2-*Acyl Derivatives of Cyclic* 1 : 3-*Diones. Part II.** *The Structures of Angustione and Dehydroangustione.*

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Angustione has been identified by synthesis as 2-acetyl-4 : 4 : 6-trimethyl*cyclo*hexane-1 : 3-dione. Further evidence for the structure of dehydroangustione has been obtained by ozonolysis.

The ketones angustione and dehydroangustione which occur in the essential oil of *Backhousia angustifolia* have been assigned the structures (I) and (II) respectively (Gibson, Penfold, and Simonsen, *J.*, 1930, 1184; Cahn, Gibson, Penfold, and Simonsen, *J.*, 1931, 286). Although these structures are based on extensive degradative studies there is no decisive evidence supporting them. In view of their unusual features we have sought unequivocal evidence.

The following properties have a particular bearing on the structural problem. Both angustione, $C_{11}H_{16}O_3$, and dehydroangustione, $C_{11}H_{14}O_3$, form copper chelate complexes, give anhydro-derivatives with hydroxylamine, substituted hydrazines, and ammonia, and condense with piperonaldehyde. Alkaline hydrolysis of angustione leads to a good yield of a compound $C_9H_{14}O_2$, formulated as 4 : 4 : 6-trimethyl*cyclo*hexane-1 : 3-dione (III) on the basis of oxidation experiments. Dehydroangustione is less susceptible to alkali but is hydrolysed by sulphuric acid to acetic acid and a β-diketone, $C_9H_{12}O_2$. As this diketone may be prepared from the diketone $C_9H_{14}O_2$ by oxidation with ferric chloride and gives $\alpha\alpha\gamma$-trimethylglutaconic acid on oxidation with sodium hypobromite, it is formulated as 4 : 6 : 6-trimethyl*cyclo*hex-4-ene-1 : 3-dione (IV). Dehydroangustione is converted quantitatively into angustione by catalytic hydrogenation.

Although structures (I) and (II) may be used to interpret the majority of the reactions

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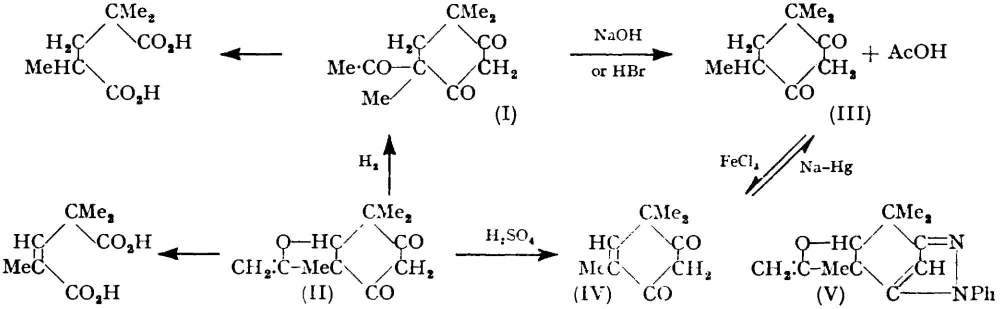
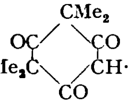
* The paper, *J.*, 1948, 50, is regarded as Part I.

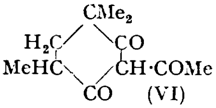
of angustione and dehydroangustione they are not entirely applicable. The compound as (II) should not give a chloroform-soluble copper derivative or a ferric chloride colour in absolute alcohol. Such *cyclo*hexane-1 : 3-diones are "*trans*-fixed" (Eistert and Riess, *Chem. Ber.*, 1954, **87**, 92, 109; Henecka, "Chemie der β-Dicarbonylverbindungen," Springer-Verlag, Berlin, 1950, p. 279) and unable to form chelate complexes. We have confirmed that the related compound 4 : 4 : 6-trimethyl*cyclo*hexane-1 : 3-dione (III) gives no chelate derivatives with iron and copper salts. The structure (I) for angustione is not excluded in this way as there is the possibility of complex formation involving the enolised *cyclo*hexane-1 : 3-dione system and the acetyl grouping.

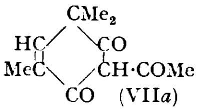


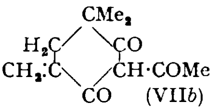
Also, the compound represented by (II) would not give anhydro-derivatives with hydroxylamine and substituted hydrazines. By Bredt's rule, such a bridged structure as (V) is excluded. In fact, the related compound dimedone gives normal mono- and di-oximes and hydrazones (Vorlander, *Annalen*, 1897, **294**, 253).

If angustione and dehydroangustione are assigned the structures (VI) and (VII*a* or *b*) respectively, there is no difficulty in accounting for all their properties. The formation of metal chelate complexes and anhydro-hydrazones has been observed (Briggs, Hassall, and Short, *J.*, 1945, 706) for the closely related compound leptospermone (VIII). The hydrolysis and oxidation reactions are readily explained in terms of the new structures. Structures (VI) and (VII*b*) have been suggested independently by Birch (*J.*, 1951, 3026), who pointed out that the nature of the condensation products formed with piperonaldehyde favoured the new structures.


(VIII)


(VI)


(VII*a*)


(VII*b*)

Evidence in support of structure (VI) for angustione has been obtained from the consideration of ultraviolet absorption spectra and by synthesis. Simple *cyclo*hexane-1 : 3-diones, in ethanol, regularly give a single strong absorption peak at approximately 255 mμ. 2-Acyl*cyclo*hexane-1 : 3-diones under these conditions are characterised by two maxima, in the region of 230 and 275 mμ. The results in the Table indicate that angustione behaves

	$\lambda_{max.}$ (mμ)	ε	Ref.
4-Methyl*cyclo*hexane-1 : 3-dione	255	12,600	1
5 : 5-Dimethyl*cyclo*hexane-1 : 3-dione	258	12,000	2
4 : 4 : 6-Trimethyl*cyclo*hexane-1 : 3-dione	255	13,200	
4 : 4 : 6 : 6-Tetramethyl-2-*iso*valeryl*cyclo*hexane-1 : 3-dione *	234	8,920	
	281	10,800	
2-Acetyl-5 : 5-dimethyl*cyclo*hexane-1 : 3-dione	231	10,000	3
	277	10,000	
2-Acetyl*cyclo*hexane-1 : 3-dione	235	14,700	4
	275	11,600	
Angustione	233	13,500	
	276	13,500	

* In *cyclo*hexane; the others in ethanol.

Refs.: 1, Meek, Turnbull, and Wilson, *J.*, 1953, 812. 2, Woodward and Blout, *J. Amer. Chem. Soc.*, 1943, **65**, 562. 3, Birch, *loc. cit.* 4, Smith, *J.*, 1953, 803.

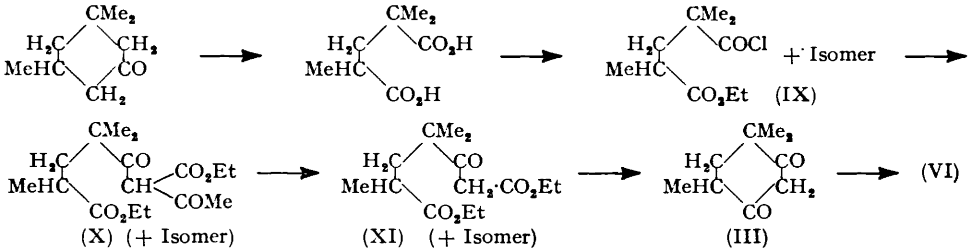
as a typical 2-acyl*cyclo*hexane-1 : 3-dione. The similarity of the ultraviolet absorption spectra of the amino-derivatives of angustione [$\lambda_{max.}$ 253, 290 mμ (ε 14,500, 14,500)] and of 2-acetyl-5 : 5-dimethyl*cyclo*hexane-1 : 3-dione [$\lambda_{max.}$ 252, 288 mμ (ε 15,850, 15,850)] provides further evidence of the presence of the 2-acyl-1 : 3-dione structure in angustione.

(±)-4 : 4 : 6-Trimethyl*cyclo*hexane-1 : 3-dione (III) has been prepared by an unambiguous route and found to be identical with the product obtained from angustione on alkaline hydrolysis. When the dione is acetylated under conditions which have been applied for the introduction of a 2-acetyl group into related *cyclo*hexane-1 : 3-dione derivatives (Dieckmann and Stein, *Ber.*, 1904, **37**, 3380), (±)-angustione is formed.

The synthesis of (±)-4 : 4 : 6-trimethyl*cyclo*hexane-1 : 3-dione involved condensation of ethyl sodioacetoacetate with the monoethyl ester chloride (IX) of ααγ-trimethylglutaric acid to yield 3 : 7-diethoxycarbonyl-5 : 5-dimethyloctan-2 : 4-dione (X) which with sodium methoxide in methanol at room temperature (Hunsdiecker, *Ber.*, 1942, **75**, 447) gave the monoketo-ester (XI). Cyclisation with sodium methoxide, followed by hydrolysis, gave 4 : 4 : 6-trimethyl*cyclo*hexane-1 : 3-dione (III). Isomers of the esters (IX), (X), and (XI) were no doubt formed in each case: no attempt was made to separate them as they lead to the same 1 : 3-dione (III).

The definition of the structure of angustione and the degradations which have been described lead to the alternative formulations (VII*a* and *b*) for dehydroangustione.

We have carried out ozonolyses in an attempt to establish one of these structures or, in the event of a mixture of isomers being involved (cf. α- and γ-irone; α- and β-citronellol; α- and β-geraniol; etc.), to obtain an indication of the proportion of (VII*b*) in the mixture. From dehydroangustione and aminodehydroangustione the maximum yield of formaldehyde was 6%. Although this result makes it very unlikely that a high concentration of (VII*b*) is present it cannot be used as an accurate measure of the proportion in dehydroangustione. There are various examples of low yields of formaldehyde from the ozonolysis of compounds containing CH_2:CRR′ groupings (Ruzicka, Seidel, Schinz, and Tavel, *Helv. Chim. Acta.*, 1948, **31**, 257). Also, there are cases where formaldehyde has been obtained from compounds which do not contain this group (Clemo and McDonald, *J.*, 1935, 1295; Karrer and Kebrle, *Helv. Chim. Acta*, 1952, **35**, 862).



Birch (*loc. cit.*) favours the structure (VII*b*) in view of the presence, in the infrared absorption spectrum of dehydroangustione, of peaks at 11·3 μ (888 cm.$^{-1}$) * and 6·1 μ (1640 cm.$^{-1}$). However, the fact that saturated hydrocarbons such as 3-ethylhexane show marked absorption near 890 cm.$^{-1}$ and both *cis*- and *trans*-3-methylpent-2-ene exhibit absorption between 1620 and 1660 cm.$^{-1}$ (Barnard, Bateman, Harding, Koch, Sheppard, and Sutherland, *J.*, 1950, 915) confirms the assumption that compounds which do not contain CH_2:CRR′ groupings may give bands in these regions. Moreover, it is not certain that with such compounds as (VII*b*) the hydrogen out-of-plane deformations of the CH_2:CRR′ group should give rise to an absorption band at 890 cm.$^{-1}$. Although the frequency of this band normally lies between narrow limits (Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 44), it has been shown for aliphatic compounds that it may be shifted to 930 cm.$^{-1}$ through conjugation with a carbonyl group (Davison and Bates,

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* Birch refers in his argument to a band at 11·75 μ but in the experimental section to a band at 11·3 μ. We have confirmed the presence of a band at 11·3 μ (888 cm.$^{-1}$), but not at 11·75 μ, and assume that the reference to the latter was a typographical error.

J., 1953, 2607). The intensity of absorption of the band at 890 cm.$^{-1}$ (38%) and others in this region is significantly less than that of bands at 1430—1500 cm.$^{-1}$ (69%) in the spectrum of dehydroangustione. If dehydroangustione existed only in the form (VII*b*) and the absorption at 890 cm.$^{-1}$ is ascribed to the $>C{=}CH_2$ group, a high intensity comparable to that at 1430—1500 cm.$^{-1}$ would be expected for this band (Werner and Sutherland, *J. Amer. Chem. Soc.*, 1952, **74**, 2689; Barnard *et al.*, *loc. cit.*)

The evidence does not permit a final decision on the composition of dehydroangustione but it does indicate that, if any of the isomer (VII*b*) is present, the proportion is small.

EXPERIMENTAL

Ultraviolet absorption spectra were determined on a Beckman spectrophotometer, model D.U. Infrared absorption spectra were determined on a Perkin-Elmer double-beam spectrometer (model 21 B), through the courtesy of Dr. Seymour Bernstein, Lederle Laboratories, New York.

αγγ- and ααγ-Trimethyladipic Acid.—Dihydro*iso*phorone (250 g.) was oxidised with 50% nitric acid (1320 c.c.) containing ammonium vanadate (1 g.), according to the procedure used in the preparation of adipic acid from *cyclo*hexanol (*Org. Synth.*, Coll. Vol. 1, 2nd edn., p. 19, note 5). No attempt was made to separate the individual components of the mixed trimethyladipic acids (147 g.).

ααγ-Trimethylglutaric Acid.—The crude mixture of trimethyladipic acids (147 g.) and manganese carbonate (12·7 g.) was heated at 230—240° until no more material distilled. The distillate was washed with sodium carbonate solution and dried, to give a mixture of 2 : 2 : 4- and 2 : 4 : 4-trimethyl*cyclo*pentanones (42 g.). No attempt was made to separate the components. Birch and Johnson (*J.*, 1951, 1493) have however recently reported the isolation of the pure compounds from a similar mixture. The mixture of ketones (40 g.) was added slowly to a well-stirred suspension of ammonium metavanadate (400 mg.) in 50% nitric acid (214 c.c.) at 90°. Then the mixture was kept at 100° for 1 hr. and finally refluxed for 30 min. The dark residue which remained after removal of the nitric acid was recrystallised from light petroleum (b. p. 60—80°) to give 20·6 g. of ααγ-trimethylglutaric acid, m. p. 97—98° (Found: C, 55·3; H, 8·2. Calc. for $C_8H_{14}O_4$: C, 55·2; H, 8·1%). The monoanilide had m. p. 164—165°. Auwers and Meyer (*Ber.*, 1890, **23**, 293) and Auwers (*Annalen*, 1896, **292**, 224) report m. p.s of 97° and 165° for the acid and anilide respectively. A further amount (7·2 g.) of the pure acid was obtained on acidification of the sodium carbonate washings of the distillate from the pyrolysis.

ααγ-Trimethylglutaric acid has been synthesised previously by the action of finely divided silver on ethyl α-bromo*iso*butyrate (Auwers and Meyer, *Ber.*, 1889, **22**, 2011). We have repeated the synthesis using this procedure and confirmed that the yield is too low to make it practicable for our purposes.

Monoethyl Ester Chlorides of αγγ- and ααγ-Trimethylglutaric Acid (IX).—ααγ-Trimethylglutaric acid (10 g.) was converted in quantitative yield into the anhydride, m. p. 92—93° (Found: C, 61·4; H, 7·69. Calc. for $C_{18}H_{12}O_3$: C, 61·5; H, 7·73%), by refluxing acetyl chloride (12·2 c.c.) in 1 hr. The anhydride (11·35 g.) and absolute ethanol (4·5 c.c.) were heated together, with exclusion of moisture, under reflux at 104° for 5 hr. The mixture was diluted with ether and washed thoroughly with 10% sodium hydrogen carbonate solution. The alkaline extract was made acid to Congo-red with hydrochloric acid and extracted with ether. Removal of the ether from the dried extract left a colourless oil (14·2 g.). This was distilled, to give a main fraction (12·6 g.), b. p. 130—131°/2 mm., n_D^{29} 1·4358 (Found: C, 59·4; H, 9·0. Calc. for $C_{10}H_{18}O_4$: C, 59·4; H, 9·0%). No attempt was made to separate the isomeric ethyl hydrogen esters.

A mixture of acid esters (26 g.) and freshly purified thionyl chloride (40 c.c.) was set aside overnight at room temperature. Excess of thionyl chloride was removed under reduced pressure and the colourless oil remaining was distilled, to give a main fraction (23·1 g.), b. p. 104—106°/4 mm. (Found: Cl, 15·7. Calc. for $C_{10}H_{17}O_3Cl$: Cl, 16·1%).

3 : 7-*Diethoxycarbonyl*-5 : 5-*dimethyloctane*-2 : 4-*dione* (X) *and* 3 : 7-*Diethoxycarbonyl*-2 : 4-*dimethyloctane*-2 : 4-*dione.*—The mixed isomeric chlorides obtained in the previous experiment (8·1 g.), in dry benzene (100 c.c.), were added gradually, with stirring, to ethyl sodioacetoacetate (from ethyl acetoacetate, 4·78 g., and sodium 0·84 g.) in benzene (100 c.c.). The temperature was kept at 4°. Then the mixture was set aside at room temperature for 14 hr. and finally refluxed for 2 hr. After cooling, more benzene was added and the mixture was extracted with

10% sodium hydrogen carbonate solution (2 × 25 c.c.). The benzene solution was dried and evaporated. When the residue was treated with successive portions of 10% aqueous sodium carbonate, the bulk dissolved slowly. The product (10·84 g.), isolated from the alkaline solution by acidification and extraction with ether, was distilled. The main fraction (8·75 g.), b. p. 132—135°/1·5 mm., was a colourless oil which gave an intense orange-red colour with ferric chloride solution (Found : C, 61·1; H, 8·5. Calc. for $C_{16}H_{26}O_6$: C, 61·1; H, 8·34%). Absorption in EtOH : $\lambda_{max.}$ 278 mμ (log ε 3·58).

1 : 5-*Diethoxycarbonyl*-3 : 3- (XI) *and* -3 : 5-*dimethylhexan*-2-*one*.—Sodium (0·713 g.) was added in small pieces to a solution, in anhydrous methanol (25 c.c.), of the esters (9·71 g.) obtained in the previous experiment. The mixture was cooled in ice until the addition was complete and then kept at room temperature for 12·5 hr. The clear yellow solution was poured into 2N-hydrochloric acid (200 c.c.). The oil which separated was extracted with ether. The residue after evaporation of the ether was distilled, to give a main fraction (4·3 g.), b. p. 100—102°/0·3 mm. (Found : C, 59·8; H, 8·63. Calc. for $C_{14}H_{24}O_5$: C, 61·7; H, 8·9%). Absorption in EtOH : $\lambda_{max.}$ 251 mμ (log ε 3·2). This product gave a red colour with ferric chloride solution. The analysis indicates that some methyl ester has been formed by ester exchange (cf. Hunsdiecker, *loc. cit.*).

4 : 4 : 6-*Trimethyl*cyclo*hexane*-1 : 3-*dione*.—The product from the previous experiment (2·92 g.), in dry ether (40 c.c.), was added to freshly prepared sodium methoxide (from 0·324 g. of sodium). After 30 min. the ether was removed and the residue kept at 100° for 1·5 hr. and at room temperature for 10 hr. Water (50 c.c.) was added and the insoluble product (1·78 g.) was extracted with ether. When the alkaline, aqueous solution was saturated with carbon dioxide, a white precipitate separated slowly. The *dione* recrystallised from light petroleum (b. p. 60—80°) as white needles (31 mg.), m. p. 131—132° (Found : C, 69·7; H, 8·7. $C_9H_{14}O_2$ requires C, 70·1; H, 9·1%). Absorption in EtOH : $\lambda_{max.}$ 255 mμ (log ε 4·08). When this product was mixed with the compound $C_9H_{14}O_2$ obtained by Cahn *et al.* (*loc. cit.*) by hydrolysis of angustione, there was no depression of m. p.

2-*Acetyl*-4 : 4 : 6-*trimethyl*cyclo*hexane*-1 : 3-*dione* (VI).—A mixture of the foregoing dione (517 mg.), acetic anhydride (2·5 c.c.), and fused sodium acetate (100 mg.) was heated at 130—135° for 3 hr., then cooled, dissolved in ether, and extracted with 10% potassium hydroxide solution (4 × 15 c.c.). The alkaline extract was acidified and extracted with ether. This ether extract was concentrated to 100 c.c., shaken for 15 min. with excess of saturated aqueous copper acetate, and then set aside for 12 hr. The residue obtained on evaporation of the ethereal extract was recrystallised from water–ethanol, to yield unchanged dione and a copper salt, m. p. 203—204°, undepressed in admixture with the copper salt of (±)-angustione (Found : C, 58·6; H, 6·6; Cu, 12·1. Calc. for $C_{11}H_{15}O_3,0{\cdot}5Cu$: C, 58·2; H, 6·7; Cu, 14·0%). (±)-Angustione was regenerated from the copper salt (30 mg.) by treatment with dilute sulphuric acid (10 c.c.). Its identity was confirmed by the preparation of the piperonylidene derivative, m. p. and mixed m. p. 166—167°.

Infrared Absorption Spectra.—Dehydroangustione (liquid) : strong bands at 5·95, 6·05, 6·40, 6·72, 6·80, 7·20; medium bands at 3·30, 3·35, 7·70, 9·70, 9·95, 11·30; weak bands at 8·05, 8·50, 9·22, 9·25, 10·35, 10·65, 11·83, 12·7, 13·5.

4 : 6 : 6-Trimethyl*cyclo*hex-4(?)-ene-1 : 3-dione (potassium bromide pellet) : strong bands at 3·30, 3·77, 5·97, 6·25, 6·45, 6·7, 6·85, 7·08, 7·25, 7:50, 7·68, 8·10, 8·20, 8·37; medium bands at 3·20, 3·58, 3·83, 9·80, 10·70, 11·07; weak bands at 8·83, 8·95, 9·25, 11·65, 13·30, 14·35.

Aminodehydroangustione (in $CHCl_3$) : strong bands at 6·13, 6·3, 6·82, 7·25, 7·52; medium bands at 2·85, 3·03, 3·30, 5·97, 7·85, 11·25; weak bands at 8·35, 8·78, 9·57, 9·78, 10·00, 10·32, 11·47, 11·83, 12·00.

Ozonolysis of Aminodehydroangustione.—An ice-cold solution of pure aminodehydroangustione (204 mg.; m. p. 151°) in purified chloroform (10 c.c.) was treated with a slow stream of ozonised oxygen (6% of ozone) for 3·5 hr. The ozonisation vessel was followed by a wash-bottle containing water (10 c.c.) to collect volatile products. The chloroform solution was evaporated and the residue treated with the aqueous solution in the wash-bottle together with further water (25 c.c.). The mixture was heated under reflux on a steam-bath for 1 hr. and then distilled into ice-water (10 c.c.) until only 5 c.c. remained. M-Sodium acetate (10 c.c.), N-hydrochloric acid (10 c.c.), and dimedone (0·45 g.) dissolved in sufficient ethanol were added to the distillate which was then heated on a water-bath for 10 min. and then left at room temperature for 12 hr. The dried precipitate (19·2 mg.) had m. p. and mixed m. p. with authentic formaldehyde–dimedone condensation product, 184—186°. This represents a yield of 6·22% of one mole of formaldehyde.

Ozonolysis of Dehydroangustione.—When dehydroangustione (267 mg.) was subjected to ozonolysis according to the conditions of Caldwell and Jones (*J.*, **1946**, 599), 10·3 mg. of formaldehyde–dimedone condensation product were obtained. This represents a yield of 2·5% of one mole of formaldehyde.

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