Cationic Platinum-Catalyzed Etherification by Intra- and Intermolecular Dehydration of Alcohols

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Abstract: Catalytic etherification of diols proceeds to give various cyclic ethers by use of cationic platinum salt, which is in situ prepared from $PtCl_2$ and $AgSbF_6$. Etherification of benzylic alcohols is also possible by intermolecular dehydration. Both of intra- and intermolecular etherifications smoothly proceed even under an atmosphere of air.

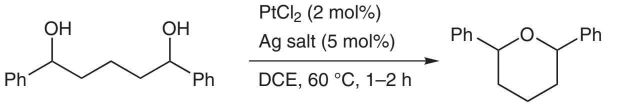
Key words: platinum, ethers, dehydration, diols, alcohols

Williamson ether synthesis is an established protocol for the synthesis of ethers from alcohols and halides, however, it is generally examined under the strongly basic conditions and a stoichiometric amount of salts is formed.[1] On the other hand, dehydration of alcohols is more direct synthesis of ethers, and protic acid catalysts[2] like amberlyst[3] and nafion-H[4] were reported for the etherification of diols. Lewis acid is another choice of a promoter for the dehydrative ether synthesis[2] and a stoichiometric amount of zinc chloride was used for the synthesis of cyclic ethers.[5] In these years, catalytic dehydrative etherifications of allylic and benzylic alcohols were also reported by use of various metal catalysts.[6,7]

We here disclose a catalytic ether synthesis using a cationic platinum salt. Intra- and intermolecular dehydrations of alcohols were examined under an atmosphere of argon and air.

We chose Pt(II) salt because of its high Lewis acidity.[8] Dehydration of 1,5-diphenylpentane-1,5-diol was examined by use of a catalytic amount of platinum dichloride in 1,2-dichloroethane (DCE) under an atmosphere of argon, however, no reaction proceeded at 60 °C (Table 1, entry 1). In order to increase Lewis acidity, silver salts were added for the generation of cationic platinum (entries 2–4). As a result, the choice of counter anion was important and 2,6-disubstituted tetrahydropyran was obtained in an excellent yield[9] by the combination of $PtCl_2$ and $AgSbF_6$ (entry 4). Argon atmosphere was not needed and no decrease of catalytic activity was observed even under an atmosphere of air (entry 5). Silver salt did not operate as a catalyst by itself (entry 6), therefore, the cationic platinum salt was an efficient catalyst for dehydrative etherification.

Table 1 Catalytic Etherification of 1,5-Diol Using Platinum Salts



Entry	Ag salt	Yield (%)
1	None	NR[c]
2	$AgBF_4$	NR[c]
3	AgOTf	78
4	$AgSbF_6$	94
5[a]	$AgSbF_6$	94
6[b]	$AgSbF_6$	NR[c]

[a] Under an atmosphere of air.
[b] Without $PtCl_2$.
[c] NR = no reaction.

Table 2 shows the results of cationic platinum-catalyzed etherification of various diols under an atmosphere of argon or air.[9,10] A 1,4-diol gave 2,5-disubstituted tetrahydrofuran under the same reaction conditions (entry 1). At higher reaction temperature, even 0.1 mol% of platinum catalyst could work efficiently to give the cyclic ether in excellent yield (entry 3). Unsymmetrical diols also reacted and di- and mono-substituted tetrahydrofurans were obtained (entries 4–6). Other aryl groups could be also tolerated as substituents on 1,5-diols and the corresponding tetrahydropyran derivatives were provided (entries 7, 8). Under the dilute reaction conditions, a 1,6-diol also cyclized to a 7-membered cyclic ether (entry 9). Not only benzylic alcohols, but alkyl alcohols were also substrates (entries 10–14). From a diol, having tertiary and primary alcohols, a 2,2-dialkyl-substituted tetrahydrofuran was obtained (entries 10, 11).[11] 1,11-Diphenylundecane-4,8-diol gave a symmetrical 2,6-dialkyl-substituted tetrahydropyran in good yield (entry 12). 2-Alkyl- and 2-alkynyl-substituted tetrahydropyrans were also provided from the corresponding diols (entries 13–15). It is noteworthy that, even under an atmosphere of air, comparable yields were achieved (entries 5, 11, 14).

Intermolecular dehydration of benzylic and allyl alcohols also proceeded by use of the cationic platinum catalyst (Table 3).[12] The reaction of 1-phenylethanol and allyl alcohol gave the corresponding ether in high yield (entry 1), moreover, the present etherification proceeded even under

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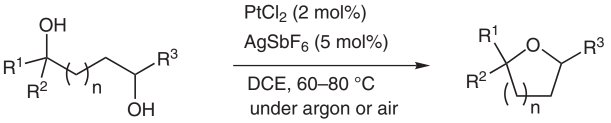
Table 2 Etherification of Various Diols by Cationic Platinum Catalyst

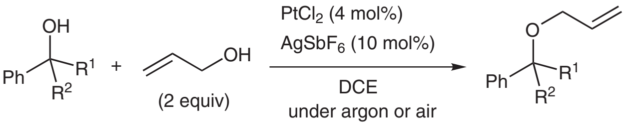


Entry	n	R^1	R^2	R^3	Temp (°C)	Time (h)	Yield (%)
1	1	Ph	H	Ph	60	0.5	97
2[a]	1	Ph	H	Ph	60	1	98
3[b]	1	Ph	H	Ph	80	0.5	95
4	1	Ph	H	Me	60	1	97
5[c]	1	Ph	H	Me	80	2	95
6	1	Ph	H	H	60	1	93
7	2	4-ClC$_6$H$_4$	H	4-ClC$_6$H$_4$	60	0.5	93
8	2	4-MeOC$_6$H$_4$	H	4-MeOC$_6$H$_4$	60	0.5	93
9[d]	3	Ph	H	Ph	60	1	75
10	1	3-Phenylpropyl	Me	H	60	2	91
11[c]	1	3-Phenylpropyl	Me	H	60	4	93
12[d]	2	3-Phenylpropyl	H	3-Phenylpropyl	70	8	77
13	2	Hexyl	H	H	80	5	78[f]
14[c]	2	Hexyl	H	H	80	4	76[f]
15[e]	2	1-Hexynyl	H	H	60	5	86

[a] PtCl$_2$ (0.5 mol%), AgSbF$_6$ (1.5 mol%).
[b] PtCl$_2$ (0.1 mol%), AgSbF$_6$ (0.5 mol%).
[c] Under an atmosphere of air. The other entries were examined under an atmosphere of argon.
[d] The concentration of diol in DCE is 0.020 M.
[e] The concentration of diol in DCE is 0.025 M.
[f] A five-membered cyclic ether (ca. 8%) was included as a side product.

an atmosphere of air without solvent (entry 2). Etherification of propargylic and tertiary alcohols occurred at room temperature (entries 3, 4). Generation of benzylic cation is probably important for the following nucleophilic addition of allyl alcohol.[13]

Table 3 Intermolecular Dehydration of Benzylic and Allyl Alcohols

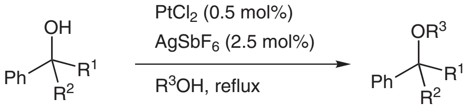


Entry	R^1	R^2	Temp (°C)	Time (h)	Yield (%)
1	Me	H	50	1.5	91
2[a]	Me	H	60	1	94
3	1-Propynyl	H	r.t.	1	75
4	Me	Me	r.t.	2	87

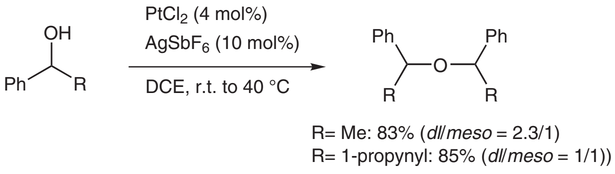
[a] Under an atmosphere of air without solvent.

In alcoholic solvents, methyl and ethyl ether syntheses from benzylic alcohols were possible using 0.5 mol% cationic platinum catalyst (Table 4). Symmetrical ethers were obtained by dimerization of alcohols, which are limited to benzylic ones (Equation 1).

Table 4 Intermolecular Etherification in Alcoholic Solvents



Entry	R^1	R^2	R^3	Time (h)	Yield (%)
1	1-Propynyl	H	Me	25	82
2	1-Propynyl	H	Et	4	67
3	Me	Me	Me	3	63



Equation 1

In summary, we developed a cationic platinum-catalyzed ether synthesis from alcohols. Catalytic intra- and intermolecular dehydration gave various cyclic and acyclic ethers. Moreover, the platinum catalyst is moisture-tolerant and the etherifications efficiently proceeded even under an atmosphere of air.

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(9) All of the 2,n-disubstituted cyclic ethers were obtained as a mixture of *dl* and *meso* isomers (ca. 1:1).

(10) **Typical Experimental Procedure for Cyclic Ethers from Diols (Table 2):** $PtCl_2$ (1.1 mg, 0.004 mmol) was placed in a flask and a 1,2-dichloroethane solution (2.0 mL) of a diol (0.20 mmol, 0.10 M) was added. To the resulting mixture was added $AgSbF_6$ (3.6 mg, 0.010 mmol) and the mixture was stirred at the temperature cited in Table 2 for 0.5–8 h. After excluding the solvent to the volume of ca. 0.5 mL under reduced pressure, the obtained mixture was purified by column chromatography (hexane–EtOAc) using silica gel to give a pure cyclic ether.

(11) 2-Methyl-2-(3-phenylpropyl)tetrahydrofuran: IR (neat): 1496, 1454, 1057, 748, 700 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.16$ (s, 3 H), 1.51–1.74 (m, 6 H), 1.82–1.95 (m, 2 H), 2.59–2.66 (m, 2 H), 3.74–3.85 (m, 2 H), 7.17–7.29 (m, 5 H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 25.8$, 26.1, 26.7, 36.5, 36.7, 40.9, 67.1, 82.5, 125.6, 128.1, 128.3, 142.5. HRMS (FAB): *m/z* calcd for $C_{14}H_{20}O$ [M^+]: 204.1514. Found: 204.1508.

(12) **Typical Experimental Procedure for Acyclic Ethers (Table 3):** $PtCl_2$ (3.2 mg, 0.012 mmol) was placed in a flask and a 1,2-dichloroethane solution (4.5 mL) of an alcohol (0.30 mmol) and allyl alcohol (0.60 mmol) was added. To the resulting mixture was added $AgSbF_6$ (10.3 mg, 0.030 mmol) and the mixture was stirred at the temperature cited in Table 3 for 1–2 h. The following procedure is the same as in ref. 10.

(13) Complete racemization of a chiral alcohol indicates that the present etherification proceeded via S_N1 pathway (Scheme 1).

Scheme 1