The Chemistry of *O*-Silylated Ketene Acetals: Synthesis of *N*-Benzoyl-L-daunosamine

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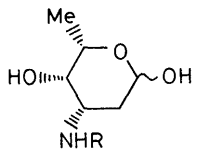
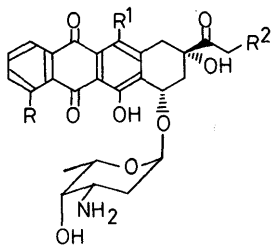
***N*-Benzoyl-L-daunosamine was synthesized with high stereoselectivity utilizing a 1,3-addition of ketene silyl acetal to the chiral nitrone, (*Z*)-[(4*S*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl]methylene[(1*S*)-1-phenylethyl]amine *N*-oxide, followed by a silyl group-transfer reaction in acetonitrile under mild conditions.**

Keywords *O*-silylated ketene acetal; L-daunosamine; chiral nitrone; diastereoselective 1,3-addition; silyl group-transfer reaction

L-Daunosamine[1] (**1a**, 3-amino-2,3,6-trideoxy-L-*lyxo*-hexose), is the carbohydrate component of several important natural and unnatural anthracycline antitumor agents, daunomycin (**2a**), adriamycin (**2b**), 4-demethoxydaunomycin (**2c**), and 11-deoxydaunomycin (**2d**). Since the amino-sugar moiety was shown to play an important role to reduce their toxicity and to change their biological activity profile, much attention has been paid to the synthesis of daunosamine and related amino-sugars, and a number of methods have been reported. Most of the syntheses were based on the use of carbohydrate precursors. Recently, approaches from non-sugar precursors have also been reported and reviewed.[2] However, the available syntheses of **1a** seem to be rather impractical. In connection with our continuing efforts to establish new, efficient methodology for the synthesis of anthracycline antibiotics,[3] we required a general practical route for the preparation of **1a**. We have reported[4] a versatile method for the diastereoselective synthesis of 2-deoxy-D-ribose by utilizing the aldol reaction of ketene silyl acetal (**3**) to 2,3-*O*-isopropylidene-D-glyceraldehyde followed by a silyl group-transfer reaction.[5] The method appeared to be applicable to the synthesis of optically pure *N*-benzoyl-L-daunosamine (**1b**). In a recent communication,[6] we reported a stereocontrolled synthesis of *N*-benzoyl-L-daunosamine utilizing a 1,3-addition of ketene methyl *tert*-butyldimethylsilyl acetal (**3a**) to the chiral nitrone followed by a silyl group-transfer reaction in acetonitrile under mild conditions. We present here a full account of this work.



1a: R=H
1b: R=COPh



2a: R=OMe, R^1=OH, R^2=H
2b: R=OMe, R^1=R^2=OH
2c: R=R^2=H, R^1=OH
2d: R=OMe, R^1=H, R^2=H

Fig. 1

Diastereoselective 1,3-Addition of Ketene Silyl Acetals to Chiral Nitrones To apply the silyl group-transfer 1,2-addition[4] of a C=O group to the silyl group-transfer 1,3-addition of a C–N unsaturated group, we initially investigated the reactions of various types of compounds (**4**—**9**) having C–N unsaturated bonds under mild conditions, considering the stability of the protected amino group, which is necessary for the synthesis of the amino-sugar. The reaction of the oxime (**4**) with **3a** gave an oxime *O*-silyl ether (**10**), but the oxime methyl ether (**5**) did not react with **3a**. The oxime acetate (**6**) was reacted with **3a** to give an *O*-silylated-1,2-addition product (**11**) of the acetyl carbonyl group. The nitrile oxide (**7**) underwent a 1,3-dipolar addition reaction to give a low yield of the addition product (**12**). Although the treatment of the imine (**8**) with **3a** failed, the iminium salt obtained by treatment with ethyl chlorocarbonate reacted with **3a** to give a

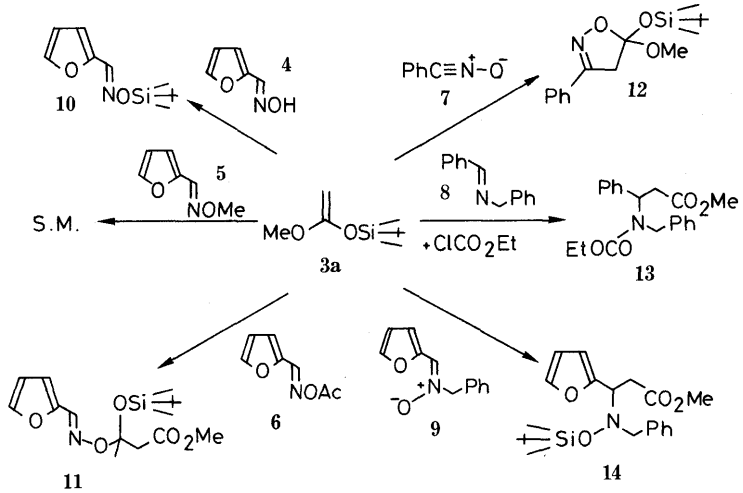
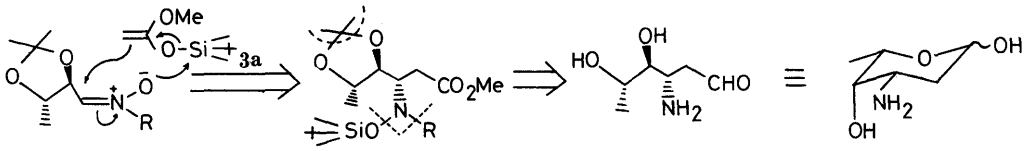
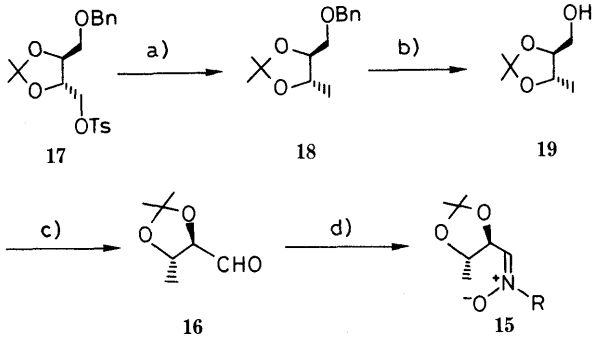


Chart 1



15 1a

Chart 2



a) $NaBH_4$, DMSO; b) [H_2] Pd-C, cat. AcOH, AcOEt;
c) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; d) RNHOH, Na_2SO_4, CH_2Cl_2

Chart 3

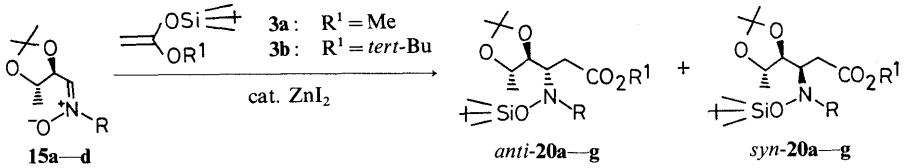
moderate yield of the addition product (**13**). The best result was obtained by the reaction of the nitrone (**9**) with **3a**. Thus, the reaction of **9** with **3a** in acetonitrile in the presence of a catalytic amount of zinc iodide yielded an *O*-silylated 1,3-addition product (**14**) quantitatively.

We describe here an efficient stereocontrolled synthesis of **1a** by a bond-forming strategy which engages the chiral *Z*-nitrone (**15**) and **3** in the silyl group-transfer 1,3-addition reaction (Chart 2).

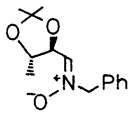
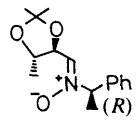
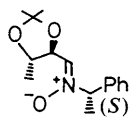
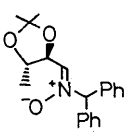
Z-Nitrones (**15a—d**) were synthesized by the following procedures. The starting chiral aldehyde (**16**) was obtained by a modification of Fronza *et al.*'s[7] and Mukaiyama *et al.*'s[8] methods. The known tosylated compounds (**17**) was obtained from commercially available diethyl L-tartrate in four steps: **17** was detosylated by sodium borohydride to give **18**, and then deprotected by hydrogenolysis to give **19**, which was converted to the aldehyde (**16**) by Swern's oxidation, then **16** was reacted with achiral and chiral *N*-alkylhydroxyamines to give the corresponding chiral *Z*-nitrones (**15a—d**) in high yields (Chart 3).

DeShong and Leginus reported[9] that the achiral *Z*-nitrone (achiral-**15a**) underwent a diastereo- and regiospecific cycloaddition to ethyl vinyl ether to give the isoxazolidine, which was converted to racemic daunosamine through severe hydrogenolysis over Pearlman's catalyst.[10] We found that the reaction of chiral nitrones (**15a—d**) with

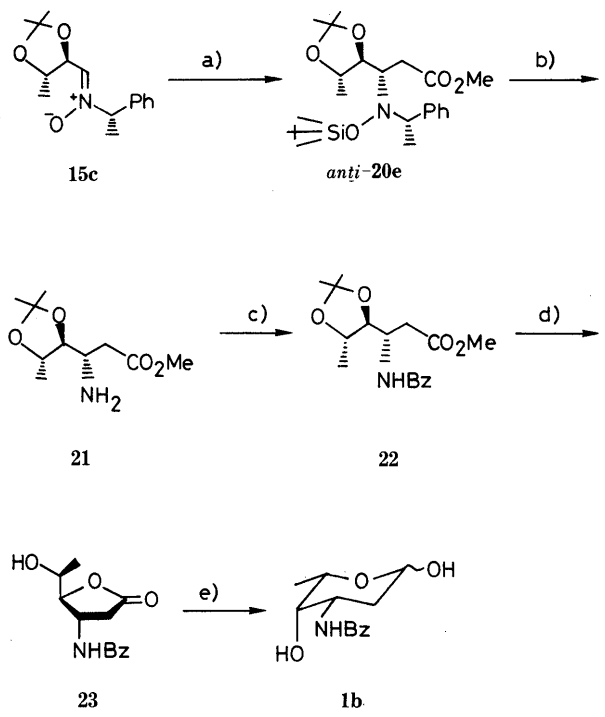
TABLE I.



15a—d *anti*-**20a—g** *syn*-**20a—g**

Nitrone	Ketene silyl acetal	Reaction conditions	Product	Yield (%)	Ratio *anti*:*syn*
 **15a**	**3a**	−78 °C, CH_3CN–CH_2Cl_2 = 1 : 1, 1.5 h	**20a**	Quant.	60 : 40
	3b	−78 °C, CH_3CN–CH_2Cl_2 = 1 : 1, 1 h	**20b**	99	83 : 17
 **15b**	**3a**	−78 °C, CH_3CN–CH_2Cl_2 = 1 : 1, 1 h	**20c**	89	88 : 12
	3b	−78 °C, CH_3CN–CH_2Cl_2 = 1 : 1, 1 h	**20d**	77	94 : 6
	3b	r.t., CH_3CN, 5 min	**20d**	32	65 : 35
 **15c**	**3a**	−78 °C, CH_3CN–CH_2Cl_2 = 1 : 1, 1 h	**20e**	Quant.	100 : 0
	3a	r.t., CH_3CN, 15 min	**20e**	Quant.	95 : 5
 **15d**	**3a**	−78 °C, CH_3CN–CH_2Cl_2 = 1 : 1, 3 h	**20f**	90	93 : 7
	3b	−78 °C, CH_3CN–CH_2Cl_2 = 1 : 1, 10 h	**20g**	85	100 : 0

r.t. = room temperature.



a) **3a**/cat. ZnI_2, CH_3CN–CH_2Cl_2 = 1 : 1, 1 h; b) [H_2] Pd–C, AcOH, r.t., 3 atm; c) PhCOCl/pyridine; d) 80% AcOH, 40°C, 1 h reflux, 5 h; e) DIBAL/THF, −78°C, 1.5 h.

Chart 4

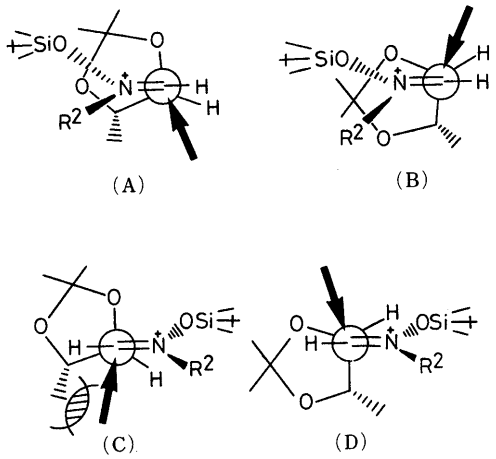


Fig. 2

ketene silyl acetals (**3a, b**) gave highly diastereoselective *O*-silylated 1,3-addition products (**20a—g**)[11] and the N–O bond in **20a—g** was proved to cleave smoothly under mild hydrogenolysis conditions to give the aminoester (**21**), which was readily converted to optically pure *N*-benzoyl-L-daunosamine (**1b**). The best result was obtained by the reaction of (*Z*)-[(4*S*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl] methylene[(1*S*)-1-phenylethyl]amine *N*-oxide (**15c**) and *O*-methyl-*O*-*tert*-butyldimethylsilyl ketene acetal (**3a**) at −78 °C in the presence of a catalytic amount of zinc iodide in CH_3CN–CH_2Cl_2 (1 : 1) for 1 h (run 6). The *O*-silylated 1,3-addition product (**20e**) was obtained in a quantitative yield with an *anti* relative stereochemistry at C-3 and C-4 (*anti* : *syn* ≧ 100 : 1). The results are summarized in Table I.

The stereochemical assignment of the adducts (**20a—g**) was established by the conversion of the adducts into the known γ-lactone (**23**)[2a,12]: Thus, the adduct (**20e**) was hydrogenated to give the aminoester (**21**), and then benzoylated to give **22**, which was converted into **23** by lactonization. The transformation of **23** into **1b** was carried out according to the known method.[12] The route is visualized in Chart 4.

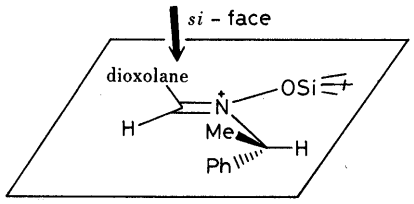


Fig. 3

While the details of the diastereoselection in the reaction of **15** and **3** remain unknown, a hypothetical model is given in Fig. 2. Addition to a diastereotopic face of a π-system is usually explained in terms of the Felkin–Ann model.[13] For the reaction of **15**, the following conformations (A—D) are considered. For conformations A and B, severe steric interactions are present between the dioxolane ring and the initially formed bulky siloxy group. For conformation C, unfavorable interactions between the incoming enolate anion and the methyl group on the dioxolane ring are present. Molecular models suggest that the attack of the enolate anion *via* conformation D is sterically required and may explain the high selectivity for the *S*-nitrone (**15c**) rather than the *R*-nitrone (**15b**) as pictured in Fig. 3.

Experimental

All melting and boiling points are uncorrected. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded on a Hitachi R-22 (90 MHz) or a JEOL JNM-GX 500 (500 MHz) spectrometer (with tetramethylsilane as an internal standard unless otherwise noted). Infrared (IR) absorption spectra were recorded on a JASCO HPIR-102 spectrometer. Low- and high-resolution mass spectra (MS) were obtained with a JEOL JMS D-300 instrument, with a direct inlet system at 70 eV. Optical rotations was measured in 1-dm cell of 1-ml capacity with a Perkin–Elmer 241 instrument. High performance liquid chromatography (HPLC) was performed on a JASCO TRI ROTAR-II. For column chromatography, E. Merck silica gel (70—230 mesh ASIM) was used.

Ketene Silyl Acetals (3a, b) Ketene silyl acetals (**3a**,[14] **3b**[15]) were prepared from the corresponding esters by the reported methods.

Compounds Having a C–N Unsaturated Bond (4—8) Compounds **4**,[16] **5**,[17] **6**,[18] **7**[19] and **8**[20] were prepared by the reported methods.

***N*-[(Furan-2-yl)methylene]benzylamine *N*-Oxide (9)** Benzyl chloride (37.6 g, 0.3 mol) was added to a stirred solution of sodium ethoxide (14.04 g, 0.27 mol) in absolute ethanol (250 ml) at room temperature. After being stirred for an additional 24 h, the mixture was concentrated *in vacuo*, and the residue was poured into chloroform (250 ml). The precipitated inorganic salt was filtered off, and the filtrate was washed with water, dried over magnesium sulfate, and evaporated *in vacuo*. The resulting solid was washed with ether and recrystallized from ether to give **9** (31 g, 57%) as colorless needles, mp 85.5—86 °C. ^{1}H-NMR ($CDCl_3$) δ: 4.34 (2H, s, CH_2Ph), 6.36 (1H, dd, *J* = 4, 2 Hz, ArH), 7.15 (6H, brs, ArH), 7.29 (1H, s, CH=N), 7.53 (1H, d, *J* = 4 Hz, ArH). *Anal.* Calcd for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.63; H, 5.51; N, 6.98.

***N*-(Furan-2-yl)methylene-*N*-(*tert*-butyldimethylsiloxy)amine (10)** Compound **3a** (451 mg, 2.4 mmol) was added to a stirred solution of **4** (222 mg, 2 mmol) and zinc iodide (33 mg, 0.1 mmol) in dry acetonitrile (4 ml) at room temperature under nitrogen, then the mixture was stirred for 2 h under the same conditions. The mixture was partitioned between ether (20 ml) and saturated aqueous solution of sodium bicarbonate (20 ml), then the aqueous layer was extracted with ether (20 ml × 3). The organic layer was washed with brine, dried over magnesium sulfate, and evaporated *in vacuo*. The residue was subjected to column chromatography on

silica gel with *n*-hexane to give **10** (427 mg, 95%) as a colorless oil, bp 80—85 °C/2 mmHg (bath temperature). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2960, 2930, 2850, 1615, 1010, 840. ^{1}H-NMR ($CDCl_3$) δ: 0.24 (6H, s, Me_2Si), 0.99 (9H, s, *tert*-BuSi), 6.47 (1H, dd, J=3.8, 1.8 Hz, ArH), 7.31 (1H, d, J=3.8 Hz, ArH), 7.42 (1H, d, J=1.8 Hz, ArH), 7.61 (1H, s, CH=N). Exact mass Calcd for $C_{11}H_{19}NO_2Si$: 225.1183. Found: 225.1163.

***N*-(Furan-2-yl)methylene-[1-(*tert*-butyldimethylsiloxy)-1-methyl-2-methoxycarbonylethyloxy]amine (11)** Compound **1a** (185 mg, 0.984 mmol) was added to a stirred solution of **6** (94 mg, 0.61 mmol) and zinc iodide (22 mg, 0.069 mmol) in dry acetonitrile (2 ml) at room temperature under nitrogen. After additional stirring of the mixture for 17 h, the mixture was worked up in a similar manner to that described above. The crude product was subjected to column chromatography on silica gel with *n*-hexane–ether (1:1) to give **11** (41 mg, 20%) as a colorless oil, bp 85—90 °C/0.2 mmHg (bath temperature). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735, 1225, 955, 840. ^{1}H-NMR ($CDCl_3$) δ: 0.12 (6H, br s, Me_2Si), 0.83 (9H, s, *tert*-BuSi), 1.68 (3H, br s, Me), 2.79 (1H, d, J=14.0 Hz, C<u>H</u>CO_2Me), 2.94 (1H, d, J=14.0 Hz, C<u>H</u>CO_2Me), 3.63 (3H, s, OMe), 6.43 (1H, dd, J=3.8, 1.3 Hz, ArH), 6.63 (1H, d, J=3.8 Hz, ArH), 7.44 (1H, d, J=1.3 Hz, ArH), 7.90 (1H, s, CH=N). *Anal.* Calcd for $C_{16}H_{27}NO_5Si$: C, 56.28; H, 7.97; N, 4.10. Found: C, 56.59; H, 8.33; N, 4.41.

3-Phenyl-5-(*tert*-butyldimethylsiloxy)-5-methoxyisoxazoline (12) Compound **3a** (376 mg, 2 mmol) and triethylamine (0.21 ml) were added to a stirred solution of benzaldochloroxime [obtained from benzaldoxime (225 mg, 1.86 mmol) by Perold *et al.*'s method[19]] in dry ether (4 ml) at room temperature under nitrogen. After being stirred for 1 h, the mixture was worked up in the same manner as described for the preparation of **10** from **4**, and the crude product was subjected to column chromatography on silica gel with *n*-hexane–ether (10:1) to give **12** (114 mg, 20%) as a colorless oil, bp 150—155 °C/0.19 mmHg (bath temperature). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2960, 2870, 1370, 1090, 845. ^{1}H-NMR ($CDCl_3$) δ: 0.14 (3H, s, MeSi), 0.26 (3H, s, MeSi), 0.93 (9H, s, *tert*-BuSi), 3.15 (1H, d, J=17.5 Hz, 4-H), 3.47 (1H, d, J=17.5 Hz, 4-H), 3.42 (3H, s, OMe), 7.2—7.8 (5H, m, Ph). Exact mass Calcd for $C_{16}H_{25}NO_3Si$-*tert*-Bu: 250.0897. Found: 250.0880.

Methyl 3-(*N*-Ethoxycarbonyl-*N*-benzylamino)-3-phenylpropionate (13) Ethyl chloroformate (120 mg, 1.11 mmol) was added to a stirred solution of **8** (216 mg, 1.11 mmol) in dry methylene chloride (1 ml), then the mixture was stirred for 20 min. Ketene silyl acetal (**3a**, 282 mg, 1.5 mmol) was added, and after 72 h, the reaction mixture was worked up in the same manner as described for the preparation of **10** from **4**. The crude product was subjected to column chromatography on silica gel with *n*-hexane–ether (5:1) to give the starting imine (**8**, 94 mg, 43%) and **13** (141 mg, 37%) as a colorless oil, bp 115—120 °C/0.22 mmHg (bath temperature). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735, 1690. ^{1}H-NMR ($CDCl_3$) δ: 1.23 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 2.89 (2H, d, J=8.1 Hz, 2-H), 3.53 (3H, s, OMe), 4.11 (1H, d, J=15.0 Hz, NCHPh), 4.20 (2H, q, J=7.0 Hz, $C\underline{H}_2CH_3$), 4.54 (1H, d, J=15.0 Hz, NCHPh), 5.67 (1H, t, J=8.1 Hz, 3-H), 6.9—7.6 (10H, m, Ph×2). Exact mass Calcd for $C_{20}H_{23}NO_4$: 341.1624. Found: 341.1606.

Methyl 3-(Furan-2-yl)-3-[*N*-benzyl-*N*-(*tert*-butyldimethylsiloxy)amino]-propionate (14) Ketene silyl acetal (**3a**, 452 mg, 2.4 mmol) was added to a stirred solution of the nitrone (**9**, 402 mg, 2 mmol) and zinc iodide (32 mg, 0.1 mmol) in dry acetonitrile (5 ml) at 0 °C under nitrogen, and then the mixture was stirred at room temperature for 1 h. The mixture was worked up in the same manner as described for the preparation of **10** from **4**. The crude product was subjected to column chromatography on silica gel with *n*-hexane–ethyl acetate (10:1) to give **14** (876 mg, quantitative) as an oil, bp 180—195 °C/0.3 mmHg (bath temperature). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735. ^{1}H-NMR ($CDCl_3$) δ: −0.16 (6H, s, Me_2Si), 0.83 (9H, s, *tert*-BuSi), 2.88 (1H, dd, J=15.2, 8.2 Hz, C<u>H</u>CO_2Me), 2.98 (1H, dd, J=15.2, 6.7 Hz, C<u>H</u>CO_2Me), 3.50 (1H, d, J=13.0 Hz, NC<u>H</u>Ph), 3.61 (3H, s, OMe), 3.80 (1H, d, J=13.0 Hz, NC<u>H</u>Ph), 4.48 (1H, dd, J=8.2, 6.7 Hz, 3-H), 6.2—6.4 (2H, m, ArH), 7.18 (5H, s, Ph), 7.32 (1H, br s, ArH). *Anal.* Calcd for $C_{21}H_{31}NO_4Si$: C, 64.75; H, 8.02; N, 3.60. Found: C, 64.92; H, 8.17; N, 3.57.

(4*S*,5*S*)-(5-Benzyloxymethyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl *p*-Toluenesulfonate (17) This was prepared by the reported method.[21]

(4*S*,5*S*)-4-Benzyloxymethyl-2,2,5-trimethyl-1,3-dioxolane (18) A solution of **17** (8.91 g, 21.9 mmol) in dry dimethyl sulfoxide (DMSO, 60 ml) was added dropwise to a stirred suspension of sodium borohydride (15.1 g, 397 mmol) in dry DMSO (100 ml) at room temperature under nitrogen, and the mixture was stirred at 50 °C for 13 h. The mixture was poured into ice-cold water (300 ml) and extracted with ether (100 ml×5). The extract was washed with water and brine, dried over magnesium sulfate, and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with *n*-hexane–ether (3:1) to give **18** (4.95 g, 96%) as an oil, bp 112 °C/0.31 mmHg. $[\alpha]_D^{21}$ +10.1° (c=1.39, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1455, 1380, 1370, 1235, 1175, 1090, 995, 910, 850. ^{1}H-NMR ($CDCl_3$) δ: 1.28 (3H, d, J=6.0 Hz, Me), 1.38 (3H, s, <u>Me</u>CMe), 1.39 (3H, s, MeC<u>Me</u>), 3.5—4.1 (4H, m, CHCHCH_2), 4.57 (2H, s, OCH_2Ph), 7.31 (5H, s, Ph). *Anal.* Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.26; H, 8.64.

(4*S*,5*S*)-4-Hydroxymethyl-2,2,5-trimethyl-1,3-dioxolane (19) A suspension of **18** (1 g, 4.237 mmol) and 10% palladium on carbon (600 mg) in ethyl acetate–acetic acid (8:1, 18 ml) was shaken under hydrogen (3 kg/cm^2) at room temperature for 24 h. The catalyst was filtered through celite, then triethylamine (10 ml) was added to the filtrate. The mixture was evaporated *in vacuo*, then the residue was subjected to column chromatography on silica gel with *n*-hexane–ether (2:1) to give **19** (550 mg, 89%) as an oil, bp 165 °C (bath temperature). $[\alpha]_D^{25}$ +0.50° (c=1.78, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3475, 1455, 1385, 1375, 1240, 1175, 1100, 1040, 990. ^{1}H-NMR ($CDCl_3$) δ: 1.28 (3H, d, J=6 Hz, Me), 1.41 (3H, s, <u>Me</u>CMe), 1.43 (3H, s, MeC<u>Me</u>), 2.45 (1H, br s, OH), 3.33—3.38 (3H, m, $CHCH_2$), 4.01 (1H, qd, J=6, 8 Hz, C<u>H</u>CH_3). Exact mass Calcd for $C_7H_{14}O_3$–Me: 131.0708. Found: 131.0724.

2,3-*O*-Isopropylidene-4-deoxy-L-threose (16) Dry DMSO (1.4 ml) was added dropwise to a stirred solution of oxalyl chloride (0.7 ml) in dry methylene chloride (18 ml) at −78 °C under nitrogen. After 5 min, a solution of **19** (350 mg, 2.40 mmol) in dry methylene chloride (4 ml) was added dropwise to the above stirred mixture. After 20 min, triethylamine (5.6 ml) was added dropwise to the mixture. After additional stirring for 20 min under the same conditions, the reaction mixture was allowed to warm to room temperature, poured into water (30 ml) and extracted with methylene chloride (20 ml×3). The extract was dried over magnesium sulfate and evaporated *in vacuo*, to give the residue, which was subjected to column chromatography on silica gel with *n*-hexane–ether (3:1) to give **16** (326 mg, 94%) as a colorless oil, bp 100—105 °C/1 mmHg (bath temperature). $[\alpha]_D^{19}$ +58.6° (c=1.87, $CHCl_3$). [lit.[7] +27.7° (c=1, $CHCl_3$)]. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1735. ^{1}H-NMR ($CDCl_3$) δ: 1.43 (9H, br s, Me×3), 3.88 (1H, dd, J=8.0, 2.2 Hz, 2-H), 4.13 (1H, qd, J=8.0, 6.0 Hz, 3-H), 9.73 (1H, d, J=2.2 Hz, CHO). MS m/z: 144 (M^+), 162 ($M^+ + H_2O$). This was used for the next reaction without further purification.

Hydroxylamines Benzylhydroxylamine,[22] (*R*)- and (*S*)-α-phenylethylhydroxylamine[23] and benzhydrylhydroxylamine[24] were prepared by the reported methods.

General Procedure for the Preparation of Nitrones (15a—d) Hydroxylamine (2.2 mmol) and sodium sulfate (500 mg) were added to a stirred solution of the aldehyde (**16**, 288 mg, 2 mmol) in methylene chloride (2 ml) at room temperature. After 15 h, the mixture was partitioned between methylene chloride (20 ml) and 5% hydrochloric acid (30 ml), and the aqueous layer was extracted with methylene chloride (20 ml×3). The extract was washed with saturated aqueous solution of sodium bicarbonate, dried over magnesium sulfate, and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with methylene chloride–ethyl acetate (20:1) to give **15a—d** (*ca.* 60%).

***N*-[[(4*S*,5*S*)-2,2,5-Trimethyl-1,3-dioxolan-4-yl]methylene]benzylamine *N*-Oxide (15a)** This (161 mg, 33% from **19**) was obtained from benzylhydroxylamine (240 mg, 1.95 mmol), sodium sulfate, the aldehyde (**16**) prepared from **19** (285 mg, 1.952 mmol), oxalyl chloride (0.7 ml), DMSO (1.4 ml), and triethylamine (5.6 ml), bp 135—140 °C/0.18 mmHg (bath temperature). $[\alpha]_D^{23}$ +42.9 (c=0.503, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1660, 1600. ^{1}H-NMR ($CDCl_3$) δ: 1.34 (3H, s, MeCMe), 1.41 (3H, s, MeCMe), 1.46 (3H, d, J=6.0 Hz, 4-Me), 4.01 (1H, qd, J=6.0, 7.5 Hz, 3-H), 4.83 (1H, dd, J=7.5, 5.8 Hz, 2-H), 4.87 (2H, s, $PhCH_2$), 6.76 (1H, d, J=5.8 Hz, CH=N), 7.39 (5H, s, Ph). Exact mass Calcd for $C_{14}H_{19}NO_3$: 249.1364. Found: 249.1369.

***N*-[[(4*S*,5*S*)-2,2,5-Trimethyl-1,3-dioxolan-4-yl]methylene][(1*R*)-1-phenylethyl]amine *N*-Oxide (15b)** This (260 mg, 60%) was obtained from **16** (236 mg, 1.639 mmol) and (*R*)-α-phenylethylhydroxylamine (226 mg, 1.65 mmol), bp 105—110 °C/0.22 mmHg (bath temperature). $[\alpha]_D^{20}$ +56.7° (c=1.45, CH_2Cl_2). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1590. ^{1}H-NMR ($CDCl_3$) δ: 1.34 (3H, s, <u>Me</u>CMe), 1.43 (3H, s, MeC<u>Me</u>), 1.43 (3H, d, J=6.2 Hz, 4-CH_3), 1.79 (3H, d, J=6.4 Hz, NCHC<u>H</u>$_3$), 3.97 (1H, qd, J=6.2, 6.4 Hz, 3-H), 4.83 (1H, dd, J=5.3, 6.4 Hz, 2-H), 6.82 (1H, d, J=5.3 Hz, CH=N), 7.22—7.47 (5H, m, Ph). MS m/z: 263 (M^+). Exact mass Calcd for $C_{15}H_{21}NO_3$–Me: 248.1287. Found: 248.1289.

***N*-[[(4*S*,5*S*)-2,2,5-Trimethyl-1,3-dioxolan-4-yl]methylene][(1*S*)-1-phenylethyl]amine *N*-Oxide (15c)** This (18 mg, 67%) was obtained from **16** (14.8 mg, 0.103 mmol) and (*S*)-α-phenylethylhydroxylamine (22 mg, 0.154 mmol), bp 130—135 °C/0.1 mmHg (bath temperature). $[\alpha]_D^{28}$ +43.8° (c=0.54, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1590. ^{1}H-NMR ($CDCl_3$) δ: 1.34 (3H, s,

MeCMe), 1.41 (3H, s, MeCMe), 1.49 (3H, d, J=6.1 Hz, 4-CH_3), 1.80 (3H, d, J=7.0 Hz, NCHCH_3), 4.03 (1H, qd, J=7.3, 6.1 Hz, 3-H), 4.80 (1H, dd, J=7.3, 5.3 Hz, 2-H), 5.01 (1H, q, J=7.0 Hz, NCHCH$_3$), 6.84 (1H, d, J=5.3 Hz, CH=N), 7.15—7.55 (5H, m, Ph). Exact mass Calcd for $C_{15}H_{21}NO_3$+H: 264.1597. Found: 264.1571.

***N*-[[(4*S*,5*S*)-2,2,5-Trimethyl-1,3-dioxolan-4-yl]methylene]benzhydrylamine *N*-Oxide (15d)** This (158.4 mg, 64%) was obtained from **16** (110 mg, 0.764 mmol) and benzhydrylhydroxylamine (228 mg, 1.146 mmol), mp 112.5—113 °C (Et_2O–*n*-hexane). $[\alpha]_D^{18}$ +30.3° (c=0.380, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1660. ^{1}H-NMR ($CDCl_3$) δ: 1.30 (3H, s, MeCMe), 1.41 (3H, s, MeCMe), 1.51 (3H, d, J=5.9 Hz, 4-CH_3), 4.08 (1H, qd, J=7.1, 5.9 Hz, 3-H), 4.91 (1H, dd, J=7.1, 5.1 Hz, 2-H), 6.19 (1H, s, CHPh$_2$), 6.85 (1H, d, J=5.8 Hz, CH=N), 7.3—7.5 (10H, m, Ph×2). Exact mass Calcd for $C_{20}H_{23}NO_3$: 325.1675. Found: 325.1674.

General Procedure for Addition Reaction of Nitrones (15a—e) with Ketene Silyl Acetals (3a, b) Ketene silyl acetal (**3**, 1.2—1.5 mmol) was added to a stirred solution of a nitrone (**15**, 1 mmol) and zinc iodide (16 mg, 0.05 mmol) in dry acetonitrile (5 ml) or dry acetonitrile–methylene chloride (1 : 1, 5 ml) under the conditions indicated in Table I. After 1—3 h, a saturated aqueous solution of sodium bicarbonate (1 ml) was added to the mixture. The reaction mixture was allowed to warm to room temperature, poured into water (25 ml), extracted with methylene chloride (20 ml×3). The extract was dried over magnesium sulfate and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with *n*-hexane–ether to give the adduct (**20**). The ratio of the mixture of the diastereomers (*anti*-**20** and *syn*-**20**) was determined by high performance liquid chromatography (HPLC, NUCLEOSIL 50-5, 4.9 mm×250 mm).

Methyl (4*S*,5*S*)-[*N*-(*tert*-Butyldimethylsiloxy)benzylamino]-4,5-(isopropylidenedioxy)hexanoates (20a) This mixture of diastereomers (51 mg, quantitative, *anti*:*syn*=60:40) was obtained from the nitrone (**15a**, 29.2 mg, 0.117 mmol), ketene silyl acetal (**3a**, 36 mg, 0.191 mmol) and zinc iodide (7 mg, 0.0191 mmol) in dry acetonitrile–methylene chloride (1 : 1, 1 ml). HPLC: *n*-hexane–Et_2O=10 : 1 (flow rate, 1.0 ml/min). t_R: *syn*-**20a**, 10.43 min; *anti*-**20a**, 11.22 min. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730. ^{1}H-NMR ($CDCl_3$) δ: −0.54 (2/5×3H, s, MeSi), −0.42 (2/5×3H, br s, MeSi), −0.23 (3/5H, br s, SiMe), −0.06 (3/5×3H, s, MeSi), 0.80 (9H, s, *tert*-BuSi), 1.2—1.5 (9H, m, MeCMe, 6-CH_3), 2.4—3.2 (2H, m, 2,2′-H), 3.79 (3H, s, OMe), 3.5—4.2 (5H, m, 3,4,5-H, NCH$_2$Ph), 7.2 (5H, s, Ph). Exact mass Calcd for $C_{23}H_{39}NO_5Si$: 437.2594. Found: 437.2583.

***tert*-Butyl (4*S*,5*S*)-3-[*N*-(*tert*-Butyldimethylsiloxy)benzylamino]-4,5-(isopropylidenedioxy)hexanoates (20b)** This mixture of diastereomers (32.7 mg, 99%, *anti*:*syn*=83 : 17) was obtained from **15a** (17.5 mg, 0.0702 mmol), ketene silyl acetal (**3b**, 21 mg, 0.095 mmol), and zinc iodide (5 mg, 0.0156 mmol) in dry acetonitrile–methylene chloride (1 : 1, 1 ml). HPLC: *n*-hexane–AcOEt=20 : 1 (flow rate, 1.0 ml/min). t_R: *syn*-**20b**, 6.64 min; *anti*-**20b**, 7.39 min. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720. ^{1}H-NMR ($CDCl_3$) δ: −0.45 (3H, br s, MeSi), −0.20 (3H, br s, MeSi), 0.78 (9H, s, *tert*-BuSi), 1.2—1.6 (9H, m, MeCMe, 6-CH_3), 1.49 (9H, s, *tert*-BuO), 2.3—2.9 (2H, m, 2,2′-H), 3.4—4.5 (5H, m, 3,4,5-H, NCH$_2$Ph), 7.2 (5H, s, Ph). Exact mass Calcd for $C_{26}H_{45}NO_5Si$: 479.3067. Found: 479.3075.

Methyl (4*S*,5*S*)-3-[*N*-(*tert*-Butyldimethylsiloxy)-(1*R*)-1-phenylethylamino]-4,5-(isopropylidenedioxy)hexanoates (20c) This mixture of diastereomers (131 mg, 89%, *anti*:*syn*=82 : 18) was obtained from **15b** (86 mg, 0.327 mmol), **3a** (92 mg, 0.49 mmol), and zinc iodide (7 mg, 0.02 mmol) in dry acetonitrile–methylene chloride (1 : 1, 1 ml). HPLC: *n*-hexane–AcOEt=25 : 1 (flow rate, 0.5 ml/min). t_R: *anti*-**20c**, 31.02 min; *syn*-**20c**, 34.20 min. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725. ^{1}H-NMR ($CDCl_3$) δ: 0.07 (12/100×3H, MeSi), 0.11 (3H, s, MeSi), 0.16 (82/100×3H, s, MeSi), 0.93 (9H, s, *tert*-BuSi), 1.21 (82/100×3H, s, MeCMe), 1.37 (82/100×3H, s, MeCMe), 1.0—1.5 (12/100×6H+6H, m, MeCMe, 6-CH_3, PhCHMe), 2.0—3.1 (2H, m, 2,2′-H), 3.57 (82/100×3H, s, OMe), 3.65 (12/100×3H, OMe), 3.2—4.4 (4H, m, 3,4,5-H, NCHPh), 7.1—7.4 (5H, m, Ph). Exact mass Calcd for $C_{24}H_{41}NO_5Si$: 451.2754. Found: 451.2755.

***tert*-Butyl (4*S*,5*S*)-3-[*N*-(*tert*-Butyldimethylsiloxy)-(1*R*)-1-phenylethylamino]-4,5-(isopropylidenedioxy)hexanoates (20d)** a) This mixture of diastereomers (310 mg, 77%, *anti*:*syn*=94 : 6) was obtained from **15b** (215 mg, 0.817 mmol), **3b** (230 mg, 1 mmol), and zinc iodide (16 mg, 0.05 mmol) in dry acetonitrile–methylene chloride (1 : 1, 8 ml).

b) This mixture of diastereomers (15 mg, 32%, *anti*:*syn*=65 : 35) was obtained from **15b** (25 mg, 0.095 mmol), **3b** (30 mg, 0.136 mmol), and zinc iodide (2 mg, 6 μmol) in dry acetonitrile (1 ml). HPLC: *n*-hexane–AcOEt=25 : 1 (flow rate, 0.5 ml/min). t_R: *syn*-**20d**, 15.34 min; *anti*-**20d**, 16.72 min. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1715. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (3H, s, MeSi), 0.16 (3H, s, MeSi), 0.93 (9H, s, *tert*-BuSi), 1.24 (3H, d, J=7.0 Hz, 6-CH_3), 1.25 (3H, s, MeCMe), 1.38 (3H, s, MeCMe), 1.41 (9H, s, *tert*-BuO), 1.41 (3H, d, J=6.7 Hz, PhCHMe), 2.18 (1H, m, 2-H), 2.36 (1H, dd, J=16.0, 5.0 Hz, 2′-H), 3.55 (2H, m, 3,5-H), 3.88 (1H, dd, J=8.2, 4.0 Hz, 4-H), 4.07 (1H, q, J=6.7 Hz, NCHPh), 7.21—7.41 (5H, m, Ph). Exact mass Calcd for $C_{27}H_{47}NO_5Si$: 493.3223. Found: 493.3224.

Methyl (3*S*,4*S*,5*S*)-3-[*N*-(*tert*-Butyldimethylsiloxy)-(1*S*)-1-phenylethylamino]-4,5-(isopropylidenedioxy)hexanoate (*anti*-20e) This (66 mg, quantitative) was obtained from **15c** (36.2 mg, 0.137 mmol), **3a** (52 mg, 0.27 mmol), and zinc iodide (3 mg, 0.01 mmol) in dry acetonitrile–methylene chloride (1 : 1, 1 ml). $[\alpha]_D^{27}$ −5.98° (c=2.59, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725. ^{1}H-NMR ($CDCl_3$) δ: 0.09 (3H, s, MeSi), 0.14 (3H, s, MeSi), 0.91 (9H, s, *tert*-BuSi), 1.11 (3H, d, J=6.0 Hz, 6-CH_3), 1.16 (3H, s, MeCMe), 1.24 (3H, s, MeCMe), 1.45 (3H, d, J=6.6 Hz, PhCHMe), 2.48 (1H, dd, J=16.6, 6.7 Hz, 2-H), 2.96 (1H, dd, J=16.6, 3.8 Hz, 2′-H), 3.05—3.45 (1H, m, 3-H), 3.5—3.7 (2H, m, 4,5-H), 3.56 (3H, s, OMe), 4.16 (1H, q, J=6.6 Hz, PhCHMe), 7.16—7.42 (5H, m, Ph). Exact mass Calcd for $C_{24}H_{41}NO_5Si$: 451.2754. Found: 451.2760.

Methyl (4*S*,5*S*)-3-[*N*-(*tert*-Butyldimethylsiloxy)-(1*S*)-1-phenylethylamino]-4,5-(isopropylidenedioxy)hexanoates (20e) This mixture of diastereomers (34.2 mg, quantitative, *anti*:*syn*=95 : 5) was obtained from **15c** (20 mg, 0.076 mmol), **3a** (16 mg, 0.082 mmol), and zinc iodide (2 mg, 6 μmol) in dry acetonitrile (1 ml). HPLC: *n*-hexane–Et_2O=25 : 1 (flow rate, 0.5 ml/min). Retention times: *syn*-**20e**, 30.95 min; *anti*-**20e**, 33.04 min.

Methyl (4*S*,5*S*)-3-[*N*-(*tert*-Butyldimethylsiloxy)benzhydrylamino]-4,5-(isopropylidenedioxy)hexanoates (20f) This mixture of diastereomers (50.4 mg, 89%, *anti*:*syn*=93 : 7) was obtained from **15d** (35.9 mg, 0.11 mmol), **3a** (32 mg, 0.166 mmol), and zinc iodide (4 mg, 0.012 mmol) in dry acetonitrile–methylene chloride (1 : 1, 1 ml). HPLC: *n*-hexane–AcOEt=25 : 1 (flow rate, 0.5 ml/min). t_R: *syn*-**20f**, 13.35 min; *anti*-**20f**, 14.50 min. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725. ^{1}H-NMR ($CDCl_3$) δ: −0.23 (3H, s, MeSi), −0.19 (3H, s, MeSi), 0.74 (9H, s, *tert*-BuSi), 1.20 (3H, d, J=6.0 Hz, 6-CH_3), 1.24 (3H, s, MeCMe), 1.32 (3H, s, MeCMe), 2.39 (1H, dd, J=15.0, 6.2 Hz, 2-H), 2.72 (1H, dd, J=15.0, 5.5 Hz, 2′-H), 3.60 (3H, s, OMe), 3.35—3.78 (2H, m, 3,5-H), 4.00 (1H, dd, J=8.6, 3.0 Hz, 4-H), 5.14 (1H, s, CHPh$_2$), 7.1—7.6 (10H, m, Ph×2). Exact mass Calcd for $C_{29}H_{43}NO_5Si$: 513.2908. Found: 513.2908.

***tert*-Butyl (3*S*,4*S*,5*S*)-3-[*N*-(*tert*-Butyldimethylsiloxy)benzhydrylamino]-4,5-(isopropylidenedioxy)hexanoate (*anti*-20g)** This (31.2 mg, 85%) was obtained from **15d** (21.9 mg, 0.012 mmol) in dry acetonitrile–methylene chloride (1 : 1, 1 ml). HPLC: *n*-hexane–AcOEt=60 : 1 (flow rate, 2.0 ml/min). t_R: *anti*-**20g**, 13.78 min. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1715. ^{1}H-NMR ($CDCl_3$) δ: −0.25 (3H, br s, SiMe), −0.18 (3H, br s, SiMe), 0.75 (9H, s, *tert*-BuSi), 1.16 (3H, d, J=5.5 Hz, 6-CH_3), 1.28 (3H, s, MeCMe), 1.32 (3H, s, MeCMe), 1.46 (9H, s, *tert*-BuO), 2.37 (1H, dd, J=16.5, 6.6 Hz, 2-H), 2.64 (1H, dd, J=16.5, 4.9 Hz, 2′-H), 3.59 (1H, qd, J=5.5, 8.6 Hz, 5-H), 3.66 (1H, ddd, J=6.6, 4.9, 1.8 Hz, 3-H), 4.00 (1H, dd, J=8.6, 1.8 Hz, 4-H), 5.16 (1H, s, CHPh$_2$), 7.15—7.46 (10H, m, Ph×2). Exact mass Calcd for $C_{32}H_{49}NO_5Si$: 555.3377. Found: 555.3372.

Methyl (3*S*,4*S*,5*S*)-3-Amino-4,5-(isopropylidenedioxy)hexanoate (21) A mixture of *anti*-**20e** (145 mg, 0.321 mmol) and 10% palladium on carbon (300 mg) in acetic acid (10 ml) was shaken at room temperature for 3 d under hydrogen (3 kg/cm^2). The mixture was filtered, then the filtrate was concentrated *in vacuo*. The residue was partitioned between methylene chloride (20 ml) and a saturated aqueous solution of sodium bicarbonate. The aqueous layer was extracted with methylene chloride (20 ml×3). The extract was dried over magnesium sulfate and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with chloroform–methanol (20 : 1) to give **21** (67.2 mg, 96%) as a syrup. $[\alpha]_D^{22}$ −8.92° (c=0.892, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3375, 1725, 1580. ^{1}H-NMR ($CDCl_3$) δ: 1.35 (3H, d, J=6.2 Hz, 6-CH_3), 1.36 (3H, s, MeCMe), 1.38 (3H, s, MeCMe), 1.40 (2H, br s, NH_2), 2.29 (1H, dd, J=15.4, 8.0 Hz, 2-H), 2.68 (1H, dd, J=15.4, 3.0 Hz, 2′-H), 3.12—3.40 (1H, m, 3-H), 3.44 (1H, dd, J=7.1, 6.0 Hz, 4-H), 3.71 (3H, s, OMe), 3.99 (1H, qd, J=7.1, 6.2 Hz, 5-H). MS m/z: 202 (M^+ − Me). This was used for the next reaction without further purification.

Methyl (3*S*,4*S*,5*S*)-3-Benzoylamino-4,5-(isopropylidenedioxy)hexanoate (22) Benzoyl chloride (52 mg, 0.37 mmol) was added to a stirred solution of **21** (53.5 mg, 0.246 mmol) in dry pyridine (2 ml) at room temperature under nitrogen. After 14 h, the mixture was evaporated *in vacuo*, and the residue was partitioned between methylene chloride (20 ml) and a saturated aqueous solution of ammonium chloride (20 ml). The aqueous layer was extracted with methylene chloride (20 ml×3), and the extract was washed with a saturated aqueous solution of sodium bicarbonate, dried over magnesium sulfate, and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with methylene chloride–ethyl acetate (50 : 1) to give **22** (71.2 mg, 90%) as colorless crystals, mp 91—

94 °C (*n*-hexane–Et_2O). $[\alpha]_D^{18}$ +22.3° (c=1.66, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3430, 1720, 1655. ^{1}H-NMR ($CHCl_3$) δ: 1.27 (3H, d, J=6.0 Hz, 6-CH_3), 1.38 (6H, s, MeCMe), 2.61 (1H, dd, J=16.2, 5.0 Hz, 2-H), 2.88 (1H, dd, J=16.2, 4.8 Hz, 2′-H), 3.69 (3H, s, OMe), 3.60—3.80 (1H, m, 4-H), 4.05 (1H, qd, J=6.0, 8.0 Hz, 5-H), 4.38—4.71 (1H, m, 3-H), 7.2—7.5 (4H, m, ArH, NH), 7.67—7.83 (2H, m, ArH). MS m/z: 321 (M^+). Exact mass Calcd for $C_{17}H_{23}NO_5$+H: 322.1652. Found: 322.1650. Calcd for $C_{17}H_{23}NO_5$–Me: 306.1339. Found: 306.1313.

L-Lyxo-3-benzoylamino-2,3,6-trideoxyhexanoic Acid γ-Lactone (23) A solution of **22** (52 mg, 0.162 mmol) in aqueous 80% acetic acid was stirred at 40 °C for 1 h, then refluxed for 5 h. The mixture was concentrated *in vacuo*, and the residue was subjected to preparative thin layer chromatography (P-TLC) on silica gel with chloroform–methanol (25:1) to give **23** (39.8 mg, 98%) as colorless crystals, mp 148—149 °C (*n*-hexane–AcOEt). $[\alpha]_D^{18}$ −19.7° (c=1.02, EtOH). [lit.[2a] mp 143—144 °C, $[\alpha]_D^{26}$ −19.4° (c=1, EtOH). The discrepancy of physical data may be ascribed to the fact that the γ-lactone gradually isomerizes to the δ-lactone.[12d]]. IR ν_{max}^{KBr} cm^{-1}: 3470, 3300, 1770, 1640, 1530. ^{1}H-NMR (acetone-d_6) δ: 1.27 (3H, d, J=5.85 Hz, Me), 2.61 (1H, dd, J=17.6, 4.0 Hz, 2-H), 3.02 (1H, dd, J=17.6, 8.8 Hz, 2′-H), 4.09 (1H, qd, J=5.85, 2.95 Hz, 5-H), 4.19 (1H, d, J=5.5 Hz, OH), 4.37 (1H, t, J=2.95 Hz, 4-H), 4.8—4.87 (1H, m, 3-H), 7.43—7.56 (3H, m, ArH), 7.90—7.93 (2H, m, ArH), 8.28 (1H, br s, NH). Exact mass Calcd for $C_{13}H_{15}NO_4$: 249.1001. Found: 249.1031.

***N*-Benzoyl-L-daunosamine (1b)** A 1.76 M solution of diisobutylaluminium hydride (DIBAL) in *n*-hexane was added to a stirred solution of **23** (10 mg, 0.04 mmol) at −78 °C under nitrogen. After additional stirring of the mixture for 1.5 h, methanol–water (4:1, 0.5 ml) was added. The reaction mixture was allowed to warm to room temperature, then a saturated aqueous solution of sodium bicarbonate (0.2 ml) was added, and the precipitate was filtered off. The filtrate was concentrated *in vacuo*, and the residue was purified by P-TLC on silica gel with benzene–acetone (4:3) to give **1b** (6.8 mg, 68%) as an 82:18 mixture of α-anomer and β-anomer. mp 154—156 °C (acetone). $[\alpha]_D^{26}$ −108° (c=0.093, EtOH). [lit.[1] mp 154—156 °C, $[\alpha]_D$ −107.5° (EtOH); lit.[12d] mp 153—155 °C (acetone), $[\alpha]_D^{20}$ −108° (c=0.1, EtOH, after 3 h)]. IR ν_{max}^{KBr} cm^{-1}: 3450, 3325, 1635, 1575, 1525. ^{1}H-NMR (DMSO-d_6) δ: signals due to α-anomer: 1.08 (3H, d, J=6.1 Hz, Me), 1.45 (1H, dd, J=12.2, 4.3 Hz, 2-H), 1.98 (1H, t dd, J=12.2, 3.2, 1.5 Hz, 2′-H), 3.49 (1H, br d, J=3.1 Hz, 4-H), 4.04 (1H, q, J=7.3 Hz, 5-H), 4.34—4.39 (1H, m, 3-H), 4.71 (1H, d, J=6.1 Hz, 4-OH), 5.14 (1H, br t, J=5.3 Hz, 1-H), 6.06 (1H, dd, J=3.7, 1.5 Hz, 1-OH), 7.4—7.55 (3H, m, ArH), 7.8—7.9 (2H, m, ArH), 7.91 (1H, d, J=7.9 Hz, NH); signal due to β-anomer: 1.14 (3H, d, J=6.7 Hz, Me), 1.59 (1H, ddd, J=12.2, 4.3, 1.8 Hz, 2-H), 1.75 (1H, td, J=12.2, 9.8 Hz, 2′-H), 3.43 (1H, dd, J=5.5, 1.8 Hz, 4-H), 3.54 (1H, br q, J=7.3 Hz, 5-H), 4.00—4.07 (1H, m, 3-H), 4.66 (1H, ddd, J=9.2, 6.1, 1.8 Hz, 1-H), 4.71 (1H, d, J=6.1 Hz, 4-OH), 6.47 (1H, d, J=6.1 Hz, 1-OH), 7.4—7.55 (3H, m, ArH), 7.8—7.9 (2H, m, ArH), 7.98 (1H, d, J=7.3 Hz, NH). MS m/z: Exact mass Calcd for $C_{13}H_{17}NO_4$: 251.1155. Found: 251.1140.

References and Notes

1) F. Arcamone, G. Cassinelli, P. Orezzi, G. Franceschi, and R. Mondelli, *J. Am. Chem. Soc.*, **86**, 5335 (1964); F. Arcamone, G. Franceschi, P. Orezzi, G. Cassinelli, W. Barbieri and R. Mondelli, *ibid.*, **86**, 5334 (1964); A. DiMarco, F. Arcamone, and F. Zunio, "Antibiotics," Vol. III, ed. by J. W. Corcoran and F. E. Hahn, Springer Verlag, New York, 1975, pp. 101—128; S. Penco, *Process Biochem.*, **15**, 12 (1980).
2) For a review, see: F. M. Hauser and S. R. Ellenberger, *Chem. Rev.*, **86**, 35 (1986) and references cited therein. Recent works after the review, see: *a*) M. Hirama, I. Nishizaki, T. Shigemoto, and S. Itoh, *J. Chem. Soc., Chem. Commun.*, **1986**, 393; *b*) Y. Kimura, T. Matsumoto, M. Suzuki, and S. Terashima, *Bull. Chem. Soc. Jpn.*, **59**, 663 (1986); H. Iida, N. Yamazaki, and C. Kibayashi, *J. Org. Chem.*, **51**, 4245 (1986); M. K. Gurjar and S. M. Pawar, *Tetrahedron Lett.*, **28**, 1327 (1987); M. Hirama, *Yuki Gosei Kagaku Kyokai Shi*, **45**, 346 (1987).
3) Y. Tamura, A. Wada, M. Sasho, K. Fukunaga, H. Maeda, and Y. Kita, *J. Org. Chem.*, **47**, 4376 (1982); Y. Tamura, M. Sasho, S. Akai, A. Wada, and Y. Kita, *Tetrahedron*, **40**, 4539 (1984); Y. Tamura, M. Sasho, S. Akai, H. Kishimoto, J. Sekihachi, and Y. Kita, *Tetrahedron Lett.*, **27**, 195 (1986); Y. Tamura and Y. Kita, *Yuki Gosei Kagaku Kyokai Shi*, **46**, 205 (1988).
4) Y. Kita, H. Yasuda, O. Tamura, F. Itoh, Y. Y. Ke, and Y. Tamura, *Tetrahedron Lett.*, **26**, 5777 (1985); Y. Kita, O. Tamura, F. Itoh, H. Yasuda, H. Kishino, Y. Y. Ke, and Y. Tamura, *J. Org. Chem.*, **53**, 554 (1988).
5) For reviews on the silyl group-transfer aldol and Michael reactions of ketene silyl acetals, see: Y. Kita, *Yakugaku Zasshi*, **106**, 269 (1986); Y. Kita, O. Tamura, and Y. Tamura, *Yuki Gosei Kagaku Kyokai Shi*, **44**, 1118 (1986).
6) Y. Kita, F. Itoh, O. Tamura, Y. Y. Ke, and Y. Tamura, *Tetrahedron Lett.*, **28**, 1431 (1987).
7) G. Fronza, C. Fuganti, P. Grassilli, and G. Marinoni, *Tetrahedron Lett.*, **1979**, 3883; G. Fronza, C. Fuganti, and P. Grasselli, *ibid.*, **21**, 2999 (1980).
8) T. Mukaiyama, Y. Goto, and S.-I. Shoda, *Chem. Lett.*, **1983**, 671.
9) P. DeShong and J. M. Legius, *J. Am. Chem. Soc.*, **105**, 1686 (1983).
10) W. M. Pearlman, *Tetrahedron Lett.*, **1967**, 1663.
11) For the reaction of ketene silyl acetals with nitrones, see: S. Tomoda, Y. Takeuchi, and Y. Nomura, *Chem. Lett.*, **1982**, 1787.
12) *a*) F. M. Hauser, R. P. Rhee, and S. R. Ellenberger, *J. Org. Chem.*, **49**, 2236 (1984); *b*) S. Brandänge and B. Lindqvist, *Acta Chem. Scand., Ser. B*, **39**, 589 (1985); *c*) S. Hanessian and J. Kloss, *Tetrahedron Lett.*, **26**, 1261 (1985); *d*) T. Hiyama, K. Nishide, and K. Kobayashi, *Chem. Lett.*, **1984**, 361.
13) M. Chérest, H. Felkin, and Z. Prudent, *Tetrahedron Lett.*, **1968**, 2199; N. T. Anh and O. Eisentein, *Nouv. J. Chim.*, **1**, 61 (1977).
14) C. Ainsworth, F. Chen, and Y.-N. Kuo, *J. Organomet. Chem.*, **46**, 59 (1972); Y. Kita, J. Segawa, J. Haruta, T. Fujii, and Y. Tamura, *Tetrahedron Lett.*, **21**, 3779 (1980).
15) S. Danishefsky, K. Vaughan, R. Gadwood, and K. Tsuzuki, *J. Am. Chem. Soc.*, **103**, 4136 (1981).
16) R. Wasylishen and T. Schaefer, *Can. J. Chem.*, **50**, 274 (1972).
17) R. G. Cooks and A. G. Varvoglis, *Org. Mass Spectrum.*, **5**, 687 (1971) [*Chem. Abstr.*, **75**, 81574*p* (1971)].
18) N. P. Kostyuchenko, A. F. Oleinik, T. I. Vozyakova, and K. Y. Novitskii, *Khim. Geterotsikl. Soedin.*, **1974**, 312 [*Chem. Abstr.*, **81**, 3251*r* (1974)].
19) G. W. Perold, A. P. Steyn, and F. V. K. von Reiche, *J. Am. Chem. Soc.*, **79**, 462 (1957).
20) F. Texier-Boullet, *Synthesis*, **1985**, 679.
21) E. Hungerbuhler and D. Seebach, *Helv. Chim. Acta*, **64**, 687 (1981).
22) L. W. Jones and M. C. Sneed, *J. Am. Chem. Soc.*, **39**, 674 (1917).
23) T. Ploński and A. Chimiak, *Tetrahedron Lett.*, **1974**, 2453.
24) O. Exner, *Chem. Listy*, **50**, 779 (1956) [*Chem, Abstr.*, **50**, 15477*f* (1956)].