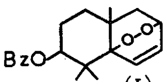
869. *Reactions of Organic Peroxides. Part I. The Reaction of Ascaridole with Ferrous Sulphate.*

By D. Brown, B. T. Davis, T. G. Halsall, and A. R. Hands.
(With an Appendix by J. V. Hatton and R. E. Richards.)

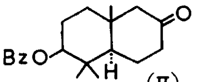
The reduction of ascaridole with ferrous ion gives the 4-hydroxy-3-isopropyl-4-methylcyclohexanones (VI) and (VII). The nuclear magnetic resonance spectra of these ketones and their Wolff–Kishner reduction products are discussed in an appendix.

Recently the epidioxide (I), which has been used as an intermediate for the synthesis of the decalone (II), was found[1] to give almost quantitatively an isomeric compound when heated in boiling ethanol. An analogous thermal rearrangement is that of the simpler epidioxide, ascaridole (III), to isoascaridole (IV) in hot xylene. As a step towards the clarification of the properties of epidioxides a further study of ascaridole has been initiated. Its chemistry up to 1945 has been reviewed by Simonsen.[2] More recently the structure of isoascaridole has been established as (IV).[3,4] Hydration of isoascaridole gives ascaridole glycol (V)[4-6] which Nelson also obtained[5] from ascaridole on treatment with saturated ferrous sulphate solution. Nelson treated ascaridole with the equivalent of 0·33 g.-atom of ferrous ion. Without cooling, he obtained combustible gas, propan-2-ol, and ascaridole glycol. With cooling, " little, if any, gas was evolved."

We have repeated this reaction following Nelson's original conditions. Besides ascaridole glycol (28%) and recovered ascaridole (34%) two reduction products have been isolated. They are two stereoisomeric hydroxy-ketones " A " and " B," both $C_{10}H_{18}O_2$. " Hydroxy-ketone A," m. p. 84° was isolated in 6·5% yield and " hydroxy-ketone B," m. p. 113·5°, in 2·5% yield. The maximum total yield of such reduction products which can be obtained with the amount of ferrous sulphate used is about 16%.



(I)



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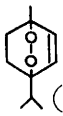

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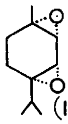

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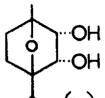

(V)

The reduction of ascaridole with titanous chloride in hydrochloric acid has been described by Paget who reported[7] the formation of propane and *p*-cresol, each in about 33% yield, together with ascaridole glycol, a substance $C_{10}H_{19}ClO_3$, m. p. 191°, and a compound, m. p. 84°, which he said was an unsaturated monocyclic glycol. We have been able to obtain a sample of Paget's compound, m. p. 84°, through the courtesy of Dr. H. T. Openshaw and have found that it is identical with " hydroxy-ketone A."

The structures of the hydroxy-ketones " A " and " B " are (VI) and (VII), assigned on the following evidence. Both contain one ketone group, forming monosemicarbazones and 2,4-dinitrophenylhydrazones, and one hydroxyl group which is not readily acetylated or benzoylated and is therefore probably tertiary. The hydroxy-ketones are saturated and hence monocyclic. With a platinum catalyst " hydroxy-ketone A " takes up one mol. of hydrogen, giving a saturated diol (XIII), m. p. 114°, which must be identical with the saturated glycol, m. p. 111—113°, obtained[7] by Paget from his " unsaturated glycol." Both hydroxy-ketones resisted attack with lead tetra-acetate and gave on Wolff–Kishner

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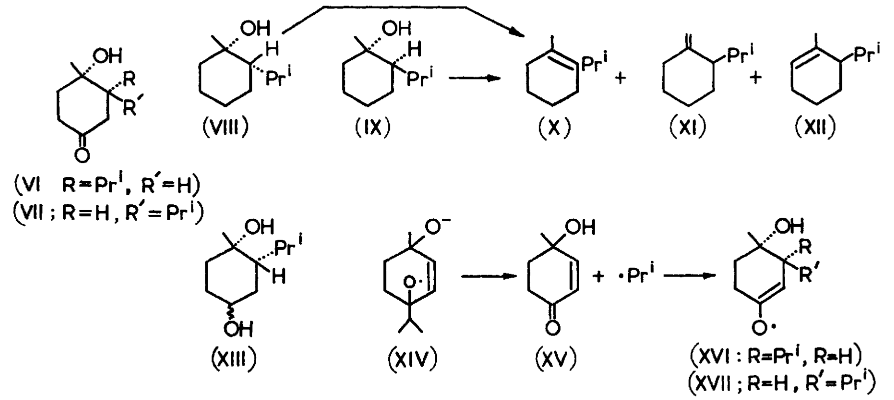
[1] Halsall, Rodewald, and Willis, *J.*, 1959, 2798.
[2] Simonsen, " The Terpenes," Cambridge Univ. Press, 1947, Vol. I, 2nd edn., p. 446.
[3] Rundquist, *Diss. Abs.*, 1956, **16**, 2313.
[4] Jacob and Ourisson, *Bull. Soc. chim. France*, 1958, 734.
[5] Nelson, *J. Amer. Chem. Soc.*, 1911, **33**, 1404.
[6] Nelson, *J. Amer. Chem. Soc.*, 1913, **35**, 84.
[7] Paget, *J.*, 1938, 829.

reduction saturated alcohols, $C_{10}H_{20}O$, " A " (VIII) and " B " (IX), which were characterised as their phenylurethanes. These reactions indicate the absence of an α- or β-hydroxy-ketone grouping.

Dehydration of " alcohol A " (VIII) with phosphoryl chloride in pyridine gave a product of which about 90% was one olefin (X) as shown by vapour-phase chromatography. Its infrared spectrum indicated that the double bond was tetrasubstituted. Similar dehydration of " alcohol B " (IX) gave a product, vapour-phase chromatography of which indicated that it was a mixture of three olefins, one being identical with that from " alcohol A." Infrared examination of the dehydration product showed that the second olefin (XI) had the grouping $>C=CH_2$ and the third (XII) the grouping $-CH=C<$. These results show that the alcohols contain the grouping $\cdot CH_2\cdot CHMe\cdot CR(OH)\cdot$ and differ in the configuration of the hydroxyl group relative to that of the hydrogen on the α-carbon atom.



(VI R=Pr^i, R′=H)
(VII ; R=H, R′=Pr^i)
(VIII) (IX) (X) (XI) (XII)
(XIII) (XIV) (XV)
(XVI : R=Pr^i, R=H)
(XVII ; R=H, R′=Pr^i)

Ozonolysis of the olefin mixture from " alcohol B " (IX) gave 2-isopropylcyclohexanone which was isolated as its 2,4-dinitrophenylhydrazone, formaldehyde which was characterised as its dimethone, and a diketone, $C_{10}H_{18}O_2$, formulated as 8-methylnonane-2,7-dione. This diketone was characterised as its bis-2,4-dinitrophenylhydrazone which was also isolated from the ozonolysis product of the olefin mixture from " alcohol A." These results lead to structures (VIII) and (IX) for alcohols " A " and " B," the stereochemistry being consistent with the dehydration products. This has been confirmed by synthesis.

2-Isopropylcyclohexanone was treated with methylmagnesium iodide. The phenylurethane of the resulting alcohol was identical with that of " alcohol A " (VIII). In the Grignard reaction the stereochemistry of the major product would be expected to be that of structure (VIII), the methyl group attacking the carbonyl group on the side away from the isopropyl group. The synthetic alcohol was dehydrated as described above and the product was identical with that from " alcohol A," consisting mainly (90%) of 1-isopropyl-2-methylcyclohexene (X). This was hydrated by the Brown hydroboronation technique [8,9] to give " alcohol B " (IX) in which the added hydrogen and hydroxyl group must be *cis*-related. The phenylurethane of the synthetic alcohol was identical with that of " alcohol B." Since the keto-group of the hydroxy-ketones cannot be situated α or β to the hydroxyl group, structures (VI) and (VII) follow for them.

The formation of the hydroxy-ketones is probably initiated by the transfer of one electron from the ferrous ion to the peroxide bridge of ascaridole to give the radical-ion (XIV) (cf. the mechanism proposed by Kharasch, Fono, and Nudenberg [10] for the reduction of α-cumyl and t-butyl hydroperoxide with ferrous ammonium sulphate). This rearranges to the unsaturated ketone (XV) and an isopropyl radical which then attacks the β-position

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[8] Brown, Murray, Murray, Snover, and Zweifel, *J. Amer. Chem. Soc.*, 1960, **82**, 4233.

[9] Brown and Zweifel, *J. Amer. Chem. Soc.*, 1959, **81**, 247.

[10] Kharasch, Fono, and Nudenberg, *J. Org. Chem.*, 1950, **15**, 763.

of the double bond of the unsaturated ketone (XV) either *cis* or *trans* to the 4-methyl group, giving the radicals (XVI) and (XVII). Acquisition of a further electron (and a proton) then leads to the hydroxy-ketones (VI) and (VII). This mechanism explains the formation of *p*-cresol and propane in Paget's work,[7] the *p*-cresol arising by dehydration and isomerisation of the unsaturated ketone (XV) and the propane by reduction of the isopropyl radical. This can also give the propan-2-ol obtained by Nelson.[5] Further evidence in support of this mechanism will be described later. Some of the results discussed in this paper have been described in a preliminary communication.[11]

The nuclear magnetic resonance spectra of the alcohols "A" and "B" and the hydroxy-ketones are discussed in an appendix.

EXPERIMENTAL

M. p.s were determined on a Kofler block and are corrected. Ultraviolet spectra were determined for ethanol solution. The alumina used for chromatography was of activity I—II and had been deactivated with 5% of 10% aqueous acetic acid.

Chromatography of Commercial Ascaridole.—Commercial ascaridole (15 g.) was dissolved in light petroleum (30 c.c.) and adsorbed on deactivated alumina (500 g.). Elution with light petroleum gave ascaridole (13·4 g.), n_D^{25} 1·4718. Elution with benzene–ether (9 : 1) gave an oil (0·63 g.), n_D^{25} 1·4687, $\nu_{max.}$ (liquid film), 3500, 1660 cm.$^{-1}$.

Action of Ferrous Sulphate on Ascaridole.—Ascaridole (30 g.) was shaken vigorously with a saturated solution of ferrous sulphate (10 g.) in water, the temperature being maintained at 30—35° by external cooling. When the evolution of heat had ceased (*ca.* 2 hr.) the mixture was extracted with chloroform (3 × 50 c.c.). The extract was dried ($MgSO_4$) and evaporated at 30°/20 mm. to a syrup (34 g.) which was dissolved in light petroleum and adsorbed on to deactivated alumina (1 kg.).

Elution with light petroleum afforded ascaridole (11·58 g., 34%), n_D^{19} 1·4723; further elution with benzene–ether afforded the following two hydroxy-ketones: (*a*) *Hydroxy-ketone A* [(±)-trans-Me,Pr^i-4-*hydroxy*-3-*isopropyl*-4-*methylcyclohexanone*] (1·97 g., 6·5%) which crystallised from ether as needles, m. p. 84° (Found: C, 70·55; H, 10·65. $C_{10}H_{18}O_2$ requires C, 70·55; H, 10·65%), $\nu_{max.}$ (in CS_2) 3630 (OH) and 1709 (C=O) cm.$^{-1}$, $\lambda_{max.}$ 2800 Å (ε 20); the *semicarbazone* formed prisms (from ethanol), m. p. 185—192° (decomp.) (Found: C, 58·15; H, 9·3; N, 18·45. $C_{11}H_{21}N_3O_2$ requires C, 58·1; H, 9·3; N, 18·5%); the 2,4-*dinitrophenylhydrazone* formed orange needles (from ethanol), m. p. 165—167° (Found: C, 55·2; H, 6·3; N, 16·1. $C_{16}H_{22}N_4O_5$ requires C, 54·8; H, 6·3; N, 16·0%). (*b*) *Hydroxy-ketone B* [(±)-cis-Me,Pr^i-4-*hydroxy*-3-*isopropyl*-4-*methylcyclohexanone*] (0·79 g., 2·5%) which crystallised from ether as plates, m. p. 113·5° (Found: C, 70·75; H, 10·85%), $\nu_{max.}$ (in $CHCl_3$) 3510 (OH) and 1705 (C=O)cm.$^{-1}$, $\lambda_{max.}$ 2850 Å (ε 15); the *semicarbazone* formed plates (from ether), m. p. 184—185° (decomp.) (Found: C, 58·15; H, 9·4%); the 2,4-*dinitrophenylhydrazone* formed orange needles (from methanol), m. p. 166—168° (Found: C, 54·9; H, 6·1; N, 15·5%).

Elution with benzene–ether (4 : 1) afforded ascaridole glycol (9·30 g., 28%), n_D^{22} 1·4780 (lit.,[12] n_D^{20} 1·4796), which was characterised as its monobenzoate, m. p. 136° (lit.,[12] m. p. 136—137°) and dibenzoate, m. p. 120—120·5° (lit., 116·5—117·5°).

Hydrogenation of Hydroxy-ketone A.—Hydroxy-ketone A (250 mg.) in ethanol (15 c.c.) was added to prereduced platinum oxide (48 mg.) in ethanol (5 c.c.) and hydrogenated at atmospheric pressure for 8 hr. (uptake 39 c.c. Calc. for 1 mol., 36 c.c.). Removal of the catalyst and evaporation afforded a solid which recrystallised from benzene to give (±)-trans-Me,Pr^i-2-isopropyl-1-*methylcyclohexane*-1,4-*diol* as plates, m. p. 111—113° (Found: C, 69·5; H, 11·8. $C_{10}H_{20}O_2$ requires C, 69·7; H, 11·7%), $\nu_{max.}$ (in Nujol) 3370 cm.$^{-1}$.

(*b*) No uptake of hydrogen occurred when palladium–charcoal was used as catalyst. Similarly, hydroxy-ketone B was not hydrogenated under these conditions.

Wolff–Kishner Reduction of Hydroxy-ketone A.—Hydroxy-ketone A (1·5 g.), 100% hydrazine hydrate (4 c.c.), and diethylene glycol (25 c.c.) were heated under reflux for 3·5 hr. in an atmosphere of nitrogen. The condenser was then removed and the mixture heated until its temperature reached 220°. The solution was then cooled, potassium hydroxide (1·5 g.) was added, and then the mixture was heated under reflux and under nitrogen for 4 hr. After

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

[12] Henry and Paget, *J.*, 1921, **119**, 1714.

dilution with water extraction with light petroleum (3 × 50 c.c.) afforded an oil which was distilled to give "*alcohol A*" [(±)-trans-Me,Pr^i-2-*isopropyl*-1-*methylcyclohexanol*] (1·1 g., 80%), b. p. 196—198°, n_D^{25} 1·4622 (Found: C, 76·8; H, 12·4. $C_{10}H_{20}O$ requires C, 76·9; H, 12·9%), $\nu_{max.}$ (in CS_2) 3597 cm.$^{-1}$. The alcohol (157 mg., 1 mol.) and phenyl isocyanate (154 mg., 1·25 mol.) were heated in a sealed tube at 80° for 24 hr.; the contents of the tube were extracted with light petroleum (b. p. 60—80°) to give an oil which was purified by chromatography to give the *phenylurethane* as crystals [from light petroleum (b. p. 60—80°)], m. p. 85° (Found: C, 73·7; H, 9·0; N, 5·1. $C_{17}H_{25}NO_2$ requires C, 74·1; H, 9·2; N, 5·1%).

Wolff–Kishner Reduction of Hydroxy-ketone B.—This was reduced in a similar manner to hydroxy-ketone A, to give "*alcohol B*" [(±)-cis-Me,Pr^i-2-*isopropyl*-1-*methylcyclohexanol*] (72%), b. p. 192—200°, n_D^{25} 1·4690 (Found: C, 76·2; H, 12·9%), $\nu_{max.}$ (in CS_2) 3500 cm.$^{-1}$. The *phenylurethane* formed crystals, m. p. 112—115°, from light petroleum (b. p. 60—80°) (Found: C, 74·1; H, 9·1; N, 5·0%).

Dehydration of Alcohol A.—Alcohol A (1·04 g.), phosphoryl chloride (4·5 c.c.), and pyridine (20 c.c.) were heated under reflux for 1·5 hr. The solution was cooled and poured on ice. It was extracted with light petroleum (4 × 20 c.c.), to give "olefin A" (0·79 g., 86%), b. p. 154—160°, n_D^{25} 1·4593 (Found: C, 86·7; H, 12·6. Calc. for $C_{10}H_{18}$: C, 86·9; H, 13·1%), no band in the infrared spectrum (CS_2 solution) attributable to an olefinic double bond, except a weak peak at 885 cm.$^{-1}$ ($>C=CH_2$), $\lambda_{max.}$ 2200 (ε 985), 2150 (ε 2075), 2100 (ε 4620), 2050 Å (ε 7080).

Dehydration of Alcohol B.—Alcohol B was dehydrated in the same manner as alcohol A, to give "olefin B" (71%), b. p. 160—164°, n_D^{25} 1·4620 (Found: C, 86·1; H, 13·0%), $\nu_{max.}$ (in CS_2) 1633 (C=C), 883 ($>C=CH_2$), and 796 cm.$^{-1}$ ($>C=CH-$).

Vapour-phase Chromatography of Olefins A and B.—Solutions of olefins A and B in light petroleum (*ca.* 20% v/v) were prepared and injected on to a 250-cm. column of benzylbiphenyl (5%) on Embacel at 100°. The flow rate of hydrogen was 56 c.c. per min. The following results were obtained:

Olefin A: Two peaks at retention times 6·4 and 5·5 min. in the ratio 1 : 10 with a faint shoulder at a higher retention time.

Olefin B: Three peaks at retention times 6·9, 6·4, and 5·4 min. in the approximate ratio 1 : 1 : 1.

Hydrogenation of Olefins A and B.—Olefins A and B were each hydrogenated in ethyl acetate in the presence of palladium–charcoal. The catalyst was removed and each solution was subjected to vapour-phase chromatography on a 250-cm. column of benzylbiphenyl (5%) on Embacel at 90°. The flow rate of hydrogen was 60 c.c. per min.

The hydrocarbon from olefin A gave two peaks (area ratio *ca.* 3 : 1) with retention times 6·3 and 7·6 min. The hydrocarbon from olefin B gave two peaks (area ratio *ca.* 3 : 1) with retention times 6·1 and 7·4 min. A mixture of the two solutions was injected and gave two peaks, of unaltered shape, with retention times 6·1 and 7·3 min.

The hydrogenated solutions were also chromatographed on a 200 cm. column of Apiezon L (20%) on Embacel at 120°. The flow rate of hydrogen was 45 c.c. per min. Both hydrocarbons gave two peaks with retention times of 10·9 and 12·9 min. These times and the peak shapes were unaltered when the solutions were mixed.

Preparation of a Benzylidene Derivative of Hydroxy-ketone A.—The ketone (340 mg., 1 mol.), benzaldehyde (2·12 g., 10 mol.), and potassium hydroxide (0·14 g.) were dissolved in ethanol (25 c.c.) and kept in the dark for 36 hr. After dilution with water, ether extraction afforded the *monobenzylidene derivative* of (±)-*trans*-Me,Pr^i-4-hydroxy-3-isopropyl-4-methylcyclohexanone; this derivative crystallised from ethanol as plates, m. p. 133—134° (Found: C, 79·0; H, 8·6. $C_{17}H_{22}O_2$ requires C, 79·0; H, 8·6%), $\nu_{max.}$ (in Nujol) 3430 (OH) and 1660 cm.$^{-1}$ (conjugated C=O), $\lambda_{max.}$ 2890 (ε 18,970), 2220 Å (ε 7590).

Ozonolysis of Olefin B.—The olefin (110 mg.) in acetic acid (10 c.c.) was treated with ozone for 21 min. and the effluent gases were passed through water (50 c.c.). After removal of the excess of ozone with nitrogen, the acetic acid solution and water were combined and steam-distilled until 100 c.c. of distillate had been collected. The distillate was neutralised to phenolphthalein with 10% sodium hydroxide solution, and dimedone (150 mg.) in methanol (8 c.c.) was added. The solution was kept overnight; formaldehyde dimethone (26 mg.), m. p. and mixed m. p. 190—192°, was formed and isolated. After the dimedone derivative had been removed by filtration the solution was again steam-distilled. The distillate (100 c.c.) was added to a solution of 2,4-dinitrophenylhydrazine (200 mg.) in methanol (12 c.c.) containing a few drops of concentrated hydrochloric acid. Extraction of this solution with chloroform and chromatography on a column of bentonite (28 g.) and kieselguhr (7 g.) gave 2-isopropylcyclohexanone 2,4-dinitrophenylhydrazone (59 mg.) as needles (from ethanol), m. p. and mixed m. p. 137—138° (Found: C, 55·6; H, 6·2; N, 17·0. Calc. for $C_{15}H_{20}N_4O_4$: C, 56·2; H, 6·3; N, 17·5%).

The solution remaining after the initial steam-distillation was extracted with ether to remove non-steam-volatile products. These were treated with the 2,4-dinitrophenylhydrazine reagent to give 8-*methylnonane*-2,7-*dione bis*-2,4-*dinitrophenylhydrazone* as prisms (from acetic acid), m. p. 166—168° (Found: C, 49·8; H, 4·9; N, 21·5. $C_{22}H_{26}N_8O_8$ requires C, 49·8; H, 4·9; N, 21·1%).

Ozonolysis of Olefin A.—Olefin A (235 mg.) in acetic acid (20 c.c.) was treated with ozone for 15 min., and the products were worked up as above. Formaldehyde dimethone (44 mg.), m. p. 190—193°, and 8-methylnonane-2,7-dione bis-2,4-dinitrophenylhydrazone (185 mg.) (prisms from chloroform), m. p. and mixed m. p. 171—172° (Found: C, 49·3; H, 4·9; N, 20·8%), identical with the compound obtained from olefin B, were obtained.

Preparation of (±)-trans-Me,Pr^i-2-*Isopropyl*-1-*methylcyclohexanol*.—Magnesium (8·5 g.) and dry ether (125 c.c.) were treated with methyl iodide (25 c.c.) in dry ether (125 c.c.) which was added dropwise. After the addition the mixture was stirred at 20° for 1 hr. 2-Isopropylcyclohexanone (10 g.) in dry ether (95 c.c.) was slowly added to the Grignard reagent with vigorous stirring. After the addition the mixture was heated under reflux for 4 hr. and then kept overnight. The Grignard complex was cooled and decomposed by dropwise addition of water and then of cold dilute hydrochloric acid. Undissolved magnesium salts were removed and the filtrate was extracted with ether, affording an oil which was distilled to give (±)-*trans*-Me,Pr^i-2-isopropyl-1-methylcyclohexanol (9·5 g., 80%), b. p. 80—82°/15 mm., n_D^{20} 1·4660 (Found: C, 76·0; H, 12·95. $C_{10}H_{20}O$ requires C, 76·9; H, 12·8%), $\nu_{max.}$ (in CS_2) 3600 cm.$^{-1}$. The alcohol was converted into its phenylurethane as described above. The phenylurethane crystallised from light petroleum as needles, m. p. 84—85°. No depression of m. p. occurred on admixture of the phenylurethane with the phenylurethane of " Alcohol A."

Dehydration of (±)-trans-Me,Pr^i-2-*Isopropyl*-1-*methylcyclohexanol*.—The alcohol (9·5 g.), " AnalaR " pyridine (80 c.c.), and phosphoryl chloride (40 c.c.; freshly redistilled) were heated under reflux for 1½ hr. The mixture was cooled, poured on ice, and extracted with light petroleum (3 × 100 c.c.). The extracts were washed with 2N-hydrochloric acid, and then with water, before they were dried ($MgSO_4$). The solvent was removed, giving an oil which was distilled to give a hydrocarbon (5 g.) which was mainly (90%) 1-isopropyl-2-methylcyclohexene, b. p. 160—165°, n_D^{22} 1·4620, $\nu_{max.}$ (liquid film) 1675 cm.$^{-1}$. Vapour-phase chromatography indicated one major component (90%) with a minor constitutent (10%). The chromatogram was identical with that of olefin A.

Conversion of the Dehydration Product of 2-*Isopropyl*-1-*methylcyclohexanol into* (±)-cis-Me,Pr^i-2-*Isopropyl*-1-*methylcyclohexanol*.—To a stirred suspension of powdered sodium borohydride (680 mg.) in tetrahydrofuran (30 c.c.) containing the dehydration product (4·7 g.) was added boron trifluoride–ether complex (3·4 g.) in tetrahydrofuran (4 c.c.) during 1 hr. under nitrogen at 20°. After the mixture had been kept for a further hour 3N-sodium hydroxide (6·4 c.c.) was added and then, after the vigorous reaction had subsided, 30% hydrogen peroxide (6·4 c.c.) was added during 1 hr. Dilution with water and extraction with ether afforded an oil which was distilled under reduced pressure, to give *cis*-Me,Pr^i-2-isopropyl-1-methylcyclohexanol (2·5 g.), b. p. 48—50°/0·01 mm., n_D^{20} 1·4670, $\nu_{max.}$ (in CS_2) 3580 cm.$^{-1}$. The phenylurethane was prepared as described above. It crystallised from light petroleum as needles, m. p. 108—111°. No depression of the m. p. occurred on admixture of the phenylurethane with the phenylurethane of " alcohol B."

The authors thank the Dow Chemical Co. Ltd. for a sample of 2-isopropylcyclohexanone. One of them (A. R. H.) thanks A. Boake, Roberts & Co. Ltd. for a research bursary.

Appendix

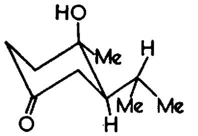
By J. V. Hatton and R. E. Richards.

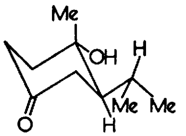
Proton spectra of ascaridole, the hydroxy-ketones " A " and " B " (VI) and (VII), and the corresponding alcohols (VIII) and (IX) were obtained with the high-resolution instrument operating at 29·92 Mc./sec. described by Leane, Richards, and Schaefer.[13] The compounds were investigated as $\sim$10% solutions in " AnalaR " chloroform since only a small amount of each was available. Chemical shifts were obtained by the side-band technique from tetramethylsilane and these are quoted in τ units. They are accurate to $\pm$0·5 c./sec.

The resonances of the olefinic protons in ascaridole (III) occur at low fields as a single line. These protons both have the same chemical shift and coupling between them is not observed. The resonance of the isopropyl group is an unsymmetrical doublet (*J* 6·5 c./sec.) due to spin coupling with the –CH proton. The doublet asymmetry arises because the coupling constant between the methyl protons and the $\geqslant$CH is of the same magnitude as the chemical shift between them.

The isopropyl group in each hydroxy-ketone, however, gives rise to a pair of doublets; for (VI), τ 8·92 and 9·4, 8·98 and 9·20; for (VII), τ 8·91 and 9·13, 9·04 and 9·25. These values indicate that the methyl groups are non-equivalent. Moreover, the chemical shift $\Delta\delta$ between the two methyl groups is 1·8 c./sec. for " ketone A " (VI) and 3·7 c./sec. for " ketone B " (VII). The factors responsible for the non-equivalence are discussed below. The methyl groups on the quaternary substituted carbon atoms have almost identical τ values, 8·60 for " ketone A " and 8·58 for " ketone B."

(XVIII)





(XIX)

The spectrum of " alcohol A " (VIII) has important differences from that of the corresponding " hydroxy-ketone A " (VI). The resonance of the isopropyl group now appears as a simple doublet (τ 8·90 and 9·10) split as before by 6·5 c./sec., indicating that the cause of the non-equivalence has been removed. Reduction of " hydroxy-ketone B " (VII) to the corresponding alcohol (IX) produces no change in the appearance of the isopropyl signal. A possible explanation of these results is provided by models of the ketones (VI) and (VII) and the alcohols (VIII) and (IX). In the hydroxy-ketone A in which the methyl and isopropyl groups are likely to be equatorial (cf. XVIII), free rotation of the isopropyl group is reduced by the steric effect of the neighbouring methyl group. The steric effect of the axial hydroxyl group is small. With the most stable conformation of the isopropyl group (cf. XVIII) one of its methyl groups will be much nearer the carbonyl group which will produce a long-range shielding, but about the same distance as the other from the axial hydroxyl group which will shield both methyl groups to the same extent. The asymmetrical shielding of the carbonyl group will give rise to the non-equivalent isopropyl resonances. Removal of the carbonyl group should eliminate this effect, as observed for the corresponding alcohol.

In " hydroxy-ketone B " (VII) the isopropyl and hydroxyl groups are likely to be equatorial and the methyl group axial (cf. XIX). The steric effects due to the equatorial hydroxyl and axial methyl groups are slightly less than in " hydroxy-ketone A," but the isopropyl group will probably take up the same conformation. Now one of the methyl groups is very close to the oxygen atom of the hydroxyl group. The shielding effect produced by it will be of much greater significance than the long-range shielding of the carbonyl group. Further, it will persist in the alcohol (IX) after the carbonyl group has been removed and the non-equivalence isopropyl resonances should therefore remain in the alcohol, as is the case.

It must be emphasised that this is a tenative explanation and other more subtle factors may be operating. Until the isopropyl signals can be observed at higher temperatures, the explanation must remain open.

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[13] Leane, Richards, and Schaefer, *J. Sci. Instr.*, 1959, **36**, 230.