Chromium(II) chloride-mediated coupling reactions of Garner aldehyde with allyl bromides: facile asymmetric synthesis of (2*R*,3*S*)-3-hydroxy-2-hydroxymethylpyrrolidine

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Chromium(II) chloride-mediated coupling reactions of 1,1-dimethylethyl (*S*)- and (*R*)-4-formyl-2,2-dimethyloxazolidine-3-carboxylates [(*S*)- and (*R*)-Garner aldehydes] (**1a**,**b**) with allyl bromides **2a**–**c** proceeded with moderate to good stereoselectivity to give the corresponding homoallyl alcohols **3a**–**d** in good yields. The homoallyl alcohol **3b** was easily transformed to (*2R,3S*)-3-hydroxy-2-hydroxymethylpyrrolidine **8**.

Introduction

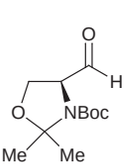
Recently, a lot of attention has been devoted to the design and synthesis of azasugars such as polyhydroxylated pyrrolidines,[1,2] pyrrolizidines,[3] indolizidines,[4] and quinolizidines,[5] in view of their remarkable inhibitory activity against glucosidases and mannosidases.[6] Therefore, they are known to possess a variety of beneficial therapeutic effects against tumor metastasis,[7] metabolic disorder,[8,9] and viral infections.[10]

During our investigation on one-electron reducing agents, such as low valent tantalum (LVT)[11] and samarium diiodide (SmI_2),[12–16] we decided to explore chromium chloride-mediated coupling reactions (Hiyama–Nozaki reaction),[17–19] which proceeded under mild conditions to give the corresponding coupling products. Though allylation of (*S*)- and (*R*)-Garner aldehydes (**1a**,**b**)[20–22] with allyl metals such as chiral titanium[23] and Grignard reagents[24] has been reported, there is little known about the Hiyama–Nozaki reaction between allyl halides and **1a**,**b**. The Garner aldehyde is a well known chiral synthon and has been converted to β,γ-alkynylglycine derivatives,[25] γ-hydroxy-β-amino alcohols and β-hydroxy amino-acids,[26] sphingosines,[24] azasugars,[27] fulleropyrrolidines,[28] and more complex natural products such as phorboxazole,[29] micropines,[30] and curacin A.[31] (*S*)-Garner aldehyde (**1**) and its antipode [(*R*)-**1**] can be easily prepared from L-serine[20,21] and D-serine,[26] respectively. To demonstrate further the versatility of these aldehydes, we decided to develop the coupling reactions of **1a**,**b** and the facile transformation of the coupling products to biologically active compounds.

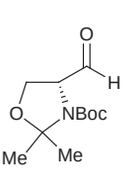
In this paper, we would like to report the chromium(II) chloride-mediated coupling reactions of **1a**,**b** with allyl halides and a facile transformation of the coupling products to (2*R*,3*S*)-3-hydroxy-2-hydroxymethylpyrrolidine.

Results and discussion

First, we examined the coupling reactions of **1a** with allyl bromide (**2a**) under several reaction conditions. The addition of



(*S*)-Garner aldehyde (**1a**)

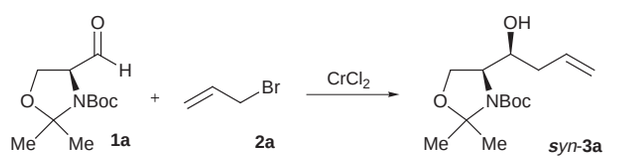


(*R*)-Garner aldehyde(**1b**)

Fig. 1

TMEDA did not give better chemical yields but did give better diastereoselectivity (entry 12 in the Table). No beneficial effect was observed when HMPA and Et_2AlCl were added (entries 10 and 13 in the Table). Methods B and C were also found to give very poor diastereoselectivity (entries 14 and 15 in the Table). The reaction conditions of entry 4 were found to be best in

Table 1 Coupling reactions of **1a** with **2a** under different reaction conditions



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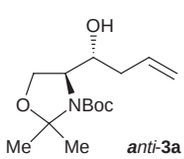
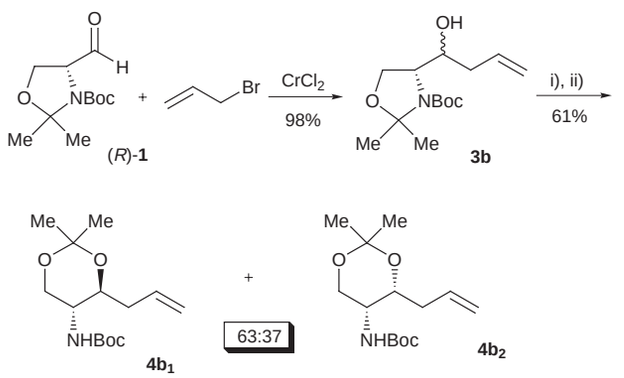


Entry	Method[a]	*T*/°C	Solvent	Additive	Total yield (%)[b]	Ratio[c]
1	A	−78	THF	none	N.R.	—
2	A	0	THF	none	5	—
3	A	0	THF	none	36[d]	45/55
4	A	rt	THF	none	98	37/63
5	A	40	THF	none	54	49/51
6	A	reflux	THF	none	72[e]	49/51
7	A	rt	CH_2Cl_2	none	0	—
8	A	rt	DMF	none	61	48/52
9	A	rt	toluene	none	56	45/55
10	A	rt	THF	Et_2AlCl	60	40/60
11	A	rt	THF	Bu^tOH	42	45/55
12	A	rt	THF	TMEDA	18[f]	27/73
13	A	0	THF	HMPA	25[f]	32/68
14	B	rt	THF	none	88	46/54
15	C	rt	THF	none	80	45/55

[a] Method A: To a THF suspension of $CrCl_2$, a mixture of **1a** and **2a** was added; Method B: **1a** was added to a mixture of $CrCl_2$ and **2a**; Method C: **2a** was added to a mixture of $CrCl_2$ and **1a**. [b] Isolated yields. [c] Ratio (*syn*/*anti*) was determined by HPLC by using chiral column AD (Daisel Chemical Co Ltd.). [d] Reaction time is 72 h. [e] Reaction time is 0.2 h. [f] Reaction time is 15 h.

terms of both chemical yield and diastereoselectivity. Namely, to a suspension of chromium chloride in THF, a THF solution of **1a** and crotyl bromide (**2b**) was added at room temperature under an argon atmosphere to give the corresponding coupling products in 98% total yield and 37 : 63 dr. At this stage, the diastereomers could not be separated by silica gel flash chromatography. To synthesize the title pyrrolidine alkaloid **8**, using **1b**, which was prepared from nonproteinogenic D-serine, the coupling reaction was carried out. To determine the structures of the coupling products and separate the diastereomers (**4b**$_1$ and **4b**$_2$), cyclic *O*,*O*′-acetals **4b**$_1$ and **4b**$_2$ were prepared from the coupling products (**3b**) and the coupling constants were measured by ^{1}H NMR.[32]



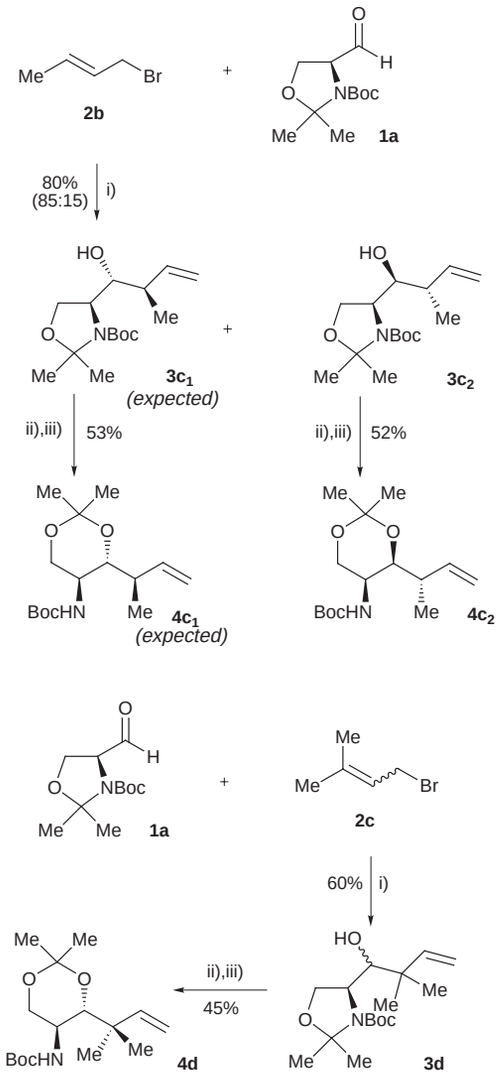
Scheme 1 Coupling reaction of **1b** with **2a** and transacetalization of homoallyl alcohol **3b** to compound **4b**$_1$ and **b**$_2$. *Reagents and conditions*: i) *p*-TsOH·H$_2$O; ii) 2,2-dimethoxypropane, *p*-TsOH·H$_2$O.

Based on the coupling constants ($J^{4,5}$) between the protons at C-4 and C-5 of the compounds **4b**$_1$ (major diastereomer) and **4b**$_2$ (minor diastereomer), of 10.0 Hz and 1.9 Hz respectively, the structures of **4b**$_1$ and **4b**$_2$ were determined as shown in Scheme 1. Further, the physical and spectral data were identical with those reported.[32]

Next, we tried to examine the coupling reactions of allyl bromides **2b**,**c** with **1a** under the reaction conditions of entry 11 in the Table (Scheme 2). The coupling reaction of **1a** with **2b** gave a mixture of two diastereomers in 80% total yield, which were easily separated. To determine the structures, each coupling product (**3c**$_1$ and **3c**$_2$) was converted to the cyclic *O*,*O*′-acetal (**4c**$_1$ and **4c**$_2$).

The coupling constants ($J^{4,5}$) between the protons at C-4 and C-5 of compounds **4c**$_1$ (major diastereomer) and **4c**$_2$ (minor diastereomer) were 9.6 Hz and 2.0 Hz, respectively. By comparison with previous work,[22] the relative configuration of C-4 and C-5 on the 1,3-dioxolane ring could be determined. Namely, since the H–H coupling constant ($J^{4,5}$) is known to be about 9 Hz for the *trans* configuration and *ca*. 1.5 Hz for the *cis* one,[22] the relative configuration of C-4 and C-5 in the compound **4c**$_1$ has to be *trans* and that in **4c**$_2$ *cis*. The physical data of **4c**$_2$ were identical with those reported.[22] So, the structure of **4c**$_2$ has been established. In general, it is known that the Nozaki–Hiyama reactions of aldehydes with crotyl halides proceed *via* the chair form transition state to give only *anti* isomers in good yields.[33] Though in this paper we have not determined the structure of **4c**$_1$ completely, it is reasonable to think that the relative configuration between C-4 and C1′ is *anti* and therefore the configuration between C-4, C-5, and C-1′ in the compound **4c**$_1$ is all-*trans*. The structures of **3c**$_1$ and **3c**$_2$ are deduced to be as shown in Scheme 2.

The coupling reaction of **1a** with isopentenyl bromide (**2c**) gave a sole product in 60% yield. After conversion of the coupling product **3d** to **4d**, the ^{1}H NMR spectrum of compound **4d** was measured. The coupling constant ($J^{4,5}$) between the protons at C-4 and C-5 of compound **4d** was 8.8 Hz, and therefore, the orientation between 5-NH group and 4-alkoxy group might be *anti*.



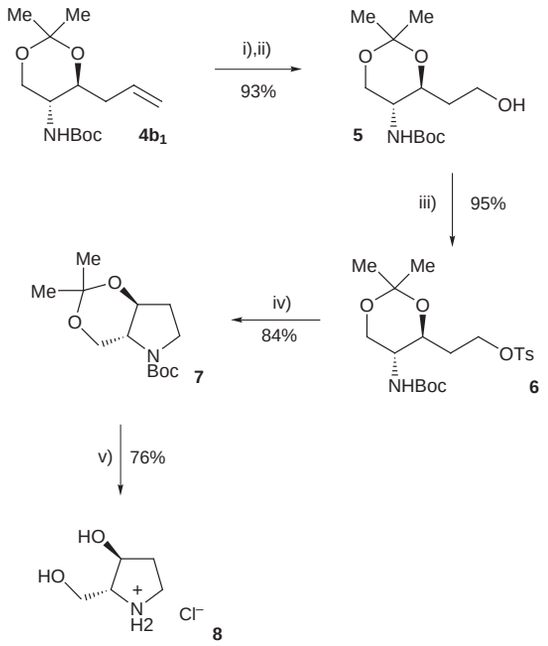
Scheme 2 Chromium(II) chloride-mediated coupling reactions of **1a** with substituted allyl bromides (**2b** and **c**). *Reagents and conditions*: i) $CrCl_2$, THF, 2.5 h; ii) *p*-TsOH, MeOH; iii) 2,2-dimethoxypropane, *p*-TsOH.

As a result, the chromium mediated coupling reactions of (*S*)- and (*R*)-Garner aldehydes (**1a**,**b**) with allyl bromides (**2a**, **b**, and **c**) proceeded *via* a Cram transition state to give *anti*-compounds predominantly, as for the coupling reactions of glyceraldehyde with allyl bromides.[34,35]

With the diastereomerically pure acetal **4b**$_1$ in hand, we examined the transformation of compound **4b**$_1$ to the pyrrolidine derivative. Ozonolysis of **4b**$_1$, followed by reductive treatment of the ozonide with sodium borohydride[36] gave the alcohol **5** in 93% yield. After tosylation of the alcohol, the treatment with sodium hydride gave the corresponding pyrrolidine (**7**) in 84% yield.

Finally, removal of the acetonide was accomplished under acidic conditions to give (2*R*,3*S*)-3-hydroxy-2-hydroxymethylpyrrolidine (**8**) in 76% yield. The melting point, optical rotation, and some spectral data such as ^{1}H NMR and IR of synthetic **8** were completely identical with those reported.[37]

In summary, we have described the chromium(II) chloride coupling reactions of **1a**,**b** with allyl bromides. The coupling reaction proceeded in good chemical yields to give the *anti*-products predominantly. Further, the effective transformation of the coupling product **4b**$_1$ to (2*R*,3*S*)-3-hydroxy-2-hydroxymethylpyrrolidine (**8**) was accomplished. The route included 8 steps from **1a** and the overall yield was 23%. As both enantiomers of **1a**,**b** were prepared easily and are commercially available, this synthetic procedure promises easy access to the



Scheme 3 Transformation of cyclic acetal **4b$_1$** to (2*R*,3*S*)-3-hydroxy-2-hydroxymethylpyrrolidine **8**. *Reagents and conditions*: i) O_3, MeOH; ii) $NaBH_4$; iii) TsCl, Et_3N, DMAP; iv) NaH; v) 5 M HCl.

enantiomer of compound **8**. Now, using the coupling products, we are trying to prepare polysubstitued pyrrolidine antibiotics and will report the results in the near future.

Experimental

General methods

Melting points were measured on a Yanagimoto micro melting point apparatus and are uncorrected. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were obtained on a Varian Gemini A-300. Chemical shifts are reported in parts per million downfield from the internal standard. Infrared spectra were recorded on a Japan Spectroscopic Co.A-100 and were recorded as λ_{max} in cm^{-1}. Optical rotations were obtained on a Japan Spectroscopic Co.DIP-360. Specific rotations $[\alpha]_D$ are reported in degrees per decimetre at 25 °C and the concentration (*c*) is given in grams per 100 mL in the specified solvent. Mass spectra were obtained on a Hitachi M-80B or Fisons VG Auto Spec instrument.

Column chromatography and flash chromatography were performed with Merck silica gel Kieselgel 60 (230–400 mesh). MPLC was conducted with a Merck silica gel Kieselgel 60. Preparative thin layer chromatography (PTLC) was carried out with Merck Kieselgel 60 F254 precoated glass (either 0.25 or 0.50 mm). All solvents were commercial grade and were distilled and dried as follows: tetrahydrofuran (THF) and diethyl ether from sodium benzophenone ketyl; MeCN from P_2O_5; CH_2Cl_2 from CaH_2. Garner aldehydes were prepared in accordance with the reported manner by Garner *et al.*[20,21] Chromium(II) chloride was purchased from Aldrich Chemical Co. and used without further purification.

Preparation of *O*,*O*′-acetals 4b$_1$ and 4b$_2$

A THF solution (5 cm^3) of **1b** (0.229 g, 1.0 mmol) and **2a** (0.242 g, 2.0 mmol) was added dropwise to a suspension of $CrCl_2$ (0.61 g, 6.0 mmol) in dry THF (10 cm^3). After stirring for 2.5 h at room temperature, sat. $NaHCO_3$ (10 cm^3) was added, and the organic layer was separated. The aqueous solution was extracted with AcOEt (2 × 10 cm^3). The combined organic phase was dried over $NaSO_4$, filtered, and evaporated *in vacuo* to give an oily residue, which was purified by flash chromatography (hexanes–AcOEt) to give the coupling products. As the diastereomeric mixture of the coupling products could not be separated at this stage, this mixture was submitted to the next reaction.

To a MeOH solution (85 cm^3) of the coupling product **3** (9.1 mmol), *p*-TsOH·H_2O (0.48 g, 2.5 mmol) was added. The resulting mixture was stirred at room temperature for 2 h. After evaporation of the solvent, sat. $NaHCO_3$–H_2O (1:1) solution (30 cm^3) was added to the residue. The aqueous phase was extracted with AcOEt (30 cm^3 × 3), and the combined organic layer was washed with sat. NaCl (40 cm^3 × 3), dried over Na_2SO_4, filtered, and evaporated to give an oily residue. The residue was purified with silica gel flash chromatography (hexanes : AcOEt = 1 : 1) to give a diastereomeric mixture of the amino diols as an oil (1.75 g, 83% yield).

To a solution of the amino diols (1.63 g, 7.1 mmol) and 2,2-dimethoxypropane (100 cm^3), *p*-TsOH·H_2O (0.28 g, 1.49 mmol) was added. After the reaction mixture was stirred at room temperature for 2 h, sat. $NaHCO_3$ (50 cm^3) was added. The aqueous phase was extracted with AcOEt (50 cm^3 × 3), and the organic layer was dried over Na_2SO_4, filtered, and evaporated to give an oily residue, which was purified with MPLC (hexanes : Et_2O : acetone = 20 : 1 : 1) to give compound **4b$_2$** (less polar component: 0.54 g, 28% yield) and **4b$_1$** (0.88 g, 46% yield), respectively. The physical data and spectral data were identical with those reported.[32]

Preparation of *O*,*O*′-acetals 4c$_1$

The coupling product **3c$_1$** (0.184 g, 68%) was obtained from **1b** (0.229 g, 1.0 mmol) and **2a** (0.270 g, 2.0 mmol). The homoallyl alcohol **3c$_1$** (0.662 g, 2.3 mmol) was transformed to compound **4c$_1$** (0.344 g, 53%) according to the method for the synthesis of **4b$_1$** and **4b$_2$**. Colorless solid (36% yield from **1a**); mp 81 °C (CH_2Cl_2); $[\alpha]_D$ +15.6 ($CHCl_3$, *c* 0.90); ν_{max}/cm^{-1} (KBr) 1680 (C=O); δ_H (pyridine-d_5, 400 MHz, 300 K) 6.12 (1H, ddd, *J* 17.0, 10.3, and 8.2), 5.26 (1H, d, *J* 17.0), 5.17 (1H, dd, *J* 10.3 and 2.1), 4.09 (1H, dd, *J* 11.8 and 2.0), 3.96 (1H, dd, *J* 11.8 and 1.9), 3.91 (1H, m), 3.78 (1H, dd, *J* 9.6 and 2.0), 2.75 (1H, m), 1.52 (9H, s), 1.47 (6H, s), 1.19 (3H, d, *J* 6.9); *m*/*z* (CI) 286 (M^+ + H) (Found: C, 62.95; H, 9.60; N, 4.90. $C_{15}H_{27}NO_4$ requires C, 63.13; H, 9.54; N, 4.91%).

Preparation of *O*,*O*′-acetals 4c$_2$

The coupling product **3c$_2$** (0.032 g, 12%) was obtained from**1b** (0.229 g, 1.0 mmol) and **2a** (0.270 g, 2.0 mmol). The homoallyl alcohol **3c$_2$** (0.286 g, 1.0 mmol) was transformed to compound **4c$_2$** (0.148 g, 52%) according to the same procedure for the synthesis of **4b$_1$** and **4b$_2$**. Colorless oil (6.2% yield from **1a**); $[\alpha]_D$ −7.72 ($CHCl_3$, *c* 1.01). The physical and spectral data of compound **4c$_2$** were identical with those reported.[22]

Preparation of *O*,*O*′-acetals 4d

The title acetal was prepared from **1a** (0.229 g, 1.0 mmol) and **2c** (0.298 g, 2.0 mmol) in 2 steps. Colorless solid [27% yield from (*S*)-**1**]; mp 65 °C (CH_2Cl_2); $[\alpha]_D$ +22.0 ($CHCl_3$, *c* 0.30); ν_{max}/cm^{-1} (KBr) 1700 (C=O); δ_H (pyridine-d_5, 300 MHz, 300 K) 7.75 (1H, d, *J* 8.6), 6.17 (1H, dd, *J* 17.6 and 10.8), 5.15 (1H, dd, *J* 17.6 and 1.4), 5.09 (1H, dd, *J* 10.8 and 1.4), 4.17 (1H, m), 3.98 (1H, dd, *J* 11.5 and 4.8), 3.80 (1H, dd, *J* 11.5, and 5.2), 3.73 (1H, d, *J* 8.8), 1.50 (9H, s), 1.45 (3H, s), 1.41 (3H, s), 1.23 (3H, s), 1.20 (3H, s); *m*/*z* (CI) 300 (M^+ + H) (Found: C, 64.30; H, 9.72; N, 4.68. $C_{16}H_{29}NO_4$ requires C, 64.18; H, 9.76; N, 4.68%).

Preparation of alcohol 5

A dry MeOH solution (26 cm^3) of compound **4b$_1$** (0.66 g, 2.4 mmol) was bubbled with O_3 at −78 °C until the solution turned blue. Excess O_3 was removed by bubbling with an Ar stream. To the reaction mixture, $NaBH_4$ (0.45 g, 11.8 mmol) was added carefully at the same temperature and the solvent was

evaporated under reduced pressure to give an oily residue. To the residue, H_2O (16 cm^3) was added. The reaction mixture was stirred at room temperature for 15 h and then extracted with Et_2O (15 cm^3 × 3), and the organic layer was dried over Na_2SO_4, filtered, and evaporated to give an oily residue, which was purified by silica gel flash chromatography (hexanes : AcOEt = 2 : 1) to give an alcohol **5** as a colorless solid (0.65 g, 98% yield); mp 77 °C (hexanes); $[\alpha]_D$ −33.9 ($CHCl_3$, *c* 1.06); ν_{max}/cm^{-1} (CH_2Cl_2) 3450 (OH, NH), 1690 (C=O); δ_H (DMSO-d_6, 300 MHz, 340 K) 6.54 (1H, br s), 4.10 (1H, t, *J* 4.8), 3.78 (1H, ddd, *J* 10.2, 8.7, and 2.6), 3.64 (1H, dd, *J* 11.4 and 6.2), 3.57 (1H, dd, *J* 11.4 and 11.4), 3.55–3.40 (2H, m), 3.26 (1H, ddd, *J* 19.2, 9.5, and 6.2), 1.78 (1H, dtd, *J* 14.0, 7.7, and 2.6), 1.46 (1H, ddt, *J* 14.0, 7.0, and 1.8), 1.42 (9H, s), 1.40 (3H, s), 1.29 (3H, s); δ_C ($CDCl_3$, 75 MHz, 300 K) 156.9, 100.4, 81.5, 73.9, 64.8, 61.7, 50.3, 36.1, 29.9, 21.3; *m/z* 276 (M^+) (Found: C, 56.65; H, 8.93; N, 5.02. $C_{13}H_{25}NO_5$ requires C, 56.70; H, 9.15; N, 5.09%).

Preparation of tosylate 6

p-TsCl (0.093 g, 0.76 mmol) was added to a dry CH_2Cl_2 solution (3.7 cm^3) of alcohol **5** (1.05 g, 3.81 mmol), Et_3N (2.1 cm^3, 15.3 mmol) and DMAP (0.093 g, 0.76 mmol) at 0 °C. Then, the reaction mixture was stirred at room temperature for 1.5 h. After the solvent was evaporated, sat. NH_4Cl (10 cm^3) was added. The reaction mixture was extracted with Et_2O (15 cm^3 × 3), and the organic layer was washed with H_2O (20 cm^3 × 3), dried over Na_2SO_4, filtered, and evaporated to give an oily residue, which was purified with silica gel flash chromatography (hexanes : AcOEt = 4 : 1) to give the corresponding tosylate **6** as a colorless oil (1.56 g, 95% yield); $[\alpha]_D$ −26.8 ($CHCl_3$, *c* 0.6); ν_{max}/cm^{-1} (film) 3400 (NH), 1700 (C=O); δ_H ($CDCl_3$, 300 MHz, 300 K) 7.79 (2H, d, *J* 8.3), 7.35 (2H, d, *J* 8.3), 4.33 (1H, br d), 4.22–4.04 (2H, m), 3.89–3.83 (1H, m), 3.63 (1H, br t), 3.49 (2H, m), 2.45 (3H, s), 2.10 (1H, m), 1.68 (1H, m), 1.42 (9H, s), 1.32 (3H, s), 1.30 (3H, s); *m/z* 430 ($M^+ + H$) (Found: C, 55.42; H, 7.25; N, 3.28. $C_{20}H_{31}NO_7S$ requires C, 55.92; H, 7.28; N, 3.26%).

Preparation of pyrrolidine 7

The tosylate **6** (1.56 g, 3.63 mmol) in dry THF (7.0 cm^3) was added dropwise to a dry THF solution (7.0 cm^3) of NaH (*ca.* 60% dispersion in mineral oil, 0.44 g, 11 mmol) at 0 °C. After stirring at room temperature for 1 h, the resulting reaction mixture was poured into ice–water (30 cm^3) and extracted with Et_2O (30 cm^3 × 3). The organic layer was washed with sat. NaCl (30 cm^3 × 3), dried over Na_2SO_4, filtered, and evaporated to give an oily residue, which was purified by silica gel flash chromatography (hexanes : AcOEt = 4 : 1) to give the corresponding pyrrolidine **7** as a colorless oil (0.78 g, 84% yield); $[\alpha]_D$ −83 ($CHCl_3$, *c* 0.63); ν_{max}/cm^{-1} (film) 1700 (C=O); δ_H ($CDCl_3$, 300 MHz, 300 K) 4.75–4.4 (1H, br s), 3.86 (1H, br t), 3.75 (1H, ddd, *J* 11.0, 9.6, and 5.7), 3.50 (1H, br d), 3.31 (1H, ddd, *J* 11.0, 11.0, and 7.0), 3.00 (1H, br t), 2.10 (1H, m), 1.78 (1H, m), 1.50 (9H, s), 1.45 (3H, s), 1.44 (3H, s); *m/z* 258 ($M^+ + H$) (Found: C, 60.38; H, 8.91; N, 5.41. $C_{13}H_{23}NO_4$ requires C, 60.68; H, 9.01; N, 5.44%).

Preparation of (2*R*,3*S*)-3-hydroxy-2-hydroxymethylpyrrolidine 8

To a MeOH solution (9.0 cm^3) of compound **7** (0.257 g, 1.0 mmol), 5.0 M HCl (30 cm^3) was added at room temperature. The reaction mixture was stirred at 60 °C for 2 h. The solvent was evaporated under reduced pressure to give a residue. After addition of H_2O (15 cm^3), the mixture was lyophilized to give a residue, which was evaporated azeotropically with EtOH–benzene (3 : 2, 15 cm^3). The solid was recrystallized from EtOH–AcOEt at −30 °C for 5 days to give the title compound **8** hydrochloride as colorless crystals (0.116 g, 76% yield); mp 118 °C (EtOH–AcOEt) (lit.,[37] mp 120 °C); $[\alpha]_D$ +43.4 (H_2O, *c* 0.33) (lit.,[36] $[\alpha]_D$ +45.7;. The spectral data were completely identical with those reported.[36])

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References

1 Y. P. Kim, M. Kido, M. Bando and T. Kitahara, *Tetrahedron*, 1997, **53**, 7501 and the references cited therein.
2 Y. J. Kim and T. Kitahara, *Tetrahedron Lett.*, 1997, **38**, 3423 and the references cited therein.
3 D. J. Robins, *Nat. Prod. Rep.*, 1995, **12**, 413 and the references cited therein.
4 H. Yoda, M. Kawauchi and K. Takabe, *Synlett*, 1998, 137 and the references cited therein.
5 J. C. Carretro, R. G. Arrayas and I. S. de Gracia, *Tetrahedron Lett.*, 1997, **38**, 8537.
6 For a review, A. D. Elben and R. J. Molyneux, in *Alkaloids: Chemical and Biological Perspective*, ed. S. W. Pelletier, Wiley, New York, 1987, vol. 5, ch. 1.
7 M. J. Humphries, K. Matsumoto, S. L. White and K. Olden, *Cancer Res.*, 1986, **46**, 5215.
8 A. D. Elbein, *Annu. Rev. Biochem.*, 1987, **56**, 497.
9 E. Truscheit, W. Frommer, B. Junge, L. Müller, D. D. Schmidt and W. Wingender, *Angew. Chem., Int. Ed. Engl.*, 1981, **20**, 744.
10 R. A. Gruters, J. J. Neefjes, M. Tersmette, R. E. Y. De Goede, A. Tulp, H. G. Huisman, F. Miedema and H. L. Ploegh, *Nature*, 1987, **330**, 74.
11 Y. Aoyagi, W. Tanaka and A. Ohta, *J. Chem. Soc., Chem. Commum.*, 1994, 1225.
12 Y. Aoyagi, T. Inariyama, Y. Arai, S. Tsuchida, Y. Matsuda, H. Tateno and A. Ohta, *Tetrahedron*, 1994, **50**, 13575.
13 Y. Aoyagi, M. Yoshimura, M. Tsuda, T. Tsuchibuchi, S. Kawamata, H. Tateno, K. Asano, H. Nakamura, M. Obokata, A. Ohta and Y. Kodama, *J. Chem. Soc., Perkin Trans. 1*, 1995, 689.
14 Y. Aoyagi, T. Manabe, A. Ohta, T. Kurihara, G.-L. Pang and T. Yuhara, *Tetrahedron*, 1996, **52**, 869.
15 Y. Aoyagi, R. Asakura, M. Kondoh, R. Yamamoto, T. Kuromatsu, A. Shimura and A. Ohta, *Synthesis*, 1996, 970.
16 Y. Aoyagi, M. Maeda, A. Moro, K. Kubota, Y. Fujii, H. Fukaya and A. Ohta, *Chem. Pharm. Bull.*, 1996, **44**, 1812.
17 Y. Okude, S. Hirano, T. Hiyama and H. Nozaki, *J. Am. Chem. Soc.*, 1977, **99**, 3179.
18 T. Hiyama, K. Kimura and H. Nozaki, *Tetrahedron Lett.*, 1981, **22**, 1037.
19 T. Hiyama, Y. Okude, K. Kimura and H. Nozaki, *Bull. Chem. Soc. Jpn.*, 1982, **55**, 561.
20 O. Garner and J. M. Park, *J. Org. Chem.*, 1987, **52**, 2361.
21 O. Garner and J. M. Park, *Org. Synth.*, 1991, **70**, 18.
22 A. Hafner, R. O. Duthaler, R. Marti, G. Rihs, P. R. Streit and F. Schwarzenbach, *J. Am. Chem. Soc.*, 1992, **114**, 2321.
23 L. Williams, Z. Zhang, F. Shao, P. J. Carroll and M. M. Joullié, *Tetrahedron*, 1996, **52**, 11673.
24 T. Läib, J. Chastanet and J. Zhu, *J. Org. Chem.*, 1998, **63**, 1709.
25 P. Meffre, L. Gauzy, E. Branquet, P. Durand and F. Le Goffic, *Tetrahedron*, 1996, **52**, 11.
26 A. Avenoza, C. Cativiela, F. Corzana, J. M. Peregrina and M. M. Zurbano, *Synthesis*, 1997, 1146.
27 P. Soro, G. Rassu, P. Spanu, L. Pinna, F. Zanardi and G. Casiraghi, *J. Org. Chem.*, 1996, **61**, 5172.
28 F. Novello, M. Prato, T. Da Ros, M. De Amici, A. Bianco, C. Toniolo and M. Maggini, *Chem. Commun.*, 1996, 903.
29 C. S. Lee and C. J. Forsyth, *Tetrahedron Lett.*, 1996, **37**, 6449.
30 A. V. Bayquen and R. W. Read, *Tetrahedron*, 1996, **52**, 13467.
31 M. Z. Hoemann, K. A. Agrios and J. Aubé, *Tetrahedron Lett.*, 1996, **37**, 953.
32 R. R. Dabrule and G. G. Hess, *Synthesis*, 1974, 197.
33 C. T. Buse and C. H. Heathcock, *Tetrahedron Lett.*, 1978, 1685.
34 M. D. Lewis and Y. Kishi, *Tetrahedron Lett.*, 1982, **23**, 2343.
35 H. Nagaoka and Y. Kishi, *Tetrahedron*, 1981, **37**, 3873.
36 J. A. Sousa and A. L. Bluhm, *J. Am. Chem. Soc.*, 1960, **25**, 108.
37 C. Hercleis and H. P. Hubmann, *Tetrahedron: Asymmetry*, 1994, **5**, 119.

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