NUCLEAR OXIDATION IN THE FLAVONE SERIES

Part X. Constitution of Gardenin

BY K. J. BALAKRISHNA AND T. R. SESHADRI

(From the Department of Chemistry, Andhra University, Waltair)

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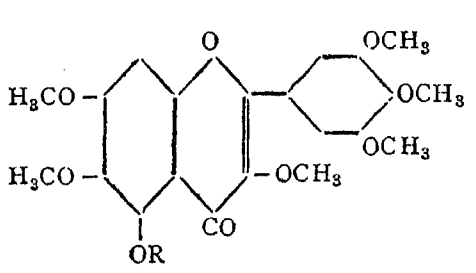
GARDENIN is the yellow crystalline component of the Dikamali gum (gum of *Gardenia lucida*) which has been used in India as a drug. It was first isolated by Stenhouse[1] and the most recent work is by Bose[2] who made a detailed study of the compound and proposed a constitution for it. He showed that the substance belonged to the group of flavones, having one hydroxyl group and six methoxyl groups. The free hydroxyl was placed in the 5-position since gardenin was sparingly soluble in alkali, gave ferric chloride colour and a condensation product with stannic chloride and was resistant to further methylation. Degradation with alkali yielded trimethyl gallic acid as a readily identified product. The ketonic half had undergone further



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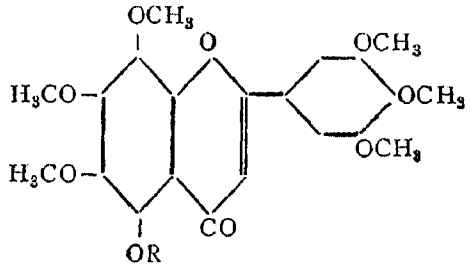
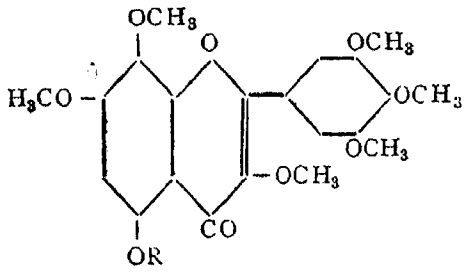


(II)

[In I to IV, R=H or CH_3]



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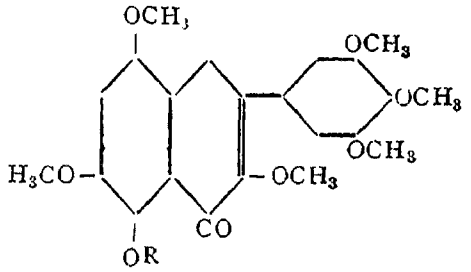

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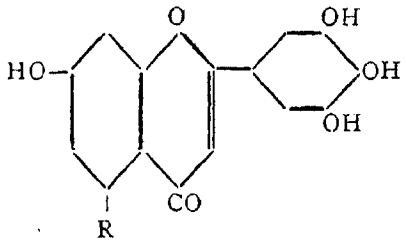


(V) R=H or OH

changes, oxidation and demethylation. The formation of the acid located three of the six methoxyl groups in the side-phenyl nucleus. There were four possible arrangements for the other three methoxyl groups in the benzo-pyrone part—3:6:7 (I), 6:7:8 (II), 3:7:8 (III), 3:6:8 (IV). Since crude nor-gardenin did not give Bargellini's test formulæ (I) and (II) were ruled out. Against formula (III) it was found that gardenin did not couple with diazotised *p*-nitraniline indicating the absence of a free nuclear position para or ortho to the phenolic hydroxyl. Further methyl gardenin was not identical with O-heptamethyl hibiscetin (III, R = CH_3). Hence by elimination of other possibilities structure (IV, R = H) was allotted by Bose to gardenin.

The above constitution for gardenin would make it a representative of an altogether unknown type of hydroxy-flavones. It was therefore felt necessary to adduce unequivocal evidence in support of this constitution and the application of the method of nuclear oxidation in the flavones has now offered an easy means of providing this support from the synthetic side.

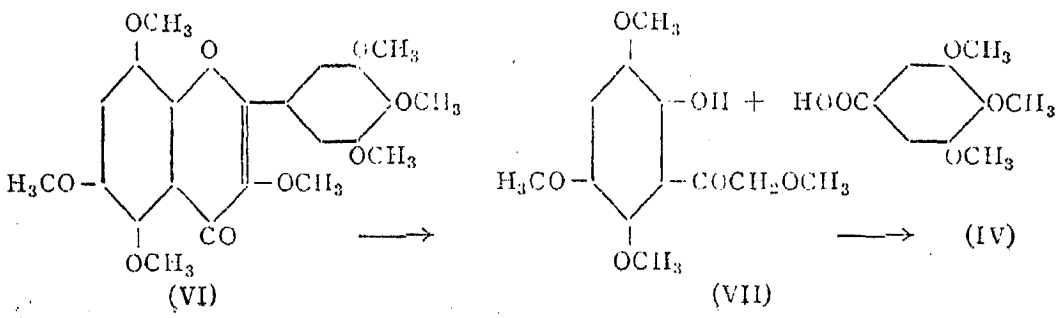
Before taking up the synthetic work a more detailed study of gardenin and of its derivatives was undertaken in order to make sure of the proposed structure. It is fairly readily obtained from the gum and an yield of 1 to 1·4% could be secured by adopting the procedure described in the experimental part. In our study of a large number of samples obtained at different times and from different places it was frequently found that several of them did not yield any gardenin, though apparently the gum samples looked genuine. But the absence of a marked yellow colour in the gum corresponded to lack of yields of gardenin. It seems to be therefore necessary to use deep yellow coloured gums in order to obtain good yeilds of the pigment.

The properties of our samples of gardenin agree with the description of previous workers. The methylation of gardenin is unusually difficult. Bose and Nath[2] obtained the methyl ether only as a pale yellow solid melting at 102° even after repeated methylation using dimethyl sulphate and aqueous sodium hydroxide. A sample of this that was sent to us, gave also a faint ferric chloride colour. Obviously the methylation was not quite complete by this process. However by using excess of dimethyl sulphate and potassium carbonate and boiling for 30 hours, a colourless product could now be obtained melting at 116–17°. Comparison of this pure product with (1) hibiscetin methyl ether[3] (III, R = CH_3), m.p. 194–6°, and (2) 6-hydroxy-myricetin methyl ether,[4] m.p. 150–51° (I, R = CH_3), showed that it is different from both of them.

By the demethylation of gardenin, nor-gardenin has now been obtained in a pure condition and its analytical results agree with the requirements of a heptahydroxy-flavone. But in its properties it is very different from hibiscetin and 6-hydroxy-myricetin. We confirm that it does not give Bargellini's test but we should here mention that though this excludes the 5:6:7-disposition of hydroxyl groups, it does not rule out the 5:6:7:8-arrangement (II) as it has been shown recently by Seshadri and Venkateswarlu[5] that calycopteretin and its analogues having the 5:6:7:8- arrangement of hydroxyl groups do not give Bargellini's test. As a matter of fact this alternative had again to be reconsidered since the colour reactions of nor-gardenin towards alkaline buffer solutions were extraordinary. The absence of any display of colour so definitely associated with flavonols having hydroxyl groups in the 3′, 4′ and 5′ positions was remarkable. Actually not only hibiscetin[3] but its isomer 6-hydroxy-myricetin,[4] myricetin[6] itself (V, R = OH) and even robinetin[7] (V, R = H) give prominent display of colours in alkaline buffer solutions. This seemed to suggest that gardenin was a flavone derivative having the 5:6:7:8-arrangement of hydroxy groups because flavones generally do not give prominent colour changes in alkaline buffer solutions. However, as shown later, this constitution was eventually found to be untenable using synthetic evidence.

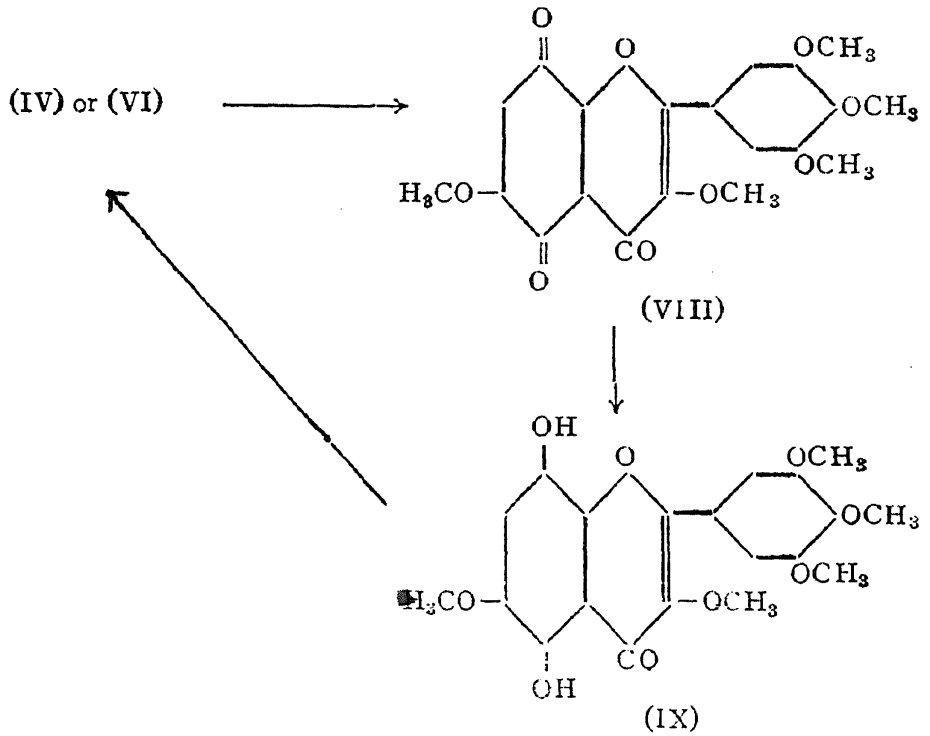
By carrying out the methylation of nor-gardenin in stages both gardenin and methyl gardenin could be obtained. This established that there was no isomeric change during the demethylation using hydriodic acid and also provided one method of preparing gardenin by partial methylation.

Alkali fission of gardenin itself does not proceed satisfactorily and produces further change in the ketonic fission product. On the other hand gardenin methyl ether (VI) undergoes fission smoothly with alcoholic potash and good yields of the ketonic part (VII) could be obtained along with trimethyl gallic acid. When these two are made to recombine using the Allan-Robinson method there is partial demethylation also and the product is found to be gardenin. These experiments confirm that gardenin belongs to the flavone group and also constitute a partial synthesis of gardenin itself.



A number of cases of partial demethylation during the Allan-Robinson condensation are now known leading to the formation of 5-hydroxy-compounds.

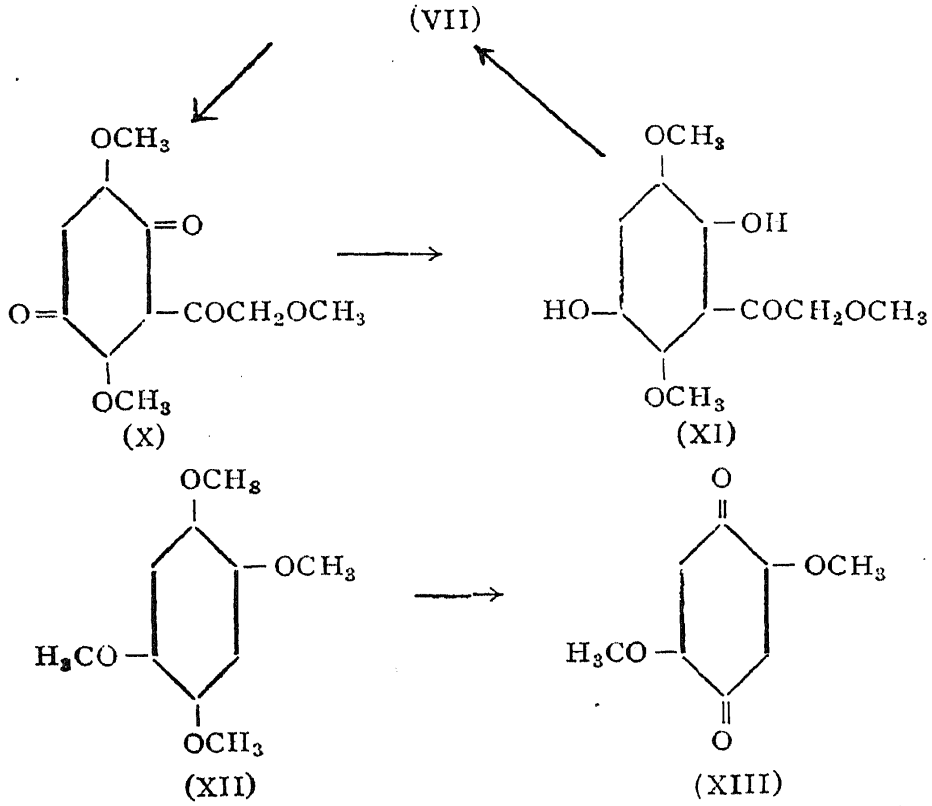
The behaviour of gardenin, as already recorded by previous workers, showed that it had a hydroxyl in the 5-position. Its preparation by the partial methylation of nor-gardenin and its partial synthesis and resistance to further methylation mentioned earlier in this paper agree with this structural feature. The boric-citric reaction[8] has now been found to be positive for the presence of the 5-hydroxyl in gardenin and 5-methoxyl in the methyl ether. With nitric acid not only gardenin (IV) but also its methyl-ether (VI) undergo change into the quinone gardeninone which is a definite indication of the presence of substituent groups in the 5 and 8 positions.[9] The quinone (VIII) could be reduced to the quinol (IX) and partial methylation of it yields again the original gardenin, whereas complete methylation yields the methyl ether. These transformations prove conclusively that nitric acid effects only oxidative demethylation and does not produce nuclear oxidation introducing fresh oxygen atoms into the nucleus. Further they constitute another easy method of preparing gardenin from its methyl ether and again confirm the location of the free hydroxyl in the 5-position.



The condensation of the fission ketone (VII) with benzoic anhydride is also accompanied by partial demethylation. But on further methylation a flavone tetramethyl ether is obtained with its melting point (118–19°) fairly close to the melting point of 5:6:7:8-tetramethoxy-flavone[10] (117–18°). But the mixed melting point is definitely lowered (95–100°). Consequently

the possibility of gardenin belonging to the 5: 6: 7: 8-hydroxy-flavone series (nobiletin series) is definitely ruled out and hence the only alternative left is that of a flavonol with the 5: 6: 8-arrangement of hydroxyls in the benzo-pyrone part. The high yield of the ketone in the fission and the facile reconstitution of gradenin would agree with the flavonol structure.

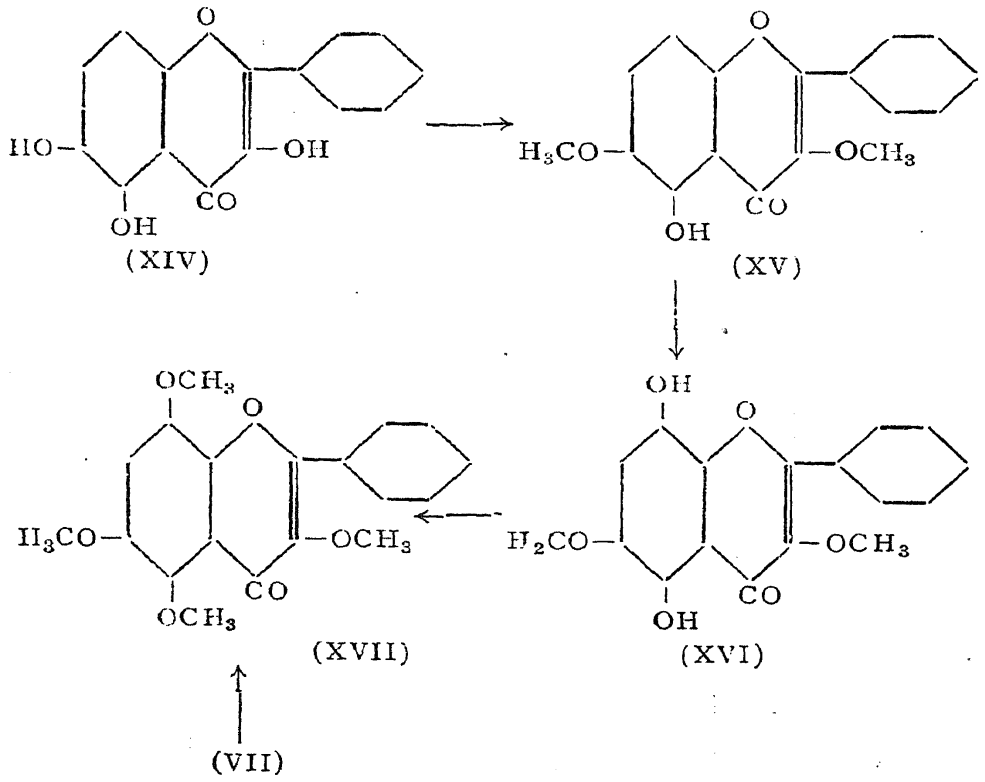
The following transformations carried out with the ketonic degradation product again agree with this idea and show definitely that it is ω-3: 5: 6-tetramethoxy-2-hydroxy-acetophenone (VII). On oxidation with nitric acid it underwent smooth oxidative demethylation yielding a quinone (X) which was neutral in properties and did not give ferric chloride colour. Estimation of methoxyl showed that it had still three methoxyls left. On reduction it formed a quinol (XI) which when partially methylated yielded the original tetramethoxy ketone. These transformations can be represented as given below.



A close analogy is provided by 1: 2: 4: 5-tetramethoxy benzene[11] (XII) which yields 2: 5-dimethoxy benzoquinone (XIII) on oxidation. In all the cases studied in the course of this work (gardenin and methyl gardenin, the fission ketone and tetramethoxy benzene) demethylation takes place only to form quinones and no extra methoxyl groups undergo removal during the process. These experiments on the ketone may be said to be complementary to those carried out on gardenin or its methyl ether. Whereas the latter give definite evidence about the presence of substituents in the 5: 8-positions, the former provide the proof for the presence of a methoxyl in

the 5-position of the ketone corresponding to the 6-position of the flavone. It may be mentioned here that with nitric acid the behaviour of 2-hydroxy-3:4:6-trimethoxy-acetophenone which has no methoxyl or hydroxyl group in the 5-position is different (unpublished work).

As already mentioned the condensation of the fission ketone (VII) with benzoic anhydride and sodium benzoate yields a compound which is different from 5:6:7:8-tetramethoxy-flavone. This led conclusively to the constitution of gardenin as a derivative of 3:5:6:8-hydroxy-flavone. Confirmation has now been obtained by comparing the above tetramethyl ether with a synthetic sample prepared by an independent route using nuclear oxidation.



The immediate starting point is 3:5:6-trihydroxy flavone (XIV) which has been recently described by Rajagopalan, Row and Seshadri.[12] It is partially methylated to yield the 3:6-dimethyl ether (XV) and subjected to oxidation with alkaline potassium persulphate. The quinol (XVI) obtained thereby is methylated when it yields 3:5:6:8-tetramethoxy flavone (XVII). In every respect it agrees with the tetramethyl ether obtained from gardenin-fission-ketone (VII) and the mixed melting point is undepressed.

The constitution of gardenin (IV, R = H) thus conclusively established, makes it the representative of a group of flavones till now unknown; the remarkable feature is that it is devoid of the 7-hydroxyl group. Compounds without this hydroxyl group are very few and are recent discoveries; primetin,

5-hydroxy-flavone, and flavone itself have so far been found to occur in nature. The marked absence of colour display in alkaline buffer solutions, already mentioned as characteristic of gardenin, is obviously bound up with the absence of this hydroxyl group since even the simpler flavonol, robinetin (V, R = H) gives this effect.

According to the theory of Robinson[13] regarding the biogenesis of anthocyanins and anthoxanthins, the 5:7-combination of hydroxyl groups in the benzopyrone part would represent the earliest stage. For the evolution of the 5:6:8-hydroxy structure as in gardenin there should be two further stages of oxidation involving the positions 6 and 8 and a stage of reduction involving position 7. Though it may not be possible to give the exact sequence of these processes the results already recorded on nuclear oxidation would suggest the following important alternatives.

$$\begin{array}{ccccc} 5:7 & \rightarrow & 5:6:7 & \rightarrow & 5:6:7:8 \\ \downarrow & & \downarrow & & \downarrow \\ \text{5-mono} & \rightarrow & 5:6 & \rightarrow & 5:6:8 \end{array}$$

The synthetic experiments described in this paper support the ready conversion of 5:6-dihydroxy compounds into 5:6:8-trihydroxy analogues. It may however be pointed out that the intermediate 5:6-dihydroxy compounds have not yet been found to occur in nature. As already indicated in an earlier paper[14] the 6-position should undergo oxidation during a stage of the skeleton when the pyrone ring is not closed whereas the 8-position is readily affected at a later stage when the pyrone ring is closed.

Experimental

Isolation of gardenin (IV, R = H)

The following procedure, for the extraction of Dikamali gum, was found to give consistently good yields of gardenin.

The gum was repeatedly digested with small volumes of boiling alcohol until the alcoholic extract was no more coloured yellow. Each time the clear supernatant liquid was decanted off quickly while hot. The total alcoholic extract was left in the refrigerator for one week. Almost all the gardenin along with some yellow resin separated out. This was filtered through fluted filters. The solid on the filter was now thoroughly shaken with hot petrol when all the resinous part went into solution. The residue was filtered and crystallised twice from alcohol. It was obtained as golden yellow needles melting at 163–64°. (Found: C, 59·8; H, 4·9; OCH_3, 44·5; $C_{21}H_{22}O_9$ requires C, 60·3; H, 5·3; OCH_3, 44·5%.) With alcoholic

ferric chloride gardenin gave an olive green colour and in aqueous alkali it was very sparingly soluble. When an alcoholic solution was acidified with hydrochloric acid and treated with magnesium powder an orange red colour was readily produced. It gave the boric-citric test characteristic of a 5-hydroxyl in the flavone nucleus.

Nor-gardenin

Gardenin (1·0 g.) was dissolved in acetic anhydride (5·0 c.c.) and hydriodic acid (10 c.c.; d, 1·7) was added with cooling under the tap. The mixture was boiled gently for one hour, cooled and diluted with water and saturated with sulphur dioxide. The bright yellow solid that separated out was crystallised from glacial acetic acid. It was obtained as micro-crystalline solid melting with decomposition at 320°. (Found: C, 51·5; H, 3·7; $C_{15}H_{10}O_9$, H_2O requires C, 51·1; H, 3·4%.) Yield, 0·6 g.

With alcoholic ferric chloride it gave a green colour which changed to blue and later gave rise to a blue precipitate. In aqueous alkali it dissolved quickly to form a reddish-brown solution. With *p*-benzoquinone in glacial acetic acid the compound produced a bright red colour followed by a reddish brown precipitate. It gave the following colour changes in buffer solutions of different p_H: p_H 8·2—light green solution changing rapidly to yellow; p_H 9·2—dissolved to give a yellow solution, no change in 24 hours; p_H 10·4—formed a deep yellow solution and turned yellowish-brown in 24 hours; p_H 11·6—golden-yellow solution slowly acquiring brown tinge and becoming pale brown red, in 24 hours changed to yellowish-brown; p_H 12·8—orange solution, brown in 2 minutes and yellowish-brown in 24 hours; sodium carbonate solution—dull green, fading rapidly to yellowish brown. With lead acetate solution it gave a red precipitate changing to brown and with sodium amalgam and absolute alcohol a brown solution followed by a brown precipitate.

Methyl gardenin (VI)

Gardenin (1·0 g.) was dissolved in dry acetone (50 c.c.) and anhydrous potassium carbonate (8·0 g.) and dimethyl sulphate (0·5 c.c.) were added. The mixture was refluxed for 30 hours. The acetone solution was filtered from the potassium salts which were washed with some more hot acetone. The acetone filtrate on concentration and dilution with water gave a colourless solid. It crystallised from a mixture of dry ethyl acetate and petroleum-ether as colourless stout rectangular rods melting at 116–17°. (Found: C, 61·4; H, 5·5; OMe, 49·6; $C_{22}H_{24}O_9$ requires C, 61·1; H, 5·6; OMe, 50·2%.) Yield 0·8 g. The compound was perfectly colourless and

insoluble in aqueous alkali and produced no colour with alcoholic ferric chloride. It gave a positive boric-citric reaction.

Complete methylation of nor-gardenin

Nor-gardenin (0·5 g.) was methylated in dry acetone (50 c.c.) using excess of dimethyl sulphate (1 c.c.) and anhydrous potassium carbonate (8·0 g.). The methyl ether, after a crystallisation from a mixture of dry ethyl acetate and petroleum-ether, was obtained as a colourless crystalline solid. The mixed melting point with methyl gardenin (VI) was undepressed.

Partial methylation of nor-gardenin

Nor-gardenin (0·2 g.) was methylated in dry acetone (25 c.c.) using dimethyl sulphate (0·28 c.c., 6 mols.) and anhydrous potassium carbonate (5·0 g.). The methylated product crystallised out of alcohol as bright yellow needles melting at 162–63°. The mixed melting point with gardenin (IV) was not depressed.

Gardeninone (VIII) and Gardeninol (IX)

Following the procedure of Bose and Nath[2] gardeninone (m.p. 222°) was prepared from gardenin and also from methyl gardenin using nitric acid (d, 1·25) and it was reduced to gardeninol. The quinol was found to melt at 190–91° as recorded by Stenhouse. With alcoholic chloride it gave a green colour which immediately changed to brown and it was soluble in aqueous alkali to form a reddish-brown solution.

Complete methylation of gardeninol (IX)

Gardeninol (IX) (0·5 g.) was dissolved in dry acetone (25 c.c.) and anhydrous potassium carbonate (8·0 g.) and dimethyl sulphate (0·8 c.c.) were added. The mixture was refluxed for 30 hours and on working up the acetone solution as in the methylations described already a colourless compound melting at 116–17° was obtained. The mixed melting point with methyl gardenin (VI) was undepressed.

Partial methylation of gardeninol

Gardeninol (IX) (0·3 g.) was dissolved in dry acetone (25 c.c.) and anhydrous potassium carbonate (5·0 g.) and dimethyl sulphate (0·08 c.c.; 1 mol.) were added. The mixture was refluxed for six hours and the acetone solution worked up as usual. The bright yellow solid product melted at 163–64° after crystallisation from alcohol. The mixed melting point with gardenin (IV) was not depressed.

Alkali fission of methyl gardenin (VI)

Methyl gardenin (VI) (1·0 g.) was treated with 8% absolute alcoholic potash (30 c.c.) and the solution was refluxed for six hours. As much of the alcohol as possible was removed by evaporation over a water-bath and the residue was treated with water. The solution was filtered through cotton and acidified with dilute sulphuric acid. The semi-solid that separated out was extracted with ether. The ether solution was repeatedly extracted with aqueous sodium bicarbonate. On acidifying this extract a colourless solid was precipitated which, when crystallised from hot water, was obtained as colourless needles melting at 167–68°. The mixed melting point with an authentic sample of trimethyl gallic acid was not depressed.

The ether solution on evaporation deposited a bright yellow semi-solid which solidified slowly. It crystallised from alcohol as bright yellow cubes (VII) melting at 88–89°. (Found: C, 56·0; H, 6·5; OCH_3, 47·9; $C_{12}H_{16}O_6$ requires C, 56·3; H, 6·3; OCH_3, 48·4%.) Yield, 0·5 g. With alcoholic ferric chloride it gave a reddish-brown colour and was soluble in aqueous alkali. Direct comparison and mixed melting point determination showed that it is different from gossypetol and quercetagetol-tetramethyl ethers.

Oxidation of the ketone (VII)

The ketone (2·0 g.) was dissolved in dry ether (150 c.c.) and fuming nitric acid (1·0 c.c.) was added. On stirring the mixture and allowing it to stand for half an hour, a bright red solid (quinone X) separated out. It was filtered and washed with ether. It crystallised from dilute acetic acid as long orange-coloured needles melting at 222–24°. (Found: OCH_3, 38·4; $C_{11}H_{12}O_6$ requires OCH_3, 38·8%.) Yield, 0·3 g. With alcoholic ferric chloride it did not give any colour. It was insoluble in sodium carbonate solution but dissolved slowly in aqueous sodium hydroxide. It liberated iodine from an acidified solution of potassium iodide.

Reduction of the quinone (X)

The quinone (X) (0·8 g.) was suspended in rectified spirit (200 c.c.) and the mixture saturated with sulphur dioxide and left overnight. The alcoholic solution was filtered and concentrated when a bright yellow solid separated out. It crystallised out of alcohol as bright yellow needles melting at 175–77°. (Found: OMe, 38·6; $C_{11}H_{14}O_6$ requires OMe, 38·4%.) With alcoholic ferric chloride it gave a green colour changing to brown and it dissolved in alkali to a reddish-brown solution.

Methylation of the quinol (XI)

The quinol (XI) (0·2 g.) was methylated in dry acetone medium (25 c.c.) using dimethyl sulphate (0·1 c.c.; 1 mol.) and anhydrous potassium carbonate (5 g.). The partially methylated compound crystallised from alcohol as a bright yellow crystalline solid melting at 87–88°. The mixed melting with the original ketone (VII) was not depressed.

Condensation of the ketone (VII) with the anhydride and sodium salt of trimethyl gallic acid.

An intimate mixture of the ketone (VII) (1·0 g.), trimethyl gallic anhydride (10·0 g.) and sodium salt of trimethyl gallic acid (4·0 g.) was heated at 175–80° under reduced pressure for three hours. The product was dissolved in boiling alcohol (50 c.c.) and an aqueous solution of potassium hydroxide (6·0 g. in 8 c.c. of water) was added to it. The mixture was boiled for 15 minutes and the alcohol was removed under reduced pressure. The residue was dissolved in water. When the aqueous solution was saturated with carbon dioxide, a bright yellow solid separated out which, after recrystallisation from alcohol, melted at 161–62°. Yield, 0·6 g. The mixed melting point with gardenin (IV) was undepressed. The condensation product was methylated in dry acetone medium using dimethyl sulphate and anhydrous potassium carbonate. The methyl ether, after a crystallisation from dry ethyl acetate, melted at 116–17°. The mixed melting point with methyl gardenin (VI) was undepressed.

Condensation of the ketone (VII) with benzoic anhydride and sodium benzoate

The ketone (1·0 g.) was intimately mixed with benzoic anhydride (10·0 g.) and sodium benzoate (4·0 g.) and the mixture was heated at 175–80° under reduced pressure for three hours. The product was worked up as before, and was obtained as a pale yellow solid (0·6 g.). It gave a green colour with alcoholic ferric chloride and was slightly soluble in aqueous alkali. It was directly methylated using dimethyl sulphate and anhydrous potassium carbonate in dry acetone medium. The tetramethyl ether (XVII) crystallised out of a mixture of ethyl acetate and petroleum-ether as stout rectangular prisms melting at 118–19°. (Found: C, 66·5; H, 5·0; $C_{19}H_{18}O_6$ requires C, 66·7; H, 5·3%.) Yield, 0·4 g. With alcoholic ferric chloride it did not give any colour and was insoluble in aqueous alkali. The mixed melting point with 5:6:7:8-tetramethoxy-flavone (m.p. 117–18°) was considerably depressed (95–100°).

3 : 6-*Dimethoxy-5-hydroxy-flavone* (*XV*)

The trihydroxy-flavone (XIV)[12] (1·0 g.) was dissolved in dry acetone (50 c.c.) and anhydrous potassium carbonate (10 g.) and dimethyl sulphate (0·7 c.c.) were added. The mixture was refluxed for six hours and the acetone solution was filtered off from the potassium salts. After concentrating the acetone solution, the product was crystallised from alcohol. It was obtained as pale yellow rectangular plates melting at 108–109°. (Found : C, 68·2; H, 5·0; $C_{17}H_{14}O_5$ requires C, 68·5; H, 4·7%.) With alcoholic ferric chloride it gave an olive-green colour and was sparingly soluble in aqueous alkali.

3 : 6-*Dimethoxy*-5 : 8-*dihydroxy flavone* (*XVI*)

The 5-hydroxy compound (XV) (1·0 g.) was dissolved in pyridine (20 c.c.) and aqueous sodium hydroxide (0·6 g. in 15 c.c. of water) was added. To the mixture an aqueous solution of potassium persulphate (1·5 g. in 30 c.c. of water) was added gradually drop by drop while the solution was stirred continuously. The solution was kept overnight and made just acid to congo-red with hydrochloric acid. The unreacted compound that separated out was filtered off and the filtrate extracted with ether to remove the last traces. Sodium sulphite (3 g.) and concentrated hydrochloric acid (20 c.c.) were added to the aqueous solution and the mixture was heated on a boiling water-bath for half an hour. The solid that separated out was filtered and crystallised from alcohol. The quinol (XVI) was thus obtained as bright yellow needles melting at 185–86°. (Found: C, 64·6; H, 4·9; $C_{17}H_{14}O_6$ requires C, 65·0; H, 4·5%.) With alcoholic ferric chloride it gave a green colour which changed to brown and it was freely soluble in aqueous alkali producing a red solution.

3 : 5 : 6 : 8-*Tetramethoxy-flavone* (*XVII*)

The 5 : 8-dihydroxy compound (XVI) (0·2 g.) was dissolved in dry acetone (25 c.c.) and anhydrous potassium carbonate (5 g.) and dimethyl sulphate (0·5 c.c.) were added. The mixture was refluxed for 30 hours and the acetone solution was worked up as in similar cases. The tetramethyl ether crystallised from ethyl acetate as stout rectangular prisms melting at 117–18°. (Found: C, 66·9; H, 5·7; $C_{19}H_{18}O_6$ requires C, 66·7; H, 5·3%.) It gave no colour with alcoholic ferric chloride and was insoluble in alkali. The mixed melting point with the tetramethoxy compound obtained from the fission ketone (VII) was undepressed.

Summary

The constitution suggested by Bose for gardenin (5-hydroxy-3 : 6 : 8 : 3′ : 4′ : 5′-hexamethoxy-flavone) has been confirmed in the following manner.

(1) Preparation of nor-gardenin and gardenin methyl ether and comparison with hibiscetin and 6-hydroxy-myricetin and their methyl ethers. There was no agreement.

(2) Oxidative demethylation of gardenin and its methyl ether. This proved that groups exist in the 5 and 8 positions.

(3) Alkali fission of methyl gardenin and study of the ketonic product. It condensed with the anhydride and sodium salt of trimethyl gallic acid to reform gardenin. Its oxidation with nitric acid and subsequent transformations showed that it has a methoxyl in the 5-position corresponding to the 6-position in gardenin.

(4) The tetramethoxy flavone obtained from the fission ketone and benzoic anhydride and sodium benzoate was not identical with 5:6:7:8-tetramethoxy-flavone, but was identical with 3:5:6:8-tetramethoxy-flavone synthetically obtained by the method of nuclear oxidation.

(5) Gardenin could be directly obtained by the partial methylation of nor-gardenin or gardeninol and by the Allan-Robinson condensation using the fission ketone and trimethyl gallic acid.

References

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