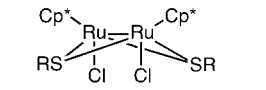
C-H Activation with Ru

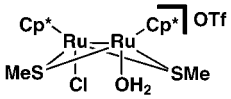
Propargylation of Aromatic Compounds with Propargylic Alcohols Catalyzed by a Cationic Diruthenium Complex**

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

We have recently disclosed that the ruthenium-catalyzed propargylation of aromatic compounds with propargylic alcohols affords the corresponding propargylated aromatic compounds in good yields with a complete regioselectivity.[1] The reactions are only catalyzed by thiolate-bridged diruthenium complexes, such as [Cp*RuCl(μ_2-SR)$_2$RuCp*Cl][2] (Cp* = η^5-C_5Me_5; R = Me (**1a**), *i*Pr (**1b**), *n*Pr (**1c**)). In this catalytic reaction, usable propargylic reagents were unfortunately strictly limited to the propargylic alcohols bearing *terminal* acetylene groups, because the reactions proceeded by an electrophilic aromatic-substitution reaction at the γ-carbon of the allenylidene intermediates, which can only be produced from this type of propargylic alcohol.[3a–c] During our study of the catalytic propargylation of aromatic compounds, we have now found that a cationic methanethiolate-bridged diruthenium complex [Cp*RuCl(μ_2-SMe)$_2$RuCp*-(OH$_2$)]OTf (**1d**; OTf = CF_3SO_3)[3d] promotes the catalytic propargylation of aromatic compounds with propargylic alcohols bearing not only *terminal* acetylene but also *internal* acetylene units. The reaction described herein provides a general preparative synthetic method for a variety of propargylated aromatic compounds. The most characteristic features of this reaction are its high atom economy and environmental friendliness, the only stoichiometric by-product being water (H_2O).



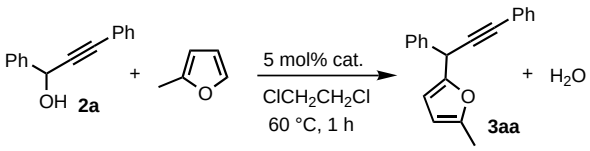
R = Me (**1a**), *i*Pr (**1b**), *n*Pr (**1c**)



R = Me (**1d**), *i*Pr (**1e**)

We investigated the propargylation of 2-methylfuran with propargylic alcohols, such as 1,3-diphenyl-2-propyn-1-ol (**2a**), with internal acetylene units. Treatment of 2-methylfuran with **2a** in 1,2-dichloroethane in the presence of **1d** (5 mol%) at 60 °C for 1 h afforded 5-methyl-2-(1,3-diphenyl-2-propynyl)furan (**3aa**) in 88% isolated yield (Table 1; entry 1).

Table 1: Propargylation of 2-methylfuran with 1,3-diphenyl-2-propyn-1-ol (**2a**).[a]



Entry	Catalyst	Yield [%][b]
1	[Cp*RuCl(μ-SMe)$_2$Cp*Ru(OH$_2$)]OTf (**1d**)	88
2[c]	[Cp*RuCl(μ-SMe)$_2$Cp*Ru(OH$_2$)]OTf (**1d**)	50
3	[Cp*RuCl(μ-S*i*Pr)$_2$Cp*Ru(OH$_2$)]OTf (**1e**)	81
4	[Cp*RuCl(μ-SMe)$_2$Cp*RuCl] (**1a**)[d]	0
5	[Cp*RuCl(μ-S*i*Pr)$_2$Cp*RuCl] (**1b**)[d]	0
6	[CpRuCl(PPh$_3$)$_2$]	0
7	[RuCl$_2$(PPh$_3$)$_3$]	0
8	[{RuCl$_2$(*p*-cymene)}$_2$]	0
9	[(indenyl)RuCl(PPh$_3$)$_2$]	0
10	[Cp*RuCl(μ$_2$-Cl)$_2$RuCp*Cl]	0

[a] All of the reactions of 2-methylfuran (1.500 mmol) with **2a** (0.300 mmol) were carried out in the presence of catalyst (0.015 mmol) in $ClCH_2CH_2Cl$ (8 mL) at 60 °C for 1 h. [b] Isolated yield. [c] At room temperature for 5 h. [d] No reaction even in the presence of NH_4BF_4.

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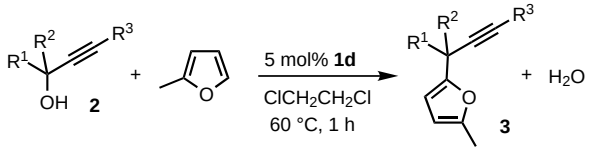
Neither other products nor regioisomers of **3aa** were detected by GLC and ^{1}H NMR. The reaction proceeded even at room temperature, but a longer reaction time was required to obtain **3aa** even in 50% isolated yield (Table 1; entry 2). The complex with the sterically demanding S*i*Pr group (**1e**) exhibited a slightly lower catalytic activity (Table 1; entry 3). It is noteworthy that neutral thiolate-bridged diruthenium complexes (**1a** and **1b**), which are known to promote the propargylation of aromatic compounds with propargylic alcohols bearing *terminal* acetylene groups,[1] did not work at all (Table 1; entries 4 and 5). Other di- and monoruthenium complexes such as $[CpRuCl(PPh_3)_2]$ ($Cp = \eta^5$-C_5H_5), $[RuCl_2(PPh_3)_3]$, $[\{RuCl_2(p\text{-cymene})\}_2]$, [(indenyl)-$RuCl(PPh_3)_2$], and $[Cp^*RuCl(\mu_2\text{-}Cl)_2RuCp^*Cl]$ were ineffective for this catalytic propargylation (Table 1; entries 6–10).

Reactions of 2-methylfuran with other propargylic alcohols bearing internal acetylene units have been similarly carried out. Typical results are shown in Table 2. The

Table 2: Propargylation of 2-methylfuran with propargylic alcohols (**2**).[a]

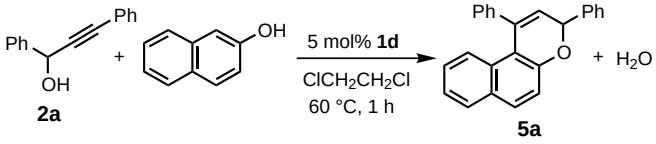


Entry		Propargylic alcohol			Yield of **3** [%][b]
		R^1	R^2	R^3	
1	**2b**	Ph	H	*n*Bu	**3ab**, 91
2	**2c**	Ph	H	*t*Bu	**3ac**, 80
3	**2d**	Ph	H	*n*-hexyl	**3ad**, 83
4	**2e**	*p*-MeC_6H_4	H	Ph	**3ae**, 91
5	**2f**	$Ph_2C{=}CH$	H	Ph	**3af**, 60
6	**2g**	Ph	Me	Ph	**3ag**, 49[c]
7[d]	**2h**	Me	Me	Ph	**3ah**, 20[e]
8[d]	**2i**	Et	H	Ph	**3ai**, 0[f]

[a] All of the reactions of 2-methylfuran (1.500 mmol) with **2** (0.300 mmol) were carried out in the presence of **1d** (0.015 mmol) in $ClCH_2CH_2Cl$ (8 mL) at 60°C for 1 h. [b] Isolated yield. [c] 2,4-Diphenyl-1-buten-3-yne (20%) was formed. [d] For 3 h. [e] 2-Methyl-4-phenyl-1-buten-3-yne (40%) was formed. [f] No reaction.

corresponding 2-propargylic furans (**3ab**–**3ae**) were obtained from various alkyl and aryl substituted propargylic alcohols (**2b**–**2e**) in excellent yields with a complete regioselectivity (Table 2; entries 1–4). The reaction with 1-alkenyl substituted propargylic alcohol (**2f**) gave the corresponding propargylic furan (**3af**) in 60% isolated yield (Table 2; entry 5). The propargylation of 2-methylfuran with 1,1-disubstituted propargylic alcohol such as 2,4-diphenyl-3-butyn-2-ol (**2g**) afforded the expected propargylic furan (**3ag**) in slightly lower yield, but together with the formation of 2,4-diphenyl-1-buten-3-yne in 20% yield (Table 2; entry 6). Similarly, the reaction with 1,1-dialkyl substituted propargylic alcohol gave both the corresponding propargylated furan (**3ah**) in only 20% yield and the conjugated enyne in 40% yield (Table 2; entry 7). On the other hand, no propargylation proceeded when 1-alkyl substituted propargylic alcohol such as **2i** was used (Table 2; entry 8).

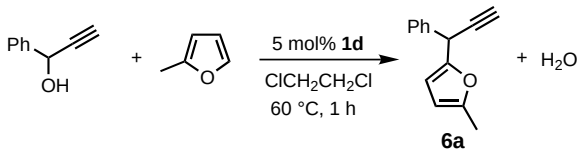
Next, the propargylation of various aromatic compounds with **2a** was examined in the presence of **1d** (5 mol%) at 60°C. Typical results are summarized in Table 3. The corresponding propargylic compounds (**4aa**–**4ad**) were obtained from a variety of heterocyclic compounds such as furan, 2,3-dimethylfuran, pyrrole, and 2-methylthiophene in good yields with a complete regioselectivity (Table 3; entries 1–4). In all cases, propargylation occurred selectively at the α position of heterocyclic rings. These results indicate that the reaction proceeds electrophilically. In the cases of electron-rich arenes such as 1,3-dimethoxybenzene, 1,3,5-trimethoxybenzene, an acetanilide derivative, and phenol, the corresponding propargylated benzene derivatives (**4ae**–**4ah**) were obtained in 91%, 73%, 41%, and 80% isolated yields, respectively (Table 3; entries 5–8). Although the reaction of 2-methoxynaphthalene with **2a** gave 1-propargylic naphthalene (**4ai**) in 94% yield (Table 3; entry 9), that of 2-naphthol afforded the unexpected 3*H*-naphtho[2,1-b]pyrane (**5a**) in 21% yield with the formation of unidentified compounds (Scheme 1).[4] The



Scheme 1. Reaction of 1,3-diphenyl-2-propyn-1-ol with 2-naphthol.

high yield formation of 1-propargylated azulene (**4aj**) was observed in the reaction of azulene with **2a** (Table 3; entry 10). No propargylation occurred under these reaction conditions, however, when naphthalene, anisole, 1,4-dimethoxybenzene, *p*-xylene, toluene, and *N,N*-dimethylaniline were used as aromatic compounds.

The complex **1d** also catalyzed the propargylation of aromatic compounds with propargylic alcohols bearing terminal acetylene groups.[1] In fact, the treatment of 2-methylfuran with 1-phenyl-2-propyn-1-ol in the presence of **1d** (5 mol%) at 60°C for 1 h afforded 2-methyl-5-(1-phenyl-2-propynyl)furan (**6a**) in quantitative yield (Scheme 2), show-

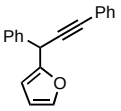
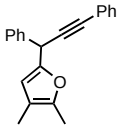
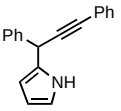
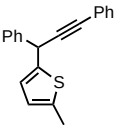
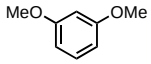
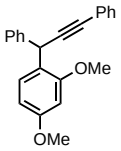
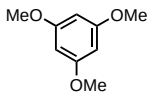
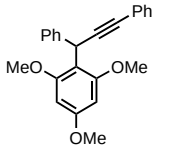
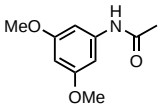
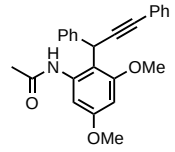
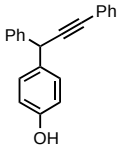
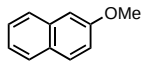
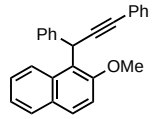
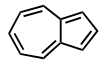
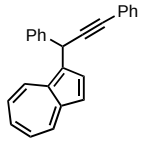


Scheme 2. Propargylation of 2-methylfuran with 1-phenyl-2-propyn-1-ol.

ing that the cationic complex exhibited almost the same catalytic activity as the neutral diruthenium complex **1a**.[1] Thus, the novel cationic methanethiolate-bridged diruthenium complex **1d** promotes the catalytic propargylation of a variety of aromatic compounds with propargylic alcohols bearing not only terminal acetylene but also internal acetylene groups.

A ^{1}H NMR spectroscopy investigation was carried out by mixing a stoichiometric amount of **1d** and **2a** at room temperature in CD_2Cl_2, but no formation of intermediates

Table 3: Propargylation of aromatic compounds with **2a**.[a]

Entry	Aromatic compound	*t* [h]	Product		Yield [%][b]
1		2		**4aa**	71
2		2		**4ab**	41
3		17		**4ac**	60
4		1		**4ad**	88
5		3		**4ae**	91
6		1		**4af**	73
7		20		**4ag**	41
8		20		**4ah**	80
9		1		**4ai**	94
10		25		**4aj**	91

[a] All of the reactions of aromatic compound (1.500 mmol) with **2a** (0.300 mmol) were carried out in the presence of **1d** (0.015 mmol) in $ClCH_2CH_2Cl$ (8 mL) at 60 °C. [b] Isolated yield.

was observed. The addition of an excess amount of 2-methylfuran to this reaction mixture, however, led to the high-yield formation of **3aa** together with an almost complete recovery of **1d**. These results may indicate that the intermediates of this catalytic reaction are too labile to be identified. Although direct evidence of the reactive intermediates has not yet been obtained, we believe that the catalytic reaction with propargylic alcohols with internal acetylene units may proceed via (η-propargyl)ruthenium species.[5,6] An electrophilic attack of the (η-propargyl)ruthenium complexes on aromatic compounds should afford the corresponding propargylated aromatic products. On the other hand, the propargylation of aromatic compounds with propargylic alcohols bearing terminal acetylene groups is considered to proceed by electrophilic attack of the cationic Cγ atom in the allenylidene intermediate, as shown previously.[1]

In summary, we have now found that the cationic diruthenium complex **1d** promotes the catalytic propargylation of aromatic compounds with propargylic alcohols bearing not only terminal acetylene but also internal acetylene units. The catalytic reaction described here provides a general and environmentally friendly preparative synthetic method (atom economical, only H_2O as byproduct) for a variety of propargylated aromatic compounds. The electrophilic aromatic-substitution reaction by free propargylic cations has been reported, but the products are either propargylated or allenylated aromatic products and/or a mixture of them, depending on the substituents of the propargylic cations.[7,8] Also, the well known Nicholas reaction requires several steps and uses a stoichiometric amount of $[Co_2(CO)_8]$ for the preparation of these compounds.[9,10] Some propargylated aromatic compounds are useful monomers in the field of material science. Further investigations for the elucidation of the detailed reaction mechanism and broadening the scope of this catalytic propargylation are currently in progress.

Experimental Section

1d: **1a** (965 mg, 1.52 mmol)[3a,b] was placed in a 50-mL flask under N_2. Anhydrous THF (20 mL) was added, and then the mixture was stirred with a magnetic stirrer at room temperature for 5 min. After the addition of AgOTf (398 mg, 1.52 mmol), the reaction flask was kept

at room temperature for 20 h. Then, the solvent was removed under reduced pressure, and the residue was recrystallized from CH_2Cl_2/*n*-hexane to give black crystals of **1d** (1.02 g, 1.26 mmol, 82%); ^{1}H NMR (270 MHz, $CDCl_3$): $\delta = 1.63$ (s, 30H), 2.51 (s, 6H), 3.30 ppm (brs, 2H); ^{13}C NMR (67.5 Hz, $CDCl_3$) $\delta = 1.1$, 10.5, 96.5 ppm; elemental analysis calcd (%) for $C_{23}H_{38}ClF_3O_4Ru_2S_3$: C 35.91, H 4.98; found: C 35.78, H 4.71.

A typical reaction of 2-methylfuran with 1,3-diphenyl-2-propyn-1-ol (**2a**) catalyzed by **1d**: **1d** was placed in a 20-mL flask (12.2 mg, 0.015 mmol) under N_2. Anhydrous $ClCH_2CH_2Cl$ (8 mL) was added, and then the mixture was magnetically stirred at room temperature for 5 min. After the addition of **2a** (62.6 mg, 0.300 mmol) and 2-methylfuran (123.2 mg, 1.500 mmol), the reaction flask was kept at 60 °C for 1 h. The solvent was concentrated under reduced pressure (aspirator), and then the residue was purified by column chromatography on SiO_2 with EtOAc/hexane (1/9) as eluent to give 5-methyl-2-(1,3-diphenyl-2-propynyl)furan (**3aa**) as a pale yellow oil (71.8 mg, 0.264 mmol, 88% yield); ^{1}H NMR (270 MHz, $CDCl_3$): $\delta = 2.23$ (s, 3H), 5.20 (s, 1H), 5.88 (d, $J = 3.0$ Hz, 1H), 6.12 (d, $J = 3.0$ Hz, 1H,) 7.27–7.47 ppm (m, 10H); ^{13}C NMR (67.5 Hz, $CDCl_3$): $\delta = 13.7$, 37.9, 83.7, 87.7, 106.1, 107.2, 123.2, 127.1, 127.7, 127.9, 128.1, 128.4, 131.6, 139.0, 151.6, 151.7 ppm; elemental analysis calcd (%) for $C_{20}H_{16}O$: C 88.20, H 5.92; found: C 88.38, H 6.09.

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Keywords: alkynes · aromatic substitution · C–H activation · ruthenium · S ligands

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