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The Structure of Xanthoperol

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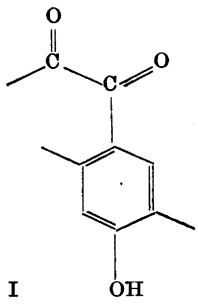
The structure V is proposed for xanthoperol, an artefact from the wood of *Juniperus communis* L. Xanthoperol is formed, without intervention of atmospheric oxygen, during the alkaline hydrolysis of wood extract from a substance having a *p*-ketophenol chromophore.

In a previous paper, the isolation of the diterpene phenol xanthoperol has been described [1], *. In the same paper, a partial structure (I) was proposed and the possibility that xanthoperol might have the structure 9,10-diketoferruginol (II) was discussed and regarded with doubt.

In continuation of the work, xanthoperol was subjected to Clemmensen reduction. As it is an α-diketone, it was considered possible that it might yield a mixture of various stages of reduction. This was also borne out by the experiment. The bulk of the reduction product was a mixture corresponding in its properties to a mixture of ferruginol (III), Δ^9-dehydroferruginol and hydroxyferruginols. As a side product a substance was isolated which showed properties corresponding to 9-ketoferruginol. On chromic oxide oxidation of the acetylated main part this same substance was obtained, besides xanthoperol. The substance, melting between 240 and 250° with decomposition, had an ultraviolet spectrum with the same shape as that of 9-ketoferruginol, *i. e.* a sharp maximum at 236 mμ (log ε 4.17) and a broad maximum at 286 mμ (log ε 4.09). The infrared spectrum likewise confirmed the conclusion that it was analogous to 9-ketoferruginol.

The reduced xanthoperol was dehydrogenated with selenium, but owing to the small amount of starting material, no pure product could be isolated. The ultraviolet spectra of some fractions of the chromatographed reaction product, however, showed full correlation with the spectrum of retenol-6 (IV) with maxima where retenol-6 has its major bands and plateaus or inflexions where retenol-6 has its side bands. These must be regarded as a strong indication that the dehydrogenation yielded retenol-6. Further evidence for the

* In the theoretical part of this paper the wave-number of the hydroxyl band is erroneously given as 3 436 cm^{-1}; it should be 3 380 cm^{-1}.



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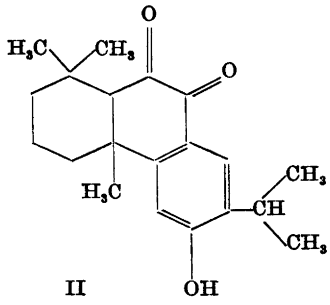

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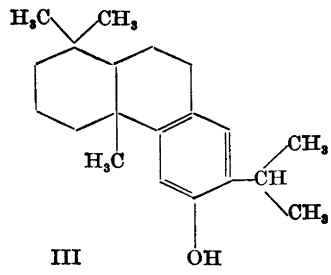

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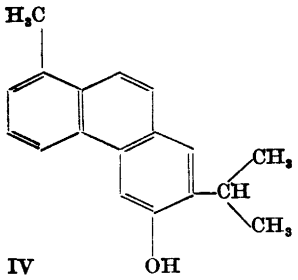

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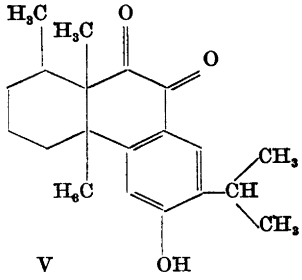

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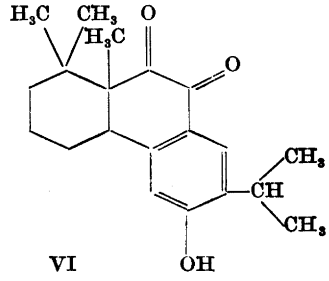

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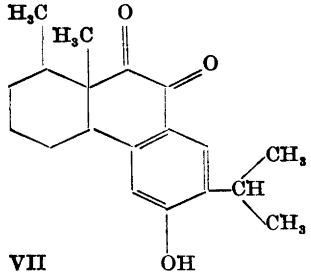

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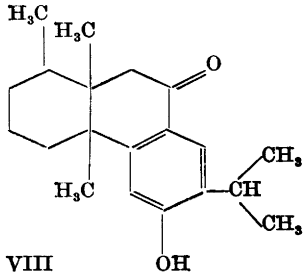

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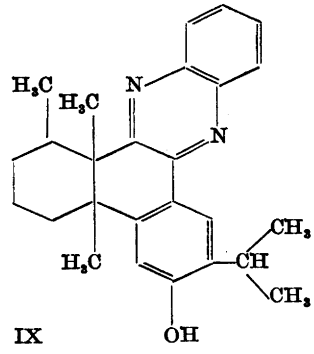

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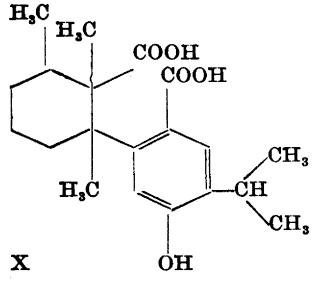

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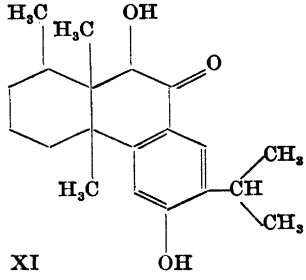

XI

presence of an *iso*propyl group in xanthoperol is afforded by the occurrence of bands at 1 163 cm^{-1} in xanthoperol and 1 172 cm^{-1} in the reduction product.

The retenol accounts for 18 carbon atoms. The remaining two carbon atoms, in the form of two methyl groups or, less probably, an ethyl group, must be placed in such positions that they are lost during the dehydrogenation, *i. e.* in the positions 1, 11 or 12, on the assumption that the aromatic ring in the partial structure (I) corresponds to the C-ring. This last assumption is strongly supported by the nature of the other compounds isolated from the wood of the juniper: ferruginol, Δ^9-dehydroferruginol and 9-ketoferruginol [2,3]. In the previous paper [1], it was shown that all structures proposed for xanthoperol where the 10-ketogroup could be enolised must be regarded with doubt. One methyl group must consequently be placed in the 11-position to hinder the enolisation. This leaves two structures: V, where a methyl group from the 1-position has migrated to the 11-position in comparison with the common diterpene phenols, and VI, where the methyl group from the 12-position has migrated to the 11-position. A third structure, the C_{19}-structure VII, which must also be taken into consideration at this stage, would apparently imply that the migration C-1—C-11 and C-12—C-13 of the methyl groups has occurred, as postulated in the case of columbin [4], with subsequent loss of the methyl group at the 13-position by aromatisation of the C-ring.

Decision can be made from among these structures by a C-methyl determination. The model 9-ketoferruginol gives the value 1.12, while xanthoperol gives 1.98. This at once excludes the structure VI as well as 9,10-diketoferruginol (II), which have the same side chains as 9-ketoferruginol. A short calculation shows that structure VII can also be ruled out. It is known that a *gem.*-dimethyl group contributes to the C-methyl determination with a value of 0.4 [5]. Hence the *iso*propyl group and the angular methyl group contribute with a joint value of 0.72. This would give the value 1.98—0.72 = 1.26 for the methyl group in the 1-position in structure VII, an obviously impossible value. If we assume that the *iso*propyl group also contributes with a value of 0.4 (the angular methyl group = 0.32), we would obtain the value 0.94 for the methyl group in the 1-position in structure V, which tallies well with the expected value. Even if one must be cautious in drawing inferences from detailed calculations of the C-methyl values, the results, nevertheless, strongly support the correctness of structure V. The reduction product, m. p. 240—250°, consequently has the structure VIII.

In most of the experiments performed, the diketo group proved to be sterically hindered. An attempt to prepare a disemicarbazone thus failed and oximation yielded only a nonresolvable mixture. Condensation with *o*-phenylene diamine gave in low yield a substance, m. p. 250—252°, which can be regarded as the corresponding quinoxaline (IX). Oxidation with periodic acid gave a quantitative recovery of xanthoperol. Treatment of xanthoperol with a large excess of alkaline hydrogen peroxide at room temperature for a long period (two days) yielded a small amount of an impure substance, m. p. 200—202°, to which the corresponding dicarboxylic acid structure X must be assigned.

Xanthoperol has a structure with no known counterpart in diterpene chemistry. It was therefore of special interest to study its formation. As

previously remarked [1], xanthoperol does not occur as such in wood. Closer examination, especially by spectrophotometry in ultraviolet, revealed that the precursor is a substance which is eluted directly after 9-ketoferruginol and that it has a chromophore which is the same or very nearly the same as the chromophore of 9-ketoferruginol. Atmospheric oxygen does not take part in the formation of xanthoperol during hydrolysis. The yield is actually higher in an atmosphere of hydrogen. The results appear to point to the structure XI or its equivalent, which would be oxidised during the hydrolysis by substances occurring simultaneously in the fractions. In spite of several attempts, the precursor could not be obtained in pure form.

EXPERIMENTAL

(All m. p. s are determined on a Kofler microscope. The microanalyses have been performed by Dr. A. Bernhardt, Mülheim, and the infrared spectra by Mr. B. C. Fogelberg, B. Sc.).

Clemmensen reduction of xanthoperol. Xanthoperol (60 mg) in ethanol-benzene (10 ml, 1:1) was reduced with amalgamated zinc (5 g) and concentrated hydrochloric acid (4 ml) at reflux temperature. After 1 1/2 h, when both layers were colourless, the heating was stopped, conc. hydrochloric acid (10 ml) was added and the mixture was allowed to stand overnight. Water was added and the solution was extracted with ether. The solvent was evaporated and the residue extracted with light petroleum, which left undissolved 0.5 mg of crystals, m. p. 240—250° (decomp.). The ultraviolet spectrum of these crystals in ethanol showed a sharp maximum at 236 mμ and a broad maximum at 286 mμ. The part soluble in light petroleum, having a maximum at 285 mμ, was acetylated with acetic anhydride and pyridine. The acetylation yielded a slowly crystallising sticky mass (44 mg), m. p. 75—95°, λ_{max} (in ethanol) 271 mμ (log k 0.92). Purification by chromatography or crystallisation did not sharpen the melting point.

Oxidation of the reduction product with chromic oxide. Xanthoperol (85 mg) was reduced as before. The reduced product was oxidised with chromic oxide (40 mg) in acetic acid (8 ml) on the water bath for 1 h. After dilution with water, the product was extracted with ether and the ether was evaporated. The residue was chromatographed on an Al_2O_3 column with light petroleum-ether-methanol. Ether-methanol eluted xanthoperol. In the ether eluates, before xanthoperol came out, about 20 mg of impure 10-deketoxanthoperol (VIII) could be demonstrated spectrophotometrically. These fractions were purified by crystallisation and sublimation, yielding 3 mg of needles, m. p. 240—250° (decomp.), λ_{max} (in ethanol) 236 mμ (log ε 4.17) 286 mμ (log ε 4.09). Principal IR-maxima (KBr): 3 280 (s), 2 920 (s), 2 835 (m), 1 642 (s), 1 590 (s), 1 568 (s), 1 502 (m), 1 464 (m), 1 385 (w), 1 366 (m), 1 340 (s), 1 309 (w), 1 288 (m), 1 257 (s), 1 192 (m), 1 172 (m), 1 055 (w), 970 (w) and 876 cm^{-1} (w). The properties of the compound resembled those of 9-ketoferruginol.

Selenium dehydrogenation of reduced xanthoperol. Reduced xanthoperol (80 mg) was mixed with selenium (300 mg) and heated at 290° for 24 h. The product was extracted with ether and the ether evaporated. The residue was chromatographed on an Al_2O_3 column with benzene-ether-methanol. The fractions eluted by ether-methanol, showing the expected ultraviolet spectra of phenanthrene derivatives, were rechromatographed. The elution was followed by spectrophotometry, but no fraction having a pure spectrum could be obtained. The purest fractions had UV-spectra of the following form: (in ethanol) maxima at 223, 258, 342 and 360 mμ, plateaus or inflexions at 270 and 308 mμ; (in *cyclo*hexane) maxima at 222, 260 and 360 mμ and plateaus or inflexions at 277, 306, 327 and 340 mμ.

Retenol-6 (IV) from 6-aminoretene. Retenol-6 was obtained from an authentic sample of 6-aminoretene by diazotisation. The product formed needles, m. p. 178—179°. (Found C 86.3; H 7.7. Calc. for $C_{18}H_{18}O$ C 86.4; H 7.3.) UV-spectrum of retenol-6: (in ethanol) mμ (log ε): 220 (4.44), 257 (4.68), 279 (4.19), 310 (4.03), 342 (3.39) and 359 (3.40); (in *cyclo*hexane) mμ (log ε): 221 (4.40), 258 (4.69), 278 (4.25), 295 (3.98), 308 (4.11), 325 (3.11), 340.5 (3.32), 357.5 (3.38).

Derivatives of xanthoperol. In attempts to prepare the disemicarbazone from xanthoperol and semicarbazide hydrochloride by heating on a water bath with sodium acetate in ethanol for one day or in pyridine-water for three days, a quantitative recovery of xanthoperol was obtained. Oximation with hydroxylamine hydrochloride in pyridine-ethanol for two days on a water bath gave crystals, m. p. 111—114°, but a sharp melting point could not be obtained by further purification.

Condensation with o-phenylene diamine. Xanthoperol (26 mg) and *o*-phenylene diamine (20 mg) were heated in acetic acid (1 ml) for 19 h on a water bath and thereafter for 2 h with reflux. Water was added and the precipitate was filtered. The precipitate was dissolved in ether and unreacted xanthoperol was extracted with 2 N sodium carbonate. After evaporation of the ether, the residue was crystallised from benzene-light petroleum, m. p. 250—252° (4 mg). The compound (IX), which was shown by paper chromatography to be free from xanthoperol, gave a deep red to violet colour with conc. sulphuric acid. λ_{max} (in ethanol) 241 mμ (log ε 4.19), 383 mμ (log ε 4.25), plateau at 260—290 mμ (log ε 4.1).

Oxidation with periodic acid. No reaction occurred between xanthoperol and periodic acid in acidic aqueous ethanol, even at water-bath temperature. The recovery of xanthoperol was quantitative in all experiments.

Oxidation with alkaline hydrogen peroxide. After preliminary experiments had shown that no reaction occurred in milder conditions, the oxidation was carried out by keeping xanthoperol (17 mg) and 30 % hydrogen peroxide (0.5 ml) in N sodium hydroxide (5 ml) for two days at room temperature. The now colourless solution was acidified and the flocky precipitate (4 mg) filtered. The precipitate (X), m. p. 200—202°, sublimed as needles from 150°. λ_{max} (in ethanol) 247 mμ (log ε 3.72), 290 mμ (log ε 3.62), Principal IR-maxima (KBr): 3 300 (broad) 2 900 (broad), 1 720 (broad), 1 680, 1 595, 1 558, 1 513, 1 460, 1 415, 1 343, 1 235, 1 165, 1 115, 940 and 872 cm^{-1}.

The formation of xanthoperol. The neutral non-hydrolysed part of the wood extract was chromatographed on an Al_2O_3 column with light petroleum-ether. Samples were taken from the fractions, which had been eluted by light petroleum-ether and ether, and UV-spectra were run in ethanol and in alkaline solution. After hydrolysis, spectra were again taken in ethanol and in alkaline solution. These spectra showed that the precursor was eluted after 9-ketoferruginol, and that it had an ultraviolet spectrum resembling that of 9-ketoferruginol: maxima at about 230 and 280 mμ in neutral and at 350 mμ in alkaline solution. The yield of xanthoperol was higher when the hydrolysis was performed in an atmosphere of hydrogen than in an atmosphere of oxygen. The precursor could not be obtained pure.

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