201. *Reactions of Organic Peroxides. Part II.*[1] *The Reduction of Dihydroascaridole.*

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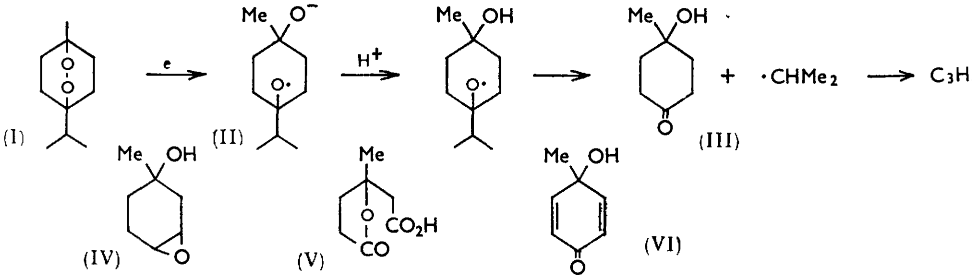
Dihydroascaridole, when reduced with ferrous sulphate or titanous chloride, gives propane and 4-hydroxy-4-methylcyclohexanone, not 3,4-epoxy-1-methylcyclohexanol as suggested by Paget. In the reduction, isopropyl radicals are produced and with cyclohexenone give 3-isopropylcyclohexanone.

In 1938 Paget[2] reduced dihydroascaridole (I) in ethanol with titanous chloride in hydrochloric acid and obtained propane in 90% yield and a corresponding amount of a compound $C_7H_{12}O_2$, containing one hydroxyl group. The second oxygen atom was said to be neither ketonic nor hydroxylic and to be similar to an " oxidic " oxygen. The compound was stable to neutral permanganate but was oxidised by Beckmann's chromic acid mixture to the lactone (V) of β-hydroxy-β-methyladipic acid. Paget therefore considered this compound to be 3,4-epoxy-1-methylcyclohexanol (IV). The genesis of such a compound is difficult to visualise and it appeared to us that it should be formulated as 4-hydroxy-4-methylcyclohexanone (III), being formed by reduction of dihydroascaridole to the radical-ion (II) and subsequent fission of this to 4-hydroxy-4-methylcyclohexanone and the isopropyl radical which is then reduced to propane. This reaction is analogous to that of ascaridole already described.[1] In this case the isopropyl radical attacks the initially formed 4-hydroxy-4-methylcyclohex-2-enone.



(I) (II) (III) (IV) (V) (VI)

Reduction of dihydroascaridole with titanous chloride gave 4-hydroxy-4-methylcyclohexanone although in lower yield than that reported by Paget. This was probably due

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[1] Part I, *J.*, 1962, 4492.
[2] Paget, *J.*, 1938, 829.

to incomplete extraction of the rather water-soluble hydroxy-ketone by the ordinary ether-extraction technique used. Its m. p. of 37—39° is lower than that reported[2] (m. p. 45°) by Paget but the same as that of synthetic 4-hydroxy-4-methylcyclohexanone. The 2,4-dinitrophenylhydrazones of the ketone from dihydroascaridole and of the synthetic ketone were identical.

Reduction of dihydroascaridole with ferrous sulphate in dilute sulphuric acid led to a much better yield (93%) of 4-hydroxy-4-methylcyclohexanone, and an almost quantitative yield of gas (presumably propane). The better yield in this case was almost certainly due to the continuous extraction of the hydroxy-ketone over a considerable period. In this case the hydroxy-ketone was converted into a *p*-nitrobenzoate with the melting point given by Paget [2] for the *p*-nitrobenzoate of his product. There is therefore no doubt that Paget's compound was 4-hydroxy-4-methylcyclohexanone and not an epoxide.

4-Hydroxy-4-methylcyclohexanone was obtained for comparison by chromic acid oxidation of 4-methylcyclohexane-1,4-diol prepared by the action of methylmagnesium iodide on 4-hydroxy- or 4-benzoyloxy-cyclohexanone. It had previously been prepared by Siegel and Bröll-Keckers [3] by hydrogenation of the hydroxy-ketone (VI). They give the melting point (37—39°) obtained in our work but lower than that given by Paget.[2] The melting point (127—129°) given for their 2,4-dinitrophenylhydrazone does not agree with those of the two samples obtained in this work.

In order to obtain evidence for the formation of isopropyl radicals and for their ability to add to cyclohexenones at the β-position of the double bond as postulated in the discussion [1] of the reduction of ascaridole with ferrous sulphate, dihydroascaridole was reduced with ferrous sulphate solution in the presence of cyclohexenone in aqueous ethanol. Only a small amount (~16%) of gas was evolved in this case, and 3-isopropylcyclohexanone (79% yield) containing a small amount of cyclohexenone was obtained.

The high yield of 3-isopropylcyclohexanone provides good evidence for the formation of isopropyl radicals and also for their ability to attack cyclohexenones. The reaction is similar in some respects to the conversion [4] of αβ-unsaturated ketones into β-methyl-substituted saturated ketones by methylmagnesium iodide in the presence of cuprous bromide. The possible extension of this reaction is now being studied.

It is not yet known whether the radical ion has independent existence, or whether it occurs only as a complex with Fe^{3+}, or even whether the sequence from the transfer of the electron to the epidioxide to the fission of the carbon–carbon bond is a concerted one.

A preliminary account of some of these results has been published.[5]

EXPERIMENTAL

M. p.s were determined on a Kofler block and are corrected.

Dihydroascaridole.—Ascaridole was hydrogenated over a platinum catalyst according to Paget's method,[2] giving dihydroascaridole as an oil, n_D^{21} 1·4645, which gave crystals, m. p. 18·2—19° (Found: C, 70·3; H, 10·45. Calc. for $C_{10}H_{18}O_2$: C, 70·6; H, 10·6%).

Reduction of Dihydroascaridole with Titanous Chloride Solution (cf. ref. 2).—Dihydroascaridole (4·6 g.) was dissolved in ethanol (5 c.c.) and added to water (50 c.c.). Commercial " 15% titanous chloride solution " (46 c.c.) was added to the dihydroascaridole solution, and the whole was stirred under carbon dioxide. After 1½ hr. the violet colour of the titanous ion had disappeared and further titanous chloride solution (16 c.c.) was added in portions until the violet colour remained. The aqueous solution was extracted with ether (4 × 25 c.c.) to give a reddish liquid (1·4 g.). This was treated in ether with charcoal and the yellow liquid so obtained was distilled. The resulting liquid (330 mg.), b. p. 124—126°/*ca.* 30 mm., n_D^{21} 1·4720, gave 4-hydroxy-4-methylcyclohexanone as crystals (from isopropyl ether), m. p. 37—39° (Paget [2] reports m. p. 45°), $\nu_{max.}$ (in CS_2) 3600 (OH) and 1715 (C=O) cm.$^{-1}$. The 2,4-dinitrophenylhydrazone was obtained as orange-yellow plates, m. p. and mixed m. p. 147—149°.

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[3] Siegel and Bröll-Keckers, *Monatsh.*, 1957, **88**, 910.

[4] Cf. Birch and Robinson, *J.*, 1943, 501.

[5] Davis, Halsall, and Hands, *Proc. Chem. Soc.*, 1961, 83.

Reduction of Dihydroascaridole with Ferrous Sulphate in Dilute Sulphuric Acid.—Dihydroascaridole (5 g.) was dissolved in 50% aqueous ethanol (50 c.c.), kept under carbon dioxide, and ferrous sulphate solution [50 c.c. of a solution containing ferrous sulphate (17·9 g.) and sulphuric acid (5·76 g. per 100 c.c.)] was added during 30 min. Meanwhile the solution was vigorously stirred and the gas evolved collected over potassium hydroxide solution. After 3 hr. 700 c.c. of gas (theoretical, 708 c.c.) had been collected. The solution was neutralised with sodium hydroxide solution and continuously extracted with ether for 2 days. The extract was distilled, to give a liquid (3·5 g., 93%), b. p. 68—76°/0·02 mm., which gave 4-hydroxy-4-methylcyclohexanone, m. p. 36—38° (Found: C, 65·85; H, 9·9. Calc. for $C_7H_{12}O_2$: C, 65·65; H, 9·4%). The *p*-nitrobenzoate was obtained as yellow plates, m. p. 155—158° (lit.,[2] m. p. 157°) (Found: C, 60·55; H, 5·55. Calc. for $C_{14}H_{15}NO_5$: C, 60·65; H, 5·4%).

Preparation of 4-*Hydroxy*-4-*methylcyclohexanone.*—4-Hydroxycyclohexanone (3·5 g., 0·03 mole), prepared [6] from 4-benzoyloxycyclohexanone,[6,7] was dissolved in ether (60 c.c.) and added dropwise at 20° to the Grignard solution from magnesium (5 g., 0·2 g.-atom), methyl iodide (12·5 c.c., 0·2 mole), and ether (75 c.c.). A white precipitate was immediately formed. The mixture was then diluted with ether (150 c.c.) and heated under reflux overnight. The Grignard complex was decomposed by iced water and then iced dilute hydrochloric acid, until the solution was just acid. After addition of sodium carbonate solution to make the solution just alkaline, continuous ether-extraction (4 days) afforded an oil (4·5 g.) containing solid. The oil and solid were taken up in acetone and kept at −20°; a crystalline precipitate was obtained of *cis*- + *trans*-1-methylcyclohexane-1,4-diol (280 mg., 7%), m. p. 80—118° (Found: C, 64·5; H, 10·7. Calc. for $C_7H_{14}O_2$: C, 64·65; H, 10·75%). The low yield is due to the formation of the insoluble complex involving the Grignard reagent and the hydroxyl group of the 4-hydroxycyclohexanone.

A higher yield (36%) of diol was obtained by the action of an excess of methylmagnesium iodide (5 equiv.) on 4-benzoyloxycyclohexanone but the reaction is complicated by the difficulty of separating the product from 2-phenylpropan-2-ol.

The mixture of diols (1·88 g.) was oxidised in acetone with 8N-chromic oxide in aqueous sulphuric acid,[8] to give 4-hydroxy-4-methylcyclohexanone (750 mg., 40%), b. p. 71—78°/0·2 mm., m. p. 35—38° (from di-isopropyl ether). The infrared spectrum was identical with that of the compound obtained by reduction of dihydroascaridole with titanous chloride. The 2,4-dinitrophenylhydrazone formed yellow plates, m. p. 146—149° (Found: C, 50·45; H, 5·45; N, 17·45. Calc. for $C_{13}H_{16}N_4O_5$: C, 50·75; H, 5·2; N, 18·2%). The *p*-nitrobenzoate was obtained as yellow crystals, m. p. 153—158°.

Reduction of Dihydroascaridole with Acidic Ferrous Sulphate Solution in the Presence of Cyclohexenone.—Dihydroascaridole (4·15 g.) and cyclohexenone (2 g.) in 50% aqueous ethanol (50 c.c.) were placed in a flask through which was passed a slow stream of carbon dioxide. Ferrous sulphate solution [41·5 c.c. of a solution containing ferrous sulphate (17·9 g. of hydrate) and sulphuric acid (5·76 g.) in 100 c.c. water] was added during ½ hr. with stirring. Propane (100 c.c.) was collected over potassium hydroxide solution. After 3 hr. the solution was steam-distilled, the distillate (500 c.c.) was extracted with ether, and the extract distilled, to give a liquid (2·27 g., 79%), b. p. 90—96°/12 mm., n_D^{20} 1·4550 (recorded,[9] for 3-isopropylcyclohexanone, n_D^{20} 1·4540), $\nu_{max.}$ 1710 cm.$^{-1}$ with a small shoulder at 1670 cm.$^{-1}$. Vapour-phase chromatography showed the amount of cyclohexenone present to be small. The liquid gave an orange-yellow 2,4-dinitrophenylhydrazone, m. p. 138—141° (Found: C, 55·9; H, 6·2; N, 18·2. Calc. for $C_{15}H_{20}N_4O_4$: C, 56·25; H, 6·25; N, 17·5%) (lit.,[9] for 3-isopropylcyclohexanone 2,4-dinitrophenylhydrazone, m. p. 138—141°). The liquid also gave a semicarbazone, m. p. 188—189° (Found: C, 60·85; H, 9·65. Calc. for $C_{10}H_{19}N_3O$: C, 60·8; H, 9·65%) (lit., for 3-isopropylcyclohexanone semicarbazone, m. p. 186—187°,[10] 194·5—195° [9]).

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[6] Jones and Sondheimer, *J.*, 1949, 615.

[7] Denby and Taylor, *J.*, 1957, 1922.

[8] Curtis, Heilbron, Jones, and Wood, *J.*, 1953, 461.

[9] Woods, Griswold, Armbrecht, Blumenthal, and Plapinger, *J. Amer. Chem. Soc.*, 1949, **71**, 2028.

[10] Crossley and Pratt, *J.*, 1915, **107**, 171.