118 (110), 117 (20), 116 (28), 91 (26), 39 (21), can be compared to that of 3-phenylpropene, m/e 118 (80.7), 117 (100), 115 (35), 91 (68), 39 (23). The NMR spectrum of **9**, 3.37, 5.05, 7.22, can be compared to that of 3-phenylpropene δ 3.32, 5.03, 5.68~6.18, 7.71.

Reaction of **9** (P = 15 W, av r = 0.8 mmol/min) was followed by GC collection, NMR, and MS analysis. The ^{1}H NMR spectrum of the cyclopropylbenzene-d_1 was δ 0.69, 0.94, 7.05, and 7.22. The ^{2}H NMR spectrum had one peak at δ 1.91. These chemical shifts can be compared to those of cyclopropylbenzene δ 0.53, 0.68, 1.64, 6.94, and 7.09. The mass spectrum, m/e (relative intensity) 119 (80.8), 118 (100), 117 (21.1), 116 (29.2), 92 (35.5), 91 (37.6), 51 (25.4), 39 (24.7), can be compared to that of cyclopropyl benzene, m/e (relative intensity) 118 (79.4), 117 (100), 115 (30.2), 91 (21.2), 39 (29.3).

Acknowledgment. This work was supported by the National Science Foundation.

Registry No. **1**, 591-93-5; **5**, 300-57-2; **6**, 873-49-4; **7**, 60604-09-3; **9**, 60468-24-8; **10**, 35024-14-7; indene, 95-13-6; 2-lithio-3-phenylpropene, 63883-88-5.

Synthesis of (2*R*,3*S*,22*R*,23*R*)- and (2*R*,3*S*,22*S*,23*S*)-2,3,22,23-Tetrahydroxy-*B*-homo-7a-oxa-5α-ergostan-7-ones, Two New Brassinolide Analogues

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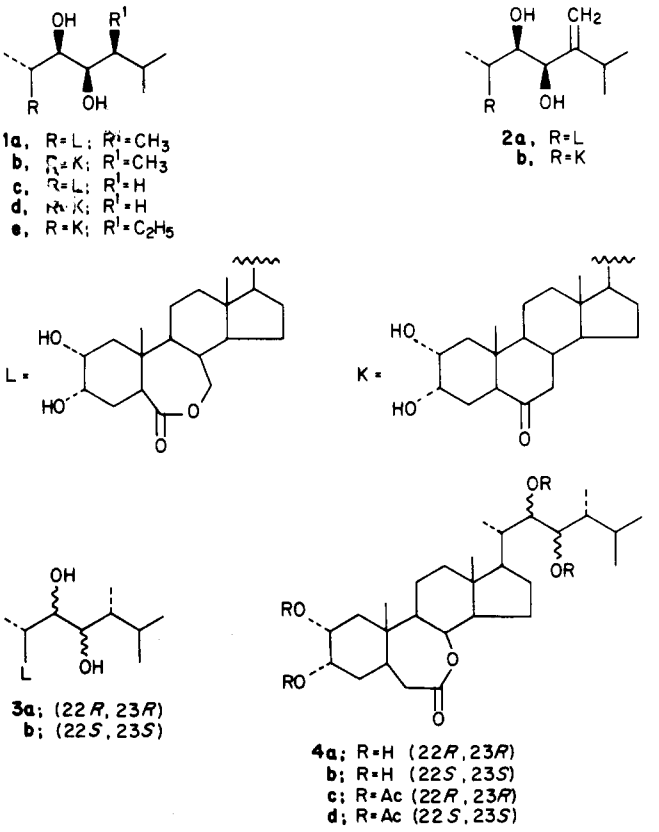
(2*R*,3*S*,22*R*,23*R*)- and (2*R*,3*S*,22*S*,23*S*)-2,3,22,23-tetrahydroxy-*B*-homo-7a-oxa-5α-ergostan-7-ones (**4a** and **4b**) were synthesized starting from the 5α-ergosta-2,7,22-triene (**7**). Osmilation of the 2,7,22 double bonds of **7** afforded the two hexols **6** which were rearranged by acidic treatment to (2*R*,3*S*,22*R*,23*R*)- and (2*R*,3*S*,22*S*,23*S*)-2,3,22,23-tetrahydroxy-5α-ergostan-7-ones (**5a** and **5b**) whose structures were determined by chemical methods. Baeyer–Villiger oxidation of the 7-oxo group of **5a** and **5b** afforded **4a** and **4b**, respectively. The triene **7** was obtained in pure form by dehydrotosylation of the 3β-hydroxy-3′,5′-dioxo-4′-phenyl-5,8[1′,2′]-1′,2′,4′-triazolidino-5α,8α-ergosta-6,22-diene 3-*p*-toluenesulfonate (**8**) and subsequent reduction with lithium dissolved in liquid ammonia of the obtained 3′,5′-dioxo-4′-phenyl-5,8[1′,2′]-1′,2′,4′-triazolidino-5α,8α-ergosta-2,6,22-triene (**9**).

The past few years have seen an increasing interest in plant growth promoting compounds which led to the discovery of a new class of plant growth steroidal hormones including brassinolide (**1a**)[1-4] and other closely related steroids such as catasterone (**1b**),[2-5] dolicholide (**2a**),[6,7] dolichosterone (**2b**),[6,7] 28-norbrassinolide (**1c**),[8] brassinone (**1d**),[8] (24*S*)-24-ethylbrassinone (**1e**),[8] and typhasterol (2-deoxycastasterone).[9]

Syntheses of brassinolide (**1a**), dolicholide (**2a**), and many brassinolide analogues (Chart I) have already been reported by different laboratories.[10-25] Structure–activity relationships of brassinosteroids with respect to the stereochemistry of the side chain were investigated by using

Chart I



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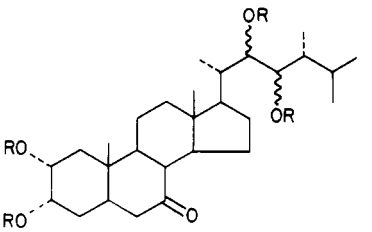
a number of bioassay systems[15,16,22] and indicate that the brassinolide isomer **3a** possessing an inverted configuration of the methyl group at C-24 is about one-tenth as active as brassinolide. The brassinolide isomer **3b** possessing an inverted configuration of the methyl group at C-24 and of the hydroxyl groups at C-22 and C-23 is as active as **3a**. On the other hand a 6-oxo or a 7-oxa-6-oxo system in ring B with cis-oriented hydroxyl groups at C-2 and C-3 were reported as necessary structural features.[16] However, isomeric compounds of brassinolide containing a 7a-oxa-7-oxo in ring B have not been available until now for testing. In the present paper we describe a facile synthesis of (2*R*,3*S*,22*R*,23*R*)- and (2*R*,3*S*,22*S*,23*S*)-2,3,22,23-tetrahydroxy-*B*-homo-7a-oxa-5α-ergostan-7-ones (**4a** and **4b**), two new isomers of brassinolide, utilizing a steroidal starting material. The structural modifications of **4a** and **4b** permit an evaluation of the structural specificity of the biological activity associated with the lactone group.

Since Baeyer–Villiger oxidation of 3β-acetoxy-5α-cholestan-7-one was reported[26] to result in C-8 migration with the formation of a 7a-oxa-7-oxo as in **4a** and **4b**, the tetrahydroxy ketones **5a** and **5b** appeared to be appropriate precursors of **4a** and **4b**.

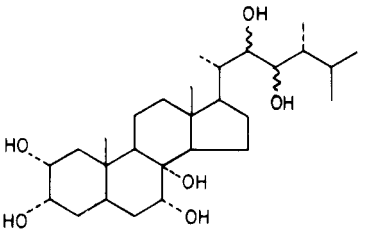
In turn the 7-keto group of **5a** and **5b** could be obtained by acidic rearrangement of the 7α,8α-glycol of the isomeric hexols **6** (Chart II). It is well-known that the 2α,3α- and 22,23-glycols are stable to acids, whereas a 7α,8α-glycol is transformed into a 7-ketone by exposure to acids via a pinacol–pinacolone rearrangement.[27,28] Hexols **6** should be accessible by oxidation with osmium tetraoxide of the ergostatriene **7**. An α-orientation of the hydroxyl groups at the 2,3,7,8-positions could be assumed on the general tendency for rear approach of osmium tetraoxide to the steroidal nucleus, while the double bond in the side chain could suffer both α and β attacks.[10,20]

With this in mind we attempted the preparation of triene **7**. A short route appeared to be the dehydrotosylation of 3β-hydroxy-5α-ergosta-7,22-diene 3-*p*-toluenesulfonate. However, either by treatment with different types of alumina[29] or with organic bases such as *sim*-collidine[30] or tetramethylguanidine, a mixture (NMR)[29] of $\Delta^{2,7,22}$- and $\Delta^{3,7,22}$-trienes was obtained, and the route was found to be unsatisfactory, because the $\Delta^{2,7,22}$ compound was difficult to separate from the $\Delta^{3,7,22}$ isomer. An alternative approach based on treatment with lithium hydride[31] of 5α-ergosta-7,22-dien-3-one 3-tosylhydrazone, resulted in a $\Delta^{2,7,22}$-triene similarly contaminated by the $\Delta^{3,7,22}$ isomer. In light of these unpromising results, it was decided to obtain the triene **7** first introducing the Δ^2 and then the Δ^7 double bond starting with 3β-hydroxy-3′,5′-dioxo-4′-phenyl-5,8[1′,2′]-1′,2′,4′-triazolidino-5α,8α-ergosta-6,22-diene 3-*p*-toluenesulfonate (**8**) prepared in two

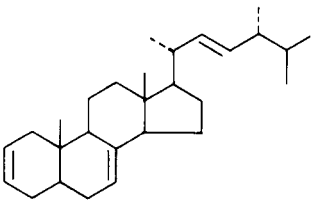
Chart II



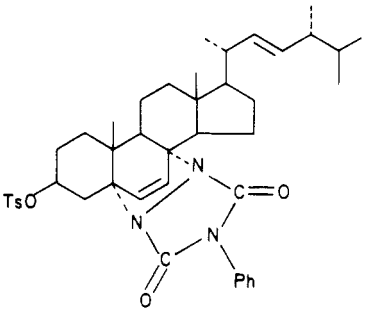
5a; R = H (22*R*, 23*R*)
b; R = H (22*S*, 23*S*)
c; R = Ac (22*R*, 23*R*)
d; R = Ac (22*S*, 23*S*)



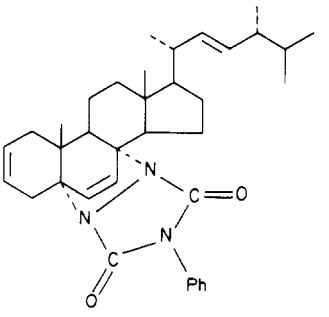
6 (22*R*, 23*R*) and (22*S*, 23*S*)



7



8



9

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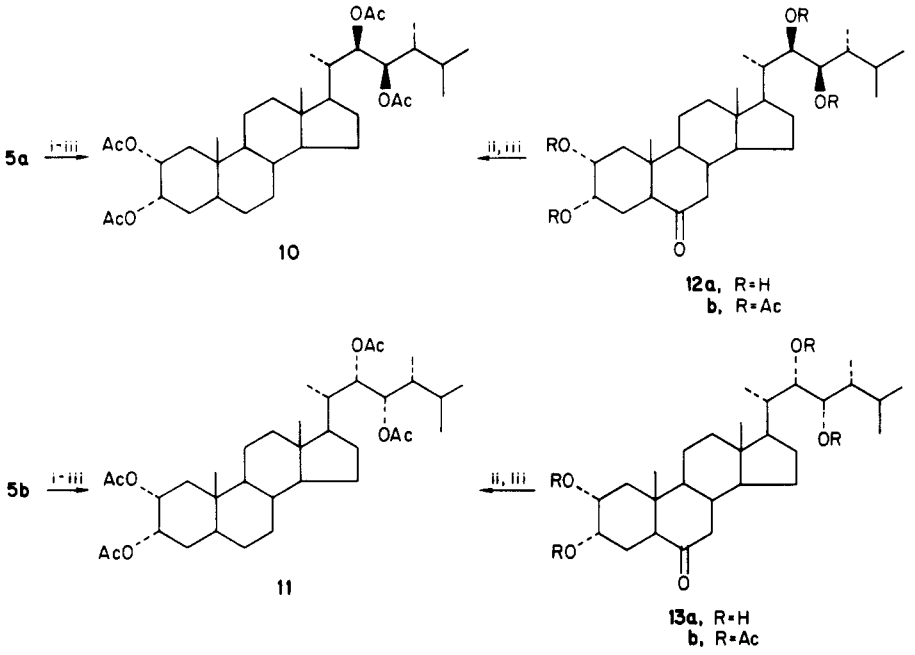
Scheme I[a]



[a] (i) Ac_2OPy; (ii) $HSCH_2CH_2SHBF_3 \cdot Et_2O$; (iii) n-Bu_3SnH.

steps from ergosterol. We hoped that the dehydrotosylation of **8** could result in the regiospecific formation of a Δ^2 double bond owing to the presence of a bulky substituent at the 5α,8α-positions of the steroid nucleus. The successive reduction of the urazole adduct with lithium dissolved in liquid ammonia[32] would have given the triene **7**. Compound **8**, when reacted with basic alumina, afforded 3′,5′-dioxo-4′-phenyl-5,8[1′,2′]-1′,2′,4′-triazolidino-5α,8α-ergosta-2,6,22-triene (**9**) uncontamined by the Δ^3-isomer.

Reduction of adduct **9** with lithium dissolved in liquid ammonia at −70 °C afforded the desired 5α-ergosta-2,7,22-triene (**7**) in good yield. The NMR spectrum of **7** exhibits a two-proton signal at δ 5.60 for the vinyl protons at C-2 and C-3 and signals at δ 5.10–5.30 for the three protons at C-7, C-22, and C-23. The chemical shifts observed for the C-18 and C-19 angular methyl groups also show good agreement with values calculated[29,33] for **7**.

Since *N*-methylmorpholine *N*-oxide and catalytic amount of osmium tetraoxide[12] failed to oxidize the Δ^7 double bond of the triene **7**, we oxidized **7** with 3 equiv of osmium tetraoxide in pyridine. The reaction proceeded slowly to give, after 5 days, a mixture of the osmate esters of hexols **6**. The structure of **6** was assigned on the basis of the reactivity of the 5α-ergosta-2,22-dien-6-one in the osmilation[10,20] and on the expected overall cis addition of the osmium tetraoxide to the α-side of the Δ^7 double bond.[28] Hexol mixture **6** showed two spots on TLC, which could be isolated only in part by column chromatography, the compounds being held strongly by silica. For this reason we did not separate them and used the mixture in the next reaction. Rearrangement of the crude mixture **6**, in dioxane containing hydrochloric acid, produced a separable mixture of the expected tetrahydroxy ketones of assigned structures (2*R*,3*S*,22*R*,23*R*)- and (2*R*,3*S*,22*S*,23*S*)-2,3,22,23-tetrahydroxy-5α-ergostan-7-ones (**5a** and **5b**). Compounds **5a** and **5b** show the correct physicochemical properties.

The orientations of the hydroxy groups at C-22 and C-23 of the more polar isomer **5a** and of the less polar **5b** (in the used solvent mixture) were assigned by chemical correlation (Scheme I). The tetrahydroxy ketones **5a** and **5b** were acetylated, and the ketone groups of the acetates **5c** and **5d** were eliminated by tri-*n*-butyltin hydride reduction of the corresponding thioketal. Comparison of the physicochemical properties of the obtained tetraacetoxy steroids with those of the compounds **10** and **11** obtained by a similar sequence of reactions starting with (2*R*,3*S*,22*R*,23*R*)- and (2*R*,3*S*,22*S*,23*S*)-2,3,22,23-tetrahydroxy-5α-ergostan-6-ones (**12a** and **13a**)[10,20] allowed the assignment of the configuration 22*R*,23*R* to **5a** and 22*S*,23*S* to **5b**.[34]

Having established the configuration of **5a** we subjected its tetraacetate **5c** to a Baeyer–Villiger oxidation in dichloromethane with trifluoroperacetic acid, for 1 h at room temperature. The reaction afforded as the only isolable substance the tetraacetoxy lactone **4c** which was purified by rapid column chromatography. The lactone structure is in agreement with the NMR (200 MHz) spectrum which shows a one-proton double doublet (J = 10.5 and 8.4 Hz) at δ 4.18 assigned to the 8β hydrogen of **4c**. The splitting is consistent with that expected for the β hydrogen at C-8 with two similar axial interactions with the hydrogens at C-9 and C-14, and the dihedral angles of about 180° showed by the Dreiding model of **4c**. In addition a one-proton double doublet was present at δ 2.72 assigned to the 6β-hydrogen (J = 10 and 15 Hz), the larger coupling corresponding to the geminal interaction and the slightly smaller splitting being due to the coupling with the 5α-hydrogen.

The tetraacetate **4c** was saponified with methanolic potassium hydroxide and subsequently acidified with concentrated hydrochloric acid to afford the title compound **4a**. When the tetraacetoxy ketone **5d** was subjected to a similar reaction sequence the 22*S*,23*S* compound **4b** was obtained.

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(34) Prof. G. Snatzke confirmed this assignment by means of the computer-assisted CD spectra obtained from **5a** and **5b** (about 1 mg each) in the presence of their molybdenum acetate complexes in Me_2SO solutions. He is going to publish this result.

Biological testing of **4a** and **4b** as plant growth promotors is in progress.

Experimental Section

All melting points are uncorrected. Infrared spectra were recorded on solutions in chloroform or Nujol mulls, and absorptions are reported as reciprocal centimeters; NMR spectra were recorded in chloroform-*d* or in pyridine-d_5 solutions and are reported in δ units relative to Me_4Si. Optical rotations were taken on chloroform solutions. The progress of all reactions and column chromatography (silica 230–400 mesh) was monitored by TLC on silica gel (HF_{254}) plates. Hexane–ethyl acetate mixtures were used as developing solvents and spots were detected by spraying with 70% sulfuric acid followed by heating.

3β-Hydroxy-3′,5′-dioxo-4′-phenyl-5,8[1′,2′]-1′,2′,4′-triazolidino-5α,8α-ergosta-6,22-diene 3-*p*-Toluenesulfonate (8). 3β-Hydroxy-3′,5′-dioxo-4′-phenyl-5,8[1′,2′]-1′,2′,4′-triazolidino-5α,8α-ergosta-6,22-diene[35] (8 g) dissolved in pyridine (100 mL) at 0 °C was treated with *p*-toluenesulfonyl chloride (8.3 g). The mixture was then allowed to warm to 23 °C and was stirred for a further 21 h. Workup afforded the tosylate **8** (8.5 g): mp 119–121 °C (from methanol); IR 1740, 1683, 1420 cm^{-1}; NMR δ 7.20–7.95 (9 H, m, overlapping, Ar H), 6.40 and 6.24 (2 H, AB q, 6- and 7-H; J_{AB} = 9 Hz), 5.10–5.25 (2 H, m, 22- and 23-H), 2.40 (3 H, s, CH_3Ph).

Anal. Calcd for $C_{43}H_{55}N_3O_5S$: C, 71.17; H, 7.59; N, 5.79. Found: C, 71.25; H, 7.81; N, 5.75.

3′,5′-Dioxo-4′-phenyl-5,8[1′,2′]-1′,2′,4′-triazolidino-5α,8α-ergosta-2,6,22-triene (9). The tosylate **8** (1 g) dissolved in toluene (20 mL) was shaken with basic alumina (17 g; grade 1) for 10 h. After filtration and repeated washing with ethyl acetate, the solution was evaporated to afford compound **9** (0.6 g) which, after crystallization from methanol, showed mp 144–146 °C; IR 1740, 1683, 1420 cm^{-1}; NMR δ 7.25–7.45 (5 H, m, Ar H), 6.40 and 6.24 (2 H, AB q, 6- and 7-H; J_{AB} = 9 Hz), 5.75 (2 H, m, 2- and 3-H), 5.10–5.25 (2 H, m, 22- and 23-H), 0.85 (6 H, s, 18- and 19-CH_3).

Anal. Calcd for $C_{36}H_{47}N_3O_2$: C, 78.12; H, 8.50; N, 7.51. Found: C, 78.25; H, 8.46; N, 7.51.

5α-Ergosta-2,7,22-triene (7). The adduct **9** (8.7 g) dissolved in dioxane (10 mL) was reacted with lithium (5 g) dissolved in liquid ammonia (250 mL) at −70 °C. After 7 h, usual workup and chromatography afforded the triene **7** (4 g) which showed mp 117–119 °C (from methanol): $[\alpha]^{20}_D$ 12 (*c* 1); NMR δ 5.60 (2 H, m, 2- and 3-H), 5.10–5.30 (3 H, m, 7-, 22-, and 23-H), 0.59 (3 H, s, 18-CH_3; calcd[29,33] 0.584), 0.80 (3 H, s, 19-CH_3; calcd[29,33] 0.776); mass spectrum, *m/e* (relative intensity) 380 (M^+), 365, 253, 105 (100).

Anal. Calcd for $C_{28}H_{44}$: C, 88.42; H, 11.58. Found: C, 88.36; H, 11.64.

(2*R*,3*S*,22*R*,23*R*)- and (2*R*,3*S*,22*S*,23*S*)-2,3,22,23-Tetrahydroxy-5α-ergostan-7-ones (5a and 5b). The triene **7** (900 mg) dissolved in pyridine (40 mL) was treated with osmium tetraoxide (2 g). The mixture was stirred at room temperature for 5 days in the dark. Then it was diluted with hexane, and the osmate esters were filtered, washed with hexane, and dissolved into a mixed solvent of ethanol and dichloromethane (1:1, 100 mL). Hydrogen sulfide was bubbled through the solution for 5 h. The formed mixture was filtered through Celite and the black residue was washed with ethanol–dichloromethane (1:1). The solvent was evaporated and the residue was dissolved in dioxane (20 mL) containing hydrochloric acid (25 μL, 37%). After 2 h the solvent was evaporated at reduced pressure, and the obtained solid was chromatographed (eluting with 50% acetone–dichloromethane) to afford **5a** and **5b**. (2*R*,3*S*,22*S*,23*S*)-2,3,22,23-Tetrahydroxy-5α-ergostan-7-one (**5b**) (500 mg): mp 142–146 °C (at 112–114 °C sintered) (from diisopropyl ether); IR 3500, 1710 cm^{-1}; NMR) δ 4.20 (1 H, m), 3.98 (2 H, m), 3.60 (1 H, m); mass spectrum, *m/e* 464 (M^+).

Anal. Calcd for $C_{28}H_{48}O_5$: C, 72.37; H, 10.41. Found: C, 72.40; H, 10.50.

The tetraacetate **5d** showed mp 124–126 °C; NMR δ 5.35–4.70 (4 H, m, overlapping, 2-, 3-, 22-, and 23-H), 2.06 (3 H, s, CH_3CO), 2.00 (6 H, s, 2 × CH_3CO), 1.98 (3 H, s, CH_3CO).

Anal. Calcd for $C_{36}H_{56}O_9$: C, 68.33; H, 8.92. Found: C, 68.40; H, 9.10.

(2*R*,3*S*,22*R*,23*R*)-2,3,22,23-Tetrahydroxy-5α-ergostan-7-one (5a) (480 mg): mp 233–236 °C (from diisopropyl ether); IR 3500, 1710 cm^{-1}; NMR (C_5D_5N) δ 4.20 (1 H, m), 3.98 (2 H, m), 3.60 (1 H, m); mass spectrum, *m/e* 464 (M^+).

Anal. Calcd for $C_{28}H_{48}O_5$: C, 72.37; H, 10.41. Found: C, 72.50; H, 10.60.

Acetylation of **5a** afforded the tetraacetate **5c** as a glass: NMR δ 5.40–4.70 (4 H, m, overlapping, 2-, 3-, 22-, 23-H), 2.06 (3 H, s, CH_3CO), 2.00 (6 H, s, 2 × CH_3CO), 1.98 (3 H, s, CH_3CO).

Anal. Calcd for $C_{36}H_{56}O_9$: C, 68.33; H, 8.92. Found: C, 68.20; H, 8.7.

(2*R*,3*S*,22*R*,23*R*)- and (2*R*,3*S*,22*S*,23*S*)-2,3,22,23-Tetrahydroxy-5α-ergostane Tetraacetates (10 and 11). (2*R*,3*S*,22*R*,23*R*)-Tetrahydroxy-5α-ergostan-6-one (**12a**)[20] (130 mg) dissolved in pyridine (3 mL) containing 4-(dimethylamino)pyridine (0.1 g) was treated with acetic anhydride (1 mL) at room temperature for 12 h. Workup afforded the corresponding tetraacetate **12b** (120 mg): mp 145–146 °C (from hexane). Treatment of **12b** (110 mg) with ethanedithiol (0.2 mL) and boron trifluoride etherate (0.2 mL) for 30 min afforded the corresponding thioketal (100 mg, glass) which was dissolved in dry benzene (5 mL) and treated with tri-*n*-butyltin hydride (0.5 mL) in the presence of 2,2′-azobis(isobutyronitrile) (3 mg). After workup the obtained product was chromatographed to afford the tetraacetate **10** (65 mg) which resisted all afforts at crystallization: NMR δ 5.40–4.70 (4 H, m, overlapping, 2-, 3-, 22-, and 23-H), 2.06 (6 H, s, 2 × CH_3CO), 2.02 (3 H, s, CH_3CO), 1.98 (3 H, s, CH_3CO); R_f 0.46 (20% ethyl acetate–benzene).

Anal. Calcd for $C_{36}H_{58}O_8$: C, 69.90; H, 9.38. Found: C, 69.75; H, 9.45.

Starting with the 7-ketone **5a** the same sequence of reaction afforded a compound having identical physicochemical properties and polarity as **10**.

Starting with **13a**, acetylation afforded **13b**: mp 108–110 °C (from hexane). Elimination of the 7-oxo group resulted into the 2*R*,3*S*,22*S*,23*S* tetraacetate **11**: mp 93–95 °C (from methanol); NMR δ 5.40–4.70 (4 H, m, overlapping, 2-, 3-, 22-, and 23-H), 2.06 (6 H, s, 2 × CH_3CO), 2.02 (3 H, s, CH_3CO), 1.98 (3 H, s, CH_3CO); R_f 0.50 (20% ethyl acetate–benzene).

Anal. Calcd for $C_{36}H_{58}O_8$: C, 69.90; H, 9.38. Found: C, 69.76; H, 9.45.

Starting with the 7-ketone **5b**, a product with the physicochemical properties and polarity of **11** was obtained.

(2*R*,3*S*,22*R*,23*R*)- and (2*R*,3*S*,22*S*,23*S*)-2,3,22,23-Tetrahydrdoxy-*B*-homo-7a-oxa-5α-ergostan-7-ones (4a and 4b). The tetraacetate **5c** (100 mg) in dichloromethane (2.5 mL) was added at 0 °C to a solution of trifluoroperacetic acid in dichloromethane prepared by adding trifluoroacetic anhydride (3.37 mL) to 30% aqueous hydrogen peroxide (0.6 mL) in dichloromethane (3.7 mL) at 0 °C. The mixture was stirred at room temperature for 1 h and then was poured into 2% potassium carbonate solution and extracted with dichloromethane. The extract was washed with water, dried, and concentrated under reduced pressure. The residue was chromatographed (eluting with 50% hexane–ethyl acetate) to afford the tetraacetoxy lactone **4c** (98 mg): a glass; NMR (200 MHz) δ 5.26 (1 H, m, 3β-H; $W_{1/2}$ = 8 Hz), 5.22 (1 H, dd, 23-H; *J* = 7 and 1.4 Hz), 5.04 (1 H, dd, 22-H; *J* = 7 and 5.4 Hz), 4.86 (1 H, m, 2β-H; $W_{1/2}$ = 12 Hz), 4.18 (1 H, dd, 8β-H; *J* = 10.5 and 8.4 Hz), 2.72 (1 H, dd, 6β-H; *J* = 10 and 15 Hz), 2.08 (3 H, s, CH_3CO), 2.05 (3 H, s, CH_3CO), 2.03 (3 H, s, CH_3CO), 1.98 (3 H, s, CH_3CO), 1.08 (3 H, s, 19-CH_3), 0.66 (3 H, s, 18-CH_3).

Anal. Calcd for $C_{36}H_{56}O_{10}$: C, 66.60; H, 8.70. Found: C, 66.50; H, 8.60.

The tetraacetate **4c** (70 mg) was treated with 5% methanolic potassium hydroxide (5 mL) under reflux for 1 h. The mixture was cooled to room temperature and acidified with hydrochloric acid (5 mL, of 6 M HCl). After stirring for 1 h, workup afforded the tetrahydroxy lactone **4a** (58 mg): mp 269–271 °C (triturated in hexane); IR 3450, 1730, 1710, 1695 cm^{-1}; NMR (C_5D_5N) δ 4.18 (1 H, dd, 8β-H; *J* = 10.5 and 8.4 Hz), 2.72 (1 H, dd, 6β-H; *J* = 10 and 15 Hz); mass spectrum, *m/e* 462 ($M^+ - H_2O$).

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Anal. Calcd for $C_{28}H_{48}O_6$: C, 70.00; H, 10.10. Found: C, 69.80; H, 10.00.

A similar Baeyer–Villiger reaction starting with the tetraacetate **5d** (100 mg) afforded the tetraacetoxy lactone **4d** (80 mg): mp 172–174 °C (from hexane); NMR δ 5.24 (1 H, m, 3β-H; $W_{1/2}$ = 8 Hz, 5.20 (1 H, dd, 22-H; J = 7 and 3 Hz), 5.08 (1 H, dd, 22-H; J = 3.5 and 3 Hz), 4.86 (1 H, m, 2β-H; $W_{1/2}$ = 12 Hz), 4.18 (1 H, dd, 8β-H; J = 10.5 and 8.4 Hz), 2.72 (1 H, dd, 6β-H; J = 10 and 15 Hz), 2.08 (6 H, s, 2 × CH_3CO), 2.05 (3 H, s, CH_3CO), 1.99 (3 H, s, CH_3CO), 1.06 (3 H, s, 19-CH_3), 0.65 (3 H, s, 18-CH_3).

Anal. Calcd for $C_{36}H_{56}O_{10}$: C, 66.60; H, 8.70. Found: C, 66.50; H, 8.60.

Saponification of **4d** (70 mg) followed by acydification afforded the tetrahydroxy lactone **4b** (55 mg): mp 97 °C (sinterizes), 146 °C (clarifies) (from hexane); IR 1730, 1710, 1695 cm^{-1}; NMR (C_5D_5N) δ 4.18 (1 H, dd, 8β-H; J = 10.5 and 8.4 Hz), 2.72 (1 H, dd, 6β-H; J = 10 and 15 Hz); mass spectrum, m/e 462 ($M^+ - H_2O$).

Anal. Calcd for $C_{28}H_{48}O_6$: C, 70.00; H, 10.10. Found: C, 69.85; H, 9.90.

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Registry No. **4a**, 93782-67-3; **4b**, 93805-92-6; **4c**, 93782-68-4; **4d**, 93782-69-5; **5a**, 90965-40-5; **5b**, 90965-39-2; **5c**, 93782-70-8; **5d**, 93782-71-9; **7**, 93782-72-0; **8**, 93782-73-1; **8** (detosylated), 10123-90-7; **9**, 93806-01-0; **10**, 93782-74-2; **11**, 93782-75-3; **12a**, 72050-71-6; **12b**, 72050-72-7; **12b** (thioketal), 93782-76-4; **13a**, 72050-69-2; **13b**, 72050-70-5; $HSCH_2CH_2SH$, 540-63-6.

α-Amino Acids as Chiral Educts for Asymmetric Products. Chirospecific Syntheses of Methyl L-Sibirosaminide and Its C-3 Epimer from L-Allothreonine

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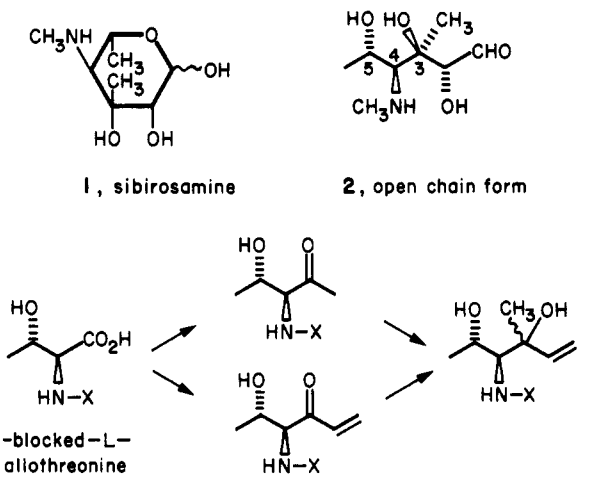
Efficient syntheses of methyl L-sibirosaminide and its C-3 epimer are described using L-allothreonine as the chiral educt. Amino acylations of organometallics with the lithium salt of *N*-(phenylsulfonyl)-L-allothreonine constitute the key carbon–carbon bond-forming steps. The resulting methyl and vinyl ketones are then converted to tertiary alcohols by a second organometallic addition, and the order of addition controls the stereochemistry at the new chiral center. Stereocontrolled functionalization of the vinyl group then leads to the amino sugars. Elaboration to the C-3 epimer of sibirosamine was achieved via a Pummerer oxidation route, while in the preparation of sibirosamine itself a selective tetraol oxidation route was used.

Largely due to their occurrence in important antibiotics,[1,2] amino sugars have elicited a substantial interest as synthetic targets for organic synthesis.[3] The challenge of creating several adjacent, functionalized chiral centers in a stereo- and enantioselective manner is chemically intriguing, and the emerging importance of the biological role of amino sugars[4] adds to the impetus for efficient construction of these molecules.

The problem of enantioselection in amino sugar synthesis is usually overcome by choosing a carbohydrate or other chiral precursor,[5,6] or occasionally by resolution of a racemic intermediate.[7] There appears to be no reported case, however, of the preparation of an amino sugar from an amino acid with retention of the amino group and its chiral integrity. This is probably due to the lack of methods for forming carbon–carbon bonds with amino acids while maintaining optical purity.

Recently, we have demonstrated some very versatile methods for performing just these operations. These methods are based on either Freidel–Crafts type amino acylations of aromatic substrates with amino acid chlorides,[8] or on the amino acylations of organometallics with lithium salts of amino acids.[8,9] The latter method appeared to be aptly suitable as the basis for a chirospecific route to amino sugar syntheses, and we set out to experimentally determine the feasibility of this concept.

Scheme I. Relationship of Sibirosamine and L-Allothreonine



Sibirosamine (**1**), derived from the potent antitumor antibiotic sibiromycin,[10,11] was chosen as our prototypical target for several reasons. First, our proposed methodology is made starkly suitable by the structural resemblance of

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