Phytochemistry, 1973, Vol. 12, pp 2733 to 2735. Pergamon Press. Printed in England.

25*S*-DIHYDRODRACOGENIN: A NEW SPIROSTAN SAPOGENIN FROM *SEMELE ANDROGYNA**

ANTONIO G. GONZÁLEZ, RAIMUNDO FREIRE, ROSENDO HERNÁNDEZ, JOSÉ A. SALAZAR and ERNESTO SUÁREZ

Department of Organic Chemistry, University of La Laguna, Instituto de Investigaciones Químicas, C.S.I.C., Tenerife, Spain

(*Received* 30 *April* 1973. *Accepted* 19 *June* 1973)

Key Word Index—*Semele androgyna*; Liliaceae; gibalbera; steroids; spirostan sapogenins; 25*S*-dihydrodracogenin.

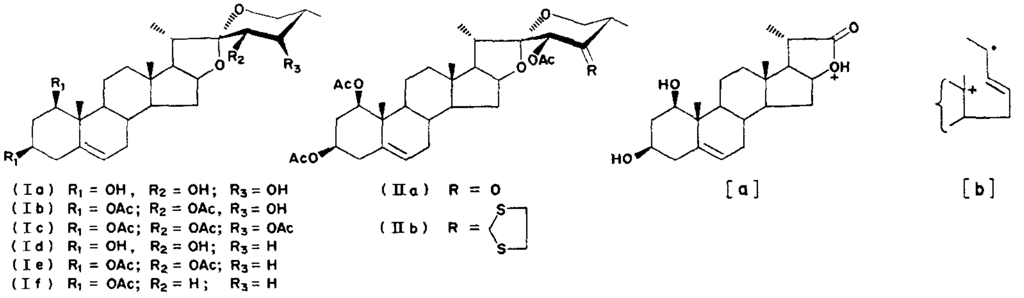
Abstract—From stems and leaves of *Semele androgyna* L. the new steroid sapogenin 25*S*-dihydrodracogenin (Ia) has been isolated and its structure confirmed by conversion into the acetates of 25*R*-dihydrosansevierigenin (Id) and ruscogenin (If) and by partial hydrogenation of dracogenin.

INTRODUCTION

IN A previous paper[1] we reported the isolation of the four new steroid sapogenins androgenin *A* and *B* and isoandrogenin A and B from stems and leaves of *Semele androgyna* L., a Canary Islands endemic. Continuing our investigations on this plant we separated a further sapogenin, named 25*S*-dihydrodracogenin (Ia), which is assigned the structure (20*S*,22*S*,23*S*,24*S*,25*S*)-spirost-5-en-1β,3β,23,24-tetrol.

RESULTS AND DISCUSSION

25*S*-Dihydrodracogenin (Ia), of empirical formula $C_{27}H_{42}O_6$, was eluted together with androgenin B,[1] the mixture being separated by preparative TLC of the acetates. In the IR,



(Ia) R_1 = OH, R_2 = OH; R_3 = OH
(Ib) R_1 = OAc; R_2 = OAc, R_3 = OH
(Ic) R_1 = OAc; R_2 = OAc; R_3 = OAc
(Id) R_1 = OH, R_2 = OH; R_3 = H
(Ie) R_1 = OAc; R_2 = OAc; R_3 = H
(If) R_1 = OAc; R_2 = H; R_3 = H

(IIa) R = O
(IIb) R =

SCHEME 1.

---

* Part XX in the series "New Sources of Steroid Sapogenins". For Part XIX see GONZÁLEZ, A. G., FREIRE, R., FRANCISCO, C. G., SALAZAR, J. A. and SUÁREZ, E. (1973) *Tetrahedron* **29**, 1731.

[1] GONZÁLEZ, A. G., FREIRE, R., HERNÁNDEZ, R., SALAZAR, J. A. and SUÁREZ, E. (1973) *Rev. Latinoam. Quím.* in press.

Ia presents absorptions for hydroxyl groups (3605, 3565, 3510, 3490 cm^{-1}) and Δ^5 (3030, 2830, 830 cm^{-1}).[2] Its MS is that expected for a spirostan sapogenin with electronegative substituent at C_{23}.[3] The base peak at *m/e* 361 corresponding to fragment [a] loses one and two molecules of water, the same being the case for fragments [a]–$C_3H_6O_2$, [b] and [b]–Me. This indicates that the androstene moiety must possess two hydroxyl groups, a third one probably being located at C_{23}. Under mild conditions, Ia forms the triacetate Ib, whose IR spectrum shows the presence of an associated hydroxyl (3520 cm^{-1}), and by refluxing with NaOAc–Ac_2O the tetraacetate Ic.

That Ib has a 1β,3β-diacetylated androst-5-ene moiety is inferred from its NMR spectrum: the singlet at 8·85 τ corresponds to the Me–C_{10} (value calculated by the method of Zürcher:[4] 8·86) and the multiplet at 4·40 ($W_{1/2}$ 10 Hz) to the H–C_6. The fact that the two protons at C_{26} appear as the *AB* part of an *ABX* system (two double doublets at 6·47 and 6·62) and the Me–C_{25} as a doublet at 9·10 (J 7 Hz) excludes positions 25, 26 and 27 for the fourth hydroxyl, which therefore must be situated at C_{24}. The proton geminal to this OH group, which in the triacetate Ib appears at 6·14 ($W_{1/2}$ 9 Hz), in the tetraacetate Ic is deshielded to 4·74. The analysis of the *AB* part in the NMR spectrum of Ib yields J_{AB} 11·8, J_{AX} 12·5 and J_{BX} 3·5 Hz; these values agree only with an equatorial Me–C_{25}. On the other hand, the doublet at 5·19, solely attributable to the proton geminal to the acetate group at C_{23}, has J 3 Hz which is incompatible with a *trans*-diaxial coupling and therefore excludes an equatorial-equatorial configuration for the 23,24-glycol. The same conclusion is also drawn from the NMR spectrum of Ic. In the IR spectrum of Ib the absorption of the hindered OH group at C_{24} is not shifted upon dilution. The length of the H bridge calculated by the formula of Kuhn[5] is 1·48 Å and the distance between an axial OH at C_{24} and the oxygen of ring E measured on a Dreiding model is 1·5 Å, while for an equatorial HO–C_{24} it would be 3·8 Å. Hence, this latter possibility is excluded.

The stereochemistry of the hydroxyl group at position 23 was determined by the following reaction sequence: oxidation of Ib with Collins reagent gave IIa, in the NMR spectrum of which the proton geminal to the acetate group appears as a singlet shifted down-field to 4·78. This confirms that Ib has an acetate group at C_{23} and a hindered OH at C_{24}. Elimination of the carbonyl *via* the thioketal IIb and subsequent Raney Ni desulfurization gave two compounds which were identified with ruscogenin acetate (If) and 25*R*-dihydrosansevierigenin acetate (Ie), the latter having been synthesized previously.[6] This confirms the existence of three hydroxyl groups at positions 1, 3 and 23, establishing their configurations as β, β and equatorial respectively, the fourth one consequently being located at C_{24} with axial configuration. Hence, Ia has the structure (20*S*,22*S*,23*S*,24*S*)-spirost-5-en-1β,3β,23,24-tetrol and therefore corresponds to 25*S*-dihydrodracogenin which we had been unable to isolate in a previous hydrogenation of the $\Delta^{25(27)}$ in dracogenin.[7] In a second attempt we now obtained the triacetate of Ia in 6% yield, in addition to the 25*R*-isomer as major product.

---

[2] SMITH, A. M. and EDDY, C. R. (1959) *Anal. Chem.* **31,** 1539.

[3] FAUL, W. H. and DJERASSI, C. (1970) *Org. Mass Spectrom.* **3,** 1187.

[4] ZÜRCHER, R. F. (1961) *Helv. Chim. Acta,* **44,** 1380.

[5] KUHN, L. P. (1952) *J. Am. Chem. Soc.* **74,** 2492; (1954) *ibid* **76,** 4323.

[6] GONZÁLEZ, A. G., FREIRE, R., GARCÍA-ESTRADA, M. G., SALAZAR, J. A. and SUÁREZ, E. (1972) *Tetrahedron* **28,** 1289.

[7] GONZÁLEZ, A. G., FREIRE, R., GARCÍA-ESTRADA, M. G., SALAZAR, J. A. and SUÁREZ, E. (1972) *Rev. Latinoam. Quim.* **3,** 8.

EXPERIMENTAL

Plant material (45 kg) was collected on the Monte de Las Mercedes (Tenerife). For experimental techniques and isolation of Ia see Ref. 1.

25S-*Dihydrodracogenin* Ia, m.p. 279–281° (Me_2CO), $[\alpha]_D$ −102° (*c* 0·13, dioxane). (Found: C, 70·36; H, 8·91. $C_{27}H_{42}O_6$ requires: C, 70·10; H, 9·15%.) $\nu_{max}^{CHCl_3}$ 3605, 3565, 3510, 3490 (OH), 3030, 2830, 830 cm^{-1} (Δ^5). MS: *m/e* 462 (M^+, 13%), 444 (60%), 426 (10%), 411 (4%), 361 ([a], 100%), 343 (55%), 325 (71%), 316 ([b], 3·5%), 301 ([b] − Me, 3·5%), 298 (10%), 287 ([a] − $C_3H_6O_2$, 74%), 283 (5%), 280 (2%), 269 (35%), 265 (4%), 251 (24%). 1, 3,23-*Triacetate* Ib, prepared from Ia with Ac_2O/pyridine at room temp. for 12 hr. Amorphous. $\nu_{m\ a}^{CS_2}$ 3520 (OH), 3040, 2840, 840 (Δ^5), 1740, 1240 cm^{-1} (OAc). NMR (100 MHz, $CDCl_3$): τ 4·40 (1H, *m*, $W_{1/2}$ 10 Hz, H–C_6), 5·19 (1H, *d*, *J* 3 Hz, H–C_{23}), 5·41 (3H, *m*, $W_{1/2}$ 30 Hz, H–$C_{1,3,16}$), 6·14 (1H, *m*, $W_{1/2}$ 9 Hz, H–C_{24}), 6·47 and 6·62 (2H, 2*dd*, J_{AB} 11·8, J_{AX} 12·5, J_{BX} 3·5 Hz, 2H–C_{26}), 7·90 (3H, *s*, AcO–C_{23}), 7·99 (6H, *s*, AcO–$C_{1,3}$), 8·85 (3H, *s*, Me–C_{10}), 9·06 (3H, *d*, *J* 7 Hz, Me–C_{20}), 9·10 (3H, *d*, *J* 7 Hz, (Me–C_{25}), 9·16 (3H, *s*, Me–C_{13}). *Tetraacetate* Ic, by refluxing Ia with Ac_2O–NaOAc for 2 hr. M.p. 190–192° (MeOH), $[\alpha]_D$ −74° (*c* 0·20, $CHCl_3$). (Found: C, 66·44; H, 8·08. $C_{35}H_{50}O_{10}$ requires: C, 66·65; H, 7·99%.) $\nu_{max}^{CS_2}$ 3030, 2840, 830 (Δ^5), 1735, 1240 cm^{-1} (OAc). NMR (60 MHz, $CDCl_3$): τ 4·40 (1H, *m*, $W_{1/2}$ 10 Hz, H–C_6), 4·74 (1H, *m*, $W_{1/2}$ 9 Hz, H–C_{24}), 5·18 (1H, *d*, *J* 4 Hz, H–C_{23}), 5·40 (3H, *m*, $W_{1/2}$ 30 Hz, H–$C_{1,3,16}$), 6·19 and 6·63 (2H, 2*dd*, J_{AB} 11·5, J_{AX} 12, J_{BX} 4 Hz, 2H–C_{26}), 7·91, 8·00, 8·03 (3H, 6H, 3H, *s*, 4 AcO), 8·85 (3H, *s*, Me–C_{10}), 9·06 (3H, *d*, *J* 7 Hz, Me–C_{20}), 9·17 (3H, *s*, Me–C_{13}), 9·22 (3H, *d*, *J* 7 Hz, Me–C_{25}).

(20S,22S,23S,25S)-*spirost*-5-*en*-1β,3β,23-*triol*-24-*one acetate* IIa. To a soln. of Ib (150 mg) in CH_2Cl_2 (15 ml) Collins reagent (500 mg) was added with stirring and the mixture kept at room temp. for 1 hr. It was poured into H_2O, extracted with $CHCl_3$ and washed with 5% aq. NaOH, 10% aq. HCl, satd aq. $NaHCO_3$ and H_2O. Preparative TLC of the residue eluting 4 × with C_6H_6–EtOAc (19:1) afforded starting material (40 mg) and IIa (110 mg), m.p. 237–239° (Me_2CO–*n*-C_6H_{12}), $[\alpha]_D$ −42° (*c* 0·33, $CHCl_3$). (Found: C, 67·51; H, 8·12. $C_{33}H_{46}O_9$ requires: C, 67·56; H, 7·90%.) $\nu_{max}^{CS_2}$ 3030, 2830, 840 (Δ^5), 1740 (CO, OAc), 1240 cm^{-1} (OAc). NMR (60 MHz, $CDCl_3$): τ 4·39 (1H, *m*, $W_{1/2}$ 10 Hz, H–C_6), 4·78 (1H, *s*, H–C_{23}), 5·43 (3H, *m*, $W_{1/2}$ 30 Hz, H–$C_{1,3,16}$), 6·17 and 6·45 (2H, 2*dd*, J_{AB} 11·5, J_{AX} 10·5, J_{BX} 9·5 Hz, 2H–C_{26}), 7·84 (3H, *s*, AcO–C_{23}), 8·00 (6H, *s*, AcO–$C_{1,3}$), 8·85 (3H, *s*, Me–C_{10}), 8·94 and 9·02 (each 3H, *d*, *J* 7 Hz), 9·15 (3H, *s*, Me–C_{13}).

(20S,22S,23S,25S)-*spirost*-5-*en*-1β,3β,23-*triol*-24-*one ethylenethioketal acetate* IIb. A soln. of IIa (102 mg) in ethanedithiol (0·75 ml) was treated with 70% $HClO_4$ (1 drop) and stirred at room temp. for 30 min, when it was poured into 10% aq. KOH and extracted with Et_2O. The organic layer was washed with 10% aq. KOH and H_2O, dried over Na_2SO_4 and evaporated *in vacuo*, yielding IIb (110 mg), amorphous. $\nu_{max}^{CS_2}$ 3030, 2830, 840 (Δ^5), 1740, 1230 cm^{-1} (OAc) NMR (60 MHz, $CDCl_3$): τ 4·39 (1H, *m*, $W_{1/2}$ 10 Hz, H–C_6), 4·72 (1H, *s*, H–C_{23}), 5·41 (3H, *m*, $W_{1/2}$ 30 Hz, H–$C_{1,3,16}$), 7·85 (3H, *s*, AcO–C_{23}), 7·99 (6H, *s*, AcO–$C_{1,3}$), 8·86 (3H, *s*, Me–C_{10}), 8·92 and 9·04 (each 3H, *d*, *J* 7 Hz), 9 21 (3H, *s*, Me–C_{13}).

25R-*Dihydrosansevierigenin* (Ie) *and ruscogenin* (If) *acetates*. A soln. of IIb (94 mg) in EtOH (15 ml) was refluxed with W-7 Raney Ni (1 g) for 2·5 hr. Dry column chromatography (C_6H_6–EtOAc, 19:1) of the residue gave If (29 mg), identified with an authentic sample (m.m.p., TLC, IR, NMR spectra superimposable), and amorphous Ie (15 mg) identified with previously synthesized material (TLC, IR, NMR spectra superimposable).[6] Saponification of Ie gave 25*R*-dihydrosansevierigenin (Id), m.p. 252–255° (MeOH), $[\alpha]_D$ −97° (*c* 0·17, $CHCl_3$); ν_{max}^{KBr} 3300 (OH), 3030, 2830, 835 (Δ^5); identified with a synthetic sample (m.m.p., TLC).[6]

25S-*Dihydrodracogenin* 1,3,23-*triacetate* (Ib) *from dracogenin* 1,3-*diacetate*. Dracogenin 1,3-diacetate (590 mg) in EtOH (50 ml) was hydrogenated over 10% Pd–C (307 mg) for 2 hr at room temp. and atm. pres. Acetylation and dry column chromatography (C_6H_6–EtOAc, 4:1) of the residue afforded 25*R*-dihydrodracogenin 1,3,23-triacetate (400 mg) identified with an authentic sample (m.m.p., TLC, IR, NMR spectra superimposable)[7] and amorphous Ib (41 mg) which showed to be identical with the triacetate of the natural product (TLC, IR, NMR spectra superimposable).

Acknowledgements—We are indebted to Dr. C. Pascual, Universität Basel, for the 100 MHz and MS spectra. One of us (R.H.) thanks the Ministerio de Educación y Ciencia for a fellowship 'Formación de Personal Investigador'. This work was realized within the Programme 1971 conceded by the Foundation 'Juan March'.