

# A NEW EFFECT OF HYDROGEN BOND FORMATION

## Part V. A Note on the Behaviour of the 8-Hydroxyl Group in Benzopyrone Derivatives

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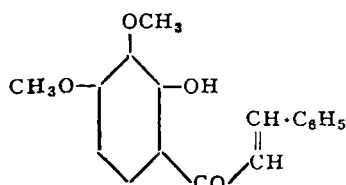
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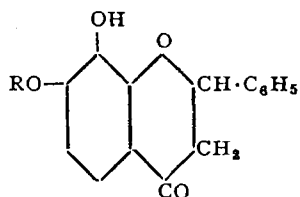
IN the isomerisation of flavones, chromones and flavanones<sup>1</sup> having the 5:7:8-arrangement of hydroxyls there was reason to believe that the 8-hydroxyl group played some important part and hence it was considered desirable to get more evidence about the reactivity of this group. It was first recorded by Baker<sup>2</sup> that 7-methoxy-8-hydroxy flavone gave a green colour with ferric chloride. A similar observation was made by Rao and Seshadri<sup>3</sup> in the case of 8-hydroxy-3:5:7:3':4'-pentamethoxy flavone which was obtained from gossypin. This would indicate the presence of chelation between the 8-hydroxyl and pyrone oxygen. The observation of Shah, Mehta and Wheeler<sup>4</sup> that in the demethylation of wogonin-5-methyl ether using anhydrous aluminium chloride in nitrobenzene solution the 8-methoxyl suffers demethylation along with the 5-methoxyl, provides further support to the existence of this chelation. But efforts to carry out partial methylation of 7:8-dihydroxy flavone have not been successful<sup>2</sup> thus showing that the chelation is only of a weak type.

The position is considerably different in the case of the corresponding flavanones. 2-Hydroxy-3:4-dimethoxy chalcone (I) undergoes demethylation with hydrobromic acid<sup>5</sup> to yield 7-methoxy-8-hydroxy flavanone (II) as a colourless substance quite free from the corresponding chalcone. Further, partial methylation of 7:8-dihydroxy flavanone (II *a*) can also be effected to give rise to a colourless monomethyl ether though slightly impure. It gives a positive ferric reaction and is insoluble in aqueous sodium carbonate and sparingly soluble in sodium hydroxide. This would indicate the existence of a stronger chelation in 8-hydroxy flavanones than in flavones. 7-Methoxy-8-hydroxy flavanone (II) has also been prepared by an alternative procedure starting with the dibenzoate of gallacetophenone-4-methyl ether (III). This is condensed with benzaldehyde in ethyl acetate solution in the presence of dry hydrogen chloride.<sup>6</sup> The dibenzoyloxy chalcone (IV) on hydrolysis with alcoholic potassium hydroxide yields 7-methoxy-8-hydroxy flavanone as the only product. The extraction of most of the product from the alkaline solution by means of ether would indicate the sparing

solubility of the compound in alkali and its formation as the only major product of the reaction shows the existence of chelation (*cf.*, Narasimhachari and Seshadri<sup>7</sup>) rendering the flavanone structure stable.



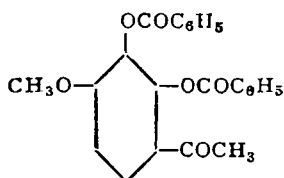
I



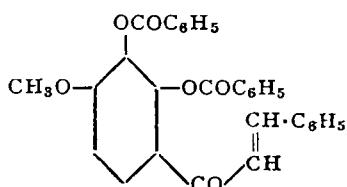
II

II, R = CH<sub>3</sub>

II a, R = H



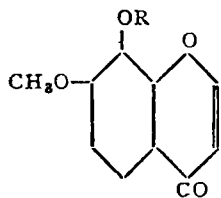
III



IV

In earlier publications<sup>8</sup> has been explained the similarity between flavanones, chromones and isoflavones in regard to the special properties of the 7-hydroxyl group. In these compounds the 7-hydroxyl undergoes methylation more readily and a methoxyl in this position is far more resistant to demethylation. In earlier work on this feature no compound with a hydroxyl or methoxyl in the 8-position was employed. In view of the interesting results mentioned above using flavanones, similar work has now been carried out with corresponding chromones and isoflavones.

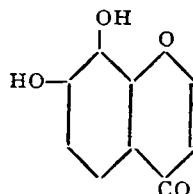
7:8-Dimethoxy chromone (V a) undergoes easy partial demethylation even with hydriodic acid at 120° giving rise to 7-methoxy-8-hydroxy chromone (V b). This substance gives an apple-green colour with ferric chloride and is soluble in sodium carbonate. It is definitely different from 7:8-dihydroxy chromone (VI) since it yields a different acetyl derivative and even



V

a, R = CH<sub>3</sub>

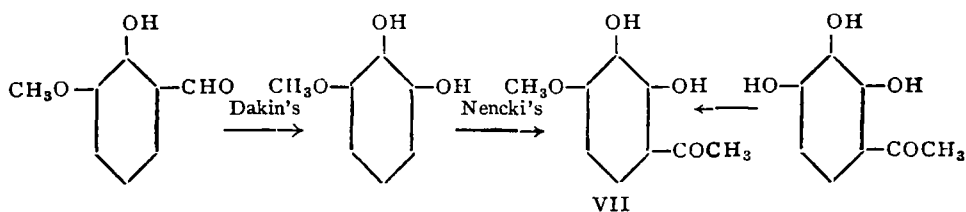
b, R = H



VI

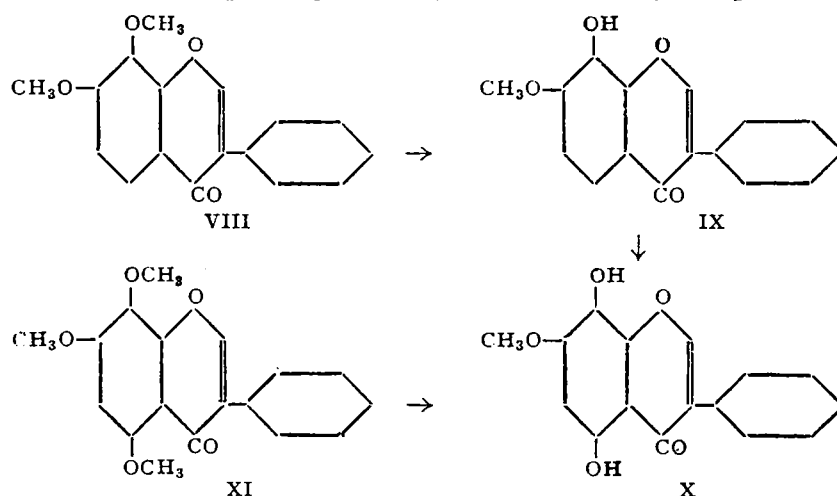
in its ferric chloride colour there is marked difference, the dihydroxy compound giving a deeper green colour. Attempts at partial methylation of 7:8-dihydroxy chromone have not been successful.

In order to establish the constitution of the above-mentioned demethylation product, 7-methoxy-8-hydroxy chromone (V *b*) has been synthesised by an independent procedure. For this and for the synthesis of 7-methoxy-8-hydroxy flavanone (II) mentioned earlier the 4-methyl ether of gallacetophenone (VII) was needed. There is some confusion in the literature about the monomethyl ether of gallacetophenone. Perkin and Wilson<sup>9</sup> carried out the methylation of monopotassium salt of gallacetophenone and claimed to have obtained in poor yield a monomethyl ether which they described as the 3-methyl ether; it was presumably the 4-methyl ether. They recorded that the product did not give colour with ferric chloride. Baker *et al.*<sup>10</sup> prepared the 4-methyl ether starting from *o*-vanillin, which was converted into monomethyl pyrogallol by Dakin's oxidation and subjected to Nencki's reaction. The preparation of 4-O-methyl gallacetophenone has now been considerably simplified by the direct methylation of gallacetophenone using one mole of dimethyl sulphate in presence of potassium carbonate. The improvement is based on the observation that the hydroxyl *para* to the ketonic group is outstandingly more reactive. This 4-methyl ether of gallacetophenone when condensed with sodium and ethyl formate yields 7-methoxy-8-hydroxy chromone (V *b*) identical with the partial demethylation product of 7:8-dimethoxy compound.



Demethylation of 7:8-dimethoxy isoflavone (VIII) gave results very similar to those of the corresponding chromone. This substance has not been reported before and has now been prepared starting from pyrogallol trimethyl ether which undergoes condensation with phenylacetyl chloride in presence of aluminium chloride to form 2-hydroxy-3:4-dimethoxy phenyl benzyl ketone; final isoflavone condensation<sup>11</sup> with ethyl formate and sodium yields 7:8-dimethoxy isoflavone. This undergoes partial demethylation with hydriodic acid to yield 7-methoxy-8-hydroxy isoflavone (IX). Its constitution has been confirmed by nuclear oxidation with alkaline persulphate whereby 7-methoxy-5:8-dihydroxy isoflavone (X) is obtained in good

yield. This product is found to be identical with the one obtained by the partial demethylation of 5:7:8-trimethoxy isoflavone (XI), and represents a successful example of nuclear oxidation from a 8-hydroxy compound to a 5:8-dihydroxy compound. The reverse oxidation process is more common. Baker<sup>12</sup> reported earlier poor yield in the oxidation of 8-hydroxy-4'-methoxy flavone to the corresponding 5:8-dihydroxy-4'-methoxy compound.



It may be mentioned here that gossypetin pentamethyl ether with a free 8-hydroxyl group, 7-methoxy-8-hydroxy chromone and isoflavone are easily soluble in aqueous sodium carbonate, whereas the corresponding 7-methoxy-8-hydroxy flavanone is insoluble.

The results recorded in this paper may be summarised as follows. The 8-hydroxyl group in chromone derivatives is involved in chelation as indicated by the positive ferric reaction. But the solubility of the 8-hydroxy compound in aqueous sodium carbonate and the inability of 7:8-dihydroxy derivatives to undergo partial methylation in the flavone, isoflavone and chromone series indicates that the chelation is only of a weak type. The chelation is considerably stronger in the flavanones which agrees with the insolubility of 7-methoxy 8-hydroxy flavanone in aqueous sodium carbonate and its very sparing solubility in aqueous sodium hydroxide and also the stability of this flavanone in alkaline medium. The effect of the 8-hydroxyl corresponds to that of the 5-hydroxyl group<sup>7</sup> and 2'-hydroxyl group<sup>13</sup> in this stabilisation.

#### EXPERIMENTAL

##### *7-Methoxy-8-hydroxy flavanone (II)*

(i) *By the demethylation of 2-hydroxy-3:4-dimethoxy chalcone (I) with hydrobromic acid.*—2-Hydroxy-3:4-dimethoxy chalcone<sup>15</sup> (1.0 g.) was

dissolved in glacial acetic acid (5 c.c.) and the solution treated with a saturated solution of hydrobromic acid in glacial acetic acid (10 c.c.). After leaving at room temperature for 24 hours it was heated on a boiling water-bath for 30 minutes, cooled and diluted with water (40 c.c.). The brown solid that separated was filtered, washed with water and crystallised first from acetone-petroleum ether mixture and subsequently from alcohol. It separated from alcohol as colourless flat needles and narrow rectangular plates, melting at 153–4°. It gave a green colour with ferric chloride in alcoholic solution. It was insoluble in aqueous sodium carbonate (5%) and sparingly soluble in aqueous sodium hydroxide. Thus it agreed in all its properties with those required for 7-methoxy-8-hydroxy flavanone (II) (Found: C, 71.0; H, 5.2;  $C_{16}H_{14}O_4$  requires C, 71.1; H, 5.2%).

(ii) *By synthesis: Gallacetophenone-4-methyl ether (VII).*—Gallacetophenone (2 g.) was refluxed in acetone solution (30 c.c.) with dimethyl sulphate (1.0 c.c.) and anhydrous potassium carbonate (2.5 g.) for 3 hours. The potassium salts were filtered off and acetone removed from the filtrate. The residue was treated with cold alcohol (10 c.c.) when an almost colourless solid separated. It was filtered and twice crystallised from excess of alcohol from which it was obtained as colourless aggregates of short prisms melting at 127–8°. It dissolved slowly in aqueous sodium carbonate giving a yellow solution and gave a deep greenish brown colour with ferric chloride in alcoholic solution (Found: C, 53.6; H, 6.4;  $C_9H_{10}O_4, H_2O$  requires C, 54.0; H, 6.0%). Yield 0.9 g. Perkin and Storey<sup>9</sup> reported the melting point of the monomethyl ether they prepared as 134–5° and Baker *et al.*<sup>10</sup> gave the melting point of 132° for the compound obtained by them. While the former reported that their product gave no colour with ferric chloride, Baker *et al.*<sup>10</sup> did not record the ferric reaction of their methyl ether.

The diacetate obtained by the acetic anhydride-pyridine method crystallised from alcohol as colourless thick rectangular plates melting at 150–1° (Found: C, 58.2; H, 4.8;  $C_{13}H_{14}O_6$  requires C, 58.7; H, 5.3%). Perkin and Storey<sup>9</sup> reported the same melting point for the diacetate of their product. Deacetylation of the pure acetate gave the dihydroxy compound (melting point and mixed melting point 127–8°).

*Dibenzoate (III).*—The benzylation of the dihydroxy monomethoxy ketone was carried out using 2 moles of benzoyl chloride and pyridine. The dibenzoate crystallised for alcohol as pale-yellow stout rhombohedral prisms melting at 185–6° (Found: C, 68.7; H, 4.5;  $C_{23}H_{18}O_6, \frac{1}{2}H_2O$  requires C, 69.2; H, 4.8%).

*Condensation with benzaldehyde.*—The above dibenzoate of gallacetophenone-4-methyl ether (1.2 g.) was dissolved in dry ethyl acetate (150 c.c.)

and benzaldehyde (0.5 c.c.) added to it. The solution was cooled in ice and a current of dry hydrogen chloride passed through it for 4 hours. It was left in the ice-bath for 24 hours and ethyl acetate removed under reduced pressure on a water-bath. The resulting 2:3-dibenzoyloxy-4-methoxy chalcone was directly hydrolysed by refluxing with alcoholic potassium hydroxide (0.8 g. in 30 c.c.) for 30 minutes. After removing alcohol under reduced pressure, water was added when a sticky mass separated which was directly taken in ether. The ether solution was marked (A) and the aqueous solution (B). On evaporating the ether solution (A) an almost colourless solid was obtained which crystallised from alcohol as colourless flat needles and narrow rectangular plates melting at 153–4°. It gave a green colour with ferric chloride in alcoholic solution and was insoluble in aqueous sodium carbonate. It was identical with 7-methoxy-8-hydroxy flavanone (II) obtained earlier and a mixed melting point with that sample was un-depressed. The aqueous solution (B) on acidification yielded a pale coloured sticky solid which was extracted with ether and the ether solution washed with sodium bicarbonate and water. When the ether extract was evaporated it gave 7-methoxy-8-hydroxy flavanone identical with the above product. Total yield 0.3 g.

*7:8-Dihydroxy flavanone (II a)*

This was claimed to have been prepared earlier by the ring closure of 2:3:4-trihydroxy chalcone obtained by direct condensation of gallacetophenone and benzaldehyde.<sup>14</sup> It has now been prepared by the demethylation of 7:8-dimethoxy flavanone with aluminium chloride in benzene solution.

7:8-Dimethoxy flavanone<sup>15</sup> (1.0 g.) was refluxed in benzene solution (20 c.c.) with anhydrous aluminium chloride (2.0 g.) for 2 hours. On distilling off benzene and decomposing the aluminium chloride complex a pale yellow solid separated. It was filtered, washed with water and after drying was crystallised from benzene when it was obtained as colourless aggregates of thin rectangular plates melting at 167–8° (Shinoda<sup>14</sup> reported the melting point of 184° for the compound obtained by him). When crystallised from alcohol 7:8-dihydroxy flavanone separated as colourless long rectangular plates and rods melting at 167–8°. It gave a deep bluish green colour with ferric chloride and was easily soluble in aqueous sodium carbonate (Found in the sample crystallised from alcohol; C, 55.9; H, 5.5; loss on drying 19.0;  $C_{15}H_{12}O_4$ , 3.5  $H_2O$  requires C, 56.4; H, 5.9; loss on drying, 19.7%. Found in a sample crystallised from benzene: C, 75.3; H, 5.7;  $C_{15}H_{12}O_4$ ,  $C_6H_6$  requires C, 75.5; H, 5.4%).

*7:8-Dimethoxy chromone (Va) and 7:8-dihydroxy chromone (VI)*

Pulverised sodium (1.0 g.) cooled in ice was treated with a solution of gallacetophenone-3:4-dimethyl ether (2.0 g.) in ethyl formate (15 c.c.). The flask was left corked in the refrigerator for 48 hours. Pieces of crushed ice were then added and since no solid separated the aqueous solution was acidified with ice-cold hydrochloric acid. The colourless solid that separated was filtered and washed with water. It was found to dissolve almost completely in aqueous sodium hydroxide. On extracting the alkaline solution with ether and evaporating the extract a very small quantity (A) (0.1 g.) of a colourless solid was obtained. It crystallised from alcohol as colourless needles, melting at 123–4°. It gave no colour with ferric chloride in alcoholic solution and was insoluble in aqueous sodium hydroxide. Kostanecki<sup>16</sup> reported 124° as the melting point for 7:8-dimethoxy chromone.

When the alkaline solution left after ether extraction was acidified it gave a colourless product which crystallised from alcohol as hexagonal prisms melting at 156–7° with evolution of gas and solidification and remelting at 202° with decomposition. Yield 1.5 g. It gave a pink colour with ferric chloride in alcoholic solution. It was insoluble in aqueous sodium carbonate but soluble in sodium hydroxide solution. Thus it agreed in all its properties with  $\omega$ -formyl-gallacetophenone-3:4-dimethyl ether (Found: C, 59.1; H, 5.7;  $C_{11}H_{12}O_5$  requires C, 58.9; H, 5.4%).

Hydriodic acid (10 c.c., sp.gr. 1.7) was added to a cooled solution of  $\omega$ -formyl-gallacetophenone-3:4-dimethyl ether (0.5 g.) in acetic anhydride (2 c.c.). The reaction mixture was then heated at 140° for 2 hours and after cooling it was diluted with sulphurous acid. The pale-pink solid that separated was crystallised from alcohol when it was obtained as rectangular prisms and prismatic rods, melting at 262–3° (decomp.). Yield 0.4 g. It gave a bright olive green colour with ferric chloride in alcoholic solution which changed to blue on dilution with water (Kostanecki reported 262° as the melting point for 7:8-dihydroxy chromone).

On methylating the above 7:8-dihydroxy chromone (0.4 g.) with excess of dimethyl sulphate (2.2 moles, 0.6 c.c.) and potassium carbonate (1.5 g.) in acetone solution (10 c.c.), 7:8-dimethoxy chromone was obtained which crystallised from dilute alcohol as colourless needles, melting at 123–4° identical in its properties with the alkali-insoluble portion (A) described above. The mixture of the two samples also melted at 123–4°. Yield 0.35 g.

*7-Methoxy-8-hydroxy chromone (Vb)*

(i) *By partial demethylation with hydriodic acid using the  $\omega$ -formyl derivative.*—The  $\omega$ -formyl derivative of gallacetophenone dimethyl ether

(0.4 g.) described in the previous experiment was dissolved in acetic anhydride (2 c.c.) and the solution treated with cooling with hydriodic acid (6 c.c., sp.gr., 1.7). The mixture was heated at 120° in an oil-bath for half an hour, after which it was cooled, diluted with sulphurous acid and the solution extracted with ether. After washing the ether solution with sodium bicarbonate, ether was evaporated and the white crystalline solid left behind was crystallised from alcohol. It separated as colourless small squares and rectangular prisms melting at 202–3°. It gave an apple green colour with ferric chloride and was soluble in aqueous sodium carbonate. It was different from 7:8-dihydroxy chromone in its reactions and properties and was identical with the product obtained by the other methods described below.

(ii) *By the partial demethylation with hydriodic acid using 7:8-dimethoxy chromone (Va).*—7:8-Dimethoxy chromone (1.0 g.) was heated in acetic anhydride solution (4 c.c.) with hydriodic acid (10 c.c., sp.gr. 1.7) at 120° in an oil-bath for 30 minutes. On working up as in similar cases and crystallising from alcohol, the product was obtained as colourless squares and rectangular prisms melting at 202–3°. It gave an apple green colour with ferric chloride and was easily soluble in sodium carbonate. It was different from 7:8-dihydroxy chromone (melting point 262°) (Found: C, 62.6; H, 4.6;  $C_{10}H_8O_4$  requires C, 62.5; H, 4.2%).

On acetylation the monoacetate was obtained which crystallised from alcohol as colourless elongated rectangular rods and prisms melting at 148–9° (7:8-diacetoxy chromone has a melting point 110°).

(iii) *By synthesis.*—Pulverised sodium (1.0 g.) cooled in ice was treated with a solution of gallacetophenone-4-methyl ether (VII) (1 g.) in ethyl formate (10 c.c.). The mixture turned gradually orange yellow and deep brown. It was left in the refrigerator for 48 hours after which it was treated with crushed ice and the clear solution acidified with hydrochloric acid. The solution was directly extracted with ether and the ether extract concentrated. On crystallising the solid thus obtained, from excess of alcohol, a small quantity (0.2 g.) separated as the first crop which, when recrystallised from alcohol was obtained as colourless small squares and rectangular prisms melting at 202–3°. It gave an apple green colour with ferric chloride and was identical with 7-methoxy-8-hydroxy chromone described in the earlier two experiments. The alcoholic solution on concentration gave a product (melting point 200–220°) which appeared to be a mixture. It was directly refluxed in alcoholic sulphuric acid (4%) solution for 20 hours. On concentrating the alcoholic solution to half the volume and diluting it with water a colourless solid was obtained, which when crystallised from alcohol,



yielded 7-methoxy-8-hydroxy chromone (melting point and mixed melting point 202–3°). Yield 0.5 g.

If in the above experiment at the end of the condensation, the solution was acidified and allowed to stand for 24 hours at room temperature and then ether extracted, the product was found to be pure 7-methoxy-8-hydroxy chromone (melting point 202–3°). Yield 0.7 g. from 1 g. of the ketone.

#### *2-Hydroxy-3:4-dimethoxy phenyl benzyl ketone*

Anhydrous aluminium chloride (20 g.) was dissolved in ice-cold dry ether (100 c.c.) and pyrogallol trimethyl ether (10 g.) in dry ether (100 c.c.) added to it. The mixture was then treated with phenyl acetyl chloride (9 c.c.) with frequent shaking and the reaction mixture left at room temperature overnight. Ether was then removed on a water-bath, and the aluminium chloride complex decomposed with ice and hydrochloric acid. The hydrolysis was completed by heating it on a water-bath for a few minutes. After cooling the product was taken up in ether, the ethereal solution first washed with sodium carbonate and then extracted four times with aqueous sodium hydroxide (10%) using 25 c.c. for each extraction. The combined alkali extract on acidification deposited a colourless solid which crystallised from alcohol as colourless small rectangular prisms melting at 106–7°. Yield 10 g. It gave a pink colour with ferric chloride (Found: C, 70.5; H, 6.2;  $C_{16}H_{16}O_4$  requires C, 70.6; H, 5.9%).

#### *7:8-Dimethoxy isoflavone (VIII)*

A solution of 2-hydroxy-3:4-dimethoxy phenyl benzyl ketone (2 g.) in ethyl formate (10 c.c.) was added to pulverised sodium (1 g.) cooled in ice and after leaving at 0° for 24 hours the mixture was treated with ice and hydrochloric acid. The colourless solid so obtained was filtered, washed with aqueous sodium hydroxide to remove the unchanged ketone and crystallised from alcohol. 7:8-Dimethoxy isoflavone separated from alcohol as stout elongated rectangular prisms melting at 133–4°. It gave no colour with ferric chloride (Found: C, 71.8; H, 5.1;  $C_{17}H_{14}O_4$  requires C, 72.3; H, 5.0%).

#### *7-Methoxy-8-hydroxy isoflavone (IX)*

Hydriodic acid (6 c.c., sp.gr. 1.7) was added slowly to a cooled solution of 7:8-dimethoxy isoflavone (0.4 g.) in acetic anhydride (2 c.c.) and the solution heated at 120° for 30 minutes.<sup>8</sup> The product that separated on diluting the solution with sulphurous acid was filtered, washed with water and crystallised from alcohol when it separated as colourless stout prisms, melting at 203–5°. Yield 0.3 g. It dissolved in aqueous sodium hydroxide

and sodium carbonate giving a yellow solution, and gave an apple green colour with ferric chloride (Found: C, 71.6; H, 4.8;  $C_{16}H_{12}O_4$  requires C, 71.6; H, 4.5%).

7-Methoxy-8-acetoxy isoflavone obtained by acetylation crystallised from ethyl acetate as colourless rectangular prisms and prismatic needles melting at 194–5° (Found: C, 69.7; H, 4.5;  $C_{18}H_{14}O_5$  requires C, 69.7; H, 4.5%). Deacetylation of the pure acetate by alcoholic hydrochloric acid yielded the original hydroxy compound (melting point and mixed melting point 203–5°). Both the hydroxy compound and the acetate differed considerably from 7:8-dihydroxy isoflavone and its acetate described below.

#### *7:8-Dihydroxy isoflavone*

(i) *By the demethylation with hydriodic acid.*—Demethylation of 7:8-dimethoxy isoflavone (0.5 g.) in acetic anhydride solution with hydriodic acid at 140° for 2 hours yielded 7:8-dihydroxy isoflavone which crystallised from alcohol as colourless flat needles and long rectangular plates melting at 218–20°. It gave an olive green colour with ferric chloride and dissolved readily in aqueous sodium carbonate. Yield 0.3 g. (Found: C, 68.3; H, 4.5; loss on drying 3.6;  $C_{15}H_{10}O_4$ ,  $\frac{1}{2} H_2O$  requires C, 68.4; H, 4.2; loss on drying 3.4%).

The diacetate crystallised from ethyl acetate as aggregates of colourless thin plates melting at 139–40° (Found: C, 64.2; H, 4.4;  $C_{19}H_{14}O_6$ ,  $H_2O$  requires C, 64.1; H, 4.5%).

(ii) *By the demethylation with aluminium chloride.*—7:8-Dimethoxy isoflavone (0.2 g.) was refluxed in benzene solution (10 c.c.) with anhydrous aluminium chloride (1 g.) for 2 hours. The dihydroxy isoflavone obtained on removing benzene and decomposing the complex crystallised from alcohol as colourless rectangular plates and needles melting at 218–20° and was identical with the product obtained in the above experiment.

#### *7-Methoxy-5:8-dihydroxy isoflavone (X)*

(i) *By the nuclear oxidation of 7-methoxy-8-hydroxy isoflavone (IX).*—A solution of sodium persulphate (1 g. in 10 c.c.) was added dropwise to a stirred solution of 7-methoxy-8-hydroxy isoflavone (0.25 g.) in aqueous sodium hydroxide (15 c.c., 1 N), the temperature being kept between 15–20°. The stirring was continued for 3 hours and the solution was kept corked for 12 hours. It was then acidified to congo red and the unreacted 7-methoxy-8-hydroxy isoflavone removed by twice extracting with ether. The aqueous solution was then treated with concentrated hydrochloric acid (10 c.c.) after the addition of sodium bisulphite (1 g.) and then heated at 90°

on a water-bath for 20 minutes. A bright yellow compound gradually separated. After cooling it was directly extracted with ether and the ethereal solution dried over anhydrous sodium sulphate. On evaporating the ether solution a bright yellow solid was left behind which crystallised from alcohol as yellow laminæ melting at 208–10° (decomp.). It gave a deep red colour with ferric chloride in alcoholic solution and dissolved readily in aqueous sodium carbonate. It agreed in its properties and reactions with a sample of 7-methoxy-5:8-dihydroxy isoflavone described below and the mixed melting point was undepressed (Found: C, 67.1; H, 4.3;  $C_{16}H_{12}O_5$  requires C, 67.6; H, 4.2%). Yield 0.6 g.

(ii) *By partial demethylation of 5:7:8-trimethoxy isoflavone (XI) with hydriodic acid.*—An acetic anhydride solution of 5:7:8-trimethoxy isoflavone<sup>17</sup> (0.5 g. in 3 c.c.) was heated with hydriodic acid (8 c.c.) at 120° for 30 minutes and the product worked up. The bright yellow 7-methoxy-5:8-dihydroxy isoflavone thus obtained crystallised from alcohol as yellow laminæ melting at 208–10° (decomp.). It gave a deep red colour with ferric chloride and was easily soluble in aqueous sodium carbonate.

#### SUMMARY

Past records indicate that an 8-hydroxyl group in a flavone is involved in chelation but it is of a weak nature. 7-Methoxy-8-hydroxy flavanone can be easily obtained by the partial methylation of 7:8-dihydroxy flavanone or the partial demethylation of 7:8-dimethoxy flavanone, and can also be directly obtained from gallacetophenone-4-methyl ether. Its preparation and properties indicate the existence of stronger chelation involving the 8-hydroxyl group. Similar experiments have been done on the preparation of 7-methoxy-8-hydroxy chromone and isoflavone. Though the partial demethylation of 7:8-dimethoxy compounds has been successful, partial methylation of the dihydroxy compounds has not been possible in these cases. The properties of the products also indicate weaker chelation in the chromone and isoflavone just as in the corresponding flavone. In the course of the synthesis of 7-methoxy-8-hydroxy flavanone and chromone independently for purpose of comparison the preparation of the intermediate gallacetophenone-4-methyl ether has been re-investigated and a convenient method has been worked out.

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