New Concept in the Allylation of Aldehydes: Regiospecific Allylation of Aldehydes by an Allyl-Transfer Reaction of Homoallylic Alcohols

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Received March 31, 1998

Allylation of carbonyl compounds with allylic organometallic reagents is one of the most fundamental and important reactions for constructing carbon−carbon bonds.[1] For example, Grignard- and Barbier-type reactions have been widely utilized for the allylation of aldehydes and ketones, in which chemo-, regio-, and stereoselectivities of the desired homoallylic alcohols are highly dependent on the nature of the metals employed. On the other hand, carbonyl−ene reactions constitute a more efficient alternative to the carbonyl addition reactions of allylic metals,[2] although the type of carbonyl enophiles that can be used is limited, e.g. formaldehyde, chloral, and glyoxylate.

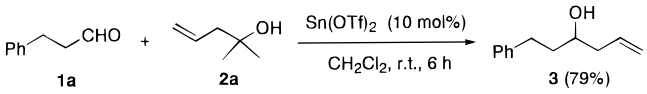
Herein, we disclose a conceptually new allylation of aldehydes: an allylic functionality of the homoallyl alcohol **2a** is transferred to the aldehyde **1a** to give the desired homoallylic alcohol **3** in the presence of a *catalytic amount* of $Sn(OTf)_2$ (Scheme 1).

Peruzzo,[3] Gambaro,[4] and Nokami[5] reported that Grignard- and Barbier-type additions of carbonyls with allyltin halides to tin homoallyl alcoholates were reversible processes. Therefore, the formation of the homoallylic alcohol **3** might be explained by assuming that an allyltin species, generated by retro-allylation[3−5] of the original homoallyl alcohol **2a** with tin(II) triflate, promotes a Grignard-type allylation of 3-phenylpropanal **1a**.

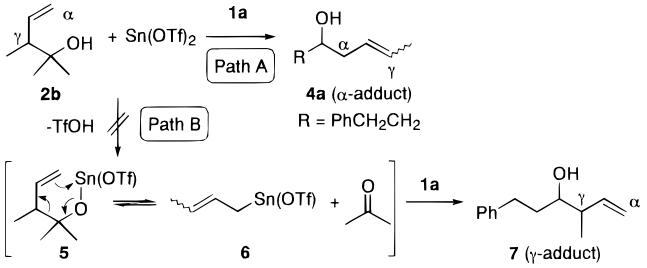
To investigate this further, we performed the allylation with 2,3-dimethyl-4-penten-2-ol **2b**, as shown in Scheme 2. Surprisingly, the reaction of **1a** with **2b** proceeded in a completely regioselective manner to afford an unexpected α-adduct 1-phenyl-5-hepten-3-ol **4a** without any detectable amount of the γ-adduct **7**.[6] This result strongly suggests that the crotyltin species **6** would not be formed by the reaction of **2b** with tin(II) triflate (path B in Scheme 2), as it is well-known that most allylic metal compounds such as **6** react with carbonyls to give γ-adducts such as **7**, predominantly or exclusively.[1]

On this basis, we propose the first synthesis of α-adducts of homoallylic alcohols **4** through an allyl-transfer reaction from the γ-adducts of homoallylic alcohols **2**, derived from acetone,[7] to the aldehydes **1**.

Scheme 1



Scheme 2



First, the allylation of **1a** with **2b** in the presence of various catalysts was examined (Table 1). The reaction of **1a** with **2b** in the presence of a catalytic amount of tin(II) triflate (10 mol %) in dichloromethane at room temperature for 6 h was carried out to afford a 9:1 mixture of *E*- and *Z*-isomers of 1-phenyl-5-hepten-3-ol **4a** in 90% yield (entry 1). Addition of molecular sieves 4 Å powder to the reaction media led to an improved yield of **4a** (95%) and a lower reaction temperature (−25 °C) (entry 2). Even with the molecular sieves 4 Å powder, zinc(II) triflate was less effective (entry 3) and the reaction with silver(I) triflate failed (entry 4). It is of interest to note that *N*-hydroxybenzenesulfonamide, which has been used as a mild acid for the acetalization of aldehydes with alcohols,[8] gave the desired alcohol **4a** (40%) although a high temperature (80 °C) was required (entry 5).

By using tin(II) triflate and molecular sieves 4 Å powder, the allylation of aldehydes **1a**−**f** with **2b** in dichloromethane afforded the expected α-adducts **4a**−**f** in high yields (70−97%) and stereoselectivities (*E*/*Z* = 6/1 to 12/1) (Table 2).

To gain some information on the Sn(II)-catalyzed allylation mechanism, a reaction with other homoallylic alcohols **2** was investigated (Table 3). The reaction of **1a** with 2-methyl-3-phenyl-4-penten-2-ol **2c** took place in a stereoselective fashion to afford only (5*E*)-1,6-diphenyl-5-hexen-3-ol **4g** (99%) without any detectable amount of its *Z*-isomer (entry 2). 2,3,3-Trimethyl-4-penten-2-ol **2e** gave the corresponding homoallylic alcohol **4i** (51%) although excess amounts of **2e** were required (entry 4).

The exclusive formation of the α-adducts **4** (Tables 1−3) and the promotion of the desired allylation by *N*-hydroxybenzenesulfonamide (Table 1, entry 5) proved that tin(II) triflate did not act in the formation of the allylic tin compounds such as **6**, by retro-allylation with the homoallylic alcohols **2**. This leads us to propose a new mechanism, as shown in Scheme 3.

In the initial stage of the reaction, the formation of the carbocation **9A** occurs through hemiacetalization of **1** and **2** to **8** with the aid of tin(II) triflate.[9] Due to the differences in stabilization between the three kinds of cation species **9A**−**C**, the rearrange-

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(5) Nokami, J.; Otera, J.; Sudo, T.; Okawara, R. *Organometallics* **1983**, *2*, 191.

(6) Some methods for the synthesis of α-adducts **4** using allylic organometallic reagents have been reported: (a) Gambaro, A.; Gains, P.; Marton, D.; Peruzzo, V.; Tagliavini, G. *J. Organomet. Chem.* **1982**, *231*, 307. (b) Gambaro, A.; Boaretto, A.; Marton, D.; Tagliavini, G. *J. Organomet. Chem.* **1984**, *260*, 255. (c) Miyake, H.; Yamamura, K. *Chem. Lett.* **1992**, 1369. (d) McNeill, A. H.; Thomas, E. J. *Tetrahedron Lett.* **1992**, *33*, 1369. (e) Kanagawa, Y.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.* **1992**, *57*, 6988. (f) Yamamoto, Y.; Maeda, N.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1983**, 742. (g) Yamamoto, Y.; Maruyama, K. *J. Org. Chem.* **1983**, *48*, 1564. (h) Guo, B. S.; Doubleday: W.; Cohen, T. *J. Am. Chem. Soc.* **1987**, *109*, 4710. (i) Iqubal, J.; Joseph, S. *Tetrahedron Lett.* **1989**, *30*, 2421. (j) Yanagisawa, A.; Habaue, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1991**, *113*, 8955. (k) Yanagisawa, A.; Habaue, S.; Yasue, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 6130.

(7) Among the various kinds of homoallylic alcohols used as an allyl donor, those derived from 2-butanone, cyclohexanone, and cyclopentanone had a similar effect to that derived from acetone. However, sterically more hindered homoallylic alcohols were less reactive.

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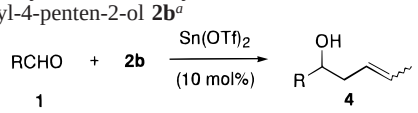
S0002-7863(98)01074-9 CCC: $15.00
Published on Web 06/17/1998

Table 1. Effect of Catalysts for Allylation of **1a** with **2b**[a]

entry	catalyst	MS-4A[b] (mg)	Temp (°C)	isolated yield (%) **4a** (*E*/*Z*)[c]	**1a**
1	$Sn(OTf)_2$		r.t.	90 (9/1)	
2	$Sn(OTf)_2$	50	−25	95 (12/1)	
3	$Zn(OTf)_2$	50	r.t.	24 (10/1)	56
4	AgOTf	50	r.t.		quant
5[d]	$PhSO_2NHOH$		80	40 (5/1)	42

[a] All reactions were performed with **1a** (1 mmol), **2b** (1.5 mmol), and catalyst (0.1 mmol) in CH_2Cl_2 (5 mL) for 6 h, unless otherwise noted. [b] Molecular sieves 4Å powder. [c] Ratios were determined by ^1H NMR (500 MHz) integration of the mixture. [d] CH_3CN (5 mL) was used as solvent.

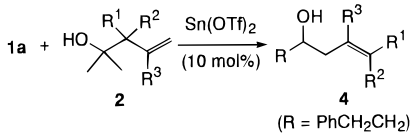
Table 2. Allylation of Aldehydes **1** with 2,3-Dimethyl-4-penten-2-ol **2b**[a]



entry	aldehyde **1** R	*T* (°C)	*t* (h)	yield[b] (%)	ratio (*E*/*Z*)
1	$PhCH_2CH_2$ (**1a**)	−25	6	95 (**4a**)[c]	12/1[d]
2	Ph (**1b**)	−25	8	94 (**4b**)[e]	11/1[f]
3[g]	*p*-$NO_2C_6H_4$ (**1c**)	r.t.	6	97 (**4c**)	6/1[f]
4	*m*-$MeOC_6H_4$ (**1d**)	r.t.	8	88 (**4d**)	8/1[f]
5	*n*-C_5H_{12} (**1e**)	−25	2	86 (**4e**)[h]	9/1[f]
6	*t*-Bu (**1f**)	−25	6	70 (**4f**)[e]	10/1[f]

[a] All reactions were performed with **1** (1 mmol), **2b** (1.5 mmol), $Sn(OTf)_2$ (0.1 mmol), and molecular sieves 4Å powder (50 mg) in CH_2Cl_2 (5 mL), unless otherwise noted. [b] Isolated yield. [c] Reference 11a. [d] Ratios were determined by ^1H NMR (500 MHz) integration of the mixture. [e] Reference 6a. [f] Ratios were determined by ^1H NMR (300 MHz) integration of the mixture. [g] $Sn(OTf)_2$ (20 mol%) was used. [h] Reference 6e and 6k.

Table 3. Allylation of 3-Phenylpropanal **1a** with Homoallylic Alcohols **2**[a]



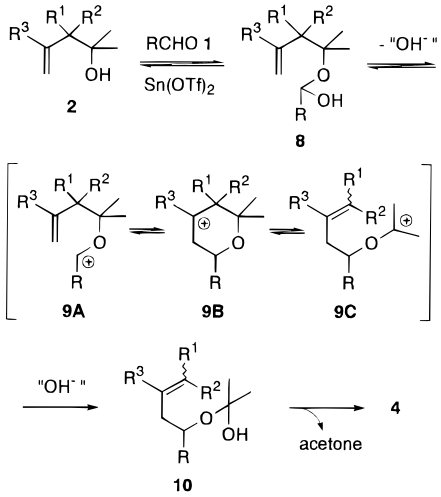
entry	homoallylic alcohol **2** R^1	R^2	R^3	isolated yield (%, *E*/*Z*)
1	Me	H	H (**2b**)	95 (12/1)[b] (**4a**)
2	Ph	H	H (**2c**)	99 (*E* only)[c] (**4g**)
3	CO_2Et	H	H (**2d**)	87 (*E* only)[c] (**4h**)
4[d]	Me	Me	H (**2e**)	51 (**4i**)
5	H	H	H (**2a**)	79 (**3**)
6	H	H	Me (**2f**)	8 (**4j**)[e,f]

[a] All reactions were performed with **1a** (1 mmol), **2** (1.5 mmol), $Sn(OTf)_2$ (0.1 mmol), and molecular sieves 4Å powder (50 mg) in CH_2Cl_2 (5 mL) at −25 °C, unless otherwise noted. [b] Ratios were determined by ^1H NMR (500 MHz) integration of the mixture. [c] *Z* isomer could not be detected by ^1H NMR (300 MHz). [d] **1a** was treated with **2d** (3.0 mmol). [e] Reference 11b. [f] See footnote 10.

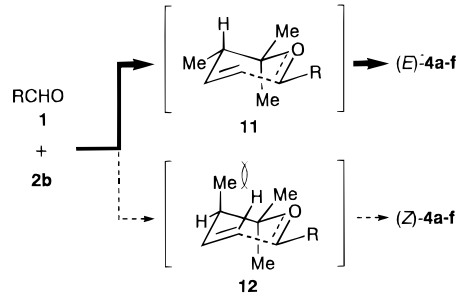
ment of **9A** produces the most stable cation **9C**, which in turn reacts with a hydroxyl equivalent generated in situ to give the α-adduct **4** together with acetone via the hemiacetal **10**. This explains the low yield of **4j**, i.e., the cation **9B** ($R^1 = R^2 = H$, R^3 = Me in Scheme 3), generated from **2f**, is stabilized by an electron-donating methyl substituent, and so the rearrangement of **9B** to **9C** is almost completely prevented (Table 3, entry 6).[10] Although the role of the molecular sieves 4 Å powder is not clear at present, it is possible that it plays an important role in the dehydroxylation of the hemiacetal **8** and the hydroxylation of the carbocation **9C** by a hydroxyl source (Table 1, entries 1 and 2).

The Sn(II)-catalyzed allylation of **1** and **2** gave predominantly the *E* homoallylic alcohols **4**. The result can be explained by cyclic chairlike transition-state models **11** and **12**, as shown in

Scheme 3



Scheme 4



Scheme 4. In the case of **2b**, the transition state **11** is preferable to **12** due to the minimization of 1,3-diaxial repulsion between the methyl substituent and hydrogen atom of the terminal olefin. Therefore, the *E*-isomers of **4a**−**h** are formed as major products (Tables 1−3). In particular, the homoallylic alcohol **2c** affords the remarkable *E* selectivity because the steric hindrance is appreciably increased by a phenyl group (Table 3, entry 2). In the case of **2e**, since the 1,3-diaxial repulsion always exists, excess amounts of **2e** are required for promotion of the desired allylation (Table 3, entry 4).

Although the reaction mechanism is not completely clear, we can assume that the reaction is accelerated to give (i) a more stable cation, (ii) a sterically less hindered homoallylic alcohol, and (iii) thermodynamically more stable olefins.

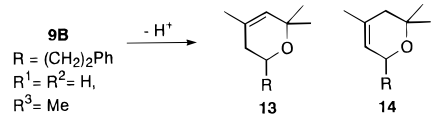
Further study to clarify the reaction mechanism and show the synthetic utility of the Sn(II)-catalyzed allylation is now in progress.

Acknowledgment. This work was financially supported by a Grant in Aid for Scientific Research from the Ministry of Education, Science, Culture, and Sports, Japan, and a Grant for Cooperative Research administered by the Japan Private School Promotion Foundation.

Supporting Information Available: Preparation information and characterization data for **3** and **4a**−**j** (5 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

JA9810742

(10) In the crude products, a considerable amount of **13** and/or **14**, which would be formed by removal of proton from stable carbocation **9B** derived by the treatment of **2f** with **1a**, were detected by GC−MS.



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