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ORIENTATION IN ISOFLAVONES

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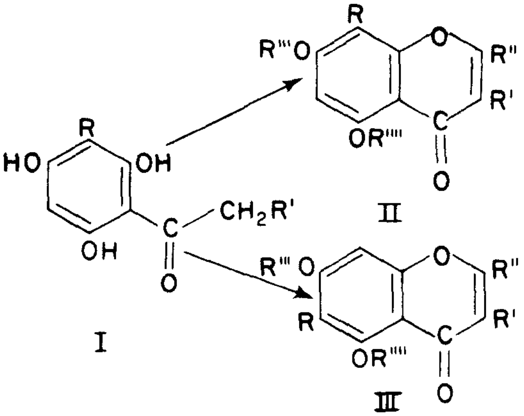
IN our earlier communication[1] it has been observed that the deoxybenzoin (I; R = Me, R' = C_6H_5) on submitting to ethoxalylation process gives a mixture of 5:7-dihydroxy-8-methyl- and 5:7-dihydroxy-6-methyl isoflavones (II and III; R = Me, R' = C_6H_5, R'' = R''' = R'''' = H) resulting from the cyclization involving 2- and 6-hydroxyl groups respectively. An explanation for the dual course of cyclization has also been advanced.



After completing this study we came across the work of Mehta and Seshadri[2] where they have reported that the deoxybenzoin of a similar type

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[1] M.O. Farooq, W. Rahman and Kh. Takrimullah Nasim, J.Org.Chem. In press (1961).

[2] A.C. Mehta and T.R. Seshadri, J.Chem.Soc. 3823 (1954).

(I; R = Me, R' = p-MeO.C_6H_4) on ethoxalylation yields finally only one isomer, 5:7-dihydroxy-4'-methoxy-6-methyl isoflavone (III; R = Me, R' = p-MeO.C_6H_4, R'' = R''' = R'''' = H). According to our explanation[1] as to the course of cyclization of the deoxybenzoins of the above type with ethoxalyl chloride, the formation of one isomer and that too of 5:6:7-orientation appeared to be inconceivable. The reinvestigation of ethoxalyation of 2:4:6-trihydroxy-3-methyl-4'-methoxydeoxybenzoin (I; R = Me, R' = p-MeO.C_6H_4) appeared of interest and therefore the present work was undertaken.

The deoxybenzoin (I; R = Me, R' = p-MeO.C_6H_4) on ethoxalylation gave a product m.p. 176-78°. This product was assigned the structure of ethyl 5:7-dihydroxy-4'-methoxy-6-methyl isoflavone-2-carboxylate (III; R = Me, R' = p-MeO.C_6H_4, R'' = CO_2Et, R''' = R'''' = H) by Mehta and Seshadri[2]. The carbethoxy isoflavone (III; R = Me, R' = p-MeO.C_6H_4, R'' = CO_2Et, R''' = R'''' = H) on hydrolysis yielded the corresponding carboxyisoflavone (III; R = Me, R' = p-MeO.C_6H_4, R'' = CO_2H, R''' = R'''' = H). The melting point of the acid is not, however, reported. The crude carboxyisoflavone on decarboxylation at 275° gave an isoflavone m.p. 210-212°. It was characterized by them as 5:7-dihydroxy-4'-methoxy-6-methyl isoflavone (III; R = Me, R' = p-MeO.C_6H_4, R'' = R''' = R'''' = H) by partial methylation to 5-hydroxy-7:4'-dimethoxy-6-methyl isoflavone (III; R = R''' = Me, R' = p-MeO.C_6H_4, R'' = R'''' = H). The latter showed no depression in melting point on admixture with the nuclear methylation product of genistein.[3]

The product m.p. 176-178° (erroneously assigned the structure of ethyl 5:7-dihydroxy-4'-methoxy-6-methyl isoflavone-2-carboxylate by Mehta and

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[3] W. Baker and R. Robinson, J.Chem.Soc. 2713 (1926).

Seshadri[2]) was found by the present authors, to be a mixture of two isomers very difficult to separate. It was, however, resolved by a careful fractional crystallization from benzene-methanol into two distinct products melting at 199-201° and 201-203°. The mixed melting point of the two isomers was found to be 176-178° as reported by the previous workers[2] for one component.

The carbethoxyisoflavone melting at 199-201° on usual hydrolysis and decarboxylation gave the corresponding carboxy- and then hydroxy-isoflavone m.p.'s 280-281° and 235-236° respectively. The latter was characterized as 5:7-dihydroxy-4'-methoxy-8-methyl isoflavone (II; R = Me, R' = p-MeO.C_6H_4, R'' = R''' = R'''' = H) by its complete methylation to 5:7:4'-trimethoxy-8-methylisoflavone (II; R = R''' = R'''' = Me, R' = p-MeO.C_6H_4, R'' = H) m.p.[4] and mixed m.p. 180°.

The carbethoxyisoflavone m.p. 201-203° (III; R = Me, R' = p-MeO.C_6H_4, R'' = CO_2Et, R''' = R'''' = H) on similar treatment as above yielded the corresponding carboxyisoflavone m.p. 288-91° (III; R = Me, R' = p-MeO.C_6H_4, R'' = CO_2H, R''' = R'''' = H) and then an isoflavone. It was characterized as 5:7-dihydroxy-4'-methoxy-6-methyl isoflavone m.p. 260-263° (III; R = Me, R' = p-MeO.C_6H_4, R'' = R''' = R'''' = H) by the preparation of its complete methyl ether m.p. 169°. It showed no depression in melting point on admixture with an authentic sample[5,6] of 5:7:4'-trimethoxy-6-methyl isoflavone (III; R = R''' = R'''' = Me, R' = p-MeO.C_6H_4, R'' = H).

The ethoxalylation of 2:4:6-trihydroxy-3-methyl-4'-methoxy deoxybenzoin (I; R = Me, R' = p-MeO.C_6H_4) resulting in the formation of isomeric isoflavones of 5:6:7- and 5:7:8-orientations lends support to our previous

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[4] W.B. Whalley, J.Amer.Chem.Soc. 75, 1059 (1953).

[5] W.B. Whalley, J.Chem.Soc. 3366 (1953).

[6] W.B. Whalley, Chem.&Ind. 277 (1953).

findings[1] and is not in agreement with the findings of Mehta and Seshadri [2]. Further confirmation to our findings has been furnished by the investigation of ethoxalylation of 2:4:6-trihydroxy-3-methyl-2'-methoxy deoxybenzoin (I; R = Me, R' = o-MeO.C_6H_4) where again in isomeric mixture of 5:6:7- and 5:7:8-isoflavones has been obtained.

The full details of this work will appear elsewhere.