Dibutyltin Oxide Catalyzed Allyl-Transfer Reaction from Tertiary Homoallylic Alcohols to Aldehydes

Akira Yanagisawa,*[a] Takahiro Aoki,[b] Takayoshi Arai[a]

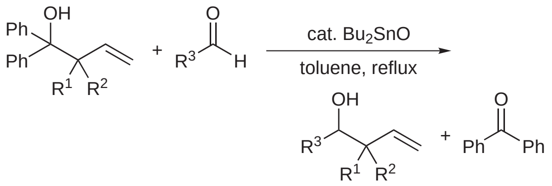
[a] Department of Chemistry, Faculty of Science, Chiba University, Inage, Chiba 263-8522, Japan

[b] Graduate School of Science and Technology, Chiba University, Inage, Chiba 263-8522, Japan
Fax +81(43)2902789; E-mail: ayanagi@scichem.s.chiba-u.ac.jp

Received 22 May 2006

Abstract: A catalytic allyl-transfer reaction from tertiary homoallylic alcohols to aldehydes was achieved using dibutyltin oxide as a catalyst in toluene under reflux conditions. Various secondary homoallylic alcohols were prepared in high yield (up to 99%). When β-alkylated tertiary homoallylic alcohols were used, branched products were exclusively obtained.

Key words: aldehydes, allylations, organometallic reagents, regioselectivity, tin



Scheme 1 Bu_2SnO-catalyzed allyl-transfer reaction from tertiary homoallylic alcohols to aldehydes

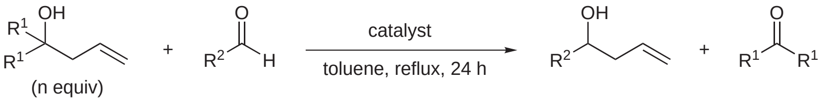
Allylation of aldehydes is a valuable method to prepare secondary homoallylic alcohols.[1] Since the homoallylic alcohol moiety is not only found in many natural products but also is able to be transformed into β-hydroxycarbonyl compounds and other useful compounds, an efficient way of obtaining this structure is desired for organic synthesis.[2] Numerous examples of Lewis acid catalyzed allylation of carbonyl compounds with allylmetals, such as allyltributyltin, have so far been reported;[3] however, the allylation method incurs industrial and environmental problems by requiring a stoichiometric amount of organometallic reagent. One promising method to solve the problem is an allyl-transfer reaction to aldehydes using tertiary homoallylic alcohols as allyl donors. Nokami and co-workers have reported that tin triflate [$Sn(OTf)_2$] catalyzes the allyl-transfer reaction providing linear secondary homoallylic alcohols via [3,3]-sigmatropic rearrangement.[4] This reaction has been further applied to the asymmetric alk-2-enylation of aldehydes catalyzed by *p*-toluenesulfonic acid or $Sn(OTf)_2$.[5,6] In contrast, Oshima and co-workers have recently found that branched secondary homoallylic alcohols are formed from similar allyl donors under the influence of a Grignard reagent and $GaCl_3$ via retro-allylation.[7] We report here a novel allyl-transfer reaction to aldehydes, catalyzed by dibutyltin oxide, that provides branched products (Scheme 1).

We have previously shown that dibutyltin dimethoxide [$Bu_2Sn(OMe)_2$] behaves as a catalyst in the aldol reaction of alkenyl trichloroacetates with aldehydes in the presence of methanol.[8] In this reaction, nucleophilic attack of the methoxide ion of the tin reagent to the alkenyl esters efficiently generates the corresponding tin enolates. We envisioned that this tin dimethoxide might promote the allyl-transfer reaction from tertiary homoallylic alcohols to aldehydes via the formation of tin alkoxides. Thus, we initially examined the reaction of diisopropyl ketone derived homoallylic alcohol with 4-nitrobenzaldehyde in the presence of 10 mol% of $Bu_2Sn(OMe)_2$ under reflux conditions for 24 h; however, the targeted product was obtained only in low yield (Table 1, entry 1). Employment of the more Lewis acidic dibutyltin dibromide and dibutyltin dichloride also resulted in unsatisfactory results (Table 1, entries 2 and 3). Gratifyingly, however, we found that dibutyltin oxide (Bu_2SnO) catalyzes the reaction, and when 20 mol% of the tin oxide was used as a catalyst, the desired homoallylic alcohol was obtained in 33% yield (Table 1, entry 4). We then attempted the reaction employing various amounts of the catalyst and the allyl donor, and found that when 25 mol% of the tin oxide and two equivalents of the tertiary homoallylic alcohol were loaded, the chemical yield reached 70% (Table 1, entry 6). Among the several allyl donors examined, benzophenone-derived homoallylic alcohol was found to be effective for the allyl-transfer reaction (Table 1, entries 8–10).

This allyl-transfer reaction was applied to diverse β-alkylated tertiary homoallylic alcohols and the results with crotyl, prenyl, and geranyl donors are summarized in Table 2.[9] The allyl-transfer reaction of β-alkylated tertiary homoallylic alcohols proceeded more smoothly than that of simple tertiary homoallylic alcohols. For example, in the reaction of the crotyl donor, not only aromatic aldehydes but α,β-unsaturated and aliphatic aldehydes also afforded the corresponding branched product in high yield (up to >99%) with moderate *syn* selectivity (Table 2, entries 1–7). In the reaction with an α,β-unsaturated aldehyde, the 1,2-adduct was formed exclusively (Table 2, entry 6). The prenyl and geranyl donors also indicated a similar regioselectivity in the reaction with

SYNLETT 2006, No. 13, pp 2071–2074
Advanced online publication: 09.08.2006
DOI: 10.1055/s-2006-948198; Art ID: U05906ST

Table 1 Optimization of the Allyl-Transfer Reaction to Aldehydes Catalyzed by Dibutyltin Catalysts[a]

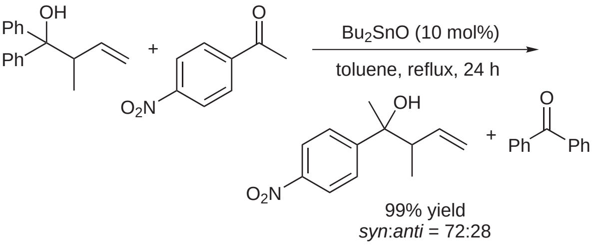


Entry	Catalyst (mol%)	n	R^1	R^2	Yield (%)[b]
1	$Bu_2Sn(OMe)_2$ (10)	1	*i*-Pr	$4\text{-}NO_2C_6H_4$	5
2	Bu_2SnBr_2 (10)	1	*i*-Pr	$4\text{-}NO_2C_6H_4$	5
3	Bu_2SnCl_2 (10)	1	*i*-Pr	$4\text{-}NO_2C_6H_4$	4
4	Bu_2SnO (20)	1	*i*-Pr	$4\text{-}NO_2C_6H_4$	33
5	Bu_2SnO (10)	2	*i*-Pr	$4\text{-}NO_2C_6H_4$	30
6	Bu_2SnO (25)	2	*i*-Pr	$4\text{-}NO_2C_6H_4$	70
7	Bu_2SnO (10)	2	Ph	$4\text{-}NO_2C_6H_4$	39
8	Bu_2SnO (10)	2	Et	1-Naphthyl	16
9	Bu_2SnO (10)	2	*i*-Pr	1-Naphthyl	26
10	Bu_2SnO (10)	2	Ph	1-Naphthyl	64

[a] Unless otherwise noted, the reaction was carried out using Bu_2SnX_2 (10–25 mol%), *tert*-homoallylic alcohol (1 or 2 equiv), and aldehyde (1 equiv) in refluxing toluene (bath temperature: 125–130 °C) for 24 h.
[b] Isolated yield of the corresponding homoallylic alcohol.

various aldehydes, though the chemical yields were lower than those given by the crotyl-transfer reaction (Table 2, entries 8–15).

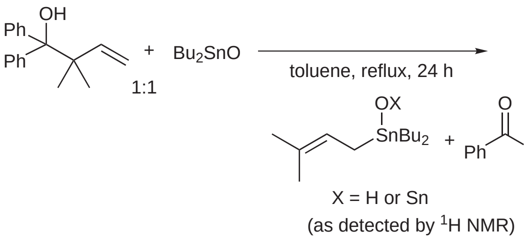
We further attempted a crotyl-transfer reaction to ketones and found that 4′-nitroacetophenone was converted to the corresponding branched product in 99% yield under the standard reaction conditions used for aldehydes (Scheme 2).



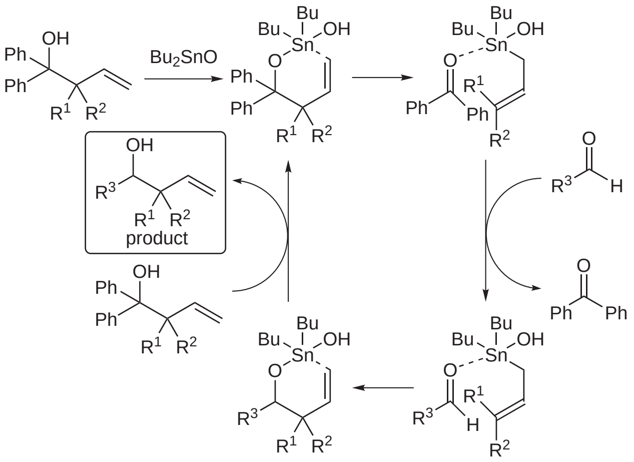
Scheme 2 Bu_2SnO-catalyzed crotyl-transfer reaction from a tertiary homoallylic alcohol to a ketone

To elucidate the catalytic mechanism of the present reaction, we performed ^1H NMR studies on a reaction of benzophenone-derived prenyl donor with an equimolar amount of Bu_2SnO in refluxing toluene for 24 h, and found that a prenyltin compound was formed (Scheme 3).

Scheme 4 provides a plausible catalytic mechanism of the allyl-transfer reaction of an allyl donor to an aldehyde. Initially, the allyl donor reacts with Bu_2SnO, forming the tin alkoxide of the tertiary homoallylic alcohol. The alkoxide then undergoes ‘retro-allylation’[4,7] to provide an

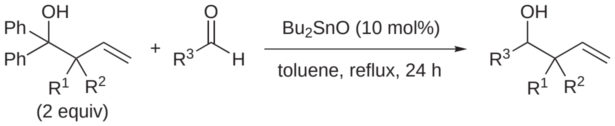


Scheme 3 Reaction of benzophenone-derived prenyl donor with Bu_2SnO for ^1H NMR studies



Scheme 4 Plausible reaction mechanism for the allyl-transfer reaction catalyzed by Bu_2SnO

Table 2 Crotyl-, Prenyl-, and Geranyl-Transfer Reactions to Various Aldehydes[a]



Entry	R^1	R^2	R^3	Yield (%)[b]	*syn*:*anti*[c]
1	Me	H	Ph	60	73:27
2	Me	H	$4\text{-}NO_2C_6H_4$	93	83:17
3	Me	H	$4\text{-}BrC_6H_4$	75	80:20
4	Me	H	$4\text{-}MeOC_6H_4$	>99	73:27
5	Me	H	2-Naphthyl	>99	68:32
6	Me	H	(*E*)-PhCH=CH	91[d]	65:35
7	Me	H	$Ph(CH_2)_2$	62	63:37
8	Me	Me	Ph	57	–
9	Me	Me	$4\text{-}NO_2C_6H_4$	84	–
10	Me	Me	$4\text{-}BrC_6H_4$	65	–
11	Me	Me	$4\text{-}MeOC_6H_4$	73	–
12	Me	Me	(*E*)-PhCH=CH	81[d]	–
13	Me	Me	$Ph(CH_2)_2$	71	–
14	$Me_2C{=}CH(CH_2)_2$	Me	Ph	63	43:57
15	$Me_2C{=}CH(CH_2)_2$	Me	$Ph(CH_2)_2$	70	48:52

[a] Unless otherwise noted, the reaction was carried out using Bu_2SnO (10 mol%), *tert*-homoallylic alcohol (2 equiv), and aldehyde (1 equiv) in refluxing toluene (bath temperature: 125–130 °C) for 24 h.
[b] Isolated yield.
[c] The *syn*:*anti* ratio was determined by ^1H NMR analysis.
[d] The 1,2:1,4 ratio was >99:1.

allylic tin compound and benzophenone. Subsequently, the allylic tin is allowed to add to the aldehyde. Finally, reaction of the resulting tin alkoxide with the allyl donor completes the catalytic cycle, yielding the secondary homoallylic alcohol (branched product) and regenerating the tin alkoxide of the allyl donor.

In conclusion, we have developed a novel, catalytic allyl-transfer reaction. By using dibutyltin oxide as a catalyst and tertiary homoallylic alcohols as allyl donors, various aldehydes were allylated with high regioselectivity. Further studies on application of the present reaction to other substrates are currently underway.

Acknowledgment

We gratefully acknowledge financial support from the Ministry of Education, Science, Sports, Culture and Technology of the Japanese Government.

References and Notes

(1) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.

(2) For reviews, see: (a) Roush, W. R. In *Comprehensive Organic Synthesis*, Vol. 2; Trost, B. M.; Fleming, I.; Heathcock, C. H., Eds.; Pergamon: Oxford, **1991**, 1. (b) Hoppe, D. In *Houben-Weyl: Methods of Organic Chemistry*, Vol. E21; Helmchen, G.; Hoffmann, R. W.; Mulzer, J.; Schaumann, E., Eds.; Georg Thieme Verlag: Stuttgart, **1995**, 1357. (c) Chemler, S. R.; Roush, W. R. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, **2000**, Chap. 11, 403.

(3) For reviews, see: (a) Yanagisawa, A. In *Comprehensive Asymmetric Catalysis*, Vol. II; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: Heidelberg, **1999**, 965. (b) Denmark, S. E.; Almstead, N. G. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, **2000**, Chap. 10, 299. (c) Kennedy, J. W. J.; Hall, D. G. *Angew. Chem. Int. Ed.* **2003**, *42*, 4732. (d) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763. (e) Yanagisawa, A. In *Comprehensive Asymmetric Catalysis*, Suppl. 2; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: Heidelberg, **2004**, 97.

(4) (a) Nokami, J.; Yoshizane, K.; Matsuura, H.; Sumida, S. *J. Am. Chem. Soc.* **1998**, *120*, 6609. (b) Sumida, S.; Ohga, M.; Mitani, J.; Nokami, J. *J. Am. Chem. Soc.* **2000**, *122*, 1310. (c) Nokami, J.; Anthony, L.; Sumida, S. *Chem. Eur. J.* **2000**, *6*, 2909. (d) Nokami, J. *J. Synth. Org. Chem., Jpn.* **2003**, *61*, 992.

(5) (a) Nokami, J.; Ohga, M.; Nakamoto, H.; Matsubara, T.; Hussain, I.; Kataoka, K. *J. Am. Chem. Soc.* **2001**, *123*, 9168. (b) Nokami, J.; Nomiyama, K.; Matsuda, S.; Imai, N.; Kataoka, K. *Angew. Chem. Int. Ed.* **2003**, *42*, 1273. (c) Nokami, J.; Nomiyama, K.; Shafi, S. M.; Kataoka, K. *Org. Lett.* **2004**, *6*, 1261. (d) Shafi, S. M.; Chou, J.; Kataoka, K.; Nokami, J. *Org. Lett.* **2005**, *7*, 2957. (e) Hussain, I.; Komasaka, T.; Ohga, M.; Nokami, J. *Synlett* **2002**, 640. (f) Kataoka, K.; Ode, Y.; Matsumoto, M.; Nokami, J. *Tetrahedron* **2006**, *62*, 2471.

(6) For other notable examples of allyl-transfer reactions to aldehydes via [3,3]-sigmatropic rearrangement, see: (a) Loh, T.-P.; Hu, Q.-Y.; Ma, L.-T. *J. Am. Chem. Soc.* **2001**, *123*, 2450. (b) Loh, T.-P.; Tan, K.-T.; Hu, Q.-Y. *Angew. Chem. Int. Ed.* **2001**, *40*, 2921. (c) Loh, T.-P.; Tan, K.-T.; Hu, Q.-Y. *Tetrahedron Lett.* **2001**, *42*, 8705. (d) Loh, T.-P.; Hu, Q.-Y.; Chok, Y.-K.; Tan, K.-T. *Tetrahedron Lett.* **2001**, *42*, 9277. (e) Crosby, S. R.; Harding, J. R.; King, C. D.; Parker, G. D.; Willis, C. L. *Org. Lett.* **2002**, *4*, 577. (f) Loh, T.-P.; Hu, Q.-Y.; Ma, L.-T. *Org. Lett.* **2002**, *4*, 2389. (g) Loh, T.-P.; Lee, C.-L. K.; Tan, K.-T. *Org. Lett.* **2002**, *4*, 2985. (h) Marumoto, S.; Jaber, J. J.; Vitale, J. P.; Rychnovsky, S. D. *Org. Lett.* **2002**, *4*, 3919. (i) Tan, K.-T.; Chng, S.-S.; Cheng, H.-S.; Loh, T.-P. *J. Am. Chem. Soc.* **2003**, *125*, 2958. (j) Cheng, H.-S.; Loh, T.-P. *J. Am. Chem. Soc.* **2003**, *125*, 4990. (k) Lee, C.-L. K.; Lee, C.-H. A.; Tan, K.-T.; Loh, T.-P. *Org. Lett.* **2004**, *6*, 1282. (l) Lee, C.-H. A.; Loh, T.-P. *Tetrahedron Lett.* **2004**, *45*, 5819. (m) Ramachandran, P. V.; Pratihar, D.; Biswas, D. *Chem. Commun.* **2005**, 1988. (n) Lee, C.-H. A.; Loh, T.-P. *Tetrahedron Lett.* **2006**, *47*, 809. (o) Lee, C.-H. A.; Loh, T.-P. *Tetrahedron Lett.* **2006**, *47*, 1641. (p) Loh, T.-P.; Chua, G.-L. *J. Synth. Org. Chem., Jpn.* **2005**, *63*, 1137.

(7) (a) Hayashi, S.; Hirano, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2005**, *7*, 3577. For other notable examples of allyl-transfer reaction to aldehydes via retro-allylation, see:. (b) Tagliavini, G.; Peruzzo, V.; Marton, D. *Inorg. Chim. Acta* **1978**, *26*, L41. (c) Peruzzo, V.; Tagliavini, G. *J. Organomet. Chem.* **1978**, *162*, 37. (d) Jones, P.; Millot, N.; Knochel, P. *Chem. Commun.* **1998**, 2405. (e) Jones, P.; Knochel, P. *Chem. Commun.* **1998**, 2407. (f) Millot, N.; Knochel, P. *Tetrahedron Lett.* **1999**, *40*, 7779. (g) Jones, P.; Knochel, P. *J. Org. Chem.* **1999**, *64*, 186. (h) Fujita, K.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *J. Org. Chem.* **2004**, *69*, 3302. (i) Hayashi, S.; Hirano, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2006**, *128*, 2210.

(8) (a) Yanagisawa, A.; Sekiguchi, T. *Tetrahedron Lett.* **2003**, *44*, 7163. (b) Yanagisawa, A.; Goudu, R.; Arai, T. *Org. Lett.* **2004**, *6*, 4281.

(9) Typical experimental procedure for crotyl-transfer reaction to aldehydes catalyzed by dibutyltin oxide (Table 2, Entry 4). Under an argon atmosphere, 4-methoxybenzaldehyde (68.1 mg, 0.50 mmol) was added to a solution of dibutyltin oxide (12.4 mg, 0.05 mmol) and crotyl donor (238 mg, 1.00 mmol) in dry toluene (2 mL) at r.t. After stirring for 30 min the mixture was heated at reflux (oil bath temperature: 125–130 °C) for 24 h and then treated with MeOH (2 mL), brine (2 mL), and solid KF (ca. 2 g) at r.t. for 2 h. The resulting precipitate was filtered off and the filtrate diluted with H_2O (30 mL) and extracted with Et_2O (3×30 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo after filtration. The residual crude product was purified by column chromatography on silica gel to give a *syn*/*anti* mixture of the corresponding homoallylic alcohol (96.0 mg, >99% yield). The *syn*/*anti* ratio was determined to be 73:27 by ^{1}H NMR analysis. Spectral data of a 73:27 mixture of the *syn* and *anti* isomers: TLC $R_f = 0.17$ (hexane–EtOAc, 7:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.82$ (d, $J = 7.0$ Hz, 0.81 H), 0.99 (d, $J = 6.8$ Hz, 2.19 H), 2.31 (br s, 1 H), 2.42 (m, 0.27 H), 2.51 (m, 0.73 H), 3.76 (s, 3 H), 4.26 (d, $J = 8.0$ Hz, 0.27 H), 4.46 (d, $J = 5.8$ Hz, 0.73 H), 4.97–5.01 (m, 1.46 H), 5.12–5.18 (m, 0.54 H), 5.64–5.74 (m, 0.73 H), 5.74–5.85 (m, 0.27 H), 6.83 (d, $J = 8.7$ Hz, 1.46 H), 6.85 (d, $J = 8.5$ Hz, 0.54 H), 7.17 (d, $J = 8.7$ Hz, 1.46 H), 7.21 (d, $J = 8.5$ Hz, 0.54 H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.4$, 16.4, 44.5, 46.1, 55.0, 55.0, 76.9, 77.3, 113.2, 113.4, 115.1, 116.3, 127.6, 127.8, 134.5, 134.7, 140.2, 140.8, 158.6, 158.9. Spectral data (^{1}H and ^{13}C NMR) of the mixture of the *syn* and *anti* isomers indicated good agreement with reported data.[10]

(10) Batey, R. A.; Thadani, A. N.; Smil, D. V.; Lough, A. J. *Synthesis* **2000**, 990.