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ISOLATION OF SAIKOGENIN E, A NEW TRITERPENE FROM BUPLEURUM FALCATUM L.

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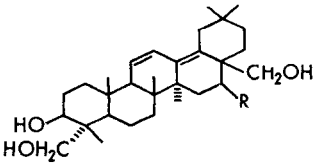
In a recent communication (1), we have described that acid hydrolysis of the crude saponin obtained from the root of Bupleurum falcatum L. afforded four new triterpenoid sapogenins, named saikogenin A (2), B, C and D, as well as the known longispinogenin (V) (3). For these new sapogenins, the structures, I, II, III and IV, have respectively been assigned.

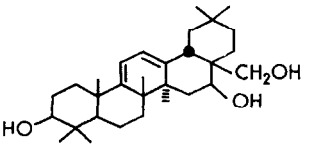
In view of the facts that saikogenin B (II) and C (III) and longispinogenin (V), isolated as the minor components, are respectively $\Delta^{9(11),12}$-, $\Delta^{11,13(18)}$- and Δ^{12}-derivatives of oleanane-3β,16β,28-triol, it was supposed that saikogenin B (II) and/or C (III) might be produced from an acid-sensitive component, which would be derived biogenetically from the ordinary Δ^{12}-derivative, during acid hydrolysis of the saponin. Thus, our investigation was directed to this point and the present paper deals with isolation and structural elucidation of a new sapogenin, now named saikogenin E (VI), which is shown to be a precursor of saikogenin B (II) and C (III).

Recently, Dugan and de Mayo (4) have described isolation of pre-senegenin, the acid-labile genuine sapogenin of Polygala senega. Isolation of saikogenin E was achieved by applying their method. The crude saponin, on thin-layer chromatography using silica gel and $CHCl_3$-MeOH-H_2O (30 : 10 : 1), is shown to consist of three main

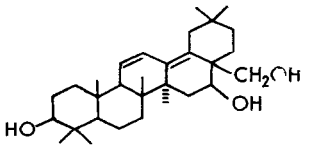


I R = β-OH; α-H

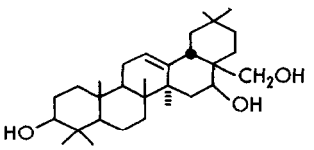
IV R = α-OH; β-H



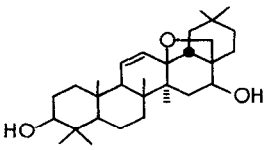
II



III



V



VI

fractions, of which the lower fraction was separated, in a fairly pure state, by column chromatography on Florisil. The fraction was oxidized with sodium metaperiodate and the product was treated with boiling ethanolic potassium hydroxide to give crude sapogenin. The top fraction obtained from chromatography on alumina was recrystallized from ethyl acetate, giving saikogenin E (VI), $C_{30}H_{48}O_3$, as plates, which began to sinter at 265° and melted at 283°, $[\alpha]_D$ +108°. The ultraviolet spectrum showed only an end absorption at 205 mμ. The infrared spectrum (Nujol) exhibited hydroxyl bands at 3445 and 3330 cm^{-1} and many sharp bands between 1189 and 883 cm^{-1} suggesting the presence of an ether linkage. Mild acetylation of saikogenin E gave

diacetate, $C_{34}H_{52}O_5$, m.p. 207-211°, $[\alpha]_D$ +111°, which showed no hydroxyl band in the infrared spectrum. Its NMR (60 Mc., in $CDCl_3$) spectrum showed signals at τ 9.15-8.90 (7 Me), 7.97 (2 Me of acetoxy groups), 6.83 and 6.02 (2H on C_{28} being involved in the ether bridge; A/B type quartet, J=7 cps), of which the bands at τ 6.83 are split with J=1.5 cps by the long-range coupling with 16α-H as expected, 5.52 (1H at C_3; quartet), 4.58 (1H at C_{16}; quartet), and 4.62 and 4.13 (2H of a two-substituted double bond; A/B type quartet, J=10.5 cps).

These data suggested the structure VI having the ether linkage between C_{28} and C_{13} for saikogenin E, in connection with saikogenin B (II) and C (III). When saikogenin E was heated with sulphuric acid in aqueous ethanol, it was readily converted into a mixture, which was shown, on examination with gas chromatography (5) of its trimethylsilyl derivative, to be saikogenin C (III)(relative retention time to cholestane 5.59) contaminated with a small amount of saikogenin B (II) (r.r.t. 4.21). After recrystallization, saikogenin C (III) was identified with an authentic specimen. Catalytic hydrogenation of saikogenin E on Adams' catalyst in acetic acid resulted in the hydrogenolysis of the allylic ether linkage as well as the double bond migration, giving longispinogenin (V).

From the above results, saikogenin E has now been proved to have the structure VI and to be a genuine sapogenin convertible into saikogenin B and C on acid treatment. Nevertheless, it is still doubtful that saikogenin B and C are produced from only a saponin corresponding to saikogenin E during acid hydrolysis.

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Note added after preparation of this paper: Just before this communication is presented, it was informed from Prof. Shoji Shibata that his group have submitted to Tetrahedron Letters a paper on isolation of the same saikogenin E. This work has been carried out independently of Prof. Shibata and appears to reach the similar result to theirs.

Note added on revision: Both the specimens of saikogenin E diacetate obtained by Shibata et al. and us have been identified by direct comparisons for which the present authors are indebted to Prof. Shibata.