Platinum(II)-catalyzed Acetal–Ene Reaction: Easy Access to Homoallylic Ethers

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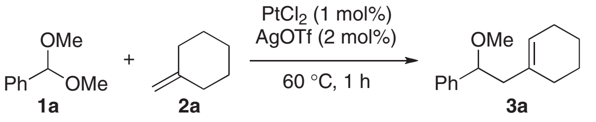
Catalytic use of $PtCl_2$ and AgX (X = OTf and SbF_6) has been found to effectively promote the intermolecular ene reaction of acetals and the tandem acetalization–ene reaction of aldehydes under solvent-free conditions.

Catalytic ene reactions using simple alkenes provide atom-economical methods for allylation of carbon electrophiles.[1] Unlike allylation reactions using allylmetals, they are not accompanied by metal wastes. The ene reaction of acetals leads to homoallylic ethers, an important class of synthetic intermediates. The intramolecular acetal–ene reaction is well established as a useful method for the construction of carbocycles and cyclic ethers;[2,3] however, the intermolecular version has been little studied.[4–6] In the course of our study of Pt(II)-catalyzed reactions, we found that combined use of $PtCl_2$ and AgX (X = OTf and SbF_6) achieved an efficient annulation of alkenols with aldehydes.[7] The reaction mechanism probably involves the formation of oxocarbenium ions by the action of a Lewis acidic Pt(II) species and subsequent intramolecular ene reaction. We herein describe that the Pt(II) catalysis is effective also in the intermolecular acetal–ene reaction under solvent-free conditions, and that it enables direct conversion of aldehydes into homoallylic ethers by a tandem acetalization–ene reaction.

The reaction of benzaldehyde dimethyl acetal (**1a**) with methylidenecyclohexane (**2a**) was initially selected to optimize the reaction conditions. Catalytic use of $PtCl_2$ (1 mol %) and AgOTf (2 mol %) in toluene at 60 °C gave the desired homoallylic ether **3a** in 64% yield (eq 1). Without solvent, the acetal–ene reaction proceeded more efficiently. Both $PtCl_2$ and AgOTf were essential to the efficient reaction.[8] With 4 equivalents of **2a**, the yield of **3a** was improved to 90%.

Various acetals were subjected to the reaction with **2a** (Table 1). Aromatic acetals **1b**–**1d** smoothly underwent the ene reaction (Entries 1–3). Use of acetal **1e** derived from 4-methoxybenzaldehyde led to an unsuccessful result, which is due to decomposition of the desired product **3e** (Entry 4). Aromatic acetal **1f** and aliphatic acetal **1g** were less reactive to **2a**, however, they could be allylated efficiently when $AgSbF_6$ was used instead of AgOTf (Entries 5–8). Acetals **1h** and **1i** were converted into **3h** and **3i** in good yield under catalysis by $PtCl_2$ and $AgSbF_6$ (Entries 9 and 10).

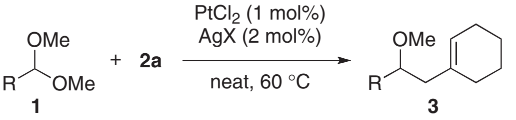


(1)

1a **2a** **3a**

2a (2 equiv), toluene: 64%
2a (2 equiv), neat: 83%
2a (4 equiv), neat: 90%

Table 1. Acetal–ene reaction with methylidenecyclohexane (**2a**)[a]

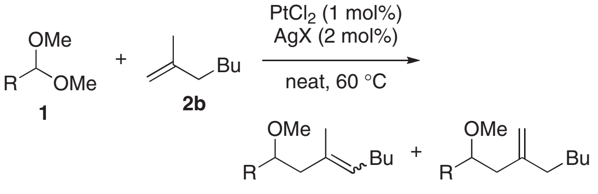


Entry	R (**1**)	X	Time/h	Yield/%[b] (**3**)
1	4-MeC_6H_4 (**1b**)	OTf	1	87 (**3b**)
2	4-ClC_6H_4 (**1c**)	OTf	1	82 (**3c**)
3	4-FC_6H_4 (**1d**)	OTf	1	76 (**3d**)
4	4-$MeOC_6H_4$ (**1e**)[c]	OTf	1.5	53 (**3e**)
5	4-$O_2NC_6H_4$ (**1f**)	OTf	2	42 (**3f**)
6	4-$O_2NC_6H_4$	SbF_6	1	78 (**3f**)
7	$Ph(CH_2)_2$ (**1g**)	OTf	2	26[d] (**3g**)
8	$Ph(CH_2)_2$	SbF_6	1	80[d] (**3g**)
9	*n*-C_8H_{17} (**1h**)	SbF_6	1	83 (**3h**)
10	*c*-C_6H_{11} (**1i**)	SbF_6	1.5	85 (**3i**)

[a]Conditions: **1** (1.00 mmol), **2a** (4.00 mmol), $PtCl_2$ (0.01 mmol), AgX (0.02 mmol), 60 °C. [b]Isolated yield. [c]At 40 °C. [d]Determined by GC.

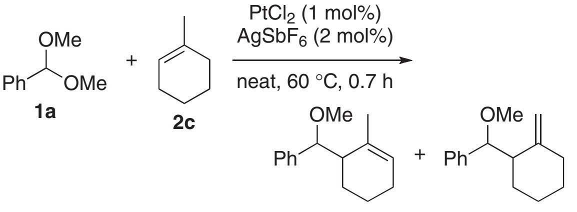
The scope of alkenes was next examined. The reaction of **1a** with 1-decene did not occur at all. In contrast, 2-methyl-1-heptene (**2b**) reacted with acetals **1a** and **1h** to afford the corresponding ene products as mixtures of regio- and stereo-isomers (eq 2). Thus *gem*-disubstituted alkenes, which are more electron-rich than monosubstituted alkenes, showed high reactivity toward the ene reaction. 1-Methylcyclohexene (**2c**), a trisubstituted alkene, was also reactive enough for the ene reaction with **1a** (eq 3).

Under the standard conditions, the reaction of **1a** with α-methylstyrene (**2d**) gave the ene product **8a** in moderate yield



(2)

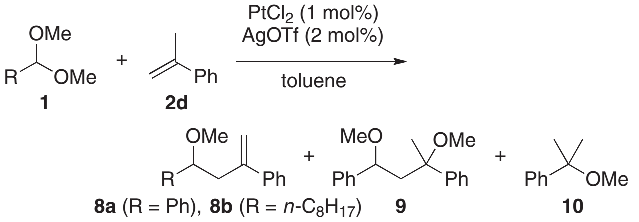
R = Ph, X = OTf, 6 h: **4a**, 71% (*E*:*Z* = 73:27) **5a**, 4%
R = *n*-C_8H_{17}, X = SbF_6, 1 h: **4b**, 72% (*E*:*Z* = 70:30) **5b**, 6%



(3)

6, 54% (dr = 66:34) **7**, 2%

Table 2. Reaction of α-methylstyrene (**2d**)[a]



Entry	**1**	Temp/°C	Time/h	GC yield/%		
				8	**9**	**10**
1[b]	**1a**	60	0.5	61	16	62
2	**1a**	60	0.5	71 (70)[c]	12	69
3[d]	**1h**	60	0.33	(73)[c]	—	—
4	**1a**	30	1	13	61	9
5	**1a**	30	3	33	53	39
6	**1a**	30	12	72	11	95

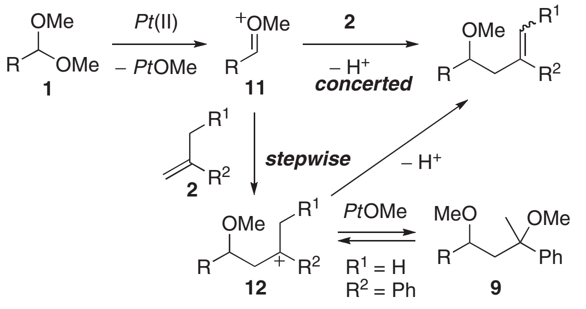
[a]Conditions: **1** (1.00 or 3.00 mmol), **2a** (4 equiv), $PtCl_2$ (1 mol %), AgOTf (2 mol %), toluene (1 mL/1 mmol of **1**). [b]Without toluene. [c]Isolated yield. [d]$AgSbF_6$ was used instead of AgOTf.

(Entry 1 in Table 2). Diether **9** and methyl ether **10** were formed as by-products. Use of toluene as solvent improved the yield of **8a** (Entry 2). A similar result was obtained in the reaction of **1h** (Entry 3). Interestingly, the reaction of **1a** with **2d** at 30 °C for 1 h gave **9** predominantly (Entry 4). The molar ratios of **8a** and **10** to **9** increased with the reaction time (Entries 5 and 6). After 12 h the yield of **8a** reached 72%. This observation is indicative of the formation of **8a** from **9**. Indeed, **9** was partially converted into **8a** under catalysis by $PtCl_2$ and AgOTf (eq 4). The presence of **2d** was effective in the elimination of methanol from **9**.

$$\mathbf{9} + \mathbf{2d} \xrightarrow[\text{toluene, 30 °C}]{PtCl_2\ (1\ mol\%),\ AgOTf\ (2\ mol\%)} \mathbf{9} + \mathbf{8a} + \mathbf{10} \qquad (4)$$

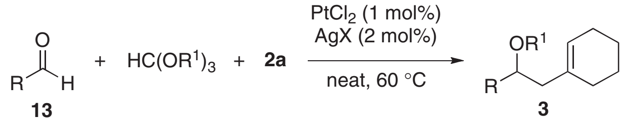
	9	**8a**	**10**
Without **2d**:	76%	11%	-
With **2d** (1 equiv):	34%	50%	24%

The present reaction probably involves the formation of an oxocarbenium ion **11** (Scheme 1). The Lewis acidic Pt(II) species generated from $PtCl_2$ and AgX would promote the C–O bond cleavage of **1**.[8] The allylation of **11** with alkene **2** can proceed by a concerted or stepwise path. The latter path consists of the formation of a cationic adduct **12** and its deprotonation. Judging from the formation of **9** and its elimination to **8a**, the reaction of **2d** would take the stepwise path. The preference for the stepwise path is likely due to the cation-stabilizing effect of the phenyl group.



Scheme 1. Plausible mechanisms for the acetal–ene reaction.

Table 3. Tandem acetalization–ene reaction[a]



Entry	R (**13**)	R^1	X	Time/h	Yield/%[b] (**3**)
1	Ph (**13a**)	Me	OTf	3	78 (**3a**)
2	Ph	Et	OTf	3	83 (**3j**)
3	$4\text{-}ClC_6H_4$ (**13c**)	Me	OTf	1.5	71 (**3c**)
4	$4\text{-}O_2NC_6H_4$ (**13f**)	Me	SbF_6	3	80 (**3f**)
5	$Ph(CH_2)_2$ (**13g**)	Me	SbF_6	1	78 (**3g**)
6	$n\text{-}C_8H_{17}$ (**13h**)	Me	SbF_6	1	96 (**3h**)
7	$n\text{-}C_8H_{17}$	Et	SbF_6	1	67 (**3k**)
8	$c\text{-}C_6H_{11}$ (**13i**)	Me	SbF_6	1	91 (**3i**)

[a]Conditions: **13** (1.00 mmol), $HC(OR^1)_3$ (1.00 or 1.20 mmol), **2a** (4.00 mmol), $PtCl_2$ (0.01 mmol), AgX (0.02 mmol), 60 °C. [b]Isolated yield.

We further attempted a direct synthesis of homoallylic ethers from aldehydes by a tandem acetalization–ene reaction. We found that orthoformates acted as effective acetalization agents. Thus the Pt(II)-catalyzed reaction of benzaldehyde (**13a**), methyl orthoformate, and **2a** gave the desired product **3a** in good yield (Entry 1 in Table 3). Use of ethyl orthoformate led to ethyl ether **3j** (Entry 2). Other aldehydes also underwent the tandem reaction efficiently (Entries 3–8).

In conclusion, we have developed the Pt(II)-catalyzed acetal–ene reaction under solvent-free conditions, which provides a convenient, green route to homoallylic ethers. More importantly, the Pt(II) catalysis is quite effective in the tandem acetalization–ene reaction of aldehydes.[9]

References and Notes

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6 Ghosez and co-workers have reported that $FeCl_3$ is an effective catalyst of intermolecular acetal–ene reaction in CH_2Cl_2. This method is slightly less efficient to the reaction of aromatic acetals and cannot be applied to the reaction with trisubstituted alkenes. A. Ladépêche, E. Tam, J.-E. Ancel, L. Ghosez, *Synthesis* **2004**, 1375.

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8 TfOH (2 mol %) also promoted the ene reaction of **1a** with **2a** (1 h, 60% yield). We cannot neglect the participation of proton catalysis. We appreciate the referee's suggestion on the reaction mechanism.

9 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

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