FIXATION OF THE AROMATIC DOUBLE BONDS IN THE CHROMONES

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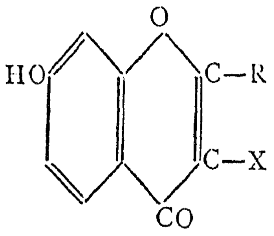
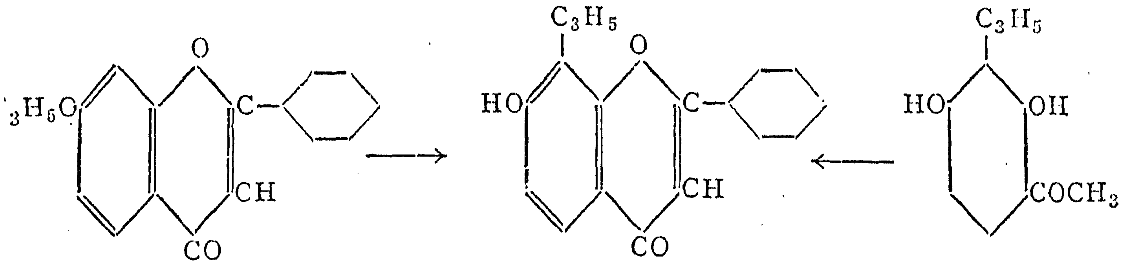
IN the course of work in progress in these laboratories relating to the preparation of aldehydes from 7-hydroxy-chromones it has been found that the incoming aldehyde group occupies position 8 indicating thereby that it is the reactive position. Wittig *et. al.*[1] and later on Baker[2] showed that when 7-acetoxy-chromones are subjected to Fries migration the acetyl group wanders only to the eighth position. These results suggested therefore the possibility of the aromatic double bonds in chromones occupying the positions as shown in (I).



where R is CH_3 or C_6H_5 and X is H or OCH_3

(I)

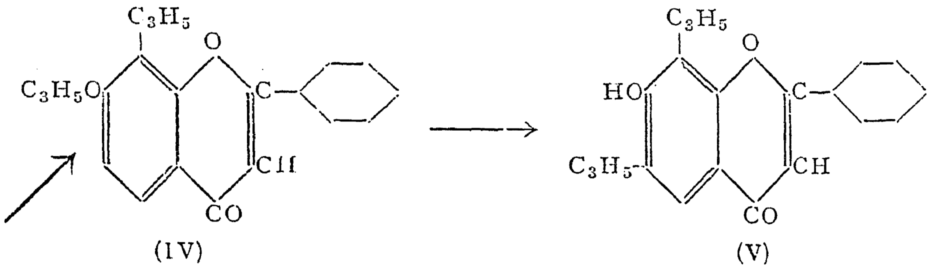
With a view to bring forward further definite evidence regarding (1) the distribution of the aromatic double bonds in the chromones and (2) the extent to which this distribution is alterable when made necessary, experiments conducted with 7-hydroxy-flavone and 2-methyl-3-methoxy-7-hydroxychromone are recorded in this paper. Since Claisen transformation of the allyl ethers offers the most reliable information regarding the position of the double bonds this reaction has been studied in detail. 7-Allyloxyflavone (II) underwent smooth and almost quantitative transformation into 8-allyl-7-hydroxyflavone (III). The constitution of the transformation product was established by its synthesis from 3-allylresacetophenone which was prepared



(II) (III)

according to the method of Baker and Lothian.[3] This gives therefore definite proof that position 8 is the reactive one in 7-hydroxyflavone and that the bond distribution is as represented in formula (I).

To find out how far this distribution is rigid the eighth position was next blocked by means of a protecting group (allyl) and the behaviour of 8-allyl-7-hydroxyflavone examined. The allyl ether of this (IV) underwent again Claisen transformation to give a good yield (75 per cent.) of an isomeric hydroxycompound which is obviously 6 : 8-diallyl-7-hydroxyflavone (V). The allyl ether has evidently reacted in the form (IV) rendering the sixth position active. The reactivity of the sixth position in compounds with substituents in position 8 was also exhibited when they were coupled in alkaline solution with diazotised *p*-nitraniline. 8-allyl-7-hydroxyflavone (III), 8-methyl-7-hydroxyflavone (VI) and 8-methyl-7-hydroxy-3-methoxyflavone[4] yielded highly coloured dyes under the above conditions. This is explicable only if structures similar to (IV) are assumed for these compounds.



Results of a similar nature were obtained from 2-methyl-3-methoxy-7-hydroxychromone. Its allyl ether (VII) underwent smooth conversion into 2-methyl-3-methoxy-7-hydroxy-8-allylchromone (VIII). The constitution of (VIII) was obtained from analogy with the compound of the 7-hydroxyflavone series. The important point to be noted however is that the allyl ether (IX) of this compound in turn underwent Claisen transformation to give an isomeric phenolic compound which is evidently 2-methyl-3-methoxy-6 : 8-diallyl-7-hydroxychromone (X). The 8-allyl-7-hydroxy chromone (VIII) further gave rise to a coloured azodye on being coupled with diazotised *p*-nitraniline. It is therefore concluded that while chromones generally react in form (I), reactivity in the isomeric form (IV) is not precluded.

Experimental

7-Allyloxyflavone (II).—A solution of 7-hydroxyflavone (2 g.) in anhydrous acetone (40 c.c.) was treated with allylbromide (5 c.c.) and anhydrous potassium carbonate (5 g.) and boiled under reflux for about six hours. The solvent was then distilled off and dilute hydrochloric acid added to the residue. An oily product was thereby obtained. It was extracted with ether and the ether solution shaken with dilute alkali so as to remove any unchanged hydroxyflavone. On removing the solvent a pale yellow crystalline solid was left behind. This was easily recrystallised from a mixture of benzene and petroleum ether (1 : 4) and thus the allyloxy compound was obtained in the form of colourless rhombic plates and rectangular prisms melting at 95–96°. The yield of the pure substance was one gram. (Found : C, 77·7 ; H, 5·1 ; $C_{18}H_{14}O_3$ requires C, 77·7 ; H, 5·0 per cent.)

8-Allyl-7-hydroxyflavone (*III*).—The above allyl ether (0·2 g.) was heated in an oil-bath at 210–15° for 2½ hours. The substance rapidly melted and the molten liquid slowly underwent conversion into a crystalline solid. After two crystallisations from alcohol it was obtained as colourless flat needles melting at 245–46°. It gave no colour with ferric chloride in alcoholic solution. (Found : C, 73·2 ; H, 5·7 ; $C_{18}H_{14}O_3$, H_2O requires C, 73·0 ; H, 5·4 per cent.) The yield of the final product was 0·12 g. and the sample was found to be identical in all respects with the one synthesised from 3-allylresacetophenone as described below :

3-Allylresacetophenone was prepared in very good yield by the method of Baker and Lothian.[3] The ketone (2·5 g.) was heated with sodium benzoate (5 g.) and benzoic anhydride (12 g.) for five hours under reduced pressure in an oil-bath at 190°. The product containing the benzoyloxyflavone was debenzoylated by boiling for half an hour with 100 c.c. of 10 per cent. alcoholic potash. The alcohol was then distilled off, water added and the resulting solution saturated with carbon dioxide. 8-Allyl-7-hydroxyflavone was precipitated as a crystalline solid. When recrystallised from alcohol it was obtained as flat needles melting at 245–46°. (Found : C, 73·0 ; H, 5·0 ; $C_{18}H_{14}O_3$, H_2O requires C, 73·0 ; H, 5·4 per cent.) Yield was one gram. A mixture of it with the sample obtained by the Claisen transformation had the same melting point.

7-Allyloxy-8-allylflavone (*IV*)—was prepared by heating the above 7-hydroxy-8-allylflavone in acetone solution with allylbromide and anhydrous potassium carbonate. On removing the solvent and adding water, a crystalline solid was produced which on further crystallisation from alcohol yielded the allyloxy compound as sheaves of thin needles melting at 145–46°. (Found : C, 79·0 ; H, 5·7 ; $C_{21}H_{18}O_3$ requires C, 79·3 ; H, 5·7 per cent.) The yield was 0·9 g. from 1 g. of the hydroxyallylflavone.

6 : *8-Diallyl-7-hydroxyflavone* (*V*).—The above allyl ether (0·4 g.) was heated for 2½ hours at 210–15°. The molten mass did not show any sign of crystallisation even after cooling. On boiling it with alcohol a small amorphous portion remained insoluble. The alcoholic solution was turbid ;

the addition of a drop of aqueous calcium chloride precipitated a small quantity of a deeply coloured high melting solid. Though the solution was now clear, it was coloured and contained some resinous matter which was precipitated by the gradual addition of water. The resin separated out first and was removed. The main product was deposited subsequently. By repeating this process of solution in alcohol and fractional precipitation with water a product melting between 180°–90° was obtained in 75 per cent. yield. Further crystallisation from alcohol and from glacial acetic acid yielded 6 : 8-diallyl-7-hydroxyflavone in the form of thin rectangular plates melting at 196–98°. The compound gave no colour with ferric chloride and was sparingly soluble in cold alkali though solution was effected by warming. On cooling the warm alkaline solution the sparingly soluble potassium salt separated as a pale yellow cotton-wool like mass. (Found : C, 78·9 ; H, 5·8 ; $C_{21}H_{18}O_3$ requires C, 79·3 ; H, 5·7 per cent.)

2-*Methyl*-3-*methoxy*-7-*allyloxychromone* (*VII*)—was obtained in an almost quantitative yield by heating 2-methyl-3-methoxy-7-hydroxychromone[5] in acetone solution with allylbromide and potassium carbonate. After removing the solvent and adding water, the solid product was macerated with cold dilute alkali in order to remove the unchanged hydroxychromone. The allyl ether was easily soluble in alcohol and crystallised out as narrow rectangular plates melting at 94–95°. (Found : C, 67·8 ; H, 6·0 ; $C_{14}H_{14}O_4$ requires C, 68·3 ; H, 5·7 per cent.)

2-*Methyl*-3-*methoxy*-7-*hydroxy*-8-*allylchromone* (*VIII*).—The transformation of the above allyl ether (VII) was effected best by heating it for 2½ hours at 200° as uniformly as possible. The product (8-allyl-7-hydroxy compound) was obtained readily pure in almost quantitative yield. It crystallised from alcohol as colourless rectangular rods melting at 183–84°. (Found : C, 64·0 ; H, 5·9 ; $C_{14}H_{14}O_4$, H_2O requires C, 63·6 ; H, 6·1 per cent.) If a higher temperature (205–15°) was employed considerable resinification took place and the transformation product had to be purified with great difficulty, whereas at a lower temperature (180–200°) the change was only partial and the resulting mixture had to be separated by using aqueous potash. The alkali-soluble portion on recrystallisation from alcohol gave the desired product, whereas the insoluble portion was the unchanged allyl ether.

2–*Methyl*–3–*methoxy*–7–*allyloxy*–8-–*allylchromone* (*IX*).—The above 7-hydroxy-8-allylchromone (VIII) was converted into the allyl ether by the procedure already described. The oily product solidified to an amorphous solid when left in the ice-chest for several hours. It was macerated with cold dilute alkali in order to remove the unchanged hydroxycompound and then extracted with small quantities of petroleum ether. A small highly coloured portion remained undissolved. By slow evaporation of the combined petroleum ether solution the required allyl ether was obtained in a colourless, crystalline form and in 90 per cent. yield. A repetition of the crystallisation from the same solvent yielded the product as rectangular rods melting at 66–68°. (Found: C, 71·2; H, 6·6; $C_{17}H_{18}O_4$ requires C, 71·3 H, 6·3 per cent.)

2-*Methyl*-3-*methoxy*-6 : 8-*diallyl*-7-*hydroxychromone* (*X*).—The preparation of this compound from the above ether (IX) was rather tedious and the yield consequently poor. The Claisen transformation was effected at 200°–05°. The viscous semi-solid product underwent partial solution when macerated for a long time with dilute sodium hydroxide. The brown solution was filtered and acidified. The colourless solid thereby precipitated was contaminated with some resinous matter. It was twice crystallised from alcohol. The first crops of crystals were contaminated with resin and were discarded. A final crystallisation from dilute acetic acid yielded the diallyl-7-hydroxychromone as thin rectangular plates melting at 120–21°. (Found: C, 69·3; H, 6·7; $C_{17}H_{18}O_4, \frac{1}{2} H_2O$ requires C, 69·2; H, 6·4 per cent.) The substance dissolved slowly in dilute sodium hydroxide and gave a pale brown colour with ferric chloride.

7-*Hydroxy*-8-*methylflavone* (*VI*).—An intimate mixture of 3-methyl resacetophenone[4] (0·5 g.), sodium benzoate (1 g.) and benzoic anhydride (3 g.) was heated under reduced pressure for 4 hours in an oil-bath at 190°. The product was then refluxed for half an hour with 10 per cent. alcoholic potash (20 c.c.) in order to effect the hydrolysis of the benzoyloxy group. After removal of the solvent the residue was dissolved in water (30 c.c.) and the clear solution saturated with carbon dioxide. The precipitated hydroxy methylflavone was crystallised from alcohol (charcoal) whereby it was obtained in the form of short colourless rectangular prisms melting at 255–57°. The alcoholic solution did not give any characteristic colour with ferric chloride. (Found: C, 70·8; H, 5·4; $C_{16}H_{12}O_3, H_2O$ requires C, 71·1; H, 5·2 per cent.)

Summary

7-Allyloxyflavone undergoes Claisen transformation to form 8-allyl-7-hydroxyflavone, the constitution of which is established from its synthesis from 3-allyl-resacetophenone. The bond distribution should therefore be as in (I). However 8-alkyl substituted derivatives undergo coupling with diazotised *p*-nitraniline to form dyes and 7-allyloxy-8-allylflavone undergoes further transformation to form 6 : 8-diallyl-7-hydroxy-flavone. Closely analogous results are obtained from 2-methyl-3-methoxy-7-hydroxy-chromone. It is therefore concluded that though the chromones generally

react in form (I) the alternative disposition of the bonds (IV) is not precluded.

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