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CHEMISTRY OF *AEGICERAS MAJUS* GAERTN—III

STRUCTURE OF AEGICERADIOL

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Abstract—Aegiceradiol, $C_{30}H_{48}O_2$, a new triterpene diol from *Aegiceras majus* Gaertn, is 3β,28-dihydroxy olean-12,15-diene and its partial synthesis from genin-A is described.

THE isolation of genin-A (Ia), isorhamnetin, and the C_{29}-triterpene alcohol, aegiceradienol (II) from the bark of *Aegiceras majus* Gaertn (Syn. *A. corniculatum* Blanco) was reported[1,2] earlier. A new triterpenoid, named aegiceradiol, is also present in the plant as a glycoside.

Aegiceradiol (IIIa), $C_{30}H_{48}O_2$, was isolated from the mixture of aglycones by chromatography and purified as its diacetate (IIIb). Easy acetylation of the compound suggests that both the hydroxyl groups (strong I.R. band in $CHCl_3$ at 3635 cm^{-1}) must be present as primary or unhindered secondary alcoholic functions.

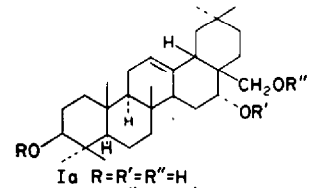
Aegiceradiol gives a positive Liebermann–Burchard test and develops a yellow colour with tetranitromethane. Hydrogenation of its diacetate over platinum and acetic acid yields erythrodiol diacetate (IV) showing that aegiceradiol is dehydroerythrodiol. In a β-amyrin skeleton possible positions[3] for the reducible double bond are C_2—C_3, C_6—C_7, C_{15}—C_{16} and C_{21}—C_{22}. Since genin-A, the congener of aegiceradiol, has a hydroxyl group at C_{16}, the 15,16-dehydroerythrodiol structure (IIIa) is favoured on biogenetic grounds.

The above structure (IIIa) was confirmed by partial synthesis of aegiceradiol from genin-A (Ia) as follows. Mild acetylation of genin-A, results in two diacetates A and B, $C_{34}H_{54}O_5$, m.p. 211–213° and 264–266° respectively. Diacetate A, on oxidation with chromium trioxide–pyridine reagent[4], yields a neutralketone, $C_{34}H_{52}O_5$, which neither gives the Zimmermann test[5] nor forms an oxime, thereby excluding positions C_3 and C_{28} for the carbonyl group. Hence, the ketone should be 16-keto erythrodiol diacetate (V) and the diacetate A represented by Ib. Diacetate A undergoes smooth dehydration with phosphorus oxychloride in pyridine yielding a product (IIIa) identical with aegiceradiol diacetate (mixed m.p. and infra-red comparison).

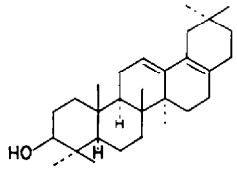
Diacetate B from its physical constants[6] should be Ic and presents an interesting example of preferential acetylation of an axial hydroxyl to a primary carbinol under mild acetylating conditions.

Aegiceradiol may be the biogenetic precursor to its C_{29}-congener, aegiceradienol

[1] K. V. Rao and P. K. Bose, *J. Indian Chem. Soc.* **36**, 358 (1959).
[2] K. V. Rao and P. K. Bose, *Sci. and Cult.* **24**, 486 (1959); *J. Org. Chem.* 1962 (In press)
[3] H. M. Smith, J. M. Smith and F. S. Spring, *Tetrahedron* **4**, 111 (1958).
[4] G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, *J. Amer. Chem. Soc.* **75**, 422 (1953).
[5] D. H. R. Barton and P. de Mayo, *J. Chem. Soc.* 887 (1954).
[6] O. Jeger, Cl. Nisoli and L. Ruzicka, *Helv. Chim. Acta* **29**, 1183 (1946).



Ia R=R'=R''=H
b R=R''=Ac; R'=H
c R=R'=Ac; R''=H



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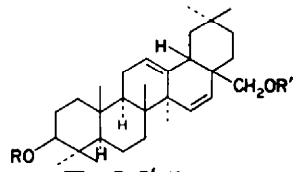
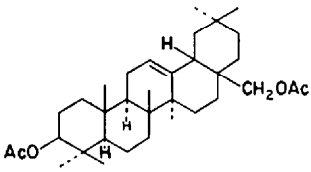
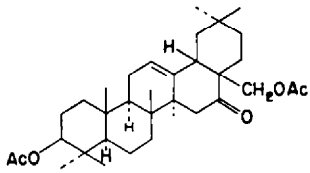


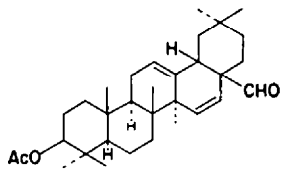
III a R=R'=H
b R=R'=Ac
c R=Ac; R'=H



IV



V



VI

(II) and the latter is probably formed by the oxidation of the primary carbinol in the former to the corresponding acid which could then undergo decarboxylation easily with the consequent double bond shift.

EXPERIMENTAL*

Isolation of the triterpenes. Air-dried powdered bark (1·2 kg) of *A. majus*† Gaertn was exhausted with ethanol (90%) under reflux and the solvent removed *in vacuo*. The dark red residue was freed from non-glycosidic material by repeated washing with ether and then dissolved in ethanol (1 l.; 50%) and heated under reflux for 4 hr, with conc HCl (200 cc). The aglycones were collected, washed, dried and extracted with ether in a Soxhlet apparatus for 30 hr. The ether extract was washed thoroughly with dil NaOH (2%) to remove *iso*rhamnetin and then with water, dried and evaporated. Extraction of the resultant semi-solid with benzene–ether (3:1; 200 cc) furnished crude *genin*-A (6·5 g) m.p. 230–235° as an insoluble residue. The remaining solution was chromatographed over alumina (400 g). Elution with light petroleum–benzene (1:1; 1 l.) and subsequent crystallizations of the residue from chloroform–methanol yielded *aegiceradienol* (0·45 g) as needles, m.p. 185–188°, $[\alpha]_D$ +74° (*c*, 0·83).

Eluting the column with benzene (1·5 l.) and crystallization of the residue from methanol furnished *aegicerin* (0·2 g) as needles, m.p. 254–256°, $[\alpha]_D^{35}$ −20·7° (*c*, 1·54). (Found: C, 78·43; H, 10·74. $C_{30}H_{48}O_3$ requires: C, 78·94; H, 10·48%).

Further elution of the column with ether–benzene (1:4; 500 cc) and crystallization of the residue from methanol gave *aegiceradiol* as a slightly impure solid (0·15 g), m.p. 220–230°.

An additional quantity of genin-A (0·5 g) could be obtained by further eluting the column with the same solvent mixture (1 l.) and ether–benzene (1:1; 1 l.).

Aegiceradiol diacetate (IIIb). The above crude aegiceradiol (150 mg) was heated with pyridine and acetic anhydride (3 cc each) over a steam-bath for 3 hr, and a benzene solution of the product passed through a column of alumina (20 g). Elution with benzene–light petroleum (3:7; 100 cc) gave aegiceradiol diacetate (IIIb, 120 mg) crystallizing from chloroform–methanol as needles, m.p. 214–215°, $[\alpha]_D^{33}$ +52·7° (*c*, 0·87). (Found: C, 78·25; H, 9·85. $C_{34}H_{52}O_4$ requires: C, 77·86; H, 9·92%). It develops a yellow colour with tetranitromethane in chloroform solution and in ethanol exhibits no selective absorption in the ultra-violet above 215 mμ.

Aegiceradiol (IIIa). Aegiceradiol diacetate (IIIb, 100 mg) was refluxed with an alcoholic solution of caustic potash (5%; 15 cc) for 3 hr. Dilution with water and isolation by means of ether gave a product which was chromatographed in benzene solution over alumina (15 g). Elution with ether–benzene (1:9; 300 cc) furnished aegiceradiol (IIIa, 75 mg) crystallizing from acetone as prisms, m.p.

* All m.p.s are uncorrected. Optical rotations were determined in chloroform at room temp. Light petroleum refers to fraction b.p. 60–80°, and alumina used for chromatography is of Brockmann's (E Merck) grade. Samples for analysis were dried *in vacuo* over phosphorus pentoxide at 110° for 12 hr.

† The plant material was collected for us by the Divisional Forest Officer, 24 Parganas, West Bengal, to whom our thanks are due.

236–238°, $[\alpha]_D^{25}$ +40·3° (*c*, 0·62). (Found: C, 81·9; H, 11·13. $C_{30}H_{48}O_2$ requires: C, 81·8; H, 10·9%).

Aegiceradiol dibenzoate. Aegiceradiol (IIIa, 100 mg) was heated with pyridine (3 cc) and benzoyl chloride (1 cc) for 3 hr at 100°. The product crystallized from benzene–ethanol, yielding aegiceradiol dibenzoate (90 mg) as microcrystalline needles, m.p. 217°, $[\alpha]_D^{25}$ +45·5° (*c*, 0·9). (Found: C, 81·12; H, 9·12. $C_{44}H_{56}O_4$ requires: C, 81·48; H, 8·64%).

Aegiceradiol 3-monoacetate (IIIc). Aegiceradiol diacetate (IIIb; 150 mg) in methanol (30 cc) was refluxed with potassium carbonate[7] (300 mg) in aqueous dioxan (1:1; 4 cc) for 3/4 hr. The product was chromatographed in benzene solution over alumina (15 g). Elution with benzene–light petroleum (1:4; 50 cc) gave only traces of unchanged aegiceradiol diacetate, m.p. 212–214°. Benzene (200 cc) eluted solids, m.p. 198–202°, which on crystallization from methanol furnished aegiceradiol 3-monoacetate (IIIc, 70 mg) as microcrystalline needles, m.p. 203–204°, $[\alpha]_D^{26}$ +44·1 (*c*, 0·34). (Found C, 79·58; H, 10·27. $C_{32}H_{50}O_3$ requires: C, 79·66; H, 10·37%). Further elution of the column with ether–benzene (1:4; 100 cc) yielded aegiceradiol (IIIa), m.p. and mixed m.p. 232–235°.

Chromic acid–acetic acid oxidation of aegiceradiol 3-monoacetate (IIIc). Aegiceradiol 3-monoacetate (IIIc, 60 mg) in glacial acetic acid (10 cc) was treated during the course of ½ hr with chromium trioxide (100 mg) in aqueous acetic acid (90%; 3 cc) and left overnight at room temp. After destroying the excess of chromic acid with methanol, the reaction mixture was poured into ice-cold water and extracted with ether. The ether extract on washing with dil NaOH (5%) gave no acidic fraction. The ether soluble residue in benzene was filtered through a column of alumina (10 g) and washed down with the same solvent (100 cc). Crystallization of the product from methanol gave VI as needles, m.p. 246–248°. (Found: C, 79·84; H, 10·32. $C_{32}H_{48}O_3$ requires: C, 80·0; H, 10·0%). It shows no colour in the Zimmermann test.

Hydrogenation of aegiceradiol diacetate (IIIb) *to erythrodiol diacetate* (IV). A solution of aegiceradiol diacetate (100 mg) in glacial acetic acid (30 cc) was shaken with reduced platinum oxide catalyst (60 mg) in an atmosphere of hydrogen at room temp and atm press. Approximately one mole of the gas at N.T.P. was taken up by the compound in 12 hr. Filtration of the catalyst and evaporation of the filtrate *in vacuo* left a residue, which after purification by chromatography over alumina, crystallized from ethanol furnishing shining needles (80 mg), m.p. 184–186°, $[\alpha]_D^{24}$ +53·6° (*c*, 0·68). It gave a yellow colour with tetranitromethane in chloroform. The m.p. of this compound was undepressed on admixture with an authentic sample[8] of erythrodiol diacetate (IV). (Found: C, 77·36; H, 9·94. $C_{34}H_{54}O_4$ requires: C, 77·52; H, 9·88%).

Partial acetylation of genin-A (Ia). Genin-A (2·5 g) in pyridine (7 cc) and acetic anhydride (3 cc) was kept at 0° for 24 hr. The product was dissolved in benzene and adsorbed over alumina (100 g). Elution with benzene–light petroleum (1:1; 1 l.) gave a colourless gum which on crystallizations from methanol yielded diacetate A (Ib, 0·8 g) as stout needles, m.p. 212–213°, $[\alpha]_D^{25}$ +30·4° (*c*, 2·5). (Found: C, 75·25; H, 10·01; $C_{34}H_{54}O_5$ requires: C, 75·27; H, 10·0%).

Eluting the column with benzene (2·5 l.) and ether–benzene (1:9; 1 l.) gave solids (1 g) which on repeated crystallizations from chloroform–methanol furnished shining needles of diacetate B (Ic), m.p. 264–266°, $[\alpha]_D^{32}$ +1·93° (*c*, 4·66). (Found: C, 75·26; H, 10·23. $C_{34}H_{54}O_5$ requires: C, 75·27; H, 10·0%). Lit.[6] m.p. 266–267°, $[\alpha]_D$ −2·2° ($CHCl_3$).

Further elution of the column with ether–benzene (1:1; 1 l.) gave only unchanged genin-A.

Oxidation of (Ib) *to* (V). A solution of diacetate A (Ib, 200 mg) in pyridine (5 cc) was added to a suspension of chromium trioxide–pyridine complex prepared from chromium trioxide (200 mg) and pyridine (10 cc) and the mixture kept at room temp for 24 hr after which it was poured into crushed ice. The separated solids were filtered, washed with dil HCl (5%) and water and then dried. The product after chromatography over alumina, furnished colourless needles of V from methanol, m.p. 211–212°, $[\alpha]_D^{25}$ −7·1° (*c*, 0·63). (Found: C, 75·45; H, 9·68. $C_{34}H_{52}O_5$ requires: C, 75·55; H, 9·63%). The compound showed no colour in the Zimmermann test and did not form an oxime under the usual conditions.

Phosphorus oxychloride dehydration of (Ib) *to* (IIIb). Diacetate A (Ib, 400 mg) was left at room temp for 16 hr with phosphorus oxychloride (3 cc) and pyridine (10 cc) and then heated on the steam-bath for 1 hr. Dilution with water, ether extraction and chromatography on alumina (20 g) furnished

[7] A 3β-acetoxy group is not attacked under these conditions. cf. C. Djerassi, E. Farkas, A. J. Lemin, J. C. Collins and F. Walls, *J. Amer. Chem. Soc.* **76**, 2969 (1954).

[8] B. Y. T. Wu and L. M. Parks, *J. Amer. Pharm. Ass, Sci. Ed.* **39**, 475 (1950).

the dehydration product (IIIb, 300 mg) which after crystallization from chloroform–methanol exhibited m.p. 214–215°, $[\alpha]_D^{33}$ +52·1° (*c*, 1·44), and strong yellow colour with tetranitromethane. (Found: C, 78·32; H, 9·93. $C_{34}H_{52}O_4$ requires: C, 77·86; H, 9·92%). The compound showed no depression in m.p. when admixed with a pure sample of aegiceradiol diacetate and gave an infra-red spectrum identical with the latter.

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