successively with four 50-mL portions of 5% HCl solution, four 50-mL portions of H_2O, and two 50-mL portions of saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated by carefully distilling off the solvents at atmospheric pressure through a 10-cm Vigreux column. The residual yellow oil was transferred to a 50-mL round-bottomed flask containing ca. 40 mg of 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulfide and distilled through a 4-cm column packed with glass helices to furnish 11.52 g (79% overall yield from methallyl alcohol) of **7b**[4] as a brilliant yellow oil: bp 68–72 °C (35 mmHg); IR (film) 2960, 2922, 1630, 1604, 1450, 1429, 1373, 1300, 1255, 1042, 932, 844 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.06 (s, 1 H), 5.94 (s, 1 H), 1.72 (s, 3 H), 0.24 (s, 9 H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 237.3, 149.6, 128.5, 15.6, −1.2; UV max (isooctane) 425 nm (ϵ 77), 222 (5990); HRMS, *m/e* calcd for $C_6H_{11}OSi$ (M^+ − 15) 127.0576, found 127.0579.

(*E*)-(1-Hydroxy-2-decenyl)trimethylsilane (6c). A 100-mL, three-necked, round-bottomed flask was equipped with an argon inlet adapter and two rubber septa. The flask was charged with (*E*)-2-decenol[19] (2.34 g, 15.0 mmol) and 20 mL of tetrahydrofuran and then cooled at −78 °C while *n*-butyllithium solution (6.50 mL of a 2.48 M solution in hexane, 16.1 mmol, 1.07 equiv) was added dropwise by syringe over 3 min. The resulting pale yellow solution was stirred at 0 °C for 15 min and then cooled at −78 °C while chlorotrimethylsilane (1.80 g, 16.5 mmol, 1.1 equiv) was added in one portion by syringe. The colorless reaction mixture was next stirred at 0 °C for 15 min and then cooled to −78 °C and treated dropwise over 10 min with 26.0 mL of a 1.74 M solution of *tert*-butyllithium in pentane (45.2 mmol, 3.0 equiv). The resulting solution was stirred at −30 °C for 6 h, and then the cold bath was removed and 6 mL of saturated aqueous NH_4Cl solution was added in one portion. The reaction mixture was diluted with 100 mL of additional saturated NH_4Cl solution and then extracted with two 100-mL portions of ether. The combined organic phases were dried over Na_2SO_4, filtered, and concentrated to provide 3.93 g of **6c** as a yellow oil, used in the next step without further purification.

Column chromatography on silica gel (elution with ethyl acetate–hexane) furnished a pure sample of **6c**: IR (film) 3450, 2980, 2940, 2875, 1710, 1675, 1470, 1255, 1085, 980, 850 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.61 (ddd, J = 1, 7, 15 Hz, 1 H), 5.50 (ddt, J = 1, 7, 15 Hz, 1 H), 3.94 (dd, J = 1, 7 Hz, 1 H), 2.07 (apparent q, J = 7 Hz, 2 H), 1.47–1.66 (br s, 1 H, OH), 1.24–1.47 (m, 10 H), 0.91 (t, J = 7 Hz, 3 H), 0.07 (s, 9 H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 131.0, 127.9, 68.5, 32.4, 31.8, 31.7, 29.7, 29.1, 22.6, 14.0, 0.1; HRMS, *m/e* calcd for $C_{13}H_{28}OSi$ (M^+) 228.1910, found 228.1908.

(*E*)-(1-Oxo-2-decenyl)trimethylsilane (7c). A 100-mL, three-necked, round-bottomed flask was equipped with an argon inlet adapter and two rubber septa. The flask was charged with *N*-chlorosuccinimide (3.04 g, 22.8 mmol, 1.5 equiv) and 40 mL of dichloromethane and then cooled at 0 °C while 2.30 mL of dimethyl sulfide (1.95 g, 31.3 mmol, 2.1 equiv) was added dropwise over 10 min by syringe. After 45 min, the reaction mixture was cooled to −25 °C, and a solution of the unpurified alcohol **6c** (3.93 g) produced in the previous reaction in 20 mL of dichloromethane was added dropwise by syringe over 5 min. The resulting mixture was stirred at −25 °C for 2.5 h and at room temperature for 30 min and then cooled at −20 °C while 3.2 mL of triethylamine (2.32 g, 23.0 mmol, 1.5 equiv) was added dropwise by syringe over 5 min. The reaction mixture was diluted with 100 mL of water and then extracted with two 100-mL portions of dichloromethane. The combined organic phases were dried over Na_2SO_4, filtered, and concentrated to afford a yellow oil. Column chromatography on silica gel (elution with ethyl acetate–hexane) provided 2.174 g (64% overall yield from 2-decenol) of **7c** as a brilliant yellow oil: IR (film) 2960, 2930, 2855, 1645, 1635, 1590, 1460, 1250, 1190, 975, 845 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.73 (dt, J = 7, 17 Hz, 1 H), 6.17 (dt, J = 1, 17 Hz, 1 H), 2.21 (apparent dq, J = 1, 7 Hz, 2 H), 1.18–1.54 (m, 10 H), 0.85 (t, J = 7 Hz, 3 H), 0.22 (s, 9 H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 236.4, 148.9, 136.4, 32.7, 31.6, 29.0, 28.9, 28.1, 22.5, 13.9, −2.0; UV max (isooctane) 424 nm (ϵ 68), 225 (10,584); HRMS, *m/e* calcd for $C_{13}H_{26}OSi$ (M^+) 226.1754, found 226.1752.

(19) (*E*)-2-Decenol was prepared in 72–92% yield from 2-decyn-1-ol by reduction with 1.5 equiv of $LiAlH_4$ in the presence of 3.0 equiv of NaOMe in THF at reflux for 3.5 h.

Acknowledgment. We thank the National Science Foundation, American Cyanamid Co., and Firmenich AG for generous financial support.

Registry No. **5a**, 107-18-6; **5b**, 513-42-8; **5c**, 18409-18-2; **6a**, 95061-68-0; **6b**, 99268-88-9; **6c**, 99268-89-0; **7a**, 51023-60-0; **7b**, 99268-90-3; **7c**, 99268-91-4; Me_3SiCl, 75-77-4; oxalyl chloride, 79-37-8.

Sn(II)–Al-Promoted Allylation of Aldehydes with Allyl Chloride in an Aqueous Solvent System

Kenji Uneyama, Nobuyoshi Kamaki, Akihiko Moriya, and Sigeru Torii*

Department of Industrial Chemistry, School of Engineering, Okayama University, Okayama 700, Japan

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Intensive studies have been accumulated on the regio- and stereoselective allylation of carbonyl compounds with allyl metallic reagents.[1] Among them, allyl stannanes are of particular value for allylation of aldehydes and ketones,[1] enones,[2] pyridinium salt,[3] and allyl acetate.[4] However, there has been no study on the recycle use of the allyl metallic reagents for allylation. Recently, we have developed a novel electrochemical recycle system for organotin reagent promoted allylation in which 2–20 mol % of metallic tin in MeOH–H_2O–AcOH can be effectively recycled for allylation of aldehydes and ketones[5] with allyl bromide. However, allyl chloride is unreactive toward metallic tin in the electrolysis conditions to make a recycling system. Because of the low cost of allyl chloride as compared with allyl bromide, it is worthy to develop an allylation with allyl chloride by the aid of recycling tin reagents.

In contrast to facile oxidative addition of metallic tin to allyl bromide[6] and iodide,[7] allyl chloride was found to be less reactive so that no successful allylation by a combination of allyl chloride and metallic tin has appeared. Recently, Nokami and Okawara[8] showed that a combination of a stoichiometric amount of metallic tin and aluminum leads to a successful allylation of carbonyl compounds using various kinds of allylic bromides. This finding suggests a possibility of activation of allyl chloride with aluminum. Meanwhile, concerning regeneration of Sn(0) from Sn(II) and Sn(IV), aluminum would be a promising metal since aluminum is less electronegative than tin so as to reduce in principle a di- and tetravalent tin to a zerovalent one. On these bases we have studied an aluminum-promoted and tin-recycled allylation process with allyl chloride where aluminum affects both oxidative addition of metallic tin to allyl chloride and reductive regeneration of Sn(0) from Sn(II) and Sn(IV) for a recycle use.

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Table I. Solvent Effect in the Allylation of Benzaldehyde with Allyl Chloride in an Organic Solvent-H_2O-AcOH System[a]

entry	organic solvent	yield of **2a** (%)[b]
1	DME–MeOH (1:1)	92
2	$(Et)_2O$–MeOH (1:1)	84
3	$MeOCH_2CH_2OH$	88
4	THF	74
5	DMF	85
6	EtOAc	77
7	MeOH	88
8	*n*-hexane	82
9	benzene	83
10	CH_2Cl_2	86

[a] Organic solvent (30 mL)–H_2O (15 mL)–AcOH (3 mL), benzaldehyde (0.1 mol), allyl chloride (0.2 mol), $SnCl_2$ (0.01 mol), Al (0.2 mol) at 40–50 °C for 6 h. [b] Isolated yield based on benzaldehyde.

First of all, Nokami's conditions were examined. A mixture of benzaldehyde, allyl chloride (2 equiv),[9] and metallic tin and aluminum (both 1 equiv) in ether–water (2:1) was stirred at room temperature for 24 h, affording 53% of 1-phenylbut-3-en-1-ol (**2a**). However, use of 0.1 equiv of metallic tin and 1 equiv of aluminum in the above conditions resulted in the formation of a trace amount of **2a**. This result suggests that a combined use of a stoichiometric amount of aluminum and tin can activate oxidative addition of tin to allyl chloride.

To generate an active zerovalent tin and recycle it, a combination of aluminum powder (2 equiv) and tin(II) chloride (0.1 equiv) was examined in a variety of mixed solvent systems. In MeOH–AcOH (4:1), which was a solvent system employed for the electrochemical tin-recycled allylation with allyl bromide,[5] no reaction occurred. Addition of water to the solvent enhanced the allylation remarkably, leading to the formation of **2a** in 88% yield. Instead of methanol, dimethoxyethane, ethylene glycol monomethyl ether, and DMF are also usable for the present purpose. Likewise, immiscible solvents with water such as hexane, methylene chloride, and ethyl acetate also provide a successful result as shown in Table I. Existence of both water and acetic acid seems to bring about activation of metallic tin for oxidative addition to allyl chloride rather than activation of the reduction process because only 15% and 4% of **2a** were obtained in MeOH–AcOH–DME (4:1:5) and MeOH–H_2O–DME (1:1:1), respectively, even if a stoichiometric amount of both metallic tin and aluminum was employed.

Next, effect of tin reagents was examined under a standard solvent system, ethylene glycol monomethyl ether–acetic acid–water (10:1:5) at 40–50 °C. Neither tin(II) chloride nor aluminum promote the allylation when it is employed alone. Even in the presence of a stoichiometric amount of metallic tin, the allylation affords **2a** in only 10% yield after 24 h when aluminum is absent. In contrast, the use of both 1 equiv of metallic tin and aluminum promotes the desired reaction to provide **2a** in 86% yield after 12 h. These results clearly demonstrate that zero valent tin accompanied with aluminum is responsible for the allylation and its activity intensively affects both the reaction rate and yield.

Then, the reductive regeneration of active zero valent tin was examined. The result is summarized in Table II. The use of 10 mol % of tin(II) chloride combined with 2 equiv of aluminum leads to 88% yield of **2a** after 4–6 h, revealing that the Sn(II)–Al system enhances the rate of

(9) In Nokami's conditions, allyl bromide was employed instead of allyl chloride.[8]

Table II. Effect of Tin Reagent in the Allylation of Benzaldehyde with Allyl Chloride in $MeOCH_2CH_2OH$–H_2O–AcOH[a]

entry	tin reagent	yield of **2a** (%)
1	$SnCl_2$	88
2	$SnSO_4$	85
3	$Sn(OAc)_2$	78
4	SnO[b]	72
5	$SnCl_4$	71
6	Sn[c]	76

[a] $MeOCH_2CH_2OH$–H_2O–AcOH (30:15:3 mL), benzaldehyde (0.1 mol), allyl chloride (0.2 mol), tin reagent (0.01 mol) at 40–50 °C for 6 h. [b] Concentrated HCl (0.5 mL) was added. [c] Concentrated HCl (0.7 mL) was added.

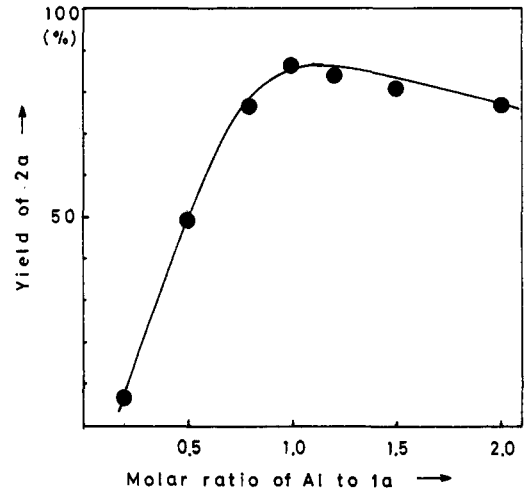


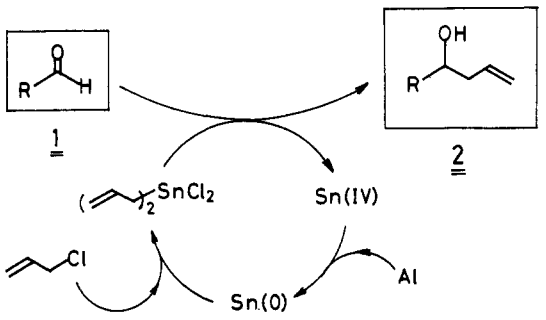
Figure 1. Relation between yield of **2a** and molar ratio of aluminum to benzaldehyde in allylation of benzaldehyde (5 mmol) with allyl chloride (10 mmol) in $MeOCH_2CH_2OH$ (1.5 mL)–H_2O (0.75 mL)–AcOH (0.15 mL) at 50 °C.

allylation as compared with a system of metallic tin and aluminum. Divalent tin reagents such as $SnSO_4$, $Sn(AcO)_2$, and SnO other than tin(II) chloride are preferable for the present purpose although tin(II) oxide must be activated with a small quantity of concentrated hydrochloric acid. Likewise, both tin(IV) chloride and a metallic tin can be similarly employed for recycle use. In contrast, butyltrichlorostannane was found to be useless presumably because it can not be reduced to Sn(0) in the present reduction conditions due to the difficulty of leaving butyl group.

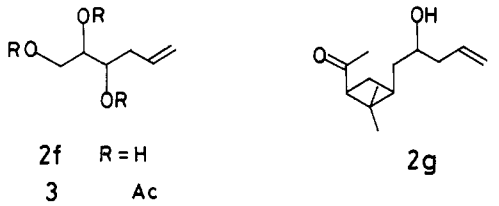
The effect of the amount of aluminum in an $SnCl_2$–Al system is shown in Figure 1. At least 1 equiv of aluminum is required to accomplish a complete conversion of benzaldehyde. A combination of metallic zinc[10] and aluminum also affects the allylation but copper fails. Taking into account of the fact that a standard redox potential of metallic tin is less negative than those of zinc and aluminum, Sn(II) is reasonably reducible by metallic aluminum and zinc.[10] Therefore, in the present allylation system, [Sn(II)–Al–H_2O–AcOH–organic solvent], aluminum reductively converts Sn(II) into Sn(0) at the initial stage, which would be activated for oxidative addition to allyl chloride by making a particular Sn–Al combined metal. After allylation, Sn(IV) is again reduced by aluminum to Sn(0) (Scheme I). It is worthwhile to note that the electrochemical reduction of Sn(II) in an MeOH–AcOH–5% HCl–Et_4NOTs(Pt) system can generate a zerovalent

(10) Allylation of carbonyl compounds by use of metallic zinc and allyl bromide is reported. (a) Petrier, C.; Einhorn, J.; Luche, J. L. *Tetrahedron Lett.* **1985**, *26*, 1449. (b) Petrier, C.; Luche, J. L. *J. Org. Chem.* **1985**, *50*, 910.

Scheme I



Scheme II



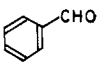
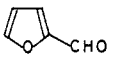
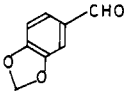
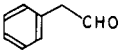
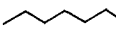
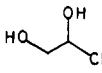
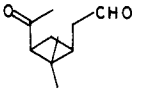
tin[11] which, however, reacts in situ slowly and less efficiently with allyl chloride, yielding **2a** (50%) along with the corresponding pinacol (30%). This result suggests that zerovalent tin alone is not enough and any activated zero-valent tin produced on a metallic aluminum surface is responsible for the efficient allylation with allyl chloride.

Results on the application of the present allylation to several aldehydes using tin(II) chloride (0.1 equiv) and aluminum (1 equiv) are summarized in Table III. Most of the aldehydes give the desired homoallyl alcohols in reasonable yields. Noteworthy is the fact that glyceraldehyde gives triol **2f** (a 1:1 mixture of diastereoisomers) in 82% yield without protecting two hydroxyl groups (Scheme II). The present allylation is useful for the selective allylation of aldehydes in the presence of a ketocarbonyl group. Thus, allylation takes place selectively at the formyl group of **1g**[12] rather than the ketocarbonyl group. In addition, a 1:1 mixture of benzaldehyde and acetophenone was subjected to allylation under the standard conditions, providing **2a** exclusively. No 2-phenylbut-3-en-2-ol was detected by VPC and ^1H NMR. Allyl chloride is so less reactive than allyl bromide that the somewhat elevated temperature (40–50 °C) was necessary as compared with allyl bromide which reacts smoothly at room temperature. Homoallyl alcohols derived from furfural[13] and piperonal[14] are unstable under the experimental conditions and the hydroxyl group was in part substituted with the methoxyethoxyl group of ethylene glycol monomethyl ether. Table III shows a comparison of the present method with the electrochemical tin-recycled allylation[5] and the Nokami's[8] method in both of which allyl bromide is a reactant, demonstrating that a satisfactory result is obtained by the present Sn(II)–Al system.

Experimental Section

The ^1H NMR spectra were measured with Me_4Si as an internal standard by JEOL FX-100 spectrometers. The IR spectra were recorded with a JASCO IRA-1 spectrometer. The MS spectrum was recorded at 60 eV with a ESCO EMD-05BG spectrometer. Elemental analyses were performed in our laboratory.

Table III. Allylation of Aldehydes with Allyl Chloride[a] in a Sn(II)–Al System

substrate		reactn time (h)	yield of 2[b] (%)
1a		4	88 (91)[d] [73][e]
1b		4	74
1c		8	83
1d		7	85 (91)[d]
1e		4	89 (87)[d] [70][e]
1f[c]		5	82 (82)[d]
1g		6	80

[a] Substrate (3 mmol), $SnCl_2$ (0.3 mmol), Al (3 mmol) in $MeOCH_2CH_2OH$ (1.5 mL)–H_2O (0.75 mL)–AcOH (0.15 mL) at 50 °C for 6 h. [b] Isolated yield. [c] **1f** (5 mmol) in MeOH (1.5 mL)–H_2O (0.75 mL)–AcOH (0.2 mL). [d] Electrochemical allylation with allyl bromide.[5] [e] Nokami's allylation with allyl bromide.[8]

Allylation of Benzaldehyde (Standard Conditions). A mixture of benzaldehyde (530 mg, 5 mmol), allyl chloride (0.82 mL, 10 mmol), $SnCl_2$ (95 mg, 0.5 mmol), and aluminum powder (135 mg, 5 mmol) in methyl cellosolve (1.5 mL), water (0.75 mL), and acetic acid (0.15 mL) was stirred in a sealed flask (30 mL) at 50–53 °C for 6 h. After neutralization with saturated $NaHCO_3$, solid substances were filtered and washed with hexane–AcOEt (3:1). To the combined filtrates was added water and organic substances were extracted with hexane–AcOEt (3:1). The extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (SiO_2, hexane:AcOEt = 5:1) to give **2a** as a colorless oil (651 mg, 88%).

The ^1H NMR and IR spectra of **2a**,[8] **2b**,[13] **2c**,[14] **2d**,[15] **2e**,[16] and **2g**[10] were consistent with those of authentic samples.

5-Hexene-1,2,3-triol (2f). A mixture of *dl*-glyceraldehyde (450 mg, 5 mmol), allyl chloride (0.82 mL, 10 mmol), $SnCl_2$ (95 mg, 0.5 mmol), and Al (135 mg, 5 mmol) in distilled MeOH (1.5 mL)–H_2O (0.75 mL)–AcOH (0.2 mL) was stirred in a sealed flask at 50–53 °C for 5 h. After addition of $NaHCO_3$, solid materials were filtered and rinsed 5 times each with 2 mL of MeOH. The combined filtrate was concentrated under reduced pressure. The residue was chromatographed with a short silica gel column (hexane–AcOEt–EtOH = 3:1:2.7), providing **2f** (540 mg, 82%) as a slightly yellow solid after drying in vacuo at 30 °C for 2 h: bp 80–83 °C (0.01 mmHg, air bath temperature); IR (neat) 3340 (OH), 1640 (C=C) cm^{-1}; ^1H NMR (acetone-d_6) δ 5.7–6.2 (m, 1 H, CH=), 4.92–5.24 (m, 2 H, CH_2=), 3.5–3.8 (m, 4 H, CHOH, CH_2OH), 2.5–3.2 (m, 3 H, OH), 2.2–2.5 (m, 2 H, CH_2). The triol **2f** is so hygroscopic that elemental analysis was performed with its triacetate **3** [a 1:1 mixture of diastereoisomers by VPC SE-30, 4 m, 140 °C]: bp 115–120 °C (2.5 mmHg); IR (neat) 1740 cm^{-1} (C=O); ^1H NMR δ 5.50–5.96 (m, 1 H, CH=), 4.96–5.35 (m, 4 H, CH_2, CHOAc), 3.95–4.48 (m, 2 H, CH_2OAc), 2.35 (t, J = 6 Hz, 2 H, CH_2), 2.14, 2.10, 2.07 (s, 9 H, AcO); MS, m/e 217 (M^+ – allyl group). Anal. Calcd for $C_{12}H_{18}O_6$: C, 55.76; H, 7.02. Found: C, 55.62; H, 7.30.

1-[2,2-Dimethyl-3-(2-hydroxy-4-pentenyl)cyclobutyl]-ethanone (2g):[10] bp 126–128 °C (2 mmHg); IR (neat) 3400 (OH), 1700 (C=O), 1640 (CH=CH_2) cm^{-1}; ^1H NMR δ 5.6–6.0 (m, 1 H, CH=), 4.96–5.24 (m, 2 H, CH_2=), 3.4–3.7 (m, 1 H, CHOH), 2.83 (t, J = 8 Hz, 1 H, CH), 1.7–2.6 (m, 5 H, CH, CH_2), 2.03 (s, 3 H,

(11) During the electrolysis, deposit of metallic tin on the cathode surface can be observed.

(12) Aldehyde **1g** was prepared by ozonolysis of α-pinene according to Eshinazi, H. E. *J. Org. Chem.* **1961**, *26*, 3072.

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CH_3), 1.30 and 1.29 (s, 3 H, CH_3), 1.2–1.7 (m, 2 H, CH_2), 0.85 (s, 3 H, CH_3). Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.55. Found: C, 74.38; H, 10.64.

Electrochemical Allylation of Benzaldehyde. A mixture of benzaldehyde (424 mg, 4 mmol), allyl chloride (2 mL, 24 mmol), $SnCl_2$ (152 mg, 0.8 mmol), and Et_4NOTs (500 mg) in MeOH (5 mL)–AcOH (1.4 mL)–5% HCl (0.5 mL) was electrolyzed in a H-type divided cell separated by a sintered glass, using platinum foils as electrode at 40–50 °C. A constant current (15 mA, 3.4 F/mol) was applied by a regulated DC power supply (Metronix Model 543B). The usual workup gave **2a** (302 mg, 51%) and benzaldehyde pinacol (270 mg, 30%) as crystals.

Registry No. **1a**, 100-52-7; **1b**, 98-01-1; **1c**, 120-57-0; **1d**, 122-78-1; **1e**, 111-71-7; **1f**, 367-47-5; **1g**, 2704-78-1; **2a**, 936-58-3; **2b**, 6398-51-2; **2c**, 6052-61-5; **2d**, 61077-65-4; **2e**, 36971-14-9; **2f** (isomer 1), 99146-85-7; **2f** (isomer 2), 99146-86-8; **2g**, 97039-57-1; $SnCl_2$, 7772-99-8; $SnSO_4$, 7488-55-3; $Sn(OAc)_2$, 638-39-1; SnO, 21651-19-4; $SnCl_4$, 7646-78-8; allyl chloride, 107-05-1; aluminum, 7429-90-5; tin, 7440-31-5; acetophenone, 98-86-2; 2-phenylbut-3-en-2-ol, 6051-52-1.

Synthesis of New Dipeptide Analogues Containing Novel Ketovinyl and Hydroxyethylidene Isosteres via Grignard Addition to Chiral α-Amino Aldehydes

Gunnar J. Hanson* and Thomas Lindberg

Department of Medicinal Chemistry, G.D. Searle & Company, Skokie, Illinois 60077

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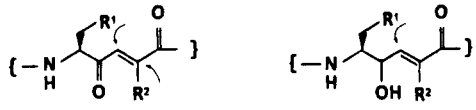
There is a tremendous amount of current interest in the study of dipeptide analogues.[1] These isosteres of natural dipeptides are proving valuable for producing mechanism-based enzyme inhibitors[2] and proteolytically stable peptides,[3] both of which hold great promise as therapeutic agents. We report the preparation of two new dipeptide analogues, ketovinyl **1** and hydroxyethylidene **2** (R^1 = phenyl, R^2 = H), which are designed to be Phe-Gly replacements; their synthesis is achieved through the novel reaction of vinylmagnesium bromide and Boc-L-phenylalaninal.



1 **2**

These particular analogues are important because they incorporate the key structural features of the known[1] trans double bond and ketomethylene/hydroxyethylene isosteres and are designed to (1) enable the preparation of potential site-directed alkylating agents[4,5] (arrows in **1** and **2** indicate possible points of attack of enzyme nucleophiles such as cysteine thiol), (2) provide a tool for drug design,[6] utilizing the conformational restriction about C-2 and C-3, (3) be used to prepare angiotensin converting enzyme inhibitors[7] based on benzoyl-Phe-Gly-Pro, and (4) function as statine mimics, for use in structure–activity studies on pepstatin-based renin inhibitors.[8]

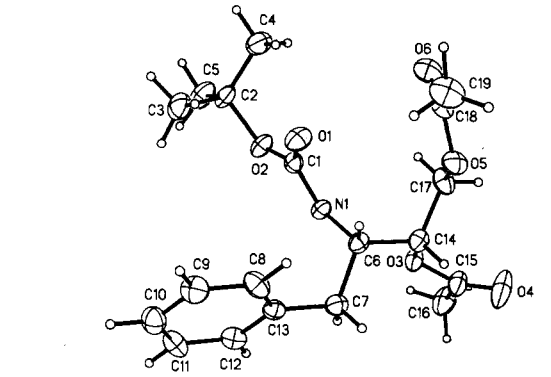
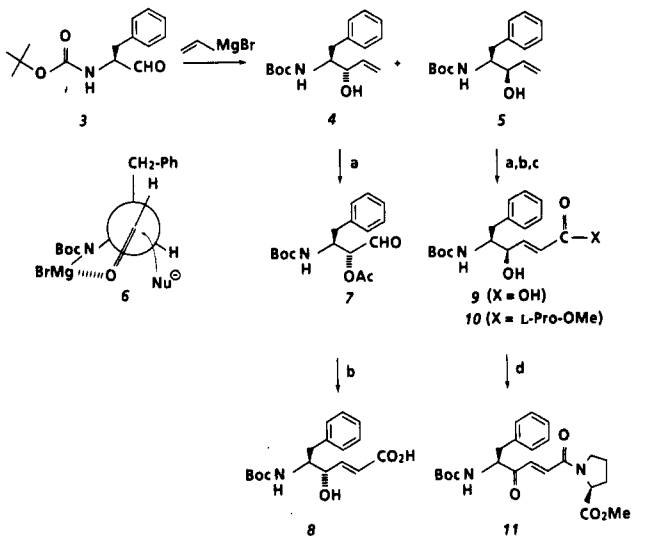


Figure 1. X-ray crystal structure of diacetate **13**.

Scheme I[a]



[a] Key: (a) Ac_2O, pyridine, room temperature; then, O_3, MeOH, followed by dimethyl sulfide workup. (b) $Ph_3P{=}CHCO_2Et$, THF, room temperature; followed by NaOH-H_2O-MeOH. (c) *i*-BuOCOCl, NMP, followed by L-Pro-OMe·HCl and NMP. (d) periodinane, CH_2Cl_2, room temperature.

Preparation of Dipeptide Analogues. Optically pure α-(acylamino)aldehydes are readily available[9] from natural α-amino acids; their reaction with Grignard reagents presents, in principle, an outstanding opportunity for the synthesis of enantiomerically pure compounds. We therefore chose Grignard addition products **4** and **5** as key synthetic intermediates.

Boc-L-phenylalanine methyl ester was reduced[10] with DIBAL in toluene to Boc-L-phenylalaninal **3**, which was treated with vinylmagnesium bromide (THF, −78 °C to room temperature) to produce a mixture (56:44) of threo and erythro allylic alcohols **4** and **5** in 66% combined yield (Scheme I). To our knowledge this is the first example of such a reaction, although the addition of saturated or-

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