Regioselective Addition of Alcohols to Internal 1-Aryl-1-alkynes Catalyzed by a Triangular Heterobimetallic Ir_2Pd Sulfido Cluster

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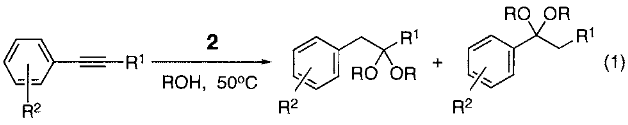
(Received April 22, 1998; CL-980304)

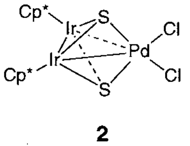
The triangular heterobimetallic sulfido cluster $[(Cp^*Ir)_2(\mu_3\text{-}S)_2PdCl_2]$ prepared from $[PdCl_2(cod)]$ and $[Cp^*IrCl(\mu\text{-}SH)_2IrCp^*Cl]$ was found to catalyze the addition of alcohols to alkynes to give the corresponding ketals. In particular, internal 1-aryl-1-alkynes were transformed into the corresponding 2,2-dialkoxy-1-arylalkanes with high regioselectivity. The analogous Ir_2PtS_2 cluster proved to be much less selective.

In recent years great efforts have been devoted to the synthesis of multinuclear transition metal-sulfur complexes,[1] because they not only provide functional models for industrial metal sulfide catalysts,[2] but also have some relevance to the active sites of metalloenzymes such as hydrogenase and nitrogenase.[3] Nevertheless, their use in catalytic organic synthesis has not been explored extensively.[4] We have long focused our attention on the syntheses, reactivities[5] and catalytic activities[5b,6-9] of multinuclear noble metal-sulfur complexes. Previously, the $PdMo_3S_4$ cubane-type cluster $[PdMo_3(\mu_3\text{-}S)_4(tacn)_3Cl][PF_6]_3$ (**1**, tacn = 1,4,7-triazacyclo-nonane) was shown to be an excellent catalyst for the stereoselective addition of alcohols[7] or carboxylic acids[8] to electron deficient alkynes and the lactonization of alkynoic acids.[9] However, cluster **1** failed to effect the intermolecular addition of alcohols to unactivated alkynes. Now we have found that the triangular Ir_2PdS_2 cluster $[(Cp^*Ir)_2(\mu_3\text{-}S)_2PdCl_2]$ (**2**, $Cp^* = \eta^5\text{-}C_5Me_5$) catalyzes the addition of alcohols to internal 1-aryl-1-alkynes to give the corresponding 2,2-dialkoxy-1-arylalkanes with high regioselectivity.

We have very recently revealed that the hydrosulfido-bridged diiridium complex $[Cp^*IrCl(\mu\text{-}SH)_2IrCp^*Cl]$ (**3**) is a versatile precursor for the synthesis of homo- and heterometallic sulfido clusters.[10] The $PdIr_2S_2$ cluster **2** was also prepared readily from complex **3** by the reaction with $[PdCl_2(cod)]$ (cod = 1,5-cyclooctadiene) in good yield.[11] When 1-phenyl-1-propyne (1.67 mmol) and a catalytic amount of cluster **2** (S/C = 30) were dissolved in MeOH and allowed to react at 50 °C, GLC analysis of the reaction mixture indicated that almost all the starting alkyne was consumed in 48 h, and 2,2-dimethoxy-1-phenylpropane (**4a**, $R^1 = R = Me$, $R^2 = H$) and 1,1-dimethoxy-1-phenylpropane (**5a**, $R^1 = R = Me$, $R^2 = H$) were formed in a 98:2 ratio (eq 1). No other products such as enol ethers were observed. After the reaction, NEt_3 was added to the mixture in order to suppress the hydrolysis of the ketals, and the catalyst was removed by passing the solution through a short silica gel column. Further purification of the products by bulb-to-bulb distillation gave **4a** and **5a** in 88% combined yield.[12]



4 **5**



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The most salient feature of this reaction is the highly regioselective formation of **4a**. Although a few transition metal catalysts such as $Na[AuCl_4]$,[13] $[PtCl_2(phosphine)_2]$ + AgOTf (OTf = OSO_2CF_3),[14] and $[RuCl\{HB(pz)_3\}(cod)]$ (pz = pyrazol-1-yl)[15] have so far been reported to promote the intermolecular addition of alcohols to unactivated alkynes, none of them have shown satisfactory regioselectivity in reactions of internal alkynes. Effect of the catalysts in the addition of MeOH to 1-phenyl-1-propyne was investigated in detail (Table 1). Neither monometallic palladium complexes including those with thiolato or thioether ligands nor iridium complexes including **3** showed catalytic activity. In addition, the combined use of $[Cp^*IrCl_2]_2$ and $[PdCl_2(cod)]$ was ineffective. Interestingly, $[(Cp^*Ir)_2(\mu_3\text{-}S)_2PtCl_2]$ (**6**),[11] the platinum analog of **2**, exhibited good activity, but its regioselectivity was not high. Some other heterobimetallic sulfido clusters containing palladium[16] were also examined as the catalyst, but they failed to give the addition products. It should also be noted that cluster **2** was recovered in 85% yield after the catalytic reaction. These observations suggest that the Ir_2PdS_2 cluster core is retained during the catalysis and is essential for the regioselective addition of MeOH to 1-phenyl-1-propyne.

Cluster **2** was found to be effective for the catalytic addition of MeOH to various alkynes. Highly regioselective formation of **4** in preference to **5** (up to 99:1) was observed with internal 1-phenyl- and 1-chlorophenyl-1-alkynes. However, 1-aryl-1-propyne with an electron donating substituent on the aryl ring

Table 1. Catalytic addition of MeOH to 1-phenyl-1-propyne[a]

Catalyst	Conv.[b] %	Yield[c] %	Ratio[d]
$[(Cp^*Ir)_2(\mu_3\text{-}S)_2PdCl_2]$ (**2**)	>99	(88)	98:2
$[Pd(OAc)_2]$	14	0	—
$[Pd(PPh_3)_4]$	8	0	—
$[PdCl_2(PhSCH_2CH_2CH_2SPh)]$	28	0	—
$[Cp^*IrCl(\mu\text{-}SH)_2IrCp^*Cl]$ (**3**)	3	0	—
$[IrCl(cod)]_2$	30	6	(35:65)
$[Cp^*IrCl(\mu\text{-}Cl)_2IrCp^*Cl]$ + $[PdCl_2(cod)]$[e]	33	0	—
$[(Cp^*Ir)_2(\mu_3\text{-}S)_2PtCl_2]$ (**6**)	>99	(96)	74:26
$[(Cp^*Ru)_2Pd_2(\mu_3\text{-}S)_2(S^iPr)(\mu\text{-}S^iPr)(PPh_3)]$	23	0	—

[a] 1-Phenyl-1-propyne, 1.67 mmol; catalyst, 56 μmol; MeOH, 2 ml; 50 °C, 48 h. [b] Determined by GLC. [c] GLC (isolated) yield. [d] **4a** : **5a**. Determined by ^1H NMR (GLC). [e] 56 μmol each.

Table 2. Catalytic addition of alcohols to alkynes by **2**[a]

Alcohol	Alkyne	Conv.[b]	Isolated yield	Ratio[c]
		%	%	
MeOH	PhC≡CMe	>99	88	98:2
EtOH	PhC≡CMe[d]	93	89	97:3
MeOH	PhC≡CEt	>99	81	99:1
MeOH	PhC≡C^{n}Bu[d]	>99	65	98:2
MeOH	p-ClC$_6$H$_4$C≡CMe	>99	95	97:3
MeOH	m-ClC$_6$H$_4$C≡CMe	>99	70	99:1
MeOH	p-TolC≡CMe	>99	82	91:9
MeOH	p-MeOC$_6$H$_4$C≡CMe	>99	59	66:34
MeOH	PhC≡CH[e]	>99	50	13:87
MeOH	^{n}HexC≡CH[f]	>99	55	0:100

[a] Alkyne, 1.67 mmol; catalyst, 56 μmol; alcohol, 2 ml; 50 °C, 48 h. [b] Determined by GLC. [c] **4** : **5**. Determined by ^{1}H NMR. [d] Alkyne, 1.12 mmol; 72 h. [e] Ethynylbenzene, 2.77 mmol. [f] 1-Octyne, 1.12 mmol; 96 h.

showed lower regioselectivity (p-Me, 91:1; p-MeO, 66:34.) Similar addition of EtOH was also effected by the action of **2**. In contrast, the reactions of terminal alkynes with MeOH afforded **5** (R^1 = H, R = Me) as the major addition products. Alkenes such as styrene and 1-phenyl-1-propene failed to react.

The present reaction of alkynes giving the corresponding ketals is considered to involve either the direct addition of an alcohol across the C≡C triple bond or the hydration of the alkyne with fortuitous water followed by the condensation with the alcohol. In fact, several transition metal compounds are known to catalyze the hydration of unactivated alkynes.[17] In order to obtain information about this point, 1-phenyl-1-propyne was allowed to react in acetone-water (4:1) in the presence of cluster **2**, but the alkyne was recovered unchanged. This result indicates that the formation of the ketal proceeds by way of the direct alkoxylation of the alkyne on the cluster. Although we must await further investigation to elucidate details of the reaction mechanism, we propose that the catalytic cycle should include the formation of an alkoxyvinyl cluster by the nucleophilic attack of an alcohol on the coordinated alkyne molecule at the palladium center of the cluster core.

This work was supported by a Grant-in-Aid for Specially Promoted Research No. 09102004 from the Ministry of Education, Science, Sports, and Culture, Japan.

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11 **2**: 74% yield. ^{1}H NMR ($CDCl_3$) δ 2.15 (s, Cp*). Anal. Found: C, 26.35; H, 3.47%. Calcd for $C_{20}H_{30}Cl_2Ir_2PdS_2$: C, 26.80; H, 3.37%. **6**: 62% yield. ^{1}H NMR ($CDCl_3$) δ 2.14 (s, Cp*). Anal. Found: C, 24.42; H, 3.17%. Calcd for $C_{20}H_{30}Cl_2Ir_2PtS_2$: C, 24.39; H, 3.07%. Details will be reported elsewhere.

12 Ketals **4** and **5** were fully characterized by ^{1}H and ^{13}C NMR.

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