CLXXVII.—*Constituents of* Myoporum lætum, *Forst. (The "Ngaio"). Part III. The Oxide Rings of Ngaione.*

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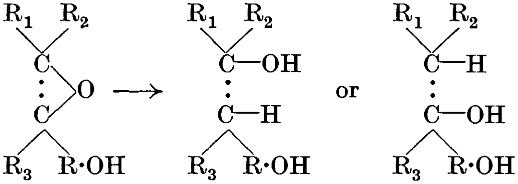
THE experiments on ngaione now to be described (see also J., 1925, **127**, 2200; 1927, 731) were carried out for the most part as a preliminary to a more exhaustive investigation of the oxide rings present in the molecule. As, however, the work has been interrupted, the results are published in their present incomplete form.

From the stability of ngaiol to water under pressure (see later), and of ngaiol and tetrahydrongaiol to acetic anhydride (*loc. cit.*), it is concluded that an ethylene oxide ring is not present in the molecule. Some ethylene oxide rings, however, show extraordinary stability, especially in dioxidic compounds. Pinol oxide, *e.g.*, is more stable than most ethylene oxides, and furyl butylene oxide (Tonnies and Staub, *Ber.*, 1884, **17**, 854) is not affected by acetic anhydride (compare also the naturally occurring diethylene oxide of linalol; and mannitol anhydride, which does not combine with water at all).

The fission of an oxide ring in ngaiol by hydrogenation has already been recorded (*loc. cit.*, 1927). By means of hydrogen and platinum-black in glacial acetic acid a different *glycol* is obtained, possibly through fission of a different oxide ring, or alternatively through fission of different oxygen bonds of the same oxide ring :

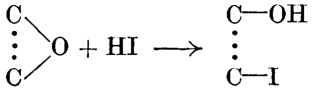


The glycols differ in their physical properties and in their colour reactions with vanillin and concentrated hydrochloric acid.

The action of halogen acids on some hydrogenated derivatives of ngaione has been studied. Tetrahydrongaiene dioxide, when treated with hydrogen chloride in glacial acetic acid solution, gave what is probably a monochloro-oxido-acetate. Tetrahydrongaiol was converted by hydrogen iodide in glacial acetic acid into a polyiodo-acetate, from which a mixture of unsaturated monohydric alcohols was obtained by reduction and saponification. From the mixture of products an alcohol, $C_{15}H_{29}\cdot OH$, was isolated, and in one instance an ethylene glycol, $C_{15}H_{30}(OH)_2$. Unsuccessful attempts were made to reduce the iodo-acetates without the formation of ethylenic linkings. Hydrogen with palladinised barium sulphate alone had no reducing effect, and addition of alkali caused elimination of hydrogen iodide with formation of several ethylenic linkings, and possibly an oxide ring. Reduction with zinc dust and glacial acetic acid, saturated with hydrogen iodide at 0°, yielded an iodine-containing product which after further reduction with zinc dust and alcohol was again unsaturated. Reduction with zinc dust and glacial acetic acid, saturated with hydrogen iodide at $-10°$, followed by reduction with zinc dust and alcohol and then by hydrogenation with platinum-black in glacial acetic acid, yielded a mixture of alcohols from which, after saponification, a paraffin alcohol, or mixture of paraffin alcohols, $C_{15}H_{31}\cdot OH$, was isolated. The isolation of this paraffin alcohol and of the ethylene glycol (see above) establishes beyond all doubt the conclusion (*loc. cit.*, 1927) that the molecule of ngaione is free from carbocyclic rings. Tetrahydrongaione gave on treatment with hydrogen iodide and glacial acetic acid an oily polyiodoketo-acetate, which by reduction and saponification was converted into a mixture of keto-alcohols.

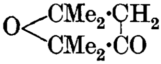
Reduction of tetrahydrongaiol with red phosphorus and constant-boiling hydriodic acid under reflux gave an oily di-iodide, which on further treatment with zinc dust and alcohol yielded a mixture of an alcohol with an unsaturated or cyclic hydrocarbon.

The formation of a monoacetate from tetrahydrongaiol suggested that the secondary alcoholic group had become esterified by the acetic acid in the presence of the hydrogen iodide, and had thus escaped reduction. A consideration of all the results indicates, however, that the problem is more complex. The formation of an acetate from tetrahydrongaiene dioxide by the action of hydrogen chloride in glacial acetic acid, the complexity of the mixture of monohydric alcohols obtained in the experiments with tetrahydrongaiol, and the formation of keto-alcohols from tetrahydrongaione all show that opening of one of the oxide rings can take place according to the equation



The alcoholic group is probably simultaneously esterified. The original secondary alcoholic group of tetrahydrongaiol is thus probably removed by conversion into the iodide and subsequent reduction.

The evidence accumulated does not permit any far-reaching speculation on the formula of ngaione. No certain indications of the absence of a furan ring have been obtained. Ngaione and ngaiol give violet colours in the pine-shaving test (compare furan and furfural, which give green colours). One would also expect a furan derivative to be rather more unstable than ngaione. On the other hand the molecular refractions of ngaione, ngaiol, and their derivatives show depressions of the order of that (average, 0·44) shown by furan derivatives (Wienhaus, *Ber.*, 1920, **53**, 1660). As with the furan compounds, the depression almost disappears on hydrogenation (*loc. cit.*, 1927). The values for the molecular refraction seem definitely to exclude the possibility of a furyl-ketone grouping of the type prepared synthetically by Asahina and Murayama (*Arch. Pharm.*, 1914, **252**, 435), $C_4OH_3\cdot COR$, which showed a large exaltation (average, approx. 1·0).

The tendency to formation of enolic acetates shown by ngaione (*loc. cit.*, 1925) is unusual for a ketone, and suggests that an esocyclic keto-oxide may be present of the type prepared by Dupont (*Compt. rend.*, 1911, **152**, 1486; **153**, 275; *Ann. Chim.*, 1913, **30**, 485),  $O<\begin{array}{l}CMe_2\cdot CH_2\\ \quad\quad\;\;|\\ CMe_2\cdot CO\end{array}$, which shows the reactions of the carbonyl group and a tendency to enolisation. The analogy can, however, only be regarded as tentative, as the properties of esocyclic keto-oxides are not well known (compare ketocineole, Cusmano and Linari, *Gazzetta*, 1912, **42**, i, 1, and the tetrahydro-γ-pyrones, Borsche and Thiele, *Ber.*, 1915, **48**, 684; 1923, **56**, 2012).

It has been shown that the vanillin–hydrochloric acid colour reaction is given by nearly all substances containing oxidic oxygen, but it is not confined to these substances.

A small quantity of an isomeride of ngaiol has been isolated, and also a monoxide, $C_{15}H_{24}O$.

EXPERIMENTAL.

Treatment of Ngaiol with Water.—No change in the physical constants was observed after ngaiol (1 part) had been heated for 10 hours with water (4 parts) in an atmosphere of carbon dioxide at 250°.

Hydrogenation of Ngaiol with Platinum-black as Catalyst.—Ngaiol (9·7 g.) in presence of platinum-black (1·1 g.; prepared by Feulgen's method; *Ber.*, 1921, **54**, 360) and 30 c.c. of glacial acetic acid absorbed 3 mols. of hydrogen during 2 hours. The resulting oil was hydrolysed with alcoholic potash, and the product isolated by means of ether. A portion of the product lost water when distilled at 0·5 mm. pressure : the distillate, b. p. 160—180°/0·5 mm., was a colourless oil with a strong sweet odour, $n_D^{20°}$ 1·4707, $d_{20°}^{20°}$ 0·9312 (Found : C, 73·4, 73·1 ; H, 11·9, 12·0. $C_{15}H_{30}O_3$ requires C, 69·7 ; H, 11·7%. $C_{15}H_{28}O_2$ requires C, 75·0 ; H, 11·7%) ; the saponification value of the acetate was 265.

The undistilled portion of the product of hydrogenation, after being freed from solvent in a vacuum at 100° (2 hours), was obtained as a slightly yellow, odourless oil, more viscous than the distillate described above. It had $d_{20°}^{20°}$ 0·966 and $n_D^{20°}$ 1·4664, whence $[R_L]_D =$ 74·03 [calc. for $C_{15}H_{28}O(OH)_2$, 73·96] (Found : C, 69·6 ; H, 11·9. $C_{15}H_{30}O_3$ requires C, 69·7 ; H, 11·7%). When treated with vanillin and concentrated hydrochloric acid, the substance slowly developed a jade-green colour. The acetate was prepared in the usual way ; saponification value, 308 [calc. for $C_{15}H_{28}O(OAc)_2$, 326].

The direct product of hydrogenation of ngaiol under the above conditions is therefore an *oxido-glycol*, $C_{15}H_{28}O(OH)_2$, different from the glycol of the same formula obtained by hydrogenation with Skita's reagent (*loc. cit.*, 1927).

Action of Hydrogen Chloride on Tetrahydrongaiene Dioxide.— A solution of the dioxide (1·1 g.) in glacial acetic acid (10 g.) was saturated with hydrogen chloride at 0° and kept in the dark for 3 days. Dilution with water then precipitated an oil, which was extracted with ether, well washed with water and with weak sodium bicarbonate solution, and dried ; removal of the solvent at 40° and finally in a vacuum over sulphuric acid left a dark, fluid oil, which did not crystallise at −20° (Found : Cl, 10·2. $C_{15}H_{28}OCl{\cdot}OAc$ requires Cl, 11·1%). The chlorine was almost completely removed by successive treatments with zinc dust and 80% alcohol, and with zinc dust and acetic acid at 100°. The resulting oil on distillation at 29 mm. pressure gave three fractions, b. p. 185—197°, 197—213°, 213—, respectively (Found for first two fractions : C, 72·1, 71·4 ; H, 11·4, 11·3. Calc. for $C_{15}H_{29}O{\cdot}OAc$: C, 71·8 ; H, 11·4%). The saponification value of the first fraction was 200 (calc. for $C_{15}H_{29}O{\cdot}OAc$, 209). The product was therefore a mixture of acetates, formed by the opening of one oxide ring.

Action of Hydrogen Iodide on Tetrahydrongaiol.—The wine-red liquid obtained when a solution of tetrahydrongaiol (5·1 g.) in glacial acetic acid (40 g.) was saturated at 0° with hydrogen iodide became turbid after some hours, and a heavy black oil gradually separated. After 2 days, ether extracted from the mixture, diluted with water, a dark brown, unstable, uncrystallisable oil (15 g.) [Found : I, 59·6.

$C_{15}H_{27}I_4 \cdot OAc$ requires I, 65·6%. $C_{15}H_{28}I_3(OAc)_3$ requires I, 59·6%. $C_{15}H_{27}OI_3$ requires I, 63·1%]. The *polyiodide* in 80% alcohol was heated with an equal weight of zinc dust on the water-bath for 1½ hours, and ether extracted from the product a mobile brownish oil with a faint odour. On distillation at 29 mm. this gave two fractions: A_1, b. p. 168—172°, $n_D^{20^\circ}$ 1·4442, $d_{20^\circ}^{20^\circ}$ 0·868; A_2, b. p. 172—, $n_D^{20^\circ}$ 1·4488 (Found for A_1: C, 75·8; H, 12·5. $C_{15}H_{29}O \cdot OAc$ requires C, 76·0; H, 12·0%). Saponification value of A_1, 178; of A_2, 188. The liquid obtained by hydrolysis of the oil with hot alcoholic potash was isolated by means of brine and ether and divided by distillation into four fractions, all of which decolorised bromine water. Analyses indicated that the product was a mixture of unsaturated monohydric alcohols with a small quantity of hydrocarbon. The second fraction had b. p. 166—173°/29 mm., $d_{20^\circ}^{20^\circ}$ 0·845, $n_D^{20^\circ}$ 1·4524, whence $[R_L]_D = 72·36$ (calc. for $C_{15}H_{29} \cdot OH \, |\overline{\overline{1}}$: $[R_L]_D$, 72·53) (Found: C, 79·8; H, 13·8. Calc. for $C_{15}H_{29} \cdot OH$: C, 79·6; H, 13·3%).

From the higher-boiling portion of the product of one treatment of tetrahydrongaiol with hydrogen iodide a very viscous, yellowish, odourless oil was obtained (0·55 g.), b. p. 200—215°/13 mm., $n_D^{20^\circ}$ 1·4655, which did not crystallise during 10 hours at $-10°$ [Found: C, 73·1; H, 13·0; *M*, by Rast's method, 248. $C_{15}H_{30}(OH)_2$ requires C, 73·7; H, 13·2%; *M*, 244. Saponification value of the acetate, 326. Calc. for $C_{15}H_{30}(OAc)_2$: S.V., 339]. The substance was thus shown to be a dihydroxypentadecane.

Reduction with palladinised barium sulphate and hydrogen. The catalyst (prepared by Schmidt's method; *Ber.*, 1919, **52**, 409) and the oily polyiodo-acetate (from 3·0 g. of tetrahydrongaiol) in absolute alcohol (30 c.c.) were stirred by means of a current of hydrogen. The reduction took place rapidly when the solution was kept slightly alkaline by frequent additions of aqueous caustic potash. After 2 hours, the solution was filtered. Extraction with ether, after addition of brine, gave an iodine-free product, from which, on hydrolysis with alcoholic potash, a light brown oil was obtained. This, on distillation at 29 mm. pressure, gave two fractions, b. p. 155—165° and 165—170°, as colourless, mobile oils with a strong aniseed odour (Found for the second fraction: C, 78·6; H, 11·8%), a third fraction, b. p. 170—180°, $d_{20^\circ}^{20^\circ}$ 0·904, $n_D^{20^\circ}$ 1·4735, as a colourless oil with a sweet odour, and a fourth fraction, b. p. 180—195°, $d_{20^\circ}^{20^\circ}$ 0·924, $n_D^{20^\circ}$ 1·4754, which was odourless (Found: C, 75·8; H, 11·3. $C_{15}H_{26}O$ requires C, 81·1; H, 11·7%. $C_{15}H_{28}O_2$ requires C, 74·9; H, 11·7%).

Reduction with zinc dust and glacial acetic acid saturated with hydrogen iodide at 0° (compare Zelinsky, *Ber.*, 1902, **35**, 2678). The polyiodo-acetate from tetrahydrongaiol (4 g.) gave by this treatment a colourless product which still contained iodine. The reduction was completed by use of zinc dust and alcohol, yielding a product which, on hydrolysis and distillation, gave a substance which seemed to be very similar to that obtained by the direct reduction of the polyiodide with zinc dust and alcohol.

The Paraffin Alcohol, $C_{15}H_{31}\cdot OH$.—A solution of tetrahydrongaiol (12 g.) in glacial acetic acid was saturated with hydrogen iodide at $-15°$, and after 3 days was treated at the same temperature with zinc dust. The product was reduced as before with zinc dust and alcohol, and the resulting acetates were distilled, and treated in glacial acetic acid with hydrogen and platinum-black, 170 c.c. of hydrogen being absorbed. After filtration from the catalyst and neutralisation with sodium carbonate, the oil was extracted with ether and hydrolysed with alcoholic potash. The product was then extracted with ether and repeatedly distilled at 29 mm. pressure, giving the *alcohol*, b. p. 168—172°/29 mm., $n_D^{20°}$ 1·4474 (1·4471—1·4481), $d_{20°}^{20°}$ 0·841, whence $[R_L]_D = 72{\cdot}64$ (calc. for $C_{15}H_{31}\cdot OH$, $[R_L]_D$, 72·99) (Found: C, 78·9; H, 14·0. $C_{15}H_{31}\cdot OH$ requires C, 78·9; H, 14·1%). It did not absorb bromine from bromine water and only slowly decolorised dilute permanganate solution in the cold.

Attempt to prepare the paraffin. The impure fractions of the saturated alcohols were treated with phosphorus pentachloride, the resulting chloride was reduced with zinc dust and alcohol and with sodium and alcohol, and the product distilled repeatedly over sodium. The resulting water-white, mobile liquid (0·50 g.) had b. p. 140—145°/29 mm., $n_D^{20°}$ 1·4431, $d_{20°}^{20°}$ 0·796, and slowly decolorised permanganate (Found: C, 83·7; H, 14·0. $C_{15}H_{32}$ requires C, 84·8; H, 15·2%). The 2·3% of oxygen may be due to the presence of an ethyl ether, formed during the reduction with zinc dust and alcohol, or with sodium and alcohol (compare reduction of myrtenyl chloride; Semmler, *Ber.*, 1907, **40**, 1368). The presence of some unsaturated hydrocarbon was also evident.

Action of Hydrogen Iodide in Glacial Acetic Acid on Tetrahydrongaione.—The ketone (3·6 g.) was treated with hydrogen iodide as described above. The yellowish oil obtained soon turned red through liberation of iodine (Found: I, 55·2. $C_{15}H_{26}OI_4$ requires I, 79·6%. $C_{15}H_{26}O_2I_2$ requires I, 51·7%. $C_{15}H_{26}OI_3\cdot OAc$ requires I, 57·5%). Examination of the product of reduction (see below) showed that the substance was probably a crude tri-iodide of a keto-acetate, with which the analysis most nearly agrees. Reduction with zinc dust in the usual way gave an oil, of which the middle fraction had a saponification value of 166. The whole product was therefore hydrolysed with alcoholic potash. Fractional distillation at 28 mm. pressure then gave three fractions, b. p. 150—170°, 170—195°, 195—, wts. 0·3 g., $n_D^{20°}$ 1·4484, 1·4529, 1·4640 (Found, respectively: C, 73·5, 76·9, 75·0; H, 11·9, 12·5, 12·2. $C_{15}H_{28}O_2$ requires C, 74·9; H, 11·7%). The first fraction was a mobile, colourless oil with an aniseed odour, the other two were yellowish, more viscous oils with fatty odours. All the fractions were unsaturated (bromine water) and yielded semicarbazones. The product of the reaction was therefore a complex mixture of keto-alcohols. The quantities of semicarbazones were too small for separation by fractional crystallisation.

Reduction of Tetrahydrongaiol with Hydriodic Acid and Red Phosphorus.—Tetrahydrongaiol (2 g.) was boiled with constant-boiling hydriodic acid (30 g.) and red phosphorus (2 g.) for 4 hours. Distillation with steam carried over a negligible quantity of light oil, which was not further examined. The heavy oily residue was extracted with ether, filtered, washed with water and alkali, dried, and freed from solvent in a vacuum over sulphuric acid (Found: I, 53·7. $C_{15}H_{30}I_2$ requires I, 54·7%. $C_{15}H_{28}OI_2$ requires I, 53·2%). Heating of tetrahydrongaiol (3 g.) under the above conditions during 20 hours with hydriodic acid gave again an oily di-iodide. It was reduced with zinc dust and alcohol in the usual way, the product was distilled in steam, extracted with ether, and divided at the ordinary pressure into two fractions, b. p. 220—240°, 240—250°, $n_D^{20°}$ 1·4465, 1·4500 (Found for the second fraction: C, 82·7; H, 13·7. $C_{15}H_{32}$ requires C, 84·8; H, 15·2%. $C_{15}H_{32}O$ requires C, 78·9; H, 14·1%). The saponification value of the acetylated product was 84. The oil was therefore a mixture of a hydrocarbon and an alcohol, the low hydrogen value indicating a cyclic or an unsaturated nature.

Colour Reactions.—Asahina, Takagi, and Hongo (*loc. cit.*, 1925; also Asano, *J. Pharm. Soc. Japan*, 1919, **454**, 99; Asahina, *Acta Phytochim.*, 1924, **2**, 1) recorded the production of a red colour when a drop of elsholtzione or atractylone was added to a solution of vanillin in concentrated hydrochloric acid. Asahina (*Acta Phytochim.*, 1924, **2**, 22) applied the reaction to a large number of furan derivatives and found that a red or red-violet colour was developed in every case with the exception of a few acids such as pyrotritaric acid.

The reaction is, however, not confined to furan derivatives, for with one exception (the oxido-glycol obtained by the hydrogenation of ngaiol with platinum-black as catalyst gave a jade-green colour) all the oxides described in this investigation have given the test. Positive tests (in some cases only after standing) have also been given by ethyl ether, acetal, *iso*amyl ether, phenetole, anisole, diphenyl ether, and dimethylpyrone, whereas negative results were obtained with citral, citronellal, borneol, menthol, camphor, acetic anhydride, and amyl benzoate. Ordinary reagent acetone, acetaldehyde, and acetophenone gave colours indistinguishable from those given by the above oxides.

An Isomeride of Ngaiol.—The strongly odorous constituent of crude ngaiol was present also in the oil obtained after treatment with phthalic anhydride, but could be separated in the first fraction, b. p. 120—190°/29 mm., on distillation. Redistillation of this fraction led to a further elimination of the odorous constituent and the isolation of a fraction, which from its physical constants appears to be an isomeride of ngaiol, b. p. 188—190°/29 mm., $d_{20^\circ}^{20^\circ}$ 1·013, $n_{D}^{20^\circ}$ 1·4794 (1·4793—1·4795) (Found: C, 71·5; H, 9·6. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·5%). The substance was a light yellow liquid with a faint, sweet odour.

A Monoxide.—The proportion of crude ngaiol that would not combine with phthalic anhydride was not large, and contained generally a small amount of ngaione. From a sample (4 g.) of the lower-boiling part (b. p. 120—180°/29 mm.) a limpid, white, faintly odorous oil was obtained by distillation over sodium, at 29 mm. pressure, b. p. 160—170°, $n_{20^\circ}^{20^\circ}$ 1·4894 (constant over the whole fraction), $d_{20^\circ}^{20^\circ}$ 0·9485, whence $[R_L]_D = 67{\cdot}06$ (calc. for $C_{15}H_{24}O\ |\overline{\overline{1}}$, 66·05; $|\overline{\overline{2}}$, 67·78) (Found: C, 81·8; H, 10·8; *M*, by Rast's method, 229. $C_{15}H_{24}O$ requires C, 81·7; H, 10·9%; *M*, 220). The fraction was therefore probably a mixture of mono- and di-cyclic oxides. It took up bromine from bromine water with formation of a black oil, slowly decolorised dilute permanganate solution, developed an immediate cherry-red colour on treatment with vanillin and concentrated hydrochloric acid, and gave a violet colour in the pine-shaving test.

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