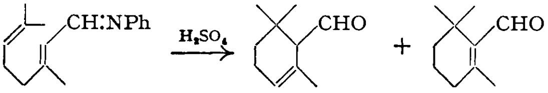
203. *Studies in the Polyene Series. Part XLI.* A New Isomerisation Product from Citral.*

By H. B. Henbest, B. L. Shaw, and George Woods.

A by-product isolated from the cyclisation of citral anil with 95% sulphuric acid has been shown to be 1-acetyl-4 : 4-dimethyl*cyclo*hexene, the main products being the α- and the β-*cyclo*citral.

The most convenient method for preparing β-*cyclo*citral is that in which citral a[illegible] is cyclised with sulphuric acid (D.R.-P. 123 747). This method has recently been i[illegible]ed by Colombi, Bosshard, Schinz, and Seidel (*Helv. Chim. Acta*, 1951, **34**, 265). Through the courtesy of Professor Schinz, who very kindly supplied us with a description of his procedure before publication, it was possible to prepare a considerable quantity of β-*cyclo*citral, required for other investigations in these laboratories.



(I) (II) (III)

The compounds known to be formed in this cyclisation are *p*-cymene, α-*cyclo*citral (II), and β-*cyclo*citral (III). These three compounds can be fairly efficiently separated by fractional distillation, but in order to procure some really pure β-*cyclo*citral, the higher-boiling fractions, consisting mostly of this isomer, were converted into the semicarbazone(s). Fractional crystallisation then gave two products, the one in larger amount proving to be β-*cyclo*citral semicarbazone (cf. Young and Linden, *J. Amer. Chem. Soc.*, 1947, **69**, 2072). The other product had a considerably higher melting point (216—218°), similar indeed to that of α-*cyclo*citral semicarbazone, but clearly differentiated from the latter by its ultraviolet light absorption—the absorption maximum at 2610 Å indicating that this new derivative had been formed from an αβ-unsaturated carbonyl compound.

Hydrolysis of the new semicarbazone afforded the parent carbonyl compound, which possesses an odour very similar to, but far more intense than, that of oil of caraway (principally carvone). Preparation of an oxime and 2 : 4-dinitrophenylhydrazone from the new ketone confirmed that it was different from carvone.

The first structures considered were those in which cyclisation had given a five-membered ring (cf. Spalding and Stevens, *ibid.*, 1949, **71**, 1687), the aldehyde group still being retained. These became untenable when it was shown that the compound was quite resis-

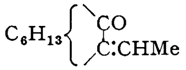
---

* Part XL, preceding paper.

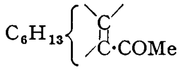
tant to aerial or silver hydroxide oxidation, and gave no colour with Schiff's reagent, and that its oxime could not be dehydrated by heating it with acetic anhydride, merely being converted into the oxime acetate. Thus an αβ-unsaturated ketone rather than an aldehyde structure was indicated.

Ozonolysis of the new ketone was next investigated. Under suitable conditions a formyl or keto-acid was isolated as its crystalline 2 : 4-dinitrophenylhydrazone, but no volatile carbonyl compound was produced in the reaction. Analysis of this 2 : 4-dinitrophenylhydrazone showed that the parent compound was a C_8-acid, and this was further confirmed by analytical data obtained with the methyl ester of this derivative.

Loss of two carbon atoms on ozonolysis suggested that the partial structures (IV*a*) or (IV*b*) might be present, of which the former could be ruled out by the non-formation of acetaldehyde on ozonolysis. Confirmation of the presence of the latter partial structure was obtained by lithium aluminium hydride reduction of the ketone to the corresponding alcohol, which on treatment with osmium tetroxide gave a triol that was readily cleaved with periodic acid to give acetaldehyde together with the same C_8-formyl or -keto-acid as obtained on ozonolysis. The presence of the acetyl group in the cyclisation product could not be detected by the iodoform test (procedure of Fuson and Tullock, *ibid.*, 1934, **56**, 1638), but under these conditions, 1-acetyl*cyclo*hexene also gave a negative result.

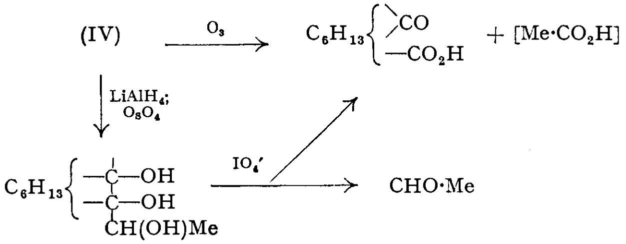
(IV*a*) 

$$C_6H_{13}\left\{\begin{array}{l}\diagdown CO\\ \diagup C{:}CHMe\end{array}\right.$$

 (IV*b*)

$$C_6H_{13}\left\{\begin{array}{l}\diagdown C\diagup\\ \quad\Vert\\ \diagup C{\cdot}COMe\end{array}\right.$$

Comparison of the light-absorption properties of the new unsaturated ketone and its derivatives with those reported for cyclic compounds containing the partial structure (IV) revealed a very close similarity to 1-acetyl*cyclo*hexene and its derivatives (cf. Hamlet, Henbest, and Jones, *J.*, 1951, 2652). This further signified that there must be a hydrogen atom attached to the carbon atom β to the carbonyl group, for replacement of this hydrogen atom by an alkyl group markedly reduces the intensity of absorption (Braude, Jones, Koch, Richardson, Sondheimer, and Toogood, *J.*, 1949, 1890; Turner and Voitle, *J. Amer. Chem. Soc.*, 1951, **73**, 1403).



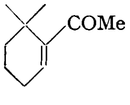
Light absorptions in ethanol.

		1-Acetyl*cyclo*hexene		Ketone	
		λ, Å	ε	λ, Å	ε
Compound	Max.	2320	12 500	2320	12 000
	Min.	2790	30	2810	30
	Max.	3080	50	3080	45
Semicarbazone	Max.	2605	24 500	2610	25 500
2 : 4-Dinitrophenylhydrazone *	Max.	2550	16 500	2550	16 800
	Min.	3120	2 000	3130	2 000
	Max.	3850	27 000	3850	27 300

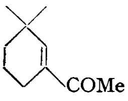
* Light absorption of both in chloroform solution.

The positions of two carbon atoms now remained to be located. The ketone was not easily aromatised, for attempted dehydrogenation with sulphur (cf. Holmes, Alcock, Demianow, Robinson, Rooney, and Sunberg, *Canadian J. Res.*, 1948, **26**, *B*, 248) led to the recovery of most of the starting material. This suggested the presence of a *gem*-dimethyl grouping.

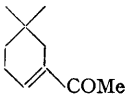
Of the four possibilities (V)—(VIII), (V) could be eliminated as this had been prepared by Chanley (*J. Amer. Chem. Soc.*, 1948, **70**, 44) and was obviously different from our



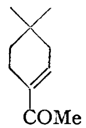
(V)



(VI)

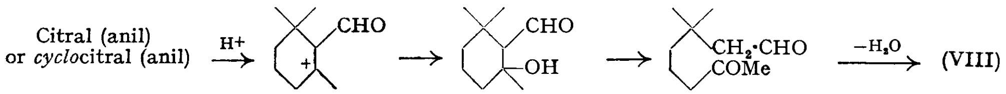


(VII)



(VIII)

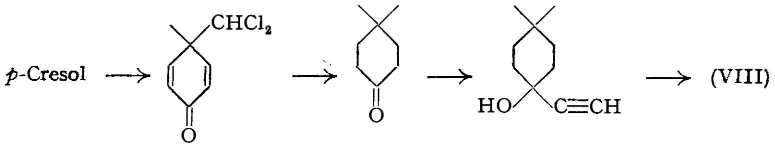
material. Consideration of the possible routes whereby (VI)—(VIII) might arise from citral, suggested that (VIII) was the only one whose formation might be accounted for by a plausible sequence of events:



Accordingly, the ketone (VIII) was synthesised from *p*-cresol by the route outlined below and shown to be identical with the product from citral.

The first stage in the isolation of the *cyclo*citral mixture involves steam-distillation of the cyclised product from dilute sulphuric acid (*i.e.*, reaction mixture diluted with ice). It seems likely that the ketone (VIII) is formed from α- and/or β-*cyclo*citral during this steam-distillation stage (by the hydration and reverse aldol changes suggested above) rather than during the cyclisation reaction. This would gain support from the observation that the yield of ketone was lower when the scale of the experiment was reduced, the time then required for the steam-distillation being correspondingly less.

This same ketone had been encountered by Haworth, Heilbron, and (W. E.) Jones (1938, unpublished work) in the course of preparing β-*cyclo*citral by the formation and cyclisation of citrylidenecyanoacetic acid. Through the courtesy of Drs. W. E. Jones and E. Haworth, who kindly provided us with a sample of their semicarbazone, a mixed m. p. determination was carried out which showed that the materials were identical. The light-absorption properties of the two semicarbazone samples were also identical, and the physical properties of the parent ketones were also in good agreement.



It is likely that a carbonyl compound isolated by Karrer and Ochsner (*Helv. Chim. Acta*, 1947, **30**, 2092) from the reaction between α- or β-*cyclo*citral (prepared from citral anil and not purified *via* crystalline derivatives) and *N*-bromosuccinimide was actually the ketone (VIII). These authors suggested a 1-formyl-2 : 6 : 6-trimethyl*cyclo*hexa-2 : 5-diene structure for their product, which cannot be correct, since a compound of this structure would absorb maximally at a wave-length >2600 Å—their reported maximum being at 2300 Å. The physical constants of the carbonyl compound and its semicarbazone given by Karrer and Ochsner agree with those of our material, and they also mention that the parent compound has an odour resembling that of kümmel (*i.e.*, caraway).

It has now been found that pure β-*cyclo*citral in ethereal solution reacts very rapidly with *N*-bromosuccinimide even at 20°, whereas the ketone (VIII) does not react appreciably under these conditions. Since β-*cyclo*citral as obtained by distillation may contain about 10% of the new ketone, it appears that the action of *N*-bromosuccinimide on this mixture is to convert the β-*cyclo*citral into non-aldehydic products, leaving the new ketone unaffected, this having then been isolated by Karrer and Ochsner as the semicarbazone.

EXPERIMENTAL

(M. p.s were determined on a Kofler block and are corrected; the light-absorption data were determined in ethanol solution with a Beckman spectrophotometer unless stated otherwise.)

Cyclisation of Citral Anil.—The method of Colombi, Bosshard, Schinz, and Seidel (*loc. cit.*) was employed; introduction of certain modifications enabled the scale of the experiment to be increased considerably. Sulphuric acid (1 l.) was diluted with ice (50 g.) and cooled to −20° with an acetone–solid carbon dioxide bath. The acid was stirred vigorously, the internal temperature being kept at −20° whilst the ethereal solution of citral anil (prepared from 152 g. of citral) was added during 45 minutes. The reaction mixture was stirred for a further 45 minutes at −15° and then poured on excess of ice and stream-distilled rapidly (about 40 minutes). Extraction of the distillate (*ca.* 1 l.) with ether gave a straw-coloured oil (95 g.; 64%). The combined product (285 g.) from three cyclisation experiments was fractionally distilled through a Widmer column with a totally condensing still head and a partial take off, the reflux ratio being 8 : 1 and the pressure 24 mm.; the fractions were:

No.	B. p.	n_D^{21}	Wt., g.	β-*cyclo*Citral, %	Ketone (VIII), %
1	35—89°	1·4711	23·5	—	—
2	89—96	1·4767	27·1	—	—
3	96—100	1·4810	21·7	—	—
4	100—102	1·4858	22·7	—	—
5	102—104	1·4900	19·0	71	13
6	104—106	1·4928	25·1		
7	106—107·5	1·4957	56·0	80	9
8	107·5—108	1·4964	48·0	85	7
9	108	1·4966	15·8	—	—

The percentages of β-*cyclo*citral and ketone (VIII) contained in fractions 5—8 are based on the quantities of pure semicarbazones obtained (see below); the remainder of the fractions were not investigated in this way. Fractions 2 and 3 consisted mainly of α-*cyclo*citral (pure compound has n_D^{18} 1·4744), and readily yielded α-*cyclo*citral semicarbazone, m. p. 201—203°. Light absorption: Maximum, 2320 Å; ε = 17 400.

Separation and Purification of the Semicarbazones.—Treatment of the fractions containing mostly β-*cyclo*citral with semicarbazide acetate in methanol solution gave a solid product, which on recrystallisation from slightly aqueous methanol gave 1-*acetyl*-4 : 4-*dimethyl*cyclo*hexene semicarbazone* as the most insoluble component. This compound formed plates, m. p. 216—218° (slight decomp.), from methanol (Found: C, 63·0; H, 8·95. $C_{11}H_{19}ON_3$ requires C, 63·1; H, 9·1%). Light absorption: see Table.

The β-*cyclo*citral semicarbazone could not be obtained pure by recrystallisation, the m. p. not being raised above 160—163° (Young and Linden, *loc. cit.*, give m. p. 167°). α-*cyclo*Citral semicarbazone was the suspected impurity, and the semicarbazone (m. p. 160—163°) was therefore dissolved in 0·75N-methanolic sulphuric acid at 20° to hydrolyse this impurity. Dilution with water gave pure β-*cyclo*citral semicarbazone (70% recovery), m.p. 165—168°.

Unpublished observations by Haworth, Heilbron, and Jones suggested that the following method would be more convenient. β-*cyclo*Citral (44 g.), as obtained by fractional distillation, was added to acetic acid (270 c.c.), and the solution then treated with semicarbazide hydrochloride (35 g.) in water (175 c.c.). The β-*cyclo*citral semicarbazone, which formed, was collected after 10 minutes, and recrystallised from aqueous methanol, yielding the pure derivative, m. p. 165—166°. The filtrate was treated with water and light petroleum (b. p. 40—60°), the latter extract yielding an oil that on treatment with semicarbazide acetate in methanol gave the new ketone semicarbazone, m. p. 216—218°.

1-*Acetyl*-4 : 4-*dimethyl*cyclo*hexene* (VIII).—Hydrolysis of the semicarbazone was carried out by the procedure described by Heilbron, Johnson, Jones, and Spinks (*J.*, 1942, 727); the homogeneous *ketone* produced had b. p. 102°/124 mm., n_D^{22} 1·4795 (Found: C, 78·75; H, 10·25. $C_{10}H_{16}O$ requires C, 78·9; H, 10·5%). Light absorption: see Table.

The 2 : 4-*dinitrophenylhydrazone* crystallised from methanol–ethyl acetate (1 : 1) as scarlet needles, m. p. 185·5—186° (Found: C, 57·9; H, 5·95. $C_{16}H_{20}O_4N_4$ requires C, 58·0; H, 6·0%). Light absorption: see Table.

The *oxime*, prepared in aqueous methanol solution, crystallised from methanol–water (1 : 1) as long needles, m. p. 103—104° (Found C, 71·8; H, 10·25. $C_{10}H_{17}ON$ requires C, 71·8; H, 10·2%). Light absorption: Maximum 2300 Å; ε = 17 100. Attempted dehydration (cf. theoretical section) of the oxime (320 mg.) by heating it under reflux with acetic anhydride (2 c.c.) led to a nearly quantitative yield of the *oxime acetate*, b. p. 160°/20 mm., n_D^{20} 1·4981 (Found:

C, 68·7; H, 9·2. $C_{12}H_{19}O_2N$ requires C, 68·8; H, 9·15%). Treatment of this compound with 2 : 4-dinitrophenylhydrazine reagent slowly gave the 2 : 4-dinitrophenylhydrazone of (VIII); it had m. p. 185—186°.

Ozonolysis of the Ketone (VIII).—A slow stream of ozonised oxygen (*ca.* 6% of ozone) was passed through a solution of the ketone (0·5 g.) in carbon tetrachloride (15 c.c.) for 45 minutes. The solvent was removed at room temperature under reduced pressure, and the residue subjected to steam distillation. The distillate gave no reaction with aqueous dinitrophenylhydrazine or dimedone reagents. The non-volatile residue was warmed at 60° for 20 minutes after the addition of 30% hydrogen peroxide solution (0·5 c.c.), and then treated with a 5% solution of 2 : 4-dinitrophenylhydrazine sulphate in 40% sulphuric acid, the resulting solution being kept overnight at 5°. The yellow precipitate was purified by extraction with 3% sodium hydrogen carbonate solution at 80°. Acidification of this extract gave a product which after recrystallisation from benzene–light petroleum weighed 340 mg. and had m. p. 123—134°. Further recrystallisation from benzene and then ethyl acetate gave 5-*keto*-3 : 3-*dimethylpentane*-1-*carboxylic acid* 2 : 4-*dinitrophenylhydrazone* as small yellow needles, m. p. 135—136° (Found: C, 50·05; H, 5·5. $C_{14}H_{18}O_6N_4$ requires C, 49·7; H, 5·4%).

A solution of this derivative (88 mg.) in methanol (10 c.c.) containing 5 drops of concentrated sulphuric acid was heated under reflux for 1 hour. The product crystallised on cooling, and recrystallisation from 80% methanol then gave the 2 : 4-*dinitrophenylhydrazone* of the methyl ester as yellow needles, m. p. 82—83° (Found: C, 50·95; H, 5·85; N, 16·15. $C_{15}H_{20}O_6N_4$ requires C, 51·15; H, 5·7; N, 15·9%). Light absorption: Maxima, 2220 and 3570 Å; $\varepsilon =$ 13 400 and 21 000; minimum, 2720 Å; $\varepsilon = 1700$.

Degradation of the Ketone (VIII) *by the Osmium Tetroxide–Periodic Acid Method.*—A solution of lithium aluminium hydride (100 mg.) in ether (10 c.c.) was added to one of the ketone (715 mg.) in ether (5 c.c.). The resulting solution was heated under reflux for 5 minutes, and the product was isolated with ether. Distillation gave the alcohol (608 mg.), b. p. *ca.* 110°/18 mm., n_D^{26} 1·4698, as a sweet-smelling oil.

A solution of osmium tetroxide (900 mg.) in dry ether (50 c.c) was added to one of the alcohol (513 mg.) in dry ether (10 c.c.) containing pyridine (1 c.c.). The solution immediately darkened in colour and within 3 minutes brown crystals were deposited. Filtration after 50 minutes yielded the triol–osmium–pyridine complex (1·59 g., 85%) as translucent brown needles.

For hydrolysis, this complex was dissolved in chloroform (40 c.c.) and shaken with 10% aqueous mannitol solution (100 c.c.) containing potassium hydroxide (1 g.). The reaction appeared to be complete after 10 minutes, for the initially brown chloroform layer had become colourless and the aqueous layer reddish-brown. The chloroform layer was washed with water (2 × 10 c.c.) and then rejected. The combined aqueous solution was extracted with ether for 11 hours to yield the *triol* (477 mg.) as a very viscous liquid. A portion was distilled at 100° (bath temp.; short-path still)/2×10^{-5} mm. (Found: C, 63·0; H, 10·5. $C_{10}H_{20}O_3$ requires C, 63·7; H, 10·6%).

(a) *Fission of the triol to give acetaldehyde.* A 10% solution of sodium metaperiodate (5 c.c.) and 2N-sulphuric acid (5 c.c.) was added to one of the triol (50 mg.) in water (30 c.c.), the mixture being shaken in nitrogen for 5 minutes. The solution was then distilled, the distillate being collected in a saturated aqueous solution of dimedone (3 c.c.). The dimedone derivative, which began to crystallise after 30 minutes, was collected after 3 days and recrystallised from ethanol–water (1 : 1) below 50°. The pure derivative (50% yield) had m. p. 139—140°, undepressed when the specimen was mixed with an authentic sample prepared from acetaldehyde (m. p. 139—140°). The dimedone derivative was also converted into its "anhydride," m. p. 177—178° undepressed when the specimen was mixed with an authentic sample, m. p. 177—178°.

(b) *Fission of the triol to the formyl acid.* The triol (350 mg.), dissolved in water (150 c.c.), was oxidised with periodic acid as before. The reaction solution was extracted with ether (5 × 15 c.c.) to give a pale yellow liquid (220 mg.), which was treated with a 5% solution of 2 : 4-dinitrophenylhydrazine in 40% sulphuric acid. After being kept at 5° for 2 days, the yellow precipitate was purified as described in the ozonolysis experiment. The product (280 mg.) had m. p. 135—136° (Found: C, 49·65; H, 5·45. Calc. for $C_{14}H_{18}O_6N_4$: C, 49·7; H, 5·4%). The m. p. was undepressed when the product was mixed with that obtained by ozonolysis. Esterification of this derivative with methanol gave the same methyl ester (m. p. and mixed m. p.) as obtained previously.

Conversion of p-*Cresol into the Ketone* (VIII).—*p*-Cresol was converted by the action of chloroform and alkali into 4-dichloromethyl-4-methyl*cyclo*hexa-2 : 5-dien-1-one by Auwers and Winternitz's method (*Ber.*, 1902, **35**, 468). This ketone was hydrogenated as described by Miller and

Adams (*J. Amer. Chem. Soc.*, 1936, **58**, 787) to 4 : 4-dimethyl*cyclo*hexanol, which was then oxidised to the corresponding ketone (cf. Auwers and Lange, *Annalen*, 1913, **401**, 315).

Dry liquid ammonia (100 c.c.) contained in a Dewar flask was saturated with acetylene; lithium (0·4 g.) was then added, and acetylene was passed in for a further 30 minutes. 4 : 4-Dimethyl*cyclo*hexanone (0·73 g.) in ether (10 c.c.) was added, and the resultant mixture was stirred for 4 hours with a slow passage of acetylene. The solvent was allowed to evaporate overnight in a slow stream of acetylene. The acetylenic alcohol was isolated with ether. Evaporation of the solvent gave the alcohol (0·77 g.), which was heated under reflux with 90% formic acid (4·5 c.c.) for 45 minutes. The product was isolated with pentane; distillation yielded the ketone (VIII) (0·47 g.), n_D^{16} 1·4794. The semicarbazone, recrystallised from methanol, had m. p. 216—219°; the oxime, recrystallised from methanol, had m. p. 103—104°; and the 2 : 4-dinitrophenylhydrazone had m. p. 183—185·5°, after recrystallisation from ethyl acetate–light petroleum (b. p. 60—80°). When the three derivatives were mixed with the corresponding compounds prepared from citral, their melting points were not depressed.

One of the authors (B. L. S.) thanks the Department of Scientific and Industrial Research for a Maintenance Grant, and another (G. W.) thanks the Ministry of Education for a F.E.T.S. Grant.

THE UNIVERSITY, MANCHESTER, 13.

[*Received, November 14th*, 1951.]