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MICROBIOLOGICAL TRANSFORMATION OF FLAVANONE

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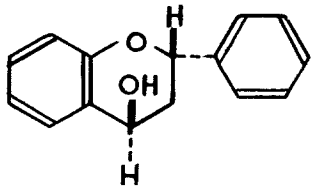
The ability of microorganisms to bring about oxidations, reductions, hydroxylations etc. renders a study of the microbial transformation of flavonoids an attractive possibility. Using flavanone as a model substrate, its microbiological transformation has been studied employing Gibberella fugikuroi as an organism.

On incubation with G. fugikuroi, flavanone undergoes various changes and several products have been isolated. A neutral product (compound A) was obtained from the ferment, which was purified by column chromatography on silica gel and repeated crystallisations. The present communication deals with the characterisation of compound A.

Compound A was obtained as colourless crystalline needles from benzene-petroleum ether (m.p. 127°; $[\alpha]_D^{25°}$ - 27.3°; c, 1.47). It analysed for the molecular formula $C_{15}H_{14}O_2$. IR bands at 2.9, 6.19, 6.3, 13.15 and 8.02 μ, suggest the presence of hydroxyl group, aromatic system, and heterocyclic ether linkage. It exhibited UV maxima at 277 and 284 mμ (log ϵ , 3.35 and 3.31) indicating a flavan structure for the compound[1]. The disappearance of the carbonyl group during fermentation and the emergence of a hydroxyl group, the neutral nature of the compound and the characteristic colour reactions[2] strongly suggest that the product should be a flavan-4-ol. The NMR spectrum (discussed below) further supports the flavan-4-ol structure and throws light on its stereochemistry also.

The low field signals (2.5 - 3.25 τ) in the NMR spectrum of compound A are attributed to the protons of the two aromatic rings. The protons at 3-position (H_{3a} and H_{3e}) appear as multiplet due to geminal and vicinal couplings at around 7.7 τ. The aliphatic protons of the heterocyclic ring form an ABMX type system in which M & X approximate to X portion of ABX system as already shown by Bolger et. al[3] for flavan-4-ols. The C-2 proton appears as a quartet (4.7 τ, $J_{2,3a} + J_{2,3e}$ = 15 cps), while the C-4 proton appears as a triplet (5.15 τ, $J_{4,3a} + J_{4,3e}$ = 6 cps). The coupling constants suggest that H-2 and H-4 are axial and quasi equitorial respectively and have trans relationship[3,4]. The compound A should therefore correspond to (-) flavan-4α-ol (I).

In connection with the above work, flavan-4β-ol (II) has also been prepared by the reduction of flavanone with $NaBH_4$[5] or by catalytic method[7]. In this case the signals due to H-2 and H-4 merge together. Although it is possible to locate the two quartets due to these protons (4.83 and 4.9 τ), it is difficult to designate as to which of the two quartets represents H-2 and H-4. However, coupling constants favour the cis structure II for flavan-4β-ol[3,4] ($J_{2 \text{ or } 4,3a} + J_{2 \text{ or } 4,3e}$ = 14 cps; $J_{4 \text{ or } 2,3a} + J_{4 \text{ or } 2,3e}$ = 17 cps). Acetylation of the hydroxyl group shows the expected segregation of the two quartets (H-2, 4.76 τ, $J_{2,3a} + J_{2,3e}$ = 14 cps; H-4, 3.76 τ, $J_{4,3a} + J_{4,3b}$ = 17 cps). The cis relationship of H-2 and H-4 is obvious from the above data.



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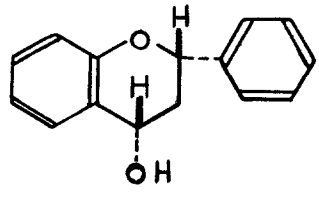

II

The hitherto reported α-isomer of flavan-4-ol was prepared by Al/Hg reduction[6] (m.p. 117-18°, Lit. m.p. 119°) and also by oximation method[7] (m.p. 116-17°, Lit. m.p. 116-117°). The NMR spectra of these products are rather complex. In addition to the expected triplet of H-4 and a quartet of H-2, a number of other peaks are discernable. A careful study of the minor peaks indicate that the samples obtained by the above two methods contain small

proportions of β-isomer also and the compounds reported earlier may in fact be mixtures. TLC examination of the products supports the above view.

The structural study of other products resulting from the microbiological transformation of flavanone using G. fugikuroi will be reported elsewhere.

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