Experimental Section

The melting points were determined on a Mel-Temp apparatus and are uncorrected. Most of the reactions were run under an inert atmosphere and anhydrous conditions. Analyses were performed by A. Bernhardt, Mülheim, Ruhr (Germany), and Galbraith Laboratories, Knoxville, Tenn.

3,5-Seco-A-norcholestane-3,5-diol Epimers (2 and 3).—A suspension of 97.0 g (0.24 mol) of 5-oxo-3,5-seco-A-norcholestan-3-oic acid (1) in 1 l. of anhydrous ether was added over a period of 40 min to 27.0 g (0.71 mol, a fourfold excess) of $LiAlH_4$ suspended in 400 ml of anhydrous ether and cooled in an ice bath. After stirring overnight the excess $LiAlH_4$ was destroyed by cautious addition of ethanol and then water. A precipitate was filtered off, washed, and dried; the ether was then evaporated to yield 89 g (94%) of solid. There was no carbonyl peak in its ir spectrum. Tlc of the product (ethanol–chloroform, 1:12, on silica gel) showed two major spots with R_f values of 0.29 and 0.37. Attempts to separate these by recrystallization from benzene or acetone were unsuccessful.

The epimers were separated by chromatography on a 2 × 20 in. silica gel column employing chloroform as the initial solvent. Tlc was used to check the fractions. The faster migrating epimer started coming off after several liters of solvent had passed through the column. A small amount (2–3% of the sample) of a fast moving side product was discarded with the forerun. After several more liters of solvent had passed through, the eluate contained a mixture of the two epimers. At this point an ether–chloroform mixture (1:10) was used until the last of the faster epimer had been eluted. The column was then washed with tetrahydrofuran, the slower epimer coming off in the first 300 ml. It was found that the best procedure was to overload the column with the epimeric mixture (about 40 g) and to simply rechromatograph the middle, mixed fractions.

3-Acetoxy-3,5-seco-A-norcholestan-5β-ol (5).—A solution of 17.50 g (0.045 mol) of 3 in 200 ml of pyridine was cooled in an ice–salt bath. To this was added dropwise 3.8 ml (a 5% excess) of acetyl chloride over a 5-min period. The reaction was cooled and vigorously stirred during and after addition. It was continued for 11 hr while the bath gradually warmed to room temperature.

The solution was poured into ice water and extracted with ether. The extract was washed with ice-cold 5% HCl until the wash remained acidic, and then with saturated NaCl solution. The extract was dryed over anhydrous Na_2SO_4 and the ether was removed to yield an oil. This was chromatographed with chloroform on a 2 × 20 in. silica gel column to yield 1.58 g of material which tlc showed to be mostly the monoacetate. The column was washed with tetrahydrofuran to give 3.7 g of solid. Since this contained a considerable amount of the starting diol, it was processed a second time as above.

All of the monoacetate fractions were combined and recrystallized from acetone–water to yield 15.04 g (83%) of 6, mp 84–86°. A small portion was recrystallized again, leading to a product melting at 85–87° with $[\alpha]^{28}D$ + 17.5° ($CHCl_3$). *Anal.* Calcd for $C_{28}H_{50}O_3$: C, 77.36; H, 11.59. Found: C, 77.83; H, 11.75.

5α-Chloro-3,5-seco-A-norcholestan-3-ol (7).—To a solution of 16.53 g (0.038 mol) of 5 in 150 ml of CCl_4 was added 50.0 g (0.19 mol) of Ph_3P. The reaction was carried out in a flamed-out flask under argon. The steroid had been dried overnight in a vacuum desiccator over Drierite and the Ph_3P was dried in an oven at 65°. The CCl_4 had been freshly distilled from P_2O_5.

The reaction mixture was magnetically stirred and kept in a 95° bath. The mixture soon became cloudy and a white precipitate started to form. After reacting for 1.75 hr it gradually turned yellow. Some ethanol was then added (the solution turned colorless) and the reaction was heated for an additional 0.75 hr. After the reaction mixture was concentrated to about one-half its original volume, 50 ml of 5% HCl was added along with about 100 ml of 95% ethanol to yield a homogeneous solution. This was refluxed for 7 hr and then stirred at room temperature for an additional 10-hr period. The solution was poured into water and extracted twice with ether. The extract was washed with water, dilute $NaHCO_3$ solution, and saturated NaCl solution, filtered through anhydrous Na_2SO_4, and brought to dryness. The residue was extracted with 40–60° ligroin and filtered to remove insoluble Ph_3PO. The filtrate was twice more concentrated and filtered, then evaporated to dryness to yield a yellow oil. The first fractions to come off contained the unhydrolized ester (tlc), and this was collected and refluxed in a solvent mixture consisting of 100 ml of ethanol, 4 ml of concentrated HCl, and 25 ml of water for 17 hr and then processed as above to purify it.

The fractions from all of the above operations that contained the desired product were combined to yield 11.68 g of oil which slowly solidified. On tlc the crude product showed three connected spots, with R_f values ($CHCl_3$ on silica gel) of 0.30, 0.35, and 0.39. From a previous run it was known that the spot with R_f 0.30 was caused by the desired product.

The crude material was recrystallized twice from acetone–water to give 7.10 g (45%) of 7 as white needles, mp 102–110°. A small amount was recrystallized further to give the analytical sample, mp 108–110°.

Anal. Calcd for $C_{26}H_{47}ClO$: C, 75.96; H, 11.53. Found: C, 76.61; H, 11.79.

3,5-α-Dichloro-3,5-seco-A-norcholestane (8).—A solution of 7.10 g (0.0173 mol) of 7 in 50 ml of CCl_4 was prepared in a flamed-out flask under argon. To this was added 21.0 g (0.08 mol) of Ph_3P and the reaction was stirred while immersed in a bath kept at 100°. A white precipitate soon formed and after 60 min the solution suddenly turned yellow. Ethanol (40 ml) and dilute HCl (1 ml of concentrated HCl + 3 ml of water) were then added (the solution became colorless) and the mixture was refluxed for an additional hour. It was poured into water and worked up as above. Tlc (40–60° ligroin on silica gel) of the resulting crude oil showed two major spots with R_f values of 0.60 and 0.83 plus several much smaller spots.

The oil was chromatographed on a 2 × 20 in. silica gel column using 40–60° ligroin. All fractions yielded oils, but the one containing only the spot with R_f 0.60 crystallized on standing overnight. Using seed crystals, this fraction and all other fractions containing that spot were crystallized from acetone as prisms. The total yield of 6.39 g (86%) of 8 was obtained, melting between 90 and 93°. The highest melting crops melted at 91–93° with $[\alpha]^{29}D$ +33.8° ($CHCl_3$).

Anal. Calcd for $C_{26}H_{46}Cl_2$: C, 72.70; H, 10,80. Found: C, 72.64; H, 10.47.

Registry No.—**5**, 21273-50-7; **7**, 21273-51-8; **8**, 21273-52-9.

Acknowledgment.—Financial aid through NASA Institutional Grant NGR-36-004-014 is greatly appreciated.

(+)-β-Eudesmol O-α-L-Arabopyranoside. A New Sesquiterpene Glycoside from *Machaeranthera tanacetifolia* (H.B.K.) Nees (Compositae)[1]

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We report the isolation and structure determination of the first glycoside of β-eudesmol. Chloroform extraction of air-dried plants of *Machaeranthera tanacetifolia* collected near Gail, Texas, afforded in 0.43% yield the new glycoside, $C_{20}H_{34}O_5$, mp 129–130°. The evidence presented below established that the compound is (+)-β-eudesmol O-α-L-arabopyranoside (1).

The new glycoside afforded (+)-β-eudesmol[2] upon periodic acid oxidation and β-L-arabinose upon hydrolysis with 0.1 *N* sulfuric acid; both products were identical with authentic samples. Nmr data for both the glycoside and its triacetate indicated that the sugar

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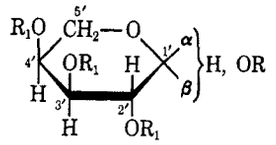
(2) We thank Dr. E. von Rudloff, National Research Council, Saskatoon, Canada, for an authentic sample of (+)-β-eudesmol.

TABLE I
NMR DATA FOR β-EUDESMOL α-L-ARABOPYRANOSIDE AND RELATED COMPOUNDS[a]



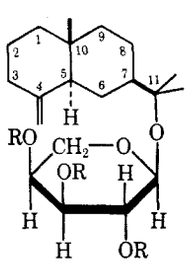
	Chemical shift, ppm						
	R			Arabopyranoside			
Compd	C_4=CH_2	C_{10} Me	C_{11} Me	$H_{1'}$	$H_{2'}$,$H_{3'}$,$H_{4'}$	$H_{5'}$	Acetates
1, R = β-eudesmol, R_1 = H	4.40 (br)[b] 4.77 (br)	0.68	1.22[b]	4.40 (br)[b]	3.40–4.10 (m)[b]	3.40–4.10[b]	
2,[c] R = β-eudesmol, R_1 = Ac	4.45 (br) 4.70 (br)	0.72	0.18 and 1.23	4.62 (br d, J = 6 cps)	4.90–5.34 (m)[b]	3.57 (dd, J = 13 and 2 cps) 4.01 (dd, J = 13 and 3 cps)	2.01 2.05 2.13
3, R = α-O-methyl, R_1 = Ac	C_1' Me 3.49			4.36 (br d, J = 6 cps)	5.05–5.40 (m)[b]	3.65 (dd, J = 13 and 2 cps) 4.09 (dd, J = 13 and 3 cps)	2.01 2.06 2.13
4, R = β-O-methyl, R_1 = Ac	C_1' Me 3.42			4.98 (br d, J = 3 cps)	5.22–5.55 (m)[b]	3.65 (dd, J = 13 and 2 cps) 3.98 (dd, J = 13 and 1.5 cps)	2.00 2.08 2.15

[a] The spectra were recorded on a Varian A-60 spectrometer in $CDCl_3$; signals were recorded in δ scale (parts per million) with TMS as an internal standard. Signals are singlets unless otherwise stated: d, doublet; dd, double doublet; m, multiplet; J = coupling constants in cycles per second. [b] Signals were overlapped. [c] Spectrum was recorded on a Varian HA-100 spectrometer.

was present in these compounds as a pyranoside (see Table I). For example, the spectrum of the triacetate (**2**) exhibited an ABX signal pattern typical for the methylene group of a $-CHOAcCH_2O-$ unit in an arabopyranose; each proton of the methylene group appeared as a double doublet at 3.57 (J = 13 and 2 cps) and 4.01 ppm (J = 13 and 3 cps), similar to the ABX pattern for the methylene group present in both α- and β-O-methyl triacetylarabopyranoside[3] (see Table I).

At this point, the only remaining structural question concerned the configuration at the anomeric carbon atom in the glycoside. Earlier studies[4] established that in α-L-tetraacetylarabopyranose the axial proton shows a coupling constant of about 6 cps while the equatorial proton in the β epimer shows a smaller coupling constant of 3 cps. We observed similar coupling constant values for the anomeric protons in the α and β forms of O-methyl triacetylarabopyranosides (see Table I, compounds **3** and **4**). The anomeric proton in the triacetate of the new eudesmol arabopyranoside showed a coupling constant of 6 cps, in accord with an α configuration.

The chemical and spectral evidence indicates that the new glycoside is (+)-β-eudesmol O-α-L-arabopyranoside and therefore corresponds to structure **1**.



1, R = H
2, R = CH_3CO

Experimental Section[5]

Isolation of (+)-β-Eudesmol O-α-L-Arabopyranoside (1).—Whole plants of *Machaeranthera tanacetifolia* (H.B.K.) Nees[6] were collected near Gail, Texas, on June 18, 1968. The air-dried ground plant material (135 g) was extracted with $CHCl_3$ and worked up in the usual manner[7] to yield 2.7 g of a thick syrup. The crude syrup was chromatographed over silica gel (70 g). Elution of the column first with benzene–acetone (4:1) afforded fractions containing impure hydrocarbon material. Elution with benzene–acetone (3:1) afforded 1.3 g of a glassy material which yielded, after standing in ether, the new compound **1** as crude crystals (0.585 g), mp 127–130°. Recrystallization from ether containing a small amount of acetone afforded pure crystals: mp 129–130°; $[\alpha]^{24}D$ +37.1° (c 0.25%, EtOH); uv (EtOH) λ_{max} 210 mμ (ε 212); ir (Nujol) 3350 (hydroxyls), 1640, and 885 cm^{-1} (double bond).

Anal. Calcd for $C_{20}H_{34}O_5$: C, 68.00; H, 9.60; O, 22.60. Found: C, 68.07; H, 9.13; O, 22.56.

Triacetyl Derivative of 1.—A solution of 40 mg of **1** in dry pyridine (0.1 ml) was added to 1.5 ml of acetic anhydride; the resultant solution was allowed to stand overnight at room temperature before work-up in the usual manner. After recrystallization of the crude product from diisopropyl ether, the triacetate **2** was obtained as needles: mp 141–142°; ir ($CHCl_3$) 1740 (carbonyls), 1640, 890 (double bond), and 1210 (acetate) cm^{-1}.

Anal. Calcd for $C_{26}H_{40}O_8$: C, 64.99; H, 8.35; O, 26.70. Found: C, 64.81; H, 8.35; O, 26.73.

Oxidative Cleavage of 1 to (+)-β-Eudesmol.—A solution of 66 mg of **1** in 5 ml of methanol was mixed with a solution of 700 mg of periodic acid hydrate and 4 drops of 10% sulfuric acid in 1.5 ml of water. The mixture was allowed to stand for 19 hr at

(3) We thank Dr. R. Bentley, University of Pittsburgh, for samples of α- and β-O-methyl L-arabopyranosides, which we acetylated by standard procedures.

(4) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *J. Amer. Chem. Soc.*, **80**, 6098 (1958).

(5) Melting points are uncorrected. Analyses were determined by Dr. Alfred Bernhardt, Mikroanalytisches Laboratorium, Elbach über Engelskirchen, West Germany.

(6) Voucher specimen, University of Texas Herbarium, no. 270186. We thank Mr. A. Birdsong, Department of Botany, University of Texas, for the plant identification.

(7) See, for example, T. J. Mabry, H. E. Miller, H. B. Kagan, and W. Renold, *Tetrahedron*, **22**, 1139 (1966).

room temperature. The solvent was removed *in vacuo* and 5 ml of water was added to the residue. The aqueous solution was extracted twice with ether and the ethereal extract was washed with aqueous saturated sodium bicarbonate. The residue from the ether extract was preparatively chromatographed on silica gel G plates (10:1 benzene–acetone). A main band at R_f 0.50 yielded an oil (25 mg), which gave, after vacuum sublimation, fine needles (15 mg), mp 79–80°[8]; the material was identical with authentic (+)-β-eudesmol[2] by nmr, ir, and specific optical rotation.

Acid Hydrolysis of 1 to β-L-Arabinose.—A solution of 100 mg of 1 in 4 ml of methanol was mixed with 4 ml of 0.1 *N* sulfuric acid; the resultant solution was heated on a steam bath for 1 hr. The solution was concentrated *in vacuo* to *ca.* 3 ml and washed with $CHCl_3$ (two 5-ml portions).[9] The aqueous layer was neutralized with calcium carbonate (150 mg). After filtration, the aqueous solution was concentrated *in vacuo* to 2 ml. Again, the solution was filtered. The aqueous filtrate was concentrated to dryness to yield a thick syrup which was extracted with hot methanol (5 ml). The methanol extract yielded a clear syrup which grew long prisms on seeding with a small crystal of β-L-arabinose. The crude crystalline mass was recrystallized from methanol (0.5 ml) to yield 10 mg of prisms which were identical with authentic β-L-arabinose by ir, mixture melting point, and specific optical rotation.

Registry No.—**1**, 21615-76-9; **2**, 21615-77-0; **3**, 21615-78-1; **4**, 14520-32-2.

(8) (+)-β-Eudesmol was reported to have mp 75–76°: J. F. J. McQuillin and J. D. Panack, *J. Chem. Soc.*, 2973 (1956).

(9) Work-up of the chloroform extract from the acid hydrolysis of the glycoside gave β-eudesmol mixed with rearranged substances (by nmr).

Nitro Steroids. I. Synthesis and Proof of Structure of 2β-Nitro-3-ethoxyestra-3,5-dien-17β-ol Acetate

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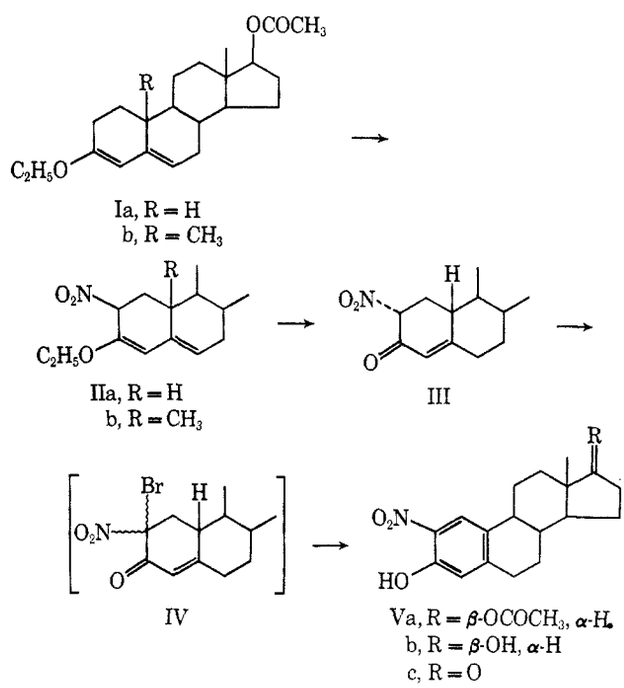
In the course of our researches in the field of estranes, we needed to prepare the compound 6-nitroestra-4-en-17β-ol-3-one as an intermediate. For this reason we repeated the reaction described in a British Patent,[1] using the 3-ethylenol ether of 19-nortestosterone acetate[2] (I) as starting material and carrying out the reaction with tetranitromethane in anhydrous ethyl ether. The nitro derivative (IIa) so obtained exhibited an infrared spectrum which was characteristic of a 3-ethoxy-$\Delta^{3,5}$ steroid (C=C bands at 1660 and 1635 cm^{-1}); however, the frequency of the NO_2 asymmetric vibration at 1550 cm^{-1} was indicative of a nitro group in a saturated position[3] and not in an unsaturated position as expected. The nmr spectrum showed two olefinic protons at *ca.* 4.47 (singlet and a doublet of doublets of which one signal fell under the singlet) assigned to C_4H and C_6H. These facts suggested that the nitro group was not in position 6, as postulated by Liisberg,[1] but probably in an allylic position, *i.e* position 2, 7, or 10.

In order to clarify the structure of IIa, the aromatization of ring A was performed as indicated in Scheme I.

SCHEME I



The enol ether IIa was hydrolyzed with concentrated hydrochloric acid in acetone to give III.[4] The nitro ketone III treated with bromine in ethyl ether afforded IV, the structure of which is only tentative and which was dehydrogenated directly with LiCl in dimethylformamide to give the nitroaromatic compound Va. Its infrared spectrum showed two aromatic bands at 1632 and 1575 cm^{-1} which were higher in frequency than the average and were typical of an aromatic nucleus substituted with a NO_2 group.[5] The nmr spectrum presented only two aromatic protons, one singlet (1H) at τ 2.02 assigned to C_1H and one singlet at τ 3.15 assigned to C_4H; these signals appeared slightly broadened by the weak coupling between *para* protons.

Acid hydrolysis of Va afforded Vb which by chromic acid oxidation gave the corresponding ketone Vc; chemical and spectral properties of Vb and Vc were in perfect agreement with those reported in the literature[6,7] for 2-nitroestradiol and 2-nitroestrone; hence, the structure of 2-nitro-3-ethoxyestra-3,5-dien-17β-ol acetate was assigned to IIa.

Information on the stereochemistry of the nitro group of IIa was furnished by the examination of its nmr spectrum. A doublet of doublets appeared at τ 5.0 (1 H) assigned to C_2H; this proton was coupled only with the C_1-methylene protons. The resonance peaks of the C_1H_e appeared as two triplets (1 H) at τ 7.47 and 7.25 (J_{gem} = 13 Hz; $J_{1,2}$ = 1.8 Hz; $J_{1,10}$ = 1.8 Hz), while the signals of the C_1H_a were hidden in the methylene envelope above τ 8.1. As the difference in chemical

(1) S. Liisberg, British Patent 883495 (1961); *Chem. Abstr.*, **57**, P3519c (1962).

(2) J. H. Zderik, H. Carpio, A. Bowers, and C. Djerassi, *Steroids*, **1**, 233 (1963).

(3) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen and Co., London, 1958, p 298.

(4) As far as the stereochemistry of the nitrogroup in compound III is concerned, the nmr spectrum indicated the α configuration on the basis of coupling constants (doublet of doublets at τ 4.75 presented J = 14 and 5 Hz).

(5) Reference 3, p 71.

(6) T. L. Patton, *J. Org. Chem.*, **24**, 1795 (1959).

(7) H. Werbin, and C. Holoway, *J. Biol. Chem.*, **223**, 651 (1956).