Synthesis of Homoallylic Alcohols from Allylic Phosphates and Aldehydes with Organoaluminum Reagent Containing Al-Sn Linkage[1)]

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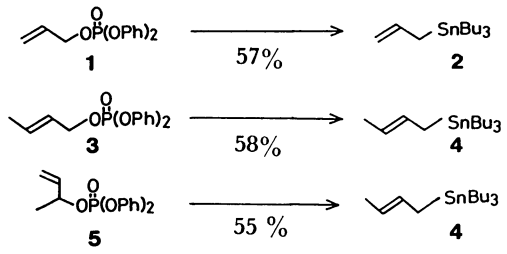
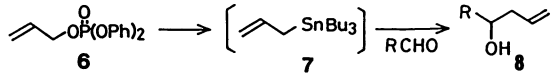
Treatment of allylic phosphates with the reagent prepared from *n*-Bu_3SnLi and Et_2AlCl or from SnF_2 and Et_2AlCl affords allyltin compounds which react with aldehydes to produce homoallylic alcohols in good yields. The formation of allyltin compounds requires the catalytic amount of $Pd(PPh_3)_4$ and proceeds with inversion of the stereochemistry predominantly.

The addition of allylmetal species[2)] to carbonyl compounds is one of the most important methods for C-C bond formation. The stereoselectivity of the reaction as well as the yields of products depend on the nature of the element such as Si,[3)] Sn,[4)] Cr,[5)] Sm,[6)] Y,[6)] Mn,[7)] Ti,[8)] and Zr.[8)] Among them the organotin compounds are widely used because of their easiness of handling and high reactivity. For instance, the reaction of allylstannanes with carbonyl compounds in the presence of Lewis acid provides erythro homoallylic alcohols with high stereoselectivity.[4b)] The allylation of carbonyl compounds also proceeds effectively with allylstannanes generated from allylic halides and tin metal[4c)] or divalent tin compounds.[4d)] Limitations associated with availability of the allylic halides[4c,d)] in these reactions have led us to examine allylic phosphates[9)] as an alternative starting material.



n-Bu_3SnLi (2 eq), Et_2AlCl (2 eq), $Pd(PPh_3)_4$ (0.1 eq)

Scheme 1.



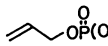
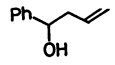
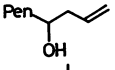
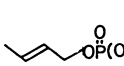
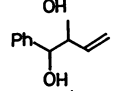
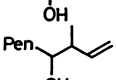
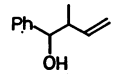
Scheme 2.

An organoaluminum reagent produced from *n*-Bu_3SnLi[10)] and Et_2AlCl, is considered to have an aluminum-tin single bond[11)] and has proved to be useful for synthetic reactions.[1)] Treatment of allyl diphenyl phosphate **1** with this reagent in the presence of $Pd(PPh_3)_4$ catalyst gave allylstannane **2** in 57% yield,[12)] and (*E*)-2-butenyl diphenyl phosphate **3** produced (*E*)-2-butenyltributylstannane **4** in 58% yield. Diphenyl 1-methyl-2-propenyl phosphate **5** also afforded (*E*)-2-butenyltributylstannane **4** contaminated by a small amount of its *Z* isomer in a 55% combined yield (Scheme 1). The yields of these products could not be improved over 70% in spite of various attempts because of the difficulty in isolating allylic stannane in a pure form.

The presence of an equimolar amount of aldehyde in this reaction system resulted in the direct formation of homoallylic alcohol **8** in good yields (Scheme 2). For example, the treatment of a mixture of allyl diphenyl phosphate and benzaldehyde with *n*-Bu_3Sn-$AlEt_2$ in the presence of $Pd(PPh_3)_4$ provided 1-phenyl-3-buten-1-ol in 82% yield after aqueous work-up. The results are summarized in Table 1.

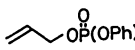
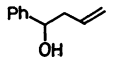
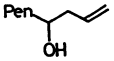
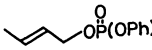
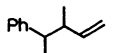
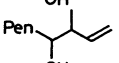
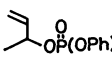
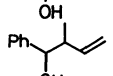
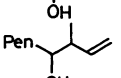
The high reaction temperature (200°C) is neces-

TABLE 1. SYNTHESIS OF HOMOALLYLIC ALCOHOLS FROM ALLYLIC PHOSPHATES AND ALDEHYDES WITH *n*-Bu_3SnLi-Et_2AlCl SYSTEM

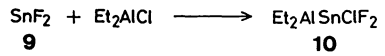
Run	Phosphates	Aldehydes	Products[a)]	Yields[b)]	*E*/*T*
1		PhCHO		82%	—
2	〃	Hexanal		70%	—
3		PhCHO		70%	(41/59)[c)]
4	〃	Hexanal		65%	(47/53)[d)]
5		PhCHO		82%	(38/62)[c)]

a) All compounds gave satisfactory spectra data. See Ref. 5. b) Isolated yields. c) Ratios of the stereoisomers (erythro and threo) were determined by the examination of ^1H-NMR signal of the methine (H-C-OH) proton. See experimental section. d) A ratio of the stereoisomer was determined by GLPC analysis. See experimental section.

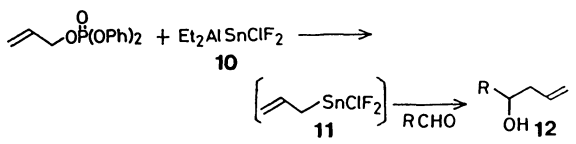
TABLE 2. SYNTHESIS OF HOMOALLYLIC ALCOHOLS FROM ALLYLIC PHOSPHATES AND ALDEHYDES WITH SnF_2–Et_2AlCl SYSTEM

Run	Phosphates	Aldehydes	Products[a]	Yields[b]	*E/T*
1		PhCHO		95%	—
2	〃	Hexanal		69%	—
3		PhCHO		96%	(33/67)[c]
4	〃	Hexanal		80%	(50/50)[d]
5		PhCHO		78%	(25/75)[c]
6	〃	Hexanal		77%	(55/45)[d]

a) All compounds gave satisfactory spectra data. See Ref. 5. b) Isolated yields. c) Ratios of the stereoisomers (erythro and threo) were determined by the examination of ^{1}H-NMR signal of the methine (H–C–OH) proton. See experimental section. d) Ratios of the stereoisomers were determined by GLPC analysis. See experimental section.



Scheme 3.



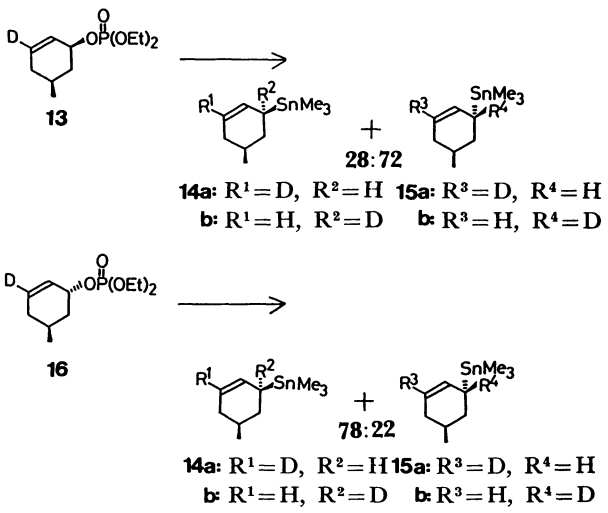
Scheme 4.

sary for the allylation of benzaldehyde with allyltributylstannane in the absence of Lewis acid.[4e] In contrast, the reaction proceeds at room temperature in the presence of Lewis acid. The stereoselectivity of the reaction between allylstannane and aldehyde depends on the nature of Lewis acids employed.[4f] In our case, Et_2Al–$OP(O)(OPh)_2$(compound **18** in Ref. 15) could behave as a Lewis acid giving poor selectivity.

Treatment of SnF_2 with an equimolar amount of Et_2AlCl in CH_2Cl_2 gave a dark red homogeneous solution. The reagent **10** thus prepared is assumed to have an aluminum–tin single bond (Scheme 3), and proved to be effective in the homoallylic alcohol synthesis from allylic phosphate and aldehyde. The results are summarized in Table 2.

The reaction is expected to involve an allylstannane **11** (Scheme 4) which has failed to be isolated. The threo stereoselectivity in the reaction with SnF_2–Et_2AlCl is slightly superior (run 3, 4) to that observed in *n*-Bu_3Sn–$AlEt_2$ reagent system.

The stereochemistry of the allylstannane synthsis from $R_3SnAlEt_2$ and allylic phosphate is shown in Scheme 5. Treatment of cis allylic phosphates **13** with Me_3Sn–$AlEt_2$ in the presence of a catalytic amount of $Pd(PPh_3)_4$ provided a mixture of cis and trans allylic stannanes **14a,b** and **15a,b** in 28:72 ratio. Both ratios of **14a**:**14b** and **15a**:**15b** were 1:1. Similar reaction of the trans isomer **16** gave **14a,b** and **15a,b** in 78:22 ratio, the ratios of **14a**:**14b** and **15a**:**15b** being 1:1 again. The stereochemistry of the allylstannanes was determined



Scheme 5.

by the examination of ^{119}Sn NMR spectra.[13] These results showed that the reaction has proceeded predominantly with the net inversion of the phosphates stereochemistry[14,15,16]

Experimental

The IR spectra were determined on a Shimadzu IR-27-G spectrometer, the mass spectra on a Hitachi M-80 machine, and the proton NMR spectra on a Varian EM-390 spectrometer and a Varian XL-200 spectrometer. The ^{119}Sn NMR and ^{13}C NMR spectra were determined on a JEOL-FX 90Q spectrometer. The chemical shifts of the proton NMR and the ^{13}C NMR are given in δ, with tetramethylsilane as an internal standard, and those of the ^{119}Sn NMR are given in δ, with tetramethylstannane as an internal standard. Tetrahydrofuran was freshly distilled from sodium benzophenone ketyl. Dichloromethane was dried over P_2O_5 and distilled. All the experiments were carried out under an argon atmosphere. Purification of products was performed by preparative thin-layer chromatography (PLC), or column chromatography on silica gel (Wakogel C-100) or alumina (Merck,

Art. 1077 Aluminiumoxid 90 aktiv neutral, 70—230 mesh). Analytical GLPC was performed with a Yanagimoto GCG-550-F and a Shimadzu GC-4CPT. Preparative GLPC was performed with a JEOL-JGC-20K apparatus.

Preparation of Allyltributylstannane with the Reagent Derived from n-*Bu*$_3$*SnLi and Et*$_2$*AlCl.* A hexane solution of butyllithium (1.6 M,† 3.8 ml, 6.0 mmol) was added to a suspension of anhydrous tin(II) chloride (0.38 g, 2.0 mmol) in THF (4.0 ml) at 0 °C. After being stirred for 20 min, the reaction mixture was treated with a hexane solution of diethylaluminum chloride (1.0 M, 2.0 ml, 2.0 mmol) at 0 °C. The resulting mixture was stirred for another 20 min, and a mixture of allyl diphenyl phosphate (0.29 g, 1.0 mmol) and Pd(PPh$_3$)$_4$ (0.12 g, 0.1 mmol) in THF (4 ml) was added. The whole was stirred for 1 h, then the reaction mixture was poured into 5% NaOH (70 ml) and extracted with ether (30 ml×3). The combined organic layers were washed with 5% NaOH (60 ml×2), dried over anhydrous sodium sulfate and concentrated. The crude product was purified by alumina column chromatography (hexane) followed by distillation (bp 120 °C/0.1 Torr,†† bath temp) to give allyltributylstannane in 57% yield as a colorless oil. This compound was identical with the authentic sample.[12a]

(E)-2-Butenyltributylstannane:[12a] The title compound was produced stereospecifically in 58% yield from (*E*)-2-butenyl diphenyl phosphate. Treatment of diphenyl 1-methyl-2-propenyl phosphate with *n*-Bu$_3$SnAlEt$_2$ as described above gave the *E* and *Z* isomeric mixture of 2-butenyltributylstannane in 55% yield. The stereochemistry was determined by ^{13}C NMR spectra.[17] The ratio of the intensity of olefinic carbon for *E*:*Z* was 10:1.

The Synthesis of Homoallylic Alcohols with the n-*Bu*$_3$*SnLi–Et*$_2$*AlCl Reagent.* A mixture of diphenyl 1-methyl-2-propenyl phosphate (0.61 g, 2.0 mmol), benzaldehyde (0.11 g, 1.0 mmol), and Pd(PPh$_3$)$_4$ (0.12 g, 0.1 mmol) was added at 0 °C to a THF solution of *n*-Bu$_3$SnAlEt$_2$ (2.0 mmol) prepared following the procedure described above. After being stirred for 1 h at room temperature, the reaction mixture was poured into 1 M hydrochloric acid (40 ml) and extracted with ether. The combined organic layers were washed with saturated NaHCO$_3$ aqueous solution, dried over anhydrous sodium sulfate, and concentrated. The purification by PLC (hexane–ethyl acetate, 5:1) gave 2-methyl-1-phenyl-3-buten-1-ol[5] in 68% yield: Bp 110 °C (bath temp, 4 Torr); IR (neat): 3400, 1635, 1492, 1011, 908, 758, 698 cm^{-1}; NMR (CCl_4): δ= 0.83 (d, *J*=7.2 Hz, 1.8 H, threo isomer), 0.94 (d, *J*=6.6 Hz, 1.2 H, erythro isomer), 2.15 (bs, 1H), 2.3—2.5 (m, 1H), 4.26 (d, *J*=6.8 Hz, 0.59 H, threo isomer), 4.43 (d, *J*=5.8 Hz, 0.41 H, erythro isomer), 4.9—5.2 (m, 2H), 5.5—5.9 (m, 1H), 7.23 (s, 5H); MS *m/z* (%): 162 (M$^+$, 0.5), 145 (10), 107 (99), 105 (36), 79 (100), 77 (96), 51 (16).

The Synthesis of Homoallylic Alcohol with SnF$_2$*–Et*$_2$*AlCl Reagent.* A hexane solution of diethylaluminum chloride (1.0 M, 2.0 ml, 2.0 mmol) was added to a suspension of anhydrous tin(II) fluoride (0.31 g, 2.0 mmol) in CH_2Cl_2 (5 ml) at 0 °C. The solution turned to red immediately. After the resulting mixture was stirred for 20 min, a mixture of diphenyl 1-methyl-2-propenyl phosphate (0.61 g, 2.0 mmol), hexanal (0.10 g, 1.0 mmol), and Pd(PPh$_3$)$_4$ (0.12 g, 0.1 mmol) was added, and the whole was stirred for 2 h at 20 °C. The reaction mixture was poured into 1 M hydrochloric acid and extracted with ether. The combined organic layers were washed with saturated NaHCO$_3$ aqueous solution, dried over anhydrous Na$_2$SO$_4$, and concentrated. The Purification by PLC (hexane–ethyl acetate, 5:1) gave an isomeric mixture of 3-methyl-1-nonen-4-ol[5] as a colorless oil (0.12 g, 80%). The isomeric ratio of the product (erythro/threo=1/1) was determined by GLPC [PEG 20 M 5%, on Celite 545, 1.5 m, 110 °C, T_r (threo)=9.0 min, T_r (erythro)=10.6 min]: Bp 90 °C (bath temp, 10 Torr); IR (CCl_4): 3380, 1638, 1260, 1081, 1000, 911 cm^{-1}, NMR (CCl_4): δ=0.92 (t, *J*=7.5 Hz, 3H), 1.04 (d, *J*=6.6 Hz, 3H), 1.0—1.6 (m, 8H), 1.80 (bs, 1H), 2.0—2.4 (m, 1H), 3.2—3.5 (m, 1H), 5.01 (dd, *J*=17.1, 2.7 Hz, 1H), 5.18 (dd, *J*=10.8, 2.7 Hz, 1H), 5.6—5.9 (m, 1H); MS *m/z* (%): 156 (M$^+$, 1.0), 133 (3), 101 (12), 83 (53), 56 (100), 55 (89), 43 (20), 41 (41).

The Stereochemical Study on the Allylic Stannane Synthesis. An ether solution of methyllithium (1.8 M, 5.0 ml, 9.0 mmol) was added to a suspension of anhydrous tin(II) chloride (0.57 g, 3.0 mmol) in THF (4 ml) at 0 °C. After being stirred for 20 min, the reaction mixture was treated with a hexane solution of Et$_2$AlCl (1.0 M, 3.0 ml, 3.0 mmol) at 0 °C. The resulting mixture was stirred for 20 min, and a mixture of *cis*- or *trans*-3-deuterio-5-methyl-2-cyclohexen-1-yl diethyl phosphate[18] (0.37 g, 1.5 mmol) and Pd(PPh$_3$)$_4$ (0.17 g, 0.15 mmol) was added. The whole was stirred for another 2 h at 20 °C, then the solution was poured into 5% NaOH (70 ml) and extracted with ether (30 ml×3). The combined organic layers were washed with 5% NaOH (60 ml×2), dried over anhydrous Na$_2$SO$_4$, and concentrated. The ratio of four isomers, **14a**, **14b**, **15a**, **15b**, was determined by the examination of ^{119}Sn NMR spectra of crude products.[13]

cis- *and* trans-*5-Methyl-2-cyclohexen-1-ol:*[18] According to the previously reported procedure,[18] *cis* isomer of the title compound was prepared from 5-methyl-2-cyclohexen-1-one[19] by reduction with lithium aluminum hydride. The aluminum triisopropoxide reduction of 5-methyl-2-cyclohexen-1-one gave the mixture of *cis* and *trans* isomers in 4:3 ratio, which was transformed into *p*-nitrobenzoates with *p*-nitrobenzoyl chloride and pyridine. Recrystallization from ethanol gave *trans* isomer which was hydrolyzed to give *trans*-5-methyl-2-clohexen-1-ol.[20] The ^{1}H NMR spectra in $CDCl_3$ for both isomers are shown as follows.

cis-*5-Methyl-2-cyclohexenyl* p-*Nitrobenzoate*: δ=1.05 (d, *J*= 6.4 Hz, 3H), 1.15—2.25 (m, 6H), 5.65—5.75 (m, 2H), 5.80—5.95 (m, 1H), 8.10—8.35 (m, 4H).

tans-*5-Methyl-2-cyclohexenyl* p-*Nitrobenzoate*: δ= 1.04 (d, *J*= 6.5 Hz, 3H), 1.15—2.25 (m, 6H), 5.49—5.60 (m, 1H), 5.80—5.95 (m, 1H), 6.05—6.20 (m, 1H), 8.10—8.35 (m, 4H).

† 1 M=1 mol·dm^{-3}.

†† 1 Torr=133.322 Pa.

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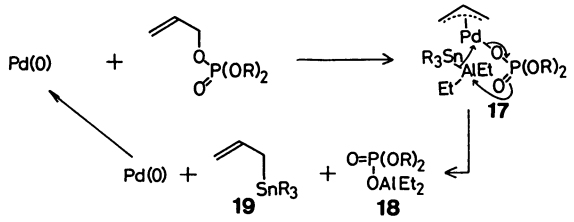

Scheme 6.

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