5. R. Kasai, M. Okihara, I. Asakawa, K. Mizutani, and K. Tanaka, Tetrahedron, 35, 1427 (1979).
6. C. Altona and C. A. G. Hasnoot, Org. Magn. Res., 13, No. 6, 417 (1980).
7. S. Seo, Y. Tomita, K. Tori, and Y. Yoshimura, J. Am. Chem. Soc., 100, No. 11, 3331 (1978).
8. M. E. Wall, C. R. Eddy, M. L. McClennan, and M. E. Klumpp, Anal. Chem., 24, 1337 (1952).
9. C. R. Eddy, M. E. Wall, and M. K. Scott, Anal. Chem., 25, 266 (1953).
10. W. H. Faul and C. Djerassi, Org. Mass Spectrom., 3, 1187 (1970).
11. M. I. Isaev, M. B. Gorovits, and N. K. Abubakirov, Khim. Prir. Soedin., 156 (1989).
12. M. S. Gonzalez, D. A. Bustos, M. Zudenigo, and E. A. Ruveda, Tetrahedron, 42, 755 (1986).
13. T. T. Gorovits, Khim. Prir. Soedin., 263 (1970).

SYNTHESIS OF 24-EPITEASTERONE

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Starting from ergosterol, the synthesis of the brassinosteroid 24-epiteasterone has been achieved by the use of a new scheme for introducing a 3β-hydroxy-6-keto group as the result of the Birch reduction of the corresponding 5α-hydroxy-Δ^7-3,6-dione.

One of the brassinosteroids of green tea Thea sinensis [Camellia sinensis viridis] is teasterone (I) [1]. This phytohormone has a fairly simple structure and, although it is substantially less active than brassinolide, may find practical use in agriculture as a plant growth regulator. Undoubted interest is also presented by its isomer 24-epiteasterone (II). It must be mentioned that brassinosteroids with the (R)-configuration of the 24-methyl group such as 24-epibrassinolide or (24R)-castasterone have recently been detected in plants [2]. In view of this one may expect the presence of compound (II) in natural sources. This hypothesis has served as an incentive for the first synthesis of 24-epiteasterol (II) from ergosterol (III), which we have now accomplished.

It is known [3] that the oxidation of ergosterol (III) with chromic acid forms the 5α-hydroxy-3,6-diketone (IV). We obtained this compound with a yield of 22% when the oxidation was performed in acetone. In the following stage, with the aim of saturating the 7(8)-double bond and hydrogenolyzing the 5-hydroxy group, the steroid so obtained was subjected to Birch reduction with an excess of lithium in a mixture of liquid ammonia and hexamethylphosphorotriamide. It was found that in this case the Birch reduction took place in a rather complex fashion. The main products, which we isolated with yields of 12 and 13%, respectively, were the steroids (V) and (VI) (see top of following page).

We established the structures of compounds (V) and (VI) by analyzing their spectra. Thus, the IR spectrum of the main product, of the Birch reduction of the hydroxydione (IV) contained the bands of a saturated C=O bond and of an OH group at 1710 and 3460 cm^{-1}, respectively. In the CD spectrum of the hydroxyketone (VI) the maximum of a negative Cotton effect was observed at 285 nm, which is characteristic for a 6-ketosteroid with a trans-A/B linkage. From this it was possible to conclude that, in the Birch reduction of compound (IV) with the formation of (VI), not only the saturation of the 7(8)-double bond and the hydrogenolysis of the 5α-hydroxy group but also the reduction of the 3-keto group to a 3-hydroxy group had taken place. In the PMR spectrum of compound (VI), the position (δ 3.58 ppm) and form of the signal of the methine proton geminal to the 3-hydroxy group were char-

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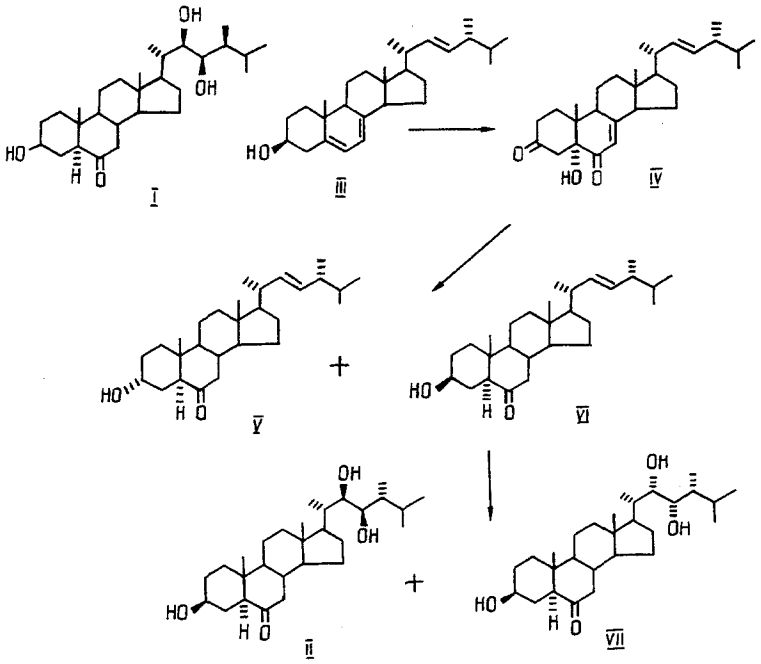

acteristic. From the half-width of the signal for this proton (W/2 = 24 Hz) it had to be assigned the axial orientation, which, in view of the presence of the trans-A/B linkage in compound (VI), unambiguously showed the β-configuration of the 3-hydroxy group. The presence in the PMR spectrum of the signals of two vinyl protons at 5.18 ppm was a proof of the retention of the 22(23)-double bond in steroid (VI). Thus, the main product of the Birch reduction of the 5α-hydroxy-Δ^7-3,6-dione (IV) had the structure of the 3β-hydroxy-6-ketone (VI).

It must be mentioned that steroid (VI) is a known intermediate in the synthesis of 24-epibrassinolide [4, 5]. Since the method of synthesizing brassinosteroids from 3β-hydroxy-6-ketones has been fairly well developed [6], the two-stage method of obtaining steroid (VI) proposed in this paper may find further practical use.

We established the structure of the minor product of the Birch reduction of the 5α-hydroxy-Δ^7-3,6-dione (IV) as the 3α-hydroxy-6-ketone (V) by an analogous analysis of its IR, CD, and PMR spectra. In this procedure, the presence in the PMR spectrum of the signals of the C_3–Hβ, C_5–Hα, and C_7–Hβ protons (δ 4.16, 2.73, and 2.31 ppm) was of great significance. The positions and forms of the signals of these protons accurately coincided with the corresponding signals in the spectrum of the brassinosteroid typhasterol, which is also a 3α-hydroxy-6-ketosteroid [7, 8].

As a result of the Criegee cis-hydroxylation of the Δ^{22}-steroid (VI) under the action of an equimolecular amount of osmium tetroxide in pyridine, the required 24-epiteasterone (II) and its (22S,23S)-isomer (VII) were obtained with yields of 26 and 65%. The structures of compounds (II) and (VII) followed from their spectral characteristics.

A study of the biological activities of brassinosteroids (II) and (VII) and also the synthesis of 24-epityphasterol from steroic (V) are in their initial stages and the results will be published later.

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EXPERIMENTAL

Melting points were determined on a Kofler block. IR spectra were obtained on a UR-20 instrument. PMR spectra were recorded in deuterochloroform on a Bruker AC-200 NMR spectrometer with a working frequency of 200 MHz. Chemical shifts are given relative to TMS as in-

ternal standard. Mass-spectrometric characteristics were obtained on a Varian MAT-311 instrument at an energy of the ionizing electrons of 70 eV. CD spectra were recorded on a Jasco J-20 spectropolarimeter.

Birch Reduction of (22E,24R)-5-Hydroxy-5α-ergosta-7,22-diene-3,6-dione (IV). With continuous stirring, a solution of 4.75 g of the hydroxyketone (IV) (obtained by the oxidation of ergosterol (III) by the method of [2]) in 160 ml of hexamethylphosphorotriamide was added to a solution of 0.90 g of lithium in 210 ml of freshly distilled liquid ammonia. The reaction mixture was stirred for 0.5 h and was then treated with an aqueous solution of ammonium chloride. After the evaporation of the ammonia, the precipitate was filtered off, and it was washed with water and dissolved in chloroform. The chloroform solution was evaporated in vacuum, and the residue was chromatographed on a column of silica gel with elution by hexane–ether (1:1). This gave 0.561 g of (22E,24R)-3α-hydroxy-5α-ergost-22-en-6-one (V). Yield 12%, mp 191-195°C (hexane–ether). Found, %: C 81.45; H 11.87. $C_{28}H_{46}O_2$. Calculated, %: C 81.10; H 11.18.

IR spectrum): ν_{max}^{KBr}, cm^{-1}: 3460 (OH), 1710 (C=O). PMR spectrum (δ, ppm): 0.68 (3H, s, 18-Me), 0.72 (3H, s, 19-Me), 0.815 (3H, d, J = 6.5 Hz, 26-Me), 0.83 (3H, d, J = 6.5 Hz, 27-Me), 0.91 (3H, d, J = 7 Hz, 28-Me), 1.01 (3H, d, J = 7 Hz, 21-Me), 2.31 (1H, dd, J_1 = 4 Hz, J_2 = 13 Hz, C_7–Hβ), 2.73 (1H, quintet, J = 8 Hz, C_5–Hα), 4.16 (1H, m, W/2 = 7 Hz, C_3–Hβ), 5.18 (2H, t, J = 5 Hz, C_{22}- and C_{23}–H). CD spectrum (c 0.08 mg/ml; methanol), nm: Δε −1.15 (290).

Further elution gave 1.12 g of (22E,24R)-3β-hydroxy-5α-ergost-22-en-6-one (VI). Yield 23%, mp 180-183°C (hexane); literature: mp 186-187°C [4]; 185-187°C [5]. Found, %: C 81.00; H 11.97. $C_{28}H_{46}O_2$. Calculated, %: C 81.10; H 11.18.

IR spectrum: ν_{max}^{KBr}, cm^{-1}: 3445 (OH), 1710 (C=O). PMR spectrum (δ, ppm): 0.67 (3H, s, 18-Me), 0.75 (3H, s, 19-Me), 0.81 (3H, d, J = 6.5 Hz, 26-Me), 0.84 (3H, d, J = 6.5 Hz, 27-Me), 0.90 (3H, d, J = 7 Hz, 28-Me), 1.00 (3H, d, J = 7 Hz, 21-Me), 3.58 (1H, m, W/2 = 24 Hz, C_3–Hα), 5.18 (2H, t, J = 5.5 Hz, C_{22}- and C_{23}–H). Mass spectrum, m/z: 414 (M^+). CD spectrum (c 0.04 mg/ml; methanol) nm: Δε − 1.89 (285).

Criegee cis-Hydroxylation of the Hydroxyenone (VI). A solution of 0.166 g of the hydroxyenone (VI) and 0.105 g of osmium tetroxide in 8 ml of pyridine was kept at room temperature for 22.5 h, and then, with stirring, a solution of 2.0 g of sodium sulfite and 1.0 ml of sulfuric acid in 20 ml of water was added over 0.5 h. After the decomposition of the osmates, the products were extracted with chloroform, and the chloroform extract was washed with water and evaporated in vacuum. The residue was chromatographed on a column of silica gel with elution by ether. This gave 0.117 g of (22S,23S,24R)-3β,22,23-trihydroxy-5α-ergostan-6-one (VII). Yield 65%, mp 195-199°C (hexane–MeOH).

IR spectrum: ν_{max}^{KBr}, cm^{-1}: 3400 (OH), 1700 (C=O). PMR spectrum (δ, ppm): 0.69 (3H, s, 18-Me), 0.76 (3H, s, 19-Me), 0.89 (3H, d, J = 6.5 Hz, 26-Me), 0.91 (3H, d, J = 7 Hz, 27-Me), 0.97 (3H, d, J = 7 Hz, 28-Me), 1.01 (3H, d, J = 7 Hz, 21-Me), 3.60 (2H, m, W/2 = 14 Hz, C_{22}–H and C_3–Hα), 3.72 (1H, m, W/2 = 12 Hz, C_{23}–H). Mass spectrum, m/z: 412 ($M^+ - 3H_2O$).

Further elution gave 0.047 g of 24-epiteasterone (II). Yield 26%, mp 220-225°C (hexane–MeOH).

IR spectrum: ν_{max}^{KBr}, cm^{-1}: 3430 (OH), 1710 (C=O). PMR spectrum (δ, ppm): 0.67 (3H, s, 18-Me), 0.76 (3H, s, 19-Me), 0.84 (3H, d, J = 6.5 Hz, 26-Me), 0.88 (3H, d, J = 6.5 Hz, 27-Me), 0.92 (3H, d, J = 7 Hz, 28-Me), 0.97 (3H, d, J = 6 Hz, 21-Me), 3.41 (1H, t, J = 5 Hz, C_{22}–H), 3.60 (1H, m, W/2 = 24 Hz, C_3–Hα), 3.70 (1H, d, J = 4 Hz, C_{23}–H). Mass spectrum, m/z: 430 ($M^+ - H_2O$).

LITERATURE CITED

1. H. Abe, T. Morishita, M. Uchiyama, S. Takatsuto, and N. Ikekawa, Agr. Biol. Chem., 48, No. 8, 2171-2172 (1984).
2. N. B. Kovganko, Khim. Prir. Soedin., No. 2, 159 (1991).
3. A. Burawoy, J. Chem. Soc., No. 3, 409-411 (1937).
4. M. J. Thompson, N. Mandawa, J. L. Flippen-Anderson, J. F. Worley, S. R. Dutky, and W. E. Robbins, J. Org. Chem., 44, No. 26, 5002-5004 (1979).
5. J. C. Ferrer, R. Lalueza, O. Saavedra, and C. Brosa, Tetrahedron Lett., 31, No. 27, 3941-3942 (1990).

6. N. V. Kovganko, Zh. Vses. Khim. Obshch. im. D. I. Mendeleeva, 35, No. 4 (1991).
7. J. A. Schneider, K. Yoshihara, K. Nakanishi, and N. Kato, Tetrahedron Lett., 24, No. 36, 3859-3860 (1983).
8. T. Yokota, M. Arima, N. Takahashi, S. Takatsutpo, S. Ikekawa, and T. Takematsu, Agr. Biol. Chem., 47, No. 10, 2419-2420 (1983).

TRITERPENE GLYCOSIDES OF Astragalus AND THEIR GENINS

XL. CYCLOCARPOSIDE B FROM Astragalus coluteocarpus

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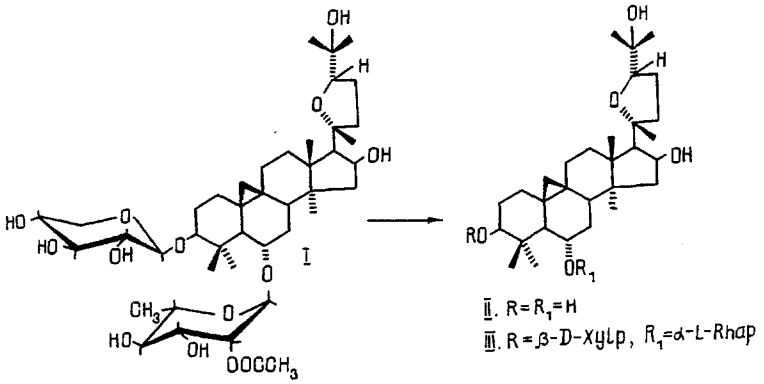
In addition to cyclosieversigenin, β-sitosterol β-D-glucopyranoside, and cyclocarposide, we have isolated another three glycosides of triterpene nature from the epigeal part of the plant Astragalus coluteocarpus Boiss. (Leguminosae). On the basis of chemical transformations and spectral characteristics, the structure of one of the new glycosides, which we have called cyclocarposide B, has been established as 20R,24S-epoxycycloartane-3β,6α,16β,25-tetraol 6-O-α-L-(2-O-acetylrhamnopyranoside) 3-O-β-D-xylopyranoside.

We have previously reported the structure of a cycloartane glycoside, cyclocarposide, isolated from the herb Astragalus coluteocarpus Boiss. (Leguminosae) [1]. Continuing the study of other components of the epigeal part of this plant, we have isolated another five compounds, which have been called substances (1)-(5) in order of increasing polarity. Cyclocarposide corresponds to a 6th substance in this series. The two weakly polar compounds (1) and (2) have been identified as cyclosieversigenin [2] and β-sitosterol β-D-glucopyranoside [3]. The present work was devoted to demonstrating the structure of substance (4), which we have called cyclocarposide B (I).

In the PMR spectrum of cyclocarposide B at 0.23 and 0.42 ppm we observed the one-proton doublets of an AB system that are characteristic for an isolated cyclopropane methylene group. This fact permitted us to assign the glycoside under consideration to the triterpenoids of the cycloartane series [2]. The formation of cyclosieversigenin (II) on the acid hydrolysis of glycoside (I) served as a proof of this conclusion.



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