SYNTHESIS OF 3,5,4′-TRIHYDROXY-6,7-METHYLENEDIOXYFLAVONE

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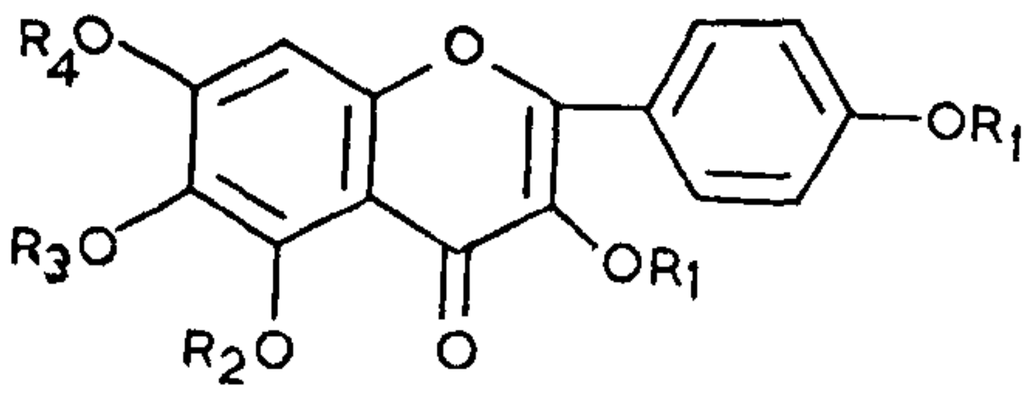
ABSTRACT

On the basis of spectral data, gomphrenol isolated from *Gomphrena globosa* and considered to be 3,5,4′-trihydroxy-6, 7-methylenedioxyflavone (I) has been now synthesised.

GOMPHRENOL isolated[1] from the leaves of *Gomphrena globosa* was considered as 3,5,4′-trihydroxy-6, 7-methylenedioxyflavone (I) based on spectral data but no synthetic support was provided. This paper reports the synthesis of I by methylenation of 3,5,6,7,4′-pentahydroxyflavone[2] (II). In order to rule out the possibility of the formation of isomeric 3,7,4′-trihydroxy-5,6-methylenedioxyflavone (III) during the methylenation reaction, II was first selectively methylated[3] to obtain 3,6,7,4′-tetrahydroxy-5-methoxyflavone (IV). On methylenation, IV yielded a compound which was characterised as 3,4′-dihydroxy-5-methoxy-6,7-methylenedioxyflavone (V) based on the following considerations. The methylenation product (*a*) analysed for $C_{17}H_{12}O_7$, (*b*) gave positive Labat test[4,5] for methylenedioxy group, (*c*) did not respond to Asahina–Inubuse test[6,7] showing a hydroxyl at C_3, (*d*) on alkali degradation gave *p*-hydroxybenzoic acid indicating another hydroxyl at C_4', (*e*) did not respond to Gibbs test[8,9] showing the absence of a free hydroxyl having an unsubstituted para position, and (*f*) on complete methylation yielded 3,5,4′-trimethoxy-6,7-methylenedioxyflavone (VI).

Selective demethylation[10,11] of C_5-methoxyl in V in the presence of the free hydroxyl at C_3 using aluminium chloride and nitrobenzene gave a compound which was characterised as 3,5,4′-trihydroxy-6, 7-methylenedioxyflavone (I) as it, unlike V, gave positive Gibbs test[8,9] showing the demethylation of C_5-methoxyl. However, during the reaction this reagent brought about demethylenation as well, thereby yielding 3,5,6,7,4′-pentahydroxyflavone (II) besides the required I. Further the direct methylenation[12] of II also gave I but the yields could not be improved. I and its trimethyl ether (VI) obtained by the direct methylation of I agreed with the corresponding compounds obtained by the first method.

The synthetic flavone could not be directly compared with the natural sample as it was not available. However, the data for I and its derivatives appear to agree with those reported[1] for the natural sample.



I, $R_1 = R_2 = H$; $R_3R_4 = -CH_2-$
II, $R_1 = R_2 = R_3 = R_4 = H$
III, $R_1 = R_4 = H$; $R_2R_3 = -CH_2-$
IV, $R_1 = R_3 = R_4 = H$; $R_2 = CH_3$
V, $R_1 = H$; $R_2 = CH_3 = R_3R_4 = -CH_2-$
VI, $R_1 = R_2 = CH_3$; $R_3R_4 = -CH_2-$

EXPERIMENTAL

3,4′-*Dihydroxy-5-methoxy-6, 7-methylenedioxyflavone* (*V*)

3,6,7,4′-Tetrahydroxy-5-methoxyflavone (IV) (3·0 g) obtained from 3,5,6,7,4′-pentahydroxyflavone (II), methylene iodide (0·9 ml), potassium carbonate (9 g) and DMF–acetone (1 : 3; 300 ml) were refluxed for 50 hr. The reaction mixture was worked up as usual and methylenation product was subjected to steam distillation to remove unreacted methylene iodide. V thus obtained crystallised from methanol as yellowish prisms (*0·45 g*), m.p. 273–74°, analysed for $C_{17}H_{12}O_7$, gave positive Labat test, yielded *p*-hydroxybenzoic acid on alkali degradation and did not give Asahina–Inubuse or Gibbs test.

3,5,4′-*Trimethoxy-6,7-methylenedioxyflavone* (*VI*)

V (0·1 g), dimethyl sulphate (0·7 ml), potassium carbonate (0·4 g) and acetone (25 ml) were refluxed for 10 hr. The reaction mixture was worked up in the usual manner. The methylation product (VI) thus obtained crystallised from ethanol as colourless micro-prisms (0·1 g), m.p. 159–60°, analysed for $C_{19}H_{16}O_7$ and gave Asahina–Inubuse test.

3,5,4′-*Trihydroxy-6,7-methylenedioxyflavone* (*I*)

V (0·15 g) in nitrobenzene (15 ml) was heated with anhydrous aluminium chloride (0·15 g) at 50° for

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30 min. The contents were treated with petroleum ether till nitrobenzene was completely eliminated and the residue was decomposed by warming with aqueous sulphuric acid (4%; 30 ml) on a steam-bath for 15 min. The demethylation product was extracted with ethyl acetate, then purified and isolated by preparative TLC using silica gel as an adsorbent and butanol:acetic acid :water (4 : 1 : 5) as the solvent system. I thus obtained crystallised from methanol as yellowish cubes, m.p. 295–96°, analysed for $C_{16}H_{10}O_7$ and gave positive Gibbs and Labat tests. UV (λ_{max}, MeOH): 260, 270, 350 nm; + $AlCl_3$: 280, 410 nm; + $AlCl_3$ + HCl : 270, 385, 410 nm.

Methylenation of 3,5,6,7,4'-*pentahydroxyflavone* (*II*)

3,5,6,7,4'-Pentahydroxyflavone (II) (1·0 g), methylene iodide (0·3 ml), potassium carbonate (3 g) and DMF–acetone (1 : 3; 100 ml) were refluxed for 50 hr and the progress of the reaction was monitored by TLC. The methylenation product I when worked up as described earlier, gave I which crystallised from methanol as yellowish cubes (0·15 g), m.p. 295-96°. I thus obtained was methylated with dimethyl sulphate and potassium carbonate in acetone to obtain its trimethyl ether (VI).

(I) and its trimethyl ether (VI) on direct comparison were found to be identical with the corresponding compounds obtained by the earlier method.

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SOME BIOLOGICAL, HAEMATOLOGICAL AND HISTOLOGICAL OBSERVATIONS IN MOLYBDENOTIC RATS

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ABSTRACT

Toxic effects of molybdenum have been experimentally established in rats. Physical examination of molybdenotic rats revealed a change in the colour of fur and retina. A rapid fall in the body weight and skeletal growth of molybdenotic rats showed its adverse effects on growth. However, the RBC, percentage of haemoglobin and haematocrit have been found elvated after molybdenum treatment. Histopathological studies on liver and kidney reflect the injurious effects.

INTRODUCTION

MOLYBDENUM (Mo) present in low concentrations in all tissues and fluids of all species plays an essential role in the animal and plant nutrition[1]. The industrial uses of molybdenum are well-known[2]. In molybdenotic rats, deficient lactation, male sterility and testicular degeneration have been observed[3]. In young rabbits molybdenotic syndrome is characterized by alopecia, dermatosis and severe anemia with a deformity in front legs[4]. Molybdenum is not acutely toxic in low concentrations[5]. A biological approach has now been made with histological and haematological parameters to study the conditions under which molybdenum participates in pathological processes in rats.