CXLIX.—*The Essential Oil of* Backhousia angustifolia. *Part II. The Isolation of Naturally Occurring β-Diketones : Angustione and Dehydroangustione.*

By Charles Stanley Gibson, Arthur Ramon Penfold, and John Lionel Simonsen.

During an investigation of the constituents of the essential oil derived from the leaves and terminal branchlets of *Backhousia angustifolia*, which grows in Queensland, Penfold (*J. Proc. Roy. Soc. New South Wales*, 1924, **57**, 300) observed that the portion of the oil which was soluble in alkali contained a substance or a mixture of substances giving crystalline derivatives with ammonia and copper carbonate. Although the boiling point of this constituent of the oil was the same for different samples of the oil, the other physical constants, more especially the refractive index, showed somewhat large variations (n_D 1·5288 and 1·5130) (*loc. cit.*, p. 308). This difference was not due solely to contamination with some other substance, since two individual ammonia derivatives, m. p. 135—137° and 153°, were prepared. Analyses and molecular-weight determinations appeared to indicate that the parent substances had the composition $C_{10}H_{14}O_3$, and this formula was provisionally adopted, although it was emphasised that evidence for the homogeneity of the substance analysed was lacking. We have now subjected the alkali-soluble fraction of this oil to a detailed investigation and have found that, depending upon conditions which remain to be determined, the substance is homogeneous and consists of either one or the other of two closely related ketones, which we have designated *angustione* and *dehydroangustione*. The constitution of the former has been rigidly established and we are able to suggest one for the latter which we regard as probably correct.

Angustione,* identical with the substance originally analysed, has now been found to have the composition $C_{11}H_{16}O_3$ and not $C_{10}H_{14}O_3$ and this has been substantiated by the preparation and analysis of a number of derivatives. The most characteristic of these is formed by the action of ammonia on angustione; this substance, m. p. 130—131°, for which we suggest the name *aminoangustione*, is not an ammonium salt but has the composition $C_{11}H_{17}O_2N$. The formation of a substance of this composition, together with the fact that a crystalline *copper* derivative, $C_{22}H_{30}O_6Cu$, m. p. 192—193°, can also be prepared, suggested that angustione was a β-diketone (compare Haas, J., 1906, **89**, 187). The existence of this structure in angustione was supported by the preparation of a *piperonylidene* derivative and by the properties of the products formed on interaction with hydroxylamine, phenylhydrazine, and *p*-bromophenylhydrazine, whereby an *anhydro-oxime*, *anhydrophenylhydrazone*, and *anhydro*-p-*bromophenylhydrazone* resulted. The presence of a pyrazole ring structure in the last derivative was proved by its reduction to a pyrazoline giving the well-known Knorr reaction. With semicarbazide an *anhydro-semicarbazone* was obtained, which, for reasons to be discussed later, we consider probably differs in constitution from the anhydro-phenylhydrazones.

In the course of his preliminary experiments Penfold (*loc. cit.*, p. 311) had observed that the ketone underwent extensive degradation when oxidised with potassium permanganate. We therefore examined the action of milder reagents. On digestion with ferric chloride in acetic acid–water solution an unsaturated crystalline substance, $C_9H_{12}O_2$, m. p. 159—160°, was obtained, which was

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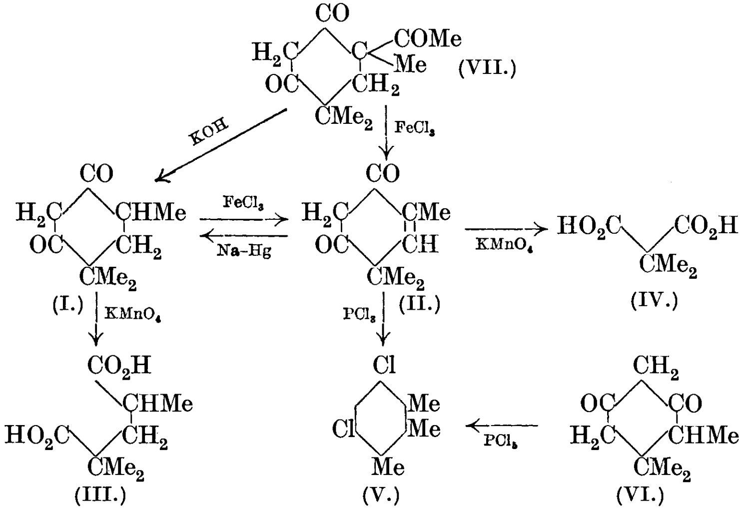
* Angustione probably occurs also in the essential oil from *Boronia thujona*, var. "A" (compare Penfold, *J. Proc. Roy. Soc. New South Wales*, 1929, **62**, 231).

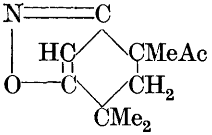
soluble in sodium bicarbonate solution and gave with ferric chloride an amethyst coloration. Oxidation of this substance with potassium permanganate gave dimethylmalonic acid, and on reduction with sodium amalgam addition of two hydrogen atoms occurred with the formation of a substance, $C_9H_{14}O_2$, m. p. 130—131°. This reduction product also gave an amethyst coloration with ferric chloride and was readily oxidised by potassium permanganate in alkaline solution, yielding ααγ-trimethylglutaric acid (III). The formation of this acid left no doubt that the substance, m. p. 130—131°, was the β-diketone, 1 : 1 : 3-*trimethyl*cyclo*hexane*-4 : 6-*dione* (I), and this view was confirmed by its oxidation with potassium hypobromite to the abovementioned substituted glutaric acid. It followed from this that the substance, m. p. 159—160°, which can also be prepared by the oxidation of 1 : 1 : 3-trimethyl*cyclo*hexane-4 : 6-dione with ferric chloride, must be the corresponding unsaturated β-diketone, 1 : 1 : 3-*trimethyl*-Δ^2-cyclo*hexene*-4 : 6-*dione* (II), which would on oxidation give dimethylmalonic acid (IV). Confirmation of this structure was obtained by the conversion of the unsaturated dione into 4 : 6-dichloro-1 : 2 : 3-trimethylbenzene (V) by the action of phosphorus trichloride, a reaction analogous to the preparation of this dichlorotrimethylbenzene by the action of phosphorus pentachloride on 1 : 1 : 2-trimethyl*cyclo*hexane-3 : 5-dione (VI) (Crossley, J., 1901, **79**, 144; Crossley and Hill, J., 1906, **89**, 881).

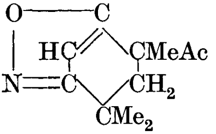


With the proof of the constitution of the product formed by the oxidation of angustione with ferric chloride and the indirect evidence that the saturated dione (I) was the primary product of the reaction, the relative positions of 9 out of the 11 carbon atoms were fixed together with those of 2 of the oxygen atoms. Although there was no direct evidence of the nature of the third oxygen, it appeared probable that the diketone contained the group Me–CO–, since if this were the case, the two remaining carbon atoms would also be accounted for. Angustione is not hydrolysed when boiled for some hours with aqueous potassium hydroxide (20%), but, when heated with an alcoholic solution of potassium hydroxide at 150° under pressure, it is degraded, yielding a mixture of 1 : 1 : 3-trimethyl-*cyclo*hexane-4 : 6-dione (I) and acetic acid. This reaction proceeds very smoothly and the yield is almost quantitative; there can therefore be no doubt that angustione must be the triketone represented by (VII). Unfortunately at this stage our material was exhausted and since later distillations have given only dehydroangustione, we have been unable to examine its reactions with potassium hypobromite and potassium permanganate. It is desirable here, before proceeding to consider the constitution of dehydroangustione, to refer to the constitution of some of the derivatives of angustione mentioned above.

The product which is obtained by the action of hydroxylamine on the ketone (p. 1193) is insoluble in alkali and gives no colour with ferric chloride; it dissolves, however, in strong mineral acids and is reprecipitated on dilution. It is probably therefore either *anhydroangustione-4-oxime* (VIII) or *anhydroangustione-6-oxime* (IX).

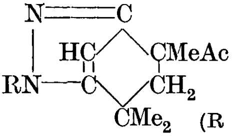
(VIII.)



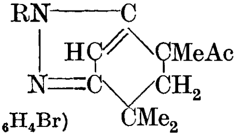


(IX.)

(X.)



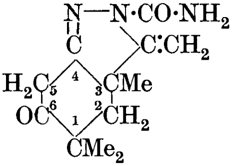
(R = Ph or p-C_6H_4Br)

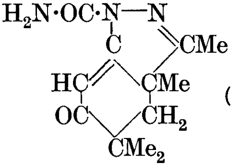


(XI.)

Similarly, two structures are possible for the products obtained by the action of phenylhydrazine and *p*-bromophenylhydrazine on angustione, namely, *anhydroangustione-4-phenylhydrazone* (X) or *anhydroangustione-6-phenylhydrazone* (XI). We have not attempted to determine the structure of these substances. As was mentioned above, the reaction with semicarbazide probably proceeds in a different manner. By the action of this reagent under suitable conditions (p. 1192) a substance is obtained which from its analysis is clearly an anhydro-derivative. It differs, however, very markedly in its properties from the anhydro-oxime and anhydro-phenylhydrazones. Although quite colourless when powdered, the crystals show a blue fluorescence and a solution of the substance in chloroform, from which it readily separates as a gel, has a marked blue colour. It is readily soluble in alkali and gives with ferric chloride an intense indigo-blue coloration. We would suggest that this derivative is either *anhydroangustione-4-semicarbazone* (XII) or

(XII.)



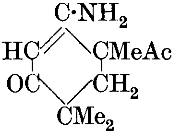


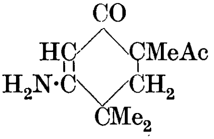
(XIII.)

anhydroangustione-ω-semicarbazone (XIII) : the presence of the potential enolic group in position 6 would account for the solubility in alkali and for the coloration with ferric chloride.

For aminoangustione, two formulæ (XIV) and (XV) are possible and in this case also we have no evidence which is correct.

(XIV.)

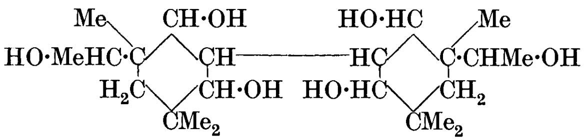




(XV.)

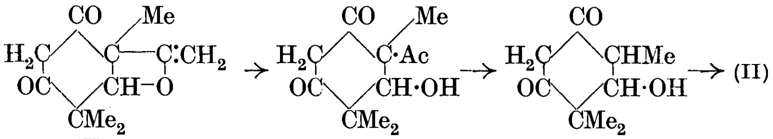
The reduction of angustione with sodium and alcohol (p. 1197) proceeds in a somewhat complex manner and we have only been able to identify two of the products : one is 1 : 1 : 3-trimethyl*cyclo*hexane-4 : 6-dione (I) resulting from the hydrolysis of the ketone, and the other, the main product of the reduction, is a bimolecular *alcohol*, $C_{22}H_{42}O_6$, probably (XVI).

(XVI.)

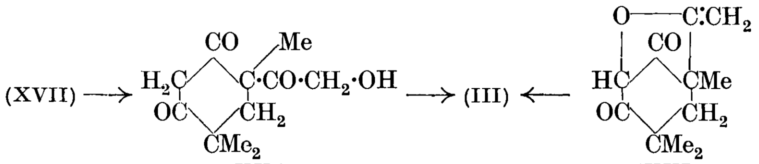


With aluminium amalgam an amorphous pinacol, $C_{22}H_{34}O_6$, m. p. 153°, is obtained, which has not been further studied.

The ketone yielding the crystalline *amino*-derivative, m. p. 151°, was at first thought to be isomeric with angustione, but careful analyses of the ketone itself and of a large number of its derivatives have shown it to contain two hydrogens less, having the composition $C_{11}H_{14}O_3$. Angustione and dehydroangustione are undoubtedly very closely related. Dehydroangustione is a β-diketone yielding an *anhydro-oxime*, *anhydro-semicarbazone*, and *anhydro*-p-*bromophenylhydrazone* ; further, it contains a reactive CH_2– group, since it forms a *piperonylidene* derivative. Unlike angustione, dehydroangustione is very resistant to the action of alkali and at 150° only slight hydrolysis occurs with the formation of 1 : 1 : 3-trimethyl-Δ^2-*cyclo*hexene-4 : 6-dione (II) : this substance is, however, obtained in excellent yield when the ketone is warmed on the water-bath with sulphuric acid (50%). Since the saturated dione (I) is not oxidised under these conditions, it is obviously not an intermediate product and it became probable, therefore, that the primary product in both reactions was a hydroxy*cyclo*hexanedione. A consideration of the various possibilities has led us to the conclusion that dehydroangustione is the β-oxide (XVII), in which case the degradation to 1 : 1 : 3-trimethyl-Δ^2-*cyclo*hexene-4 : 6-dione would proceed with the intermediate formation of (XVIII) and (XIX).


(XVII.) (XVIII.) (XIX.)

When dehydroangustione is oxidised with potassium permanganate, it yields a mixture of ααγ-trimethylglutaric acid and dimethylmalonic acid, the latter being formed in greater quantity. With potassium hypobromite l-*ααγ-trimethylglutaric acid* is obtained together with a substance having the composition $C_8H_{10}O_3$. The constitution of this substance has not been determined, but it is derived apparently from 1 : 1 : 3-trimethyl-Δ^2-*cyclo*hexene-4 : 6-dione, since preliminary experiments have shown that it can be prepared by the action of potassium hypobromite on this. The formation of ααγ-trimethylglutaric acid by the oxidation of dehydroangustione can be explained only if we assume that during the oxidation hydration occurs to some extent in the reverse direction, yielding the hydroxy-ketone (XX). We recognise that this reaction is unusual and when further material becomes available we propose to attempt to establish rigidly the constitution of dehydroangustione.

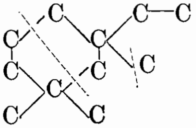

(XX.) (XXI.)

A substance having the alternative formula (XXI) would probably give a piperonylidene derivative and would undoubtedly yield ααγ-trimethylglutaric acid on oxidation, but its hydrolysis to the unsaturated dione involves obvious difficulties. Furthermore it would be unlikely to yield a copper derivative.

As is the case with angustione, two formulæ are possible for all the derivatives of dehydroangustione which have been prepared. It is, however, unnecessary to consider these in detail, as we have been unable to distinguish between them. Attention may perhaps be directed to the properties of the anhydro-semicarbazone which resemble closely those of anhydroangustionesemicarbazone. It has, however, been prepared in two isomeric forms, m. p. 138—139° and 173—175° (see p. 1199). On reduction with sodium and alcohol dehydroangustione yields the same products as angustione.

Mention has been made already of the fact that angustione and dehydroangustione differ in their physical constants and this difference is shown also in their molecular refractions, that of angustione being 54·09 and of dehydroangustione 54·5. If we accept formula (VII) for angustione, the molecular refraction calculated from the Eisenlohr 1910 values (Eisenlohr, "Spectrochemie Organischen Verbindungen," p. 48) is 50·59 and the ketone therefore shows the large molecular exaltation of 3·5 units. It is difficult to find a substance of similar structure to determine how far such an exaltation is abnormal, since the *cyclo*hexanediones are usually solids. A somewhat similar substance is 4-acetyl-1-methyl*cyclo*hexan-3-one, which was prepared by Léser (*Ann. Chim.*, 1902, **26**, 239). The molecular refraction of this ketone is 44·07 and the calculated value is 41·38, giving an exaltation of 2·79. Since this substance contains only two carbonyl groups, the exaltation is evidently of the same order. With dehydroangustione the molecular exaltation is even more marked, since the calculated value in this case is 49·53 if no allowance is made for the oxide ring. A high value is perhaps to be anticipated owing to the presence of the extracyclic ethylenic linkage. Any theoretical deductions from these values would be premature, but it appears justifiable to assume that a large molecular exaltation is to be expected in all *cyclo*hexanediones.

In angustione and dehydroangustione we have, so far as we are aware, the first instance of the occurrence in nature of β-diketones. Since they contain eleven carbon atoms, they are obviously not simple derivatives of isoprene, but the formulæ which have been



(XXII.)

assigned to them are built up from two isoprene nuclei, as will be seen by reference to the partial formula (XXII). Whether the ketones are formed by condensation with a molecule of formaldehyde or by the degradation of a substance containing fifteen carbon atoms, we have no means of determining. It is, however, of interest to note that they contain the "ionone" ring the presence of which has recently been shown to occur in carotin (Karrer and Helfenstein, *Helv. Chim. Acta*, 1929, **12**, 1142).

Although the two ketones described in this communication are the first natural β-diketones to be investigated in detail, the presence of substances having similar reactions has been observed in other eucalyptus oils. Of these the most important and most readily available is leptospermol, which occurs in the oil derived from the leaves and terminal branches of *Leptospermum flavescens* (Penfold, *J. Proc. Roy. Soc. New South Wales*, 1921, **45**, 51). This ketone is at present being studied by one of us (A. R. P.) and Dr. W. F. Short and it has been found to be a β-diketone.

EXPERIMENTAL.

Angustione.

The ketone, which had been separated from the oil by the method described previously (*loc. cit.*, p. 308), was purified either through its amino- or copper derivative. It was regenerated from the former by gentle warming with dilute aqueous alkali (10%), the temperature not being allowed to rise above 50° and the liberated ammonia being removed under diminished pressure. The solution was acidified with dilute sulphuric acid, and the ketone isolated by extraction with ether. From the copper derivative the ketone was obtained by the decomposition of an ethereal solution with dilute sulphuric acid. When purified by either of these methods *angustione* had b. p. 129°/15 mm., $d_{20^\circ}^{20^\circ}$ 1·089, $n_D^{20^\circ}$ 1·5137, $[\alpha]_{5461}$ −5·56°, $[R_L]_D$ 54·09 [Found *: (from amino-derivative) C, 67·2; H, 8·0; (from Cu derivative) C, 67·5; H, 8·1. $C_{11}H_{16}O_3$ requires C, 67·3; H, 8·1%].

Angustione is a colourless viscid oil with a faint and somewhat unpleasant smell; when pure it can be kept in a loosely stoppered bottle for months without becoming discoloured. It does not yield a crystalline bromide or react with hydrogen bromide in acetic acid solution at 0°, but with hydrogen iodide it gives an unstable crystalline derivative. It was recovered unchanged after digestion with acetic anhydride, and a benzoyl derivative could not be prepared. Its alcoholic solution gives with ferric chloride an intense orange-red coloration.

Aminoangustione (XIV or XV).—When angustione in light

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* The majority of the analyses recorded in this paper are microanalyses and where two analyses are given they were made with different preparations.

petroleum solution was treated with dry ammonia, an amorphous white solid, probably an ammonium salt, separated. This was readily soluble in water and when the aqueous solution was warmed the sparingly soluble amino-derivative was precipitated. This can however, be prepared more conveniently by the method described previously (*loc. cit.*, p. 309). It is best purified by crystallisation from *cyclo*hexane, in which it is somewhat sparingly soluble, and from which it separates in well-formed massive prisms, m. p. 130—131°. In absolute alcohol solution ($c = 0{\cdot}9163$, $l = 4$), $\alpha_{5461} - 0{\cdot}31°$ was observed, whence $[\alpha]_{5461} = -8{\cdot}6°$ (Found : C, 68·0, 67·9; H, 8·6, 8·8; N, 7·2. $C_{11}H_{17}O_2N$ requires C, 67·7; H, 8·7; N, 7·2%).

Aminoangustione is readily soluble in all the ordinary organic solvents with the exception of light petroleum, but it is very sparingly soluble in water, melting under this solvent when heated. It gives with ferric chloride the same coloration as the parent ketone. It is stable to mineral acids, but it is readily decomposed by hot alkalis with liberation of ammonia. It cannot apparently be acetylated by digestion with acetic anhydride. When it is treated in chloroform solution with bromine, a sparingly soluble oil separates, which crystallises rapidly in leaflets melting below 0°. This substance is probably a perbromide, since, on removal of the solvent under diminished pressure, a red gum remains from which aminoangustione can be recovered on trituration with ammonia.

The *copper* derivative of angustione was prepared most conveniently by the treatment of a light petroleum solution of the ketone with copper acetate, ammonia being added to neutralise the acetic acid liberated. The derivative, which was very readily soluble in ether and alcohol, crystallised from either benzene or dilute alcohol in blue prisms, m. p. 192—193° (Found : C, 58·5, 58·2; H, 6·5, 6·9; Cu, 14·0. $C_{22}H_{30}O_6Cu$ requires C, 58·2; H, 6·6; Cu, 14·0%). It does not react with methyl iodide in benzene solution.

Anhydroangustione-4(or ω)-*semicarbazone* (XII or XIII).—When a mixture of angustione (4 g.), semicarbazide hydrochloride (3·75 g.), dissolved in the minimum quantity of water, and sodium bicarbonate (2·8 g.) was kept for 3 days with occasional shaking, a viscid oil formed. The solution was cleared by the addition of alcohol and after 2 days the crystalline solid which had separated was collected; a further quantity was obtained by addition of water to the filtrate (yield, 3·2 g.). After trituration with ether, which removed a small quantity of a yellow impurity, the *semicarbazone* was recrystallised by solution in hot chloroform and addition of an equal volume of hot benzene. If allowed to cool slowly, the semicarbazone crystallised in soft serrated needles, m. p. 145° (decomp.), but if the solution was rapidly cooled, a gel was obtained : the same phenomenon was observed when a hot concentrated chloroform solution was rapidly cooled. The solution showed a marked blue fluorescence (Found : C, 61·6 ; H, 7·4. $C_{12}H_{17}O_2N_3$ requires C, 61·3 ; H, 7·2%). The semicarbazone is readily soluble in water, giving a colourless solution, which on boiling clouds with the separation of an oil; it is soluble in alkali and its alcoholic solution gives with ferric chloride an intense indigo-blue coloration. In aqueous solution it reduces an ammoniacal solution of silver oxide with the formation of a silver mirror.

Anhydroangustione-4(or 6)-*phenylhydrazone* (X or XI).—This derivative was obtained in a somewhat poor yield when an alcoholic solution of the ketone was kept for some days with an excess of phenylhydrazine acetate. It crystallised from alcohol, in which it was readily soluble, in small plates, m. p. 119—120° (Found : C, 76·0 ; H, 7·4. $C_{17}H_{20}ON_2$ requires C, 76·1 ; H, 7·5%).

Anhydroangustione-4(or 6)-p-*bromophenylhydrazone* (X or XI) crystallised from alcohol, in which it was somewhat sparingly soluble, in faintly brown prisms, m. p. 191° (Found : C, 58·5 ; H, 5·3 ; Br, 23·1. $C_{17}H_{19}ON_2Br$ requires C, 58·8 ; H, 5·5 ; Br, 23·0%). The *p*-bromophenylhydrazone was insoluble in alkali and gave no colour with ferric chloride in alcoholic solution. When it was reduced with sodium and alcohol, a substance was obtained which gave Knorr's pyrazoline reaction.

Anhydroangustione-4(or 6)-*oxime* (VIII or IX).—A mixture of angustione (9 g.), hydroxylamine hydrochloride (3·5 g.), and sodium acetate (4·1 g.) in alcohol (35 c.c.) was heated on the water-bath for 2 hours. After about 15 minutes a blue colour developed which disappeared on further heating. The reaction mixture was distilled in steam, the volatile oil extracted with ether, the ether dried and evaporated, and the residual oil distilled under diminished pressure (22 mm.) : the whole boiled at 150—152°. The colourless viscid oil, which had a strong basic smell, partly crystallised on keeping. The solid was collected, drained on porous porcelain, and recrystallised from dilute methyl alcohol; it was then obtained in needles melting not quite sharply at 41—43° (Found : C, 68·0 ; H, 7·6. $C_{11}H_{15}O_2N$ requires C, 68·4 ; H, 7·8%). The *anhydro-oxime* was insoluble in alkali but readily soluble in concentrated hydrochloric acid, being reprecipitated on dilution. It did not give a crystalline picrate or chloroplatinate.

Piperonylideneangustione.—To a mixture of equimolecular proportions of angustione and piperonal dissolved in alcohol, piperidine (one drop) was added, and the solution heated to boiling. After some days a yellow crystalline solid had been deposited ; it crystallised from alcohol, in which it was very sparingly soluble, in bright sulphur-yellow, soft needles, m. p. 166—167° (Found: C, 69·6; H, 5·9. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·0%).

Oxidation of Angustione.—(A) *With ferric chloride.* 1 : 1 : 3-*Trimethyl*-Δ^2-cyclo*hexene*-4 : 6-*dione* (II). A mixture of the ketone (15 g.), ferric chloride (40 g.), acetic acid (60 c.c.), and water (130 c.c.) was boiled for 8 hours and, after remaining over-night, distilled in steam until the aqueous distillate no longer deposited a solid on saturation with ammonium sulphate. A red resinous solid remained in the distillation flask. The distillate, after saturation with ammonium sulphate, was extracted with ether, the extract dried over sodium sulphate, and the solvent evaporated; the residual red oil was warmed under diminished pressure until free from acetic acid and the crystalline solid which separated was mixed with light petroleum (b. p. 40—60°) and collected. The filtrate on distillation under diminished pressure (11 mm.) boiled at 125—135° and gave an oil from which, on cooling, a further quantity of solid could be obtained, but which consisted mainly of unchanged angustione.

1 : 1 : 3-*Trimethyl*-Δ^2-cyclo*hexene*-4 : 6-*dione* crystallised from dilute alcohol in long needles or from light petroleum–benzene in soft needles, m. p. 159—160° (Found: C, 71·0; H, 7·8. $C_9H_{12}O_2$ requires C, 71·1; H, 7·9%). It was readily soluble in the ordinary organic solvents with the exception of ether, in which it was somewhat sparingly soluble, and of light petroleum, in which it was very sparingly soluble. It was somewhat soluble in hot water and the solution gave with ferric chloride an amethyst coloration. It was not readily attacked by concentrated sulphuric acid and could be heated with this reagent to 110° without marked discoloration. In chloroform solution the dione rapidly absorbed bromine with the liberation of hydrogen bromide and on evaporation of the solvent 5-*bromo*-1 : 1 : 3-*trimethyl*-Δ^2-cyclo*hexene*-4 : 6-*dione* remained, which crystallised from dilute alcohol in iridescent prisms, m. p. 126—127° (Found: C, 46·9; H, 4·8; Br, 34·3. $C_9H_{11}O_2Br$ requires C, 46·7; H, 4·7; Br, 34·6%).

When the dione was warmed with phosphorus trichloride, evolution of hydrogen chloride occurred, and a pasty solid separated on cooling. This was dissolved in benzene, and the solution decanted from phosphorous acid, washed with alkali, and evaporated. The residual solid crystallised from dilute acetone in glistening leaflets, m. p. 77—78° (Crossley and Hills, *loc. cit.*, give 76·5°), and was evidently 4 : 6-dichloro-1 : 2 : 3-trimethylbenzene (V) (Found: C, 57·3; H, 5·4. Calc.: C, 57·1; H, 5·3%).

When an alcoholic solution of equimolecular proportions of the dione and piperonal was treated with a drop of piperidine and warmed for a few minutes, a crystalline solid was obtained. This separated from alcohol in prisms, decomp. 208—210°. Although the *substance* itself was quite colourless, it dissolved in hot alcohol to yield a bright yellow solution, the colour disappearing on cooling. The constitution of this substance was not determined, but it consists apparently of two molecules of the dione combined with one of piperonal and analysis indicates that it is a reduction product (compare p. 1196) (Found: C, 70·9; H, 7·5. $C_{26}H_{32}O_6$ requires C, 70·9; H, 7·3%).

(B) *With potassium ferricyanide.* A mixture of the ketone (13 g.), potassium ferricyanide (176 g.), water (400 c.c.), and potassium hydroxide solution (10%; 600 c.c.) was gently boiled for 3 hours. The cooled solution was acidified, saturated with ammonium sulphate, and extracted with ether. After removal of the solvent the residual oil was distilled in steam; a crystalline solid passed over, leaving a red resinous residue (3·7 g.). The distillate, after saturation with ammonium sulphate, was extracted with ether, and the extract dried and evaporated. The residue, which crystallised, was drained on porous porcelain to remove some adhering oil and recrystallised from dilute alcohol; it was then obtained in soft needles which were apparently homogeneous and melted sharply at 141°. Specimens from two distinct preparations were analysed and showed the substance to be a mixture of 1 : 1 : 3-trimethyl*cyclo*hexane-4 : 6-dione and 1 : 1 : 3-trimethyl-Δ^2-*cyclo*hexene-4 : 6-dione (Found: C, 70·4, 70·5; H, 8·4, 8·7%). This was confirmed by bromination of the mixture, the bromide, m. p. 126—127° (p. 1194), being readily obtained, and by reduction with sodium amalgam, whereby it was converted quantitatively into the saturated dione, m. p. 130—131° (compare p. 1196). The 1 : 1 : 3-trimethyl*cyclo*hexane-4 : 6-dione present in the mixture was optically active; in alcoholic solution, $c = 5{\cdot}453$, $l = 2$, $\alpha_{5461} + 0{\cdot}12°$, $[\alpha]_{5461} + 1{\cdot}04°$.

Oxidation of 1 : 1 : 3-*Trimethyl*-Δ^2-cyclo*hexene*-4 : 6-*dione*.—The dione (2 g.), dissolved in sodium carbonate solution, was oxidised with potassium permanganate (2·5%) at 0°, a current of carbon dioxide being passed through the solution. On completion of the oxidation (250 c.c. $KMnO_4$) the manganese dioxide sludge was separated, and the liquid evaporated to a small bulk in a current of carbon dioxide. The acidified solution was repeatedly extracted with ether, the solvent dried and evaporated, and the residue, which immediately solidified, crystallised from hot water; it separated in glistening tablets, decomp. 185—186°. This decomposition point was not depressed on admixture with an authentic specimen of dimethylmalonic acid (Found: C, 45·7; H, 5·8. Calc.: C, 45·4; H, 6·1%).

Reduction of 1 : 1 : 3-*Trimethyl*-Δ^2-cyclo*hexene*-4 : 6-*dione*. 1 : 1 : 3-*Trimethyl*cyclo*hexane*-4 : 6-*dione* (I).—The unsaturated dione (0·5 g.), dissolved in sodium carbonate solution, was reduced with sodium amalgam (2·5%; 80 g.), a current of carbon dioxide being passed through the solution during the reaction. After completion the aqueous solution was concentrated and acidified with dilute sulphuric acid and the solid (0·35 g.) which separated was collected and recrystallised from light petroleum (b. p. 60—80°); it was then obtained in glistening prisms, m. p. 130—131° (Found: C, 70·2; H, 8·9. $C_9H_{14}O_2$ requires C, 70·1; H, 9·1%). 1 : 1 : 3-*Trimethyl*cyclo*hexane*-4 : 6-*dione* is readily soluble in all the ordinary organic solvents with the exception of light petroleum; it is somewhat sparingly soluble in water and its solution gives with ferric chloride an amethyst coloration. In chloroform solution it readily absorbs bromine with evolution of hydrogen bromide and on removal of the solvent a gum remains which cannot be induced to crystallise.

With piperonal the saturated dione reacts in an exactly analogous manner to the unsaturated dione (p. 1195) to yield a *substance* crystallising from alcohol in soft glistening prisms, m. p. 192—193°. Its solution in hot alcohol is bright yellow, although the substance itself is colourless. Analysis appears to show that it is formed by the interaction of two molecules of the dione with one of piperonal with loss of water and addition of four atoms of hydrogen (Found: C, 70·6; H, 8·3. $C_{26}H_{36}O_6$ requires C, 70·3; H, 8·1%).

Oxidation of 1 : 1 : 3-*Trimethyl*cyclo*hexane*-4 : 6-*dione*.—(A) *With ferric chloride.* A mixture of the dione (1 g.), ferric chloride (4 g.), water (15 c.c.), and acetic acid (3 c.c.) was boiled for 4 hours and then distilled in steam; an oil passed over, which crystallised, and a red resin remained in the distillation flask. After saturation of the distillate with ammonium sulphate the solid which separated was collected and recrystallised from dilute alcohol, forming needles, m. p. 158—159°. It was identified as 1 : 1 : 3-trimethyl-Δ^2-*cyclo*hexene-4 : 6-dione by the method of mixed melting point and by the preparation of the bromide, m. p. 126—127°.

(B) *With potassium permanganate.* The dione (4 g.), dissolved in sodium carbonate solution, was treated at 0° with potassium permanganate (2·5%), a current of carbon dioxide being passed through the solution during the oxidation. On completion of the reaction (370 c.c. $KMnO_4$) the manganese dioxide sludge was removed, and the filtrate evaporated to a small bulk, acidified, and extracted with ether. On removal of the solvent an oil was obtained which partly crystallised. The solid was separated by solution in hot light petroleum (b. p. 40—60°), in which the oil was insoluble, and it was finally crystallised from water, from which it was obtained in leaflets, m. p. 97° (Found: C, 55·0; H, 8·1. Calc.: C, 55·1; H, 8·0%). This acid was identical (mixed m. p.) with the acid prepared by oxidation of the dione with potassium hypobromite (see below) and consisted of $\alpha\alpha\gamma$-trimethylglutaric acid.

(C) *With potassium hypobromite.* A solution of the dione (2 g.) in potassium hydroxide solution (10 c.c.; KOH, 1 g.) was added all at once to a potassium hypobromite solution (Br_2, 6·5 g.; KOH, 6 g.; H_2O, 30 c.c.); bromoform separated immediately and the temperature rose to about 30°. After 1 hour, the bromoform was drawn off, the excess of hypobromite removed with sulphur dioxide, and the solution concentrated, acidified, and extracted with ether. On removal of the solvent a crystalline solid (2·2 g.) remained, m. p. 95—97°. It crystallised from water in leaflets, m. p. 97° (not depressed by admixture with acid from B). The identity of this acid with $\alpha\alpha\gamma$-trimethylglutaric acid was confirmed by the preparation of the anhydride, needles, m. p. 95°, and the anilide, needles, m. p. 165° (Auwers and Meyer, *Ber.*, 1890, **23**, 305; Auwers, *Annalen*, 1896, **292**, 224, give 95—96° and 165° respectively). The anilide was analysed (Found: N, 5·6. Calc.: N, 5·6%).

Action of Potassium Hydroxide on Angustione.—A mixture of the ketone (11·7 g.), potassium hydroxide (7 g.), water (6 c.c.), and alcohol (14 c.c.) was heated at 150° in a sealed tube for 3 hours. The liquid, which contained a crystalline potassium salt in suspension, was diluted with water, the alcohol removed on the water-bath, and the cold solution acidified; a crystalline solid mixed with some oil then separated. The solid (4·1 g.) was collected and washed with light petroleum (b. p. 40—60°) to remove the oil; when recrystallised from petroleum (b. p. 60—80°), it separated in glistening prismatic needles, m. p. 131—132° (Found: C, 70·4; H, 8·8. $C_9H_{14}O_2$ requires C, 70·1; H, 9·1%). This substance was identified as 1 : 1 : 3-trimethyl*cyclo*hexane-4 : 6-dione by the preparation of the piperonal derivative, m. p. 192—193°.

The filtrate from which the dione had been separated was extracted with ether and, after being made alkaline with sodium carbonate solution, evaporated to dryness on the water-bath. The residual salts were extracted with absolute alcohol, and the alcohol evaporated after filtration. The crystalline residue consisted essentially of sodium acetate, since on admixture with alcohol and sulphuric acid ethyl acetate was formed, whilst on the addition of silver nitrate to an aqueous solution silver acetate was precipitated. After recrystallisation from hot water the silver salt was analysed (Found: Ag, 64·9. Calc.: Ag, 64·7%).

Reduction of Angustione with Sodium and Alcohol.—To a solution of the ketone (20 g.) in gently boiling alcohol (300 c.c.), sodium

(30 g.) was gradually added. After all the sodium had dissolved, steam was passed through the solution; after removal of the alcohol, a very pungent-smelling oil (A) distilled. The residue in the flask consisted of a viscid oil (B), which partly solidified.

The oil (A) was dissolved in ether, dried, recovered (6 g.), and distilled under diminished pressure (12 mm.). The first fraction, a mobile pungent oil, distilled mainly at about 90°, and the remainder, which was very viscid, at 140—150°. All attempts to prepare crystalline derivatives of these substances have been unsuccessful and they have not been identified.

The residue (B) was shaken with a little ether, and the solid (4·1 g.) collected and recrystallised from ethyl acetate, in which it was somewhat sparingly soluble. The *alcohol* crystallised in soft needles, m. p. 196—197°, which were lævorotatory in alcohol, $c = 0{\cdot}4467$, $l = 2$, α_{5461} $-0{\cdot}09°$, $[\alpha]_{5461}$ $-10{\cdot}23°$ [Found: C, 65·3; H, 10·7; *M* (Rast), 406. $C_{22}H_{42}O_6$ requires C, 65·6; H, 10·4%; *M*, 404].

The alkaline solution from which the alcohol had been separated was acidified; the oil deposited partly crystallised. After draining on porous porcelain, the solid was recrystallised from light petroleum (b. p. 60—80°), separating in prismatic needles, m. p. 130—131°, and was identified as 1 : 1 : 3-trimethyl*cyclo*hexane-4 : 6-dione (Found: C, 70·3; H, 9·1. Calc.: C, 70·1; H, 8·7%).

Dehydroangustione (XVII).

Dehydroangustione, after purification through its copper derivative, had b. p. 126—127°/11 mm., $d_{20°}^{20{\cdot}5°}$ 1·103, $n_{\mathrm{D}}^{20{\cdot}5°}$ 1·5255, $[\alpha]_{5461}$ $-2{\cdot}03°$, $[R_L]_{\mathrm{D}}$ 54·5 (Found: C, 67·9; H, 7·5. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·2%). It gives in alcoholic solution with ferric chloride the same orange-red coloration as angustione. The following derivatives were prepared by methods identical with those used for the preparation of the analogous derivatives of angustione.

Aminodehydroangustione crystallised from *cyclo*hexane in glistening prismatic needles or from much hot water in leaflets, m. p. 151°. It was lævorotatory in alcoholic solution, $c = 3{\cdot}98$, $l = 2$, α_{5461} $-0{\cdot}41°$, $[\alpha]_{5461}$ $-1{\cdot}76°$ (Found: C, 68·3, 68·2; H, 8·0, 7·8. $C_{11}H_{15}O_2N$ requires C, 68·4; H, 7·8%).

Aminodehydroangustione cannot be acetylated, being recovered unchanged after prolonged digestion with acetic anhydride. When kept for some days in alcoholic solution with semicarbazide acetate, it is converted into anhydrodehydroangustionesemicarbazone.

The *copper* derivative crystallised from benzene, in which it was somewhat more soluble than the corresponding derivative of angustione, in blue needles, m. p. 188—190° (Found: 58·8, 58·5; H, 6·0, 6·0. $C_{22}H_{26}O_6Cu$ requires C, 58·7; H, 5·8%).

Anhydrodehydroangustione-4(or 6)-*semicarbazone* was obtained in two forms. The α-semicarbazone crystallised from chloroform–benzene in prismatic needles, decomp. 138—139° (Found : N, 17·7. $C_{12}H_{15}O_2N_3$ requires N, 18·0%). When a hot concentrated solution of the α-semicarbazone was rapidly cooled, a gel was obtained which crystallised on gentle warming. The solid, m. p. 164°, obtained was now very sparingly soluble in chloroform and quite colourless, no longer showing the blue fluorescence of the α-semicarbazone. The β-*semicarbazone* crystallised from dilute alcohol in small prisms, decomp. 173—175° (Found : C, 57·8; H, 6·9. $C_{12}H_{15}O_2N_3,H_2O$ * requires C, 57·4; H, 6·8%). Both semicarbazones gave the same deep blue colour with ferric chloride.

Anhydrodehydroangustione-4(or 6)-p-*bromophenylhydrazone* crystallised from alcohol in almost colourless prisms, m. p. 247—248° (Found : C, 59·1; H, 5·0. $C_{17}H_{17}ON_2Br$ requires C, 59·1; H, 4·9%).

Anhydrodehydroangustione-4(or 6)-*oxime*. A mixture of the ketone (2·1 g.), hydroxylamine hydrochloride (2·5 g.), and sodium hydroxide (1·5 g. in water, 5 c.c.) with sufficient alcohol to give a clear solution was kept for 3 hours and then diluted with water. The *anhydro-oxime* thus precipitated crystallised from dilute alcohol in glistening needles, m. p. 79—80°. It was dextrorotatory in alcoholic solution : $c = 3{\cdot}09$, $l = 2$, $\alpha_{5461} + 0{\cdot}15°$, $[\alpha]_{5461} + 4{\cdot}95°$ (Found : C, 69·1; H, 7·0. $C_{11}H_{13}O_2N$ requires C, 69·1; H, 6·8%).

Piperonylidenedehydroangustione separated from alcohol in yellow needles, m. p. 169—170° (Found : C, 70·0; H, 5·8. $C_{19}H_{18}O_5$ requires C, 69·6; H, 5·5%).

Oxidation of Dehydroangustione.—(A) *With potassium permanganate*. A mixture of the ketone (5 c.c.) and acetone (200 c.c.) was cooled to 0°, and finely powdered potassium permanganate gradually added. After the addition of 6 g. the oxidation became very slow; water (20 c.c.) was added and a further quantity of permanganate (10 g.). After the whole had remained over-night in the ice-box, the manganese dioxide sludge was separated and thoroughly washed with boiling water and the aqueous extract was evaporated to a small bulk in a current of carbon dioxide. The acetone on evaporation left a brown liquid, which was added to the main extract. The aqueous solution was acidified and extracted with ether (10 times), the extract dried, and the solvent evaporated. The residual oil, which had a strong odour of acetic acid, slowly crystallised when kept in a vacuum over potassium hydroxide. The solid was mixed with acetyl chloride and warmed on the water-bath for 2

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* Sufficient material was not available to determine whether this addition of water was constitutional.

hours, and the excess of acetyl chloride removed. When the residual solid was triturated with ice-cold sodium bicarbonate solution, a portion dissolved. The residue, $\alpha\alpha\gamma$-trimethylglutaric anhydride, m. p. 95°, was dissolved in boiling water; on cooling, $\alpha\alpha\gamma$-trimethylglutaric acid crystallised in leaflets, m. p. 97° (Found : C, 55·3; H, 8·0. Calc.: C, 55·1; H, 8·0%).

The sodium bicarbonate solution was acidified and extracted with ether; the solid which remained after removal of the solvent crystallised from water in tablets, decomp. 185—186°, and was identified as dimethylmalonic acid by the method of mixed melting point.

(B) *With potassium hypobromite.* Dehydroangustione (9·8 g.) in potassium hydroxide solution (40 c.c.; KOH, 3·7 g.) was added to a solution of potassium hypobromite (KOH, 17 g.; Br_2, 24 g.; H_2O, 100 c.c.); bromoform was immediately deposited with considerable rise in temperature. After 1 hour, the excess of the hypobromite was removed with sulphur dioxide and the bromoform (4—5 g.) separated. The solution was acidified, saturated with ammonium sulphate, and extracted with ether (10 times) and the ether was dried and evaporated. The residual oil was distilled in steam and the distillate, which contained a heavy oil, was saturated with ammonium sulphate and extracted with ether. The oil (5 g.) left on removal of the solvent was distilled under diminished pressure (11 mm.); it boiled at 125—130° and partly crystallised on keeping. The solid was collected, washed with light petroleum, and recrystallised from this solvent, separating in long prismatic needles, m. p. 88·5° (Found: C, 62·3; H, 6·6. $C_8H_{10}O_3$ requires C, 62·3; H, 6·5%). This *substance*, which, as has already been mentioned, has not been identified, gives no colour with ferric chloride in aqueous solution.

The filtrate from which the substance, m. p. 88·5°, had been removed did not crystallise on keeping and was found to consist essentially of unchanged dehydroangustione.

The aqueous residue from the steam distillation was made alkaline, concentrated, acidified, and extracted with ether. On evaporation of the solvent an oil was obtained which partly crystallised. On trituration with hot light petroleum the greater part dissolved, leaving a red resinous residue; evaporation of the light petroleum left colourless crystals which separated from hot water in glistening leaflets, m. p. 91—92°. There can be no doubt that this acid was *l-$\alpha\alpha\gamma$-trimethylglutaric acid*; in water, $c = 1{\cdot}123$, $l = 2$, α_{5461} $-0{\cdot}19°$, $[\alpha]_{5461}$ $-16{\cdot}9°$ (Found: C, 55·2; H, 8·0. $C_8H_{14}O_4$ requires C, 55·1; H, 8·0%).

Action of Potassium Hydroxide on Dehydroangustione.—Dehydroangustione was heated with an alcoholic solution of potassium hydroxide under the same conditions as those used for the hydrolysis of angustione. On completion of the reaction the tube contained a sparingly soluble potassium salt which crystallised in prisms. The reaction product, which was an oil, was dissolved in light petroleum (b. p. 40—60°) and kept for some days in the ice-box; the crystalline solid (yield, 0·3 g. from 10 g.) that had separated was recrystallised from light petroleum–benzene; it separated in felted needles, m. p. 159—160°, and was identified as 1 : 1 : 3-trimethyl-Δ^2-*cyclo*hexene-4 : 6-dione by the method of mixed melting point and by analysis (Found: C, 71·2; H, 8·0. Calc.: C, 71·1; H, 7·9%).

Action of Sulphuric Acid on Dehydroangustione.—A mixture of the ketone (5 c.c.), sulphuric acid (10 c.c.), and water (10 c.c.) was heated on the water-bath for 8 hours. The oil slowly dissolved and a deep red colour developed, some sulphur dioxide being liberated. The cooled solution was diluted with water and the solid which separated (3·4 g.) was recrystallised from dilute alcohol; it was obtained in needles, m. p. 159—160°, and was identified as 1 : 1 : 3-trimethyl-Δ^2-*cyclo*hexene-4 : 6-dione. The hydrolysis can also be effected with dilute sulphuric acid (10%), but owing to the sparing solubility of the ketone the time required is very much longer.

Reduction of Dehydroangustione.—Dehydroangustione was reduced with sodium and alcohol in the same manner as angustione (p. 1197). The products obtained were identical, but in this case a considerable quantity of a viscid red oil was also formed. The yields of the various products from 20 g. of ketone were: dione, 2 g.; bimolecular alcohol, 3 g.; oil volatile in steam, 5 g.

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