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Monoallylation of 1,2-Diols by Pd/Sn Bimetallic Catalysis

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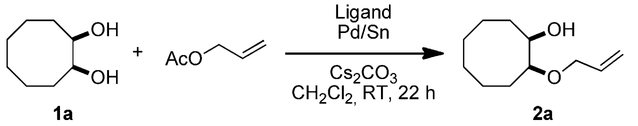
Selective transformation of 1,2-diols is highly important in synthetic organic chemistry and a variety of methods for the selective monoalkylation of 1,2-diols have been reported, which required an excess amount of 1,2-diols in most cases.[1] In the past, many stoichiometric methods have been developed, such as reductive cleavage of acetals,[2] use of polymer resins,[3] thallium salts,[4] monosodium salts,[5] silver oxide,[6] dibutyltin oxide,[7] arylboronic acids,[8] and direct allylation of 1,2-diols through intramolecular dehydrohalogenation.[9] On the other hand, only a few catalytic reactions were reported with limited successful examples using tin dichloride,[10] palladium salts,[11] phase-transfer catalysts,[12] and crown ether.[13] In particular, selective monoallylation of 1,2-diols is quite important in these types of transformation because the allyl group can be utilized as a protecting group and convertible synthetic foothold. However, no successful monoallylation of 1,2-diols have been reported in catalytic methods.[2–13]

Recently, we reported the effective methods for monoacylation of 1,2-diols with dimethyltin dichloride[14] or copper(II) salts[15] as catalysts and also developed the selective monoalkylation of 1,2-diols catalyzed by copper(II) chloride or arylboronic acids.[16] However, these catalysts gave insufficient catalytic activity with only a narrow scope of substrates for monoallylation of 1,2-diols. Therefore, we examined other catalyst systems and found that combined catalysts composed of a transition metal and Lewis acid promoted monoallylation of 1,2-diols effectively. Herein, we describe the efficient selective monoallylation of 1,2-diols by Pd/Sn bimetallic catalysis.

Initial studies were aimed at finding effective catalyst systems for the selective monoallylation of 1,2-diols. Palladium and tin salts were focused on because palladium salts were known to be good catalysts in the allylation of mono-ols and the ability of tin salts to selectively activate 1,2-diols has been already examined.[14,17] A broad range of phosphine ligands, palladium catalyst precursors, and tin salts were evaluated and selected results were shown in Table 1. First of all, the investigation of phosphine ligands in the monoallylation of *cis*-1,2-cyclooctanediol (**1a**) with allyl acetate in the presence of cesium carbonate was conducted in dichloromethane at room temperature (Table 1, entries 1–7). DPPB was proven to be a superior bidentate phosphine ligand, although most of the phosphine ligands gave excellent results. A series of palladium sources were screened and palladium(II) acetate showed the highest catalytic activity (Table 1, entries 3 and 8–11). The influence of tin salts was

Table 1. Optimization of the catalytic system.[a]



Entry	Ligand	Pd	Sn	Yield [%][b]
1	DPPE[c]	$Pd(OAc)_2$	Me_2SnCl_2	84
2	DPPP[d]	$Pd(OAc)_2$	Me_2SnCl_2	92
3	DPPB[e]	$Pd(OAc)_2$	Me_2SnCl_2	94
4	DPPPent[f]	$Pd(OAc)_2$	Me_2SnCl_2	90
5	DPPHex[g]	$Pd(OAc)_2$	Me_2SnCl_2	90
6	DPPBz[h]	$Pd(OAc)_2$	Me_2SnCl_2	93
7	DPPF[i]	$Pd(OAc)_2$	Me_2SnCl_2	89
8	DPPB[e]	$PdCl_2$	Me_2SnCl_2	87
9	DPPB[e]	$[Pd(acac)_2]$[j]	Me_2SnCl_2	73
10	DPPB[e]	$[Pd_2dba_3]$[k]	Me_2SnCl_2	60
11	DPPB[e]	$[Pd(dba)_2]$[k]	Me_2SnCl_2	83
12	DPPB[e]	$Pd(OAc)_2$	Bu_2SnCl_2	82
13	DPPB[e]	$Pd(OAc)_2$	Oc_2SnCl_2	78
14	DPPB[e]	$Pd(OAc)_2$	Ph_2SnCl_2	86
15	DPPB[e]	$Pd(OAc)_2$	Bu_2SnO	80
16	DPPB[e]	$Pd(OAc)_2$	none	60
17	none	$Pd(OAc)_2$	none	0
18	DPPB[e]	none	Me_2SnCl_2	0
19	none	none	Me_2SnCl_2	0

[a] Reaction conditions: *cis*-1,2-cyclooctanediol **1a** (0.5 mmol), allyl acetate (1.5 mmol), ligand (0.125 mmol), Pd (0.05 mmol), Sn (0.05 mmol), Cs_2CO_3 (0.75 mmol), CH_2Cl_2 (3 mL), room temperature, 22 h. [b] Yield of the isolated product. [c] 1,2-Bis(diphenylphosphino)ethane. [d] 1,3-Bis(diphenylphosphino)propane. [e] 1,4-Bis(diphenylphosphino)butane. [f] 1,5-Bis(diphenylphosphino)pentane. [g] 1,6-Bis(diphenylphosphino)hexane. [h] 1,2-Bis(diphenylphosphino)benzene. [i] 1,1′-Bis(diphenylphosphino)ferrocene. [j] acac = acetylacetonate. [k] dba = dibenzylideneacetone.

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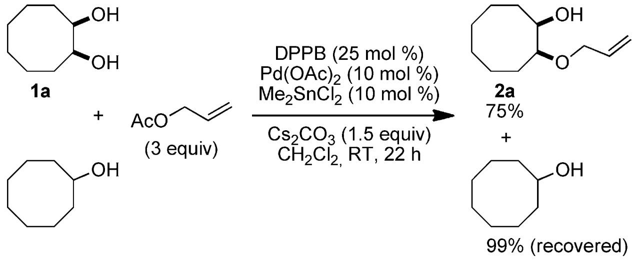
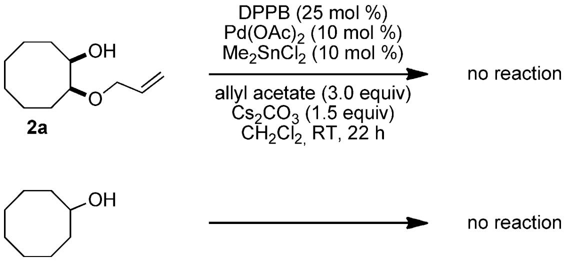
investigated and dimethyltin dichloride was found to be the most suitable (Table 1, entries 3 and 12–15). On the other hand, the allylation reaction without tin salts led to a decrease in yield (Table 1, entry 16), and the catalytic systems composed of only palladium(II) acetate, dimethyltin dichloride with DPPB, or only dimethyltin dichloride did not work at all (Table 1, entries 17–19). In addition, this catalytic system showed quite high chemoselectivity (Scheme 1). The catalytic allylation with a 1:1 mixture of *cis*-1,2-cyclooctanediol and cyclooctanol was conducted to give the monoallyalted product and unreacted cyclooctanol in 75 and 99% yields, respectively. The mono-ols such as *cis*-2-(allyloxy)-cyclooctanol **2a** and cyclooctanol did not react at all under the same reaction conditions (Scheme 2). These results regarding the catalytic systems and chemoselectivity suggested that palladium(II) acetate with DPPB was fundamental for the induction of allylation and dimethyltin dichloride was effective for the selective recognition and reactivity enhancement of diols by bidentate complexation,[18] which could not be achieved effectively in the case of *cis*-2-(allyloxy)-cyclooctanol **2a**.



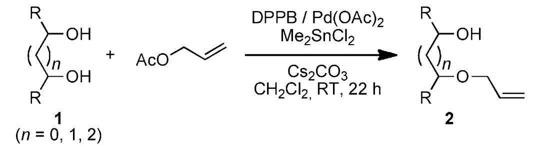
Scheme 1. Allylation using *cis*-1,2-cyclooctanediol and cyclooctanol.

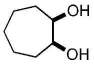
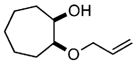
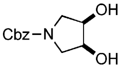
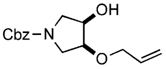
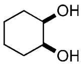
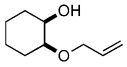
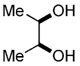
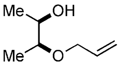
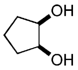
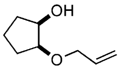
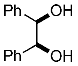
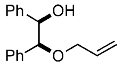
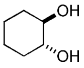
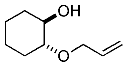
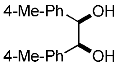
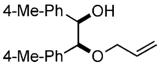
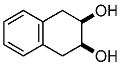
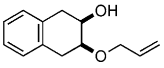
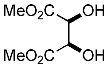
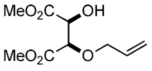
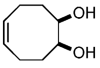
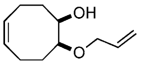
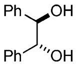
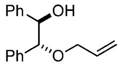
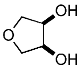
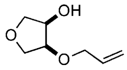
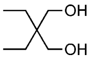
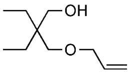
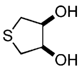
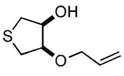
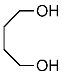
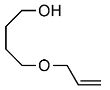


Scheme 2. Allylation using *cis*-2-(allyloxy)-cyclooctanol or cyclooctanol.

Investigation of various symmetric diols in the allylation with the Pd/Sn bimetallic catalyst using allyl acetate was conducted (Table 2). Although *cis*-1,2-cycloheptanediol (**1b**) and *cis*-1,2-cyclohexanediol (**1c**) led to excellent yields (Table 2, entries 1 and 2), the allylation of *cis*-1,2-cyclopentanediol (**1d**) gave the product **2d** in 74% yield (Table 2, entry 3). The *trans*-isomer **1e** was also a good substrate in this catalytic monoallylation, affording the product in 99%

Table 2. Scope of diols.[a]

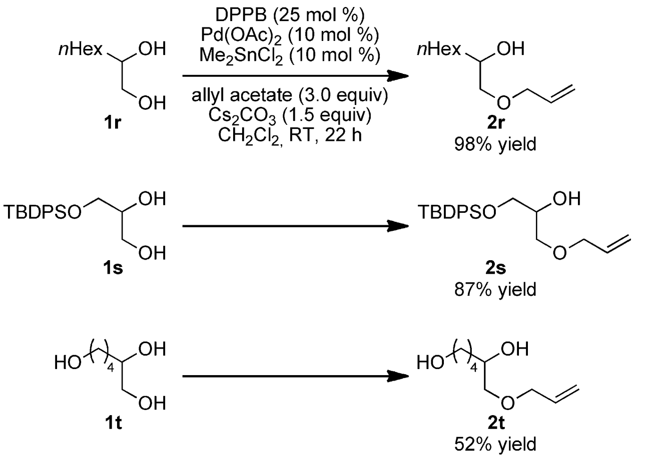


Entry	Substrate **1**		Product **2**		Yield [%][b]	Entry	Substrate **1**		Product **2**		Yield [%][b]
1	**1b**		**2b**		99[d]	9	**1j**		**2j**		98
2	**1c**		**2c**		90[d]	10	**1k**		**2k**		99[d]
3	**1d**		**2d**		74[d]	11	**1l**		**2l**		87
4	**1e**		**2e**		99[d]	12	**1m**		**2m**		98
5	**1f**		**2f**		97	13[c]	**1n**		**2n**		45
6	**1g**		**2g**		88	14	**1o**		**2o**		91
7[c]	**1h**		**2h**		99[d]	15	**1p**		**2p**		77
8	**1i**		**2i**		97	16	**1q**		**2q**		0

[a] Reaction conditions: diol **1** (0.5 mmol), allyl acetate (1.5 mmol), DPPB (0.125 mmol), $Pd(OAc)_2$ (0.05 mmol), Me_2SnCl_2 (0.05 mmol), Cs_2CO_3 (0.75 mmol), CH_2Cl_2 (3 mL), room temperature, 22 h. [b] Yield of the isolated product. [c] Allyl acetate (2.0 equiv). [d] Yields were determined by GC.

yield (Table 2, entry 4). The reaction with cyclic *cis*-1,2-diols containing π bonds proceeded with no side product to give excellent results (Table 2, entries 5 and 6). The heterocyclic *cis*-3,4-diols containing oxygen, sulfur, and nitrogen were examined. This type of heterocyclic substrate did not decrease the reaction rate (Table 2, entries 7–9). The allylation of aliphatic linear *meso*-1,2-diols **1k** proceeded efficiently as expected, affording the quantitative yield (Table 2, entry 10). Although the linear *meso*-1,2-diols with aromatic rings were easily converted to the desired monoallylated compounds (Table 2, entries 11 and 12), the substrate with ester groups gave a moderate yield (Table 2, entry 13). The *threo*-hydrobenzoin **1o** also reacted with ally acetate smoothly with 91 % yield (Table 2, entry 14). Although the 1,3-diol **1p** was suitable for this allylation method (Table 2, entry 15), the allyaltion reaction of 1,4-diol **1q** did not take place at all (Table 2, entry 16).

On the other hand, unsymmetrical linear substrates that contain primary and secondary alcohols in one molecule were examined under the same reaction conditions (Scheme 3). Only the primary alcohol moiety in diols **1r** and **1s** was allylated and the products **2r** and **2s** were obtained in 98 and 87 % yields, respectively.[19,20] The allylated glycerol derivative **2s** is known as a useful intermediate for biologically active agents.[21] This reaction system was also effective for triol **1t**, leading to an acceptable yield without any other allylated compounds.[22]



Scheme 3. Allylation of unsymmetrical substrates.

In summary, we have developed the efficient selective monoallylation of 1,2-diols with Pd/Sn bimetallic catalysis. This process was successfully applied to various diols, such as cyclic 1,2-diols containing π bonds, heterocyclic 1,2-diols, and an aliphatic 1,3-diol, as well as aliphatic cyclic and linear 1,2-diols. In addition, the catalyst system achieved high chemoselectivity even in the presence of a 1:1 mixture of *cis*-1,2-cyclooctanediol and cyclooctanol. This selective allylation could be useful for synthetic studies because it was carried out under mild conditions. Further efforts will be focused on the development of an asymmetric version in our research group.

Experimental Section

Representative procedure for selective monoallylation of 1,2-diols (Table 1, entry 3): Under an atmosphere of air, a round-bottomed flask was charged with palladium(II) acetate (11.2 mg, 0.05 mmol), 1,4-bis(diphenylphosphino)butane (53.3 mg, 0.125 mmol), dimethyltin dichloride (11.0 mg, 0.05 mmol), *cis*-1,2-cyclooctanediol **1a** (72 mg, 0.5 mmol), and cesium carbonate (245 mg, 0.75 mmol). Then, dichloromethane (3 mL) was added followed by allyl acetate (150 mg, 1.5 mmol) and the mixture was stirred at room temperature for 22 h. After this time water was added and the resulting mixture was extracted with ethyl acetate and the combined organic layers were dried with anhydrous magnesium sulfate. After filtration, the volatile components were removed with a rotary evaporator. Purification of the crude product through silica gel column chromatography (hexane/ethyl acetate = 10:1) gave 86 mg (0.47 mmol, 94 % yield) of the allylated product **2a**.

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Keywords: allylation · bimetallic catalysis · diols · palladium · tin

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