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Carbon–carbon bond formation by reactions of allylic alcohol with enoxysilane in the presence of Ir-complex

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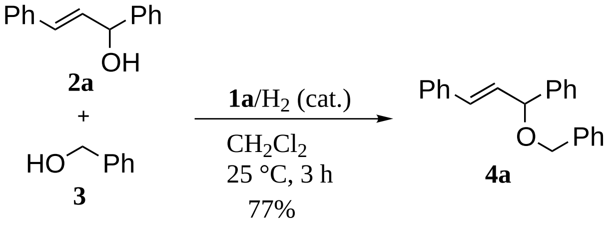
Abstract—Substitution of allylic alcohols to form a carbon–carbon bond is accomplished by a simple reaction of the allylic alcohol itself with an enoxysilane, catalyzed by [Ir(cod)(PPh$_3$)$_2$]X which is activated by H_2 molecule. The anion part X of the complexes plays an important role to enhance the rate and product yields of the reactions. The efficacy of the catalyst increases with switching X in the order of $PF_6^-<ClO_4^-<TfO^-$. © 2002 Elsevier Science Ltd. All rights reserved.

Cationic Ir(I) complexes are interesting in their prominent ability as a catalyst precursor for the hydrogenation of highly substituted alkenes[1] in which the direction of the incoming hydrogen is controlled by the hydroxy group contained in the substrates.[2] A second feature of these complexes is the high performance for the isomerization of olefinic double bonds in allylic alcohols,[3] silyloxyallyl compounds,[4] and alkenes containing a trimethylsilyl group at a remote position.[5] On the other hand, some alkoxy iridium complexes[6] formed by oxidative addition of an alcohol have been scrutinized in relation to transfer hydrogenation of alkynes[7] and asymmetric hydrogenation of ketones[8] or imines.[9] However, there are no examples of the hydroxy function of alcohols behaving as a leaving group in reactions catalyzed by a cationic Ir(I) complex[10] or by Brønsted acid. We focussed on finding this type of catalytic reaction. We report here that the hydroxy group of allylic alcohols is readily substituted by benzyl alcohol or an enoxysilane in the presence of a catalytic amount of a cationic Ir(I) complex.

At the first stage of this project, it was observed that [Ir(cod)(PPh$_3$)$_2$]PF$_6$ (**1a**) activated by H_2 works as a catalyst for substitution of the hydroxy group at the allylic position and for isomerization of alkenes. 3-Benzyloxy-1,3-diphenyl-1-popene (**4a**) was isolated in 77% yield with the concomitant formation of a trace amount of 1,3-diphenylpropan-1-one by simply stirring a CH_2Cl_2 solution of **2a** (0.72 mmol), benzyl alcohol (**3**, 0.79 mmol) and **1a** (0.037 mmol) for 3 h at 25°C (Eq. (1)). On the other hand, 1,1-dibenzyloxy-3-phenylpropane (43%) was isolated as the sole product in a reaction of cinnamyl alcohol with **3** under similar conditions.



(1)

The result of Eq. (1) implies that the hydroxy group of **2a** was kicked off to form a cationic site at the allylic carbon in the presence of **1a**. This stimulated us to design Ir-catalyzed C–C bond forming reactions between an allylic alcohol and an enoxysilane as a facile homologation method, because we have already found that enoxysilane behaves as a good nucleophile in Ir(I)-catalyzed aldol-type and Michael-type couplings.[11] Thus, we arranged a series of Ir-catalyzed reactions between allylic alcohol **2** and enoxysilane **5**.

A coupling product **6aa** was isolated in 54% yield with the concomitant formation of **7a** (14%) and **8a** (17%), when a mixture of **2a** (1 mmol) and **5a** (2 mmol) was heated for 21 h at 80°C in a sealed tube containing 2 mol% of **1a** activated in advance by H_2 gas at −78°C.

Keywords: allylic substitution; cationic Ir(I) complex; allylic alcohols; enoxysilanes.

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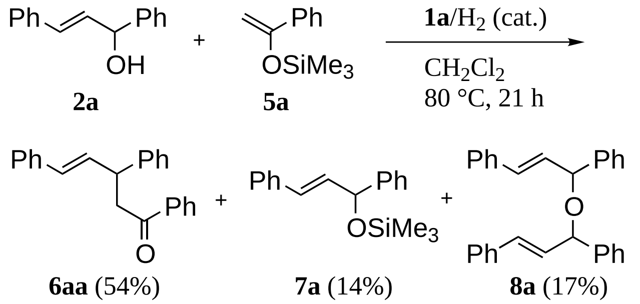


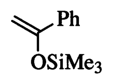
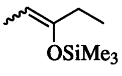
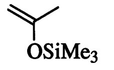
(2)

Detailed results are summarized in Table 1. This type of coupling to form **6aa** proceeded even at 25°C, though slow addition of **2a** through a micro-feeder was required in order to suppress the formation of **8a**. It is noted that the yield of **6aa** was lower than in the reaction of **2a** itself in the reactions using **7a** and the acetate of **2a** as the starting substrate (entries 4 and 5 in Table 1).

In contrast to **5a**, enoxysilane **5b** derived from pentan-3-one gave poor yield of **6ab** under similar conditions using **1a** as a catalyst (entry 6 in Table 1). However, this defect was surmounted by tuning the anion part of [Ir(cod)(PPh$_3$)$_2$]X. When complexes **1b** (X = ClO$_4$)[12] and **1c** (X = OTf, trifluoromethanesulfonate) were used as a catalyst, rate acceleration and improvement in the yield of **6ab** were observed in the reaction of **2a** with **5b** (entries 7 and 8 in Table 1). In particular, **1c** brought about significant acceleration and high selectivity for the formation of **6ab**, whereas the diastereoselectivity of **6ab** could not be improved by the choice of catalyst. Similarly, **1c** accelerated the coupling rate to give **6aa** and **6ac** in the reactions of **2a** with **5a** and **5c**, respectively (entries 3 and 9 in Table 1).

The present type of allylic substitution was extended to some other alcohols as illustrated in Eq. (3). Two regioisomers were formed in the reaction of unsymmetrically substituted allylic alcohols. The results are summarized in Table 2. 1-Phenyl-2-buten-1-ol **2b** reacted readily with **5a** to give a pair of regioisomers, **6ba** and **6ba′** (entry 1 in Table 2). In sharp contrast to **2b**, 4-phenyl-3-buten-2-ol **2c** was not amenable to the allylic substitution, but the trimethylsilyl ether derived from **2c** was the sole product in the reaction with **5a** catalyzed by **1a** (entry 3 in Table 2). Only 7% yield of **6ca** was isolated in a similar reaction catalyzed by **1c** (entry 4 in Table 2). On the other hand, an additional methyl group on the carbinol carbon of **2c** remarkably enhanced the lability of the hydroxy group as a leaving group to give **6eb′** and **6ec′** (identical with **6db** and **6dc**, respectively) with high regioselectivity as exemplified in the reactions of **2e** with **5b** and **5c** (entries 9 and 10 in Table 2). The identical products **6db** and **6dc** were also obtained with high selectivity in the reactions of **2d** with the corresponding enoxysilane. The rate of the reactions was much enhanced by using TfO$^-$ as the anion part, X of **1**, whereas the ratio of diastereomers did not

Table 1. Reactions of **2a** with enoxysilanes in the presence of **1**[a]

Entry	Enoxysilane	[Ir(cod)(PPh$_3$)$_2$]X (1)		Conditions	Yield (%) of products[b]			
		X	mol %	°C/h	6		7a	8a
1	 5a	PF$_6$	2	80/21[c]	aa	54	14	17
2		PF$_6$	2	25/24[d]	aa	62	9	22
3		OTf	1	25/4	aa	60 (65)	5 (0)	22 (0)
4[e]	5a	PF$_6$	2	80/18[c]	aa	39	0	0
5[f]	5a	PF$_6$	2	80/19[c]	aa	26	0	0
6	 5b[g]	PF$_6$	3	80/23[c]	ab	24[h]	13	0
7		ClO$_4$	2	25/24	ab	79[h]	12	0
8		OTf	1	25/3	ab	92[h] (87)	3 (0)	0 (0)
9	 5c	OTf	1	25/2	ac	77 (73)	22 (8)	0 (0)

[a] Reactions were carried out in a CH$_2$Cl$_2$ (5 ml) solution containing **2a** (1 mmol), an enoxysilane (2 mmol), and **1**.

[b] The value in parentheses is the result obtained in the presence of 1 mole % of CF$_3$SO$_3$H instead of **1c**.

[c] A solution containing substrates and catalyst was stirred in a sealed tube.

[d] A solution of **2a** was added to a solution containing **5a** and **1a** at the rate taking 2 h for completion.

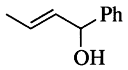
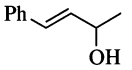
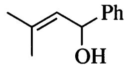
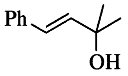
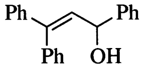
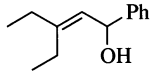
[e] Trimethylsilyl ether (**7a**) was used instead of **2a**.

[f] Acetate of **2a** was used instead of **2a**.

[g] *E*:*Z* ≈ 3:7

[h] A mixture of two diastereomers (ratio ≈ 56:44)

Table 2. Reactions of allylic alcohols with enoxysilanes in the presence of **1**[a]

Entry	Allylic alcohol	Enoxysilane	Catalyst **1**		Conditions	Product (**6** and/or **6'**)		
			X	mol %	°C/h	Yield (%) of **6** or **6'**		Ratio of isomers[b]
1	**2b** 	**5a**	PF_6	2	25/12	**6ba**	42	58:42[d]
2		**5c**	OTf	1	25/1	**6bc**	57[c]	46:54[d]
3	**2c** 	**5a**	PF_6	2	25/12	**6ca**	0[e]	—
4		**5a**	OTf	1	25/2	**6ca**	7[f]	52:48[d]
5	**2d** 	**5b**	PF_6	3	25/12	**6db**	78	56:44[g]
6		**5b**	ClO_4	2	25/15	**6db**	91	53:47[g]
7		**5b**	OTf	1	25/2	**6db**	93	54:46[g]
8		**5c**	OTf	1	25/2	**6dc**	94	93:7[d]
9	**2e** 	**5b**	ClO_4	2	25/12	**6eb'**	56	51:49[g]
10		**5c**	OTf	1	25/14	**6ec'**	81	6:94[d]
11	**2f** 	**5b**	PF_6	2	25/20	**6fb**	54	59:41[g]
12	**2g** 	**5b**	ClO_4	2	25/24	**6gb**	73	54:46[g]

[a] A CH_2Cl_2 (1. 5 ml) solution of **2** (1 mmol) was added to a CH_2Cl_2 (3.5 ml) solution containing **5** (2 mmol) and **1** at the rate taking 2 h for completion.

[b] The ratio was estimated from the ^{1}H NMR spectrum of the corresponding crude product.

[c] A mixture of ethers (32%) **8b** and **8c** was formed concomitantly.

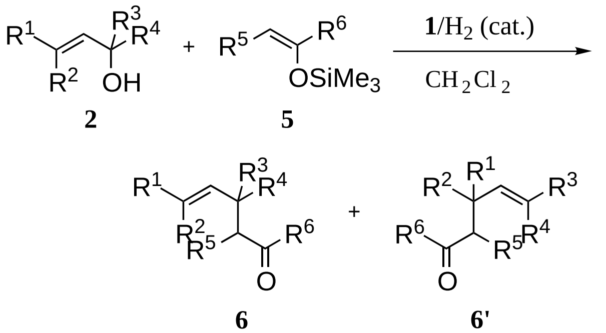
[d] This ratio shows **6**:**6'**.

[e] Trimethylsilyl ether (**7c**) was obtained in 76% yield.

[f] Trimethylsilyl ether (**7c**, 12%) and a mixture of ethers (50%) were formed concomitantly.

[g] This value shows the ratio of two diastereomers of **6** or **6'** which are not specified at present.

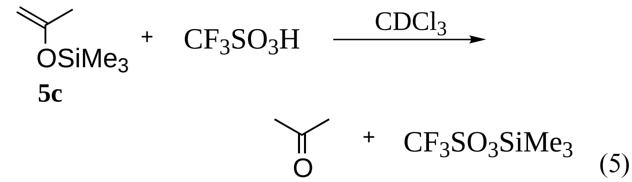
vary so much regardless of X (entries 5, 6 and 7 in Table 2). Other alcohols **2f** and **2g** reacted with **5b** to give the corresponding product **6fb** and **6gb**, respectively (entries 11 and 12 in Table 2). Regioselectivity was not observed in the reaction of **2b**; however, a less substituted site was selected preferentially as the connecting site in the reaction of models containing different numbers of substituents on the two allylic termini. Unfortunately, diastereo-control in these reactions was not satisfactory similarly to the results reported in transition-metal catalyzed substitution of allylic esters.[13]



(3)

We have postulated the presence of an Ir–Si species on the basis of the appearance of a new trimethylsilyl signal in accord with the decrease of an Ir–H species in the ^{1}H NMR spectrum of a stoichiometric mixture of **1** activated by H_2 gas and **5c**.[11a] The rate of the corresponding interaction strongly depended on the anionic part of **1**: the rate increases in the order of **1a** (X = PF_6)<**1b** (X = ClO_4)<**1c** (X = OTf). Although the precise behavior of the Ir-species is obscure at present, this appreciable rate deviation on the anionic part of **1** seems to reflect the remarkable rate acceleration in the present allylic substitution. This rate acceleration can be elucidated by the intervention of XH which may be formed by the equilibrium as shown in Eq. (4).[14] In fact, the presence of catalytic amount of CF_3SO_3H instead of **1c** realized the substitution of **2a** with the efficiency similar to **1c** (entries 3, 8 and 9 in Table 1). However, we observed that free CF_3SO_3H reacts rapidly with an equivalent mole of **5c** to form Me_3SiOTf and acetone in $CDCl_3$ (Eq. (5)). Formation of Me_3SiOTf was not observed in the ^{1}H NMR spectrum ($CDCl_3$) of a mixture of $[Ir(H)_2(cod)(PPh_3)_2]OTf$ and four equivalent moles of **5c**. Excess of **5c** remained intact for over 2 h in the sample. Unfortunately, the participation of CF_3SO_3H cannot be completely excluded in the present transformation as shown in Eqs. (2) and (3), because the starting allylic alcohol may behave as a proton source. Detailed study on this point is now in progress.

$$[Ir(H)_2(cod)(PPh_3)_2]X \rightleftharpoons Ir(H)(cod)(PPh_3)_2 + HX \quad (4)$$



(5)

Mechanistic consideration aside, the most important point of this transformation is the fact that allylic alcohols themselves are suitable for the substitution using an enoxysilane as a nucleophile. Our finding provides a new variation in the allylic substitution regardless of the source of catalyst. Although remarkable difference in the efficiency of catalyst is not observed between **1c** and CF_3SO_3H at present, the following points are advantageous for the use of Ir complexes as a catalyst: (i) the required quantity of catalyst is precisely controlled by weight, because they are solid stable in the atmosphere, (ii) the required property as a catalyst can be adjusted by tuning ligands and (iii) the present transformation is extendable to an asymmetric version by choosing prompt ligands.

In summary, we have found that the hydroxy group of allylic alcohols behaves as a leaving group in the presence of a catalytic amount of $[Ir(cod)(PPh_3)_2]X$ activated in advance by H_2 to form a carbon–oxygen bond or a carbon–carbon bond at the allylic position. It should be stressed that the present method is performed by simply stirring a mixed solution of the substrates under almost neutral conditions, though considerable effort is required for the control of regio- and stereochemistry at present.

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References

1. (a) Crabtree, R. H. *Acc. Chem. Res.* **1979**, *12*, 331; (b) Suggs, J. W.; Cox, S. D.; Crabtree, R. H.; Quirk, J. M. *Tetrahedron Lett.* **1981**, *22*, 303.
2. Crabtree, R. H.; Davis, M. W. *J. Org. Chem.* **1986**, *51*, 2655.
3. Baudy, D.; Ephritikhine, M.; Felkin, H. *Chem. Commun.* **1978**, 694.
4. Ohmura, T.; Yamamoto, Y.; Miyaura, N. *Organometallics* **1999**, *18*, 413.
5. Matsuda, I.; Kato, T.; Sato, S. *Tetrahedron Lett.* **1986**, *27*, 5747.
6. (a) Milstein, D.; Calabrese, J. C.; Williams, I. D. *J. Am. Chem. Soc.* **1986**, *108*, 6387; (b) Lapido, F. L.; Kooti, M.; Merola, J. S. *Inorg. Chem.* **1993**, *32*, 1681; (c) Newman, L. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1985**, *107*, 5314; (d) Glueck, D. S.; Winslow, L. J. N.; Bergman, R. G. *Organometallics* **1991**, *10*, 1462; (e) Tani, K.; Iseki, A.; Yamagata, T. *Angew. Chem., Int. Ed.* **1998**, *37*, 3381.
7. Tani, K.; Iseki, A.; Yamagata, T. *Chem. Commun.* **1999**, 1821.
8. Mashima, K.; Abe, T.; Tani, K. *Chem. Lett.* **1998**, 1199 and 1201.
9. Kainz, S.; Brinkmann, A.; Leitner, W.; Pfalz, A. *J. Am. Chem. Soc.* **1999**, *121*, 6421.
10. In the previous report on the Ir(I)-catalyzed substitution of allylic alcohols, the process of the reaction is elucidated by presuming intervention of a malonate ester derived from allylic alcohols: Takeuchi, R.; Kashio, M. *J. Am. Chem. Soc.* **1998**, *120*, 8647.
11. (a) Matsuda, I.; Hasegawa, Y.; Makino, T.; Itoh, K. *Tetrahedron Lett.* **2000**, *41*, 1405; (b) Matsuda, I.; Makino, T.; Hasegawa, Y.; Itoh, K. *Tetrahedron Lett.* **2000**, *41*, 1409.
12. It is known that perchlorate compounds are explosive. Although we have not experienced an explosion in the reaction using **1b**, manipulations with this reagent should be performed with care.
13. (a) Godleski, S. A. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 4, p. 585; (b) Tsuji, J. In *Palladium Reagents and Catalysts*; John Wiley & Sons: New York, 1995; p. 290; (c) Harrington, P. J. In *Comprehensive Organometallic Chemistry II*; Abel, E. W.; Stone, F. G. A.; Wilkinson, G., Eds.; Pergamon Press: Oxford, 1995; Vol. 12, p. 797; (d) Trost, B. M.; Varanken, D. L. V. *Chem. Rev.* **1996**, *96*, 395; (e) Recent successful examples of diastereocontrol for allylic substitutions: Trost, B. M.; Surivet, J.-P. *J. Am. Chem. Soc.* **2000**, *122*, 6291; (f) Braun, M.; Laicher, F.; Meier, T. *Angew. Chem., Int. Ed.* **2000**, *39*, 3494.
14. The authors thank one of the reviewers who pointed out the possibility of this equilibrium and gave the opportunity to add the results of control experiments using CF_3SO_3H.