NUCLEAR REDUCTION IN THE 5-POSITION OF ANTHOXANTHINS

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In continuation of our earlier publication,[1] the nuclear reduction of the 5-hydroxyl group in anthoxanthins is considered in this paper. There are actually more compounds without this hydroxyl group than without the 7-hydroxyl group. The following are the most important among flavones and flavonols: pratol (7-hydroxy 4′-methoxy flavone), fisetin (3 : 7 : 3′ : 4′-tetrahydroxy flavone), auranetin (3 : 6 : 7 : 8 : 4′-pentamethoxy flavone), robinetin (3 : 7 : 3′ : 4′ : 5′-pentahydroxy flavone), kanugin (3 : 3′ : 7-trimethoxy-4′ : 5′-methylenedioxy flavone), karanjin (3-methoxy-7 : 8-furano flavone). It was suggested previously by Seshadri and co-workers[2] that these compounds should arise from more fundamental 5 : 7-dihydroxy compounds by a process of reduction in the 5-position taking place at some stage of their evolution. In the case of auranetin it appeared that this happened to be the last stage.[3] In support of this theory as model laboratory experiments, the conversion of chrysin, apigenin, galangin and quercetin into the corresponding 5-desoxy compounds has been carried out. They are first methylated to produce their partial methyl ethers having only the 5-hydroxyl free. These readily form their tosyl derivatives which undergo smooth reduction with hydrogen in the presence of Raney nickel catalyst at room temperature to yield the 5-desoxy compounds (7-methoxy-, 3 : 7-dimethoxy-, 7 : 4′-dimethoxy- and 3 : 7 : 3′ : 4′-tetramethoxy flavones). The immediate product of reduction is in each case a mixture containing the unchanged compound, but the separation can be easily effected by following the two methods which are given in detail in the experimental part.

Experimental

Chrysin, apigenin, galangin and quercetin were subjected to partial methylation using the required quantity of dimethyl sulphate and excess of anhydrous potassium carbonate in acetone solution.[4]

Tosylation

A solution of each of the above partial methyl ethers (5-hydroxy flavones) (0·01 mole) in dry acetone was refluxed with toluene-*p*-sulphonyl chloride

(0·03 mole; excess) and ignited potassium carbonate (20–25 g.) on a water-bath until the product gave no colour with alcoholic ferric chloride (15 hours). Acetone was then removed and the residue was treated with cold aqueous potash (5%, 100 c.c.), when the tosyl esters separated as a fine powder. They were filtered, washed with water and a few c.c. of warm alcohol and then crystallised from the same solvent. Yield, nearly quantitative. The particulars of these tosyl esters are given below: 5-Tosyloxy tecto-chrysin separated in the form of colourless rhombic tablets melting at 207–8° (Found: C, 65·4; H, 4·2; $C_{23}H_{18}SO_6$ requires C, 65·4; H, 4·2%). 5-Tosyloxy apigenin dimethyl ether formed colourless prismatic needles melting at 185–86° (Found: C, 63·8; H, 4·6; $C_{24}H_{20}SO_7$ requires C, 63·7; H, 4·4%). 5-Tosyloxy-galangin dimethyl ether came out as colourless rectangular plates melting at 164–65° (Found: C, 64·0; H, 4·6; $C_{24}H_{20}SO_7$ requires C, 63·7; H, 4·4%). 5-Tosyloxy-quercetin tetramethyl ether crystallised as colourless small prismatic needles melting at 146–47° (Found: C, 58·8; H, 5·1; $C_{26}H_{24}SO_9$, H_2O requires C, 58·8; H, 4·9%).

Raney nickel Reduction

The tosyl ester (1 g.) was dissolved in alcohol (300–400 c.c.) and Raney nickel, prepared according to the method of Mozingo,[5] (3 teaspoon-ful) added. A stream of purified hydrogen gas was passed for 1 hour through this mixture which was shaken vigorously all the time. The solution was decanted off; the nickel residue decomposed with dilute hydrochloric acid and the resulting mixture extracted with ether (Ether solution E). The alcoholic solution was concentrated to 25 c.c. under diminished pressure and the concentrate was mixed with the residue left after evaporating off the ether solution (E). This alcoholic solution was then refluxed with aqueous potash (1·5 g. in 1 c.c.) for 40 minutes; alcohol was removed in vacuum and the resulting mixture (M) treated in two ways:

(i) Aqueous sodium hydroxide (5%, 50 c.c.) was added and the whole mixture extracted with ether. The ether solution, after being dried over anhydrous sodium sulphate, was concentrated and the residue was crystallised as given below.

(ii) The mixture (M) was acidified and the solid product filtered, washed with water and dried. It was dissolved in absolute alcohol and exactly 1 mole of alcoholic sodium hydroxide (calculated on the tosyl ester taken) was added to it. Alcohol was removed on a water-bath as quickly as possible and the residue left was extracted with benzene leaving behind the sodium salt of the unchanged 5-hydroxy flavones. The benzene solution on evaporation gave the desoxy compounds which could be crystallised as follows.

7-Methoxy flavone

It crystallised from ethyl acetate-petroleum ether and melted at 110°, undepressed with an authentic sample obtained by methylation of 7-hydroxy flavone with dimethyl sulphate using the potassium carbonate-acetone method. Robinson and Turner[6] also reported its m.p. as 110°. It exhibits blue fluorescence in concentrated sulphuric acid.

Pratol-methyl ether (7 : 4′-Dimethoxy flavone)

When crystallised from methyl alcohol it came out as colourless needles melting at 143–44° as reported by Tambor.[7] It also dissolves in concentrated sulphuric acid to give a yellow solution showing blue fluorescence.

3 : 7-*Dimethoxy flavone*

It crystallised from methyl alcohol as colourless rectangular prisms melting at 125–6° alone or when mixed with an authentic sample prepared from synthetic 7-hydroxy-3-methoxy flavone by dry methylation with dimethyl sulphate.

Fisetin tetramethyl ether (3 : 7 : 3′ : 4′-Tetramethoxy flavone)

It was obtained as colourless needles (m.p. 149–50°) when crystallised from ethyl acetate-petroleum ether and recrystallised from ethyl acetate (Allan and Robinson[8] reported the melting point as 150°). The melting point was considerably depressed when mixed with quercetin 3 : 7 : 3′ : 4′-tetramethyl ether, and moreover the product did not give any ferric reaction.

SUMMARY

Partial methyl ethers of chrysin, apigenin, galangin and quercetin have been subjected to nuclear reduction in the 5-position through their tosyloxy compounds. The products are 7-methoxy flavone, pratol methyl ether, 3 : 7-dimethoxy flavone and fisetin tetramethyl ether respectively.

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