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Abstract

Full Text

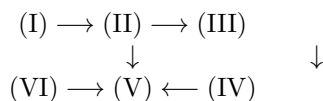
Chemistry

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A New Synthesis of 3-Hydroxyflavone, Flavonol

(Presented by Academician M. I. Kabachnik on 15 III 1963)

Flavonol (V), which is the structural basis of quercetin, its 3-rutinoside rutin, and other bioflavonoids, was synthesized earlier in our laboratory (^{1,2}) from *o*-benzyloxyphenyl- ω -nitrostyryl ketone (I).



On treatment with concentrated hydrochloric acid in glacial acetic acid, simultaneous debenylation of (I) and ring closure occur. The resulting 3-nitroflavanone (II) was converted by reaction with diazomethane into the methyl ester of nitronic acid (III), which disproportionates on moderate heating to the oxime of 3-ketoflavanone (IV) and formaldehyde. Heating (IV) in dilute acetic acid in the presence of pyruvic acid gave flavonol (V).

An alternative oxidative route is known for the conversion of *o*-hydroxyphenylstyryl ketones (chalcones) into flavonols by the Algar–Flynn–Oyamada reaction (^{3–5}). Under the conditions of this reaction, on treatment with hydrogen peroxide in an alkaline medium, we isolated nitroketone epoxide (VI) from I. Figure 1 shows the light-absorption spectra in the ultraviolet region for benzyloxychalcone (I) and epoxide (VI). The shape of the curve for (I) closely resembles the spectra of trans-chalcones (⁶), while that for VI resembles the absorption curve of 2-benzyloxychalcone epoxide (⁷).

The difference in the mechanism of cyclization of I and VI under the same conditions is striking. Under the action of concentrated hydrochloric acid in glacial acetic acid on VI, debenylation and cyclization readily occur to give flavonol V, with spontaneous elimination of the nitro group.

The debenylation and cyclization reaction can be described as a single process beginning with nucleophilic S_N2 substitution at the methylene group of the benzyl residue (⁷) of the protonated epoxide molecule (VII):



Fig. 1

Figure 1: Fig. 1

Fig. 2

Figure 2: Fig. 2

The hypothetical intermediate compound (VIII) that is formed should be unstable in a polar solvent upon heating. In the course of cleavage of the epoxide grouping and formation of the flavone ring, the hydroxyl at the α -carbon atom is located in the cis-position to the hydrogen of the β -carbon atom. This may be the cause of favorable steric prerequisites for trans-elimination of the elements of nitrous acid from (VIII) and the formation of flavonol.

Experimental Part

o-Benzoyloxyphenyl- ω -nitrostyryl ketone epoxide (VI). To a solution of 2.05 g of o-benzoyloxyphenyl- ω -nitrostyryl ketone (I) in 140 ml of acetone at 0° is added a mixture, previously cooled to 0°, of 3.5 ml of 2 N sodium hydroxide solution, 4.5 ml of 15% hydrogen peroxide, and 7 ml of methyl alcohol. The reaction mass is stirred for 30 min at 0°, diluted with 100 ml of chilled water, and left to stand for 4 h at $-(2-1)^\circ$.

The precipitate that separates is filtered off and washed with an acetone–water mixture 1:1 (2 portions of 10 ml). Yield 1.70 g (77.62%). After crystallization from alcohol, colorless lustrous needles are obtained. M.p. 118–119°, λ_{\max} 260 m μ and 327 m μ , lg ϵ 4.12 and 3.71, respectively.

Found, %: C 70.30; 70.44; H 4.71; 4.52; N 3.76; 3.98
C₂₂H₁₇NO₅. Calculated, %: C 70.40; H 4.53; N 3.73

Fig. 1. Absorption spectrum in the ultraviolet region in 95% alcohol: 1–o-benzoyloxyphenyl- ω -nitrostyryl ketone (I), 2–o-benzoyloxyphenyl- ω -nitrostyryl ketone epoxide (VI)

3-Hydroxyflavone, flavonol (V). A mixture of 0.82 g of o-benzoyloxyphenyl- ω -nitrostyryl ketone epoxide (VI), 16 ml of glacial acetic acid, and 1.6 ml of conc. HCl is heated on a boiling water bath for 15 min, cooled to 15–18°, 20 ml of water is added, and the mixture is left to stand for 12 h at 3–5°. The separated small yellow crystals are isolated, washed with 50% alcohol, and recrystallized from alcohol. Light-yellow needles are obtained.

Fig. 2. Absorption spectrum in the infrared region of o-benzoyloxyphenyl- ω -nitrostyryl ketone epoxide (VI) (KBr pellet)

Yield 0.31 g (62%). Mp 167–168°. A mixed-melting-point test of the obtained substance (mp 167–168°) with a known sample of 3-hydroxyflavone (mp 168–

169°) gives no depression (mp 166.5-167.5°). λ_{\max} 239, 305, and 347 $m\mu$, $\lg \varepsilon$ 4.29, 4.12, and 4.27, respectively.

Found, %: C 75.58; 75.49; H 4.31; 4.36
C₁₅H₁₀O₃. Calculated, %: C 75.63; H 4.37

The elemental analyses were carried out under the supervision of V. M. Rakova. The IR spectra were obtained under the supervision of L. V. Luk' yanova.

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REFERENCES CITED

1. G. I. Samokhvalov, M. K. Shakhova et al., ZhOKh, **31**, 1147 (1961).
2. M. K. Shakhova, M. I. Budagyants et al., ZhOKh, **32**, 2832 (1962).
3. J. Algar, J. Flynn, Proc. Roy. Irish Acad., **42B**, 1 (1934); Chem. Abstr., **29**, 161 (1935).
4. T. Oyamada, J. Chem. Soc. Japan, **55**, 1256 (1934); Bull. Chem. Soc. Japan, **10**, 182 (1935); Chem. Abstr., **29**, 4358, 5112 (1935).
5. T. S. Wheeler, Rec. Chem. Progr., **18**, 133 (1957).
6. W. B. Black, R. Lutz, J. Am. Chem. Soc., **75**, 5990 (1953).
7. R. Bognár, J. Stefanovsky, Tetrahedron, **18**, 143 (1962).

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