

A NEW EFFECT OF HYDROGEN BOND FORMATION (CHELATION)

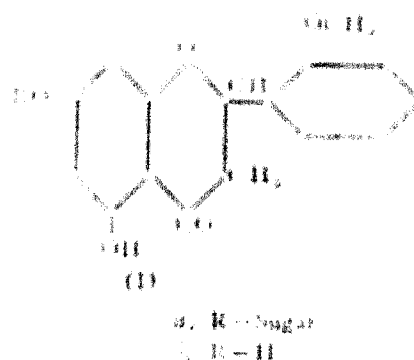
Part IV. Abnormal Behaviour of 2-Hydroxy Flavanones

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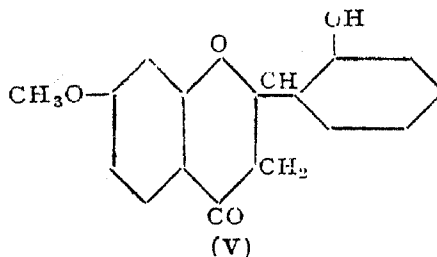
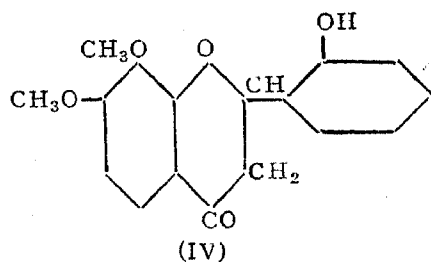
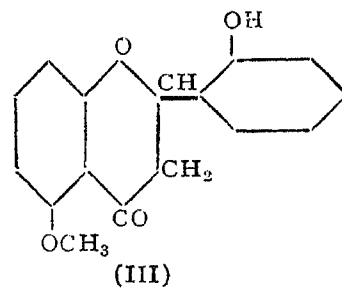
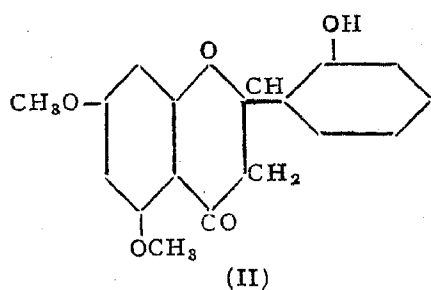
ANTHOKYANTHINS with a substituent in the 2-position are rare in nature and citronetin has been considered to be the only representative of this type among flavanones. It was found to be present in the peels of *Citrus limon ponderosa* as its glycoside citroum (Ia) by Yamamoto and Oshima¹ who gave it the constitution of 8-7-dihydroxy-2-methoxy flavanone (Ib). By the fusion of the glycoside with potash they claimed to have isolated the phloroglucinol part containing the sugar residue and *o*-methoxy-hydrocoumaric acid. Later Shinoda and Sato² reported the synthesis of a compound of this constitution from phloroglucinol and *o*-methoxy cinnamoyl chloride by the Friedel and Crafts reaction. But there is no agreement between the natural and synthetic products and their derivatives. Citronetin obtained from citroum was given a melting point of 224 while the compound obtained by synthesis had a melting point of 224-25. Their methyl ethers also did not agree in their melting points. Further it has been noticed by us that the Friedel and Crafts reaction with *o*-methoxy cinnamoyl chloride and phloroglucinol does not proceed smoothly and that good results are obtained only with the trimethyl ether of phloroglucinol.



In view of these discrepancies it was planned to investigate the preparation of 2-hydroxy flavanones and their derivatives and their conversion to the corresponding flavones and flavonols. In the course of this work

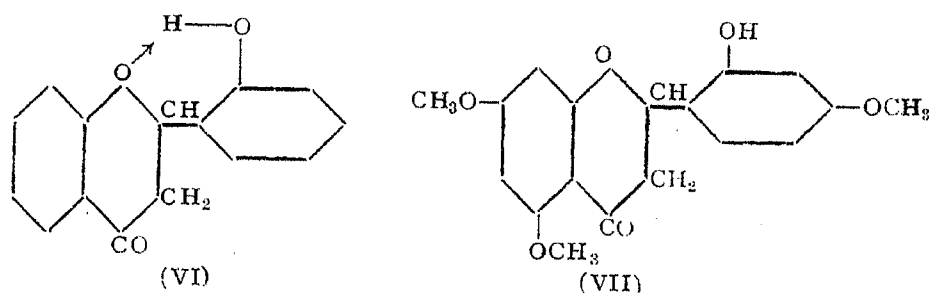
were noticed certain extraordinary features which had not been observed before and some of these are discussed in this communication.

The following ketones were condensed with salicylaldehyde in the presence of cold aqueous alcoholic potash: (i) phloracetophenone dimethyl ether, (ii) γ -resacetophenone monomethyl ether, (iii) gallacetophenone 3:4-dimethyl ether, and (iv) resacetophenone 4-methyl ether. The initial yellow colour of the solutions very rapidly changed to deep red and on acidification after 48 hours the products were almost colourless and crystalline in all the cases except in the last one where a semi-solid mass was obtained. With all the products a bright red colour was developed when their alcoholic solutions were treated with magnesium and hydrochloric acid and the Boric-Citric reaction³ was negative. These reactions indicated that they consisted of flavanones and they were free from chalcones. The products seemed to be quite pure and their structures should be correctly represented by formulæ II to V. In a test case phloracetophenone-4:6-dimethyl ether and salicylaldehyde were condensed by the acid method of Russel and Todd.⁴ Besides a deeply coloured product (probably a pyrylium salt) a colourless crystalline compound was obtained in the more soluble fraction and it was found to be identical with the product obtained by the alkali method.



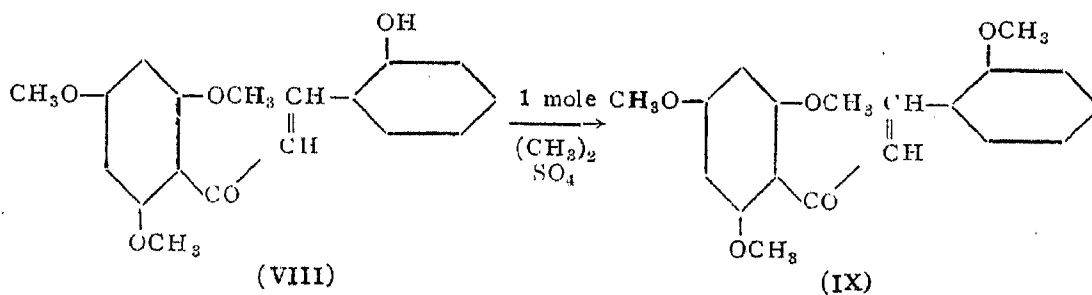
An extraordinary characteristic of the above-mentioned 2'-hydroxy flavanones is the prominent ferric chloride colour in alcoholic solution. They are also sparingly soluble in aqueous alkali and highly resistant to methylation. These properties are reminiscent of 5-hydroxy flavanones⁵ and should be attributed to the existence of chelation involving the 2'-hydroxyl and the oxygen atom of the pyranone ring as shown in formula VI. Since the

chelate ring consists of six atoms it could be expected to be stable but no earlier observation has been recorded regarding the existence of chelate rings of this type and of their stability. That ether oxygen can act as donor in hydrogen bond formation is fairly well recognised and the existence of this phenomenon was brought out prominently in the study of hydrogen bonds by the Raman effect by Murty and Seshadri.⁶



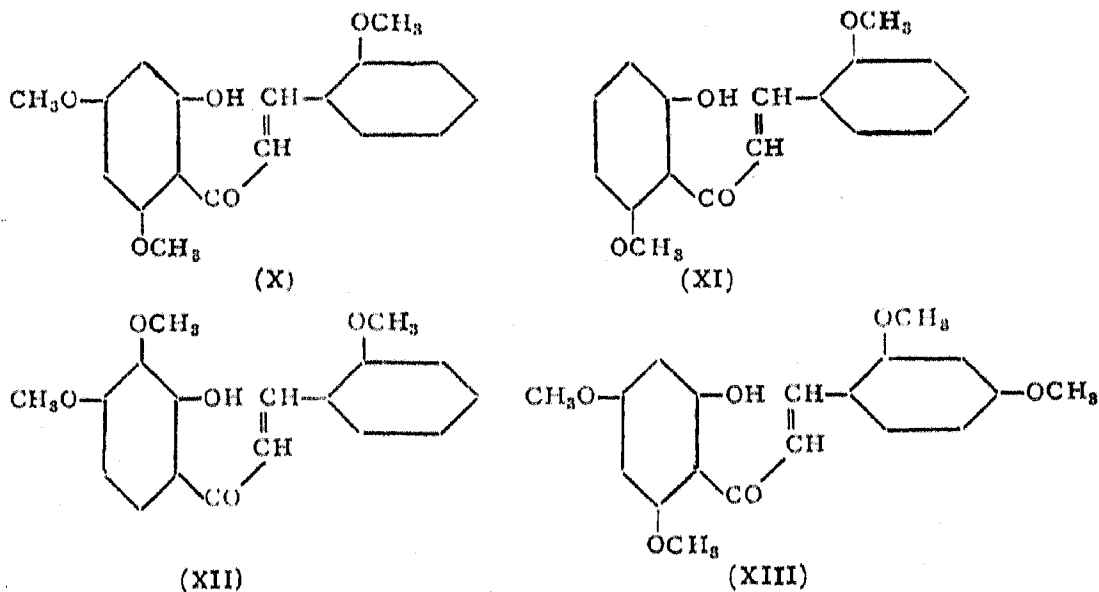
As a further extension of this study the condensation of phloracetophenone dimethyl ether with the 4-methyl ether of resorcyaldehyde was also carried out. The behaviour of the product was exactly the same and its constitution should be that of the 2'-hydroxy flavanone (VII). The exclusive formation of 2'-hydroxy flavanones under conditions of chalcone condensation seems to be attributable to the existence of the above-mentioned chelation which renders the flavanone structure highly stable. In this respect also the 2'-hydroxyl group resembles in its effect the 5-hydroxyl, which has been shown to stabilise the flavanone ring in the earlier papers of this series.⁵

From the experiments discussed above it would appear that the products are flavanones because free hydroxyl groups were present in the 2- and 2'-positions of the intermediate chalcones, the former rendering the closure of the flavanone ring possible and the latter stabilising it. In order to verify this conclusion two sets of experiments were conducted. In the first, a fully methylated ketone, phloracetophenone trimethyl ether was condensed with salicylaldehyde. The product was a chalcone (VIII) giving no colour with magnesium and hydrochloric acid but responding to the Boric-Citric reaction. This substance was already reported by Cullinane and Philpott⁷ and can be fully methylated to the tetramethoxy chalcone (IX), identical



with the sample prepared by the chalcone condensation between phloracetophenone trimethyl ether and salicylaldehyde methyl ether and by the condensation of phloroglucinol trimethyl ether and *o*-methoxy cinnamoyl chloride in cold ether solution by means of aluminium chloride.

The second set of experiments employed the methyl ether of salicylaldehyde and the first three *o*-hydroxy acetophenones mentioned earlier. In many of the condensations 2-hydroxy chalcones (X to XII) were obtained. It was at the same time observed that in certain condensations the products were mainly the corresponding 2'-hydroxy flavanones which after a few crystallisations were found to be identical with the samples obtained earlier using salicylaldehyde for the condensation. Similar results were obtained using phloracetophenone dimethyl ether and resorcydaldehyde dimethyl ether. In one of the condensations a pure 2-hydroxy chalcone⁸ (XIII) was produced while in some others a mixture consisting mostly of the 2'-hydroxy flavanone was produced.



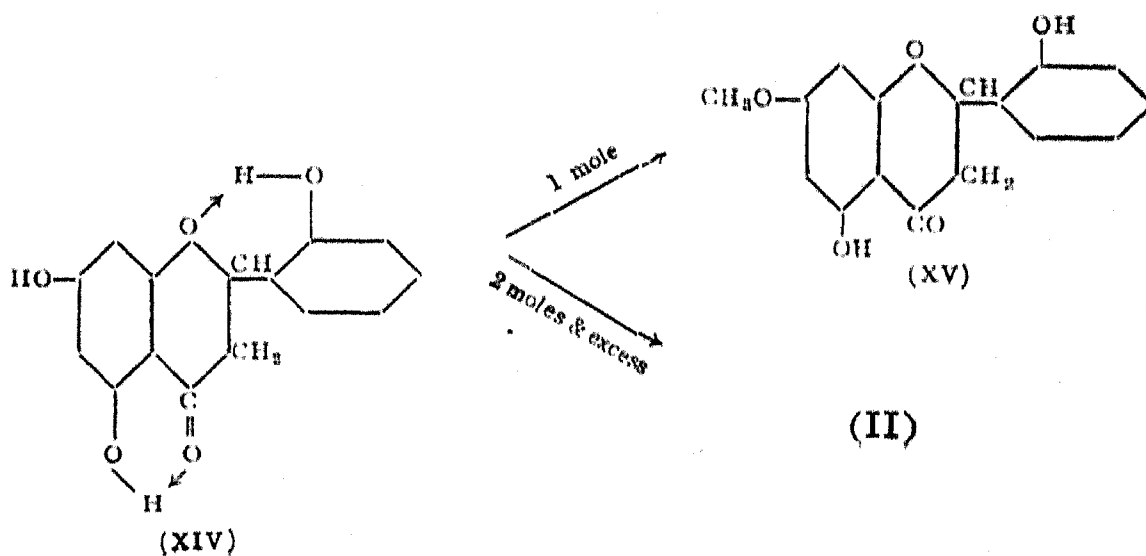
The demethylation of the 2'-methoxyl group in alkaline medium in the cold is quite unusual and it would appear that the initial flavanone ring closure which has been reported to take place in other cases of chalcones⁹ even in alkaline medium renders the demethylation of 2'-methoxyl easy. The highly alkaline conditions used in these condensations seem also to play an important part for when a mild alkali like sodium ethoxide is employed this demethylation does not take place to any appreciable extent and 2-hydroxy chalcones are invariably obtained.

Another interesting observation was made when the above-mentioned 2-hydroxy chalcones were refluxed with alcoholic sulphuric acid (4%) to

bring about flavanone ring closure. With ring closure simultaneous demethylation of the 2'-position also takes place yielding in quantity the corresponding 2'-hydroxy flavanone. This further confirms the conclusion already arrived at that a methoxyl in the 2'-position of a flavanone is highly susceptible to demethylation.

For the demethylation of flavanones hydriodic acid has not been found to be successful since some unknown changes occur. On the other hand the use of anhydrous aluminium chloride for this purpose has been found to be quite convenient.¹⁰ The hydroxy flavanones thus obtained are colourless and crystalline in appearance. The most unexpected observations of this work were made in the experiments on the methylation of hydroxy flavanones mentioned above. Complete methylation of these does not occur even under the most efficient conditions using dimethyl sulphate and anhydrous potassium carbonate in dry acetone medium. In previous studies on the methylation of hydroxy flavanones it was shown that of all the hydroxyls the 7-hydroxyl is the most reactive and partial mono-methyl ethers could be satisfactorily obtained.¹¹ Further methylation without opening the pyranone ring is possible so long as the 5-hydroxyl group is free. As soon as this is also methylated the oxygen ring opens up and eventually fully methylated chalcones result.⁵

In the course of the present work the first case to be examined was 5:7:2'-trihydroxy flavanone (XIV); with one mole of dimethyl sulphate it yields the 7-monomethyl ether (XV) and with 2 moles 5:7-dimethoxy-2'-hydroxy flavanone (II) with the pyranone ring still in tact and the product identical with that obtained by direct condensation of phloracetone



phenone dimethyl ether and salicylaldehyde. Prolonged heating with large excess of dimethyl sulphate did not bring about further methylation.

7:8:2'-Trihydroxy flavanone yielded only 7:8-dimethyl ether with excess dimethyl sulphate and 5:2'-dihydroxy flavanone gave only the 5-methyl ether. Thus the 2'-hydroxyl group is not only more resistant to methylation than the 5-hydroxyl but it cannot be methylated at all by methods now employed. This is a very remarkable result and the special features of the concerned chelate structure (VI) which would account for this phenomenon are not at present comprehensible.

In the light of the special features connected with 2'-hydroxy flavanones and the related chalcones certain difficulties reported in earlier literature become explicable. In the course of their synthesis of morin, Kostanecki, Lampe and Tambor¹¹ prepared 2-hydroxy-4:6:2':4'-tetramethoxy chalcone; when they converted it into the corresponding flavanone by the usual method they obtained only poor yields. Further they had difficulty in converting it into the flavonol, the conversion being accompanied by partial demethylation. They concluded that the resulting morin trimethyl ether had a free hydroxyl group in the 5-position due to this partial demethylation. But such a demethylation of the 5-methoxyl group during the flavonol conversion was not noticed in other similar cases (*eg.*, kaempferol methyl ether by Kostanecki *et al.*¹³). In view of our observations that the same 2-hydroxy-4:6:2':4'-tetramethoxy chalcone undergoes demethylation at the 2'-position during isomerisation to the flavanone, complications should be expected in the progress of their synthesis.

More recently Cullinane and Philpott⁷ experienced difficulty in preparing 2-hydroxy-4:6:2':4'-tetramethoxy chalcone; their product melted at 128° while our sample had a melting point of 152–53° agreeing with the description of Kostanecki *et al.*⁸ The lower melting point is obviously due to contamination with the corresponding 2'-hydroxy flavanone formed in the condensation. Their conditions involving some heating would have favoured the demethylation of the 2'-position. As already mentioned the most satisfactory method for obtaining these methoxy chalcones seems to be the use of sodium ethoxide as the condensing agent.

EXPERIMENTAL

5:7-Dimethoxy-2'-hydroxy flavanone (II)

(i) To a solution of phloracetophenone dimethyl ether (2.5 g.) and salicylaldehyde (1.4 c.c.) in alcohol (30 c.c.) was added potassium hydroxide (10 g. in 10 c.c. of water) with shaking. It was kept in an air-tight flask

or two days, when the solution turned deep red. It was then diluted with water and acidified after cooling with hydrochloric acid. The pale yellow solid that separated was filtered, washed with a saturated solution of sodium bicarbonate and finally with water. It crystallised from alcohol as aggregates of colourless plates melting at 85–86°. Yield 2 g. It gave a deep blue colour with concentrated nitric acid, a violet colour with ferric chloride and a red colour with magnesium and hydrochloric acid. It was sparingly soluble in aqueous sodium hydroxide (Found: C, 61.9; H, 6.2; $C_{17}H_{16}O_6$, 1.5 H_2O requires C, 62.4; H, 5.8%). Even after sublimation at reduced pressure on a water bath the compound had the same melting point and did not lose its water of crystallisation.

(ii) Through a solution of phloracetophenone dimethyl ether (2 g.) and salicylaldehyde (0.8 c.c.) in ethyl acetate cooled in ice, dry hydrogen chloride gas was passed for three hours when a deep brown coloured solid was formed. After leaving for 24 hours in the ice-chest the solid was filtered and was found to be amorphous (m.p. above 300°); this was not examined further. On distilling off ethyl acetate from the filtrate a pale yellow solid separated which crystallised from alcohol as colourless plates melting at 85–86°, identical with the product of experiment (i).

5:7:2'-Trihydroxy flavanone (XIV)

To a solution of 5:7-dimethoxy-2'-hydroxy flavanone (1 g.) in benzene (50 c.c.) anhydrous aluminium chloride (4 g.) was added and the mixture refluxed on a water bath for 2 hours. Benzene was then removed by distillation and the complex decomposed with ice and hydrochloric acid when a white solid separated out. The mixture was kept in a hot water bath for a few minutes to complete the decomposition. On cooling a colourless solid separated which crystallised from alcohol in the form of colourless rectangular prisms melting at 195–96° (Shinoda and Sato gave m.p. 185–87° for nor-citronetin). It dissolved readily in aqueous sodium carbonate and gave a pink colour with ferric chloride. It could be recovered unchanged from its alkaline solution on acidification (Found: C, 61.7; H, 4.9, loss on drying 6.8%; $C_{15}H_{12}O_5$, H_2O requires C, 62.1; H, 4.8, loss on drying 6.2%).

Methylation

(a) *With one mole of dimethyl sulphate (7-methoxy-5:2'-dihydroxy flavanone) (XV).*—A solution of 5:7:2'-trihydroxy flavanone (1.6 g.) in dry acetone (100 c.c.) was refluxed with dimethyl sulphate (0.6 c.c.) and anhydrous potassium carbonate (2 g.) for 6 hours. It was then filtered,

the residue washed with warm acetone and acetone distilled off. 7-Methoxy-5:2'-dihydroxy flavanone crystallised from alcohol in the form of colourless aggregates of rhombohedral prisms melting at 134–35°. It gave a deep violet colour with ferric chloride and a blue colour with concentrated nitric acid (Found: C, 67.1; H, 5.3; $C_{16}H_{14}O_5$ requires C, 67.2; H, 4.9%).

(b) *With two moles of dimethyl sulphate (5:7-dimethoxy-2'-hydroxy flavanone) (II).*—5:7:2'-Trihydroxy flavanone (0.3 g.) was methylated with dimethyl sulphate (0.26 c.c., 2 moles) and anhydrous potassium carbonate (1 g.) in acetone solution for 16 hours. The product crystallised from alcohol in the form of aggregates of plates melting at 85–86°. It agreed in all its properties and reactions with 5:7-dimethoxy-2'-hydroxy flavanone and a mixed melting point with the sample obtained earlier was undepressed.

(c) *With excess dimethyl sulphate.*—The trihydroxy flavanone was refluxed with dimethyl sulphate (excess) and potassium carbonate for 48 hours. On working up as usual the product was found to be the dimethoxy-monohydroxy-flavanone (II).

2-Hydroxy-4:6:2'-trimethoxy chalcone (X)

This was reported earlier by Bargellini and Peratoner.¹⁴ In two experiments phloracetophenone dimethyl ether and salicylaldehyde methyl ether in alkaline medium gave mostly the 5:7-dimethoxy-2'-hydroxy flavanone at room temperature. However by carrying out the reaction at 0° and working up as usual 2-hydroxy-4:6:2'-trimethoxy chalcone was obtained which crystallised from alcohol as bright yellow rectangular plates and needles melting at 113–14° (Bargellini and Peratoner reported m.p. 106–08°). It gave only a brown colour with nitric acid and a reddish brown colour with ferric chloride. On reduction with magnesium and hydrochloric acid it did not develop any red colour (Found: C, 68.6; H, 5.7; $C_{18}H_{18}O_5$ requires C, 68.8; H, 5.7%).

Isomerisation with alcoholic sulphuric acid

The above chalcone (0.5 g.) was refluxed in alcoholic sulphuric acid solution (50 c.c., 4%) for 24 hours. On concentrating under reduced pressure and diluting the solution with water a colourless crystalline solid was obtained. It was filtered, washed with water and crystallised from alcohol when it separated in the form of colourless rectangular plates melting at 85–86°. The product could easily be sublimed under reduced pressure on a water bath when it was obtained as thick plates, m.p. 85–86°. It was identical in all its properties with 5:7-dimethoxy-2'-hydroxy flavanone

(II) and a mixed melting point with the sample obtained in an earlier experiment was undepressed.

2:4:6:2'-Tetramethoxy chalcone (IX)

Method I.—Phloracetophenone trimethyl ether (2 g.) and salicylaldehyde methyl ether (2 c.c.) in alcohol (50 c.c.) were treated with a solution of potassium hydroxide (6 g. in 6 c.c.) and the solution left corked for two days. On diluting with water and cooling a pale yellow solid separated which was filtered and washed with water. It crystallised from alcohol as stout rectangular prisms melting at 124–25°. It was insoluble in aqueous alkali and gave no colour with ferric chloride (Found: C, 69.1; H, 6.3; $C_{19}H_{20}O_4$ requires C, 69.5; H, 6.1%).

Method II.—Anhydrous aluminium chloride (10 g.) was dissolved in dry ether with cooling and phloroglucinol trimethyl ether added to it. The mixture was cooled in ice and treated with *o*-methoxy cinnamoyl chloride (4 g.) with shaking. It was kept at 0° for half an hour and at the room temperature for 12 hours. Ether was then distilled off and the complex decomposed with ice and hydrochloric acid. The product was filtered, washed with dilute hydrochloric acid and water. It crystallised from alcohol as big pale yellow rectangular prisms melting at 124–25°. It was identical with the sample obtained in Method I.

Method III.—2:4:6-Trimethoxy-2'-hydroxy chalcone (0.5 g.) was methylated with excess of dimethyl sulphate and potassium carbonate in acetone solution. The tetramethoxy chalcone crystallised from alcohol as stout prisms melting at 124–25° and was identical with the samples obtained above.

5:7:4'-Trimethoxy-2'-hydroxy flavanone (VII)

(i) Phloracetophenone dimethyl ether (3 g.) and resorcyaldehyde-4-methyl ether (2.7 g.) were condensed in alkaline medium as described earlier for similar cases. The product obtained on acidification crystallised from alcohol as colourless plates melting at 86–87° and after sublimation melted at the same temperature. It gave a blue colour with conc. nitric acid, a violet colour with ferric chloride and a red colour with magnesium and hydrochloric acid. Thus it agreed in its properties with those required for a flavanone (Found: C, 62.4; H, 5.6; $C_{18}H_{18}O_4 \cdot H_2O$ requires C, 62.1; H, 5.8%).

(ii) 5:7:2':4'-Tetrahydroxy flavanone described below was methylated with excess of dimethyl sulphate and potassium carbonate in acetone solution for 20 hours. The product crystallised from alcohol as rectangular

plates and prisms melting at 86–87° and was identical with the product of the above experiment (i).

5:7:2':4'-Tetrahydroxy flavanone

A solution of 5:7:4'-trimethoxy-2'-hydroxy flavanone (0.5 g.) in benzene (10 c.c.) was treated with anhydrous aluminium chloride (2.5 g.) and the product worked up as in similar demethylation given before. The product crystallised from alcohol as colourless prisms melting at 184–86°. It gave a pink colour with ferric chloride in alcoholic solution and dissolved readily in aqueous sodium carbonate (Found: C, 55.5; H, 4.8; $C_{15}H_{12}O_8$, $2H_2O$ requires C, 55.5; H, 4.9%).

2-Hydroxy-4:6:2':4'-tetramethoxy chalkone (XIII)

Kostanecki and Tambor⁸ employed aqueous sodium hydroxide for the condensation. In our experiment the same general procedure as was used in the case of salicylaldehyde methyl ether was adopted. It was found that in one of the condensations the product was found to be pure chalkone and was obtained in good yield. It crystallised from alcohol as yellow stout rhombohedral prisms melting at 152–53°. It gave no colour with concentrated nitric acid and magnesium and hydrochloric acid. In alcoholic solution it gave a brown colour with ferric chloride.

However it was found that in a number of condensations the product was mostly the 2'-hydroxy flavanone (VII) agreeing with the earlier sample. Even under exactly the same conditions as adopted by Kostanecki and Tambor the same demethylation of the 2'-position was noticed. It should be noted in this connection that Cullinane and Philpott⁷ report a melting point of 128° for this chalkone; their sample was probably a mixture.

Isomerisation with alcoholic sulphuric acid

The pure chalkone obtained above was refluxed with alcoholic sulphuric acid (50 c.c., 4%) for 24 hours and the solution concentrated under reduced pressure. The solid that separated on dilution was filtered and crystallised from alcohol. It separated as colourless thin plates melting at 84–85°. It was identical in all its properties and reactions with 5:7:4'-trimethoxy-2'-hydroxy flavanone and a mixed melting point with the sample described earlier was undepressed.

5-Methoxy-2'-hydroxy flavanone (III)

(i) 5-Methoxy-2'-hydroxy flavanone obtained by condensing 2-hydroxy-6-methoxy acetophenone and salicylaldehyde in alkali crystallised from alcohol in the form of colourless long rectangular prisms melting at 55–56°,

It gave a green colour with nitric acid and a red colour with magnesium and hydrochloric acid (Found: C, 66.4; H, 6.0; $C_{18}H_{14}O_4$, H_2O requires C, 66.7; H, 5.6%).

(ii) 5:2'-Dihydroxy flavanone described below was methylated with dimethyl sulphate (1.1 mole) and anhydrous potassium carbonate in acetone solution (16 hours). The methyl ether crystallised from alcohol as colourless long rectangular prisms melting at 55–56°, was identical with the product of experiment (i) and the mixed melting point with it was not depressed.

5:2'-Dihydroxy flavanone

On demethylating the above compound with aluminium chloride as in previous cases 5:2'-dihydroxy flavanone was obtained which crystallised from alcohol as rectangular prisms melting at 153–54°. It gave a deep reddish violet colour with ferric chloride and dissolved in aqueous sodium hydroxide (Found: C, 70.2; H, 5.0; $C_{15}H_{12}O_4$ requires C, 70.3; H, 4.7%).

2-Hydroxy-6:2'-dimethoxy chalcone (XI)

When aqueous sodium hydroxide was used for the chalcone condensation the reaction was accompanied by the usual demethylation of the 2'-position resulting in the formation of 2'-hydroxy flavanone. However by adopting the following method the pure chalcone could be obtained.

Sodium (3 g.) was dissolved in absolute alcohol (20 c.c.) and to this was added a solution of 2-hydroxy-6-methoxy acetophenone (1.4 g.) and salicylaldehyde methyl ether in alcohol. After leaving the mixture in the refrigerator for 2 days it was diluted with water, extracted with ether and the aqueous solution acidified with hydrochloric acid. A semi-solid mass was obtained which solidified on keeping in ice. It was filtered, washed with aqueous sodium bicarbonate and finally with water. On crystallising from alcohol it was obtained as bright orange red stout rhombic prisms melting at 96–97°. It gave a reddish brown colour with ferric chloride, no colour with conc. nitric acid and no red colour with magnesium and hydrochloric acid (Found: C, 71.8; H, 5.5; $C_{17}H_{16}O_4$ requires C, 71.8; H, 5.7%).

7:8-Dimethoxy-2'-hydroxy flavanone (IV)

(i) This was obtained from gallacetophenone dimethyl ether and salicylaldehyde. The product crystallised from alcohol as colourless stout rectangular prisms melting at 79–80°, gave a violet colour with ferric chloride and a red colour with magnesium and hydrochloric acid (Found: C, 60.7; H, 6.0; $C_{17}H_{16}O_5$, 2 H_2O requires C, 60.7; H, 5.9%).

(ii) Methylation of 7:8:2'-trihydroxy flavanone with excess of dimethyl sulphate gave only the 2'-hydroxy flavanone identical in all its reactions with the above sample.

7:8:2'-Trihydroxy flavanone

This was obtained by demethylation of 7:8-dimethoxy-2'-hydroxy flavanone with anhydrous aluminium chloride. It separated from alcohol as colourless aggregates of needles melting at 165–66°. It gave a bluish violet colour with ferric chloride and dissolved readily in aqueous sodium carbonate (Found: C, 58.5; H, 5.3; $C_{15}H_{12}O_5$, 2 H_2O requires C, 58.4; H, 5.2%).

2-Hydroxy-3:4:2'-trimethoxy chalcone (XII)

Gallacetophenone dimethyl ether (2 g.) and salicylaldehyde methyl ether (2 g.) were condensed in alcoholic solution in the presence of potassium hydroxide (6 g.). On working up as in similar cases the product crystallised from alcohol as bright yellow prisms melting at 103–04°. It gave a reddish brown colour with ferric chloride and no colour with magnesium and hydrochloric acid (Found: C, 68.4; H, 5.9; $C_{18}H_{18}O_5$ requires C, 68.8; H, 5.7%).

7:2'-Dihydroxy flavanone

7-Methoxy-2'-hydroxy flavanone obtained from peonol and salicylaldehyde separated only as a semi-solid mass and could not be crystallised. It was directly demethylated with aluminium chloride in benzene solution. The dihydroxy flavanone crystallised from alcohol as prismatic needles melting at 132–33°, and it gave a deep red colour with ferric chloride (Found: C, 62.0; H, 5.5; $C_{15}H_{12}O_4$, 2 H_2O requires C, 61.7; H, 5.5%).

SUMMARY

In view of the discrepancies in the properties of the natural and synthetic citronetin, a detailed study of 2'-hydroxy flavanones and related compounds has been made. The condensation of a number of 2-hydroxy acetophenones with salicylaldehyde and 4-methoxy salicylaldehyde yields exclusively flavanones. Protection of both the ortho hydroxyl groups of the ketone as well as the aldehyde gives the corresponding methylated chalcones. Chalcones are again formed even if a 2-methoxy ketone is condensed with an ortho hydroxy aldehyde. On the other hand, when the hydroxyl of the ketone is kept free and only the ortho hydroxyl group of the aldehyde is etherified, the product is found to be a chalcone or flavanone, depending on the conditions. Lower temperature and milder alkali avoid demethylation of

the 2'-methoxyl group and tend to produce 2'-methoxy chalcones, otherwise a flavanone is formed with the 2'-hydroxyl group free. Even during chalcone-flavanone conversion with alcoholic sulphuric acid demethylation of the 2'-methoxyl group takes place. It is clear that a free 2'-hydroxyl group stabilises the flavanone structure such as a similar group in the 5 position; and a methoxyl group in this position in a flavanone is very readily demethylated. This could be attributed to the presence of chelation between this hydroxyl and the ether oxygen of the pyranone ring. Demethylation of these flavanones can be conveniently effected using aluminium chloride to yield the hydroxy flavanones. By employing different quantities of dimethyl sulphate partial methyl ethers of the hydroxy flavanones have been obtained. A special feature is the extraordinary resistance of the 2'-hydroxyl group in a flavanone, which cannot be methylated at all under drastic conditions. These observations explain the difficulties experienced by certain workers in the preparation and utilisation of these types of compounds.

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