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Studies on Components of Evodiae Fructus. III.[1] Structure of Rutaevin and Dehydrolimonin

YOSHIO HIROSE

Faculty of Pharmaceutical Sciences, Kumamoto University[2]

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It has been reported in the previous paper[1] that rutaevin (I), mp 300° (decomp.), was reexamined to be found in the fruits of *Evodia rutaecarpa* HOOKER fill. et THOMSON, Rutaceae. The molecular formula, $C_{26}H_{30}O_9$, had been first put forward for I by Fujita.[3]

The present paper deals with the structures of I and dehydrolimonin (II),[4] the latter of which was obtained by oxidation of limonin (III) with iodine and sodium acetate. Rutaevin (I) is occurring along with III, $C_{26}H_{30}O_8$,[5] and evodol (IV), $C_{26}H_{28}O_9$,[6] as non-N bitter principles in the sume plant.

Treatment of I with aqueous sodium hydroxide afforded a diosphenol which was proved to be identical with IV by mixed melting point determination and infared (IR) spectrum comparison. It suggests that the mild alkaline reaction caused air-oxidation between C-5 and C-6 of I to yield IV. I was also converted to IV by the oxidation with active manganese dioxide. On account of these findings I has been formulated as 6-hydroxylimonin. In the nuclear magnetic resonance (NMR) spectrum of I, both the signals of H-6 at 4.725 ppm and H-5 at 3.325 ppm show the almost singlet patterns. The observation strongly suggested that H-5 of III was axial.[5] At this point, since III was converted to IV by autoxidation[5] and I to IV by air-oxidation, it would be very probable that H-5 of I is also axial. Consequently H-6 of I must be equatorial, and the structure of rutaevin (I) has been represented by the formula of 6-β-hydroxylimonin (I).

It had been reported[4] that treatment of III with iodine, sodium acetate and potassium iodide as a catalyzer afforded II, $C_{26}H_{28}O_8$. The IR spectrum of II shows the bands at 1688 and 1640 cm^{-1} indicating the keto carbonyl group and the conjugated double bond. The signal at 6.28 ppm (1H, singlet) must be due to H-6 of the newly produced double bond between C-5 and C-6 of III.

On the basis of the above findings dehydrolimonin has been presented by the formula II.

Experimental[7]

Hydrolysis of Rutaevin (I)——I (250 mg) was heated on a water bath 2 or 5% NaOH solution (100 ml) to be dissolved for 30 min. After cooling, the reaction mixture was acidified with dil.HCl. The separated precipitate was recrystallized from aceton to colorless needles, mp 282° (decomp.). This substance was

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1) Part II: Y. Hirose, K. Kondo, H. Arita, and A. Fujita, *Syōyakugaku Zasshi* (Japan. *J. Phamacog.*), **21**, 126 (1967).

2) Location: *5-1, Ōe-hon-machi, Kumamoto.*

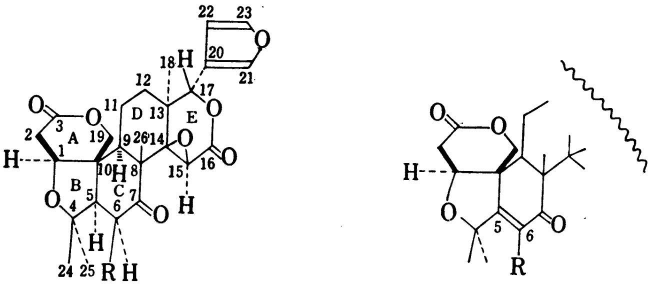
3) A. Fujita, *Yakugaku Zasshi*, **69**, 72 (1949).

4) A. Fujita and Y. Hirose, *Yakugaku Zasshi*, **74**, 365 (1954).

5) D.H.R. Barton, S.K. Pradhan, S. Sternhell, and J.E. Templeton, *J. Chem. Soc.*, **1961**, 255; S. Arnott, A.W. Davie and J.M. Robertson, *ibid.*, **1961**, 4183.

6) Y. Hirose, *Chem. Pharm. Bull.* (Tokyo), **11**, 535 (1963).

7) The NMR spectra were measured on a LNM C-100 (100 Mc) spectrometer attached with a magnetic resonance accumulator, JNM-Ra of Japan Electron Optics Lab. Co., a Model H-6013 and a Model R-20 NMR spectrometer of Hitachi Ltd. in CF_3COOH, $CDCl_3$ and pyridine-d_5. The chemical shifts and the coupling constants were recorded respectively in δ and cps value using tetramethylsilane (TMS) as the internal reference. Limonin derivatives were not sufficiently soluble in $CDCl_3$, DMSO-d_6, C_6D_6 and acetone-d_6 to measure NMR spectra.



I : R=OH
III: R=H5)

II: R=H
IV: R=OH5,6)

Chart 1

identified with IV by mixed mp determination and IR comparison. IR cm^{-1} (KBr): 3420, 3340—3280 (ν_{O-H}), 1742 ($\nu_{C=O}$,δ-lactone), 1692 ($\nu_{C=O}$, keto carbonyl group), 1669 (diosphnol), 3170, 1503, 875 ($\nu_{C=H}$, $\nu_{C=C}$, δc-H of furan). *Anal.* Calcd. for $C_{26}H_{28}O_9$: C, 64.45; H, 5.83. Found: C, 64.56; H, 5.90.

Oxidation of Rutaevin (I)——I (250 mg) in $CHCl_3$(300 ml) was refluxed with active MnO_2 (2.5 g) for 70 hr. The filtrate was concentrated. The obtained precipitate was recrystallized from acetone to colorless needles, mp 282° (decomp.). This substance was identical with IV.

Rutaevin (I)——Prepared by the method of the literature.1) mp 300° (decomp.). *Rf* 0.4 (TLC, $CHCl_3$: $CH_3COOC_2H_5$=1:1 (solvent system), C_2H_5OH solution of *p*-N-dimethylaminobenzaldehyde, and conc.HCl (coloring reagents). Molecular weight 486 (Mass Spectrum *m/e*). *Anal.* Calcd. for $C_{26}H_{30}O_9$: C, 64.18; H, 6.22. Found: C, 64.34; H, 6.23. IR cm^{-1} (KBr): 3124, 1594 and 1504, 867 (ν_{C-H}, $\nu_{C=C}$, δ_{C-H} of furan), 3520 (ν_{C-H}), 1770 ($\nu_{C=O}$, δ-lactone), 1743 ($\nu_{C=O}$, δ-lactone), 1711 ($\nu_{C=O}$, keto carbonyl group). NMR (100 Mc, saturated solution in CF_3COOH): 7.49 (2H, singlet (containing a little coupling constant (*J*)), H-21 and H-23), 6.425 (1H, singlet (containing a little *J*), H-22), 5.725 (1H, singlet, H-17), 4.725 (2H, singlet overlapping with triplet, $J_{H-6e, H-5a}$=*ca.* 0, H-6*e*, and $J_{H-1e, H-2a}$8)=3, $J_{H-1e, H-2b}$8)=3, H-1*e*), 4.62 (1H, doublet, *J*=12, H-19a8)), 4.47 (1H, doublet, *J*=12, H-19b8)), 4.29 (1H, singlet, H-15), 3.325 (1H, quartet, *J*=*ca.* 0, H-5*a*), 3.225 (1H, quartet, *J*=15.5 and 3, H-2a), 3.03 (1H, quartet, *J*=15.5 and 3, H-2b), 1.54 (3H, singlet, CH_3), 1.47 (3H, singlet, CH_3), 1.42 (3H, singlet, CH_3), 0.84 (3H, singlet, CH_3).

Dehydrolimonin (III)——Prepared by the method of the literature.4) mp 312° (decomp.). IR cm^{-1} (KBr): 3162, 1590 and 1504, 874 (ν_{C-H}, $\nu_{C=C}$, δ_{C-H} of furan), 1750 and 1731 ($\nu_{C=O}$, δ-lactone), 1687 ($\nu_{C=O}$, keto carbonyl group), 1638 ($\nu_{C=C}$). NMR (100Mc, saturated solution in CF_3COOH): 7.44 (2H, singlet, H-21 and H-23), 6.39 (1H, singlet, H-22), 6.28 (1H, singlet, H-6), 5.67 (1H, singlet, H-17), 4.99 (1H, doublet, *J*=15, H-19a), 4.19 (1H, doublet, *J*=15, H-19b), 4.60 (1H, triplet, *J*=3 and 3, H-1*e*), 4.26 (1H, singlet, H-15), 3.375 (1H, quartet, *J*=18 and 3,H-2a), 3.125 (1H, quartet, *J*=18 and 3, H-2b), 2.93 (1H, quartet, *J*=8 and 2, H-9), 1.56 (6H, singlet, $CH_3\times 2$), 1.14 (6H, singlet, $CH_3\times 2$).

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8) The each two protons of H-2 and H-19 were affixed with the optional marks of a and b.