SYNTHETICAL EXPERIMENTS IN THE
CHROMONE GROUP

Part XXVII. Coupling of 5-Hydroxyflavone, 5-Hydroxy-6-methoxyflavone and Tectochrysin with Diazotized Aniline. New Synthesis of 5:6-Dihydroxyflavone, Baicalein, and 5:6:8-Trihydroxyflavone

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The coupling of 6-hydroxyflavone with diazotized aniline in the 5-position has been used for the synthesis of 5:6-dihydroxyflavone, and the behaviour of 5-hydroxyflavone and its derivatives towards diazotized aniline has now been studied. 5-Hydroxyflavone in pyridine-alcohol containing caustic soda and ammonia coupled with diazotized aniline. The azo dye, presumably (II), gave on reduction a primary amine which should then be 8-amino-5-hydroxyflavone (III). The diazonium salt from (III) was unusually stable, but on slow boiling with 50% sulphuric acid until the concentration was about 80% decomposition with evolution of nitrogen took place. The product was 5:6-dihydroxyflavone and not primetin (I). The constitution of the azo dye from 5-hydroxyflavone was therefore examined. When

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\text{Ph-N=N} \quad \text{H}_2\text{N} \quad \text{Ph}
\]

\[
\text{HO} \quad \text{O} \quad \text{Ph}
\]

\[
\text{OH} \quad \text{COCH}_3
\]

2-acetyl-4-benzeneazoresorcinol (IV) was heated with benzoic anhydride and sodium benzoate, the product was a benzeneazo-5-hydroxyflavone
different from (II) and formulated as (V). Cyclization of (IV) in this direction to form (V), and not (II), is to be expected on account of chelation of the azo and o-hydroxyl groups. The constitution of (II) and (V) as the 8- and 6-benzeneazo derivatives of 5-hydroxyflavone was confirmed by the fact that (II) could be methylated by means of dimethyl sulphate and potassium carbonate in acetone solution, while (V) was resistant to methylation. Reduction of (V) and diazotization of the aminophenol (VI) thus obtained gave a diazo-oxide in the same manner as 5-amino-6-hydroxyflavone.\(^1\) The amine agreed in its properties with 6-amino-5-hydroxyflavone prepared from 6-acetyl-5-hydroxyflavone by Sugasawa\(^2\) except for a slight difference in the melting point. The melting point observed was 181\(^\circ\) (Sugasawa, 177\(^\circ\)). Vigorous hydrolysis of the diazo-oxide with sulphuric acid gave 5 : 6-dihydroxyflavone. Sugasawa\(^2\) has stated that all his attempts to replace the amino by hydroxyl in 6-amino-5-hydroxyflavone were unsuccessful.

Since the aminophenols (III) and (VI) were isomeric and not identical compounds, the former was 8-amino-5-hydroxyflavone, and the formation of 5 : 6-dihydroxyflavone, and not 5 : 8-dihydroxyflavone, from (II) and (V) has to be explained by postulating the opening of the pyrone ring under the drastic conditions of acid treatment of the diazonium salt, followed by cyclization in the alternative direction. Such rearrangements have been recorded by Wesseley,\(^3\) Baker\(^4\) and Seshadri\(^5\) during demethylation of flavones containing methoxyl groups in the 5 : 8-positions with hydroiodic acid. It was observed in the present work that by boiling with 32% hydrochloric acid or 50–80% sulphuric acid, 8-amino-5-hydroxyflavone (III) was converted into the 6-amino compound (VI), and primetin into 5 : 6-dihydroxyflavone.

When 2-hydroxy-6-methoxyacetophenone\(^6\) was coupled with benzene diazonium chloride, the dye obtained had the anticipated structure (VII), and was different from the product (VIII) of the methylation of 2-acetyl-4-benzeneazoresorcinol (IV) with one mole of dimethyl sulphate in acetone solution in the presence of potassium carbonate. When (VII) was submitted to the Robinson reaction with benzoic anhydride the result was unexpected. Instead of 6-benzeneazo-5-hydroxyflavone (V) or its methyl ether, 8-benzene-
azo-5-hydroxyflavone (II) was obtained. Demethylation occurred, apparently by a direct attack of the anhydride on the methoxyl group, immediate cyclization to (II) then taking place. Demethylation during the Robinson reaction was noticed by Baker in the case of 2:5-dihydroxy-6-methoxy-acetophenone, but the cyclization of the flavone proceeded in the direction to be anticipated and the product was 5:6-dihydroxyflavone.

The condensation of 2-acetyl-4-benzeneazo-resorcinol with benzaldehyde gave the chalcone (IX), which did not undergo cyclization to a flavone by the action of selenium dioxide in amyl alcohol or xylene.

5-Methoxyflavone was first prepared by Simonis and Danishevski, and 5-hydroxyflavone by Sugasawa. Seshadri and co-workers synthesized 5-hydroxyflavone by converting 2-benzoyloxy-6-methoxyacetophenone (X) to the diketone (XI) by means of sodamide in toluene at 100°, cyclization of the diketone to 5-methoxyflavone and demethylation. They also obtained it by debenzoylation of 3-benzoyl-5-hydroxyflavone with alcoholic sodium carbonate. 2-Acetylresorcinol dibenzoate, when treated with sodium ethoxide in absolute alcohol, gave 6-benzoyloxy-2-hydroxydibenzoylmethane (XII), which was converted into 5-hydroxyflavone by the action of glacial acetic acid and fused sodium acetate.

2-Acetylresorcinol dibenzoate, dissolved in ether or boiling benzene and treated with sodamide, gave a compound which is formulated as the triketone (XIII) since it gave 3-benzoyl-5-hydroxyflavone by refluxing with glacial acetic acid and sodium acetate.

Chrysin was partially methylated to tectochrysin (XIV) by treatment with one mole of dimethyl sulphate in acetone solution in the presence of potassium carbonate. Tectochrysin (XIV) coupled with benzenediazonium
chloride to form a monoazo dye, formulated as 8-benzeneazotectochrysin (XV), by analogy with the behaviour of 5-hydroxyflavone. Reduction of (XV) with zinc dust in alcohol-acetic acid yielded the amine (XVI). The diazonium salt from (XVI) was even more difficult to decompose than that from (III), prolonged boiling with 80% sulphuric acid being necessary. Under these conditions, some general decomposition was unavoidable and the product, which gave all the characteristic colour reactions of baicalein, could not be isolated in pure crystalline form. However, on boiling the amine (XVI) with 32% hydrochloric acid for 24 hours, baicalein 7-methyl ether (XVII), agreeing in all its properties with the substance described by Sastri and Seshadri, was obtained in good yield. Thus treatment with hydrochloric acid resulted in hydrolysis of the amine, accompanied by a rearrangement of 5:8-dihydroxy-7-methoxyflavone (XVIII) to 5:6-dihydroxy-7-methoxyflavone (XVII). Demethylation of (XVII) yielded baicalein (XIX), which was first isolated from a natural source by Shibata, Nakamura and Iwata, but synthesized earlier by Bargellini. A more recent synthesis is due to Sastri and Seshadri.

5-Hydroxy-6-methoxyflavone (XX) was prepared by methylating 5:6-dihydroxyflavone with one mole of dimethyl sulphate in acetone in the
presence of potassium carbonate; and also by partially demethylating 5:6-dimethoxyflavone with aluminium chloride in ether at room temperature. With diazotized aniline, (XX) gave 8-benzeneazo-5-hydroxy-6-methoxyflavone (XXI), which was reduced to the amine (XXII).

When the amine was treated for 24 hours with boiling 32% hydrochloric acid and the product, which did not contain nitrogen, was acetylated, the acetyl derivative on hydrolysis with alcoholic hydrochloric acid yielded 5:6:8-trihydroxyflavone (XXIII) prepared by Rajagopalan, Seshadri and Varadarajan by a different route.

**EXPERIMENTAL**

6-Benzoyloxy-2-hydroxydibenzoylmethane (XII)

2-Acetylresorcinol dibenzoate (2 g.) was added to a solution of sodium ethoxide (from 0.6 g. of sodium) in absolute alcohol (40 c.c.). The mixture was frequently shaken until the ester completely went into solution (1 hr.). There was a rapid change of the colour of the solution from pale yellow to green. On leaving overnight at room temperature the reaction mixture set to a dark greenish brown gel, which was acidified with ice-cold dilute acetic acid. After 4 hours the crystalline precipitate was filtered and crystallized from aqueous alcohol. The mixture of plates and needles (0.71 g.) melted at 124° (Found: C, 72.9; H, 4.3. C_{22}H_{16}O_{5} requires C, 73.3; H, 4.4%). The alcoholic solution develops a reddish brown colour with ferric chloride.

The filtrate after separation of the crude diketone deposited a brown precipitate (0.1 g.) which crystallized from alcohol in colourless needles, m.p. 157°, undepressed when mixed with 5-hydroxyflavone.

5-Hydroxyflavone

6-Benzoyloxy-2-hydroxydibenzoylmethane (1.4 g.) was refluxed for 5 hours with glacial acetic acid (15 c.c.) containing fused sodium acetate (3 g.). The product was poured into water and the brown precipitate crystallized from alcohol in needles (1 g.), m.p. 157°.

2:6-Dihydroxytribenzoylmethane (XIII)

(a) 2-Acetylresorcinol dibenzoate (2 g.) was dissolved in dry ether (40 c.c.) in a pressure bottle. Finely powdered sodamide (3 g.) was added, the bottle stoppered and mechanically shaken for 6 hours. The light green precipitate was filtered and cautiously added to ice-cold dilute acetic acid. The yellow precipitate was collected and crystallized successively from benzene and from ethyl acetate. The yellow elongated plates melted at 180–81° (Found: C, 73.4; H, 4.4. C_{26}H_{18}O_{5} requires C, 73.3; H, 4.4%).
(b) 2-Acetylresorcinol dibenzoate (2 g.) was dissolved in dry benzene (20 c.c.), finely powdered sodamide (3 g.) added and the mixture refluxed for 6 hours. The pale green product was filtered, washed with benzene, sucked dry, and gradually stirred into ice-cold dilute acetic acid. Successive crystallization of the yellow precipitate (1 g.) from benzene and from ethyl acetate gave yellow plates, m.p. 181°. The m.p. was not depressed by mixing with the product obtained by method (a), but when mixed with 3-benzoyl-5-hydroxyflavone prepared according to Baker, the m.p. was 160–65°. The alcoholic solution gives a deep brownish purple colour with ferric chloride.

3-Benzoyl-5-hydroxyflavone

A solution of the triketone from the previous experiment (0·5 g.) in glacial acetic acid (5 c.c.) containing fused sodium acetate (1 g.) was refluxed for 6 hours and poured into water. The product crystallized from a mixture of alcohol and acetic acid in yellow rods (0·4 g.), m.p. 178–79°, undepressed when mixed with 3-benzoyl-5-hydroxyflavone prepared according to Baker.

8-Benzeneazo-5-hydroxyflavone (II)

A solution of benzenediazonium chloride, prepared as usual from aniline (2 g., 2·5 mol.), hydrochloric acid (32%, 6 c.c.), alcohol (30 c.c.) and sodium nitrite (1·8 g. in 10 c.c. water) was gradually added at 0° to a solution of 5-hydroxyflavone (2 g.) in alcohol (80 c.c.), pyridine (14 c.c.), 20% aqueous caustic soda (2 c.c.) and ammonia (d. 0·88; 2 c.c.). During addition of the diazonium solution and for 6 hours thereafter, the mixture was mechanically stirred and maintained at 0°. It was then left overnight in a refrigerator and the brown precipitate that separated was collected, boiled with 10% hydrochloric acid for a few minutes, filtered and crystallized from acetic acid. The orange plates (1·5 g.) melted at 214–15° (Found: N, 8·2. C_{21}H_{14}O_{2}N_{2} requires N, 8·2%). The alcohol solution gives a reddish brown colour with ferric chloride, and a deep red coloration with aqueous sodium hydroxide. Acetylation of the dye in the usual manner with acetic anhydride and pyridine gave the acetyl derivative, which crystallized from alcohol in orange-yellow needles, m.p. 186° (Found: N, 7·5. C_{22}H_{16}O_{4}N_{2} requires N, 7·3%).

8-Benzeneazo-5-methoxyflavone

8-Benzeneazo-5-hydroxyflavone (1 g.), dissolved in boiling anhydrous acetone (20 c.c.) was treated with dimethyl sulphate (1·25 g.) and freshly ignited potassium carbonate (4 g.) during 15 hours. On pouring into water and removal of acetone on the water-bath, the product crystallized from
glacial acetic acid in orange plates, m.p. 206-08°, depressed to 172-80° when mixed with 8-benzeneazo-5-hydroxyflavone (Found: N, 7·9. C_{22}H_{16}O_{3}N_{2} requires N, 8·0%). The yellow alcoholic solution gives no colour with ferric chloride or aqueous caustic soda.

8-Amino-5-hydroxyflavone (III)

8-Benzeneazo-5-hydroxyflavone (1 g.) suspended in a boiling mixture of alcohol (80 c.c.) and acetic acid (10 c.c.) was treated under reflux with zinc dust (2 g.). There was a vigorous reaction, the red solid gradually dissolved and the red solution became orange yellow in colour. Boiling was continued 10 minutes longer, the hot solution was filtered, and the zinc was extracted thrice with 5 c.c. portions of hot alcohol. The filtrate was cooled and diluted with water. The compound that separated was filtered and crystallized from dilute alcohol. The brownish yellow rods (0·6 g.) melted at 204-05° (Found: N, 5·7. C_{15}H_{14}O_{3}N requires N, 5·5%). The orange yellow alcoholic solution turns dark greenish brown on the addition of a drop of alcoholic ferric chloride. The compound is insoluble in aqueous caustic soda, and gives a yellow solution in conc. sulphuric acid.

5-Hydroxyflavone-8-diazonium sulphate and 5:6-dihydroxyflavone

8-Amino-5-hydroxyflavone (0·1 g.) was suspended in a mixture of water (10 c.c.) and conc. sulphuric acid (0·5 c.c.). On boiling the mixture, the orange compound became colourless and gradually dissolved. The mixture was filtered and the small amount of residue extracted again with a mixture of water (10 c.c.) and concentrated sulphuric acid (0·5 c.c.). The combined filtrates on cooling deposited the amine sulphate as microscopic needles. The suspension was cooled to 5° and sodium nitrite (0·04 g.) in water (1 c.c.) was added with stirring. The crystals first became reddish brown, but completely went into solution in 10 minutes, giving a clear, pale brown solution. After 20 minutes, excess nitrous acid was destroyed by the addition of urea and the diazonium solution gradually added to a boiling mixture of water (20 c.c.) and concentrated sulphuric acid (10 c.c.). After the addition, a drop of the boiling mixture was tested every 5 minutes with alkaline β-naphthol for the presence of the diazonium salt. When the volume of the boiling mixture decreased to about 15 c.c., there was a vigorous effervescence due to evolution of nitrogen, the orange-yellow colour of the solution changed to brown, and the solution failed to give a red colour with alkaline β-naphthol indicating complete hydrolysis of the diazonium salt. The mixture was cooled and added to ice and water. The brownish yellow precipitate was collected, washed with water and crystallized from dilute alcohol (norit). The yellow needles (0·03 g.) melted at 188-90°, not
depressed by mixing with an authentic sample of 5:6-dihydroxyflavone prepared from 6-hydroxyflavone.¹

On acetylation by refluxing with acetic anhydride and pyridine, 5:6-diacetoxyflavone, m.p. 166-67°C, was obtained.

5-Hydroxyflavone-8-azo-β-naphthol, prepared by coupling alkaline β-naphthol with diazotized 8-amino-5-hydroxyflavone, crystallized from nitrobenzene in elongated plates, m.p. 288-90° (Found: N, 6.4. C_{25}H_{18}O_{4}N_2 requires N, 6.9%).

3-Acetyl-2-hydroxy-4-methoxyazobenzene (VIII)

2-Acetyl-4-benzeneazoresorcinol (0.5 g.), dimethyl sulphate (0.25 g., 1 mol.) and freshly ignited potassium carbonate (1 g.) in benzene were heated under reflux for 8 hours. The reaction mixture was diluted with water and the benzene layer extracted 4 times with 5% aqueous caustic soda. Acidification of the alkaline extract gave an orange substance which crystallized from alcohol in needles, m.p. 90° (Found: N, 10.1. C_{15}H_{14}O_{3}N_2 requires N, 10.4%). The alcoholic solution gives a pale reddish brown colour with ferric chloride. The solution in conc. sulphuric acid is pale orange in colour.

After extraction with alkali, the benzene layer was evaporated to dryness; the residual dimethyl ether crystallized from alcohol in orange plates, m.p. 110° with previous shrinking (Found: N, 10.3. C_{15}H_{14}O_{3}N_2 requires N, 9.9%).

3-Acetyl-4-hydroxy-2-methoxyazobenzene (VII)

A solution of benzenediazonium chloride prepared from aniline (0.6 g., 1 mol.) was gradually added to a solution of 2-acetylsorcinol monomethyl ether (1.1 g.) in alcohol (40 c.c.) and pyridine (6 c.c.) at 0°. The mixture was left overnight in a refrigerator, and the light orange precipitate collected, treated with hydrochloric acid to remove pyridine, washed and crystallized from alcohol. The orange needles (1 g.) melted at 100° with shrinking at 97° (Found: N, 10.7. C_{15}H_{14}O_{3}N_2 requires N, 10.4%). The alcoholic solution gives a deep brown colour with ferric chloride.

8-Benzeneazo-5-hydroxyflavone (II)

3-Acetyl-4-hydroxy-2-methoxyazobenzene (2.3 g.) was intimately mixed with benzoic anhydride (3.5 g.) and sodium benzoate (12 g.) and heated at 180-90° for 10 hours. Hydrolysis was effected by means of caustic potash (22 g.) in alcohol (240 c.c.) on the water-bath for 40 minutes. Alcohol was removed under reduced pressure, the residue diluted with water and saturated with carbon dioxide. The orange yellow precipitate was filtered, washed
with water and crystallized from acetic acid. The orange plates (1.9 g.) melted at 215°, not depressed by admixture with 8-benzeneazo-5-hydroxy-flavone obtained by coupling 5-hydroxyflavone with benzene diazonium chloride.

6-Benzeneazo-5-hydroxyflavone (V)

2-Acetyl-4-benzeneazoresorcinol (4 g.) was intimately mixed with benzoic anhydride (60 g.) and sodium benzoate (10 g.) and heated at 180-90° for 10 hours. The reddish brown product was treated on the water-bath with alcohol (300 c.c.) and caustic potash (34 g. in 40 c.c. water) during 40 minutes. Most of the alcohol was removed under reduced pressure, the residue diluted with water and saturated with carbon dioxide. The reddish brown precipitate was filtered, washed with water and crystallized from acetic acid. The orange-yellow rods (3 g.) melted at 210°, lowered to 170-88° when mixed with 8-benzeneazo-5-hydroxyflavone (II) (Found: N, 8.4. C_{21}H_{14}O_{2}N_{2} requires N, 8.2%). The alcoholic solution gives a reddish brown colour with ferric chloride. The acetyl derivative crystallized from alcohol in light orange needles, m.p. 195° (Found: N, 7.6. C_{23}H_{16}O_{4}N_{2} requires N, 7.3%).

6-Benzeneazo-5-hydroxyflavone was subjected to methylation under the conditions used for methylating compound (II). The product crystallized from acetic acid in orange rods, m.p. 206°, not depressed by mixing with 6-benzeneazo-5-hydroxyflavone. Methylation therefore had not taken place.

6-Amino-5-hydroxyflavone (VI)

6-Benzeneazo-5-hydroxyflavone (1 g.) in boiling alcohol (60 c.c.) and acetic acid (10 c.c.) was treated with zinc dust (2 g.). The orange red solution changed to a deep brownish grey. More zinc dust (0.5 g.) was added, the mixture refluxed for 10 minutes longer, filtered hot, and the residue extracted thrice with 5 c.c. portions of hot alcohol. The filtrate was diluted with water and the yellow precipitate collected and crystallized by dissolving in hot alcohol (Norit), diluting to slight turbidity and cooling. The yellow elongated plates (0.6 g.) melted at 181° with previous shrinking (Found: N, 5.7. C_{16}H_{11}O_{3}N requires N, 5.5%). Sugasawa describes the amine as golden yellow plates melting at 177°. The alcoholic solution turns an intense reddish brown with ferric chloride. With concentrated sulphuric acid, a yellow solution is obtained. The substance does not dissolve in aqueous caustic soda.

Conversion of 6-amino-5-hydroxyflavone into 5:6 dihydroxyflavone

6-Amino-5-hydroxyflavone (0.3 g.) was boiled with water (30 c.c.) and sulphuric acid (98%; 3 c.c.). The yellow crystals changed to white and
then dissolved. On cooling, colourless crystals of the amine sulphate were deposited. On addition of sodium nitrite (0.5 g.), the crystals gradually disappeared, and a yellow precipitate of the diazo-oxide then separated. This was filtered, washed with water and dried (Found: N, 9·6. C_{15}H_{8}O_{3}N requires N, 10·6%).

A suspension of the diazo-oxide from 0.3 g. of the amine was added to a boiling mixture of water (30 c.c.) and 98% sulphuric acid (30 c.c.). The brownish yellow solution was boiled to about 45 c.c., when there was a vigorous evolution of nitrogen and the dark orange brown solution gave no indication of coupling with alkaline β-naphthol. The brown precipitate obtained on cooling crystallized from dilute alcohol in yellow needles (0·1 g.), m.p. 188–89°, not altered when mixed with 5:6-dihydroxyflavone. On acetylation in the usual way 5:6-diacetoxyflavone melting at 166° was obtained.

Action of hydrochloric acid on 8-amino-5-hydroxyflavone (III)

8-Amino-5-hydroxyflavone (0·1 g.) was treated with boiling 16% hydrochloric acid (20 c.c.) for 20 hours. The deep brown precipitate was collected and identified as an amine hydrochloride, m.p. 230–35°. Treatment with aqueous sodium bicarbonate, and crystallization from dilute alcohol gave yellow elongated plates (0·06 g.) which melted at 178°, not depressed by mixing with 6-amino-5-hydroxyflavone. A further quantity of this amino-hydroxyflavone was recovered by neutralizing the hydrochloric acid filtrate with sodium bicarbonate.

6-Amino-5-hydroxyflavone was recovered unchanged by treatment with boiling 16% hydrochloric acid for 20 hours, followed by neutralization with sodium bicarbonate.

Action of hydrochloric acid on primetin (I)

A solution of primetin (0·05 g.) in alcohol (1 c.c.) and 32% hydrochloric acid (3 c.c.) was refluxed for 20 hours and poured into water. The yellow precipitate crystallized from dilute alcohol in needles, m.p. 189°, not depressed by admixture with 5:6-dihydroxyflavone prepared from 6-hydroxyflavone. The substance also exhibited all the reactions of 5:6-dihydroxyflavone.

Action of 80% sulphuric acid on primetin

Primetin (0·05 g.) was refluxed with 98% sulphuric acid and water (5 c.c.) for 45 minutes. After cooling and diluting with water, the yellow precipitate was collected and crystallized from dilute alcohol. The yellow needles shrunk at 170° and melted at 180–85°, and gave all the reactions of 5:6-dihydroxyflavone.
3-Benzeneazo-2: 6-dihydroxyphenyl styryl ketone (IX)

2-Acetyl-4-benzeneazoresorcinol (1.06 g.) and benzaldehyde (1.3 g., 3 mols.) in absolute alcohol (20 c.c.) were treated with caustic potash (15 g. in 20 c.c. water), and left overnight at room temperature. The reaction mixture was added to crushed ice and hydrochloric acid. The bright red precipitate crystallized from glacial acetic acid in deep red plates, m.p. 178° (Found: N, 7.9. C₂₁H₁₈O₃N₂ requires N, 8.1%).

8-Benzeneazo-3-benzoyl-5-hydroxyflavone

A solution of benzenediazonium chloride prepared from aniline (0.3 g.) was gradually added to a solution of 3-benzoyl-5-hydroxyflavone (0.3 g.) in alcohol (15 c.c.), pyridine (2 c.c.), caustic soda (0.3 c.c. of 20% solution) and ammonia (d. 0.88; 0.3 c.c.) at 0°. On leaving overnight in a refrigerator, the brown precipitate was collected and crystallized from acetic acid. The orange needles (0.15 g.) melted at 247-49° (Found: N, 6.6. C₂₈H₁₈O₄N₂ requires N, 6.37%). The acetyl derivative crystallized from alcohol in needles, m.p. 184° (Found: N, 5.9. C₂₈H₂₀O₅N₂ requires N, 5.7%).

8-Benzeneazotectochrysin (XV)

Benzenediazonium chloride from aniline (1 g.) was gradually added to a solution of tectochrysin (0.8 g.) in pyridine (12 c.c.), alcohol (60 c.c.), 5 N caustic soda solution (0.75 c.c.) and ammonia (d. 0.88; 1.2 c.c.) at 0°. On leaving overnight in a refrigerator, the orange precipitate was filtered, treated with hydrochloric acid (32%) in which it partly dissolved and diluted with water. The red precipitate crystallized from acetic acid in orange needles (0.6 g.), m.p. 232° (Found: N, 7.6. C₂₈H₁₈O₄N₂ requires N, 7.8%). The substance gives an orange solution with conc. sulphuric acid and a brown colouration with alcoholic ferric chloride.

8-Benzeneazo-5: 7-dimethoxyflavone

8-Benzeneazotectochrysin (0.1 g.), dry acetone (10 c.c.), dimethyl sulphate (0.5 g.) and freshly ignited potassium carbonate (2 g.) were heated for 15 hours on a water-bath. The product was poured into water, excess acetone removed on a water-bath and the precipitate crystallized from alcohol. The orange needles melted at 207-08° (Found: N, 7.8. C₂₈H₁₈O₄N₂ requires N, 7.3%). The substance gives no ferric chloride reaction and is insoluble in aqueous caustic soda.

8-Aminotectochrysin (XVI)

8-Benzeneazotectochrysin (1 g.) in boiling alcohol (60 c.c.) and glacial acetic acid (10 c.c.) was treated with zinc dust (2.0 g.). After 10 minutes,
when the colour of the solution had become orange, zinc was filtered off and extracted thrice with 5 c.c. portions of boiling alcohol. Dilution of the filtrate and extracts with water gave an orange-yellow precipitate, which crystallized from dilute alcohol in fine yellow needles (0.7 g.) and melted at 197° with previous shrinking (Found: N, 4.7. C_{18}H_{13}O_{4}N requires N, 4.9%). The alcoholic solution develops a brown colouration with ferric chloride. With aqueous sodium hydroxide the aminophenol turns red, but does not dissolve. It dissolves in hot hydrochloric acid and sulphuric acid, the colourless salts being deposited on cooling. On the addition of sodium nitrite, the salts gradually dissolve leaving a trace of a fluffy residue and the diazonium salts couple with alkaline β-naphthol to form a brownish red dye.

**Baicalein 7-methyl ether (XVII)**

8-Aminotectochrysin (0.8 g.) was refluxed for 24 hours with 25% hydrochloric acid (45 c.c.) and the mixture filtered hot. The residue was washed with hot water, and crystallization from alcohol gave yellow plates (0.4 g.), m.p. 219° (Found: C, 67.4; H, 4.3. C_{18}H_{13}O_{5} requires C, 67.6; H, 4.3%). A deep green colour similar to that produced with 5: 6-dihydroxyflavone is produced when a drop of ferric chloride is added to an alcoholic solution of the substance. With aqueous caustic soda it develops an orange-red colour and a greenish brown precipitate then separates. With sodium amalgam in absolute alcohol, a transient orange colour appears which rapidly changes to a dark greenish blue; after some minutes a brown precipitate is formed. With conc. sulphuric acid a yellow non-fluorescent solution is obtained. An alcoholic solution gives an orange yellow precipitate with alcoholic lead acetate. All these properties agree with those recorded by Sastri and Seshadri for baicalein 7-methyl ether.

**5: 6-Diacetoxy-7-methoxyflavone**

Baicalein 7-methyl ether (0.1 g.) was acetylated in the usual manner; the diacetyl derivative crystallized from alcohol in colourless plates, m.p. 239-40° (Found: C, 65.3; H, 4.5. C_{20}H_{19}O_{7} requires C, 65.2; H, 4.3%).

**5: 6: 7-Trimethoxyflavone**

Baicalein 7-methyl ether (0.1 g.) was treated for 8 hours with boiling acetone (20 c.c.), dimethyl sulphate (0.5 c.c.) and freshly ignited potassium carbonate (1 g.). On dilution with water and removal of acetone on a water-bath, the trimethyl ether separated as a crystalline solid which crystallized from dilute alcohol in narrow rectangular plates, m.p. 166° (Seshadri et al., 14-17 quote the m.p. 165-66°).
Baicalein (XIX)

The 7-methyl ether (0.1 g.) was treated with boiling hydriodic acid (d. 1.5; 4 c.c.) and acetic anhydride (4 c.c.) for 4 hours. On pouring into saturated sodium bisulphite solution, the yellow precipitate was collected and crystallized from dilute alcohol. The yellow plates melted at 264° and gave all the reactions described by Seshadri and others for baicalein (Found: C, 66.6; H, 3.7. C_{15}H_{10}O_{5} requires C, 66.7; H, 3.7%).

8-Benzeneazo-5-hydroxy-6-methoxyflavone (XXI)

Benzenediazonium chloride prepared from aniline (1 g.) was gradually added to a solution of 5-hydroxy-6-methoxyflavone (0.5 g.) in alcohol (60 c.c.), pyridine (12 c.c.), 5 N caustic soda (0.6 c.c.) and ammonia (d. 0.88; 2 c.c.) at 0°. The orange dye crystallized from acetic acid in dull orange elongated plates (0.5 g.), m.p. 233-34° (Found: N, 7.8. C_{22}H_{16}O_{4}N_{2} requires N, 7.9%). A reddish brown colour is developed when a drop of ferric chloride is added to its alcholic solution. It gives an orange solution with alcoholic caustic soda and a scarlet solution with conc. sulphuric acid.

8-Amino-5-hydroxy-6-methoxyflavone (XXII)

8-Benzeneazo-5-hydroxy-6-methoxyflavone (0.5 g.) in a boiling mixture of alcohol (60 c.c.) and acetic acid (10 c.c.) was treated with zinc dust (2 g.) during 15 mins. Worked up as described earlier, the amine crystallized from dilute alcohol in brown elongated plates (0.3 g.), m.p. 210° (Found: N, 5.2. C_{15}H_{12}O_{4}N requires N, 4.9%). An alcoholic solution gives with ferric chloride a green colouration, changing to greenish brown. The solution in conc. sulphuric acid is yellow.

Hydrolysis of 8-amino-5-hydroxy-6-methoxyflavone: 5:6:8-Trihydroxyflavone (XXIII)

The amine (XXII; 0.2 g.) was refluxed with 32% hydrochloric acid (20 c.c.) for 24 hours, when the diazotization test was negative. On cooling the yellowish brown precipitate (0.15 g.) was collected, dried and acetylated by refluxing with acetic anhydride (10 c.c.) and pyridine (1 c.c.) for 2 hours. The product was poured on crushed ice and the precipitate of 5:6:8-triacetoxyflavone crystallized from alcohol. The shining rectangular plates melted at 217° (Rajagopalan et al. quote m.p. 214°) (Found: C, 63.2; H, 4.3. C_{21}H_{16}O_{8} requires C, 63.6; H, 4.0%).

The acetyl derivative (0.05 g.) was hydrolysed by heating with alcohol (10 c.c.) and 32% hydrochloric acid (2 c.c.) for 30 mins. The solution was diluted and excess alcohol removed under vacuum. The orange yellow
product crystallized from dilute alcohol in sheaves of yellow needles, m.p. 236° (Found: C, 67.4; H, 4.0. \( \text{C}_{15}\text{H}_{10}\text{O}_7 \) requires C, 66.7; H, 3.7%). It gives a brown colour with alcoholic ferric chloride and a red solution with aqueous caustic soda which becomes paler and finally yellow on standing. These properties are in agreement with those described by Rajagopalan et al.\(^{18}\)

**SUMMARY**

The coupling of 5-hydroxyflavone with benzenediazonium chloride led to an azo dye which was different from the compound obtained by the Robinson flavone condensation on 2-acetyl-4-benzeneazoresorcinol and benzoic anhydride. The two compounds are shown to be the 8- and 6-benzeneazo derivatives of 5-hydroxyflavone respectively. The conversion of both the azo dyes into 5:6-dihydroxyflavone is described.

Tectochrysin was converted to baicalein 7-methyl ether by coupling with benzenediazonium chloride, followed by reduction of the azo dye to the amine and treatment of the latter with hydrochloric acid. Baicalein was obtained by demethylation of the 7-methyl ether. The same series of reactions carried out on 5-hydroxy-6-methoxyflavone\(^{25}\) led to 5:6:8-trihydroxyflavone.

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**REFERENCES**

7. Simonis and Danishevski .. *Ber.*, 1926, 59B, 2914.