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Rhodium-Catalyzed Reductive Allylation of Conjugated Aldehydes with Allyl Acetate

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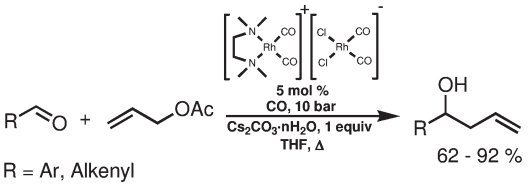


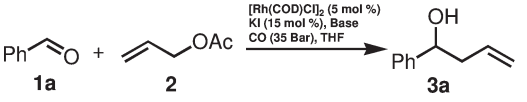
Reductive allylation of aryl and alkenyl aldehydes with allyl acetate catalyzed by the ionic diamine carbonyl rhodium complex, $[Rh(TMEDA)(CO)_2][RhCl_2(CO)_2]$, under a carbon monoxide atmosphere afforded the corresponding homoallylic alcohols in good isolated yields.

A typical carbonyl allylation reaction is usually stoichiometric in nature and involves the use of allyl boron, allyl silane, or allyl metal reagents (e.g., allyl tin), which are either not simple to prepare, moisture and air sensitive (e.g., allyl Mg or Li), or toxic.[1] Some of the available catalytic methods such as Umani−Ronchi−Keck[2] or Lewis base-catalyzed allylation[3] also require similar types of reagents. It is quite apparent, therefore, that a catalytic method that employs readily available allyl alcohol or its corresponding acetate as a source of the allyl fragment is more desirable. On the other hand, most of the existing methods for catalytic allylation with palladium or nickel catalysts and allyl alcohol or allyl acetate require the use of more than stoichiometric amounts of reductants (e.g., $SnCl_2$) assisting in the formation of a transition metal allyl complex.[4] The excellent Lewis acid-free alternatives to these methods are described in recent reports on ruthenium-catalyzed nucleophilic carbonyl allylation[5a−c] and enantioselective iridium-catalyzed carbonyl allylation with allyl acetate.[6] To our knowledge, the only report on Rh-catalyzed carbonyl allylation with allyl alcohol involves the use of more than a stoichiometric amount of $SnCl_2$.[7] We, therefore, initiated research to address the rhodium-catalyzed allylation of carbonyls to determine whether the reaction is possible with allyl acetate under Lewis acid-free conditions.

We now describe a rhodium-catalyzed Lewis acid-free reductive allylation of conjugated aldehydes using allyl acetate as a source of the allyl group, furnishing the corresponding homoallylic alcohols in good isolated yields.

In our initial experiment, the allylation reaction of benzaldehyde **1a** was carried out with the $[Rh(COD)Cl]_2$ catalyst, potassium iodide, and 2 equiv of allyl acetate **2** under 35 bar of carbon monoxide in THF at 120 °C and gave none of the desired 1-phenylbuten-1-ol **3a** (Table 1, entry 1).

TABLE 1. Reductive Allylation of Benzaldehyde by Use of $[Rh(COD)Cl]_2$/KI as the Catalytic System



entry	Cs_2CO_3 (equiv)	**2** (equiv)	*t* (h)	*T* (°C)	conversion (mol %)[a]	yield (mol %)[a]
1		2	24	120	−[b]	
2	1	2	24	120	48	84[d]
3	0.6	2	72	100	75	87[d]
4	0.6	4	48	100	80 (74)[c]	94[d]

[a]Determined by GC. [b]No reaction occurred. [c]Isolated yield after purification by column chromatography. [d]Accompanied by some unidentified products.

However, addition of 1 equiv of an inorganic base, cesium carbonate, resulted in the formation of **3a** in 48% conversion and 84% selectivity (Table 1, entry 2). Carrying out the reaction with 0.6 equiv of Cs_2CO_3 at 100 °C for 72 h afforded **3a** in 75% conversion and 87% selectivity (Table 1, entry 3). The use of 4 equiv of allyl acetate decreased the reaction time from 72 to 48 h and the reaction occurred affording slightly higher conversion than that realized when effecting the reaction with 2 equiv of **2** (Table 1, entry 3 vs 4).

To determine whether the nature of the base has any influence on the reaction, and to investigate the possibility of decreasing the reaction time to 24 h with no loss in conversion and selectivity, we carried out the allylation

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(4) See for example: (a) Masuyama, Y.; Takahara, J. P.; Kurusu, Y. *J. Am. Chem. Soc.* **1988**, *110*, 4473. (b) Masuyama, Y.; Ito, T.; Tachi, K.; Ito, A.; Kurusu, Y. *Chem. Commun.* **1999**, 1261. (c) Hirashita, T.; Kambe, S.; Tsuji, H.; Omori, H.; Araki, S. *J. Org. Chem.* **2004**, *69*, 5054. (d) Jang, T.-S.; Keum, G.; Kang, S.-B.; Chung, B.-Y.; Kim, Y. *Synthesis* **2003**, *5*, 775. (e) Fontana, G.; Lubineau, A.; Scherrmann, M.-C. *Org. Biomol. Chem.* **2005**, *3*, 1375. (f) Masuyama, Y.; Hayashi, R.; Otake, K.; Kurusu, Y. J. *Chem. Soc., Chem. Commun.* **1988**, 44. (g) Kimura, M.; Tomizawa, T.; Horino, Y.; Tanaka, S.; Tamaru, Y. *Tetrahedron Lett.* **2000**, *41*, 3627.

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(6) (a) Kim, I. S.; Ngai, M.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 6340. (b) Kim, I. S.; Ngai, M.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 14891.

(7) Masuyama, Y.; Kaneko, Y.; Kurusu, Y. *Tetrahedron Lett.* **2004**, *45*, 8969.

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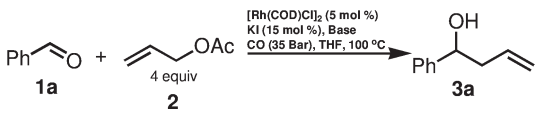
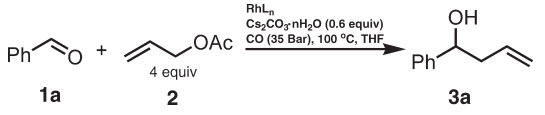
TABLE 2. Investigation of the Influence of the Base on the Allylation of Benzaldehyde Effected by the $[Rh(COD)Cl]_2$/KI Catalytic System



entry	base (equiv)	t (h)	conversion (mol %)[a]	yield (mol %)[a]
1	Cs_2CO_3 (0.6)	48	80(74)[b]	94
2	Cs_2CO_3 (2)	48	85	91
3	$SrCO_3$ (2)	24	—[c]	
4	K_2CO_3 (2)	24	56	62[d]
5	$KHCO_3$ (2)	24	37	64[d]
6	$Ba(OH)_2$ (2)	24	—[c]	
7	DBU (2)	24	—[c]	

[a]Determined by GC. [b]Isolated yield after purification by column chromatography. [c]No reaction occurred. [d]Accompanied by some unidentified products.

TABLE 3. Allylation of Benzaldehyde Catalyzed by Different Rh Complexes



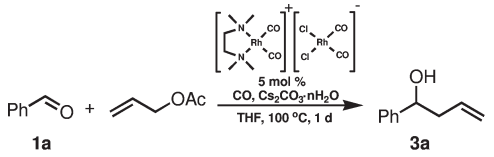
entry	Rh source (mol %)	t (h)	conversion (mol %)[a]	yield (mol %)[a]
1	$[Rh(COD)Cl]_2$ (5)[b]	48	80(74)[c]	94[d]
2	$RhCl(PPh_3)_3(CO)$ (5)	24	50	85[d]
3	$RhCl(PPh_3)_3$ (5)	24	60	80[d]
4	[Rh(COD)]OTf (5)	24	48	69[d]
5	[Rh(dppb)(COD)][BF_4] (5)	24	36	73[d]
6	$[Rh(TMEDA)(CO)_2]$ $[RhCl_2(CO)_2]$ (5)	24	77(65)[c]	88[d]
7	$[Rh(TMEDA)(CO)_2]$ $[RhCl_2(CO)_2]$ (5)[e]	24	—[f]	

[a]Determined by GC. [b]KI (15 mol %). [c]Isolated yield after purification by column chromatography. [d]Accompanied by some unidentified products. [e]N_2 (35 bar) was used instead of CO. [f]No reaction occurred.

reaction in the presence of a range of bases. As the results in Table 2 show, the use of $SrCO_3$, $Ba(OH)_2$, and DBU was not effective for the production of **3a** (Table 2, entries 3, 6, and 7); on the other hand, the use of K_2CO_3 and $KHCO_3$ produced **3a** in low conversion and selectivity (Table 2, entries 4 and 5). When the allylation reaction was carried out with 2 equiv of Cs_2CO_3 for 48 h, **3a** was formed in slightly higher conversion (Table 2, entry 2).

Although the allylation of benzaldehyde can be effected in 48 h with the conditions outlined in Table 1, entry 4, we thought that we could shorten the reaction time by using a complex other than the initially chosen $[Rh(COD)Cl]_2$ as the catalyst. The influence of the rhodium source on the allylation of benzaldehyde was tested by employing several Rh(I) complexes listed in Table 3. The results presented in Table 3 indicate that the most effective catalyst for the reaction was the ionic diamine carbonyl rhodium complex, $[Rh(TMEDA)(CO)_2]^+[Rh(Cl)_2(CO)_2]^-$, which gave conversions and selectivities similar to those obtained with $[Rh(COD)Cl]_2$ for a shorter reaction time of 24 h (Table 3, entry 6 vs entry 1). Allylation carried out under N_2 instead of CO gave no product. It is evident, therefore, that although

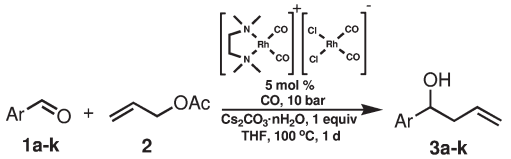
TABLE 4. Optimization of the Allylation Reaction Conditions



entry	catalyst (mol %)	Cs_2CO_3 (equiv)	CO (bar)	conversion (mol %)[a]	yield (mol %)[a]
1	5	0.6	35	77(65)[b]	88[c]
2	5	1	10	92(87)[b]	95[c]
3	7.5	1.25	35	90	93[c]
4	7.5	1.25	20	98	91[c]
5	7.5	1.25	10	95	92[c]

[a]Determined by GC. [b]Isolated yield after purification by column chromatography. [c]Accompanied by some unidentified products.

TABLE 5. Rh-Catalyzed Allylation of Aromatic Aldehydes[a]



entry	product	Ar	isolated yield (%)
1	**3a**	Ph	87
2	**3b**	4-methylphenyl	80
3	**3c**	4-isopropylphenyl	83
4	**3d**	2-methoxyphenyl	85
5	**3e**	2-methylphenyl	62
6	**3f**	2-chlorophenyl	88
7	**3g**	2-bromophenyl	92
8	**3h**	4-bromophenyl	83
9	**3i**	4,4′-biphenyl	77
11	**3j**	naphthyl	89
12	**3k**	4-carbamoylphenyl	78

[a]Reaction conditions: substrate, 2 mmol; $[Rh(TMED)(CO)_2][RhCl_2(CO)_2]$, 5 mol % ; $Cs_2CO_3 \cdot nH_2O$, 2 mmol; allyl acetate, 8 mmol; THF, 10 mL; CO, 10 bar; 100 °C.

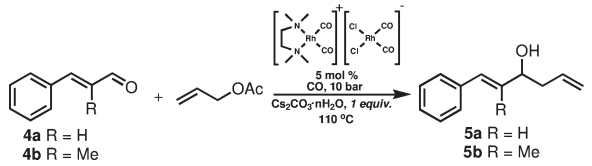
the carbon monoxide fragment does not appear in the reaction product, the presence of CO is necessary for the reaction.

The reaction conditions outlined in Table 3, entry 6, were further optimized by varying the catalyst and the base concentration, and by changing the pressure of CO. The results in Table 4 indicate that the most optimal conditions are those presented in entry 2, affording 1-phenylbuten-1-ol **3a** in 92% conversion, 95% selectivity, and 87% isolated yield.

Using the optimal reaction conditions, a range of aryl aldehydes were tested for the allylation reaction. The results presented in Table 5 demonstrate that substrates **1a**−**d** and **1f**−**k** afford the corresponding homoallylic alcohols **3a**−**d** and **3f**−**k** in good isolated yields. 1-(2-Methylphenyl)buten-1-ol **3e** was isolated in a somewhat lower yield of 62%. The location and the nature of the halogen substituent have little effect on the performance of the reaction (Table 5, entries 6−8).

To determine whether the Rh-catalyzed reductive allylation reaction can be extended to α,β-unsaturated aldehydes,

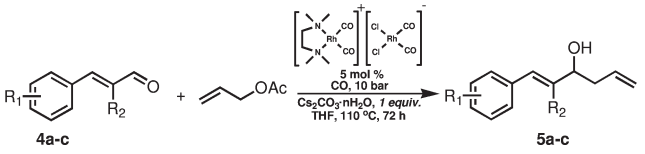
TABLE 6. Reductive Allylation of Alkenyl Aldehydes



entry	solvent	*t* (h)	conversion (mol %)[a]	yield (mol %)[a]
1[b]	THF	24	60	95
2[b]	THF	72	78	91
3[b]	THF	96	85	53[c]
4[b]	benzene	24	—[d]	
5[b]	acetonitrile	24	41	38[c]
6[e]	$[CH_3(CH_2)_{13}P(C_6H_{13})_3]PF_6$[f]	24	—[d]	

[a]Determined by GC. [b]R = H. [c]Selectivity decreased due to the oxy-Cope rearrangement of **5a**. [d]No reaction occurred. [e]R = Me. [f]CYPHOS IL 110.

TABLE 7. Reductive Allylation of Alkenyl Aldehydes[a]



entry	product	R_1	R_2	isolated yield (%)
1	**5a**	H	H	79
2	**5b**	H	Me	85
3	**5c**	4-*t*-Bu	Me	69

[a]Reaction conditions: substrate, 2 mmol; $[Rh(TMEDA)(CO)_2][RhCl_2(CO)_2]$, 5 mol %; $Cs_2CO_3 \cdot nH_2O$, 2 mmol; allyl acetate, 8 mmol; THF, 10 mL; CO, 10 bar; 110 °C.

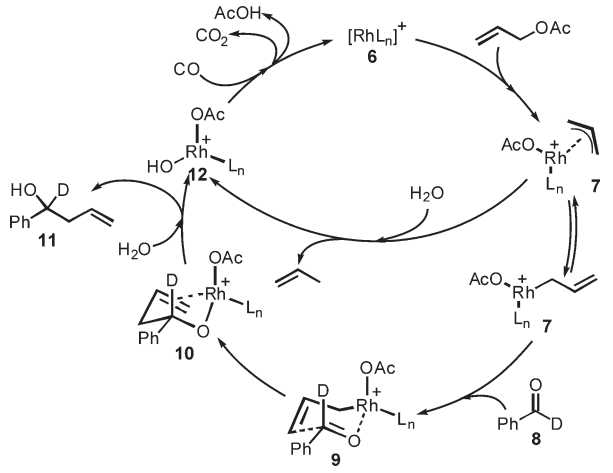
cinnamaldehyde **4a** was reacted under conditions suitable for the alkylation of aryl aldehydes. The results summarized in Table 6 show that allylation of cinnamaldehyde **4a** required higher temperatures and longer reaction times than those needed for aryl aldehydes **1a**−**k**. At the same time, reaction times longer than 72 h led to a decrease in selectivity due to the oxy-Cope rearrangement of the homoallylic alcohol **5a** into the corresponding aldehyde (Table 6, entry 3). The use of benzene, acetonitrile, and phosphorus-based ionic liquid as the reaction solvents was also tested (Table 6, entries 4−6).

As one can see from the results, no product was formed during the reaction conducted in benzene and the phosphonium ionic liquid (Table 6, entries 4 and 6). In acetonitrile the oxy-Cope rearrangement proceeded faster than that in THF (Table 6, entry 5 vs entry 1). On the basis of the results shown in Table 6, we can conclude that the optimal conditions for the reductive allylation of cinnamaldehyde are these found in Table 6, entry 2.

Using the optimal conditions, substituted cinnamaldehydes were evaluated for the alkylation reaction. The results presented in Table 7 demonstrate that substrates **4a**−**c** afford the corresponding homoallylic alcohols **5a**−**c** in good isolated yields.

To gain an insight into the mechanism of the reaction, we conducted an experiment using benzaldehyde-*1-d* (**8**). Isolation of **11** with retention of deuterium label excludes

SCHEME 1. The Suggested Mechanism for Rh-Catalyzed Allylation



formation of a Rh-acyl intermediate. Generation of propene indicated a competing hydrolytic decomposition of Rh(III) allyl as a side reaction.[8] Allylation of **1a** in the presence of D_2O (2 mmol) gave nondeuterated product **3a** and ^{2}H-enriched propene.[9]

Taking into account the aforementioned results, we propose a mechanism for the Rh-catalyzed allylation reaction with allyl acetate (Scheme 1). Generated Rh(III) allyl complex **7**[10] reacts with aldehyde in a Barbier-type fashion[7] through an intermediate **9** to form alkoxy−Rh(III) complex **10**, which then undergoes hydrolysis;[11] subsequent reduction of hydroxy−Rh(III) complex **12** by CO regenerates the catalyst **6**.

In conclusion, a variety of aryl and alkenyl aldehydes undergo allylation by allyl acetate, using the ionic diamine carbonyl rhodium complex, $[Rh(TMEDA)(CO)_2]^+[Rh(Cl)_2(CO)_2]^-$, under carbon monoxide to give the corresponding homoallylic alcohols in good isolated yields.

Experimental Section

General Procedure for the Rhodium-Catalyzed Reductive Allylation of Aryl Aldehydes with Allyl Acetate. A glass liner containing the substrate (2 mmol), $[Rh(TMEDA)(CO)_2][RhCl_2(CO)_2]$ (5 mol %), $Cs_2CO_3 \cdot nH_2O$ (2 mmol), allyl acetate (8 mmol), and THF (10 mL) was placed in a 45 mL autoclave equipped with a magnetic stirring bar. The autoclave was flushed three times with carbon monoxide and then pressurized to 10 bar.[12] The autoclave was placed in

(8) Propene was trapped as 1,2-dibromopropane by slowly passing the gas mixture through a solution of Br_2 in $CHCl_3$; an excess of Br_2 was removed by treating the solution with aq Na_2SO_3. 1,2-Dibromopropane was detected by GC-MS analysis (*m*/*z* 202 ([M^+] 2%), 123 (97), 121 (100), 107 (4), 105 (4), 95 (5), 93 (6), 81 (5), 78 (5)). Formation of propene explains the need for an excess of allyl acetate for the reaction.

(9) See the Supporting Information, pp S49 and S50.

(10) See for example: (a) Payne, M. J.; Cole-Hamilton, D. J. *J. Chem. Soc., Dalton Trans.* **1997**, 3167. (b) Hayashi, T.; Okada, A.; Suzuka, T.; Kawatsura, M. *Org. Lett.* **2003**, *5*, 1713.

(11) Cs_2CO_3 contained 1.96% of H_2O (determined by TGA); water may be produced during the reaction from H_2CO_3 generated by trapping AcOH with Cs_2CO_3. Regeneration of 0.5 equiv of H_2O and entrapment of AcOH define the role of Cs_2CO_3 in the reaction.

(12) Carbon monoxide is a highly poisonous gas; please see the Supporting Information for the safety requirements.

an oil bath preset to 100 °C on a stirring hot plate. After 24 h, the autoclave was removed from the oil bath and cooled to room temperature prior to the release of CO gas. The reaction mixture was concentrated in vacuum, and the residue was purified by flash chromatography with use of 20% ethyl acetate in hexanes as eluant to afford the product.

Acknowledgment. We are grateful to the National Sciences and Engineering Research Council for support of the research.

Supporting Information Available: Experimental procedures and copies of ^{1}H and ^{13}C NMR spectra of synthesized compounds. This material is available free of charge via the Internet at http://pubs.acs.org.