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PHOTOOXYGENATION OF ROTENONE

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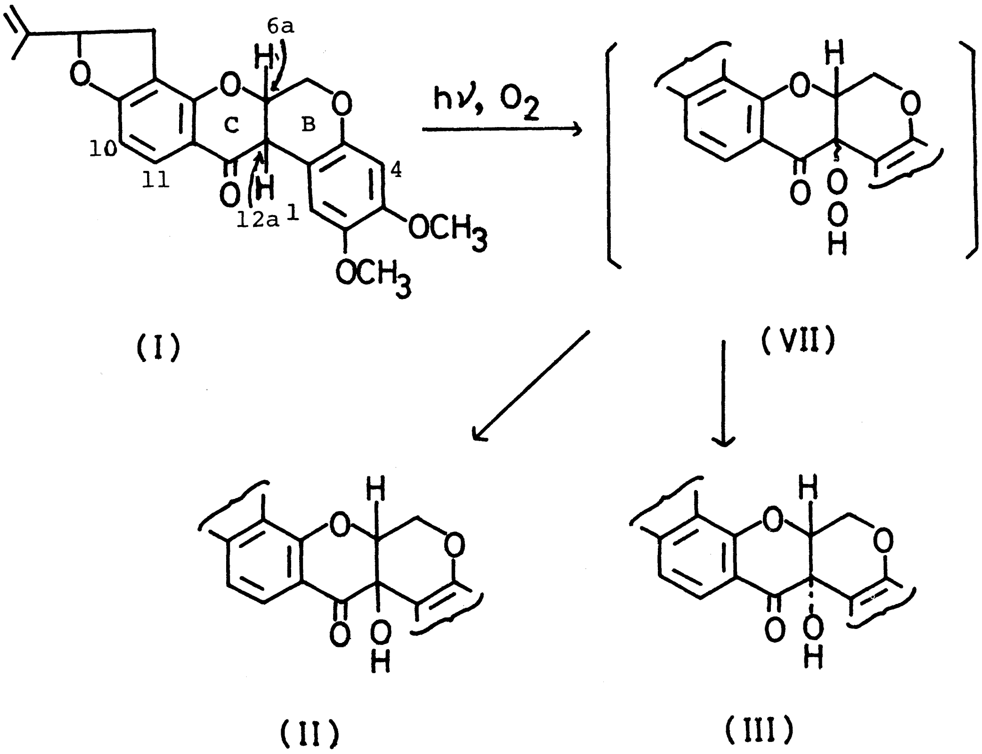
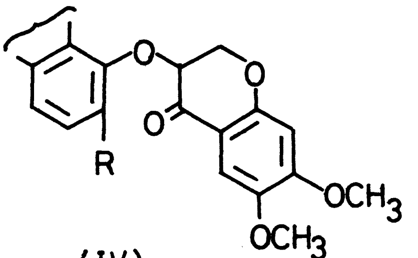
In the photooxygenation of rotenone(I) in pyridine solution, two isomers of rotenolones, $6a\beta,12a\beta$- and $6a\beta,12a\alpha$-rotenolones (II and III), were obtained besides dehydrorotenone(V) and rotenonone(VI). As one of acidic products, a keto-acid(IVa) was also isolated.

It has been known that four diastereoisomers of rotenolones can be made by aerating an alkaline solution of naturally occurring (-)-rotenone,together with dehydrorotenone and rotenonone.[1,2] The structures and the stereochemistry for these isomers of rotenolones on the B/C ring junction have been studied in detail by Crombie and Godin.[2] In the works on photodegradation of rotenoids, Suginome, Yomezawa, and Masamune[3a] and the present authors[3b] reported the photooxidation of dehydrorotenone, and Cheng, Yamamoto, and Casida demonstrated in recent paper[4] that irradiation of rotenone in oxygenated methanol solution with ultraviolet light affords O-demethyl rotenone, $6a_\beta,12a_\beta$-rotenolone, dehydrorotenone,rotenonone and three acids.

Present communication[5] mainly deals with rotenolones and an acidic product which were produced by the photooxygenation at position 12a of (-)-rotenone(I) in pyridine solution. From the chromatographic and spectral data, rotenolones obtained here were assigned to be $6a_\beta,12a_\beta$-rotenolone(II) as a cis isomer and $6a_\beta,12a_\alpha$-rotenolone(III) as a trans one, in contrast to the case of the oxygenation in alkaline solution. Keto-acid, which was isolated from the acidic fraction, was assigned to be the structure IVa.

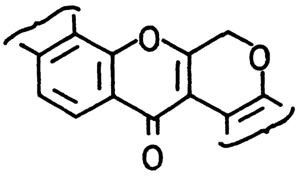
In a typical run, a pyridine solution(150ml) of (-)-rotenone(I,3.0g) in a Pyrex flask was irradiated with a 400W high pressure mercury lamp under bubbling oxygen for 3hr at 45°C. The amount of carbon dioxide(25mg) evoluted was assayed by converting it to barium carbonate. Only a fraction of the reaction mixture was subjected to the determination of dehydrorotenone(V,5.3%) and rotenonone(VI, 1.2%) by isotope dilution method using the corresponding ^{14}C-labeled compounds.[6] Subsequently, after removal of the solvent from the remaining reaction mixture, the residue was separated into neutral, phenolic and acidic fractions in the usual way. From the neutral fraction, unchanged rotenone(0.87g) was removed as a carbon



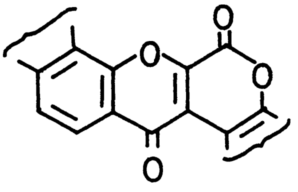


(IV)

a R= COOH
b R= COOMe
c R= CHO



(V)



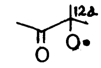
(VI)

tetrachloride solvate, and then chromatographic separation of the residue was carried out on a column of silica gel with benzene-chloroform eluents and two compounds were isolated

One of the two compounds(16%), which was precipitated as an amorphous solid by the addition of cyclohexane to the ether solution, presented $[\alpha]_D$-167°(c=0.17, $CHCl_3$) and M^+410(mass spectroscopy). The compound was identified to be II by comparing the spectral data and the thin layer chromatograms with those of 6aβ,12aβ-rotenolone which was prepared by the oxidation of (-)-rotenone(I) with potassium dichromate in acetic acid.$^{2)}$ Further, since 6aα,12aα- and 6aβ,12aβ-isomer of rotenolones have retention times of 8.8min and 10.4min respectively, in gas chromatographic-mass spectrometric analysis(OV-17, 0.5%, 1m, 262°C, He gas 30ml/min), the compound(II) was confirmed to be 6aβ,12aβ-rotenolone from its retention time, but 6aα,12aα-isomer which is inverted at position 6a and 12a of (-)-rotenone could not be detected in products of the present oxygenation.[7)] Therefore, it was considered that the inversion at position 6a of rotenone did not occur in the present condition.

Another compound(6%) was crystallized as white prisms from chloroform-ethanol, mp 202-203°(decomp), $[\alpha]_D^{18}$+334°(c=0.3,$CHCl_3$), M^+410, $C_{23}H_{22}O_7$(requires: C67.31; H5.40. found: C67.47; H5.34%); UV(EtOH)λmax 236(ε15400) and 293nm(18000); IR($CHCl_3$) 3585, 3472 and 1690(carbonyl)cm^{-1}; NMR($CDCl_3$), δppm 1.80(s,$-CH_3$), 3.83 3.87(s,$-2OCH_3$), 6.37(s,H_4), 7.77(s,H_1), 6.55(d,H_{10}, J=8.7Hz) and 7.81(d,H_{11}, J=8.7Hz). Ir and nmr spectra of the compound are similar to those of the mixture[2)] of trans-rotenolones and especially, the absorption value of the carbonyl and the magnitude of the chemical shift for hydrogen atoms at the position 1 support the structure of trans-rotenolone.[2,8)] On other hand, when (-)-rotenone was oxidized with potassium dichromate where no inversion occurs at position 6a of rotenone[2)], a small amount of 6aβ,12aα-rotenolone(III) as trans-stereoisomer could be separated chromatographically. The compound showed mp 202-203° and $[\alpha]_D^{16}$+321°(c=0.37,$CHCl_3$), and its spectral data were identical with those of the compound produced photochemically. From these results, present compound was assigned to be 6aβ,12aα-rotenolone(III), although the values of the melting point and the optical rotation do not agree with those given by Crombie and Godin[2)] for 6aβ,12aα-rotenolone which was separated by fractional crystallization from a mixture of two trans-rotenolones.[9)] In addition, the evidences of the chemical structures for the compound(II) and (III) were obtained from the mass spectra, in which the fragmentation patterns of these compounds are similar to those which have been observed from 12a-hydroxy rotenoids[10)] ($m/e410 \longrightarrow m/e208 \xrightarrow[m^*206]{} m/e207$), and also from the fact that the treatment of either the compound(II) or (III) with 10% sulfuric acid afforded 6a,12a-dehydrorotenone(V).

Keto-acid(IVa,20mg) separated from the acidic fraction was precipitated as white blocks from ethyl acetate and dioxane-ethanol, mp 232-233°, $[\alpha]_D$-62°(c=0.18, dioxane), M^+426, $C_{23}H_{22}O_8$(requires: C64.78; H5.20. found: C64.95; H5.12%); UV ($CHCl_3$)λmax 242(ε20600), 273(19800) and 342nm(6500); IR(KBr) 1690cm^{-1}; NMR($CDCl_3$) of its methyl ester(IVb), δppm 1.70(s,$-CH_3$), 3.84, 3.88 and 3.95(s,$-3OCH_3$), 6.50 (s,H_4), 7.26(s,H_1), 6.64(d,H_{10}, J=8.8Hz) and 7.82(d,H_{11}, J=8.8Hz). The structure of the compound(IVa) was determined by comparison with the spectral data of keto-aldehyde(IVc) prepared from rotenolone.[2)] It was suggested that the compound has the same skeleton as the keto-aldehyde, since the uv spectrum of the compound(IVa) was similar to that of IVc(λmax 241, 282 and 340nm). In the mass spectrum of the compound(IVb), base peak is m/e208, and peaks due to the predominant fragmentation are m/e207(72%), 206(37%), 180(60%), 165(17%) and 137(17%). The series of these ions are common in the spectrum of keto-aldehyde(IVc) and are, moreover, of about the same relative intensity. These ions may, therefore, be considered as coming from the molecular skeleton of IV.

Photochemical oxygenation of rotenone in pyridine may also be initiated by ejection of the hydrogen atom at position 12a.[4)] Resulting hydroperoxides(VII) which are the mixture of cis and trans B/C form would be led to the corresponding cis and trans rotenolones. Although trans forms of rotenolone were not detected by the photooxygenation of rotenone in methanol,[4)] both cis and trans rotenolones were obtained in this experiment and the ratio of the yield was about 3:1. This result is probably due to the fact that rotenolones were relatively stable during oxygenation in basic media.[1)] Further, it is reasonable to consider that the keto-acid(IVa) was produced by the β-fission of the oxyradical  which was formed from the peroxyradical or the hydroperoxide(VII).

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References and notes

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9) In connection with these disagreements, Professor L. Crombie kindly pointed out in the private comminucation whether we dealt with a solvated compound or the compound which included an impurity. However, such possibilities could not be recognized from the further experiments. Although we cannot present definite information to the disagrrement of these values, it is considered that certain amount of 6aα,12aβ-rotenolone was still contained in the 6aβ,12aα-rotenolone because the separation of two isomers of rotenolone by fractional recrystallization was very difficult.
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