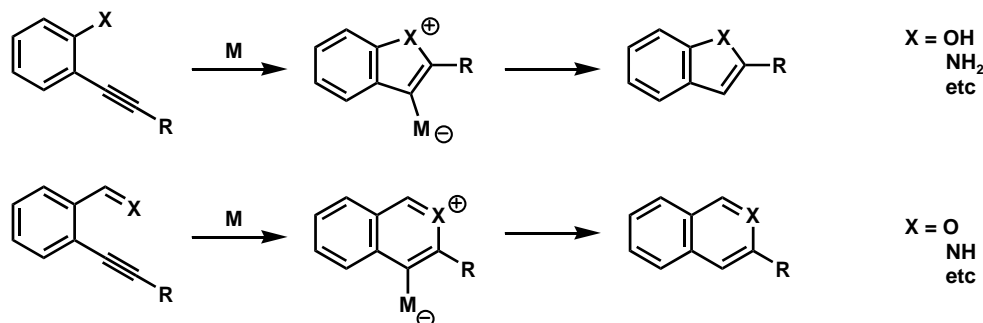
Contents

1. W(CO)₅(thf)-catalyzed generation of carbonyl ylide and tandem reaction with alkene
2. CpRu⁺L₃-catalyzed *anti*-Markovnikov hydration of terminal alkynes
3. Control of π -alkyne and vinylidene complex

1. W(CO)₅(thf)-catalyzed generation of carbonyl ylide and tandem reaction with alkene

generally studied reactions involving π -alkyne metal complex

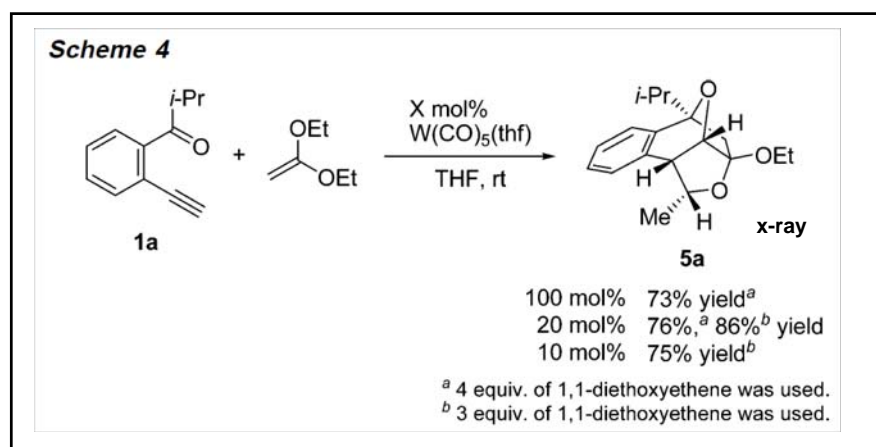
For review of Pt, Au, see ; *Angew. Chem. Int. Ed.* 2007, 46, 3410.
other metals ; *J. Org. Chem.* 2007, 72, 7817.



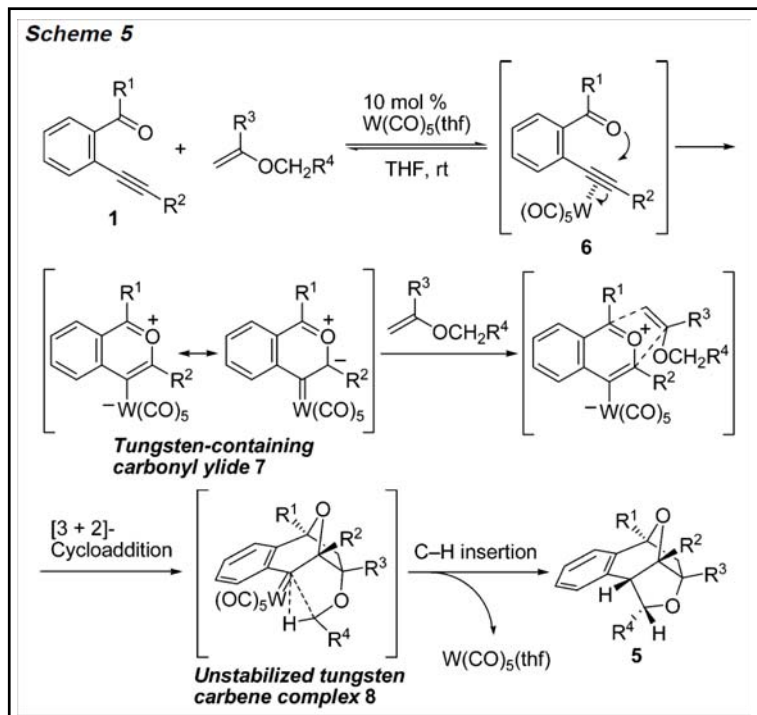
1st. report. (Pd) (pyrrole)
Utimoto et al. *Tetrahedron Lett.* 1981, 22, 4277.

Generation and Reaction of Tungsten-Containing Carbonyl Ylides: [3 + 2]-Cycloaddition Reaction with Electron-Rich Alkenes

Iwasawa et al. *JACS* 2001, 123, 5814. (commun.)
JACS 2005, 125, 2709. (full)



+ postulated mechanism



Scheme 6

+ Tungsten-containing carbonyl ylide

+ Minute mechanistic consideration is presented below

Table 1

R³

+ Not only ketene acetal but also alkyl vinyl ether is applicable

entry 7, 8

+ aryl aldehyde is applicable

entry 8

+ internal alkyne is applicable

Table 1. Reaction of Various *o*-(1-Alkynyl)phenyl Ketones with Electron-Rich Alkenes^a

entry	R ¹	R ²	R ³	R ⁴	time	yield/%		
1	<i>i</i> -Pr	H	1a	OC ₂ H ₅	CH ₃	5a	23 h	75
2	<i>i</i> -Pr	H	1a	H	<i>n</i> -C ₃ H ₇	5b	1 week	50
3	Me	H	1b	OC ₂ H ₅	CH ₃	5c	4 days	84
4	Me	H	1b	H	<i>n</i> -C ₃ H ₇	5d	2 days	74
5	<i>n</i> -Pr	H	1c	OC ₂ H ₅	CH ₃	5e	2 days	81
6	<i>n</i> -Pr	H	1c	H	<i>n</i> -C ₃ H ₇	5f	8 h	77
7 ^b	H	H	1d	H	<i>n</i> -C ₃ H ₇	5g	4 h	94
8	H	Me	1e	H	<i>n</i> -C ₃ H ₇	5h	16 h	69

^a 10 equiv of *n*-butyl vinyl ether and 3 equiv of 1,1-diethoxyethene were used. ^b Including an about 5% yield of an isomeric product concerning the substituent R⁴.

Not all the alkenes have a suitable carbon-hydrogen bond for tungsten-carbenoid intermediate to insert.

It is well known that metal-carbenoid can readily insert into a silicon-hydrogen bond of silanes.

+ silicon trapping of intermediate tungsten-carbenoid

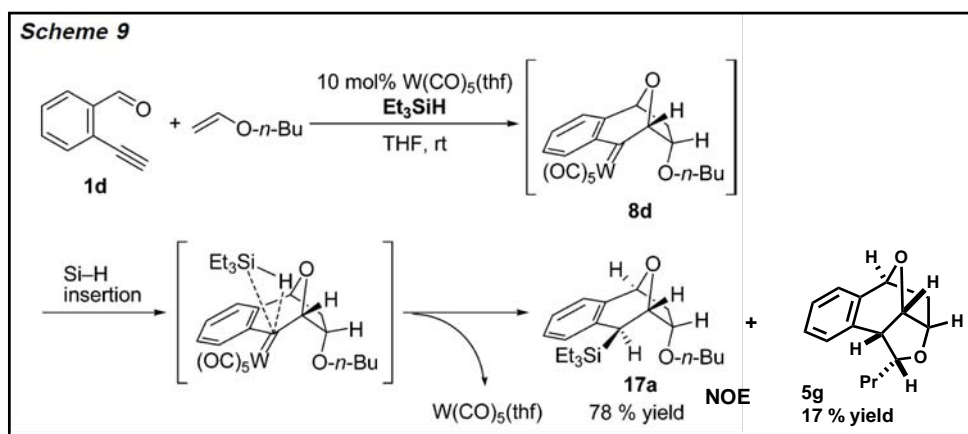


Table 2. Reaction of 1d with Various Alkenes in the Presence of Silanes^a

entry	R	R ₃ SiH	yield/%		ratio 17:5g
			17	5g	
1	O- <i>n</i> -Bu	Et ₃ SiH	78, 17a	17	82:18
2		<i>t</i> -BuMe ₂ SiH	40, 17b	53	43:57
3		Ph ₃ SiH	4, 17c	84	5:95
4		<i>i</i> -Pr ₃ SiH	<3 17d	93	<3:>97
5		EtMe ₂ SiH	85, 17e	6	93:7
6	O- <i>t</i> -Bu	Et ₃ SiH	74, 17f		
7	OSiMe ₃	Et ₃ SiH	70, 17g		
8	CH ₂ SiMe ₃	Et ₃ SiH	59, 17h		
9	Ph	Et ₃ SiH	44, 17i		

^a Except **17i**, all products were obtained as a single stereoisomer, the structure of which was confirmed to be as shown above by the measurement of NOE. In the case of entry 9, a diastereomer concerning the substituent R was produced in a ratio of 98:2.

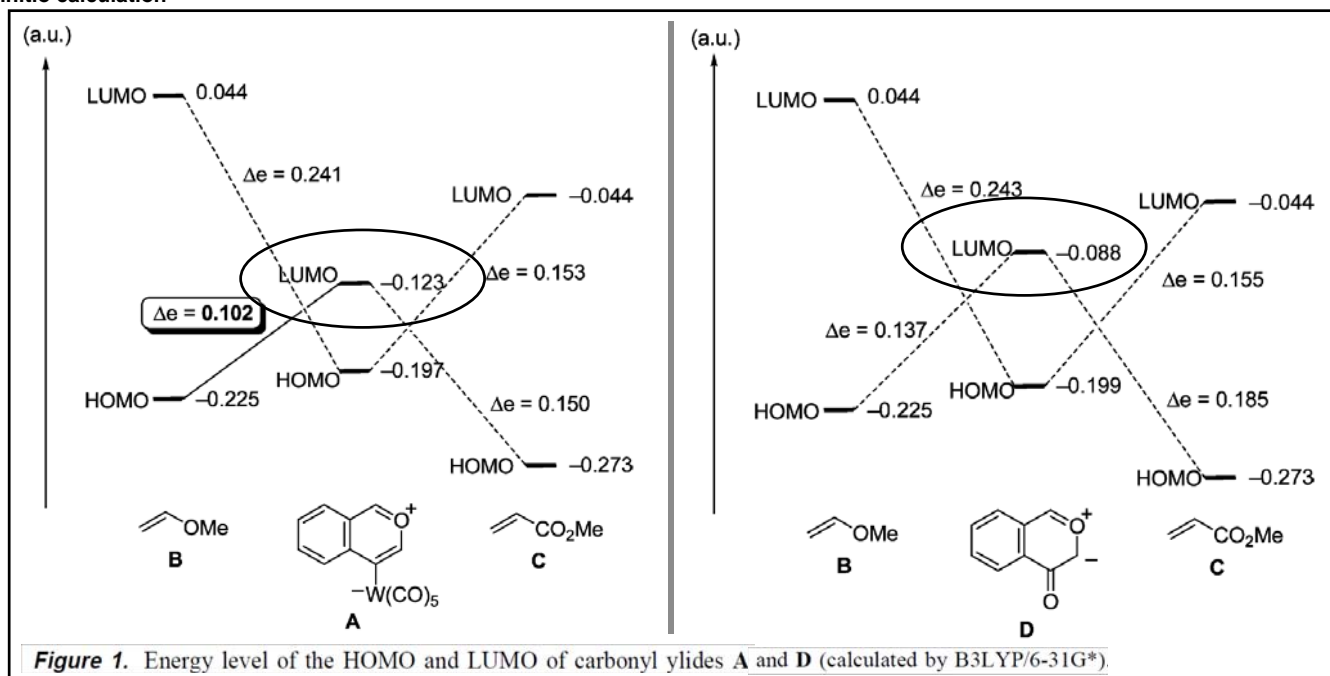
entry 1 - 4
large silane : C-H insertion occurred predominantly.

entry 5
Small EtMe₂SiH was effective.

entry 6 - 9
silyl enol ether, allyl silane, styrene were applicable. → expansion of substrate scope to ones having no C-H bond to insert
1-octene and methyl acrylate : No Rxn.

+ To gain insight into the reactivity of the tungsten-containing carbonyl ylide

Ab initio calculation



(lan12dz basis set was used for the W atom, and the 6-31 basis sets were used for the other atoms)

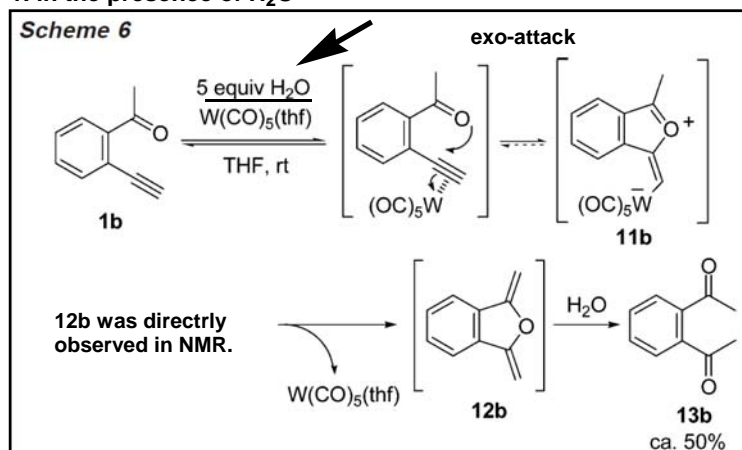
*LUMO of ylide **A** is considerably lower than that of ylide **D**. (probably because of the strong electron-withdrawing nature of the tungsten carbonyl)

normal carbonyl ylide :
react with electron deficient alkene preferentially
tungsten-containing ylide :
react with electron rich alkene preferentially

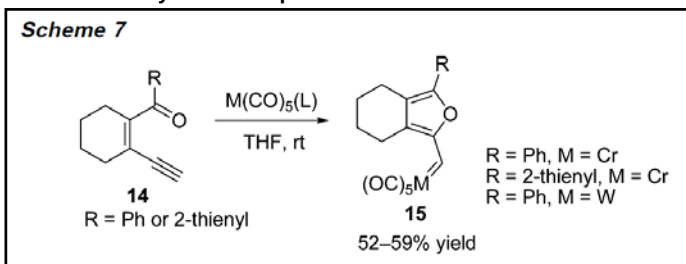
+ Mechanistic consideration

1. in the presence of H₂O

cf. Scheme 6 in page 2
endo-attack



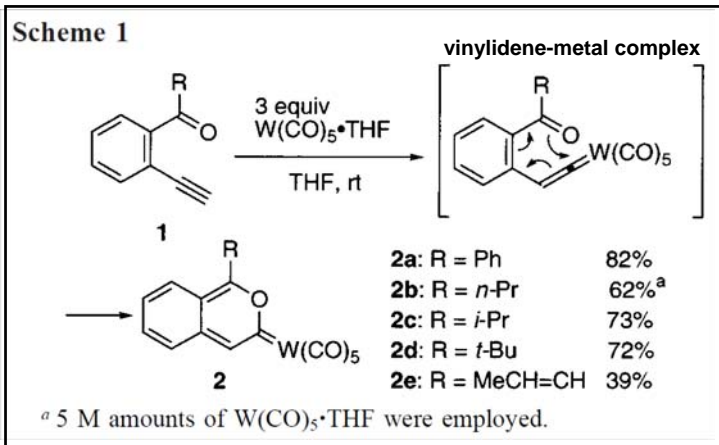
isolation of alkydene complex



Uemura et al. *J. Organomet. Chem.* 2002, 645, 228.

In the presence of H₂O instead of alkene,
13b was obtained probably through 11b.

3. in the absence of alkene & H₂O



Iwasawa et al. JACS 2000, 122, 10226.

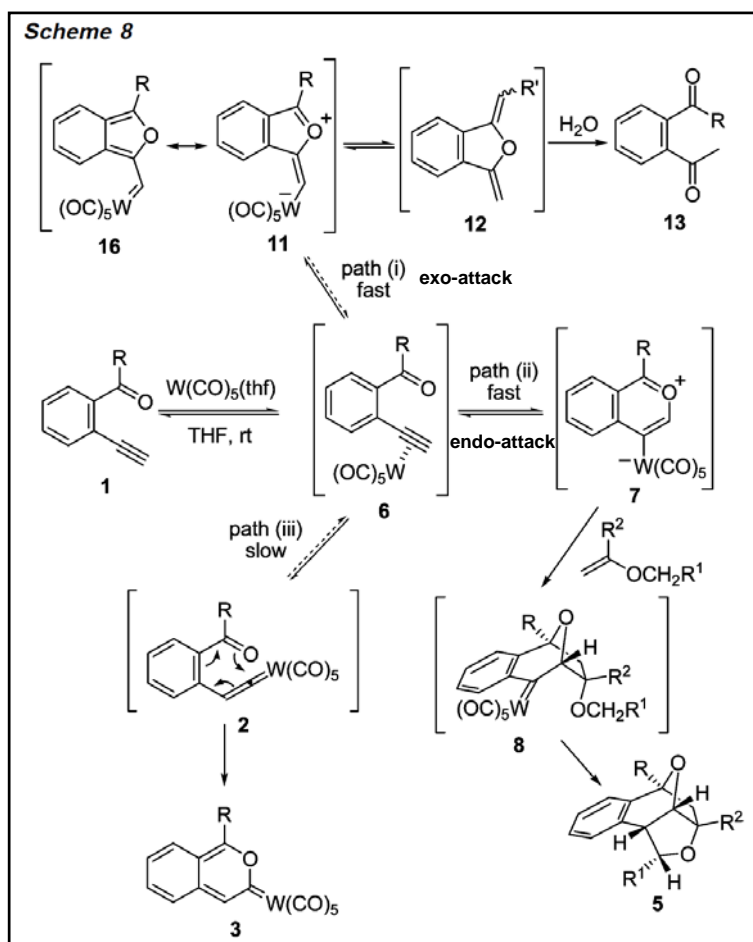
Scheme 1

2 was isolated by silica gel chromatography and characterized by ¹³C NMR (typical carbene carbon δ = 230.9 ppm) and elemental analysis.

In the absence of alkene and H₂O,

2 was obtained probably through metalvinylidene intermediate.

+ Dynamic equilibria to account for these experimental results



+ Path (i) and (ii) would be faster than path (iii).

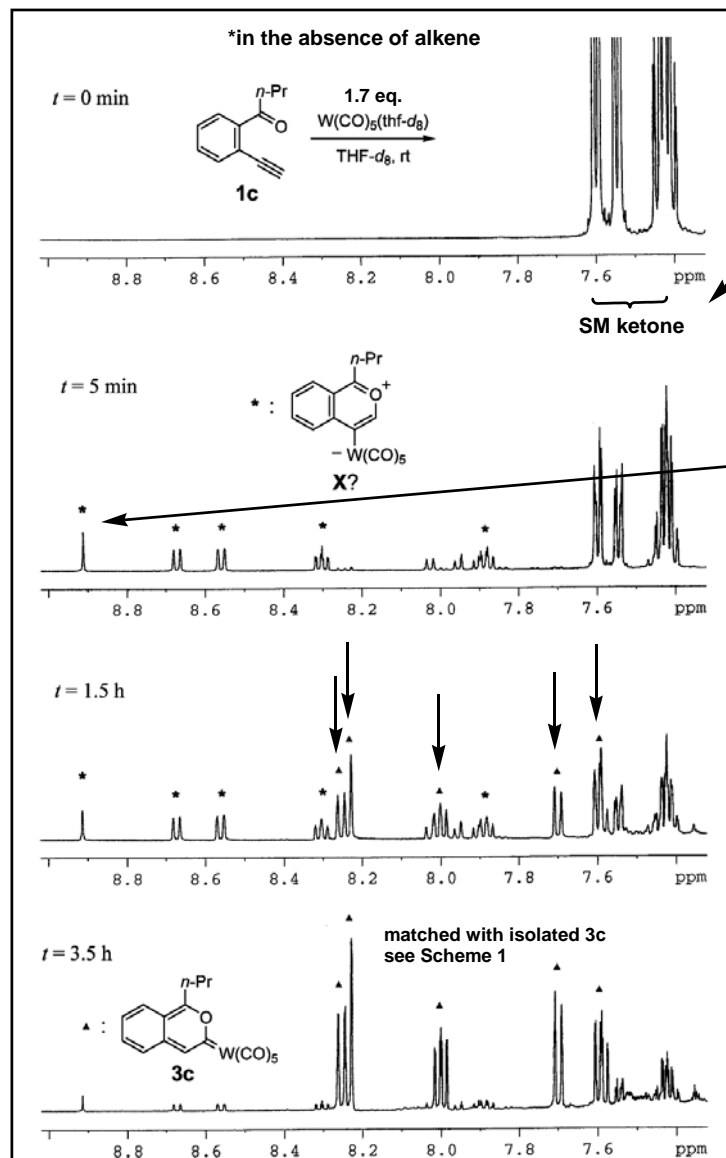
+ Path (i) and path (ii) would be under rapid equilibrium.

+ Therefore, in the presence of a reagent capable of trapping intermediate 11 or 7 (H₂O or alkene), the reaction proceeds through path (i) or (ii).

+ In the absence of such trapping reagents, vinylidene complex 2 would form slowly and to give 3 through an irreversible electrocyclic.

+ Observation of the tungsten-containing carbonyl ylide

1. ¹H NMR time course

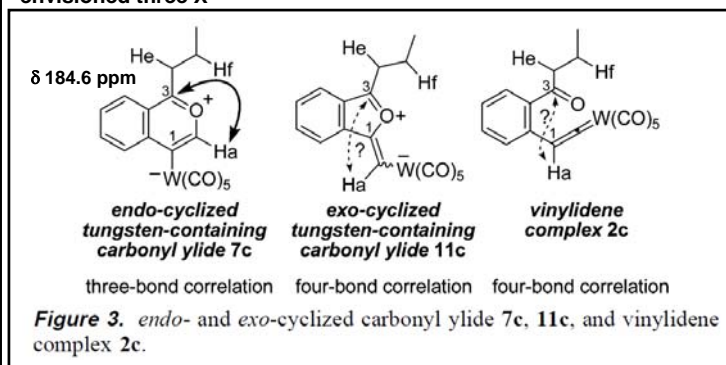


* New species have much lower electron density than the SM ketone

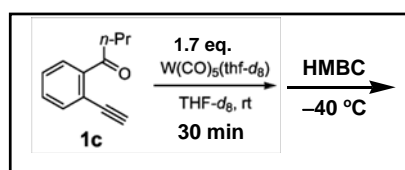
* X disappeared and 3c became a major product after 3.5 h.

* singlet at 8.92 ppm

envisioned three X



2. HMBC

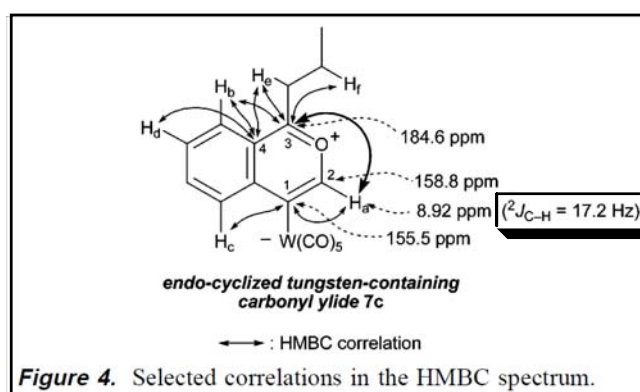
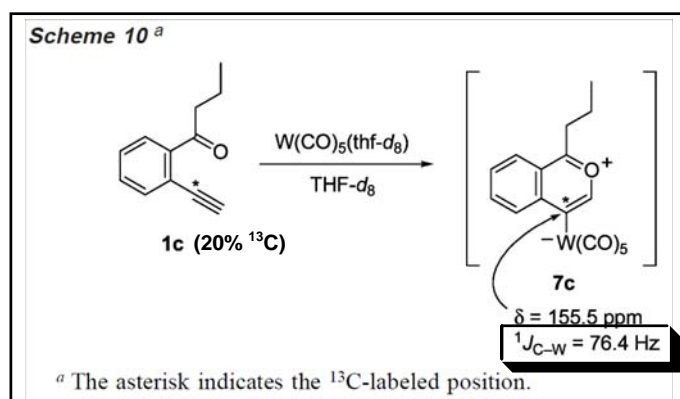


δ 184.6 ppm (¹³C) : correlation with H(e) and H(f) → C 3

C 3 : correlation with singlet at δ 8.92 ppm (¹H) = H(a)

X would be endo-cyclized carbonyl ylide 7c

3. ¹³C-¹⁸³W coupling



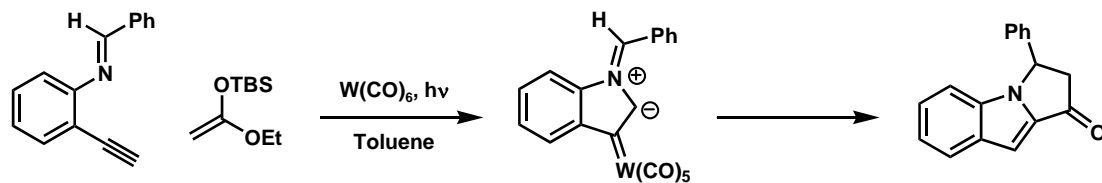
* ¹⁸³W has 1/2 nuclear spin (other isotopes of tungsten have no nuclear spin)

* A set of satellite peaks should be observed in ¹³C NMR spectrum at the carbon directly bonded to tungsten.

* 76.4 Hz (¹J_{C-W}) (C1 - W) in ¹³C NMR spectrum and 17.2 Hz (²J_{C-H}) (Ha - C1) in ¹H NMR spectrum were observed.

: direct bonding between C1 and W

+ Other application

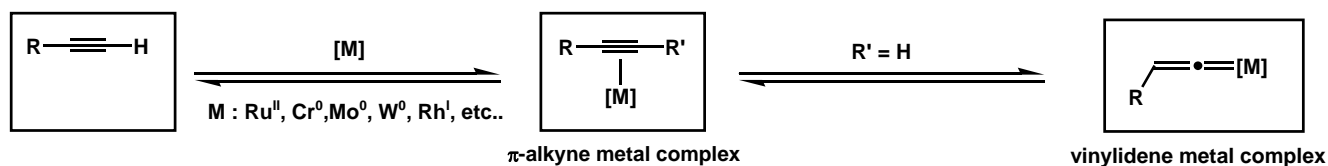


Tungsten-containing azomethine ylide

Iwasawa et al. *JACS* 2002, 124, 11592.

2. CpRu⁺L₃-catalyzed *anti*-Markovnikov hydration of terminal alkynes

* general features of metal vinylidene complex

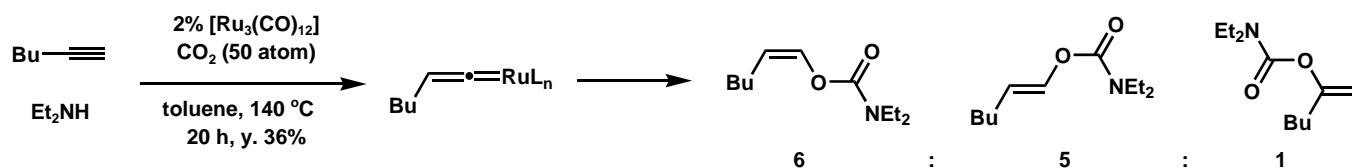


Three types of reactions are commonly investigated.

review ; *Chem. Asian J.* 2008, 3, 164.

1. nucleophilic addition to the α-carbon atom

1st example of a metal vinylidene complex as a catalytic species

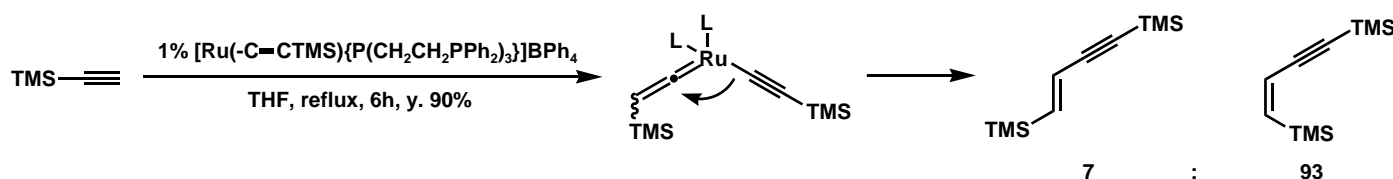


Y. Sasaki, P. H. Dixneuf *J. Chem. Soc. Chem. Commun.* 1986, 790.

other nucleophiles ; carboxylic acid, alcohol, epoxide, carbonyl, thiol, amine, phosphine, enolate, enamine

2. [1,2]-alkyl migration from the metal center to the α-carbon atom

alkyne dimerization

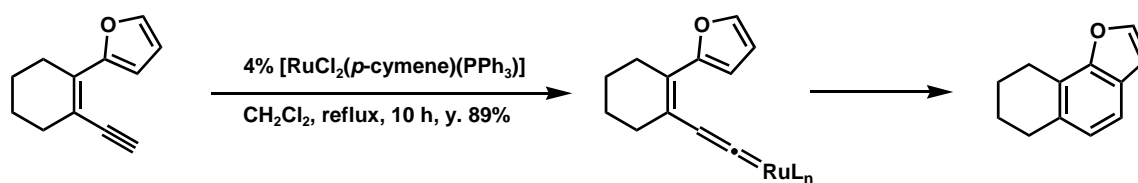


Bianchini et al. *JACS* 1991, 113, 5453.

For earlier work by Yamazaki, see ; *J. Chem. Soc. Chem. Commun.* 1976, 841.

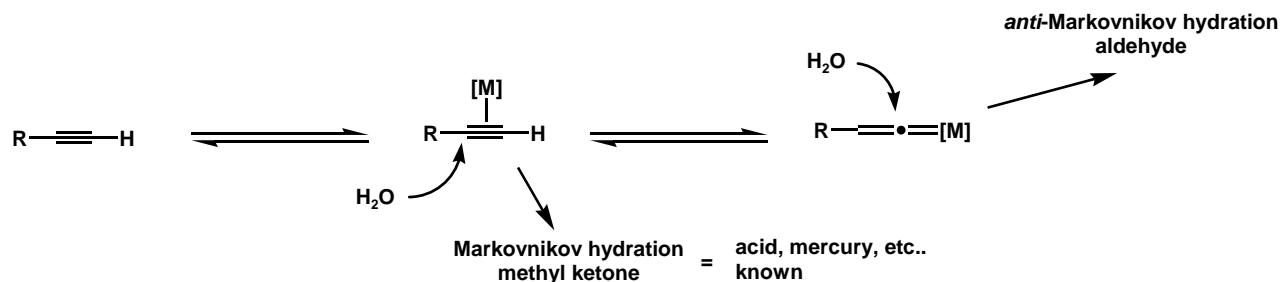
3. Pericyclic reactions

1st example of 6π electrocyclization onto a catalytic vinylidene intermediate

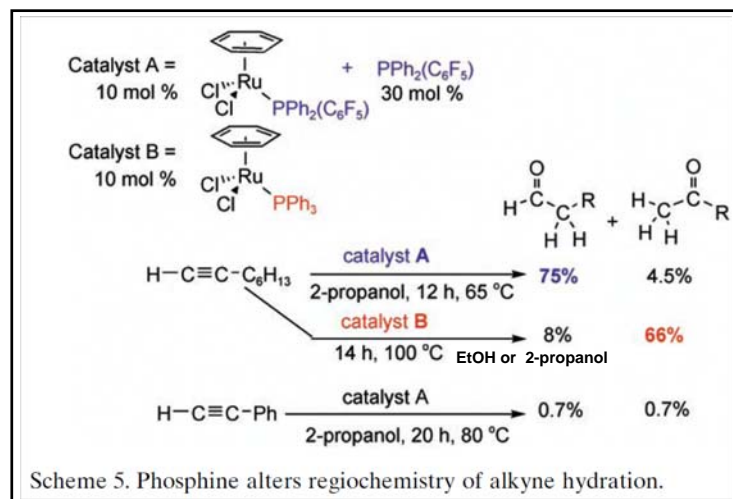


C. A. Merlic, M. E. Pauly *JACS* 1996, 118, 11319.

*CpRu⁺L₃-catalyzed *anti*-Markovnikov hydration of terminal alkynes



1st report : M. Tokunaga, Y. Wakatsuki *Angew. Chem. Int. Ed.* 1998, 37, 2867.



* By tuning phosphine ligand, they could produce aldehyde or ketone.

* not so good selectivity

* high catalyst loading

* Phenylacetylene, *tert*-butylacetylene were not applicable.

Improvement (use of RuCpCl(dppm))

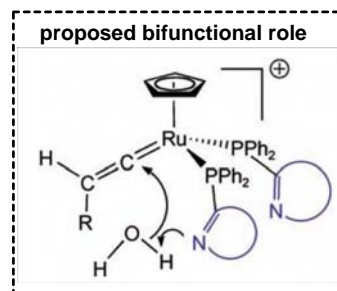
Wakatsuki et al. *Org. Lett.* 2001, 3, 735.

Combined Effects of Metal and Ligand Capable of Accepting a Proton or Hydrogen Bond Catalyze *Anti*-Markovnikov Hydration of Terminal Alkynes**

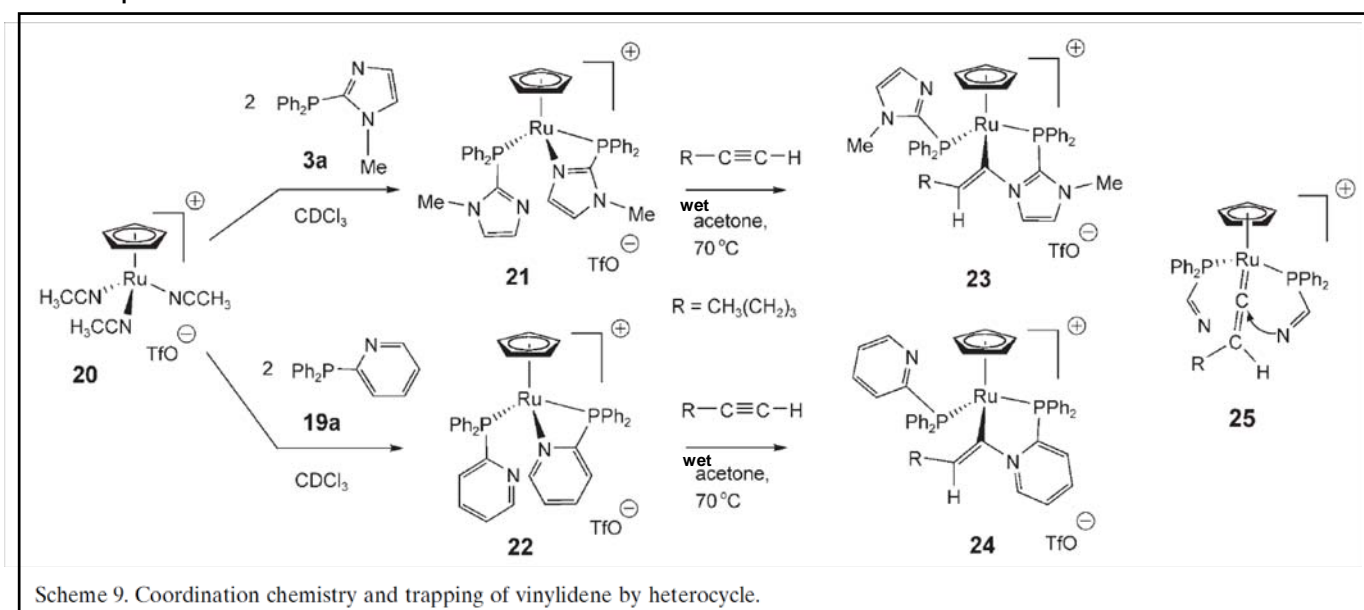
Grotjahn et al. *Angew. Chem. Int. Ed.* 2001, 40, 3884.

JACS 2004, 126, 12232.

Chem. Euro. J. 2005, 11, 7146.



1st attempt

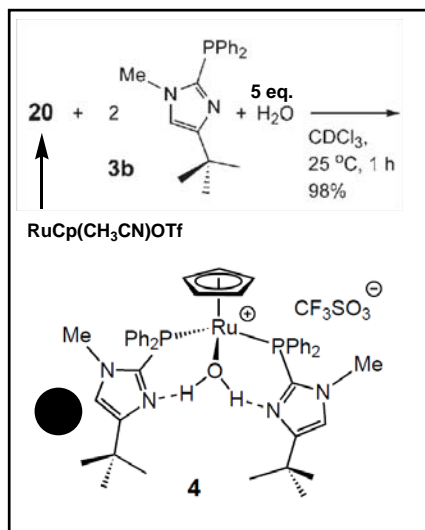


Scheme 9. Coordination chemistry and trapping of vinylidene by heterocycle.

21, 22 : The same ligand is coordinated in two different environments, one chelating, the other not.

The reaction with alkyne didn't afford aldehyde, but 23 and 24. (2D NMR and X-ray)

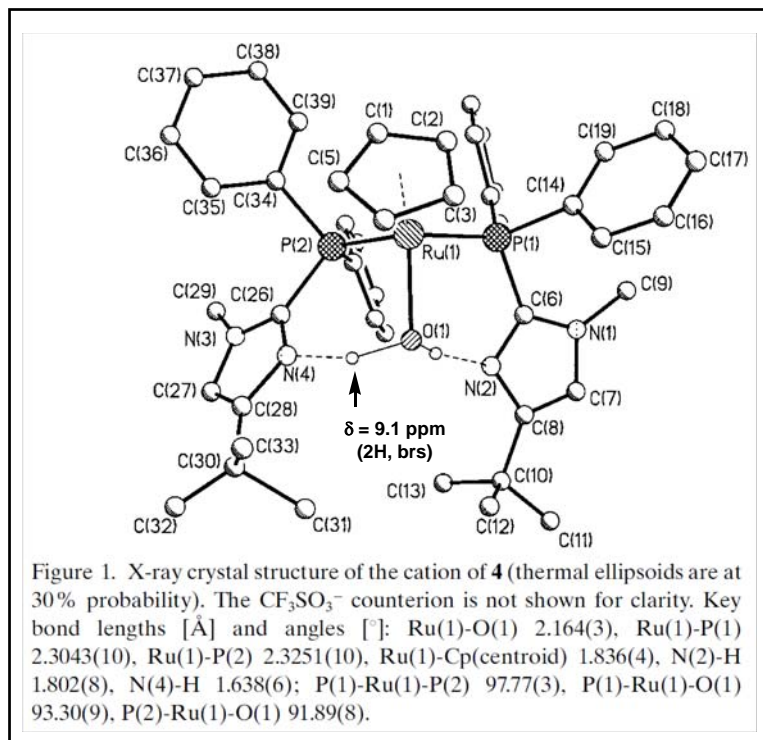
* sterical environment tuning



+ To hinder the direct attack of nitrogen at vinylidene carbon, bulky substituent was introduced.

+ H₂O was incorporated.

+ Two hydrogen bond



* scope and limitations

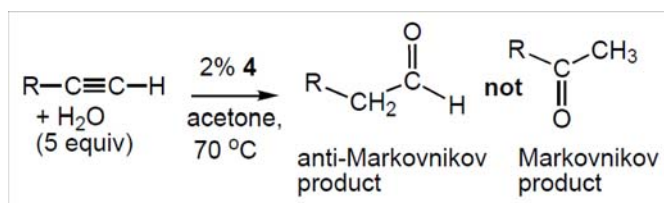
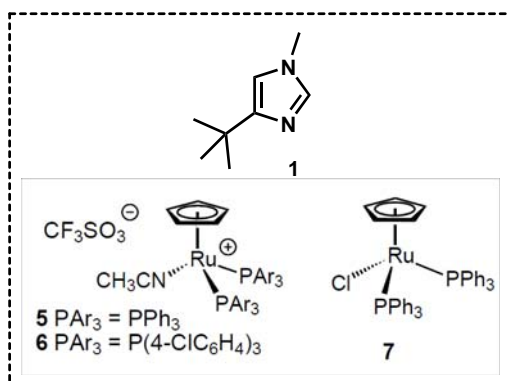


Table 1. Catalysis of alkyne hydration [see Eq. (1)].^[a]

Entry	Catalyst	Alkyne substituent R	Aldehyde yield [%] after reaction time			Selectivity ^[b]
			3 h	21 h	later [h]	
1	4	Bu	39	92	96 [36]	1000
2	4	PhCH ₂ CH ₂	40	88	92 [46]	150
3	4	(CH ₃) ₃ C	3.5	21	91 ^[c]	≥ 130
4	4	Ph	9.6	20	54 ^[d]	135
5	4	Ph ^[e]	24	64	75 [42]	32
6	4	TBSO-CH ₂ ^[f]	28	91	96 [36]	≥ 200
7	4	THPO-CH ₂ ^[g]	35	83	86 [50]	≥ 400
8	4	NC(CH ₂) ₃	34	96	98 [40]	n.d. ^[h]
9	5	Bu	0.1	0.3	n.d.	n.d.
10	6	Bu	0.3	0.5	n.d.	n.d.
11	6 + 1	Bu	< 0.1	< 0.1	n.d.	n.d.
12	6 + Et₃N	Bu	0	0	n.d.	n.d.
13	7	Bu	0.3	1.0	1.2 ^[i]	n.d.

[a] Conditions: 0.5 mmol alkyne, 5 equiv water, 2 mol% catalyst, and (Me₃Si)₄C internal standard in [D₆]acetone (1 mL) heated in a sealed NMR tube in an oil bath (67–72 °C). Yields and products identified by ¹H and in some cases ¹³C NMR data. See Supporting Information for full details. [b] Ratio of aldehyde (value shown) to ketone (assigned value of 1). Authentic sample of ketone added at end of reaction period. See Supporting Information for full details. [c] Yield 49% after 68 h; 91% after an additional 108 h at 88–91 °C. [d] Yield 54% after three additions of 2 mol% **4** and 36–45 h heating each time. [e] Using 10 mol% catalyst with substrate concentration of 0.2M. [f] TBS = (CH₃)₂(*t*Bu)Si. [g] THP = 3,4,5,6-tetrahydropyran-2-yl. [h] n.d. = not determined. [i] After 7 d at 90 °C.

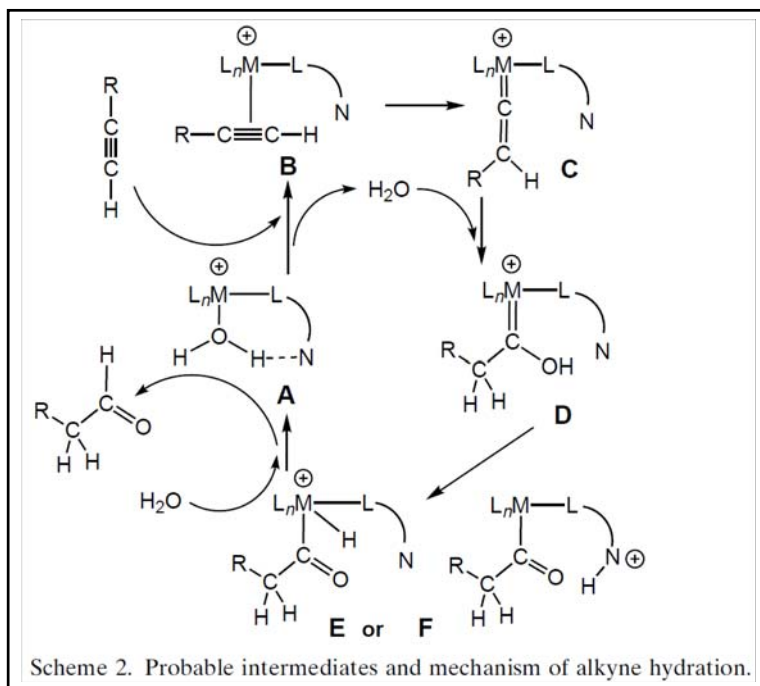


entry 3, 4, 5
tert-Butylacetylene and phenylacetylene were applicable although sluggish reaction

entry 8
Nitrile didn't inhibit the reaction
(Wakatsuki catalyst was inhibited by nitrile.)

entry 11 and 12
Proper placement of imidazole is crucial for efficient catalysis.

* Postulated mechanism



H₂O has to be exchanged to alkyne substrate.

(Two phosphine seemed to stay on the metal because added phosphine did not change the hydration rate)

Imidazole

+ facilitate conversion from B to C ?

+ activate H₂O ? (C to D)

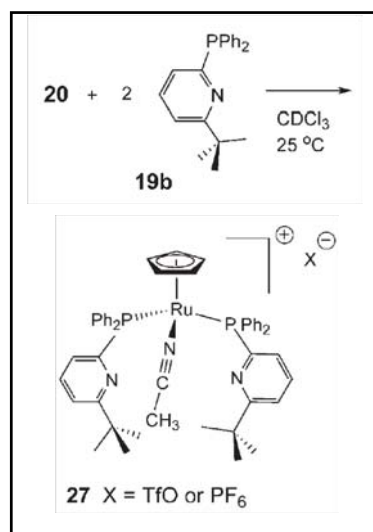
* facilitate conversion from D to E via F (proton shuttle) ?

* stabilize the catalyst by hydrogen bonding ?

so far, not clear

*next report

* JACS 2004, 126, 12232.



reduced hydrogen bonding to open catalytically active site for alkyne binding

entry 3, 4, 5

Phenylacetylene and electron-rich arylacetylene were applicable.

entry 6

Nitrile inhibited the reaction.

entry 10

in situ deprotection

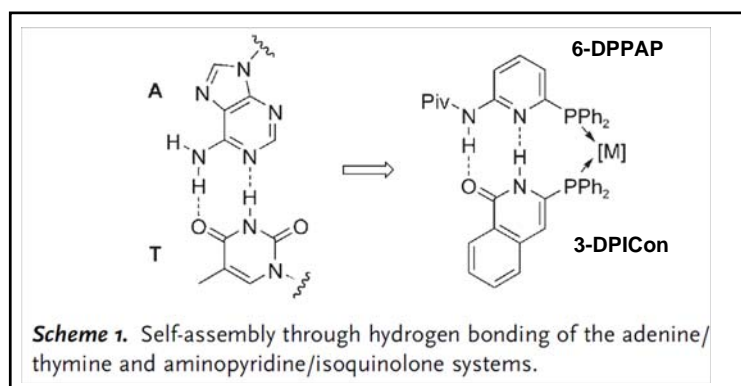
Table 2. Scope of Alkyne Hydration^a

entry	alkyne	aldehyde yields		
		1 h	3 h	later (time)
1	CH ₃ (CH ₂) ₆ C≡CH	55.0	99.9	nd
2 ^b	CH ₃ (CH ₂) ₆ C≡CH	nd	30.2 ^b	98.6 (48 h)
3	C ₆ H ₅ C≡CH	11.8	33.1	99.8 (20 h)
4	4-MeOC ₆ H ₄ C≡CH	14.0	42.7	99.8 (24 h)
5	4-O ₂ NC ₆ H ₄ C≡CH	0.31 ^d	nd	nd
6	N≡C(CH ₂) ₃ C≡CH	3.6	12.0	97.8 (96 h)
7	HC≡C(CH ₂) ₄ C≡CH	47.7 ^c	nd	71.2^c (8 h)
8	THPOCH ₂ C≡CH	26.1	76.2	98.0 (9 h)
9	TsNHCH ₂ CH ₂ C≡CH	nd	97.0 ^e	98.1^e (6 h)
10	CH ₃ C≡CSi(CH ₃) ₃	6.7 ^f	24.3 ^f	100^f (66 h)
11	(CH ₃) ₂ C(OH)C≡CH	nd	nd	80.7^g (168 h)
12	1-ethynylcyclohexene	nd	nd	41.0^{g-h} (168 h)

^a Unless otherwise specified, using **6** (2 mol %), H₂O (5 equiv), acetone, 70 °C, initial alkyne concentration 0.50 M. ^b Room-temperature reaction with 5 mol % catalyst; 30.2% after 5.5 h. ^c Yields of dialdehyde and ynal (double and single hydration products) at 1 and 8 h = 27.9 + 19.8 and 51.6 + 19.6%, respectively. ^d In addition, 2.1% of corresponding alkane and deactivated catalyst. No further reaction seen. ^e Product formed as 1:8 mixture of aldehyde and its cyclized form (*N*-tosyl-2-hydroxypyridine). ^f Product is propanal. ^g Room-temperature reaction. ^h 34.2 and 6.9% β,γ- and isomerized α,β-unsaturated aldehydes, respectively.

Self-Assembled Bidentate Ligands for Ru-Catalyzed *anti*-Markovnikov Hydration of Terminal Alkynes**

Breit et al. *Angew. Chem. Int. Ed.* 2006, 45, 1599.

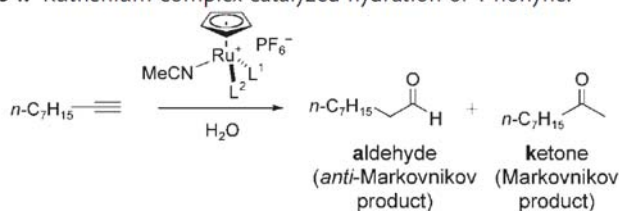


concept

adenine / thymine in DNA
 ↓ mimic
 aminopyridine / isoquinolone
 through hydrogen bonding

* Search for appropriate catalyst

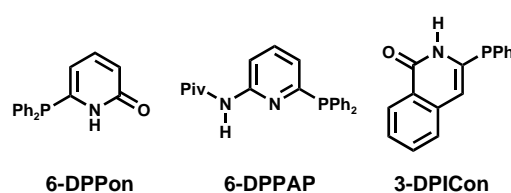
Table 1: Ruthenium complex-catalyzed hydration of 1-nonyne.



Entry	Cat.	L ¹ [^a]	L ² [^a]	t [h]	a [%] ^[b]	k [%] ^[b]
1	1	PPh ₃	PPh ₃	140	1.2	18
2	2 ^[c]	dppy	dppy	168	4.0	2.4
3	3	dppe	—	168	2.1	20
4	4 ^[c]	6-DPPon	6-DPPon	168	2.1	25
5	5	6-DPPAP	3-DPICon	26	94	0
6	6 ^[c]	6-DPPAP	6-DPPAP	72	39	3.8
7	7	3-DPICon	3-DPICon	48	1.9	0

[a] dppy: 2-diphenylphosphinopyridine, dppe: 1,2-bis(diphenylphosphino)ethane, 6-DPPon: 6-diphenylphosphino-2-pyridone, 6-DPPAP: 6-diphenylphosphino-*N*-pivaloyl-2-pyridine, 3-DPICon: 3-diphenylphosphinoisoquinolone. [b] Yield calculated from GC response factors relative to hexadecane internal standard. a = aldehyde, k = ketone. [c] η^1 -P, η^2 -P,N coordination of the phosphinopyridine with replacement of the acetonitrile ligand.

Ligand



entry 6 and 7

Heterodimer is responsible for the result.

*characterization of catalyst 5

- + ³¹P NMR : two doublet (around 50 Hz, ²J(P-P) = 35.9 Hz)
- + ¹H NMR : substantial shift of NH signals of two ligands to lower field
- + X-ray

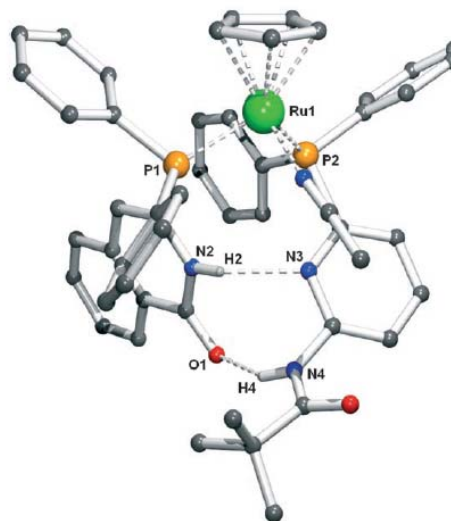


Figure 2. PLATON plot of 5 (H atoms bound to the carbon atoms and the PF₆⁻ counterion are omitted for clarity). Selected interatomic distances [Å] and angles [°]: Ru1-P1 2.3366(7), Ru1-P2 2.3193(8), H2...N3 2.811(3), O1...H4 2.846(3); P1-Ru1-P2 98.20(3), N2-H2...N3 135.35(3), O1...H4-N4 147.50(3).

* Scope and limitations

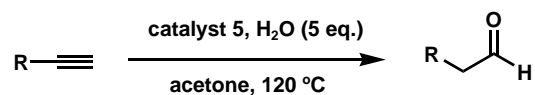
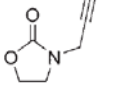
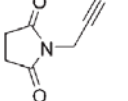
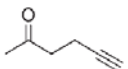
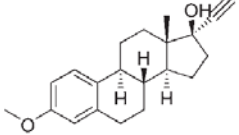


Table 3: Regioselective hydration of functionalized terminal alkynes with **5** as the catalyst.

Entry	Substrate	5 [%]	t [h]	a/k [%] ^[a]	Yield [%] ^[b]
1	$n\text{-C}_7\text{H}_{15}-\text{C}\equiv\text{C}-\text{H}$	2	26	> 99:1	89
2	$\text{Ph}-\text{C}\equiv\text{C}-\text{H}$	2	26	> 99:1	73
3	$\text{N}(\text{CH}_2)_3-\text{C}\equiv\text{C}-\text{H}$	10	96	> 99:1	78
4	$(\text{CH}_2)_6-\text{C}\equiv\text{C}-\text{H}$	10	78	99:1 ^[c]	82
5		5	70	> 99:1	87
6		5	72	99:1	65
7	$\text{BnO}-\text{CH}_2-\text{CH}_2-\text{C}\equiv\text{C}-\text{H}$	5	48	99:1	83
8	$\text{BzO}-\text{CH}_2-\text{CH}_2-\text{C}\equiv\text{C}-\text{H}$	5	50	87:13	74
9		5	28	96:4	91
10 ^[d]		10	124	> 99:1	61

[a] Determined by GC analysis and ¹H NMR spectroscopy. a = aldehyde, k = ketone. [b] Yield of isolated product. [c] Ratio of decane-1,10-dial/9-oxodecanal. [d] Reaction performed at 70 °C.

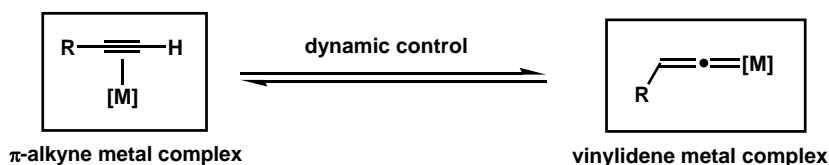
The origin of the catalytic activity remains unknown.

Hydrogen bonding network incorporates H₂O so that addition proceeds readily and regioselectively ?

3. Control of π -alkyne and vinylidene complex

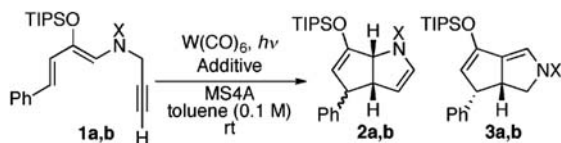
Efficient Control of π -Alkyne and Vinylidene Complex Pathways for the $W(CO)_5(L)$ -Catalyzed Synthesis of Two Types of Nitrogen-Containing Bicyclic Compounds

Iwasawa et al. JACS 2008, 130, 802.



* condition optimization

Table 1. $W(CO)_5(L)$ -Catalyzed Reaction of Dienol Silyl Ethers **1a,b**



entry	X	1a,b	$W(CO)_6$ (mol %)	additive (100 mol %)	time	yield (%)	
						2 (α -Ph/ β -Ph)	3
1	Ts	1a	10	—	1.5 h	68 (67:33)	0
2			100	Et_3N	15 min	0	80
3			100	$n-Bu_3N$	1 h	0	57
					(15 min) ^a	(4) ^a	(73) ^a
4			100	DABCO ^b	40 min	0	81
5			10	Et_3N	2 h	0	0
6			10	$n-Bu_3N$	2 h	0	32
7	Ms	1b	10	—	1.5 h	85 (60:40)	0
8			10	Et_3N	2 h	0	61
9			10	$n-Bu_3N$	2 h	0	93
10			3	$n-Bu_3N$ ^c	3.5 h	0	92

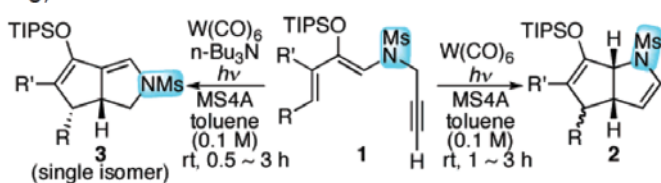
^a Dilution conditions (0.01 M). ^b Run using 50 mol %. ^c Run using 30 mol %.

Addition of *tert*-amine controlled the product distribution.

The use of *N*-Ms instead of *N*-Ts improved the yield.

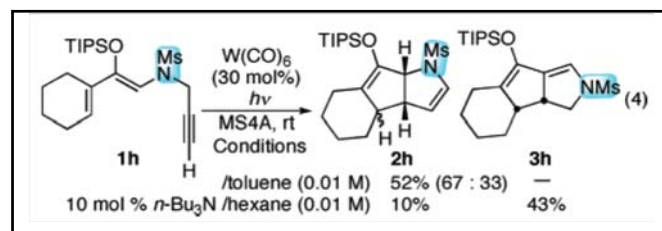
* scope and limitations

Table 2. $W(CO)_5(L)$ -Catalyzed Reaction of Dienol Silyl Ethers (**1b–g**)



entry	R	R'	1	$W(CO)_6$ (mol %)	$n-Bu_3N$ (mol %)	yield (%) (α -R/ β -R)
1	Ph	H	1b	10	—	2b : 85 (60:40)
				3	30	3b : 92
2	2-furyl	H	1c	5	—	2c : 70 (60:40)
				5	50	3c : 82
3	1-naphthyl	H	1d	30	—	2d : 64 (40:60)
				10	100	3d : 74
4	Ph	Me	1e	30	—	2e : 65 (47:53)
				5	50	3e : 80
5	<i>i</i> -Pr	H	1f	10	—	2f : 67 (60:40) ^a
				10	10	3f : 50 (2f : 10%) ^b
6	<i>c</i> -hexyl	H	1g	10	—	2g : 74 (60:40) ^a
				10	10	3g : 59 (2g : 11%) ^b

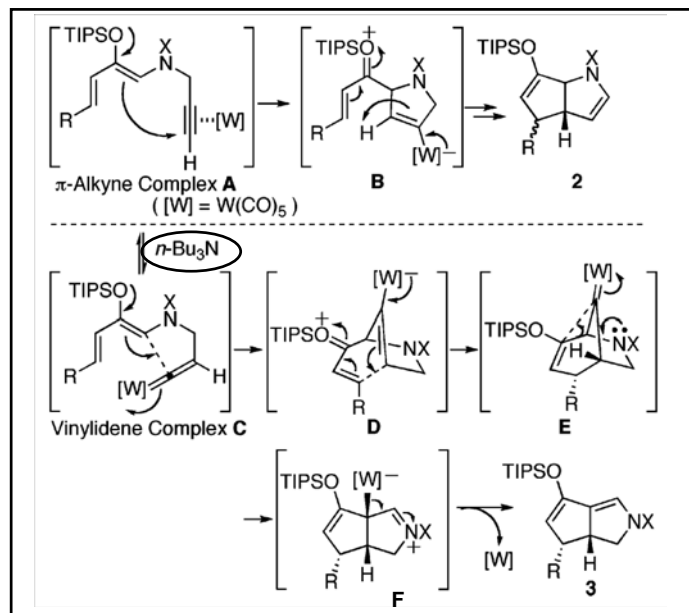
^a Dilution conditions (0.01 M). ^b Dilution conditions (0.01 M) in hexane.



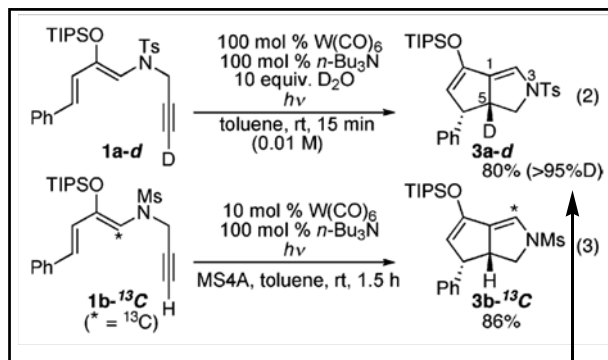
entry 5 and 6

In the case of alkyl substituted diene, small amounts of **2** were obtained even in the amine-promoted reaction.

* proposed mechanism



* deuterium- and ^{13}C -labeling experiments to support the proposed mechanism



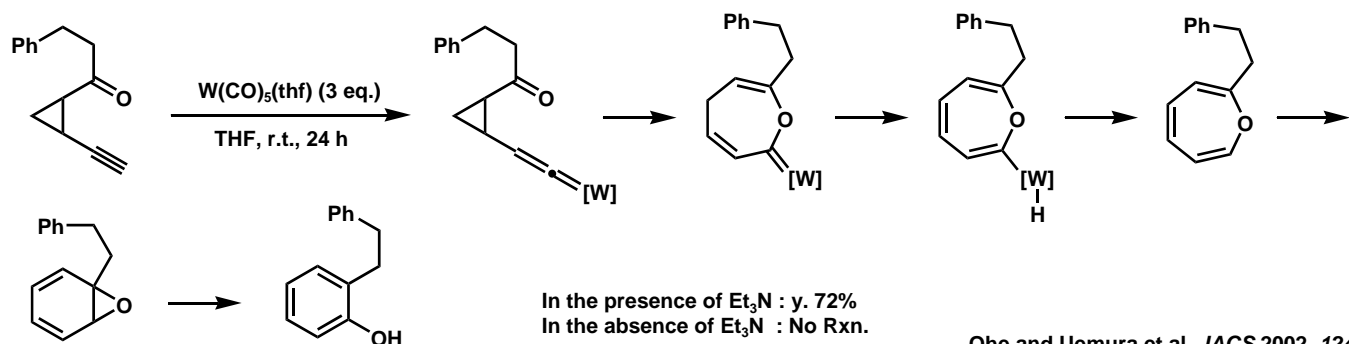
without D_2O : 46% D incorporation

A to C
The presence of amine would facilitate the formation of vinylidene complex

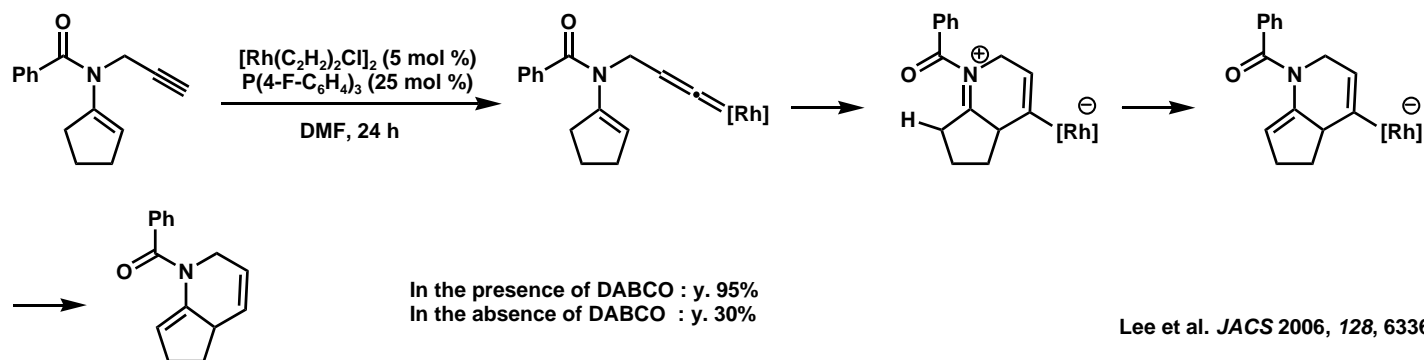
E to F
1,2-alkyl migration aided by electron donation from nitrogen

* Effect of amine

Similar effect of amine has been suggested.



Ohe and Uemura et al. *JACS* 2002, 124, 526.



Lee et al. *JACS* 2006, 128, 6336.