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Synthesis of the Tricyclic ABC Ring Subunit of Mazamine A

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Abstract: A new approach to the construction of the pyrrolo[2, 3 -i] isoquinoline, the core structure of manzamine A, is described.

Introduction

Manzamine A, isolated from the Okinawan marine sponge *Haliclona sp.* by Higa in 1986 [1] and independently by Nakamura in 1987 from the marine sponge *Pellina sp.* [2], is a structurally complex polycyclic alkaloid with cytotoxic, antileukemic and antibacterial activities. Its unique structure and significant biological activity have stimulated many synthetic studies, culminating in the syntheses of several fragments and subunits. From a review of the papers published, there are two main strategies, Diels-alder reaction [3-13] and asymmetric synthesis [14-21], involved in the approach to the total synthesis of manzamine A. Generally, the tricyclic ABC ring, the core structure of manzamine A, was chosen as the first synthetic target because it consists of all of the five stereogenic carbons. We have previously tried the Diels-Alder reaction route [22] and were prompted to investigate a new strategy towards the total synthesis of manzamine A. In this paper, we report the synthesis of the pyrrolo[2,3-i] isoquinoline, the core structure of manzamine A, as outlined in Scheme 1.

Results and Discussion

Cyclopentenone as a commercially available starting material in the route to the synthesis of the tricyclic ABC ring subunit **I** of manzamine A was treated with a Grignard reagent, derived from the reaction of 2-(3-chloropropyl)-1,3-dioxolane with magnesium, and the resulting enolate further reacted face-selectively with allyl bromide to only afford a trans-isomer **2** [23] (Scheme 2). Treatment of the compound **2** with aqueous hydrochloric acid induced sequential acetal hydrolysis and intramolecular aldol condensation, thus giving the bicyclic annulation product **3** [24, 25]. Under these conditions, only the α-hydroxy isomer was produced. Alcohol **5**, which could be easily prepared under normal reactions, reacted with SESNHBoc under Mitsunobu conditions [26] to offer carbamate **6** in 52% yield. The lower yield was due to steric hindrance of the

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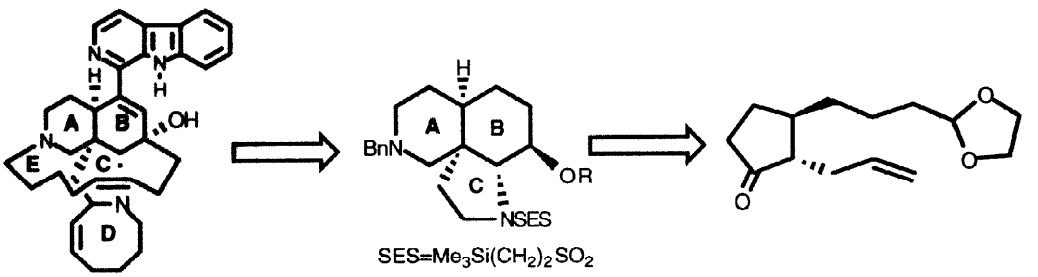
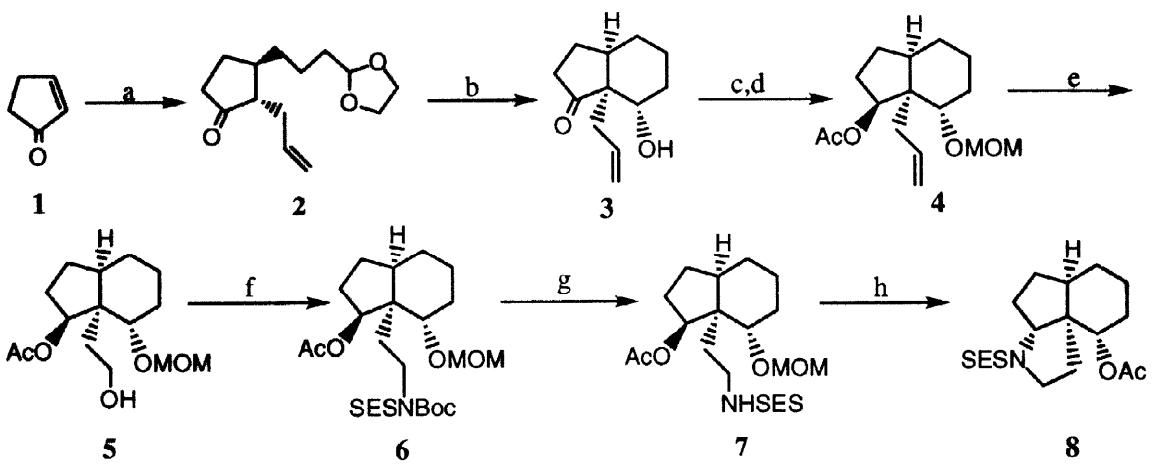
protective group MOM at the β-position. With sulfonamide **7**, which was produced by removal of the protective group Boc with magnesium chloride [27], in hand, we attempted to eliminate the protective group MOM with TFA in dichloromethane. However, the desired product was not formed and only unexpected tricyclic compound **8** was yielded.



Scheme 1.

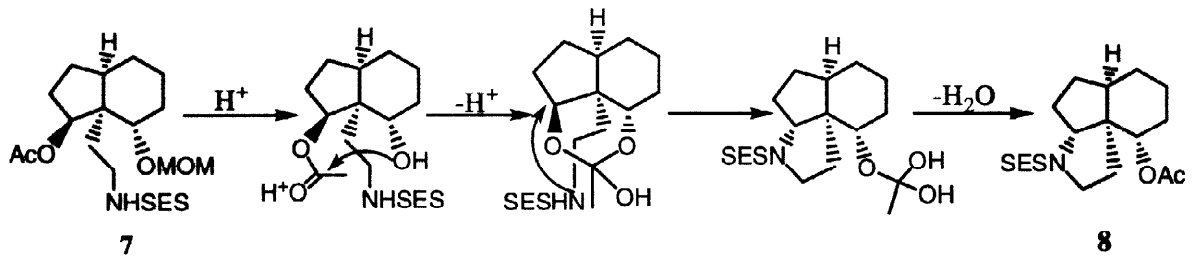


(a) 2-(3-chloropropyl)-1,3-dioxolane, Mg, THF; CuBr • Me_2S, Me_2S; Allyl bromide, HMPA; (b) 2N HCl, CH_3COCH_3, 78%; (c) MOMCl, $^iPr_2NEt$, CH_2Cl_2, 75%; (d) $NaBH_4$, MeOH; Ac_2O, Et_3N, CH_2Cl_2, ~100% in 2 steps; (e) OsO_4, NMO, CH_3COCH_3:H_2O=10:1; $NaIO_4$, THF; $NaBH_4$, MeOH, 99% in 3 steps; (f) SESNHBoc, Ph_3P, DEAD, THF, 52%; (g) $MgCl_2$, CH_3CN, reflux, 86%; (h) TFA, CH_2Cl_2, 81%.

Scheme 2.

The reaction probably underwent a six-membered cyclic intermediate to generate the compound **8** (Scheme 3). At first, the protective group MOM was removed in a proton medium, and then the resulting

hydroxy group attacked the protonated carbonyl group in an intramolecular manner to form the six-membered cyclic intermediate. Finally, the nitrogen atom replaced the oxygen atom on the five-membered ring *via* a just-behind nucleophilic attack, resulting in the formation of a new five-membered heterocycle containing a nitrogen atom, followed by dehydration to afford the tricyclic compound **8** which was recrystallized from a mixed solvent of hexane and chloroform to provide colourless crystals whose structure was unambiguously determined by an X-ray crystallographic analysis (Fig. 1).



7 8

Scheme 3.

Therefore, we adjusted the route to the tricyclic ABC ring subunit **I** of manzamine A, as outlined in Scheme 4. The compound **3** was converted into olefin **9** by subsequent protection of the hydroxy group with acetic anhydride, reduction of the carbonyl with sodium borohydride and protection of the resulting alcohol with chloromethyl methyl ether. Since the acetate group of **9** was at the α-position, it would impede the later Mitsunobu reaction. In order to effect a smooth Mitsunobu reaction, the α-acetate group of **9** should be trasformed into its β-isomer to decrease the hindrance.

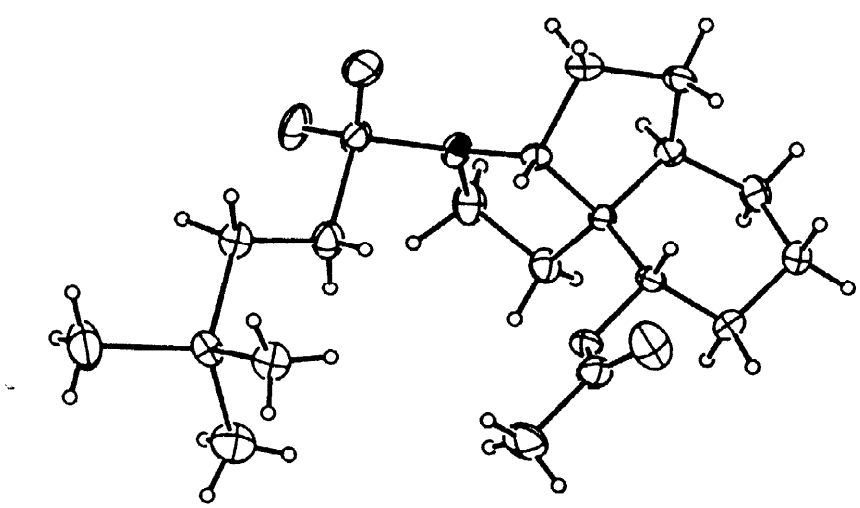
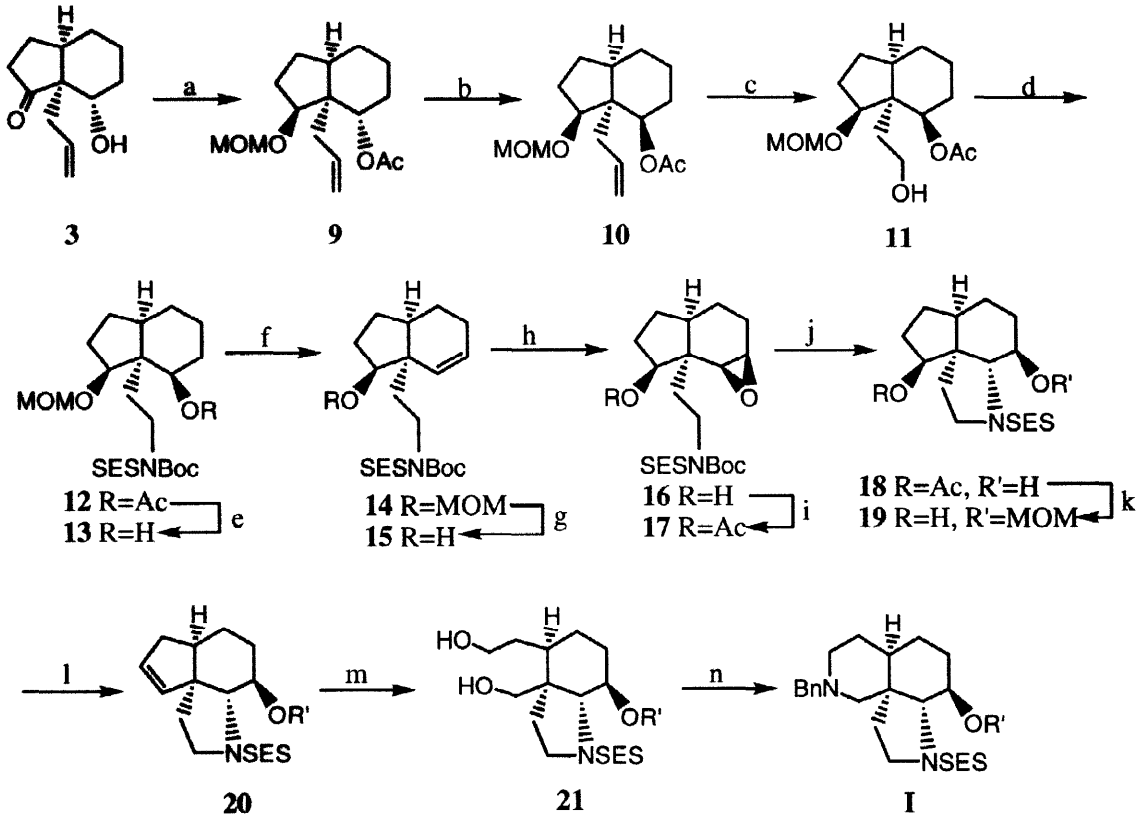


Fig. 1 The ORTEP Drawing of 8



(a) Ac_2O, Et_3N, DMAP, CH_2Cl_2, 81%; $NaBH_4$, MeOH; MOMCl, $^iPr_2NEt$, CH_2Cl_2, 93% in 2 steps; (b) 2N LiOH (aq.), MeOH; Swern Oxid., 86% in 2 steps; $NaBH_4$, MeOH; Ac_2O, Et_3N, DMAP, CH_2Cl_2, 93% in 2 steps; (c) OsO_4, NMO; $NaIO_4$, THF; $NaBH_4$, MeOH, 90% in 3 steps; (d) SESNHBoc, Ph_3P, DEAD, THF, 100%; (e) 2N LiOH (aq.), MeOH, 94%; Boc_2, Et_3N, CH_2Cl_2, 84%; (f) MsCl, Et_3N, CH_2Cl_2; DBU, PhH, 60 °C, 84% in 2 steps; (g) *p*-TsOH, MeOH, 90%; (h) $VO(acac)_2$, TBHP, PhH, reflux; (i) Ac_2O, Et_3N, DMAP, CH_2Cl_2; (j) $MgCl_2$, CH_3CN, reflux, 50% in 3 steps; (k) MOMCl, $^iPr_2NEt$, CH_2Cl_2; 2N LiOH (aq.), MeOH, 82% in 2 steps; (l) MsCl, Et_3N, CH_2Cl_2; DBU, PhH, reflux, 60% in 2 steps; (m) O_3, CH_2Cl_2, -78 °C and then Me_2S; $NaBH_4$, MeOH, 67% in 2 steps; (n) MsCl, Et_3N, CH_2Cl_2; $BnNH_2$, KF, DMF, ~60 °C, 69% in 2 steps.

Scheme 4.

The conversion of the α-isomer **9** into the β-isomer **10** was easily carried out under normal conditions in high yield. Oxidative cleavage of the double bond of the olefin **10** with osmium tetroxide and sodium periodate, followed by reduction of the resulting aldehyde with sodium borohydride, gave alcohol **11**. Just as we anticipated, treatment of the alcohol **10** with SESNHBoc under the Mitsunobu conditions afforded carbamate **12** in almost quantitative yield. Although many trials were carried out to remove the acetyl group selectively in the presence of the protective group Boc, the results were not satisfactory. When the

compound **12** was treated with 2N aqueous lithium hydroxide in methanol, both protective groups Ac and Boc were eliminated. The resulting product was protected with Boc_2O again to offer acohol **13** in very good overall yield. The olefin **14** was easily prepared by mesylation of **13** with methanesulfonyl chloride, followed by treatment with DBU [28]. With the olefin **14** in hand , we attempted to remove the protective group MOM selectively so that we could carry out stereoselective epoxidation of the homoallyl alcohol in the next step. *p*-Toluenesulfonic acid was found to be a proper deprotective reagent. It could effectively remove the protective group MOM to give the homoallylic acohol **15** in high yield. Although the epoxidation of the homoallylic alcohol **15** with *t*-butyl hydroperoxide in the presence of transition metal vanadium [29, 30] as a catalyst only afforded the desired epoxide **16**, it was difficult to know when the reaction finished since the spots of both the starting material and the epoxide **16** on the TLC plate were at the same position. In addition, the epoxide **16** was not stable under the reaction condition. After the epoxidation of **15** was quenched, the product was directly used for the next experiments until a stable tricyclic compound **18** was obtained without purification. When the protective group Boc was cleaved with magnesium chloride in anhydrous acetonitrile, the resulting nitrogen anion spontaneously attacked the epoxide to give a ring-closure product **18**. Now, we have prepared the B and C rings of the tricyclic ABC ring subunit **I** and next we will construct its A ring, a six-membered azacycle.

In order to construct the A ring, the five-membered carbon ring has to be opened and a nitrogen atom is then introduced to close the six-membered ring A. After the compound **18** was transformed into alcohol **19** under normal reaction conditions, we found that a mixture of α- and β-mesylates was produced when **19** was treated with methanesulfonyl chloride in dichloromethane at -20 °C and the reaction temperature was gradually elevated to room temperature. Higher reaction temperature was needed to convert the α-mesylate into olefin **20** than in the case of the β-isomer. With the olefin **20** in hand, we wished to cleave the double bond to open the five-membered carbon ring. Several attempts were made to cleave the double bond of **20** however, no positive results were obtained. Finally, we found that ozone was a good cleaving reagent only in dry dichloromethane at -78 °C. The olefin **20** was treated with ozone, followed by reduction of the resulting ozonide with sodium borohydride, to afford diol **21**. The tricyclic ABC ring subunit **I** of manzamine A was successfully synthesized by treatment of the mesylate of the diol **21** with benzyl amine [31, 32].

Experimental Section

General. Infrared(IR) spectra were recorded on a Jasco A-202 spectrophotometer and are recorded in cm^{-1}. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded on JNM-EX 270 and JNM-α 400 instruments. They were also used for recording carbon nuclear magnetic resonance(^{13}C-NMR) spectra. Chemical shifts are given in ppm downfield from tetramethylsilane(TMS). Coupling constants are given in Hz. ^{1}H-NMR shift correlation spectroscopy (COSY), double resonance and ^{1}H-^{13}C correlation experiments were occasionally used for signal assignments. HRMS measurements were performed on a Hitachi M-80 instrument. THF was distilled from sodium metal and dichloromethane was distilled from phosphorous

pentoxide. Benzene was dried over sodium metal. Reactions requiring an inert atmosphere were carried out under argon. Column chromatography was performed using 70-230 mesh silica gel.

***trans*-2-Allyl-3-[3-(1,3-dioxolan-2-yl)propylcyclopentanone (2).** To a solution of 43.0 g (0.2 mol) of pyridinium chlorochromate in 100 ml of dichloromethane was dropwise added another solution of 11.0 g (0.1 mol) of 4-chloro-1-butanol in 100 ml of dichloromethane and the resulting mixture was stirred at room temperature for 4 hours. Ether was added and filtered through a celite bed. The filtrate was concentrated *in vacuo* to give the crude corresponding aldehyde.

To a solution of the aldehyde in 120 ml of benzene were added 17 ml of ethylene glycol and 1.2 g of *p*-toluenesulfonic acid. The resulting mixture was stirred under reflux with a water-separator overnight and then cooled to room temperature. Ethyl acetate was added and the mixture was washed with brine, dried over sodium sulfate and concentrated *in vacuo*. The residue was chromatographed, eluting with hexane-ethyl acetate (2:1), to give 7.0 g of 2-(3-chloropropyl)-1,3-dioxolane (47% in 2 steps) as a colourless oil. ^{1}H-NMR(270 MHz, $CDCl_3$), δ 4.89(1H, t, J=4.29), 3.91(4H, m), 3.58(2H, t, J=6.27), 1.84(4H, m).

To a solution of 4.0 g (0.17 mol) of magnesium in 35 ml of dry THF were added 1 ml of newly distilled 2-(3-chloropropyl)-1,3-dioxolane and 0.5 ml of ethyl iodide respectively under argon, and the resulting mixture was lightly refluxed until the reaction took place. The mixture was then stirred at room temperature and another 22 ml of new distilled 2-(3-chloropropyl)-1,3-dioxolane was added to keep the reaction mixture under light reflux (the mixture was heated to reflux if needed). After addition, the mixture was stirred at 60 °C until the magnesium was exhausted completely, and cooled to room temperature to give a Grignard reagent solution.

The above Grignard reagent solution was diluted with 30 ml of dry THF under argon and cooled to -75 °C. A solution of 6.4 g of copper bromide(I) with dimethyl sulfide complex in 58 ml of dry dimethyl sulfide was added slowly under stirring at -75 °C over 1 hour. After the addition, the resulting mixture was stirred at -75 °C for 1 hour and another solution of 11.5 ml of newly distilled cyclopentenone in 23 ml of dry THF was then added dropwise over 40 minutes. The mixture was stirred at -75 °C for an additional 3 hours. Next, 55 ml of dry hexamethylphosphoramide and 30 ml of dry allyl bromide were added respectively at -75 °C and the reaction mixture was stirred until the temperature rose gradually up to room temperature. The reaction was quenched with saturated aqueous ammonium chloride and the mixture was extracted with ethyl acetate. The combined extracts were washed with brine, dried over sodium sulfate and concentrated *in vacuo*. The residue was subjected to silica gel column chromatography, eluting with hexane-ethyl acetate (3:2), to give 18.2 g of the cyclopentanone **2** (52%) as a pale yellow oil. IR(film), υ 3080, 2980, 1740, 1640 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 5.66(1H, m), 5.00(1H, d, J=15.83), 4.96(1H, d, J=7.92), 4.82(1H, t, J=4.30), 3.87(4H, m), 2.31(3H, m), 2.10(2H, m), 1.78(6H, m), 1.35(3H, m); HRMS(M^+) calcd. for $C_{14}H_{22}O_3$ 238.1568, found 238.1573.

1α-Allyl-6α-hydro-9-oxobicyclo[4.3.0]nonan-2α-ol (3). A mixture of 0.32 g (1.34 mmol) of the cyclopetanone derivative **2**, 0.5 ml of 2N aqueous HCl and 5 ml of acetone was stirred at 50 °C for 24 hours. The mixture was then cooled to room temperature and extracted with ethyl acetate. The combined extracts were washed with saturated aqueous sodium bicarbonate and brine, dried over sodium sulfate, concentrated *in vacuo* and chromatographed, eluting with hexane-ethyl acetate (3:2), to afford 0.21 g (81%) of the alcohol **3** as a colourless oil. IR(film), υ 3500, 3100, 2950, 1730, 1640cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 5.52(1H, m), 5.07(1H, d, J=16.83), 5.05(1H, d, J=11.55), 2.72(1H, dd, J=6.27, 14.18), 2.40(2H, m), 2.16(2H, m), 1.81(2H, m), 1.54(6H, m); ^{13}C-NMR(270 MHz, $CDCl_3$), δ 216.7, 134.5, 118.2, 75.8, 62.2, 44.0, 39.8, 36.7, 31.2, 29.7, 26.5, 22.5;); HRMS(M^+) calcd. for $C_{12}H_{18}O_2$ 194.1305, found 194.1269.

9β-Acetoxy-1α-allyl-6α-hydro-2α-methoxymethoxybicyclo[4.3.0]nonane (4). To a solution of 0.12 g (0.62 mmol) of the alcohol **3** in 3 ml of dichloromethane were added 0.21 ml (1.2 mmol) of ethyldiisopropylamine and 0.1 ml (1.2 mmol) of chloromethyl methyl ether respectively. The resulting mixture was stirred at room temperature overnight, and the solvent was then removed under reduced pressure. The residue was subjected to silica gel column chromatography, eluting with hexane-ethyl acetate (2:1), to give 0.11 g of a protected product as a colourless oil in 75% yield. ^{1}H-NMR(270 MHz, $CDCl_3$), δ 5.59(1H, m), 5.02(1H, d, J=15.50), 5.01(1H, d, J=10.87), 4.63(1H, d, J=6.93), 4.49(1H, d, J=6.93), 3.70(1H, t, J=4.29), 3.32(3H, s), 2.72(1H, dd, J=5.94, 14.68), 2.42(1H, ddd, J=5.94, 9.24, 19.46), 2.20(3H, m), 1.80(2H, m), 1.58(5H, m), 1.30(1H, m).

To a solution of 0.74 g (3.1 mmol) of the protected product in 20 ml of methanol was added sodium borohydride in batches at -10 °C until the starting material was reduced completely. Excess amount of sodium borohydride was treated with saturated aqueous ammonium chloride and the mixture was extracted with ethyl acetate. The combined extracts were washed with brine, dried over sodium sulfate and concentrated *in vacuo* to give the crude corresponding alcohol.

To the alcohol were added 15 ml of dry toluene, 2 ml of pyridine and 1.2 ml of acetic anhydride respectively. The resulting mixture was stirred at 80 °C overnight. The solvent was removed under reduced pressure and the residue was subjected to silica gel column chromatography, eluting with hexane-ethyl acetate (2:1), to offer 0.78 g (89%) of the acetate **4**. IR(film), υ 3057, 2950, 1740, 1640 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 5.84(1H, m), 5.00(2H, m), 4.83(1H, d, J=6.93), 4.60(1H, d, J=6.60), 3.70(1H, m), 3.37(3H, s), 2.42(1H, dd, J=6.93, 14.18), 2.15(2H, m), 2.01(3H,s), 1.86(2H, m), 1.51(8H, m); HRMS(M^+) calcd. for $C_{16}H_{26}O_4$, 282.1830, found 282.1890.

9β-Acetoxy-1α-(2-hydroxy)ethyl-6α-hydro-2α-methoxymethoxybicyclo[4.3.0]nonane (5). To a solution of 0.78 g (2.77 mmol) of **4** and 0.65 g (5.53 mmol) of 4-methylmorpholine N-oxide in 15 ml of a mixed solvent (acetone:water=10:1) in an ice-bath was added 1 ml of osmium tetroxide in *t*-butanol (0.2 M), and the resulting mixture was stirred under argon in the ice-bath overnight. Sodium hydrogensulfite was then added and stirred for an additional half an hour. Water was added to dissolve the salt and the mixture was

extracted three times with ethyl acetate. The combined extracts were washed successively with 5% aqueous acetic acid, saturated aqueous sodium bicarbonate and brine, dried over sodium sulfate and concentrated *in vacuo* to give the crude corresponding diol.

To a solution of the diol in 15 ml of THF in an ice-bath was added another solution of 1.18 g (5.53 mmol) of sodium periodate in 7 ml of water, and the resulting mixture was stirred in the ice-bath for 1 hour. Ethyl acetate and water were then added and the water layer was extracted with ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate and concentrated *in vacuo* to leave the crude corresponding aldehyde.

To a solution of the aldehyde in 15 ml of methanol was added sodium borohydride in batches at -50 °C ~ -30 °C until the aldehyde was reduced completely, and the reaction was then quenched with saturated aqueous ammonium chloride. The mixture was extracted with ethyl acetate and the combined extracts were washed with brine, dried over sodium sulfate, concentrated *in vacuo* and chromatographed, eluting with hexane-ethyl acetate-methanol (2:10:1), to give 0.78 g of the alcohol **5** in 99% overall yield as a colourless oil. IR(film), υ 3500, 2980, 1750 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 5.09(1H, t, J=8.57), 5.88(1H, d, J=6.60), 4.67(1H, d, J=6.93), 3.70(3H, m), 3.47(1H, m), 3.40(3H, s), 2.25(2H, m), 2.03(3H, s), 1.88(2H, m), 1.59(9H, m).

***t*-Butyl *N*-2-[(9β-acetoxy-6α-hydro-2α-methoxymethoxy)bicyclo[4.3.0]nonan-1α-yl] ethyl, *N*-2-(trimethylsilyl)ethanesulfonylcarbamate (6).** To a solution of 6 mg of the alcohol **5**, 5 mg of *t*-butyl 2-(trimethylsilyl)ethanesulfonylcarbamate, SESNHBoc and 10 mg of triphenylphosphine in 0.5 ml of dry THF under argon in an ice-bath was added 10 μl of diethyl azodicarboxylate slowly, and the resulting mixture was stirred in the ice-bath for half an hour and then at room temperature overnight. The solvent was removed under reduced pressure and the residue was separated on TLC plate, eluting with hexane-ethyl acetate (1:1), to give 6 mg of the carbamate **6** in 52% yield. ^{1}H-NMR(270 MHz, $CDCl_3$), δ 5.00(1H, t, J=7.58), 4.77(1H, d, J=6.60), 4.58(1H, d, J=6.60), 3.86(1H, m), 3.63(3H, m), 3.34(2H, m), 3.33(3H, s), 2.20(2H, m), 2.01(3H, s), 1.90(2H, m), 1.58(, 9H, m), 1.50(9H, s), 0.95(2H, m), 0.03(9H, s).

***N*-[2-(9β-Acetoxy-6α-hydro-2α-methoxymethoxy)bicyclo[4.3.0]nonan-1α- y l] e t h y l 2 - (trimethylsilyl)ethanesulfonamide (7).** A mixture of 0.14 g (0.26 mmol) of the carbamate **6**, 60 mg (1.0 mmol) of magnesium chloride and 5 ml of dry acetonitrile was stirred under reflux for 5 hours and then cooled to room temperature. Ethyl acetate was added and the mixture was washed with brine, dried over sodium sulfate and concentrated *in vacuo*. The residue was subjected to silica gel column chromatography, eluting with hexane-ethyl acetate (1:1), to give 90 mg of the sulfonamide **7** in 82% yield. IR(film), υ 3400, 2930, 1740 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 5.10(1H, t, J=8.58), 4.92(1H, t, J=6.54), 4.82(1H, d, J=7.60), 4.63(1H, d, J=6.93), 3.70(1H, m), 3.37(3H, s), 3.20(2H, m), 2.90(2H, m), 2.20(1H, m), 2.04(2H, m), 2.03(3H, s), 1.91(2H, m), 1.55(8H, m), 1.02(2H, m), 0.04(9H, s); HRMS(M^+) cald. for $C_{20}H_{39}NO_6SiS$ 449.2264, found 449.2257.

The tricyclic compound 8. To a solution of 5 mg of the sulfonamide **7** in 0.5 ml of dichloromethane was added 50 μl of triflouroacetic acid, and the resulting mixture was stirred at room temperature for 2.5 hours. The reaction was then quenched with saturated aqueous sodium bicarbonate and the mixture was extracted with ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate, concentrated *in vacuo* and chromatographed, eluting with hexane-ethyl acetate (2:1), to leave 3.5 mg of the ring-closing product **8** in 81% yield as white solid. m.p. 103-105 °C; IR(film), υ 2950, 1740cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 4.80(1H, dd, J=3.96, 10.56), 3.85(1H, dd, J=7.59, 11.22), 3.61(1H, m), 3.36(1H, m), 2.84(2H, m), 2.21(3H, m), 2.05(3H, s), 1.65(9H, m), 1.33(1H, m), 1.01(1H, m), 0.03(9H, s); ^{13}C-NMR(270 MHz, $CDCl_3$), δ 170.6, 71.9, 66.9, 57.5, 48.0, 47.1, 43.2, 32.5, 29.7, 28.9, 28.8, 24.6, 21.3, 19.9, 10.0, -2.0; HRMS(M^+) calcd. for $C_{18}H_{33}NO_4SiS$ 387.1897, found 387.1812. Crystal data for **8** ($C_{18}H_{33}NO_4SiS$) are as follows: monoclinic, P2/c; a = 10.134 (2), b = 20.269 (1), c = 10.457 (1) Å; b = 97.57 (1)°, V = 2129.2 (6) Å^3; R = 0.055 for 2637 reflections. Tables of atomic parameters, bond lengths and bond angles have been deposited with The Cambridge Crystallographic Data Centre.

2α-Acetoxy-1α-allyl-6α-hydro-9β-methoxymethoxybicyclo[4.3.0]nonane (9). To a solution of 3.0 g (15.5 mmol) of the alcohol **3** in 50 ml of dry dichloromethane were added 4.5 ml (31.0 mmol) of triethylamine, 0.3 g (3.1 mmol) of 4-dimethylaminopyridine and 3.0 ml (3.1 mmol) of acetic anhydride respectively and the resulting mixture was stirred at room temperature for 6 hours. The reaction was quenched with saturated aqueous sodium bicarbonate and the mixture was extracted with ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate, concentrated *in vacuo* and chromatographed, eluting with hexane-ethyl acetate (2:1), to give 2.94 g (81%) of the corresponding acetate. IR(film), υ 3070, 2930, 1740, 1640 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 5.54(1H, m), 5.03(1H, t, J=6.72), 5.01(1H, d, J=10.22), 5.00(1H, d, J=16.82), 2.50(2h, m), 2.14(3H, m), 2.01(3H, s), 1.90(2H, m), 1.57(5H, m), 1.30(1H, m). HRMS(M^+-AcOH) calcd. for $C_{14}H_{20}O_3$ 176.1199, found 176.1176.

To a solution of 7.26 g (30.8 mmol) of the acetate in 75 ml of methanol was added sodium borohydride in batches at -20 °C ~ -10 °C until the starting material was reduced totally. The reaction was quenched with saturated aqueous ammonium chloride and the mixture was extracted with ethyl acetate. The combined extracts were washed with brine, dried over sodium sulfate and concentrated *in vacuo* to afford the crude corresponding alcohol.

To a solution of the alcohol in 75 ml of dichloromethane were added 11 ml of ethyldiisopropylamine and 5.2 ml of chloromethyl methyl ether respectively, and the resulting mixture was stirred at room temperature overnight. Saturated aqueous ammonium chloride was added and the aqueous layer was extracted with ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate, concentrated *in vacuo* and chromatographed, eluting with hexane-ethyl acetate (2:1), to give 8.09 g of the acetate **9** in 93% yield in 2 steps as a colourless oil. IR(film), υ 3120, 2950, 1730, 1650 cm^{-1}. ^{1}H-NMR(270 MHz, $CDCl_3$), δ 5.81(1H, m), 5.19(1H, dd, J=4.62, 10.72), 5.10(1H, d, J=11.55), 5.09(1H, d, J=16.51), 4.54(2H, d, J=12.22), 4.52(1H, d, J=12.22), 3.84(1H, t, J=8.25), 3.33(3H, s), 2.53(1H, dd, J=7.26, 14.52), 2.28(1H, dd, J=7.26, 14.19),

2.03(2H, m), 2.01(3H, m), 1.80-1.35(9H, m); ^{13}C-NMR(270 MHz, $CDCl_3$), δ 170.2, 134.1, 118.0, 95.3, 81.5, 69.5, 55.2, 37.7, 32.1, 27.5, 26.5, 23.5, 22.7, 21.5, 18.8; HRMS(M^+) calcd. for $C_{16}H_{26}O_4$ 282.1829, found 282.1770.

2β-Acetoxy-1α-allyl-6α-hydro-9β-methoxymethoxybicyclo[4.3.0]nonane (10). A mixture of 7.34 g (26.0 mmol) of **9** and 2N aqueous lithium hydroxide in 60 ml of methanol was stirred at ~50 °C for 19 hours. The mixture was then cooled to room temperature and extracted with ethyl acetate. The combined extracts were washed with brine, dried over sodium sulfate, concentrated *in vacuo* and chromatographed, eluting with hexane-ethyl acetate 2:1), to give 6.27 g of the corresponding alcohol in quantitative yield. IR(film), υ 3550, 3150, 2950, 1635 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 5.81(1H, m), 5.10(1H, d, J=10.56), 5.09(1H, d, J=16.50), 4.65(1H, d, J=17.82), 4.63(1H, d, J=17.82), 3.99(2H, m), 3.38(3H, s), 2.52(1H, dd, J=7.59, 14.36), 2.24(1H, dd, J=7.59, 14.35), 2.10(1H, m), 1.90(1H, m), 1.80-1.35(9H, m); ^{13}C-NMR(270 MHz, $CDCl_3$), δ 133.5, 117.2, 95.0, 82.2, 68.2, 54.5, 47.8, 36.2, 29.4, 27.5, 26.3, 22.5, 22.4, 18.3; HRMS(M^+) calcd. for $C_{14}H_{24}O_3$ 240.1724, found 240.1727.

To a solution of 16.1 ml (0.16 mol) of oxalyl chloride in 190 ml of dry dichloromethane under argon was slowly added 26 ml of dry dimethyl sulfoxide at -75 °C. After addition, the mixture was stirred at this temperature for 1 hour and another solution of 6.27 g (26.3 mmol) of the above alcohol in 100 ml of dry dichloromethane was then added dropwise. The mixture was stirred at -75 °C for 1 hour. Next, 55 ml of dry triethylamine was added and the reaction mixture was gradually warmed to -25 °C under stirring for 6 hours and quenched with saturated aqueous ammonium chloride. The mixture was elevated to room temperature and extracted with ethyl acetate. The combined extracts were washed with brine, dried over sodium sulfate, concentrated *in vacuo* and chromatographed, eluting with hexane-ethyl acetate (2:1), to give 5.36 g of the corresponding ketone in 86% yield. IR(film), υ 3125, 2980, 1710, 1650cm^{-1}; ^{1}H-NMR(270MHz, $CDCl_3$), δ 5.55(1H, m), 5.03(2H, m), 4.49(1H, d, J=12.44), 4.47(1H, d, J=12.44), 3.91(1H, t, J=2.64), 3.25(3H, s), 2.78(1H, dd, J=5.61, 13.2), 2.25(3H, m), 2.05-1.50(9H, m); HMRS(M^+) calcd. for $C_{14}H_{22}O_3$ 238.1567, found 238.1558.

To a solution of 0.2 g (0.79 mmol) of the ketone in 3 ml of methanol was added sodium borohydride in batches at -20 °C ~ -10 °C until the ketone was reduced totally. The reaction was quenched with saturated aqueous ammonium chloride and the mixture was extracted with ethyl acetate after it was warmed to room temperature. The combined extracts were washed with brine, dried over sodium sulfate and concentrated *in vacuo* to give crude alcohol.

To a solution of the above alcohol in 3 ml of dichloromethane were added 0.35 ml (2.4 mmol) of triethylamine, 20 mg of 4-dimethylaminopyridine and 0.16 ml (1.6 mmol) of acetic anhydride respectively and the resulting mixture was stirred at room temperature for 6 hours. Saturated aqueous ammonium chloride was added and the mixture was extracted with ethyl acetate. The combined extracts were washed with brine,

dried over sodium sulfate, concentrated *in vacuo* and chromatographed, eluting with hexane-ethyl acetate (2:1), to afford 0.18 g of the acetate **10** in 93% yield in 2 steps. IR(film), υ 3080, 2950, 1740, 1640cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 5.77(1H, m), 5.04(1H, d, J=10.6), 4.93(1H, d, J=16.1), 4.95(1H, t, J=4.96), 4.59(2H, s), 3.86(1H, dd, J=4.95, 8.91), 3.34(3H, s), 2.01(3H, s), 1.70(7H, m), 1.49(2H, m), 1.30(1H, m); ^{13}C-NMR(270 MHz, $CDCl_3$), δ 169.2, 133.5, 117.6, 95.8, 84.0, 72.7, 54.8, 49.4, 40.3, 39.0, 30.4, 27.2, 27.0, 26.4, 21.1, 18.9; HRMS(M^+) calcd. for $C_{16}H_{26}O_4$ 282.1830, found 282.1890.

2α-Acetoxy-1α-(2-hydroxy)ethyl-6α-hydro-9β-methoxymethoxybicyclo[4.3.0]nonane (11). To a solution of 4.92 g of **10** in 90 ml of a mixed solvent (acetone:water=10:1) in an ice bath were added 4.0 g of 4-methylmorpholine N-oxide and 4.5 ml of osmium tetroxide in *t*-butanol (0.2 M) respectively and the resulting mixture was stirred under argon in the ice bath for 18 hours. Sodium hydrogensulfide was added and the mixture was stirred in the ice bath for an additional one hour. Ethyl acetate and water were added and the aqueous layer was extracted with ethyl acetate. The combined organics were washed successively with 5% aqueous acetic acid, saturated aqueous sodium bicarbonate and brine, dried over sodium sulfate and concentrated *in vacuo* to give crude diol.

To a solution of the above diol in 150 ml of THF in an ice bath was added another solution of 7.3 g of sodium periodate in 44 ml of water and the resulting mixture was stirred in the ice bath for 2 hours. Water was added and the aqueous layer was extracted with ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate and concentrated *in vacuo* to afford crude aldehyde.

To a solution of the above aldehyde in 40 ml of methanol was added sodium borohydride in bacthes at -50 °C ~ -40 °C until the aldehyde was reduced completely and the reaction was then quenched with saturated aqueous ammonium chloride and the mixture was extracted with ethyl acetate. The combined extracts were washed with brine, dried over sodium sulfate and concentrated *in vacuo*. The residue was subjected to silica gel column chromatography, eluting with hexane-ethyl acetate-methanol (2:10:1), to give 4.48 g of the alcohol **11** in 90% yield in 3 steps as a colourless oil. IR(film), υ 3500, 2980, 1750 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 5.13(1H, t, J=5.61), 4.62(2H, dt, J=6.60, 6.27), 3.69(1H, dd, J=5.28, 8.91), 3.70(2H, m), 3.37(3H, s), 2.31(1H, br.), 2.09(1H, m), 2.04(3H, s), 1.90-1.45(11H, m), 1.33(1H, m); ^{13}C-NMR(270 MHz, $CDCl_3$), δ 169.4, 95.8, 85.5, 72.1, 57.9, 55.0, 47.6, 40.8, 38.8, 29.7, 26.5, 25.2, 21.1, 17.4, 14.7; HRMS(M^+) calcd. for $C_{15}H_{26}O_5$ 286.1778, found 286.1871.

***t*-Butyl *N*-2-(2β-acetoxy-6α-hydro-9β-methoxymethoxybicyclo[4.3.0]nonan-1α-yl) ethyl *N*-2-(trimethylsilyl)ethanesulfonylcarbamate (12).** To a solution of 4.48 g (15.7 mmol) of **11**, 12.1 g of triphenylphosphine and 6.41 g of t-butyl 2-(trimethylsilyl) ethanesulfonylcarbamate, SESNHBoc in 120 ml of dry THF under argon in an ice bath was added 2.7 ml of diethyl azodicarboxylate slowly and the resulting mixture was stirred in the ice bath for half an hour and then at room temperature overnight. The solvent was removed under reduced pressure and the residue was subjected to silica gel column chromatography, eluting with hexane-ethyl (2:1), to give 9.26 g of the carbamate **12** in quantitative yield. ^{1}H-NMR(270 MHz,

$CDCl_3$), δ 5.00(1H, s, br), 4.62(2H, q, J=6.60), 3.90(1H, dd, J=5.30, 8.58), 3.70(2H, m), 3.32(3H, s), 3.29(2H, m), 2.10(1H, m), 2.02(3H, s), 1.90-1.40(12H, m), 1.49(9H, s), 0.87(2H, m), 0.04(9H, s).

***t*-Butyl *N*-2-[6α-hydro-2α-hydroxy-9β-methoxymethoxybicyclo[4.3.0]nonan-1α-yl] ethyl 2-(trimethylsilyl)ethanesulfonylcarbamate (13).** To a solution of 2.56 g of **12** in 40 ml of methanol was added 30 ml of 2N aqueous lithium hydroxide and the resulting mixture was stirred at ~ 65 °C for 11 hours. The mixture was extracted with ethyl acetate after it was cooled to room temperature. The combined extracts were washed with brine, dried over sodium sulfate, concentrated *in vacuo* and chromatographed, eluting with hexane-ethyl acetate (1:2), to give 2.41 g of the corresponding sulfonamide in 94% yield in 2 steps. IR(film), υ 3550, 3180, 2950, 1742 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 4.95(1H, t, J=6.27), 4.67(2H, s), 4.12(1H, dd, J=3.96, 8.58), 3.78(1H, dt, J=4.29, 6.27), 3.40(3H, s), 3.18(2H, dt, J=6.93, 6.27), 3.07(1H, d, J=6.27), 2.91(2H, m), 2.11(1H, m), 1.90(1H, m), 1.80-1.55(8H, m), 1.44(2H, m), 1.25(1H, m), 0.99(2H, m), 0.04(9H, s); ^{13}C-NMR(270 MHz, $CDCl_3$), δ 95.4, 84.7, 69.4, 54.8, 48.7, 46.9, 41.3, 37.4, 36.5, 30.3, 29.3, 26.9, 25.7, 17.5, 9.05, -2.3; HRMS(M^+) calcd. for $C_{18}H_{37}NO_5SiS$ 407.2160, found 407.2196.

To a solution of 4.50 g (11.1 mmol) of the sulfonamide, 1.8 ml of dry triethylamine and 0.3 g of 4-dimethylaminopyridine in 50 ml of dry dichloromethane under argon in an ice bath was added another solution of 3.0 ml of di-*t*-butyl dicarbonate in 20 ml of dry dichloromethane and the resulting mixture was stirred in the ice bath for 1.5 hours. Saturated aqueous ammonium chloride was added and the mixture was extracted with ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate and concentrated *in vacuo*. The residue was subjected to silica gel column chromatography, eluting with hexane-ethyl acetate (2:1), to give 4.7 g of the carbamate **13** in 84% yield. IR(film), υ 3570, 2900, 1730 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 4.70(2H, d, J=1.65), 4.14(1H, dd, J=4.29, 8.58), 3.82(1H, br), 3.73(2H, t, J=8.25), 3.40(3H, s), 3.36(2H, m), 3.02(1H, d, J=4.62), 2.15(1H, m), 1.99(1H, m), 1.90-1.43(10H, m), 1.48(9H, s), 1.30(1H, m), 0.95(2H, m), 0.06(9H, s); ^{13}C-NMR(270 MHz, $CDCl_3$), δ 150.2, 95.6, 85,2, 83.3, 69.8, 55.2, 50.3, 49.2, 43.5, 41.6, 36.5, 30.8, 29.7, 27.1, 27.0, 25.5, 16.8, 10.3, -2.2; HRMS(M^+) calcd. for $C_{23}H_{45}NO_7SiS$ 507.2683, found 507.2674.

***t*-Butyl *N*-2-(6α-hydro-9β-methoxymethoxybicyclo[4.3.0]non-2-en-1α-yl)ethyl *N*-2-(trimethylsilyl) ethanesulfonylcarbamate (14).** To a solution of 1.89 g (3.4 mmol) of **13** in 25 ml of dry dichloromethane were added 1.2 ml of dry triethylamine and 0.6 ml (7.5 mmol) of methanesulfonyl chloride respectively at -50 °C and the resulting mixture was gradually warmed to room temperature under stirring for 15 hours. The reaction was quenched with saturated aqueous ammonium chloride and the aqueous phase was extracted with ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate and concentrated *in vacuo* to leave the crude corresponding mesylate.

To a solution of the mesylate in 25 ml of dry benzene was added 1.5 ml of 1,8-diazabicyclo[5.4.0]-7-undencene and the resulting mixture was stirred under argon at 60 °C for 21 hours. The reaction mixture was

cooled to room temperature and the solvent was removed under reduced pressure. The residue was subjected to silica gel column chromatography, eluting with hexane-ethtyl acetate (2:1), to afford 1.54 g of the olefin **14** in 85% yield in 2 steps as a pale yellow oil. IR(film), υ 2950, 1725 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 5.87(1H, m), 5.60(1H, d, J=10.23), 4.65(2H, s), 3.65(3H, m), 3.35(2H, m), 3.30(3H, s), 2.01-1.40(11H, m), 1.45(9H, s), 0.94(2H, m), 0.03(9H, s); ^{13}C-NMR(270 MHz, $CDCl_3$), δ 150.2, 128.5, 127.7, 95.3, 84.8, 83.4, 54.8, 49.5, 45.1, 43.5, 38.8, 37.3, 28.6, 27.2, 23.5, 23.4, 20.3, 9.8, -2.4; HRMS(M^+) calcd. for $C_{23}H_{43}NO_6SiS$ 489.2577, found 489.2552.

***t*-Butyl *N*-2-(6α-hydro-9β-hydroxy)bicyclo[4,3,0]non-2-en-1α-yl)ethyl *N*-2-(trimethylsilyl)ethane sulfonylcarbamate (15).** A mixture of 0.11 g of **14**, 10 mg of *p*-toluenesulfonic acid and 1 ml of methanol was stirred at room temperature for 24 hours. The solvent was removed under reduced pressure and the residue was subjected to silica gel column chromatography, eluting with hexane-ethyl acetate (2:1), to give 90 mg of the alcohol **15** in 90% yield. IR(film), υ 3550, 2950, 1730, 1450 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 6.03(1H, dt, J=11.22, 5.56), 5.56(1H, d, J=11.23), 3.75(3H, m), 3.35(2H, m), 1.95(2H, m), 1.78(4H, m), 1.57(5H, m), 1.53(9H, s), 0.95(2H, m), 0.04(9H, s); ^{13}C-NMR(270 MHz, $CDCl_3$), δ 151.2, 131.5, 127.2, 83.8, 80.3, 50.2, 46.7, 43.5, 39.3, 38.3, 31.2, 27.5, 25.5, 25.3, 21.0, 10.3, -2.3; HRMS(M^+) calcd. for $C_{21}H_{39}NO_5SiS$ 445.2316, found 445.2409.

3aβ, 4β -(2'β-Acetoxy)cyclopentano-7β-hydroxy-4α, 5, 6, 7α , 7aβ -pentahydro-1-[2-(trimethylsilyl)ethanesulfonyl]indoline (18). To a solution of 0.53 g (1.19 mmol) of **15** and 0.28 g of $VO(acac)_2$ in 8 ml of benzene was added 1.7 ml of *t*-butyl hydroperoxide in toluene (3.59 M) dropwise at room temperature and the resulting mixture was stirred under reflux until the colour of the reaction solution changed from deep red to green. The reaction mixture was then cooled to room temperature and diluted with ethyl acetate. The mixture was washed with aqueous sodium hydrogensulfite solution and brine, dried over sodium sulfate, and concentrated *in vacuo* to give crude epoxide.

To a solution of the epoxide and 0.51 ml of dry triethylamine in 9 ml of dichloromethane in an ice bath were added 46 mg of 4-dimethylaminopyridine and 0.24 ml of acetic anhydride respectively, and the resulting mixture was stirred in the ice bath for 1 hour. Saturated aqueous sodium bicarbonate was added and the mixture was extracted with ethyl acetate. The combined extracts were washed with brine, dried over sodium sulfate and concentrated *in vacuo* to give the corresponding acetate.

A mixture of the above acetate and 0.73 g of magnesium chloride in 30 ml of dry acetonitrile was stirred under argon at 80°C for 20 hours and then cooled to room temperature. The mixture was diluted with ethyl acetate and washed with brine, dried over sodium sulfate, concentrated *in vacuo* and chromatographed, eluting with hexane-ethyl acetate (1:1), to give 0.24 g of the tricyclic compound **18** in 50% yield in 3 steps. IR(film), υ 3500, 2900, 1740 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 4.91(1H, t , J=6.60), 3.86(1H, d, J=8.91), 3.45(2H, m), 3.30(1H, t, J=9.24), 3.05(2H, m), 2.13(3H, s), 2.07(3H, m), 1.90-1.49(8H, m), 1.03(2H, m),

0.04(9H, s); ^{13}C-NMR(270 MHz, $CDCl_3$), δ 170.5, 80.7, 73.2, 63.7, 52.8, 48.8, 45.5, 38.3, 34.7, 28.6, 27.5, 25.3, 23.3, 20.7, 9.5, -2.2; HRMS(M^+) calcd. for $C_{18}H_{33}NO_5SiS$ 403.1847, found 403.1886.

3aβ, 4β-(2'β-Hydroxy)cyclopentano-7β-methoxymethoxy-4α, 5, 6, 7α, 7aβ-pentahydro-1-[2-(trimethylsilyl)ethanesulfonyl]indoline (19). To a solution of 0.17 g (0.42 mmol) of **18** in 4 ml of dry dichloromethane in an ice bath were added 0.33 ml of ethyldiisopropylamine and 0.15 ml of chloromethyl methyl ether respectively, and the resulting mixture was stirred at room temperature for 8 hours. Ethyl acetate was added and the mixture was washed with brine, dried over sodium sulfate and concentrated *in vacuo* to leave a residue.

A mixture of the above residue and 0.6 ml of 2N aqueous lithium hydroxide in 1 ml of methanol was stirred at room temperature for 24 hours. The mixture was extracted with ethyl acetate and the combined extracts were washed with brine, dried over sodium sulfate, concentrated *in vacuo* and chromatographed, eluting with hexane-ethyl acetate (1:1), to give 0.14 g of the alcohol **19** in 82% yield in 2 steps. IR(film), υ 3470, 2950 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 4.72(2H, d, J=3.30), 4.02(1H, br), 3.92(1H, d, J=4.52), 3.84(1H, t, J=4.92), 3.73(1H, m), 3.39(3H, s), 3.21(1H, m), 2.95(2H, m), 1.94-1.56(11H, m), 1.05(2H, m), 0.05(9H, s); ^{13}C-NMR(270 MHz, $CDCl_3$), δ 94.4, 80.1, 73.7, 60.8, 54.5, 47.0, 45.6, 38.4, 37.0, 31.5, 27.3, 24.2, 9.3, -2.5; HRMS(M^+) calcd. for $C_{18}H_{35}NO_5SiS$ 405.2003, found 405.1976.

3aβ, 4β-Cyclopenta-2'-eno-7β-methoxymethoxy-4α, 5, 6, 7α , 7aβ-pentahydro-1-[2-(trimethylsilyl)ethanesulfonyl]indoline (20). To a solution of 0.47 g (1.16 mmol) of **19** in 15 ml of dry dichloromethane were added 2.4 ml of dry triethylamine and 0.8 ml of methanesulfonyl chloride respectively at -70 °C, and the resulting mixture was stirred at -70 °C for half an hour and stirred in an ice bath for 4 hours. The reaction was quenched with saturated aqueous ammonium chloride and the mixture was extracted with ethyl acetate. The combined extracts were washed with brine, dried over sodium sulfate and concentrated *in vacuo* to provide a residue.

A mixture of the above residue and 0.4 ml of 1,8-diazabicyclo[5.4.0]-7-undencene in 20 ml of dry benzene was stirred under argon at 60 °C for 24 hours. The solvent was removed under reduced pressure and the residue was subjected to silica gel column chromatography, eluting with hexane-ethyl acetate (2:1), to give 0.27 g of the olefin **20**. IR(film), υ 3050, 2950, 1450 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 5.77(2H, s), 4.70(2H, d, J=1.65), 3.81(1H, m), 3.57(2H, m), 3.36(3H, s), 3.31(3H, m), 3.01(3H, m), 2.40(1H, dd, J=7.92, 18.15), 2.18(2H, m), 1.94-1.50(6H, m), 1.05(2H, m), 0.04(9H, s); ^{13}C-NMR(270 MHz, $CDCl_3$), δ 135.8, 129.3, 95.7, 76.8, 67.0, 56.8, 55.3, 48.8, 46.5, 40.7, 36.9, 34.7, 25.5, 22.6, 10.0, -1.8; HRMS(M^+) calcd. for $C_{18}H_{33}NO_4SiS$ 387.1897, found 387.1708.

4β-(2-Hydroxy)ethyl-3aβ-hydroxymethyl-7β-methoxymethoxy-4α, 5, 6, 7α, 7aβ-pentahydro-1-[2-(trimethylsilyl)ethanesulfonyl]indoline (21). To a solution of 47 mg of **20** in 4 ml of dry dichloromethane was introduced ozone at -78 °C until the starting material was oxidated totally. Dimethyl sulfide was then

added and the resulting mixture was stirred at room temperature for 3 hours. The solvent was removed under reduced pressure to give the corresponding ozonide.

To a solution of the ozonide in 1 ml of methanol was added sodium borohydride in batches at 0 °C ~ room temperature until the ozonide was reduced completely. The reaction was then quenched with saturated aqueous ammonium chloride and the mixture was extracted with ethyl acetate. The combined extracts were washed with brine, dried over sodium sulfate, concentrated *in vacuo* and chromatographed, eluting with hexane-ethyl acetate (1:5), to give the diol **21** in 67% yield in 2 steps. IR(film), υ 3550, 2980 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 4.74(2H, q), 4.36(1H, s, br), 3.81(1H, m), 3.78(1H, d), 3.65(3H, m), 3.41(3H, s), 3.34(2H, m), 2.90(2H, m), 1.80(2H, m), 1.65(5H, m), 1.56(2H, m), 1.03(2H, m), 0.04(9H, s); ^{13}C-NMR(270 MHz, $CDCl_3$), δ 96.1, 73.5, 67.0, 66.1, 60.8, 55.8, 49.2, 47.4, 46.8, 33.8, 33.2, 31.8, 25.0, 21.8, 9.9, -2.0.

2-Benzyl-3, 4, 4aα, 5, 6, 7α, 7aβ, 9, 10-nonahydro-8-[2-(trimethylsilyl)ethanesulfonyl] pyrrolo[2, 3-i]isoqinoline (I). To a solution of 10 mg of **21** in 1 ml of dry dichloromethane in an ice bath were added 80 μl of dry triethylamine and 20 μl of methanesulfonyl chloride respectively, and the resulting mixture was stirred under argon in the ice bath for 3.5 hours. Saturated aqueous ammonium chloride was added and the aqueous layer was extracted with ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate and concentrated *in vacuo* to give the corresponding dimesylate.

To a solution of the above dimesylate in 0.5 ml of N,N-dimethylformamide were added 14 mg of potassium flouride and 26 μl of benzylamine respectively, and the resulting mixture was stirred at 60 °C for 6 hours. The mixture was diluted with ethyl acetate and washed with brine, dried over sodium sulfate and concentrated *in vacuo*. The residue was subjected to thin layer chromatography, eluting with hexane-ethtyl acetate (1:3), to give 8 mg of the tricyclic ABC subunit **I** in 69% yield in 2 steps. IR(film), υ 3060, 2950, 1640, 1490 cm^{-1}; ^{1}H-NMR(270 MHz, $CDCl_3$), δ 7.29(5H, m), 4.71(2H, s), 3.70(3H, m), 3.37(3H, s), 3.32(2H, m), 2.93(3H, m), 2.14(2H, m), 1.85(2H, m), 1.57(9H, m), 1.05(2H, m), 0.03(9H, s); HRMS(M^+) calcd. for $C_{25}H_{42}N_2O_4SiS$ 494.2631, found 494.2439.

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