483. *The Isolation and Structure of Geigerinin, a Guaianolide.*

By J. P. De Villiers.

A new bitter principle, geigerinin, has been isolated from *Geigeria aspera* Harv. It is a guaianolide containing two easily esterified hydroxyl groups and a vinyl group, and gives chamazulene on dehydrogenation. The structure (V) is proposed for geigerinin, though an isomer remains a possibility.

" Vermeerbos " (*Geigeria* spp.) grows abundantly in many parts of South Africa and is annually responsible for heavy losses of sheep due to " vermeersiekte " (vomiting disease). From *Geigeria aspera* Harv., Rimington and Roets[1] isolated geigerin and vermeerin. As a result of later work by Perold[2] and by Barton and Levisalles,[3] structure (I) was established for geigerin.

A new sesquiterpenoid lactone, geigerinin, has now been isolated from *G. aspera*. Its presence, together with geigerin, has also been demonstrated by paper chromatography in *G. africana* Gries., the species mainly responsible for " vermeersiekte."

Geigerinin, $C_{15}H_{22}O_4$, contains a γ-lactone group (infrared maximum at 1761 cm.$^{-1}$), two easily acetylated hydroxyl groups, and a double bond. Dehydrogenation with palladium–charcoal gave chamazulene, showing that geigerinin has the usual carbon skeleton of the guaianolides[4] (II), or the alternative structure with the lactonised hydroxyl at position 8. Ozonolysis of geigerinin yielded formaldehyde, indicating that the double bond is in a vinyl group. The position and intensity of the ultraviolet absorption of geigerinin ($\lambda_{max.}$ 209, log ε 4) require the double bond to be conjugated with the carbonyl group of the lactone, and the double bond must therefore be in the 13,14-position in (II). Similar ultraviolet absorption is ascribed by Büchi and Rosenthal[5] to the unsaturated lactone chromophore in helenalin (III). Geigerinin shows a strong infrared peak at 820 cm.$^{-1}$ which is absent from the spectrum of dihydrogeigerinin. Helenalin, containing a

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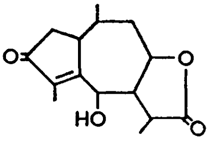
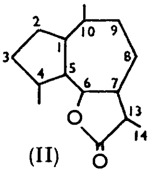
[1] Rimington and Roets, *Onderstepoort J. Vet. Sci.*, 1936, **7**, 485.
[2] Perold, *J.*, 1957, 47.
[3] Barton and Levisalles, *J.*, 1958, 4518.
[4] Čekan, Herout, and Šorm, *Chem. and Ind.*, 1954, 604.
[5] Büchi and Rosenthal, *J. Amer. Chem. Soc.*, 1956, **78**, 3860.

trisubstituted double bond and an unsaturated lactone, shows two peaks at 820 and 830 cm.$^{-1}$, neither being shown by tetrahydrohelenalin.[6]

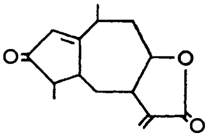
Geigerinin reduced 1 mol. of periodate, indicating vicinal hydroxyl groups, and, as the ease of acetylation makes it unlikely that either hydroxyl is tertiary, the only possible positions for the hydroxyls are 2,3 or 8,9 in (II). Heating geigerinin with alumina in an attempt to dehydrate it [7] gave a new compound, anhydrogeigerinin, $C_{15}H_{20}O_3$. This shows no infrared hydroxyl absorption, but has an additional carbonyl band at 1739 cm.$^{-1}$ indicative of a *cyclo*pentanone. Like geigerinin, it has only one double bond, and its ultraviolet spectrum is identical with that of geigerinin, except for the shoulder caused by the isolated ketone group at 290 mμ. As the only possibilities for a *cyclo*pentanone system are with the carbonyl group at position 2 or 3 in (II), anhydrogeigerinin has the structure (IV) and geigerinin the structure (V).



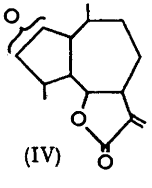
(I)



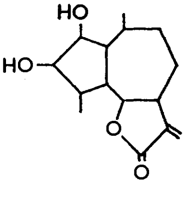
(II)



(III)



(IV)



(V)

An alternative series of structures with the lactonised hydroxyl in position 8 has, however, not been excluded.

EXPERIMENTAL

Ultraviolet spectra were measured for 96% ethanol solutions in a Unicam S.P. 500 spectrophotometer. The infrared spectra were measured in a Perkin-Elmer Model 21 spectrophotometer for potassium bromide discs. M. p.s are corrected. *Geigeria aspera* was obtained through the courtesy of Mr. Tom du Toit from his farm " Schaapplaats " near Wolwehoek, Orange Free State.

Geigerinin.—Ground, air-dried *G. aspera* was extracted with cold chloroform. Removal of the solvent gave a viscous, dark green tar, which was dissolved in 1 : 4 v/v aqueous ethanol and extracted repeatedly with pentane. The ethanol solution was boiled with charcoal and filtered. The clear yellow-brown filtrate was diluted with brine to give an aqueous phase, containing 30% of ethanol and 5% of sodium chloride, which was extracted with chloroform until it had a light straw colour and was no longer bitter. Removal of the chloroform left a very viscous tar.

Chromatography of this tar on acid-washed alumina, with 3 : 1 benzene–chloroform as eluant, gave two major fractions, the first being a complex mixture and the second consisting essentially of geigerin. Subsequent elution of the column with ethanol and removal of the solvent afforded a yellow-green viscous oil. Trituration of this residue with acetone yielded white crystalline *geigerinin*, which on recrystallisation from methanol had m. p. 202—203°, $[\alpha]_D^{29}$ $-10{\cdot}7°$ (*c* 2·3 in ethanol), $\lambda_{max.}$ 209 mμ (log ε 4) (Found: C, 67·4; H, 8·6%; equiv., by lactone titration, 266. $C_{15}H_{22}O_4$ requires C, 67·6; H, 8·3%; *M*, 266).

The molecular weight was determined from crystallographic measurements by Mr. G. Gafner (National Physical Research Laboratory, C.S.I.R., Pretoria) who reports: " Cell dimensions were measured from oscillation and Weissenberg photographs and are: $a = 13{\cdot}745$ Å, $b = 7{\cdot}796$ Å, $c = 13{\cdot}291$ Å, $\beta = 92°$. The density was determined by flotation to be 1·24 g./c.c.

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[6] Adams and Herz, *ibid.*, 1949, **71**, 2546.

[7] Cook, Loudon, and McCloskey, *J.*, 1954, 4176.

On the assumption of 4 mol./unit cell, this gives a molecular weight of 266 ± 4. The only systematic absence is (0*k*0) absent for *k* odd. Laue symmetry is $2/m$, thus the space group is $P2_1$."

Geigerinin was soluble in ethanol and very sparingly soluble in acetone, chloroform, carbon disulphide, or water. It did not give a colour with ferric chloride or tetranitromethane. It was insoluble in sodium hydrogen carbonate solution, but dissolved slowly in aqueous sodium hydroxide; only polymeric material was recovered on acidification. With acetic anhydride–perchloric acid it readily yielded a *diacetate* as white rods, m. p. 158°, $[\alpha]_D^{28}$ −33·9° (*c* 4·2 in ethanol) (Found: C, 65·5; H, 7·7; Ac, 26·0. $C_{19}H_{26}O_6$ requires C, 65·1; H, 7·4; Ac, 25·3%). On hydrogenation over Adams platinum oxide in ethanol, geigerinin absorbed 1·01 mol. of hydrogen, to give *dihydrogeigerinin*, m. p. 152—154°, $[\alpha]_D^{28}$ +15·3° (*c* 2·1 in ethanol), $\lambda_{max.}$ 219 (log ε 2·6) (Found: C, 66·7; H, 9·1. $C_{15}H_{24}O_4$ requires C, 67·1; H, 9·0%). Acetylation gave *dihydrogeigerinin diacetate*, m. p. 171—172°, $[\alpha]_D^{28}$ −48° (*c* 0·5 in ethanol) (Found: C, 64·9; H, 8·3; Ac, 24·4. $C_{19}H_{28}O_6$ requires C, 64·8; H, 8·0; Ac, 24·4%).

Dehydrogenation of Geigerinin.—Geigerinin (0·75 g.) and 30% palladised charcoal (100 mg.) were heated to 330° in two lots for 2 hr. in nitrogen. The mixture was extracted with pentane and ethanol (10 ml.), and the residue heated for a further hour. After being washed with water and dried, the extracts were chromatographed on alumina to give an intense blue oil (19·9 mg.), $\lambda_{max.}$ 244, 283, 343, and 365 mμ (log ε 4·28, 4·41, 3·41, and 3·1, respectively). With 1,3,5-trinitrobenzene, black needles (5 mg.) were obtained which, on recrystallisation from ethanol, had m. p. 132—133° alone or mixed with the chamazulene adduct.

Ozonolysis of Geigerinin.—Geigerinin (500 mg.) in acetic acid (15 ml.) was treated with a stream of oxygen, containing 15 mg. of ozone/min., for 45 min. The mixture was steam-distilled into aqueous dimedone. On neutralisation of the distillate a precipitate was formed (113 mg., 20%) which had m. p. 191° alone or mixed with formaldehyde dimethone.

Periodate Oxidation.—Geigerinin (0·1407 g.) was dissolved in ethanol (5 ml.), 2M-potassium periodate (2 ml.) added, and the solution made up to 10 ml. with water. After 24 hr. the solution (2 ml.) was added to potassium iodide solution, excess of standard sodium arsenite added, and the solution titrated with standard iodine. Geigerinin consumed 1·37 g.-atom of oxygen per mole.

Anhydrogeigerinin.—Geigerinin (500 mg.), mixed with alumina (1 g.), was heated at 180—190°/2 mm. During 16 hr. 210·6 mg. of sublimate were collected, chiefly as a glass which crystallised as feathery needles. Recrystallisation from methanol gave *anhydrogeigerinin*, m. p. 152—153°, $[\alpha]_D^{28}$ +65° (*c* 0·8 in ethanol), $\lambda_{max.}$ 209 mμ (log ε 4), shoulder 290 mμ (log ε 1·5), $\nu_{max.}$ 1770 (γ-lactone) and 1739 cm.$^{-1}$ (*cyclo*pentanone) (Found: C, 72·2; H, 8·2. $C_{15}H_{20}O_3$ requires C, 72·6; H, 8·1%). It gave no tetranitromethane colour and on microhydrogenation absorbed 1·2 mols. of hydrogen. Anhydrogeigerinin gave an orange 2,4-*dinitrophenylhydrazone*, m. p. 235° (Found: C, 58·6; H, 5·6. $C_{21}H_{24}O_6N_4$ requires C, 58·9; H, 5·6%).

Mr. G. Gafner is thanked for the crystallographic measurements and Mr. D. F. Gouws for technical assistance. The gift of a sample of chamazulene–trinitrobenzene adduct by Dr. G. W. Perold of the South African Iron and Steel Industrial Corporation, and many helpful discussions with Dr. P. R. Enslin are gratefully acknowledged.

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