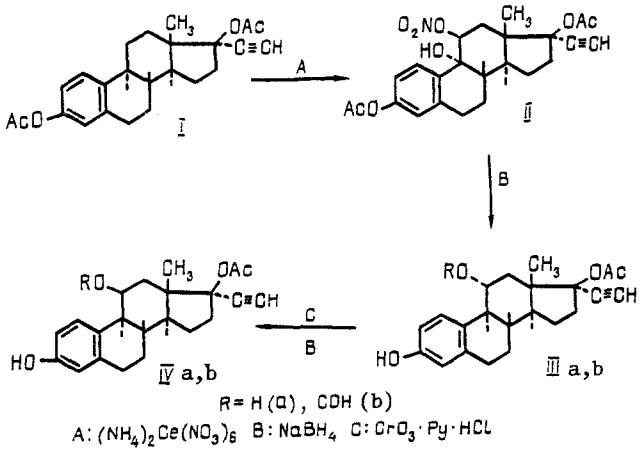
FORMATES OF STEREOISOMERIC 17α-ETHYNYL-11-HYDROXYESTRADIOLS

V. M. Rzheznikov

UDC 547.689.6

In the 11-hydroxyestrogen series a unique example of a pair of epimers with diametrically opposed biological activities is known: 17α-ethynyl-11β-methoxyestradiol is a powerful estrogen [1], while its 11α- epimer exhibits an antiestrogenic effect [2]. Among the analogous 11-formates, only the formate of 11β-hydroxyestrone, with a high hormonal activity, is known [3].

On the basis of the method that we have developed for obtaining 17α-ethynyl-11α-hydroxyestradiol [4], we have synthesized both stereoisomeric formates (IIIb and IVb).



17α-Estradiol diacetate (I) was oxidized with cerium ammonium nitrate to the hydroxy nitrate (II), which was then reduced with sodium tetrahydroborate to the 11α-carbinol (IIIa). Passage from the 11α- to the 11β- derivative was effected by the classical route: oxidation with pyridine chlorochromate followed by reduction of the ketone with $NaBH_4$. The formylation of the carbinols (IIIa and IVa) with 88% formic acid [3] took place regioselectively with the formation of the 11-formates (IIIb and IVb).

17β-Acetoxy-17α-ethynyl-11α-formyloxyestradiol (IIIb): mp 249-252°C (MeOH), $[\alpha]_D$ −142° (c 0.73; $CHCl_3$). UV spectrum ($\lambda_{max}^{ethanol}$, nm): 277.5 (log ε 3.18). IR spectrum (ν_{max}^{KBr}, cm^{-1}): 3400-3415, 3240 (O–H); 2110 (C≡CH); 1735, 1710, 1680 (absent from the spectrum of a solution in $CHCl_3$), 1260, 1235, 1180-1190, 1025 (OAc, OFr); 1585, 1500 (Ar). PMR (80 MHz, C_5D_5N): 0.875 (3H, s, CH_3-18), 1.90 (3H, s, Ac), 3.01 (1H, s, C≡CH), 5.58 (1H, m, J = 10 and 5 Hz, H-11), 8.26 (1H, s, OCOH).

The formate (IVb): mp 121-124° [benzene–hexane (3:1)]. $[\alpha]_D$ −9° (c 0.86; $CHCl_3$). UV spectrum: 280, 286 (sh.) (3.22; 3.18). IR spectrum: 3425-3440, 3300; 1745, 1718, 1245, 1230, 1195, 1170, 1020; 1620, 1500.* PMR ($CDCl_3$): 1.01 (3H, s), 2.01 (3H, s), 2.56 (1H, s), 6.0 (1H, m, J = 5 and 3 Hz), 7.95 (1H, s).*

The formate (IVb) exhibited an estrogenic activity 1.6 times exceeding the effect of estradiol, while the epimer (IIIb) was antiestrogenic, inhibiting the action of estradiol by 20%.

LITERATURE CITED

1. G. Azadian-Boulanger and D. Bertin, Chimie Thérapeutique, 8, 451 (1973).

*Interpretation as in the example given above.

All-Union Endocrinological Scientific Center, Russian Academy of Medical Sciences, Moscow. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 729-730, September-October, 1991. Original article submitted January 14, 1991.

0009-3130/91/2705-0645$12.50

2. L. Ferband, F. Labric, P. A. Kelly, and J. P. Raynaud, Biol. Reprod., 18, 99 (1978).
3. A. Segaloff and R. B. Gabbard, Steroids, 43, 111 (1984).
4. V. M. Rzheznikov, USSR Inventor's Certificate No. 1,395,639 (1988); Byull Izobret, No. 18, 99 (1988).

STEROID GLYCOSIDES OF Solanum tuberosum

II. TUBEROSIDE F

P. K. Kintya, T. I. Prasol, and N. E. Mashchenko

UDC 547.918+547.917

The presence of steroid glycosides in potato seeds has been reported previously [1]. In the present paper we give a proof of the structure of a new glycoside isolated from seeds of Solanum tuberosum L., which we have called tuberoside F (I).

Tuberoside F (mp 152-153°C, $[\alpha]_D^{20}$ −127°, c 2.5; MeOH), which was obtained in the individual state by the repeated chromatography on a silica gel column of a methanolic extract of potato seeds, gave a positive reaction with the Ehrlich reagent [2]. In the products of acid hydrolysis we identified yamogenin (mp 201°C, $[\alpha]_D$ −120° (c 1.0; $CHCl_3$); $[M^+]$ 414; IR spectrum: 890 < 920 cm^{-1}), which was the basis for considering the aglycon of tuberoside F to be (25S)-furost-5-ene-3β,22α,26-triol.

GLC of the aldononitrile derivatives [3] of the monosaccharides of (I) showed the presence of galactose, rhamnose, and glucose in a ratio of 1:1:1.

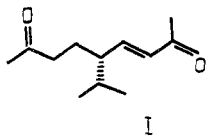
The methyl 3,4,6-tri-O-methyl-D-galactopyranoside, methyl 2,3,4-tri-O-methyl-L-rhamnopyranoside, and methyl 2,3,4,6-tetra-O-methyl-D-glucopyranoside obtained after the methanolysis of Hakomori-permethylated [4] tuberoside F showed the direct attachment of the galactose residue to the aglycon.

Methylation and the methanolysis of the permethylate of yamogenin rhamnogalactopyranoside (II), mp 236-238°C, $[\alpha]_D^{20}$ −63° (c 1.7; pyridine), obtained, together with yamogenin galactopyranoside (mp 230-233°C; $[\alpha]_D^{20}$ −91°, c 1.0; CH_3OH) and yamogenin, as the result of the mild hydrolysis of (I), showed the identity of (II) with tuberoside C [1].

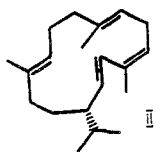
A confirmation of the furostanol nature of (I) may be considered to be its oxidative cleavage [5] and the presence of free glucose and compound (II) in the products of the enzymatic hydrolysis of tuberoside F with β-glucosidase.

The configurations of the glycosidic centers were determined from the differences in the molar rotations of the initial glycosides, of the progenins, and of the aglycon [6].

According to all the facts presented, tuberoside F corresponds to the structure of (25S)-furost-5-ene-3β,22α,26-triol 26-O-β-galactopyranoside 3-O-[O-L-rhamnopyranosyl-(1 → 2)-β-D-galactopyranoside].



I



II

LITERATURE CITED

1. P. K. Kintya and T. I. Prasol, Khim. Prir. Soedin., No. 4 (1991).
2. S. Hijosawa, M. Huton, T. Komori, et al., Chem. Pharm. Bull., 16, 1162 (1968).

Institute of Ecological Genetics, Moldavian Academy of Sciences, Kishinev. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 730-731, September-October, 1991. Original article submitted October 29, 1990; revision submitted January 31, 1991.

 0009-3130/91/2705-0646$12.50