Rhenium-catalyzed Coupling of 2-Propynyl Alcohols and Several Nucleophiles via Dehydration

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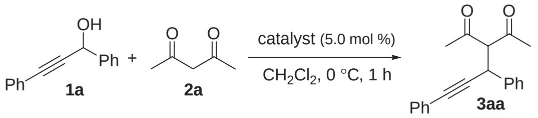
Treatment of 2-propynyl alcohols with several nucleophiles in the presence of a catalytic amount of a rhenium complex, $[ReBr(CO)_3(thf)]_2$, gave coupling products via dehydration. In these reactions, C–C, C–O, and C–S bonds can be constructed under mild conditions.

Cross-coupling reactions between organometallic reagents and organohalides or triflates are powerful and effective methods to synthesize more complex compounds efficiently.[1] However, these reactions provide metal halides or triflates as side products. One strategy that eliminates such side products is cross-coupling reaction via dehydration, which is an atom economical and environmentally friendly approach. Therefore, there have recently been many reports on carbon–carbon bond formation via dehydration. Some examples of these include reactions between 2-propynyl alcohols and allylsilanes,[2] alkynylsilanes,[2d] active methylene compounds,[3] ketones,[4] and aromatic compounds.[2b,2c,5] Carbon–heteroatom bond–formation reactions using 2-propynyl alcohols have also been reported.[6,7] We report herein dehydrative coupling reactions between 2-propynyl alcohols and several carbon and heteroatom nucleophiles.

Treatment of 2-propynyl alcohol **1a** with 2,4-pentanedione (**2a**) in the presence of a catalytic amount of a rhenium complex, $Re_2(CO)_{10}$, in dichloromethane at 0 °C for 1 h, gave a trace amount of the coupling product **3aa** (Table 1, Entry 1). The use of rhenium(I) complexes, $ReCl(CO)_5$ and $ReBr(CO)_5$, did not provide **3aa** (Table 1, Entries 2 and 3). The optimal catalyst was the rhenium complex $[ReBr(CO)_3(thf)]_2$, which provided the desired product **3aa** in 93% yield (Table 1, Entry 4).[8,9] Rhenium chlorides, $ReCl_3$ and $ReCl_5$, also afforded **3aa** in good yields (Table 1, Entries 5 and 6). However, high-valent rhenium complexes, $ReOCl_3(PPh_3)_2$ and Re_2O_7, did not work well (Table 1, Entries 7 and 8). Although the manganese complex, $Mn_2(CO)_{10}$, did not exhibit any catalytic activity (Table 1, Entry 9), $FeCl_3$, $InCl_3$, and $BiCl_3$ promoted the coupling reaction in moderate yields (Table 1, Entries 10–12).

A 2-propynyl alcohol having an alkyl group at the terminal position of the acetylene moiety, **1b**, also afforded the coupling product **3ba**, quantitatively (Table 2, Entry 1). In contrast, when using a secondary 2-propynyl alcohol bearing a terminal acetylene moiety **1c**, and a tertiary 2-propynyl alcohol **1d**, the yields of the adducts, **3ca** and **3da**, were low (Table 2, Entries 2 and 3). 2-Propynyl alcohols **1c** and **1d** were consumed in both cases; however, in Entry 3, a conjugate enyne, which would be formed by dehydration of **1d**, was not observed. 1-Phenyl-1-pentyn-3-ol and 3-phenyl-2-propyn-1-ol did not produce a coupling product.

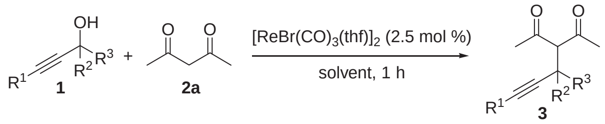
Table 1. Investigation of several catalysts[a]



Entry	Catalyst	Yield/%[b]	Entry	Catalyst	Yield/%[b]
1	$Re_2(CO)_{10}$[c]	trace	7	$ReOCl_3(PPh_3)_2$	0
2	$ReCl(CO)_5$	0	8	Re_2O_7[c]	31
3	$ReBr(CO)_5$	0	9	$Mn_2(CO)_{10}$[c]	trace
4	$[ReBr(CO)_3(thf)]_2$[c]	93	10	$FeCl_3$	78
5	$ReCl_3$	82	11	$InCl_3$	54
6	$ReCl_5$	72	12	$BiCl_3$	64

[a] **1a** (1.0 equiv), **2a** (1.0 equiv). [b] ^1H NMR yield. [c] 2.5 mol %.

Table 2. Reactions between several 2-propynyl alcohols **1** and 2,4-pentanedione (**2a**)[a]



Entry	R^1	R^2	R^3		Solvent	Temp/°C		Yield/%[b]
1[c]	$^nC_6H_{13}$	Ph	H	**1b**	CH_2Cl_2	40	**3ba**[d]	96 (>99)
2[e]	H	Ph	H	**1c**	CH_3NO_2	80	**3ca**	14 (14)
3[e]	Ph	Me	Me	**1d**	CH_3NO_2	0	**3da**	10 (10)

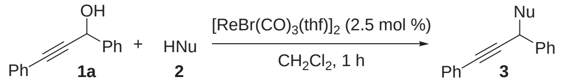
[a] **1** (1.0 equiv), **2a** (1.0 equiv). [b] Isolated yield. Yield determined by ^1H NMR is reported in parentheses. [c] **2a** (3.0 equiv). [d] ca. 3:1 mixture of keto and enol forms. [e] **2a** (2.0 equiv).

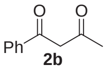
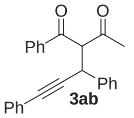
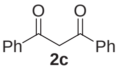
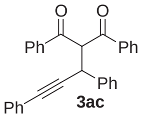
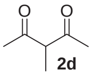
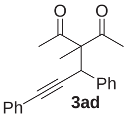
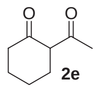
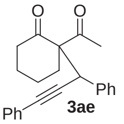
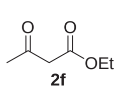
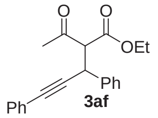
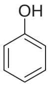
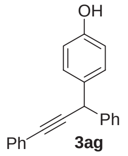
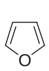
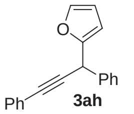
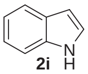
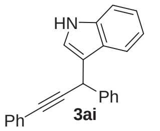
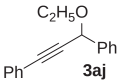
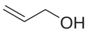
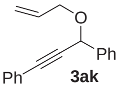
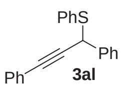
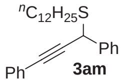
By using the rhenium catalyst, $[ReBr(CO)_3(thf)]_2$, several substrates could be employed as nucleophiles under mild conditions (Table 3). 1,3-Diketones **2b**–**2e** worked well as nucleophiles, and the coupling products **3ab**–**3ae** were obtained in excellent to quantitative yields (Entries 1–4).[10,11] β-Keto ester **2f** gave the coupling product **3af** in 84% yield (Entry 5).[11] Phenol (**2g**), furan (**2h**), and indole (**2i**) substrates also acted as carbon nucleophiles, and afforded the corresponding coupling products **3ag**–**3ai** (Entries 6–8). C–O and C–S bonds were formed using ethanol (**2j**), allyl alcohol (**2k**), thiophenol (**2l**), and 1-undecanethiol (**2m**), 2-propynyl ethers, **3aj** and **3ak**, and 2-propynyl thioethers, **3al** and **3am**, were obtained in 62%–85% yields (Entries 9–12).

Although there has been a report on transition-metal-catalyzed reactions between 2-propynyl acetates and silyl enol ethers (Nicholas-type reaction),[12,13] efficient reactions using 2-propynyl alcohols have not been reported to date. By using a rhenium complex, $[ReBr(CO)_3(thf)]_2$, as a catalyst, the reactions of 2-propynyl alcohols, **1e** or **1f**, with silyl enol ether, **2n**, proceeded, and γ-alkynylketones **3en** and **3fn** were obtained in 96% and 72% yields, respectively (eq 1).[14]

Based on our previous report,[2d] the reaction mechanism is proposed as follows: (1) formation of a 2-propynyl cation via dehydroxylation; (2) nucleophilic attack of a nucleophile to the propargyl cation; and (3) deprotonation.

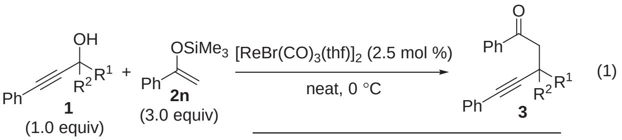
Table 3. Reactions between 2-propynyl alcohol **1a** and several nucleophiles **2**[a]



Entry	HNu	Temp/°C	Product	Yield/%[b]
1	 **2b**	0	 **3ab**	94 (99)[c]
2	 **2c**	0	 **3ac**	94 (99)
3	 **2d**	0	 **3ad**	83 (91)
4	 **2e**	40	 **3ae**	89 (93)[c]
5	 **2f**	0	 **3af**	84 (85)[c]
6[d]	 **2g**	0	 **3ag**	81 (84)
7[d]	 **2h**	25	 **3ah**	37 (39)
8[e]	 **2i**	40	 **3ai**	44 (46)
9[d]	C_2H_5OH **2j**	40	 **3aj**	79 (84)
10[d]	 **2k**	40	 **3ak**	85 (90)
11[f]	PhSH **2l**	0	 **3al**	85 (86)
12[d]	$^{n}C_{12}H_{25}SH$ **2m**	40	 **3am**	62 (63)

[a] **1a** (1.0 equiv), **2** (1.0 equiv). [b] Isolated yield. Yield determined by ^{1}H NMR is reported in parentheses. [c] ca. 1:1 mixture of two diastereomers. [d] **2** (3.0 equiv), 3 h. [e] Solvent-free conditions. 3 h. [f] **2** (2.0 equiv).

In summary, we have succeeded in rhenium-catalyzed coupling reactions between 2-propynyl alcohols and several nucleophiles to construct C–C, C–O, and C–S bonds efficiently under mild conditions.[15] Reactions between 2-propynyl alcohols and silyl enol ethers, which are usually difficult, also proceeded. We hope that these reactions will prove to be effective transformations, and will provide useful insights into synthetic organic chemistry.

 (1)

R^1	R^2		Time	**3**	
4-(MeO)C_6H_4	H	**1e**	1 h	**3en**	96%
Ph	Me	**1f**	3 h	**3fn**	72%

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8 The higher activity of [ReBr(CO)$_3$(thf)]$_2$ compared with ReCl(CO)$_5$ and ReBr(CO)$_5$ may be due to the smooth dissociation of the THF ligand.
9 Investigation of solvents: hexane 53%; toluene 89%; 1,2-dichloroethane 92%; THF 52%; acetone 71%; nitromethane 34%; acetonitrile 0%.
10 There have been a few reports on coupling reactions between 2-propynyl alcohols and 1,3-diketones. See: a) V. Cadierno, J. Gimeno, N. Nebra, *Adv. Synth. Catal.* **2007**, *349*, 382. b) W. Huang, J. Wang, O. Shen, X. Zhou, *Tetrahedron* **2007**, *63*, 11636. See also: Refs. 3 and 4.
11 Although Brønsted acids also promote the reaction, higher temperature is necessary. See: Refs. 3 and 10b.
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14 When the reactions were carried out in dichloromethane, **2n** was decomposed, and the coupling reactions of **2n** with **1e** or **1f** did not proceed.
15 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

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