Transposition of Allylic Alcohols into Carbonyl Compounds Catalyzed by Rhodium–Phosphinine Complexes

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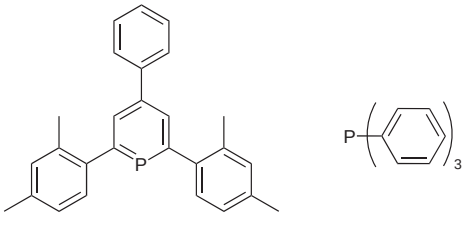
Abstract: The isomerization of a variety of allylic alcohols with formation of the corresponding saturated carbonyl compounds is readily accomplished by a new catalyst system comprising rhodium and a trisubstituted phosphinine (phosphabenzene derivative), especially when the Rh complex is activated by hydrogen prior to the transposition reaction.

Key words: green chemistry, homogeneous catalysis, isomerization, phosphorus, rhodium

We recently showed that the use of mixtures of monodentate P-ligands provides a combinatorial means to control diastereoselectivity in Rh-catalyzed olefin hydrogenation of chiral allylic alcohols.[1] The members of the library of ligands used included simple aryl- and alkylphosphines, phosphinites, phosphites and phosphinines (phosphabenzenes). In most cases a side product was observed, namely a saturated ketone resulting from an internal redox process. When using the triaryl-substituted phosphinine **1** (Figure 1), this undesired isomerization was most prominent.[1] Since the targeted transition-metal-catalyzed isomerization of allylic alcohols is an atom-economical method of significant synthetic value,[2,3] we decided to focus our attention on this process (Scheme 1). Here we show that Rh complexes of ligand **1**, especially when activated by H_2, are in fact excellent catalysts, surpassing the efficiency of traditional analogues based on triphenylphosphine (**2**). This finding constitutes yet another example of the useful application of phosphinines as ligands in transition metal-catalyzed reactions,[4] originally introduced by Breit in selective hydroformylation[5] and by Zennek and Mathey in Fe-catalyzed pyridine synthesis.[6]



1 **2**

Figure 1

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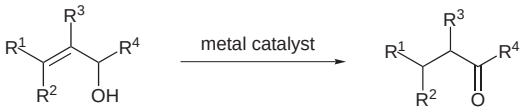
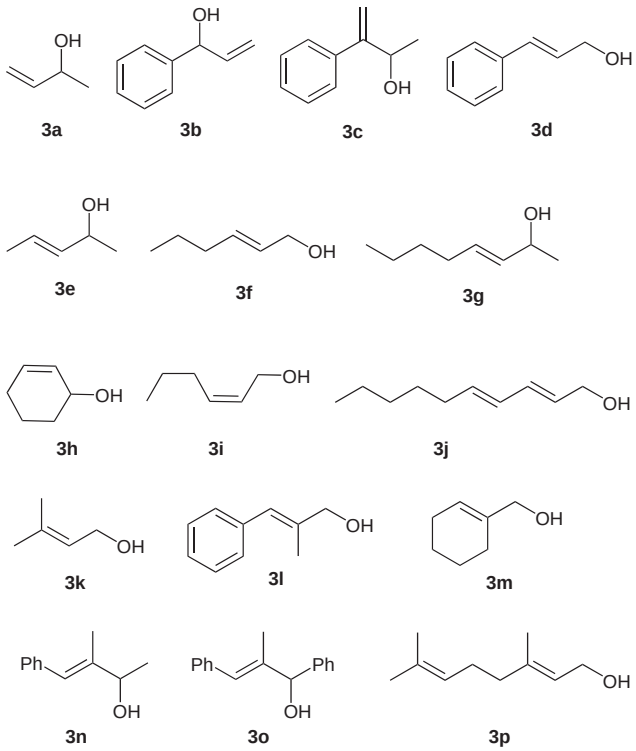


3 **4**

Scheme 1 Transition-metal-catalyzed isomerization of allylic alcohols with formation of carbonyl compounds

In the present study sixteen allylic alcohols **3a**–**p** (Figure 2) were subjected to isomerization. Based on previous work using Rh catalysts or other transition-metal analogues,[2,3] it is known that the reaction becomes more difficult as the degree of substitution around the olefinic double bond increases.



3a **3b** **3c** **3d** **3e** **3f** **3g** **3h** **3i** **3j** **3k** **3l** **3m** **3n** **3o** **3p**

Figure 2

Exploratory experiments were first performed with allylic alcohol **3c**. In procedure A, $Rh(NBD)_2BF_4$ (NBD = norbornadiene) was treated with two equivalents of phosphinine **1** or phosphine **2** under an Ar atmosphere and stirred for 30 minutes. Then the complex was used as a catalyst in the isomerization of **3c** under various conditions. In

procedure B, the same protocol was applied, except that following the treatment of the Rh salt with the respective ligand, the mixture was stirred under 1.3 bar H_2 for 30 minutes with formation of an activated species, presumably a Rh hydride. Following H_2 displacement by Ar, the activated form of the Rh complex was used in catalysis. Table 1 shows the results.

It can be seen that the activation of the Rh complex with H_2 prior to catalysis (Method B) results in a much more active catalyst, especially when using dioxane as the solvent (e.g., entry 2 vs. 1, or entry 4 vs. 3). The side-products include various reduction and/or coupling products, which reduce selectivity. We then proceeded to test the other allylic alcohols using Method B, although full optimization in each case was not attempted (Table 2).[7]

Table 1 Optimization of the Isomerization **3c** → **4c** Using 2 mol% of Rh Complexes[a]

Entry	Ligand	Method	Solvent	Temp. (°C)	Time (h)	Conv. (%)	Selectivity (%)
1	2	A	Dioxane	60	12	30	30
2	2	B	Dioxane	60	12	91	77
3	1	A	Dioxane	60	12	30	100
4	1	B	Dioxane	60	1	100	100
5	1	A	CH_2Cl_2	23	16	1	100
6	1	B	CH_2Cl_2	23	1	17	100
7	1	B	CH_2Cl_2	23	16	100	72

[a] Method A: no H_2 pretreatment. Method B: H_2 pretreatment. $Rh(NBD)_2BF_4$ used in all cases; conversion and selectivity by GC and GC-MS determinations.

Table 2 Isomerization of Allylic Alcohols **3a**–**p** with Formation of **4a**–**p** Using 2 mol% of H_2 Activated $Rh(\mathbf{1})_2BF_4$[a]

Entry	Allylic alcohol	Solvent	Temp. (°C)	Time (h)	Conv. (%)	Selectivity (%)
1	**3a**	CH_2Cl_2	23	0.5	100	100
2	**3b**	Dioxane	60	1	100	93
3	**3c**	Dioxane	60	1	100	100
4	**3d**	Dioxane	60	3.5	100	100
5	**3e**	CH_2Cl_2	23	0.5	100	100
6	**3f**	CH_2Cl_2	23	0.5	100	98
7	**3g**	Dioxane	60	1	100	97
8	**3g**	CH_2Cl_2	23	6	100	81
9	**3h**	Dioxane	60	12	85	84
10	**3i**	CH_2Cl_2	23	0.5	100	100
11	**3j**	Dioxane	60	12	51	8
12	**3k**	Dioxane	60	6	100	100
13	**3k**	CH_2Cl_2	23	16	100	90
14	**3l**	Dioxane	60	1	99	98
15	**3l**	CH_2Cl_2	23	16	73	72
16	**3m**	CH_2Cl_2	23	0.5	100	100
17	**3n**	Dioxane	60	2	100	100
18	**3o**	Dioxane	60	12	19	100
19	**3p**	Dioxane	60	12	70	33

[a] Method B; conversion and selectivity by GC and GC-MS determinations.

As shown in Table 2, allylic alcohols with diverse substitution patterns including monosubstituted (entries 1, 2) disubstituted (entries 3–10), and trisubstituted substrates (entries 12, 17), can be transformed smoothly into the corresponding saturated aldehydes or ketones in the presence of H_2 activated Rh(**1**)$_2$BF$_4$ under mild conditions. Exceptions are substrates **3j** (entry 11) and **3p** (entry 19), which provide rather sensitive aldehydes, as well as the highly substituted allylic alcohol **3o** (entry 18). Of particular note is the efficient isomerization of the trisubstituted allylic alcohol **3n** (entry 17). This compound (or analogues) is isomerized efficiently only by very few catalysts.[2a,3g,3k]

Extensive structural studies of the activated Rh complexes involving ligands **1** and **2** have not been performed. However, preliminary NMR and ESI-MS experiments show the presence of species of the type Rh(**1**)$_2$[H]$_n$BF$_4$ in which NBD has been cleaved by hydrogenation. Apparently, the Rh hydrides are more active than the starting Rh complex prior to treatment with H_2. The reason for this activation is unclear at this time, but the observation suggests that similar activation of other transition-metal complexes[2,3] used in the isomerization may also be possible. The mechanism may be different from Ru-catalyzed isomerizations.[3]

In summary, a new and active catalyst system for the isomerization of allylic alcohols with formation of the saturated carbonyl compounds has been developed. It is based on the Rh complexes of a trisubstituted phosphinine ligand. For optimal results, activation by H_2 treatment of the Rh–phosphinine complex is best carried out prior to the isomerization reaction.[7]

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(7) **General Procedure for the Isomerization of Allylic Alcohol.**
A dry 5-mL Schlenk flask under an atmosphere of argon was charged with a 5.4 mM solution of P-ligand (0.5 mL) in dry CH_2Cl_2 and a 5.4 mM solution of [Rh(NBD)$_2$]BF$_4$ (0.25 mL) in CH_2Cl_2. The mixture was stirred for 30 min at r.t., then stirred for an additional 30 min under 1.3 bar H_2. The CH_2Cl_2 and H_2 were removed by Ar displacement under reduced pressure, then 0.5 mL of CH_2Cl_2 and a 67.5 mM solution of an allylic alcohol in CH_2Cl_2 (1 mL) were added. The isomerization was carried out for the periods given. The reaction solution was passed through a small amount of silica gel and selectivity and conversion were determined by gas chromatography (GC and GC-MS).