Palladium-Catalyzed Carbonyl Allylation by Allylic Alcohols with $SnCl_2$

Jun P. Takahara, Yoshiro Masuyama,* and Yasuhiko Kurusu

Contribution from the Department of Chemistry, Sophia University, 7-1 Kioicho, Chiyoda-ku, Tokyo 102, Japan. *Received July 1, 1991*

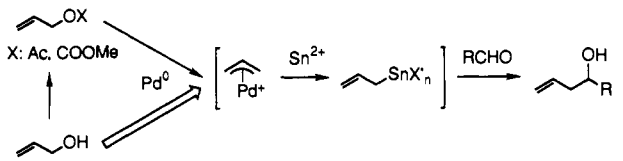
Abstract: Allylic alcohols can be applied to carbonyl allylation via the formation of π-allylpalladium complexes, using palladium as catalyst and $SnCl_2$ as a reducing agent. This reaction has chemoselectivity: The reactivity order of allylating agents is allylic carbonate > allylic alcohol > allylic acetate, and that of carbonyl compounds is aldehyde > ketone. High regioselection was observed in polar solvents such as DMF, DMI, and DMSO; carbonyl compounds apparently attacked the more substituted allylic position of π-allylpalladium complexes to afford only one regioisomer. Diastereocontrol in the carbonyl allylation of aromatic aldehydes by (*E*)-2-butenol was achieved by the choice of polar solvents; use of DMSO at 25 °C led to syn selection, while anti selection was found at −10 °C in THF. The addition of H_2O in any solvent accelerated the carbonyl allylation and enhanced both regioselectivity and the diastereoselectivity. Anti selection in DMF, DMI, and THF–H_2O can be explained by the chair form of the six-membered cyclic transition state, while syn selection in DMSO allows us to propose an acyclic antiperiplanar transition state. An NMR spectroscopic investigation demonstrated that the actual allylating agent in dry medium was allyltrichlorotin: ^1H, ^{13}C, and ^{119}Sn NMR spectra of the reaction of allyl alcohol with $PdCl_2(PhCN)_2$–$SnCl_2$ in DMF-d_7 corresponded to those of the reaction of allyl chloride with $PdCl_2(PhCN)_2$–$SnCl_2$ in DMF-d_7.

Introduction

Nucleophilic substitution of π-allylpalladium complexes has been considered for possible application to the synthesis of a wide range of natural products and other complex organic molecules.[1] Such nucleophilic substitution contains important themes of chemo-, regio-, and stereocontrol. If the π-allylpalladium complex would be applied not only as an electrophile but also as a nucleophile, the chemistry of π-allylpalladium complex could be further developed in organic syntheses. The utilization of π-allylpalladium complex as a nucleophile has been designed by the transformation of allylic esters to allylic metal compounds with palladium(0) catalyst and low-valent metals, which have been applied to carbonyl allylation.[2] We have reported that stannous chloride is more effective as a reducing low-valent metal than other low-valent metals in palladium-catalyzed chemo- and regioselective carbonyl allylation by allylic esters.[3]

Allylic halides, esters, and ethers, from which π-allylpalladium intermediates are derived with palladium(0) complex, are frequently prepared from stable and tractable allylic alcohols. Therefore, the direct formation of π-allylpalladium complexes from allylic alcohols, which yields savings in resources and energy, is one of the important themes in palladium-catalyzed allylation. However, such formation of π-allylpalladium complexes from allylic alcohols usually requires either severe reaction conditions or a reagent such as AsO_3 for promoting the elimination of hydroxide.[4] Here we report about *the palladium-catalyzed carbonyl allylation by allylic alcohols with* $SnCl_2$ via the formation of π-allylpalladium complexes (Scheme I); we cover the fundamental aspects of chemo-, regio-, and diastereoselectivity,[5] the detection of an actual allylating agent by NMR spectroscopic investigation, solvation-controlled diastereoselection,[6] applications, and limitations.

Scheme 1



Results and Discussion

Carbonyl Allylation via Apparent Charge Reversal of π-Allylpalladium Complex. The addition reaction of 2(*E*)-butenol (**1**) to benzaldehyde was examined under various conditions. The results are summarized in Table I. Palladium catalysts such as $Pd(PPh_3)_4$, $PdCl_2$dppe, $PdCl_2(PPh_3)_2$, $PdCl_2(PBu_3)_2$, $PdCl_2\{P(OMe)_3\}_2$, $PdCl_2(PhCN)_2$, and $PdCl_2(MeCN)_2$ can be used in this carbonyl allylation by allylic alcohol with $SnCl_2$ (Table I, entries 5–11). $PdCl_2(PhCN)_2$ and $PdCl_2(MeCN)_2$ are superior to other Pd complexes bearing phosphine ligands with regard to stability to air and reactivity to this allylation. The allylations with other tin-reducing agents such as Sn,[7] $Sn(OAc)_2$, and SnF_2,[8] instead of $SnCl_2$, were not found to occur significantly under the same conditions. This allylation needed more than 2 equiv of $SnCl_2$ (Table I, entries 1–4). Thus, $SnCl_2$ may function during two steps: elimination of the hydroxy group and reduction of the π-allylpalladium complex. Although 1 equiv of 2(*E*)-butenol (**1**) to aldehyde should be sufficient to complete the reaction, a little excess of **1** was used for the sake of effective addition. Many kinds of solvents which dissolve $SnCl_2$, such as DMF, 1,3-dimethyl-2-

(1) (a) Trost, B. M.; Verhoeven, T. R. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergamon Press: Oxford, 1982; Vol. 8, p 802. (b) Hegedus, L. S. In *Comprehensive Carbanion Chemistry*; Buncel, E., Durst, T., Eds.; Elsevier: Amsterdam, 1984; p 30. (c) Heck, R. F. In *Palladium Reagents in Organic Syntheses*; Academic Press: London, 1985; p 117. (d) Tsuji, J. In *The Chemistry of the Metal-Carbon Bond*; Hartley, F. R., Patai, S., Eds.; Wiley: New York, 1985; Vol. 3, p 163.

(2) (a) Trost, B. M.; Herndon, J. W. *J. Am. Chem. Soc.* **1984**, *106*, 6835. (b) Matsubara, S.; Wakamatsu, K.; Morizawa, Y.; Tsuboniwa, N.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1196. (c) Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 1195. (d) Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1987**, *28*, 215. (e) Masuyama, Y.; Kinugawa, N.; Kurusu, Y. *J. Org. Chem.* **1987**, *52*, 3702. (f) Qiu, W.; Wang, Z. *J. Chem. Soc., Chem. Commun.* **1989**, 356. (g) Zhang, P.; Zhang, W.; Zhang, T.; Wang, Z.; Zhou, W. *J. Chem. Soc., Chem. Commun.* **1991**, 491.

(3) (a) Masuyama, Y.; Hayashi, R.; Otake, K.; Kurusu, Y. *J. Chem. Soc., Chem. Commun.* **1988**, 44. (b) Masuyama, Y.; Otake, K.; Kurusu, Y. *Tetrahedron Lett.* **1988**, *29*, 3563.

(4) (a) Atkins, K. E.; Walker, W. E.; Manyik, R. M. *Tetrahedron Lett.* **1970**, 3821. (b) Haudegond, J.-P.; Chauvin, Y.; Commereuc, D. *J. Org. Chem.* **1979**, *44*, 3063. (c) Lu, X.; Lu, L.; Sun, J. *J. Mol. Catal.* **1987**, *41*, 245. (d) Lu, X.; Jiang, X.; Tao, X. *J. Organomet. Chem.* **1988**, *344*, 109. (e) Bergbreiter, D. E.; Weatherford, D. A. *J. Chem. Soc., Chem. Commun.* **1989**, 883.

(5) Preliminary report: Masuyama, Y.; Takahara, J. P.; Kurusu, Y. *J. Am. Chem. Soc.* **1988**, *110*, 4473.

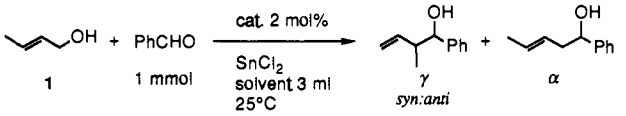
(6) Preliminary report: Masuyama, Y.; Takahara, J. P.; Kurusu, Y. *Tetrahedron Lett.* **1989**, *30*, 3437.

(7) (a) Mukaiyama, T.; Harada, T. *Chem. Lett.* **1981**, 1527. (b) Nakami, J.; Otera, J.; Sudo, T.; Okawara, R. *Organometallics* **1983**, *2*, 191. (c) Mandai, T.; Nokami, J.; Yano, T.; Yoshinaga, Y.; Otera, J. *J. Org. Chem.* **1984**, *49*, 172. (d) Petrier, C.; Einhorn, J.; Luche, J. L. *Tetrahedron Lett.* **1985**, *26*, 1449. (e) Boga, C.; Savoia, D.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Organomet. Chem.* **1988**, *353*, 177.

(8) (a) Mukaiyama, T.; Harada, T.; Shoda, S. *Chem. Lett.* **1980**, 1507. (b) Harada, T.; Mukaiyama, T. *Chem. Lett.* **1981**, 1109.

0002-7863/92/1514-2577$03.00/0

Table I. Addition Reaction of 2(*E*)-Butenol (**1**) to Benzaldehyde under Various Conditions



entry	alcohol (mmol)	catalyst	$SnCl_2$ (mmol)	solvent	time (h)	yield[a] (%)	ratio[b] (syn:anti:α)
1	1.0	$PdCl_2(PhCN)_2$	1.0	DMF	216	40	25:75:0
2	1.0	$PdCl_2(PhCN)_2$	1.5	DMF	216	62	26:74:0
3	1.0	$PdCl_2(PhCN)_2$	2.0	DMF	216	80	24:76:0
4	1.0	$PdCl_2(PhCN)_2$	3.0	DMF	216	77	23:77:0
5	1.5	$PdCl_2(PhCN)_2$	3.0	DMI	24	75	29:71:0
6	1.5	$PdCl_2(MeCN)_2$	3.0	DMI	24	64	30:70:0
7	1.5	$PdCl_2(PPh_3)_2$	3.0	DMI	48	68	29:71:0
8	1.5	$Pd(PPh_3)_4$	3.0	DMI	48	64	29:71:0
9	1.5	$PdCl_2\{P(OMe)_3\}_2$	3.0	DMI	65	67	18:82:0
10	1.5	$PdCl_2$dppe	3.0	DMI	169	16	19:81:0
11	1.5	$PdCl_2(PBu_3)_2$	3.0	DMI	169	9	21:79:0
12	1.5	$PdCl_2(PhCN)_2$	3.0	DMSO	136	34	65:35:0
13	1.5	$PdCl_2(PhCN)_2$	3.0	EG	37	78	58:42:0
14	1.5	$PdCl_2(PhCN)_2$	3.0	DMF	63	89	30:70:0
15	1.5	$PdCl_2(PhCN)_2$	3.0	DMF[c]	15	77	18:82:0
16	1.5	$PdCl_2(PhCN)_2$	3.0	BuOH	64	72	36:58:6
17	1.5	$PdCl_2(PhCN)_2$	3.0	EtOH	72	79	38:41:21
18	1.5	$PdCl_2(PhCN)_2$	3.0	THF	25	72	22:25:53
19	1.5	$PdCl_2(PhCN)_2$	3.0	DME	142	22	41:3:56
20	1.5	$PdCl_2(PhCN)_2$	3.0	ether	72	8	4:2:94

[a] Isolated yields of regio- and/or diastereoisomer based on benzaldehyde. [b] The ratio was determined by ^1H NMR (GX-270) and GC (PEG 20M, 0.25 mm × 30 m). [c] H_2O (1 mL) was added.

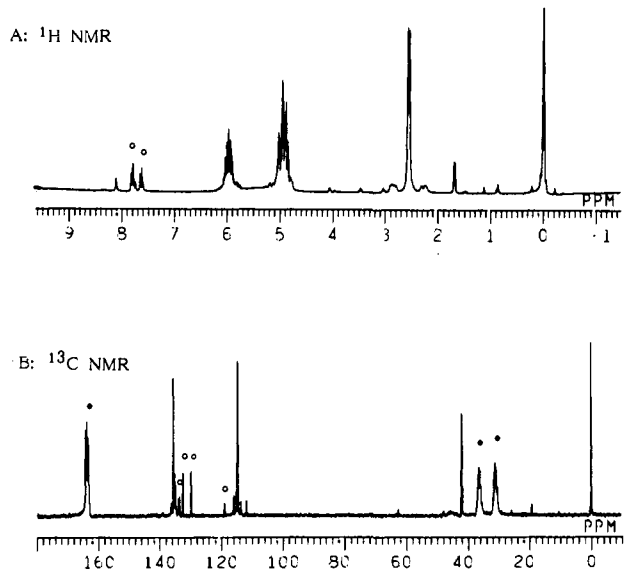


Figure 1. Spectra of the reaction of 2-propenol (**2**) with $PdCl_2(PhCN)_2$–$SnCl_2$ in DMF-d_7: (○) PhCN; (●) DMF-d_7.

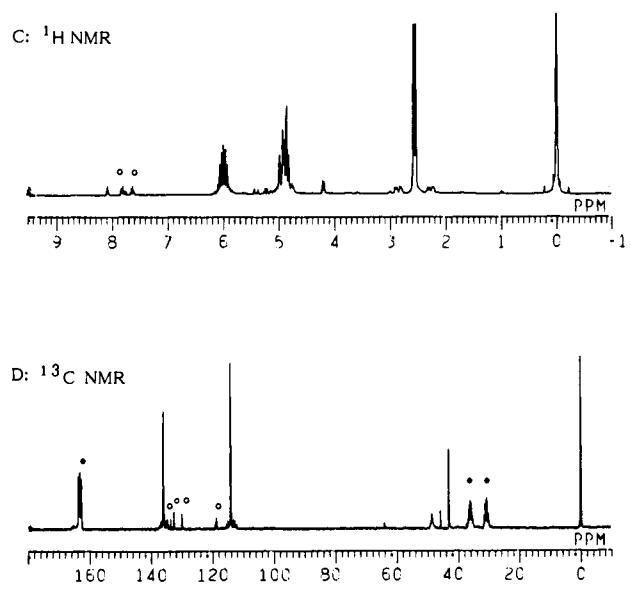


Figure 2. Spectra of the reaction of 3-chloropropene (**3**) with $PdCl_2(PhCN)_2$–$SnCl_2$ in DMF-d_7: (○) PhCN; (●) DMF-d_7.

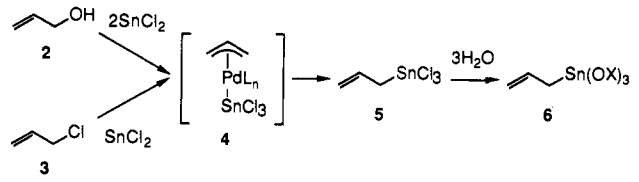
imidazolidinone (DMI), DMSO, EtOH, BuOH, DME, THF, and ethylene glycol (EG), can be employed in the carbonyl allylation by **1** with $PdCl_2(PhCN)_2$–$SnCl_2$ (Table I, entries 5 and 12–19). The larger the dielectric constant, the higher the regioselectivity (γ-addition). Addition of the butenyltin intermediate,[9] derived from **1**, probably occurred regioselectively at the γ-position in a polar solvent such as DMI, DMSO, DMF, and EG, to afford only a single regioisomer (Table I, entries 5 and 12–14). On the other hand, use of ether, which did not dissolve $SnCl_2$, depressed the yield and led to the opposite α-addition (Table I, entry 20). Although carbonyl allylations using allylic organometallic reagents are usually inhibited by the presence of H_2O, the palladium-catalyzed carbonyl allylation with $SnCl_2$ can be accelerated by the addition of H_2O (entry 15).[10] As mentioned above, air- and moisture-stable $PdCl_2(PhCN)_2$ is a better catalyst, and we recommend use of 1.5 equiv of 2(*E*)-butenol (**1**) and 3.0 equiv of stannous chloride to benzaldehyde (Table I, entry 5).

Determination of Actual Allylating Agent. The detection of an actual allylating agent, namely an allylic tin intermediate, was carried out by NMR spectroscopic investigation as an opening to the enigmas in this palladium-catalyzed carbonyl allylation by allylic alcohols: (1) This reaction required 2 equiv of $SnCl_2$ to allylic alcohol, and (2) the addition of H_2O accelerated the allylation. We first carried out direct ^1H and ^{13}C NMR observation of the reaction of 2-propenol (**2**; 1 mmol) and $SnCl_2$ (2 mmol)

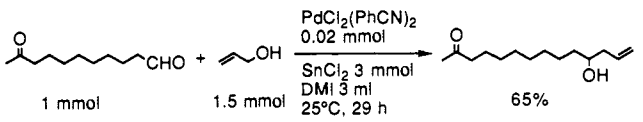
(9) For addition reaction of allylic tin compounds to carbonyl compounds, see: (a) Kumar Das, V. G.; Chu, C.-K. *The Chemistry of the Metal-Carbon Bond*; Wiley: New York, 1985; Vol. 3, p 41. (b) Tagliavini, G. *Rev. Si Ge Sn Pb* **1985**, *8*, 237. (c) Yamamoto, Y. *Aldrichim. Acta* **1987**, *20*, 45. (d) Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987; p 211.

(10) Furlani, D.; Marton, D.; Tagliavini, G.; Zordan, M. *J. Organomet. Chem.* **1988**, 341, 345 and references cited therein. Reference 7b,c.

Scheme II



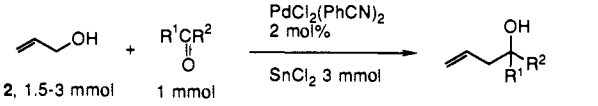
Scheme III



with $PdCl_2(PhCN)_2$ (0.04 mmol) in DMF-d_7 (0.5 mL) at 25 °C (sample I; spectra A and B in Figure 1). After 48 h, the starting **2** was completely consumed. The ^1H and ^{13}C NMR spectra of a major detectable product are almost the same as those of 3-chloropropene (**3**; 1 mmol) and $SnCl_2$ (1 mmol) with $PdCl_2(PhCN)_2$ (0.01 mmol) in DMF-d_7 (0.5 mL) (sample II; spectra C and D in Figure 2). The ^{13}C NMR spectrum is the same as that of 2-propenyltrichlorotin (**5**).[11] 2-Propenyltrichlorotin (**5**) should therefore be prepared from 2-propenol (**2**) via the formation of π-allylpalladium trichlorostannate (**4**).[12] A minor product, having broad ^{13}C peaks as shown on spectrum F in Figure 3, is obtained in the reaction of 2-propenol (**2**), and the ^{13}C chemical shifts resemble those of **5**. Thus, the minor product also seems to consist of a 2-propenyltin moiety. The ^{119}Sn NMR spectra of samples I and II were measured to confirm the structure of the major product (25 °C, DMF-d_7, Me_4Sn as an external reference compound). In the two samples, the ^{119}Sn peak (−326.7 ppm) of $SnCl_2$ has almost disappeared. Sample I showed two signals (−490.4 and −503.6 ppm). On the other hand, sample II showed a fairly sharp signal (−488.3 ppm). When we added six equimolar amounts of D_2O to sample I, the spectrum changed to one signal (−503.6 ppm). To support the above assumption, we observed the alteration of the ^{13}C chemical shifts of the allyl species, while adding a controlled amount of D_2O to samples I and II. The ^{13}C NMR spectra between 110 and 140 ppm are shown in Figure 3, spectra E–J. If one equimolar amount of D_2O was added to sample II, C_2 (136.0 ppm) and C_3 (114.2 ppm) shifted to upfield and downfield to each form two peaks C_2' (135.9 ppm) and C_2'' (135.6 ppm) and C_3' (114.5 ppm) and C_3'' (114.7 ppm) for two different allyl species (spectrum I). The signals of spectrum I resembled those of spectrum F. On continual addition of D_2O to the sample showing spectrum F, the peaks for C_2' and C_3' became less intense and the peaks for C_2'' and C_3'' became more intense. The peaks for C_2' and C_3' finally disappeared. The final allyl species should be an allyltin compound having no Sn^{IV}–Cl bond. From the results above, signals for the major allyl species in spectrum B are assigned to 2-propenyltrichlorotin (**5**) and the minor allyl species seems to be an propenylhydroxytin derivative (**6**).[13] A reaction path is illustrated in Scheme II. The detection of **5** indicates that $SnCl_2$ possesses two functions: that of assisting elimination of the hydroxy group and that of reducing the π-allylpalladium complex. The addition of D_2O produces the hydrated allylic tin species (**6**), which may be active for the carbonyl allylation.

Chemoselection in Carbonyl Allylation by Various Allylic Alcohols. The allylation by 2-propenol (**2**) can be applied not only to aldehydes but also to ketones at room temperature without additives such as cesium fluoride and tetrabutylammonium bromide, in contrast to allylic esters.[14] The results are summarized in Table II. The allylation of acetophenone at 50 °C enhanced the yield of 2-phenylpent-4-en-2-ol, with the production of 4-phenyl-1,3-pentadiene (6%) as a byproduct. Addition to 4-*tert*-butylcyclohexanone occurred predominantly from an equatorial direction (syn:anti = 94:6).[15,16,40] Addition of **2** to ketones is slower than that to aldehydes. Thus, chemoselective addition to an aldehyde can be realized in the presence of a ketone (Scheme III). Differences in reactivity between allylic alcohol and allylic esters were investigated using 2(*Z*)-butene-1,4-diol and its ester derivatives. The results are shown in Table III. The examination of the chemoselectivity between an allylic alcohol and an allylic acetate with 4-acetoxy-2(*Z*)-butenol demonstrates the higher reactivity of the allylic alcohol. The product is the same as that found in the addition of 1,4-diacetoxy-2(*Z*)-butene. This result suggests that the hydroxy group reacts with $SnCl_2$ to form a better leaving group than the acetoxy group, since (1) oxidative addition of allylic alcohols to palladium(0) complex is usually much slower than that of allylic acetates and (2) the carbonyl allylation by

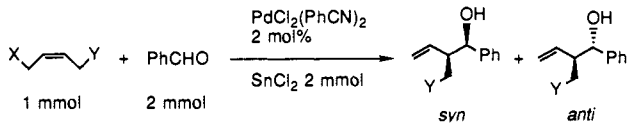
Table II. Allylation of Various Carbonyl Compounds by 2-Propenol (**2**)



carbonyl compound	solvent	temp (°C)	time (h)	yield[a] (%)
heptanal	DMI	25	38	77
10-undecenal	DMI	25	39	65
crotonaldehyde	DMI	25	26	36
cinnamaldehyde	DMI	25	24	81
piperonal	DMI	25	39	88
benzaldehyde	DMI	25	25	74
benzaldehyde	THF	25	24	83
acetophenone	DMI	25	96	36
acetophenone	DMI	50	45	59[b]
cyclohexanone	DMF	25	68	98
2-methylcyclohexanone	DMF	25	67	51
4-*tert*-butylcyclohexanone	DMF	25	142	89[c]
cycloheptanone	DMF	25	67	45
cyclododecanone	DMF	25	118	55

[a] Isolated yields. [b] 4-Phenyl-1,3-pentadiene was obtained as a by-product in 6% yield. [c] syn:anti = 94:6.

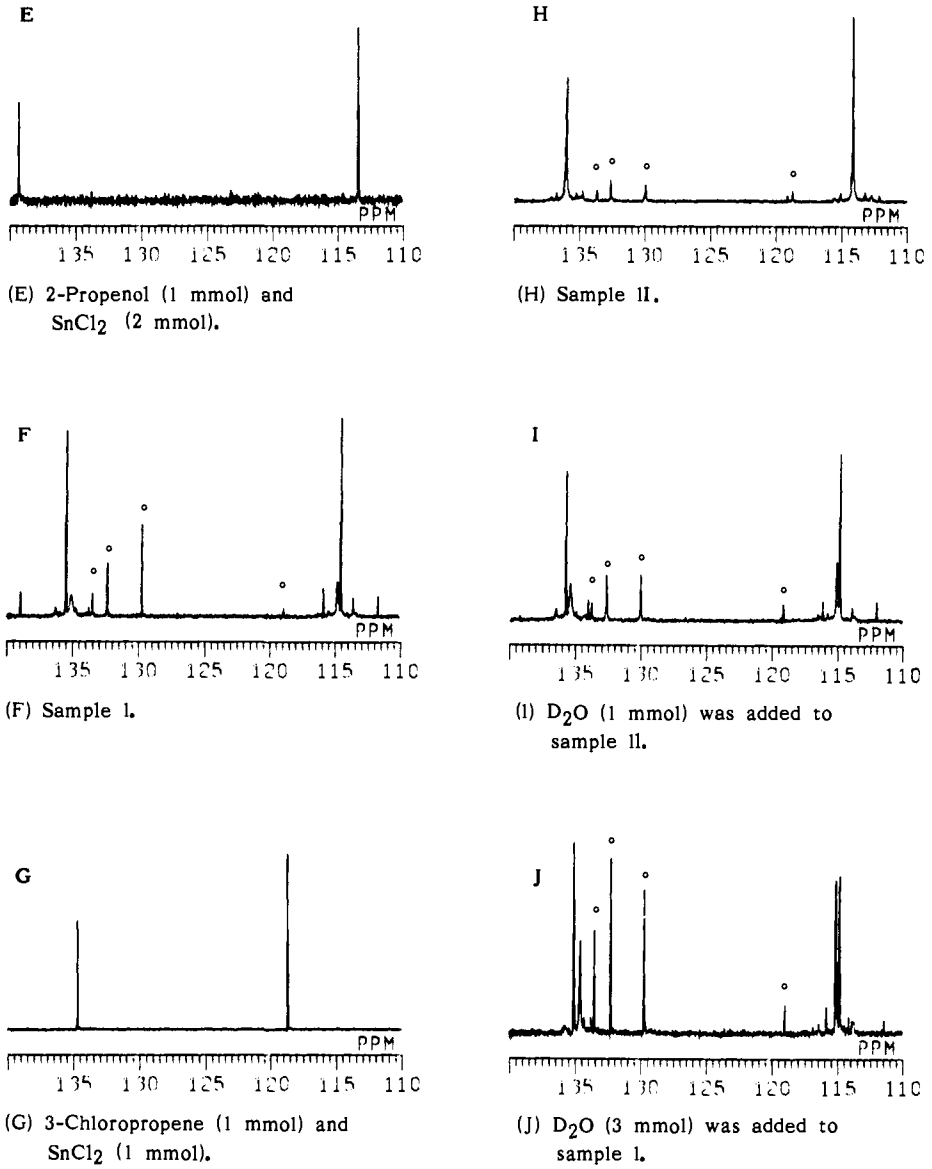
Table III. Chemoselection to Allylic Derivatives in Allylation of Benzaldehyde



allylic derivative				ratio[b]
X	Y	time (h)	yield[a] (%)	(syn:anti)
OH	OH	43	60	35:65
OAc	OAc	123	61	28:72
OH	OAc	101	56	31:69
OCO_2Me	OH	53	56	32:68

[a] Isolated yields. [b] After the adduct was converted to 1,3-dioxane derivatives, the configuration was determined by following the results reported in ref 18.

(11) Denmark, S. E.; Wilson, T.; Willson, T. M. *J. Am. Chem. Soc.* **1988**, *110*, 984.
(12) Musco, A.; Pontellini, R.; Grassi, M.; Sironi, A.; Meille, S. V.; Ruegger, H.; Ammann, C.; Pregosin, P. S. *Organometallics* **1988**, *7*, 2130.
(13) Poller, R. C. In *Comprehensive Organic Chemistry*; Jones, D. N., Ed.; Pergamon: Oxford, 1979; Vol. 3, p 1073.
(14) Masuyama, Y. Unpublished results. Palladium-catalyzed allylation of acetophenone by allyl acetate with $SnCl_2$ did not occur at 60 °C in DMI. However, the addition of cesium fluoride or tetrabutylammonium bromide (TBA) caused the allylation of acetophenone at 60 °C for 48 h in 19% and 48% yields, respectively. *2-Propenyltrihalotin intermediate*, which is more active than 2-propenylacetoxydihalotin in the absence of TBA, may be prepared from π-allylpalladium complex and stannous chloride with TBA, or *pentacoordinated 2-propenyltin compound*, which is effective for the allylation, may be prepared from tetracoordinated 2-propenyltin compound and TBA.
(15) (a) Naruta, Y.; Ushida, S.; Maruyama, K. *Chem. Lett.* **1979**, 919. (b) Hiyama, T.; Okude, Y.; Kimura, K.; Nazaki, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 561.
(16) Wu, Y.-D.; Houk, K. H. *J. Am. Chem. Soc.* **1987**, *109*, 908.



(E) 2-Propenol (1 mmol) and $SnCl_2$ (2 mmol).

(H) Sample II.

(F) Sample I.

(I) D_2O (1 mmol) was added to sample II.

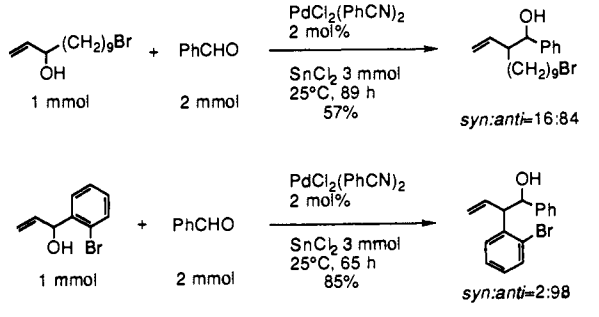
(G) 3-Chloropropene (1 mmol) and $SnCl_2$ (1 mmol).

(J) D_2O (3 mmol) was added to sample I.

Figure 3. ^{13}C NMR spectra in DMF-d_7 of the influence of D_2O (O, PhCN).

allylic alcohols requires at least two equimolar amounts of $SnCl_2$, in contrast with that by allylic esters. On the other hand, an allylic carbonate is more reactive than an allylic alcohol. As a result, the order of the reactivity of leaving groups is OCO_2Me > OH > OAc in the palladium-catalyzed carbonyl allylation with $SnCl_2$.[17] Aryl, vinyl, and alkyl bromides did not cause palladium-catalyzed homocoupling or cross-coupling reactions with $SnCl_2$ under the same conditions as the carbonyl allylation by allylic alcohols. Therefore, allylic alcohols bearing either an aliphatic or an aromatic bromide can be applied chemoselectively to produce the corresponding homoallylic alcohols, as shown in Scheme IV. These results demonstrate that oxidative addition of allylic alcohols to Pd(0) is faster than that of aryl bromides under these conditions.[19]

Scheme IV



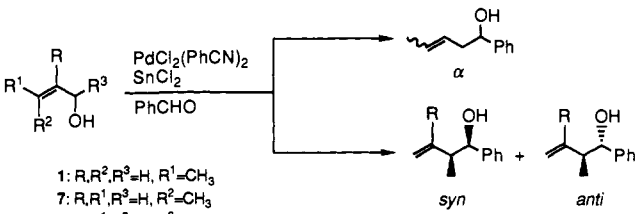
Solvation-Induced Regiocontrol and Diastereocontrol. The regio- and diastereoselection in the allylation of benzaldehyde by 2-(*E*)-butenol (**1**) was changed by the choice of solvents as shown in Table I. Here, the effects of solvents and H_2O for the regio- and diastereoselection in the allylation of benzaldehyde were investigated in detail at different temperatures. The results are summarized in Table IV. THF in the allylation by 2(*E*)-butenol (**1**) cannot be applied to regio- (γ-addition) and diastereoselection (anti selection) at 25 °C but can be at lower reaction temperatures (<−10 °C; Table IV, entries 1–6). The reaction did not proceed at −40 °C in THF. This palladium-catalyzed carbonyl allylation with $SnCl_2$ was accelerated by the addition of H_2O to any polar solvent used.[6] Furthermore, in the presence of H_2O, the reaction is more selective with respect to both γ-addition (regiocontrol) and syn/anti addition (diastereocontrol). Use of THF–H_2O or DME–H_2O medium led to highly selective anti addition without α-addition even at 25 °C (Table IV, entries 7–9 and 15–17), and

(17) For reactivity between allylic acetates, allylic carbonates, and allylic alcohols, see: (a) Tsuji, J.; Shimizu, I.; Minami, I.; Ohashi, Y. *Tetrahedron Lett.* **1982**, *23*, 4809. (b) Tsuji, J.; Shimizu, I.; Minami, I.; Ohashi, Y.; Sugiura, T.; Takahashi, K. *J. Org. Chem.* **1985**, *50*, 1523 and ref 3b.

(18) Koga, K.; Yamada, S. *Chem. Pharm. Bull.* **1972**, *20*, 526.

(19) (a) Nwokogu, G. C. *J. Org. Chem.* **1985**, *50*, 3900. (b) Trost, B. M.; Walchli, R. *J. Am. Chem. Soc.* **1987**, *109*, 3487.

Table IV. Dependence of Diastereoselection on Solvent[a]



1: R,R²,R³=H, R¹=CH₃
7: R,R¹,R³=H, R²=CH₃
8: R,R¹,R²=H, R³=CH₃
9: R,R¹=CH₃, R²,R³=H
10: R,R²=CH₃, R¹,R³=H

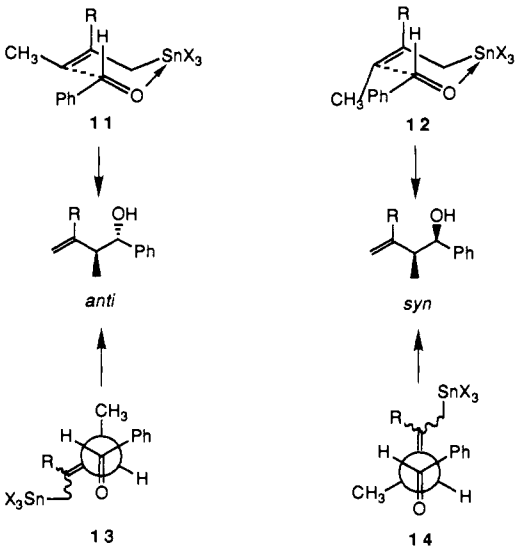
entry	alcohol	solvent (mL)	H_2O (mmol)	temp (°C)	time (h)	yield[b] (%)	ratio[c] (syn:anti:α)
1	1	THF (5)		50	24	67	23:23:54
2	1	THF (3)		25	25	72	22:25:53
3	1	THF (3)		0	95	80	16:78:6
4	1	THF (3)		−10	139	81	9:91
5	1	THF (3)		−15	135	62	7:93
6	1	THF (3)		−20	120	21	3:97
7	1	THF (3.5)	5	25	7	76	20:79:1
8	1	THF (3.5)	12	25	9	74	16:84
9	1	THF (4)	25	25	13	70	17:83
10	1	DMI (3)		50	7	65	49:51
11	1	DMI (3)		25	36	63	29:71
12	1	DMF (3)		25	63	89	30:70
13	1	DMF (3)	4	25	39	71	25:75
14	1	DMF (3)	63	25	15	77	18:82
15	1	DME (6)		25	142	22	41:3:56
16	1	DME (8)	6	25	90	67	31:64:5
17	1	DME (3)	56	25	17	99	29:71
18	1	EG (3)		25	37	78	58:42
19	1	EG (3)	5	25	36	85	43:57
20	1	EG (3)	56	25	17	99	17:83
21	1	DMSO (3)		25	136	34	65:35
22	1	DMSO (3)	2	25	91	45	74:26
23	1	DMSO (3)	3	25	88	84	86:14
24	1	DMSO (3)	10	25	88	75	83:17
25	1	DMSO (3)	20	25	69	77	68:32
26	1	DMSO (3)	28	25	77	65	49:51
27	1	DMSO (3)	43	25	50	71	39:61
28	1	DMSO (3)	56	25	47	76	27:73
29	1	DMSO (3)	63	25	43	42	22:78
30	1	DMSO (3)	169	25	70	70	16:84
31	7	DMSO (3)		25	138	24	75:25
32	7	DMSO (3)	3	25	95	51	84:16
33	7	DMSO (3)	173	25	95	48	79:21
34	7	DMI (3)		25	47	67	66:34
35	7	THF (4)		−10	139	71	77:23
36	7	THF (4)	12	0	76	73	70:30
37	7	THF (4)	12	25	6	80	56:44
38	8	DMSO (3)	3	25	92	95	84:16
39	8	DMSO (3)	174	25	55	60	24:76
40	8	DMI (3)		25	24	75	29:71
41	8	THF (3)	11	25	6	91	27:73
42	9	DMSO (3)		25	134	15	10:90
43	9	DMSO (3)	6	25	134	46	9:91
44	9	DMSO (3)	5	25	109	83	27:73[d]
45	9	DMSO (3)	54	25	68	67	3:97
46	9	THF (4)	26	25	47	63	16:81:3
47	10	DMSO (3)	4	25	130	19	43:57
48	10	DMSO (3)	4	25	113	87	38:62[d]
49	10	DMSO (3)	62	25	71	88	81:19
50	10	THF (4)	13	25	35	79	84:13:3

[a] The allylation of benzaldehyde (1 mmol) by allylic alcohol (1.5 mmol) is carried out with $PdCl_2(PhCN)_2$ (0.02 mmol) and $SnCl_2$ (3 mmol). [b] Isolated yields based on benzaldehyde. [c] The ratio was determined by GC (capillary column PEG 20 M, 0.25 mm × 30 m). [d] A 3-mmol portion of allylic alcohol was used.

in the case of DMF and EG, addition of H_2O increased anti selectivity (Table IV, entries 12–14 and 18–20). On the other hand, surprisingly, control of the amount of H_2O in DMSO medium permitted both syn selection (a small amount of H_2O) and anti selection (a large amount of H_2O) (Table IV, entries 21–30). In a solvent such as THF–H_2O or DMSO–H_2O (a large amount), 3-buten-2-ol (**8**) and 2-methylbut-2(*E*)-enol (**9**) as well as 2(*E*)-butenol (**1**) caused anti addition (Table IV, entries 39, 41, 45, and 46) and (*Z*)-allylic alcohols, namely 2(*Z*)-butenol (**7**) and 2-methylbut-2(*Z*)-enol (**10**), caused syn addition (Table IV, entries 33, 37, 49, and 50). These results can be explained by chair forms of six-membered cyclic transition states **11** and **12** (Scheme V).[20] The decrease of syn selectivity in the addition of 2(*Z*)-butenol (**7**) in THF (entry 37) may be dependent on the preparation of a 2(*E*)-butenyltin intermediate via the rapid isomerization of the *anti*-π-allylpalladium complex to the syn complex. On the contrary, the (*Z*)-**10** bearing 2-methyl group exhibited high syn selectivity (entry 50), which is probably due to the suppression of isomerization of anti complex to syn complex by steric hindrance of the 2-methyl group. Additions of butenols ((*E*)-**1** and (*Z*)-**7**) in DMSO–H_2O (a small amount) medium led to syn selection without depending upon the double-bond geometry (Table IV, entries 23 and 32). Thus, this selection suggests the existence of an acyclic antiperiplanar transition state **14** (Scheme V).[20] Both 2-methylbutenols ((*E*)-**9** and (*Z*)-**10**) caused anti addition in DMSO–H_2O (a small amount) medium (Table IV, entries 43 and 47). This anti addition cannot be accounted for by either the six-membered cyclic transition state or the acyclic antiperiplanar transition state. Since (1) an *anti*-π-allylpalladium complex derived from 2-methylbut-2(*Z*)-enol (**10**) has isomerized to a syn complex very little in THF–H_2O and DMSO–H_2O (a large amount) and (2) the reactions of butenols ((*E*)-**1** and (*Z*)-**7**) have proceeded via an acyclic transition state **14** in DMSO–H_2O (a small amount), we propose one possible acyclic transition state, namely the acyclic synclinal transition state **13** in the reactions of 2-methylbutenols ((*E*)-**9** and (*Z*)-**10**) in DMSO-H_2O (a small amount).[6,21,22] Steric hindrance, due to the 2-methyl group in (*E*)-**9** and (*Z*)-**10**, which is more bulky than a 2-proton in (*E*)-**1** and (*Z*)-**7**, presumably leads to the more favorable synclinal transition state **13** rather than to the antiperiplanar transition state **14**. In contrast to other solvents such as THF, DMI, or DMF, DMSO should strongly coordinate to the Sn(IV) of the allylic tin intermediates, thus disturbing the formation of the six-membered cyclic transition states **11** and **12**. The rate of the allylation

Scheme V

Six-Membered Cyclic Transition States in THF–H_2O



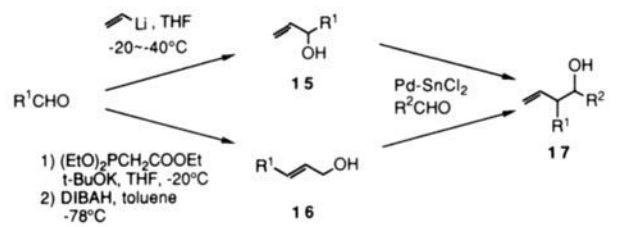
Acyclic transition states in DMSO–H_2O (a small amount)

(20) (a) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555. (b) Yamamoto, Y.; Maruyama, K. *Heterocycles* **1982**, *18*, 357. (c) Reetz, M. T. *Organotitanium Reagents in Organic Synthesis*; Springer-Verlag: Berlin, 1986; p 162. (d) Yamamoto, Y. *Acc. Chem. Res.* **1987**, *20*, 243.

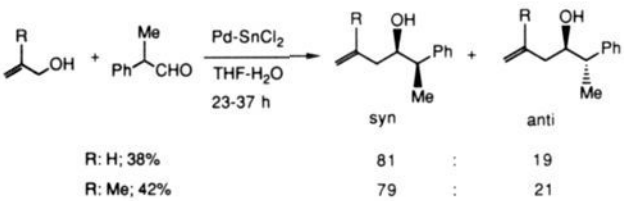
(21) (a) Denmark, S. E.; Weber, E. J.; Wilson, T. M.; Willson, T. M. *Tetrahedron* **1989**, *45*, 1053. (b) Denmark, S. E.; Henke, B. R.; Weber, E. *J. Am. Chem. Soc.* **1987**, *109*, 2512. (c) Denmark, S. E.; Weber, E. J. *J. Am. Chem. Soc.* **1984**, *106*, 7970. (d) Denmark, S. E.; Weber, E. J. *Helv. Chim. Acta* **1983**, *66*, 1655.

(22) Mikami, K.; Kawamoto, K.; Loh, T.-P.; Nakai, T. *J. Chem. Soc., Chem. Commun.* **1990**, 1161.

Scheme VI



Scheme VII



in DMSO is slower than that in THF or DMI, since the aldehyde is not activated by coordination to the Sn(IV) of the intermediate. A small amount of H_2O seems to cause the hydrolysis of Sn(IV)–Cl bonds to activate the allylic tin intermediates, while a large amount of H_2O in DMSO seems not only to hydrolyze the Sn(IV)–Cl bonds but also to rupture the coordination of DMSO to the Sn(IV).

Steric and Electronic Effects of Substituents for Solvation-Induced Regiocontrol and Diastereocontrol. Desirable diastereoselection in the 2-butenol/benzaldehyde system can be achieved by the choice of solvent.[23] We have investigated the steric and electronic effects of the substituents of the allylic alcohol and the aldehyde for regio- and diastereoselection. The results are summarized in Table V. The rate of allylation was more affected by the steric hindrance of the 1- or (*E*)-3-substituent of the allylic alcohols than by that of the aldehydes. The rate was also dependent upon the electrophilicity of the aldehyde (Table V, entries 1–6).[24] Both 1-substituted allylic alcohol **15** and (*E*)-3-substituted allylic alcohol **16** react with the aldehyde at room temperature to give one regioisomer, **17**; its diastereomer ratio prepared from **15** is almost the same as that prepared from **16** (Scheme VI). Therefore, 1-substituted **15**, which can be prepared more easily than (*E*)-3-substituted **16**, can be generally applied to this carbonyl allylation. The reaction of allylic alcohols bearing a bulky substituent at the 3-position with bulky aldehydes, as an exception, led to an apparent α-regioselection in THF–H_2O to produce (*E*)-homoallylic alcohols (Table V, entries 25 and 35).[25-27] Usual γ-addition of 3-substituted allyltin intermediates, derived from the allylic alcohols with Pd–$SnCl_2$, to bulky aldehydes should be suppressed by steric hindrance between both of the bulky substituents (cyclohexyl and phenyl groups). 1-Substituted allyltin intermediates, which slightly existed in an equilibrium state, might consequently cause α-addition to afford the (*E*)-homoallylic alcohols. Steric and electronic effects of substituent R^3 of aldehyde for solvation-controlled diastereoselection in the carbonyl allylation were investigated using 2(*E*)-butenol and 3-buten-2-ol. In the cases of benzaldehyde derivatives, the diastereoselection is dependent on the choice of solvents but independent of the electronic effect of para substituents (Table V, entries 1–6). Heptanal exhibited low diastereoselectivity in either THF–H_2O or DMSO–H_2O (Table V, entries 7–9 and 13–14). Bulky cyclohexanecarboxaldehyde underwent anti addition in both THF–H_2O and DMSO–H_2O (Table V, entries 10–12 and 15–16). The reaction of (*E*)-allylic alcohols, bearing a bulky substituent such as cyclohexyl and phenyl at 1- or 3-position, with bulky aldehydes exhibited high anti selection in DMSO–H_2O (Table V, entries 26, 33, and 36) in contrast with syn selectivity in the reaction of (*E*)-2-butenol with benzaldehyde (Table IV, entry 23).[28] Less active (3-cyclohexyl-2-propenyl)tin or cinnamyltin intermediate may be able to cause the addition only via six-membered cyclic transition state, which has a smaller entropy difference to product than the acyclic transition state does.[29]

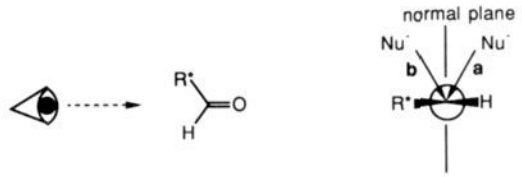
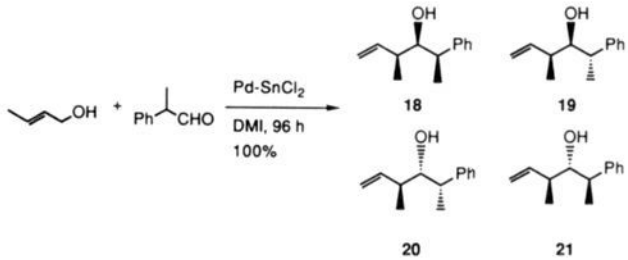
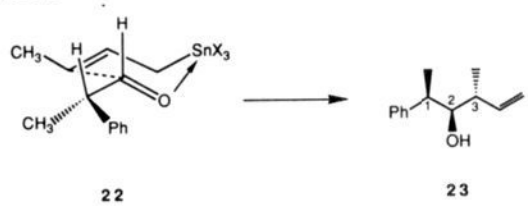


Figure 4. (Route a) The usual trajectory of attack of nucleophile Nu^- on carbonyl compound R*CHO; (route b) a proposed trajectory in carbonyl allylation via a six-membered cyclic transition state.

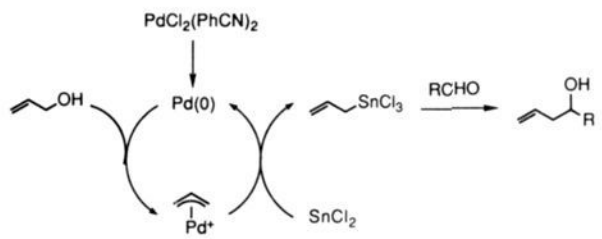
Scheme VIII



Scheme IX



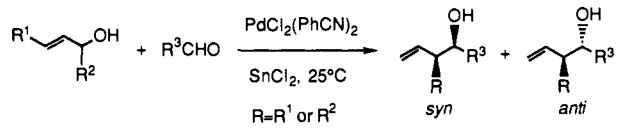
Scheme X



1,2-Asymmetric Induction on the Pd–$SnCl_2$ System. This carbonyl allylation was applied to 1,2-asymmetric induction, as realized in the addition reaction of allylic alcohols to 2-phenylpropanal, which has a stereocenter at the 2-position, with $PdCl_2(PhCN)_2$–$SnCl_2$ at 25 °C in DMI or THF–H_2O. 2-Propenol and 2-methyl-2-propenol exhibited the same syn diastereoselec-

(23) Keck, G. E.; Abbott, D. E.; Boden, E. P.; Enholm, E. J. *Tetrahedron Lett.* **1984**, *25*, 3927.
(24) Yamataka, H.; Nishikawa, K.; Hanafusa, T. *Chem. Lett.* **1990**, 1711.
(25) (a) Yamamoto, Y.; Maeda, N.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1983**, 742. (b) Yamamoto, Y.; Yatagai, H.; Ishihara, Y.; Maeda, N.; Maruyama, K. *Tetrahedron* **1984**, *40*, 2239.
(26) Hoffmann, R. W.; Ditrich, K.; Koster, G.; Sturmer, R. *Chem. Ber.* **1989**, *122*, 1783 and literature cited therein.
(27) (a) Boaretto, A.; Marton, D.; Tagliavini, G. *J. Organomet. Chem.* **1987**, *321*, 199. (b) Gambaro, A.; Ganis, P.; Marton, D.; Peruzzo, V.; Tagliavini, G. *J. Organomet. Chem.* **1982**, *231*, 307. (c) Hull, C.; Mortlock, S. V.; Thomas, E. J. *Tetrahedron Lett.* **1987**, *28*, 5343.
(28) Koreeda, M.; Tanaka, Y. *Chem. Lett.* **1982**, 1299.
(29) The carbonyl allylation by active allylic tin intermediates, which was controlled by enthalpy, proceeded smoothly in either THF–H_2O or DMSO–H_2O, as shown in Table IV. The allylation via the six-membered cyclic transition state in DMI or THF–H_2O was generally faster than that via acyclic transition state in DMSO–H_2O. Bulkiness and/or delocalization of sp^2 electrons of allylic tin intermediates such as ((*E*)-3-cyclohexyl-2-propenyl)tin and (*E*)-cinnmayltin lower the enthalpy difference between reactants and products, so that the entropy difference between transition states and products may control the allylation. Since the entropy difference between the six-membered cyclic transition state and the product is smaller than that between the acyclic transition state and the product, the six-membered cyclic transition state is probably favorable for the allylation even in DMSO–H_2O.

Table V. Addition of 1- or (*E*)-3-Substituted Allylic Alcohols to Aldehydes



entry	allylic alcohol R^1	allylic alcohol R^2	aldehyde R^3	solvent[a]	time (h)	yield[b] (%)	ratio[c] (syn:anti)
1	Me	H	*p*-$MeO_2CC_6H_4$	DMSO–H_2O	43	90	77:23
2	Me	H	*p*-ClC_6H_4	DMSO–H_2O	120	84	70:30
3	Me	H	*p*-$MeOC_6H_4$	DMSO–H_2O	240	79	82:18
4	Me	H	*p*-$MeO_2CC_6H_4$	DMF	38	99	22:78
5	Me	H	*p*-ClC_6H_4	DMF	125	50	22:78
6	Me	H	*p*-$MeOC_6H_4$	DMF	173	70	36:64
7	Me	H	*n*-C_6H_{13}	DMI	72	65	45:55
8	Me	H	*n*-C_6H_{13}	THF–H_2O	26	72	49:51
9	Me	H	*n*-C_6H_{13}	DMSO–H_2O	117	27	60:40
10	Me	H	c-C_6H_{11}	DMI	72	76	14:86
11	Me	H	c-C_6H_{11}	THF–H_2O	72	66 (10)	14:86
12	Me	H	c-C_6H_{11}	DMSO–H_2O	116	13	29:71
13	H	Me	*n*-C_6H_{13}	DMI	96	75	45:55
14	H	Me	*n*-C_6H_{13}	THF–H_2O	72	90	46:54
15	H	Me	c-C_6H_{11}	DMI	96	97 (2)	18:82
16	H	Me	c-C_6H_{11}	THF–H_2O	72	65	32:68
17	*n*-Pr	H	Ph	DMI	96	83	11:89
18	*n*-Pr	H	Ph	THF–H_2O	48	82	20:80
19	*n*-Pr	H	Ph	DMSO–H_2O	120	83	70:30
20	i-Pr	H	Ph	THF–H_2O	50	36	3:97
21	c-C_6H_{11}	H	*n*-C_6H_{13}	DMI	96	56	33:67
22	c-C_6H_{11}	H	*n*-C_6H_{13}	THF–H_2O	70	55 (7)	40:60
23	c-C_6H_{11}	H	*n*-C_6H_{13}	DMSO–H_2O	172	20	22:78
24	c-C_6H_{11}	H	Ph	DMI	116	69	3:97
25	c-C_6H_{11}	H	Ph	THF–H_2O	96	(45)	
26	c-C_6H_{11}	H	Ph	DMSO–H_2O	172	57	3:97
27	H	c-C_6H_{11}	Me	DMI	68	19 (6)	46:54
28	Ph	H	Me	DMI	72	73	6:94
29	Ph	H	Me	THF–H_2O	72	67	8:92
30	Ph	H	Me	DMSO–H_2O	190	17	6:94
31	Ph	H	Ph	DMI	73	79	7:93
32	Ph	H	Ph	THF–H_2O	42	67	0:100
33	Ph	H	Ph	DMSO–H_2O	169	57	3:97
34	Ph	H	c-C_6H_{11}	DMI	70	59	0:100
35	Ph	H	c-C_6H_{11}	THF–H_2O	64	(66)	
36	Ph	H	c-C_6H_{11}	DMSO–H_2O	94	37	1:99
37	H	*p*-MeO-C_6H_4	Me	DMI	75	71	8:92
38	H	*p*-NC-C_6H_4	Me	DMI	87	75	6:94

[a] THF–H_2O; THF, 3 mL; H_2O, 10 mmol. DMSO–H_2O: DMSO, 3 mL; H_2O, 3 mmol. [b] Isolated yields. Figures in parentheses are yields of α-adducts. [c] The ratio was determined by ^1H NMR (Jeolco GX-270) and by GC (capillary column; PEG 20 M, 0.25 mm × 30 m).

tivity, which may be explained by Cram's rule (Scheme VII). The addition of 2(*E*)-butenol to 2-phenylpropanal caused 1,2-syn-2,3-anti addition (Scheme VIII; **18**:**19**:**20**:**21** = 22:14:60:4).[25b] This selection can be explained by a combination of the Felkin model and the six-membered cyclic transition-state model, namely transition state **22** (Scheme IX).[30]

Conclusions

This palladium-catalyzed carbonyl allylation by allylic alcohols with $SnCl_2$ proceeds smoothly in organic medium containing water, as shown in Scheme X. $PdCl_2(PhCN)_2$ acts on the carbonyl allylation as a catalyst in organic medium containing water under air. This reaction implies that allylic alcohols function as synthons of allylic carbanions. The actual allylating agents in dry medium are allylic trichlorotins. The carbonyl allylation by allylic alcohols can achieve high chemo-, regio-, and diastereoselection by the choice of solvent and can be applied to 1,2-asymmetric induction.

Experimental Section

General Methods. ^1H NMR spectra (tetramethylsilane as an internal reference) were taken in $CDCl_3$ solution on a JEOL 270-MHz GX-270 FT-NMR; chemical shifts are given in ppm units, and peak forms are described with the following symbols: br (broadened), s (singlet), d (doublet), t (triplet), q (quartet), m (unsolved multiplet). Coupling constants, *J*, are reported in Hz. IR spectra were recorded on a Hitachi 265-50 spectrometer; peaks are reported in cm^{-1}. Mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded on a JEOL JMS-D300 spectrometer, with an ionization voltage of 70 eV. Gas chromatographic analysis (GC) was performed on an Ohkura Model 103 fitted with a flame ionization detector (PEG 20M capillary column, 0.25 mm × 30 m). Column temperatures are reported in °C. Retention time (t_R/min) and integrals were obtained from a Shimadzu C-R6A recorder. HPLC purification was carried out on a Japan Analysis Industry CO. Ltd. LC-908. TLC analyses were carried out with silica gel plates (Merck Art. 5735), column chromatography was carried out with silica gel (Merck silica gel 60 Art. 7734), and preparative TLC was carried out with a Harrison centrifugal thin-layer chromatotron (Merck Kiesel-gel 60 PF_{254} Art. 7749). All solvents had been dried over desiccant and had been distilled before being used. Most organic compounds used were commercial samples purified by distillation or recrystallization.

(30) Mori, I.; Bartlett, P. A.; Heathcock, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 7199. In general, the trajectory of attack of nucleophile Nu^- on aldehyde R*CHO shifts from the normal plane (the plane perpendicular to the R*CH and containing the C=O bond) to the opposite side of a bulky stereocenter R* (route a in Figure 4). Hence, the diastereofacial selection is not so strongly affected by the stereocenter R*, which is far from the trajectory a. On the contrary, the high 1,2-syn selectivity of the 2,3-anti product (**20**:**21** = 94:6) in this palladium-catalyzed carbonyl allylation suggests that the diastereofacially selective attack of allyltin intermediate is strongly affected by the stereocenter R*. The six-membered cyclic transition state **22** seems to serve for a fixation of trajectory b (Figure 4) in the direction of the sterically more demanding R*. The low 1,2-syn selectivity of the 2,3-syn product (**18**:**19** = 64:36) suggests that most of the 2,3-syn product was produced not via a six-membered cyclic transition state (substituents of aldehyde (R) take pseudoaxial position) but by an acyclic transition state.

Diastereomeric ratios were determined by ^1H NMR and GC analysis (accuracy ±1%).

Catalysts and Materials. Palladium catalysts were prepared by the literature procedure.[1c] 1-Substituted allylic alcohols were prepared by the reaction of aldehydes with vinylmagnesium bromide in Et_2O.[31] (*E*)-3-Substituted allylic alcohols were prepared by the reaction of aldehydes and ethyl diethylphosphonoacetate with *t*-BuOK, followed by the reduction with DIBAL in THF.[32] (*Z*)-3-Substituted allylic alcohols were prepared by the hydrogenation of the corresponding propargyl alcohols with Pd on $BaSO_4$ and quinoline.[33]

Carbonyl Allylation by Allylic Alcohol with Pd–$SnCl_2$. A typical procedure is as follows: To a mixture of $SnCl_2$ (0.57 g, 3 mmol), benzaldehyde (0.11 g, 1 mmol), and (*E*)-2-butenol (0.11 g, 1.5 mmol) in DMI (3 mL) was added $PdCl_2(PhCN)_2$ (0.02 mmol) at ambient temperature under a nitrogen atmosphere. After being stirred for 25 h, the mixture was diluted with 120 mL of a mixed solvent (ether:dichloromethane = 2:1) and washed successively with aqueous 10% HCl solution (10 mL), aqueous $NaHCO_3$ solution (10 mL), water (10 mL), and brine (10 mL). The extracts were dried over anhydrous $MgSO_4$. Then evaporation of solvent and purification by column chromatography on silica gel (hexane:ethyl acetate = 7:1) afforded 0.12 g (0.74 mmol, 74%) of 2-methyl-1-phenylbut-3-en-1-ol as a colorless oil.

The structures of the following alcohols were confirmed by the comparison of spectroscopic values with those of authentic samples in the literature: 2-methyl-1-phenylbut-3-en-1-ol,[34] 1-phenylpent-3-en-1-ol,[25b] 1-decen-4-ol,[35] hept-1,5-dien-4-ol,[36] 1-phenylhex-1,5-dien-3-ol,[37] 1-phenylbut-3-en-1-ol,[38] 1-(2-propenyl)cyclohexan-1-ol,[35] 2-methyl-1-(2-propenyl)cyclohexan-1-ol,[39] 1-(2-propenyl)-4-*tert*-butylcyclohexan-1-ol,[40] 3-methyldec-1-en-4-ol,[36] 2-phenylhex-5-en-3-ol,[25,36] 5-methyl-2-phenylhex-5-en-3-ol,[41] 4-methyl-2-phenylhex-5-en-3-ol.[25]

Tetradeca-1,13-dien-4-ol: colorless oil; R_f = 0.53 (hexane:EtOAc = 3:1); ^1H NMR 1.28–1.46 (m, 14 H, H-6–12), 1.82 (br, 1 H, OH), 1.99–2.10 (m, 2 H, H-5), 2.10–2.20 (m, 1 H, H-3), 2.20–2.35 (m, 1 H, H-3), 3.58–3.68 (m, 1 H, H-4), 4.89–5.03 (m, 2 H, CH_2=C–), 5.07–5.17 (m, 2 H, CH_2=C–), 5.72–5.91 (m, 2 H, C=CH–); IR (neat) 3350, 3060, 2900, 2840, 1635, 1450, 1430, 1070, 990, 910, 720; MS (rel intens) *m/e* 210 (0.3, M^+), 192 (0.4, $[M - H_2O]^+$), 169 (1, $[M - C_3H_5]^+$), 151 (3, $[M - (C_3H_5 + H_2O)]^+$), 109 (6), 95 (17, $C_7H_{13}^+$), 83 (6, $C_6H_{11}^+$), 81 (10), 69 (9), 67 (9, $C_5H_9^+$), 57 (4), 55 (12, $C_4H_7^+$); Anal. Calcd for $C_{14}H_{26}O$: C, 79.94; H, 12.46. Found: C, 80.11; H, 12.81.

1-(3,4-Methylenedioxyphenyl)but-3-en-1-ol:[42] colorless oil; R_f = 0.25 (hexane:EtOAc = 3:1); ^1H NMR 2.45 (ddd, *J* = 1.10, 6.60, and 6.96, 2 H, H-2), 2.60 (br, 1 H, OH), 4.56 (t, *J* = 6.60, 1 H, H-1), 5.07 (dd, *J* = 1.10 and 10.26, 1 H, (*E*)-CH_2=C–), 5.09 (dd, *J* = 1.10 and 17.22, 1 H, (*Z*)-CH_2=C–), 5.74 (ddt, *J* = 6.96, 10.26, and 17.22, 1 H, C=CH–), 5.89 (s, 2 H, OCH_2O), 6.73 (d, *J* = 1.10, 2 H, aryl-H), 6.81 (d, *J* = 0.73, 1 H, aryl-H); IR (neat) 3360, 3060, 2880, 2780, 1630, 1600, 1480, 1440, 1240, 1040, 990, 920; MS (rel intens) *m/e* 192 (0.6 M^+), 175 (5), 174 (10, $[M - H_2O]^+$), 151 (6, $[M - C_3H_5]^+$), 144 (3), 117 (4), 116 (11), 115 (15), 93 (6), 65 (5), 63 (4). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.61; H, 6.33.

2-Phenylpent-4-en-2-ol:[43] colorless oil; R_f = 0.28 (hexane:EtOAc = 7:1); ^1H NMR 1.53 (s, 3 H, H-1), 2.18 (br, 1 H, OH), 2.48 (dd, *J* = 8.43 and 13.74, 1 H, H-3), 2.67 (dd, *J* = 6.59 and 13.74, 1 H, H-3), 5.10 (dd, *J* = 1.10 and 10.63, 1 H, (*E*)-CH_2=C–), 5.11 (dd, *J* = 1.10 and 16.86, 1 H, (*Z*)-CH_2=C–), 5.61 (dddd, *J* = 6.59, 8.43, 10.63, and 16.86, 1 H, C=CH–), 7.19–7.45 (m, 5 H, aryl-H); IR (neat) 3400, 3010, 2950, 2900, 2850, 1445, 750, 690; MS (rel intens) *m/e* 144 (4, $[M - H_2O]^+$), 129 (9, $[M - (H_2O + CH_3)]^+$), 128 (5), 121 (29, $[M - C_3H_5]^+$), 105 (6, $PhCO^+$), 77 (10, Ph^+). Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.41; H, 8.73.

1-(2-Propenyl)cycloheptan-1-ol:[44] colorless oil; R_f = 0.26 (hexane:EtOAc = 5:1); ^1H NMR 1.33–1.76 (m, 12 H, cyclo-CH_2), 2.23 (dd, *J* = 1.14 and 7.57, 2 H, –CH_2C=C), 2.47–2.51 (m, 1 H, OH), 5.06–5.16 (m, 2 H, CH_2=C–), 5.90 (ddt, *J* = 7.58, 10.23, and 16.85, 1 H, –CH=C); IR (neat) 3495, 3080, 2940, 1640, 1450, 970, 910; MS (rel intens) *m/e* 154 (0.4 M^+), 136 (2, $[M - H_2O]^+$), 113 (17, $C_7H_{12}OH^+$), 95 (19, $[C_7H_{12}OH - H_2O]^+$), 93 (3), 79 (4), 69 (5), 67 (8), 55 (11). Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.81; H, 11.78.

1-(2-Propenyl)cyclododecan-1-ol:[15b] colorless oil; R_f = 0.58 (hexane:EtOAc = 5:1); ^1H NMR 1.25–1.61 (m, 22 H, cyclo-CH_2), 2.17 (dd, *J* = 1.14 and 7.58, 2 H, –CH_2C=C), 5.08–5.19 (m, 2 H, CH_2=C–), 5.92 (ddt, 7.58, 10.23, and 16.86, 1 H, –CH=C); IR 3400, 3060, 2940, 1635, 1450, 990, 910; MS (rel intens) *m/e* 224 (0.6, M^+), 206 (2, $[M - H_2O]^+$), 183 (5, $C_{12}H_{22}OH^+$), 109 (4), 95 (6), 83 (9), 82 (7), 81 (6), 79 (4), 69 (5), 67 (8), 55 (10). Anal. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.16; H, 12.76.

11-Hydroxytetradec-13-en-2-one: white solid; mp 64–66 °C; R_f = 0.18 (hexane:EtOAc = 3:1); ^1H NMR 1.14–1.59 (m, 12 H, H-4–9), 1.75 (br, 1 H, OH), 2.14 (s, 3 H, H-1), 2.05–2.20 (m, 2 H, H-10), 2.20–2.38 (m, 2 H, H-12), 2.42 (t, *J* = 7.5, 2 H, H-3), 3.60–3.71 (m, 1 H, H-11), 5.12 (d, *J* = 11.3, 1 H, (*E*)-CH_2=C–), 5.13 (d, *J* = 18.2, 1 H, (*Z*)-CH_2=C–), 5.76–5.92 (m, 1 H, –CH=C); IR (KBr) 3300, 3060, 2900, 2840, 1710, 1450, 1400, 1150, 1090, 1000, 900, 710; HRMS calcd for $C_{14}H_{26}O_2$ ($[M]^+$) 226.1931, found 226.1926.

2-(Acetoxymethyl)-1-phenylbut-3-en-1-ol: colorless oil (syn:anti = 4:6); R_f = 0.23 (benzene:acetone = 20:1); ^1H NMR syn isomer 2.00 (s, 3 H, CH_3CO), 2.50–2.65 (br, 1 H, OH), 2.67–2.81 (m, 1 H, H-2), 3.97 (dd, *J* = 6.60 and 10.94, 1 H, CH_2OAc), 4.11 (dd, *J* = 6.60 and 10.94, 1 H, CH_2OAc), 4.64–4.71 (m, 1 H, H-1), 4.96–5.04 (m, 1 H, CH_2=C–), 5.08–5.30 (m, 1 H, CH_2=C–), 5.59 (ddd, *J* = 8.60, 10.60, and 17.0, 1 H, –CH=C), 7.23–7.35 (m, 5 H, aryl-H), anti isomer 2.00 (s, 3 H, CH_3CO), 2.50–2.65 (br, 1 H, OH), 2.67–2.81 (m, 1 H, H-2), 4.16 (dd, *J* = 6.60 and 10.94, 1 H, CH_2OAc), 4.31 (dd, *J* = 6.60 and 10.94, 1 H, CH_2OAc), 4.64–4.71 (m, 1 H, H-1), 5.13 (dd, *J* = 1.6, and 17.2, 1 H, (*Z*)-CH_2=C–), 5.22 (dd, *J* = 1.6 and 10.6, 1 H, (*E*)-CH_2=C–), 5.77 (ddd, *J* = 8.6, 10.6, and 17.2, 1 H, –CH=C), 7.23–7.35 (m, 5 H, aryl-H); IR (neat) 3380, 3080, 1735, 1640, 1500, 1450, 1380, 990, 910, 700; MS (rel intens) *m/e* 129 (4), 107 (10, $PhCHOH^+$), 105 (14, $PHCO^+$), 79 (8, $[Ph + 2H]^+$), 77 (8, Ph^+), 54 (23). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.91; H, 7.27. Found: C, 70.88; H, 7.46.

2-(9-Bromononanyl)-1-phenylbut-3-en-1-ol: colorless oil (syn:anti = 2:8); R_f = 0.33 (hexane:EtOAc = 5:1); ^1H NMR syn isomer 1.15–1.37 (m, 14 H, H-2′–8′), 1.86 (q, *J* = 6.96, 2 H, H-1′), 2.24 (d, *J* = 1.83, 1 H, OH), 2.29 (m, 1 H, H-2), 3.37 (t, *J* = 6.96, 2 H, H-9′), 4.54–4.60 (m, 1 H, H-1), 5.02–5.06 (m, 2 H, CH_2=C–), 5.49 (ddd, *J* = 9.16, 10.26, and 16.86, 1 H, –CH=C), 7.23–7.36 (m, 5 H, aryl-H), anti isomer 1.15–1.37 (m, 14 H, H-2′–8′), 1.86 (q, *J* = 6.96, 2 H, H-1′), 2.24 (d, *J* = 1.83, 1 H, OH), 2.29 (m, 1 H, H-2), 3.37 (t, *J* = 6.96, 2 H, H-9′), 4.37 (dd, *J* = 1.83 and 8.06, 1 H, H-1), 5.14 (dd, *J* = 2.20 and 17.22, 1 H, (*Z*)-CH_2=C–), 5.22 (dd, *J* = 2.19 and 10.25, 1 H, (*E*)-CH_2=C–), 5.64 (ddd, *J* = 9.16, 10.26, and 17.22, 1 H, –CH=C), 7.23–7.36 (m, 5 H, aryl-H); IR (neat) 3350, 3050, 2950, 1640, 1000, 920, 750, 700, 650; MS (rel intens) *m/e* 336 (0.4, $[M(^{81}Br) - H_2O]^+$), 334 (0.4, $[M(^{79}Br) - H_2O]^+$), 157 (0.5), 150 (0.6), 143 (3), 129 (14), 128 (3), 107 (27, $PhCHOH^+$), 105 (5, $PhCO^+$), 79 (6, $[Ph + 2H]^+$), 77 (5, Ph^+), 55 (5). Anal. Calcd for $C_{19}H_{29}BrO$: C, 64.59; H, 8.27. Found: C, 64.57; H, 8.28.

2-(2-Bromophenyl)-1-phenylbut-3-en-1-ol: colorless oil (syn:anti = 2:98); R_f = 0.20 (hexane:EtOAc = 7:1); ^1H NMR anti isomer 2.48 (d, *J* = 2.20, 1 H, OH), 4.18 (dd, *J* = 6.22 and 8.43, 1 H, H-2), 4.86 (dd, *J* = 2.20 and 6.23, 1 H, H-1), 5.05 (d, *J* = 17.22, 1 H, (*Z*)-CH_2=C–), 5.15 (d, *J* = 10.26, 1 H, (*E*)-CH_2=C–), 6.15 (ddd, *J* = 8.43, 10.26, and 17.22, 1 H, –CH=C), 6.90–7.76 (m, 9 H, aryl-H); IR (neat) 3400, 3050, 1630, 1600, 1490, 1410, 1110, 990, 910, 760, 700, 650; MS (rel intens) *m/e* 198 (5, $^{81}BrC_6H_4 - C_3H_5^+$), 196 (5, $^{79}BrC_6H_4 - C_3H_5^+$), 117 (4), 116 (5), 115 (7), 107 (23, $PhCHOH^+$), 79 (14), 77 (8, Ph^+). Anal. Calcd for $C_{16}H_{15}BrO$: C, 63.38; H, 4.99. Found: C, 63.31; H, 4.97.

2,3-Dimethyl-1-phenylbut-3-en-1-ol: white solid; mp 41 °C (syn:anti = 97:3); colorless oil (syn:anti = 5:95); R_f = 0.23 (hexane:EtOAc = 7:1); GC (column temp 160) t_R = 26.4 (anti), 29.1 (syn); ^1H NMR syn isomer 1.00 (d, *J* = 6.84, 3 H, 2-CH_3), 1.75 (s, 3 H, 3-CH_3), 2.30 (br, 1 H, OH), 2.42–2.53 (m, 1 H, H-2), 4.75 (d, *J* = 4.88, 1 H, H-1), 4.79 (s, 1 H, CH_2=C), 4.86 (s, 1 H, CH_2=C), 7.28–7.36 (m, 5 H, aryl-H), anti isomer 0.79 (d, *J* = 6.84, 3 H, 2-CH_3), 1.79 (s, 3 H, 3-CH_3), 2.30 (br, 1 H, OH), 2.42–2.53 (m, 1 H, H-2), 4.38 (d, *J* = 9.28, 1 H, H-1), 4.99

(31) (a) Kharash, M. S.; Reinmuth, O. *Grignard Reaction of Nonmetallic Substance*; Prentice-Hall: New York, 1954; p 138. (b) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; Benjamin: Reading, MA, 1972; p 817.

(32) (a) Boutagy, J.; Thomas, R. *Chem. Rev.* **1974**, *74*, 87. (b) Wadsworth, W. S. *Org. React.* **1977**, *25*, 73.

(33) Cram, D. J.; Allinger, N. L. *J. Am. Chem. Soc.* **1956**, *78*, 2518.

(34) Yamamoto, Y.; Yatagai, H.; Maruyama, K. *J. Am. Chem. Soc.* **1981**, *103*, 1969.

(35) Katzenellenbogen, J. A.; Lenox, R. S. *J. Org. Chem.* **1973**, *38*, 326.

(36) Wilson, S. R.; Guazzaroni, M. E. *J. Org. Chem.* **1989**, *54*, 3087.

(37) Hoffmann, R. W.; Herold, T. *Chem. Ber.* **1981**, *114*, 375.

(38) Smith, G. G.; Voorhees, K. J. *J. Org. Chem.* **1970**, *35*, 2182.

(39) Abehaim, D.; Henry-Basch, E.; Freon, P. *Bull. Soc. Chim. Fr.* **1969**, 4038.

(40) Gaudemar, M. *Tetrahedron* **1976**, *32*, 1689.

(41) Heathcock, C. H.; Kiyooka, S.; Blumenkopf, T. A. *J. Org. Chem.* **1984**, *49*, 4214.

(42) Uneyama, K.; Kamaki, N.; Moriyama, A.; Torii, S. *J. Org. Chem.* **1985**, *50*, 5396.

(43) Hiyama, T.; Obayashi, M.; Nakamura, A. *Organometallics* **1982**, *1*, 1249.

(44) Kramer, G. W.; Brown, H. C. *J. Org. Chem.* **1977**, *42*, 2292.

(s, 2 H, CH_2=C), 7.28–7.36 (m, 5 H, aryl-H); IR (KBr) 3380, 2980, 1950, 1640, 1450, 1370, 1280, 1200, 1120, 1020, 890, 820, 700, 560; MS (rel intens) *m/e* 176 (0.5, M^+), 158 (0.9, $[M - H_2O]^+$), 143 (2, $[M - (H_2O + CH_3)]^+$), 107 (19, $PhCHOH^+$), 105 (3, $PhCO^+$), 79 (14, $[Ph + 2H]^+$), 77 (Ph^+), 70 (22), 55 (7). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.90; H, 9.43.

2-Methyl-1-[4-(methoxycarbonyl)phenyl]but-3-en-1-ol: colorless oil (syn:anti = 7:3–3:7); R_f = 0.14 (hexane:EtOAc = 7:1); GC (column temp 195) t_R = 39.4 (anti), 41.9 (syn); ^1H NMR syn isomer 0.97 (d, *J* = 6.82, 3 H, 2-CH_3), 2.54 (m, 1 H, H-2), 2.95 (br, 1 H, OH), 3.87 (s, 3 H, CO_2CH_3), 4.61 (d, *J* = 5.30, 1 H, H-1), 5.01 (d, *J* = 16.66, 1 H, (*Z*)-CH_2=C), 5.01 (d, *J* = 10.98, 1 H, (*E*)-CH_2=C), 5.72 (ddd, *J* = 7.19, 10.98, and 16.66, 1 H, –CH=C), 7.32 (d, *J* = 7.95, 2 H, aryl-H), 7.92 (d, *J* = 7.95, 2 H, aryl-H), anti isomer 0.87 (d, *J* = 6.81, 3 H, 2-CH_3), 2.45 (m, 1 H, H-2), 3.07 (br, 1 H, OH), 3.86 (s, 3 H, CO_2CH_3), 4.44 (d, *J* = 7.19, 1 H, H-1), 5.09 (d, *J* = 16.66, 1 H, (*Z*)-CH_2=C), 5.10 (d, *J* = 10.98, 1 H, (*E*)-CH_2=C), 5.76 (ddd, *J* = 7.99, 10.98, and 16.66, 1 H, –CH=C), 7.34 (d, *J* = 8.33, 2 H, aryl-H), 7.94 (d, *J* = 8.33, 2 H, aryl-H); IR (neat) 3450, 3080, 2960, 1735, 1640, 1610, 1580, 1510, 1300, 1200, 1100, 1030, 910, 840; MS (rel intens) *m/e* 163 (2), 105 (5, $PhCO^+$), 91 (3, $C_7H_7^+$), 78 (2), 59 (8). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.68; H, 7.36.

1-(4-Chlorophenyl)-2-methylbut-3-en-1-ol.[45] The structure of this alcohol was determined by the spectroscopic comparison with that of an authentic sample prepared from 2-butenyltributyltin and 4-chlorobenzaldehyde:[23] colorless oil (syn:anti = 7:3–2:8); R_f = 0.32 (hexane:EtOAc = 7:1); GC (column temp 175) t_R = 44.0 (anti), 47.7 (syn); ^1H NMR syn isomer 0.95 (d, *J* = 6.81, 3 H, C-2-CH_3), 2.34–2.55 (m, 2 H, OH, H-2), 4.48 (dd, *J* = 2.65 and 5.30, 1 H, H-1), 4.95–5.05 (m, 2 H, CH_2=C–), 5.68 (ddd, *J* = 7.01, 10.60, and 17.00, 1 H, –CH=C), 7.13–7.20 (m, 4 H, aryl-H), anti isomer 0.83 (d, *J* = 6.81, 3 H, 2-CH_3), 2.34–2.55 (m, 2 H, OH, H-2), 4.27 (d, *J* = 7.57, 1 H, H-1), 5.09–5.17 (m, 2 H, CH_2=C–), 5.73 (ddd, *J* = 7.95, 9.85, and 17.80, 1 H, –CH=C), 7.13–7.20 (m, 4 H, aryl-H); IR (neat) 3400, 3080, 2960, 1640, 1600, 1500, 1420, 1100, 1020, 920, 830, 750; MS (rel intens) *m/e* 143 (12), 141 (36), 113 (6), 111 (2), 77 (17, Ph^+).

1-(4-Methoxyphenyl)-2-methylbut-3-en-1-ol:[46] R_f = 0.45 (hexane:EtOAc = 3:1); GC (column temp 180) t_R = 36.0 (syn), 38.0 (anti); ^1H NMR syn isomer 1.00 (d, *J* = 6.81, 3 H, 2-CH_3), 2.42 (br, 1 H, OH), 2.51 (m, 1 H, H-2), 3.75 (s, 3 H, OCH_3), 4.46 (d, *J* = 5.68, 1 H, H-1), 4.95–5.02 (m, 2 H, CH_2=C–), 5.69 (ddd, *J* = 7.19, 9.84, and 17.80, 1 H, –CH=C), 6.83 (d, *J* = 8.71, 2 H, aryl-H), 7.17 (d, *J* = 8.71, 2 H, aryl-H), anti isomer 0.82 (d, *J* = 6.81, 3 H, 2-CH_3), 2.42 (br, 1 H, OH), 2.50–2.54 (m, 1 H, H-2), 3.75 (s, 3 H, OCH_3), 4.18 (d, *J* = 7.95, 1 H, H-1), 5.06 (d, *J* = 17.04, 1 H, (*Z*)-CH_2=C–), 5.06 (d, *J* = 10.22, 1 H, (*E*)-CH_2=C–), 5.89 (ddd, *J* = 7.57, 10.22, and 17.04, 1 H, –CH=C), 6.82–6.85 (m, 2 H, aryl-H), 7.18–7.23 (m, 2 H, aryl-H); IR (neat) 3440, 3060, 2960, 2830, 1670, 1600, 1500, 1470, 1300, 1240, 1180, 1030, 1000, 910, 810; MS (rel intens) *m/e* 138 (4), 137 (47, $[MeOC_6H_4CH$=$OH]^+$), 135 (4), 109 (9), 94 (5), 77 (7, Ph^+). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.92; H, 8.49.

1-Cyclohexyl-2-methylbut-3-en-1-ol:[23] colorless oil (syn:anti = 2:8); R_f = 0.30 (hexane:EtOAc = 7:1); GC (column temp 135) t_R = 15.2 (anti), 17.4 (syn); ^1H NMR syn isomer 1.01 (d, *J* = 6.82, 3 H, 2-CH_3), 1.06–1.94 (m, 12 H, cyclo-CH, cyclo-CH_2, OH), 2.34–2.44 (m, 1 H, H-2), 3.20 (t, *J* = 5.68, 1 H, H-1), 5.04–5.13 (m, 2 H, CH_2=C–), 5.55–5.88 (m, 1 H, –CH=C), anti isomer 1.03 (d, *J* = 6.82, 3 H, 2-CH_3), 1.06–1.94 (m, 12 H, cyclo-CH, cyclo-CH_2, OH), 2.34–2.44 (m, 1 H, H-2), 3.10 (t, *J* = 5.68, 1 H, H-1), 5.04–5.13 (m, 2 H, CH_2=C–), 5.55–5.88 (m, 1 H, –CH=C); IR (neat) 3400, 3070, 2920, 2850, 1640, 1450, 1380, 1110, 1000, 910; MS (rel intens) *m/e* 168 (0.2, M^+), 113 (20, $[C_6H_{11}CH$=$OH]^+$), 95 (100, $[M - (C_4H_7 + H_2O)]^+$), 83 (14, $C_6H_{11}^+$), 69 (11), 67 (15), 56 (27), 55 (27, $C_4H_7^+$). Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.55; H, 11.95.

1-Phenyl-2-propylbut-3-en-1-ol:[28] colorless oil (syn:anti = 7:3–1:9); R_f = 0.31 (hexane:EtOAc = 7:1); GC (column temp 170) t_R = 26.6 (anti), 29.2 (syn); ^1H NMR syn isomer 0.90–1.05 (m, 3 H, propyl-CH_3), 1.20–1.71 (m, 4 H, propyl-CH_2), 2.37–2.61 (m, 2 H, OH, H-2), 4.66–4.69 (m, 1 H, H-1), 5.26 (dd, *J* = 2.27 and 17.04, 1 H, (*Z*)-CH_2=C–), 5.35 (dd, *J* = 2.27 and 10.22, 1 H, (*E*)-CH_2=C–), 5.71 (ddd, *J* = 9.09, 10.22, and 17.04, 1 H, –CH=C), 7.33–7.49 (m, 5 H, aryl-H), anti isomer 0.90–1.05 (m, 3 H, propyl-CH_3), 1.20–1.71 (m, 4 H, propyl-CH_2), 2.37–2.61 (m, 2 H, OH, H-2), 4.50 (dd, *J* = 1.52 and 7.57, 1 H, H-1), 5.10 (dd, *J* = 2.27 and 17.04, 1 H, (*Z*)-CH_2=C–), 5.17 (dd, *J* = 2.27 and 10.22, 1 H, (*E*)-CH_2=C–), 5.62 (ddd, *J* = 9.09, 10.22, and 17.04, 1 H, –CH=C), 7.33–7.49 (m, 5 H, aryl-H); IR (neat) 3420, 3050, 2950, 1640, 1600, 1500, 1460, 1380, 1120, 1000, 920, 760, 700; MS (rel intens) *m/e* 190 (0.2, M^+), 172 (0.2, $[M - H_2O]^+$), 143 (3), 129 (10), 128 (5), 107 (25, $PhCHOH^+$), 105 (5, $PhCO^+$), 91 ($C_7H_7^+$), 79 (11, $[Ph + 2H]^+$), 77 (8, Ph^+), 55 (3). Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.54. Found: C, 82.13; H, 9.64.

2-(1-Methylethyl)-1-phenylbut-3-en-1-ol: colorless oil (syn:anti = 1:9); R_f = 0.31 (hexane:EtOAc = 7:1); GC (column temp 170) t_R = 24.5 (anti), 25.8 (syn); ^1H NMR anti isomer 0.82 (d, *J* = 6.83, 3 H, ^{i}Pr-CH_3), 0.85 (d, *J* = 6.83, 3 H, ^{i}Pr-CH_3), 1.47 (m, 1 H, ^{i}Pr-CH), 2.08 (br, 1 H, OH), 2.16 (ddd, *J* = 4.40, 8.79, and 9.76, 1 H, H-2), 4.67 (d, *J* = 8.79, 1 H, H-1), 5.12 (dd, *J* = 2.44 and 17.09, 1 H, (*Z*)-CH_2=C–), 5.30 (dd, *J* = 2.44 and 10.26, 1 H, (*E*)-CH_2=C–), 5.81 (ddd, *J* = 9.76, 10.26, and 17.09, 1 H, –CH=C), 7.24–7.35 (m, 5 H, aryl-H); IR (neat) 3400, 3050, 2980, 1640, 1600, 1460, 1390, 1370, 1160, 1120, 1000, 930, 750, 690; MS (rel intens) *m/e* 97 (4), 84 (13), 81 (4), 71 (4), 70 (10), 69 (13), 67 (3), 57 (7), 55 (17). Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.54. Found: C, 81.98; H, 9.60.

3-Cyclohexyldec-1-en-4-ol: colorless oil (syn:anti = 4:6); R_f = 0.41 (hexane:EtOAc = 7:1); GC (column temp 170) t_R = 32.0 (anti), 34.0 (syn); ^1H NMR syn isomer 0.88 (t, *J* = 6.08, 3 H, H-10), 0.96–1.80 (m, 23 H, H-3, H-5–9, cyclo-CH, cyclo-CH_2), 3.66–3.72 (m, 1 H, H-4), 5.02 (dd, *J* = 2.65 and 17.04, 1 H, (*Z*)-CH_2=C–), 5.13 (dd, *J* = 2.65 and 10.22, 1 H, (*E*)-CH_2=C–), 5.50 (dt, *J* = 10.22 and 17.14, 1 H, –CH=C), anti isomer 0.88 (t, *J* = 6.08, 3 H, H-10), 0.96–1.80 (m, 23 H, cyclo-CH, cyclo-CH_2, H-3, H-5–9), 3.66–3.72 (m, 1 H, H-4), 5.02 (dd, *J* = 2.65 and 17.04, 1 H, (*Z*)-CH_2=C–), 5.17 (dd, *J* = 2.65 and 10.22, 1 H, (*E*)-CH_2=C–), 5.70 (dt, *J* = 10.22 and 17.04, 1 H, –CH=C); IR (neat) 3400, 3080, 2900, 1640, 1450, 1380, 1120, 1000, 920; MS (rel intens) *m/e* 220 (0.4, $[M - H_2O]^+$), 124 (9, $[C_6H_{11}CHCH$=$CH_2]^+$), 95 (4), 82 (14), 81 (9), 68 (4), 55 (15). Anal. Calcd for $C_{16}H_{30}O$: C, 80.61; H, 12.68. Found: C, 80.60; H, 12.72.

2-Cyclohexyl-1-phenylbut-3-en-1-ol: colorless oil (syn:anti = 1:9); R_f = 0.33 (hexane:EtOAc = 7:1); GC (column temp 195) t_R = 48.8 (anti), 51.9 (syn); ^1H NMR syn isomer 1.00–1.19 (m, 6 H, cyclo-CH_2-3′,4′,5′), 1.40–1.48 (m, 1 H, cyclo-CH), 1.57–1.77 (m, 4 H, cyclo-CH_2-2′,6′), 1.94 (br, 1 H, OH), 2.12 (dt, *J* = 7.93 and 9.77, 1 H, H-2), 4.75 (d, *J* = 7.93, 1 H, H-1), 4.83 (dd, *J* = 2.44 and 17.09, 1 H, (*Z*)-CH_2=C–), 4.97 (dd, *J* = 1.83 and 10.38, 1 H, (*E*)-CH_2=C–), 5.34–5.44 (m, 1 H, –CH=C), 7.24–7.36 (m, 5 H, aryl-H), anti isomer 1.00–1.19 (m, 6 H, cyclo-CH_2-3′,4′,5′), 1.40–1.48 (m, 1 H, cyclo-CH), 1.57–1.77 (m, 4 H, cyclo-CH_2-2′,6′), 1.94 (br, 1 H, OH), 2.12 (dt, *J* = 7.93 and 9.77, 1 H, H-2), 4.68 (d, *J* = 7.93, 1 H, H-1), 5.07 (dd, *J* = 1.83 and 17.09, 1 H, (*Z*)-CH_2=C–), 5.24 (dd, *J* = 2.44 and 10.38, 1 H, (*E*)-CH_2=C–), 5.81 (dd, *J* = 9.76, 10.38, and 17.09, 1 H, –CH=C), 7.24–7.36 (m, 5 H, aryl-H); IR (neat) 3450, 3080, 2920, 2850, 1450, 1110, 990, 910, 740, 700; MS (rel intens) *m/e* 124 (9), 107 (34, $PhCHOH^+$), 82 (6), 81 (5), 79 (10, $[Ph + 2H]^+$), 77 (5, Ph^+), 67 (3), 55 (3). Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.49; H, 9.89.

4-Cyclohexyl-1-phenylbut-3-en-1-ol: colorless oil; R_f = 0.32 (hexane:EtOAc = 7:1); ^1H NMR 0.97–1.37 (m, 6 H, cyclo-CH_2), 1.61–1.70 (m, 4 H, cyclo-CH_2), 1.87–1.98 (m, 1 H, cyclo-CH), 2.18 (br, 1 H, OH), 2.31–2.50 (m, 2 H, H-2), 4.64 (t, *J* = 6.44, 1 H, H-1), 5.33 (dt, *J* = 6.44 and 15.52, 1 H, H-3), 5.50 (dd, *J* = 6.44 and 15.52, 1 H, H-4), 7.21–7.33 (m, 5 H, aryl-H); IR (neat) 3350, 3020, 2900, 1630, 1600, 1500, 1450, 1040, 960, 750, 700; MS (rel intens) *m/e* 212 (4, $[M - H_2O]^+$), 130 (8), 129 (6), 121 (3), 107 (19, $PhCHOH^+$), 91 (4, $C_7H_7^+$), 79 (9, $[Ph + 2H]^+$), 77 (4, Ph^+), 67 (3), 55 (2). Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.46; H, 9.61.

Mixture of 3-Cyclohexylpent-4-en-2-ol and 5-Cyclohexylpent-4-en-2-ol. These alcohols were not separated: colorless oil; R_f = 0.19 (hexane:EtOAc = 7:1); GC (column temp 130) 3-cyclohexylpent-4-en-2-ol t_R = 19.9 (syn), 22.5 (anti), 5-cyclohexylpent-4-en-2-ol t_R = 26.5 (*E* isomer); ^1H NMR 3-cyclohexylpent-4-en-2-ol, syn isomer 0.80–2.20 (m, 13 H, cyclo-CH_2, cyclo-CH, OH, H-3), 1.10 (d, *J* = 6.05, 3 H, H-1), 3.80–3.95 (m, 1 H, H-2), 5.05 (d, *J* = 17.5, 1 H, (*Z*)-CH_2=C–), 5.17 (d, *J* = 10.0, 1 H, (*E*)-CH_2=C–), 5.72 (dt, *J* = 10.0 and 17.5, 1 H, –CH=C), anti isomer 0.80–2.20 (m, 13 H, cyclo-CH_2, cyclo-CH, OH, H-3), 1.77 (d, *J* = 6.05, 3 H, H-1), 3.80–3.95 (m, 1 H, H-2), 5.05 (d, *J* = 17.5, 1 H, (*Z*)-CH_2=C–), 5.22 (d, *J* = 10.0, 1 H, (*E*)-CH_2=C–), 5.51 (dt, *J* = 10.0 and 17.5, 1 H, –CH=C), 5-cyclohexylpent-4-en-2-ol 0.80–2.20 (m, 14 H, cyclo-CH_2, cyclo-CH, OH, H-1, H-3), 3.70–3.80 (m, 1 H, H-2), 5.35 (dt, *J* = 7.50 and 15.0, 1 H, H-4), 5.50 (dd, *J* = 6.25 and 15.0, 1 H, H-5). Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 76.98; H, 11.85.

3-Phenylpent-4-en-2-ol:[28] colorless oil (anti >95%); R_f = 0.28 (hexane:EtOAc = 7:1); GC (column temp 165) t_R = 28.5 (syn), 31.4 (anti); ^1H NMR syn isomer 1.23 (d, *J* = 6.43, 3 H, H-1), 1.68 (br, 1 H, OH), 3.23 (t, *J* = 8.27, 1 H, H-3), 4.04 (dq, *J* = 6.44 and 8.27, 1 H, H-2), 5.11 (d, *J* = 10.60, 1 H, (*E*)-CH_2=C–), 5.12 (d, *J* = 18.17, 1 H, (*Z*)-CH_2=C–), 6.08–6.13 (m, 1 H, –CH=C), 7.18–7.34 (m, 5 H, aryl-H), anti isomer 1.06 (d, *J* = 6.43, 3 H, H-1), 2.02 (br, 1 H, OH),

(45) Servens, C.; Pereyre, M. *J. Organomet. Chem.* **1971**, *26*, C4.
(46) Wider, L.; Seebach, D. *Helv. Chim. Acta* **1982**, *65*, 1085.

3.16 (t, J = 8.27, 1 H, H-3), 3.97 (dq, J = 6.44 and 8.27, 1 H, H-2), 5.21 (d, J = 18.17, 1 H, (Z)-CH_2=C-), 5.23 (d, J = 10.60, 1 H, (E)-CH_2=C-), 6.12 (ddd, J = 8.27, 10.60, and 18.17, 1 H, -CH=C), 7.18-7.34 (m, 5 H, aryl-H); IR (neat) 3400, 3050, 2950, 1640, 1600, 1490, 1410, 1110, 990, 920, 760, 700; HRMS calcd for $C_{11}H_{14}O$ ([M^+]) 162.1044, found 162.1040. Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.47; H, 8.74.

1,2-Diphenylbut-3-en-1-ol:[28] colorless oil (anti >95%); R_f = 0.10 (hexane:EtOAc = 7:1); ^{1}H NMR syn isomer 2.73 (d, J = 2.57, 1 H, OH), 3.88 (d, J = 5.15, 1 H, H-2), 4.56-4.65 (m, 1 H, H-1), 5.00-5.15 (m, 2 H, CH_2=C-), 5.82 (ddd, J = 5.15, 10.30, and 17.04, 1 H, -CH=C), 6.93-7.24 (m, 10 H, aryl-H), anti isomer 2.73 (d, J = 2.57, 1 H, OH), 3.46 (dd, J = 7.69 and 8.84, 1 H, H-2), 4.68 (dd, J = 2.57 and 7.69, 1 H, H-1), 5.01 (ddd, J = 0.76, 1.52, and 17.04, 1 H, (E)-CH_2=C-), 5.12 (ddd, J = 0.76, 1.52, and 10.30, 1 H, (Z)-CH_2=C-), 6.15 (ddd, J = 8.84, 10.30, and 17.04, 1 H, -CH=C), 6.99-7.21 (m, 10 H, aryl-H); IR (neat) 3400, 3050, 1630, 1600, 1490, 1410, 1110, 990, 910, 760, 700; MS (rel intens) 224 (0.3, M^+), 206 (1, [$M - H_2O$]$^+$), 118 (18), 117 (10, [PhCHCH=CH_2]$^+$), 115 (5), 107 (18, $PhCHOH^+$), 105 (5, $PhCO^+$), 91 (15, $C_7H_7^+$), 79 (11, [Ph + 2H]$^+$), 77 (8, Ph^+). Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 85.71; H, 7.29.

1-Cyclohexyl-2-phenylbut-3-en-1-ol:[28] colorless oil (anti >95%); R_f = 0.39 (hexane:EtOAc = 7:1); GC (column temp 195) t_R = 51.2 (anti), 54.1 (syn); ^{1}H NMR anti isomer 1.08-1.37, 1.59-1.85 (m, 12 H, cyclo-CH, cyclo-CH_2, OH), 3.44 (dd, J = 7.20 and 9.08, 1 H, H-2), 3.53 (m, 1 H, H-1), 5.16 (dd, J = 1.52 and 17.04, 1 H, (Z)-CH_2=C-), 5.20 (dd, J = 1.52 and 10.22, 1 H, (E)-CH_2=C-), 6.14 (ddd, J = 9.09, 10.22, and 17.04, 1 H, -CH=C), 7.15-7.34 (m, 5 H, aryl-H); IR (neat) 3450, 3050, 2900, 1640, 1600, 1500, 1450, 1390, 1130, 990, 920, 760, 700; MS (rel intens) m/e 230 (0.6, M^+), 212 (1, [$M - H_2O$]$^+$), 118 (24), 117 (8, [PhCHCH=CH_2]$^+$), 115 (5), 95 (11), 91 (4, $C_7H_7^+$), 77 (2, Ph^+), 67 (3), 55 (5). Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.48, H, 9.74.

1-Cyclohexyl-4-phenylbut-3-en-1-ol: colorless oil; R_f = 0.30 (hexane:EtOAc = 7:1); ^{1}H NMR 0.89-1.89 (m, 12 H, cyclo-CH_2, cyclo-CH, OH), 2.25 (dd, J = 4.01 and 7.76, 1 H, H-2), 2.39-2.47 (m, 1 H, H-2), 3.39-3.47 (m, 1 H, H-1), 6.22 (ddd, J = 6.44, 7.76, and 15.90, 1 H, H-3), 6.45 (d, J = 15.91, 1 H, H-4), 7.15-7.36 (m, 5 H, aryl-H); IR (neat) 3400, 3050, 2900, 1600, 1500, 1450, 1040, 960, 740, 690; MS (rel intens) m/e 130 (3), 129 (3), 118 (24), 117 (11, [PhCH=CHCH$_2$]$^+$), 115 (5), 95 (13), 91 (6, $C_7H_7^+$), 67 (4), 55 (5). Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.40; H, 9.70.

3-(4-Methoxyphenyl)pent-4-en-2-ol: white solid mp 57 °C (syn:anti = 8:92); R_f = 0.20 (hexane:EtOAc = 6:1); GC (column temp 180) t_R = 24.1 (syn), 26.6 (anti); ^{1}H NMR syn isomer 1.21 (d, J = 6.06, 3 H, H-1), 2.16 (br, 1 H, OH), 3.18 (t, J = 8.33, 1 H, H-3), 3.76 (s, 3 H, OCH_3), 3.91 (dq, J = 6.06 and 8.33, 1 H, H-2), 5.05-5.12 (m, 2 H, CH_2=C-), 6.00 (ddd, J = 8.33, 9.84, and 17.42, 1 H, -CH=C), 6.85 (m, 2 H, aryl-H), 7.10 (m, 2 H, aryl-H), anti isomer 1.05 (d, J = 6.06, 3 H, H-1), 2.16 (br, 1 H, OH), 3.11 (t, J = 8.33, 1 H, H-3), 3.75 (s, 3 H, OCH_3), 3.91 (dq, J = 6.06 and 8.33, 1 H, H-2), 5.16 (d, J = 16.66, 1 H, (Z)-CH_2=C-), 5.19 (d, J = 10.60, 1 H, (E)-CH_2=C-), 6.08 (ddd, J = 8.71, 10.60, and 16.66, 1 H, -CH=C), 6.84 (d, J = 8.71, 2 H, aryl-H), 7.10 (d, J = 8.71, 1 H, aryl-H); IR (KBr) 3440, 3060, 2960, 2830, 1670, 1600, 1500, 1470, 1300, 1240, 1180, 1030, 1000, 910, 810; MS (rel intens) m/e 192 (4, M^+), 174 (2, [$M - H_2O$]$^+$), 149 (14), 148 (100), 147 (95, [CH_2=CH - C_6H_4OMe]$^+$), 133 (17), 117 (13), 115 (15), 103 (9), 91 (14, $C_7H_7^+$), 78 (5), 77 (7, Ph^+). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.91; H, 8.53.

3-(4-Cyanophenyl)pent-4-en-2-ol: colorless oil (syn:anti = 1:9); R_f = 0.59 (hexane:EtOAc = 1:1); ^{1}H NMR syn isomer 1.22 (d, J = 6.44, 3 H, H-1), 2.79 (br, 1 H, OH), 3.34 (dd, J = 6.44 and 8.33, 1 H, H-3), 4.03 (quintet, J = 6.44, 1 H, H-2), 5.15-5.28 (m, 2 H, CH_2=C-), 5.93-6.30 (m, 1 H, -CH=C), 7.40 (d, J = 8.33, 2 H, aryl-H), 7.63 (d, J = 8.33, 2 H, aryl-H), anti isomer 1.09 (d, J = 6.44, 3 H, H-1), 2.79 (br, 1 H, OH), 3.30 (dd, J = 6.44 and 8.71, 1 H, H-3), 4.03 (quintet, J = 6.44, 1 H, H-2), 5.18 (d, J = 17.04, 1 H, (Z)-CH_2=C-), 5.25 (d, J = 10.23, 1 H, (E)-CH_2=C-), 6.09 (ddd, J = 8.71, 10.23, and 17.04, 1 H, -CH=C), 7.37 (d, J = 8.33, 2 H, aryl-H), 7.60 (d, J = 8.33, 2 H, aryl-H); IR (neat) 3450, 2980, 2230, 1640, 1570, 1450, 1210, 1150, 1080, 920, 830; MS (rel intens) m/e 146 (37), 145 (10), 144 (27), 143 (100), 142 (81), 117 (18), 116 (26), 115 (18). Anal. Calcd for $C_{12}H_{13}NO$: C, 76.98; H, 7.00; N, 7.48. Found: C, 76.95; H, 7.03; N, 7.37.

Acknowledgment. This work was supported by Grant-in-Aid for Scientific Research No. 02640407 from the Ministry of Education, Science and Culture, Japan.

Chiral Phosphine Ligands Modified by Crown Ethers: An Application to Palladium-Catalyzed Asymmetric Allylation of β-Diketones

Masaya Sawamura, Hiroshi Nagata, Hiroaki Sakamoto, and Yoshihiko Ito*

Contribution from the Department of Synthetic Chemistry, Faculty of Engineering, Kyoto University, Kyoto 606-01, Japan. *Received August 23, 1991*

Abstract: Chiral ferrocenylphosphine ligands modified by monoaza or diaza crown ethers of varying ring sizes and linker chain lengths (**8a-e**, **9**) were synthesized. The reaction of the phosphine ligand modified by monoaza-18-crown-6 (**8b**) and the di-μ-chlorobis(π-allyl)dipalladium(II) complex in $CDCl_3$ produced the π-allylpalladium(II) complex chelated by the two phosphorus atoms of **8b**, leaving the crown ether moiety free. The ^{1}H{^{1}H} nuclear Overhauser effect study of the π-allylpalladium(II) complex suggests that the aza crown ether moiety of chiral ligand **8b** is located at the proper position to interact with an incoming nucleophile. The palladium catalyst which was prepared in situ by mixing the crown ether-modified chiral ligands and $Pd_2(dba)_3$·$CHCl_3$ was examined for stereoselectivity and catalytic activity in the asymmetric allylation of unsymmetrically substituted β-diketones under solid-liquid, two-phase reaction conditions using potassium fluoride as an insoluble base in mesitylene. The ligands bearing monoaza-18-crown-6 or 1,10-diaza-18-crown-6 with an appropriate length of linker chain (**8b** and **8d**, respectively) significantly accelerated the allylation and showed fairly high enantioselectivity (up to 75% ee). It is proposed that a ternary complex involving a crown ether, a potassium cation, and an enolate anion attacks a π-allylpalladium(II) intermediate.

Asymmetric synthesis employing a chiral metal catalyst is a subject of considerable interest, since a small amount of chiral material can produce a large amount of chiral product.[1] Among the many examples of catalytic asymmetric reactions, palladium-catalyzed asymmetric allylation or allylic alkylation, which involves a (π-allyl)palladium(II) intermediate, has been one of the most studied, and several successful results achieving enantioselectivity of over 80% ee have been reported.[2-9] In general,

(1) For reviews, see: (a) Ojima, I.; Clos, N.; Bastos, C. *Tetrahedron* **1989**, *45*, 6901. (b) Noyori, R.; Kitamura, M. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Springer-Verlag: Berlin, 1989; Vol. 5, p 115. (c) Brunner, H. *Synthesis* **1988**, 645.

(2) (a) Auburn, P. A.; Mackenzie, P. B.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2033. (b) Mackenzie, P. B.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2046.

0002-7863/92/1514-2586$03.00/0