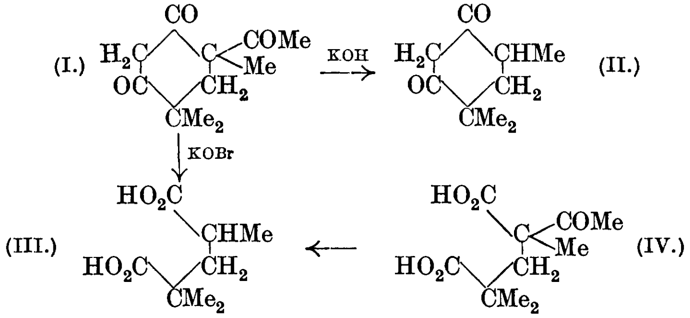
XXXVIII.—*The Essential Oil of* Backhousia angustifolia. *Part III. The Constitutions of Angustione and Dehydroangustione.*

By ROBERT SYDNEY CAHN, CHARLES STANLEY GIBSON, ARTHUR RAMON PENFOLD, and JOHN LIONEL SIMONSEN.

THE chief constituents of the essential oil of *Backhousia angustifolia* have been shown (J., 1930, 1184) to be two β-diketones, angustione and dehydroangustione. It has now been found that these ketones occur together in the natural oil, one or the other predominating. The constitution of angustione (I) was based in the first place on its hydrolysis with sodium hydroxide to 1 : 1 : 3-trimethyl*cyclo*hexane-4 : 6-dione (II) and acetic acid, and the correctness of this view has been confirmed by the work now described.

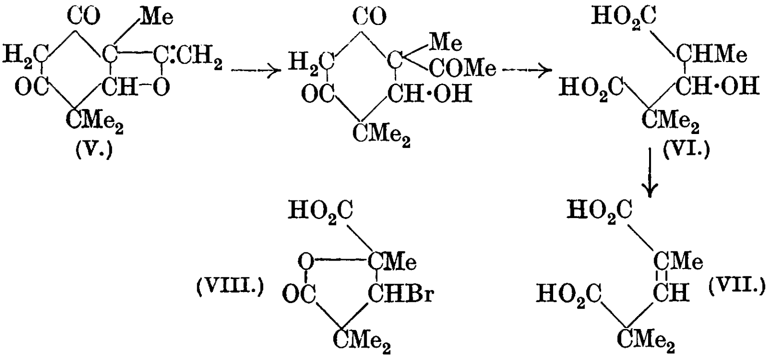


Angustione is converted quantitatively by oxidation with potassium hypobromite solution into *l*-ααγ-trimethylglutaric acid (III). The main product of oxidation with potassium permanganate in acetone solution is a liquid acid, which, although it could not be characterised by any crystalline derivative, is probably the ketonic acid (IV), since it is oxidised smoothly by sodium hypobromite solution to *l*-ααγ-trimethylglutaric acid.

It was tentatively suggested (*loc. cit.*, p. 1189) that dehydroangustione was represented by (V) and, in view of the somewhat unusual oxide ring, a further study of its reactions was desirable. A preliminary investigation of its oxidation with potassium hypobromite had shown that ααγ-trimethylglutaric acid (see below) and a neutral substance, $C_8H_{10}O_3$, m. p. 88·5°, volatile in steam, were formed. The latter substance has now been identified as the anhydride of *cis*-ααγ-trimethylglutaconic acid (VII), which was described by Perkin and Smith (J., 1904, **85**, 157). Its constitution was established by it hydration to *cis*-ααγ-trimethylglutaconic acid, m. p. 125°.

According to Perkin and Smith this acid yields on bromination a dibromide, m. p. 168°, but we have been unable to isolate this; we found it to be unstable, passing into the *lactone* of *β-bromo-γ-hydroxy-ααγ-trimethylglutaric acid* (VIII).

The formation of *cis*-ααγ-trimethylglutaconic acid by the oxidation of dehydroangustione is in agreement with the constitution originally assigned to the ketone, since it would result from the dehydration of hydroxy-ααγ-trimethylglutaric acid (VI), the reaction proceeding in accordance with the scheme :



That this correctly represents the course of the reaction is proved by the isolation from the reaction mixture of a small quantity of an acid, $C_8H_{14}O_5$, m. p. 156°, which is identical with the *trans*-β-hydroxy-ααγ-trimethylglutaric acid (VI) described by Perkin and Smith (J., 1903, **83**, 776). The acid is converted, on reduction with hydriodic acid and red phosphorus, followed by sodium and amyl alcohol, into ααγ-trimethylglutaric acid. The hydroxy-acid, like *cis*- and *trans*-caronic acids (compare Baeyer, *Ber.*, 1896, **29**, 2796), behaves on titration as a monobasic acid; the second carboxyl group can, however, be shown to be present, if an excess of alkali is added to a hot solution.

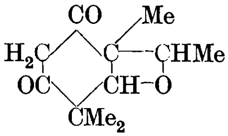
These degradation products from dehydroangustione are strong evidence for the correctness of the constitution assigned to that ketone. In the previous work, we were, however, unable to explain satisfactorily the isolation, in addition, of ααγ-trimethylglutaric acid. The catalytic hydrogenation of dehydroangustione has now shown that the ketone which was oxidised contained a small quantity of angustione and it is from the latter that ααγ-trimethylglutaric acid was produced.

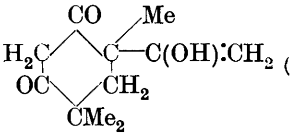
When dehydroangustione in alcoholic solution is treated with hydrogen in the presence of a palladium–norite catalyst, the reduction proceeds rapidly, but ceases when about 80% of the hydrogen required for the presence of one ethylenic linkage has been absorbed. The product is *dl*-angustione and is homogeneous. Its identity is established by acid hydrolysis to 1 : 1 : 3-trimethyl*cyclo*hexane-4 : 6-dione. Whilst the racemisation of dehydroangustione on reduction hardly calls for comment, since a group directly attached to the centre of asymmetry is involved, it is not without interest that the angustione present as an impurity is also racemised. It is possible that the norite behaves here in a similar manner to the animal charcoal in the conversion of α-benziloxime into β-benziloxime (Taylor and Marks, *Nature*, 1930, **125**, 636).

The *dl*-angustione prepared by the reduction of dehydroangustione agreed closely in its physical properties with the natural ketone described previously, except for a marked discrepancy in the refractive index, $n_{\rm D}^{20^\circ}$ 1·5087 in place of 1·5137. This difference is due to the fact that the previous sample of the ketone was contaminated with dehydroangustione, and a new specimen of the natural ketone, which was purified through its amino-derivative, was found to have a similar value, $n_{\rm D}^{20^\circ}$ 1·5092. Since the catalytic hydrogenation of dehydroangustione had shown it to be contaminated with angustione, a considerable quantity of the ketone was very carefully purified by prolonged fractional crystallisation of its amino-derivative. The refractive index, $n_{\rm D}^{20^\circ}$ 1·5313, of the pure ketone regenerated from this was very much higher than that observed previously. A calculation shows that the ketone used for the catalytic hydrogenation, which had $n_{\rm D}^{20^\circ}$ 1·5254, must have contained 26% of angustione, in satisfactory agreement with that shown by the absorption of hydrogen (21%).*

Whilst the reduction of dehydroangustione to angustione provides strong confirmatory evidence of the correctness of the structure assigned to the unsaturated ketone, it seems somewhat remarkable that the oxide ring should be reduced preferentially to the ethylenic linkage. The formation of the saturated oxide (IX) might have been anticipated and not the enolic form of angustione (X).

(IX.)





(X.)

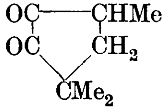
The oxidation of 1 : 1 : 3-trimethyl-Δ^2-*cyclo*hexene-4 : 6-dione with sodium hypobromite gives *cis*-ααγ-trimethylglutaconic acid as the main product. At the same time a small quantity of a substance,

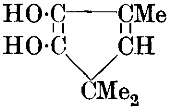
---

* These revised values for the refractive indices of angustione and dehydroangustione alter slightly their molecular refractions, which now become $[R_L]_{\rm D}$ 54·0 and 54·77 respectively.

$C_8H_{12}O_2$, which has phenolic properties is formed. This unstable substance passes on keeping into a red oil and is possibly the 1 : 2-diketone (XI) or the dienol (XII), since on treatment with bromine in chloroform solution it yields an ochreous bromide, which is decomposed by water with formation of the substituted glutaconic acid. The instability of the substance and the extremely small quantity available for investigation have rendered a further study of its reactions impossible.

(XI.)





(XII.)

Note on the Parachors of Angustione and Dehydroangustione.

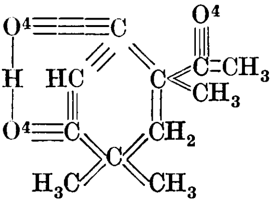
[By OWEN JOHN EVANS and FREDERICK GEORGE SOPER].

Since the dehydroangustione molecule differs from that of angustione by the loss of two hydrogen atoms and the gain of a four-membered ring, the parachors of the two ketones should differ by 22·6 units. It was thought that it might prove possible to obtain confirmation of the structure assigned to dehydroangustione by a comparison of the parachors.

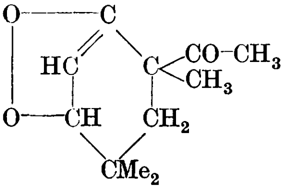
The angustione used was the *dl*-ketone, which had been prepared by the catalytic hydrogenation of dehydroangustione (p. 287), and two specimens of dehydroangustione were examined. Sample (A) had been regenerated from aminodehydroangustione recrystallised once from *cyclo*hexane and, from its refractive index, contained 18% of angustione; sample (B) was prepared from very carefully purified aminodehydroangustione. This was crystallised three times from dilute alcohol, digested once with a small quantity of *cyclo*hexane, and finally recrystallised from benzene; it then melted at 151—152°.

The surface tensions were measured by the method of maximum bubble pressure as modified by Sugden (J., 1924, **125**, 27), pure benzene being used to standardise the apparatus. The values obtained at 20° for *dl*-angustione and dehydroangustione (sample B) were 34·9 and 36·7 dynes/cm. respectively, and dehydroangustione (sample A) gave the value 36·0 dynes/cm. These values for the surface tension give for the parachor of angustione 442 ([*P*] calc., 462·1) and for that of dehydroangustione 435 ([*P*] calc., 439·5), the densities at 20° being 1·083 and 1·103 respectively.

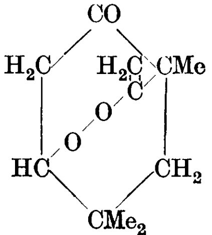
The observed negative anomalies cannot be considered to question the accepted formulæ for these ketones, since negative anomalies of similar magnitude have been noticed in phorone and its derivatives (Sugden, J., 1928, 410) and for other β-diketones (Sugden, J., 1929, 316). To explain such observations the formation of odd electron linkages, as in formula (XIII), and/or the replacement of double bonds by ring structures have been suggested. Such replacement of the double bonds in two of the carbonyl groups to give the bridged structure (XIV) or (XV) has been suggested to us by Dr. Sugden for angustione and would account for a large proportion of the observed deficiency of 20 units. Although there is no chemical evidence for the peroxide structure in angustione, a peroxide formula is assigned to ascaridole.



[P] 445·0.
(XIII.)



[P] 447·4.
(XIV.)



[P] 445·1.
(XV.)

A determination of the Ramsay–Shields constant indicated that angustione is a normal liquid, so the negative anomaly cannot be attributed to association. (The temperature coefficient of the surface tension is — 0·072 dyne/cm. per degree ; d^{40° 1·074 ; Ramsay–Shields constant 2·05.)

The anomaly for dehydroangustione (— 4·5 units) is much less serious and part of this may be due to the *gem*-dimethyl group, which would tend to reduce the ring strain and to lower the parachor by a few units (Sugden, J., 1928, 411).

EXPERIMENTAL.

Angustione.

Action of Hydrogen Bromide on Angustione.—A mixture of the ketone (5 g.) and hydrobromic acid (*d* 1·5 ; 20 c.c.) was heated on the water-bath for 12 hours. The clear solution was cooled and after the addition of water (50 c.c.) a solid separated which crystallised from light petroleum in prismatic needles, m. p. 130—131°, and was identified as 1 : 1 : 3-trimethyl*cyclo*hexane-4 : 6-dione. It was optically inactive.

Oxidation of Angustione.—(1) *With potassium hypobromite.* The ketone (6·5 g.) in potassium hydroxide solution (KOH, 2·5 g. ; H_2O, 30 c.c.) was added all at once to a solution of potassium hypobromite (KOH, 11·2 g. ; Br_2, 16 g. ; H_2O, 60 c.c.) ; a considerable rise in temperature occurred and bromoform separated. After extraction with ether, and removal of the excess of hypobromite with sulphur dioxide, the solution was acidified, saturated with ammonium sulphate, and extracted with ether. Evaporation of the extract left an oil, from which, by distillation in steam, a little unchanged ketone was removed : the remaining aqueous solution was evaporated, and the crystalline residue was extracted with hot light petroleum (b. p. 60—80°), which left a small quantity of a yellow oil undissolved. The light petroleum solution was evaporated, and the residue crystallised from hot water, from which it separated in leaflets, m. p. 91—92°. It was identified as *l*-$\alpha\alpha\gamma$-trimethylglutaric acid : in water it had $[\alpha]_{5461} - 12{\cdot}0°$ ($c = 1{\cdot}546$, $l = 2$, $\alpha_{5461} - 0{\cdot}37°$) (Found : C, 55·1; H, 7·8. Calc.: C, 55·1; H, 8·0%).

(2) *With potassium permanganate.* The ketone (5 g.) in acetone (100 c.c.) was treated gradually with potassium permanganate (8 g.), the temperature being maintained at 0°. The acidic products were isolated in the usual manner; after distillation in steam to remove a small quantity of unchanged ketone, a yellow oil was obtained, which showed no tendency to crystallise. The acid was therefore dissolved in alkali and treated with an excess of sodium hypobromite solution, which caused a copious separation of bromoform. The acid resulting from the oxidation crystallised from water in leaflets, m. p. 90—91°, and was identified as *l*-$\alpha\alpha\gamma$-trimethylglutaric acid : $c = 2{\cdot}265$, $l = 2$, $\alpha_{5461} - 0{\cdot}45°$, $[\alpha]_{5461} - 9{\cdot}71°$.

Dehydroangustione.

p-*Toluidinodehydroangustione.*—A mixture of the ketone (2 g.), *p*-toluidine (2·2 g.), and zinc chloride (0·5 g.) was heated at 140—150° for 2 hours. The oil obtained was dissolved in ether, and the solution filtered from an insoluble crystalline zinc salt, washed with dilute sulphuric acid and with sodium carbonate solution, dried, and evaporated; a viscid oil remained, which gradually crystallised. Recrystallised from dilute acetone, it formed needles, m. p. 63—65° (Found : N, 5·3. $C_{18}H_{21}O_2N$ requires N, 4·9%). p-*Toluidinodehydroangustione* is extremely difficult to purify, since it is very soluble in all the ordinary organic solvents and unless cooled to 0° tends to separate as an oil.

Action of Hydrogen Bromide on Dehydroangustione.—A mixture of the ketone (5 g.) and hydrobromic acid (*d* 1·5 ; 20 c.c.) was heated on the water-bath until a clear solution was obtained (4 hours); water (70 c.c.) was then added. The solid which separated melted at 156—157° after crystallisation from dilute alcohol and was identified as 1 : 1 : 3-trimethyl-Δ^2-*cyclo*hexene-4 : 6-dione.

Reduction of Dehydroangustione. dl-*Angustione.*—Dehydroangustione ($n_D^{20°}$ 1·5254) (29·8 g.) in alcohol (200 c.c.) was, after the addition of palladised norite (1 g.), shaken in an atmosphere of hydrogen : absorption (2724 c.c.; calc., 3440 c.c.) was complete in 50 minutes. An excess of ammonia was added to the filtered liquid, and the alcohol removed on the water-bath; dl-*aminoangustione* (27·5 g.), m. p. 138—139°, then separated as a crystalline solid. A further small quantity was obtained on evaporation of the filtrate. *dl*-Aminoangustione crystallised from *cyclo*hexane in conglomerates of sharp prisms, which on exposure to the air became matte and then melted at 139—140°. It was optically inactive in alcoholic solution (Found : C, 67·9; H, 8·5. $C_{11}H_{17}O_9N$ requires C, 67·7; H, 8·7%).

The amino-derivative was hydrolysed with alkali (*loc. cit.*, p. 1191), dl-*angustione* being obtained, b. p. 127°/14 mm., $d_{20°}^{20°}$ 1·083, $n_D^{20°}$ 1·5087 (Found : C, 67·0; H, 8·1. $C_{11}H_{16}O_3$ requires C, 67·3; H, 8·1%). The ketone was characterised by the preparation of the copper derivative, which crystallises from benzene in fine blue needles, m. p. 203—204°.

dl-*Anhydroangustione*-4(or 6)-*oxime* was obtained when the ketone was treated in alcoholic solution with hydroxylamine hydrochloride and sodium hydroxide. It crystallised from dilute methyl alcohol in fine needles, m. p. 57—58°, softening slightly below this temperature (Found : N, 7·4. $C_{11}H_{15}O_2N$ requires N, 7·2%).

When *dl*-angustione is hydrolysed with hydrogen bromide under the conditions described on p. 290, it yields 1 : 1 : 3-trimethyl*cyclo*hexane-4 : 6-dione, m. p. 130—131°, in a quantitative amount.

Oxidation of Dehydroangustione with Sodium Hypobromite.—For the oxidation of the ketone the following method was found to be more convenient than that previously described (*loc. cit.*, p. 1200). The ketone (9·8 g.) in sodium hydroxide solution (NaOH, 3 g.; H_2O, 40 c.c.) was added all at once to a solution of sodium hypobromite (NaOH, 18 g.; Br_2, 36 g.; H_2O, 150 c.c.); bromoform was immediately deposited and the temperature rose to 40°. After 1 hour the bromoform (11·5 g.) was separated, the excess of hypobromite removed with sulphur dioxide, the solution acidified, saturated with ammonium sulphate, and extracted ten times with ether, and the ether dried and evaporated. The residual oil was distilled in steam, until no further solid separated on saturation of the distillate with ammonium sulphate (about 3 litres). The steam distillate (A) was made alkaline, concentrated, acidified, and extracted with ether; on removal of the solvent a crystalline solid (2·5 g.) remained. This decomposed at 125° and was identified as *cis*-$\alpha\alpha\gamma$-trimethylglutaconic acid by conversion into the anhydride, m. p. 88·5° (see p. 294).

The residue from the steam distillate was extracted with ether, and the extract dried and evaporated; a crystalline solid, mixed with some oil, (5 g.) remained. This was repeatedly extracted with hot light petroleum (b. p. 60—80°); a yellow oil (2·5 g.) (B), left undissolved, gradually crystallised. The light petroleum extract on evaporation yielded a solid, identified as *l*-$\alpha\alpha\gamma$-trimethylglutaric acid, which, as mentioned on p. 287, originates from angustione present in the dehydroangustione.

The solid (B) melted somewhat indefinitely at 138° and was best purified by extraction with hot benzene and repeated crystallisation from water, in which it was extremely readily soluble, and from which it separated in large prisms, m. p. 156—157° (Found : C, 50·3; H, 6·9; *M*, 192. Calc. for $C_8H_{14}O_5$: C, 50·5; H, 7·4; *M*, 190). It agreed in its properties with the *trans*-β-hydroxy-$\alpha\alpha\gamma$-trimethylglutaric acid described by Perkin and Smith (*loc. cit.*, p. 776). It was sparingly soluble in ether, benzene, toluene, chloroform, and light petroleum and in alkaline solution it was stable to potassium permanganate. It differed from $\alpha\alpha\gamma$-trimethylglutaric acid and *cis*-$\alpha\alpha\gamma$-trimethylglutaconic acid in that it did not give a sparingly soluble copper salt when its aqueous solution was treated with copper acetate. On reduction with hydriodic acid (*d*, 1·7) and red phosphorus at 170—180°, followed by reduction with sodium in amyl-alcoholic solution, it gave $\alpha\alpha\gamma$-trimethylglutaric acid, m. p. 97—98°, both alone and after admixture with an authentic specimen.

Oxidation of 1 : 1 : 3-*Trimethyl*-Δ^2-cyclo*hexene*-4 : 6-*dione with Sodium Hypobromite.*—To an ice-cold solution of the ketone (9·2 g.) in sodium hydroxide (NaOH, 4·5 g.; H_2O, 50 c.c.) was added all at once a solution of sodium hypobromite (NaOH, 25 g.; Br_2, 27·6 g; H_2O, 150 c.c.). The temperature rose to 40° and bromoform separated. After 1 hour, the bromoform was removed, the excess of hypobromite destroyed with sulphur dioxide, and the acidified solution, after saturation with ammonium sulphate, extracted with ether. After removal of the solvent the residue (8 g.) was shaken with sodium carbonate solution, the solution saturated with carbon dioxide, and the crystalline solid (A) (1·8 g.), which remained undissolved, was collected. The filtrate was extracted with ether; on removal of the solvent, a solid (B) (0·4 g.) was obtained. The alkaline solution (C) was reserved.

The fractions (A) and (B) were combined and purified by solution in sodium hydroxide solution and precipitation by carbon dioxide. The solid was then recrystallised from light petroleum, from which it separated in fine needles, m. p. 85—86° (Found in air-dried material: C, 68·7; H, 8·6. $C_8H_{12}O_2$ requires C, 68·6; H, 8·6%). This *substance*, which gives with ferric chloride in alcoholic solution a purple coloration, is somewhat unstable. If placed in a vacuum over sulphuric acid, it liquefies slowly, giving a red oil, and the same change occurs when it is kept for some weeks in a sample tube. In chloroform solution it readily absorbs bromine and on evaporation of the solvent a red oil is obtained which, when triturated with light petroleum, is converted into a red solid. This dissolves in water to give a colourless solution, which on evaporation deposits fine needles, decomp. 125°. It was identified as *cis*-$\alpha\alpha\gamma$-trimethylglutaconic acid (Found : C, 55·9 ; H, 7·4. Calc. : C, 55·8 ; H, 7·0%).

The alkaline solution (C) was acidified and extracted with ether. On removal of the solvent a solid was obtained which, crystallised from light petroleum (b. p. 60—80°), gave a sparingly soluble fraction in leaflets, m. p. 88·5°, and a more readily soluble fraction in needles, decomp. 125°. The latter was identified as *cis*-$\alpha\alpha\gamma$-trimethylglutaconic acid (Found : C, 55·7 ; H, 7·1. Calc. : C, 55·8 ; H, 7·0%) ; when heated above its melting point, it was converted into the anhydride, m. p. 88·5°, identical with the less soluble fraction referred to above, and on reduction with sodium in amyl-alcoholic solution it gave $\alpha\alpha\gamma$-trimethylglutaric acid. The substance, m. p. 88·5°, was identical with that having this melting point, the preparation of which from dehydroangustione was described previously (*loc. cit.*, p. 1200).

When *cis*-$\alpha\alpha\gamma$-trimethylglutaconic acid was treated with bromine under the conditions used by Perkin and Smith (*loc. cit.*, p. 158), and the resulting solid recrystallised from benzene, evolution of hydrogen bromide occurred : on cooling, the *lactone* of *β-bromo-γ-hydroxy-ααγ-trimethylglutaric acid* separated in well-formed prisms, m. p. 147—148° (Found : Br, 32·0 ; *M*, 253. $C_8H_{11}O_4Br$ requires Br, 31·9% ; *M*, 251).

UNIVERSITY COLLEGE OF NORTH WALES, BANGOR.
GUY'S HOSPITAL MEDICAL SCHOOL (UNIVERSITY OF LONDON),
LONDON, S.E.1.
TECHNOLOGICAL MUSEUM, SYDNEY.

[*Received, January* 12*th*, 1931.]