21. *Rubber, Polyisoprenes, and Allied Compounds. Part I. The Synthesis of Low-molecular Polyisoprenes of the Rubber and the Squalene Type.*

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A synthesis for dihydrofarnesene, $H{\cdot}[CH_2{\cdot}CMe{:}CH{\cdot}CH_2]_3{\cdot}H$, has been devised which appears to be capable of utilisation in the formation of other low-molecular dihydropolyisoprenes,

$$H{\cdot}[CH_2{\cdot}CMe{:}CH{\cdot}CH_2]_n{\cdot}H,$$

in which the individual isoprene units are uniformly arranged in head-to-tail fashion. This synthesis, starting from geraniol, gives a triene hydrocarbon which differs in one of its additive properties from a product described as dihydrofarnesene in the literature. The reason for the difference has been investigated.

A new synthesis for squalene has been devised which appears to be capable of utilisation in the formation of other symmetrical dihydropolyisoprenes, $H{\cdot}[CH_2{\cdot}CMe{:}CH{\cdot}CH_2]_n{\cdot}[CH_2{\cdot}CH{:}CMe{\cdot}CH_2]_n{\cdot}H$, of the squalene type. This starts from geranylacetone and the Grignard derivative from 1 : 4-dibromobutane.

FOR various purposes in connexion with the investigation of rubber it has been desired to obtain low-molecular, open-chain polyisoprenes in which a uniform head-to-tail arrangement of the isoprene units is strictly maintained. A dimeric rubber in the form of dihydromyrcene,

$$H{\cdot}(CH_2{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{:}CH{\cdot}CH_2){\cdot}H,$$

is obtainable by reduction of the myrcene hydrocarbon present in Bay oil (*Pimenta acris*), and a hexameric polyisoprene is available in the form of squalene, a well-known component of certain fish-liver oils; but in the latter case the hydrocarbon is not of the rubber type, since the head-to-tail arrangement of C_5-units extends only from each end of the molecule to the middle. No other low-molecular, open-chain polyisoprenes, save one which is discussed below, are known, and there is no general method of passing with structural certainty up the polyisoprene series.

The possibility of obtaining a useful selection of relatively low-molecular, straight-chain polyisoprenes from isoprene itself by direct polymerisation has been examined concurrently with this work, but the triple requirement of rigid maintenance of the head-to-tail arrangement of units, the exclusion of all chain-branching arising from the 1 : 2-additive tendency of the diene molecules, and the fairly precise regulation of the chain-length, is a severe handicap to success. The obvious synthetic alternative to the polymeric method, amounting to the building-up of the chain unit by unit by formal organic methods, could not be other than laborious and expensive, and hence it seemed useful before embarking on it to explore the possibility of applying a third procedure, based on the Wurtz and the Grignard reaction.

Bifunctional Grignard reactions have been known in the saturated series for many years. Von Braun and Sobecki (*Ber.*, 1911, **44**, 1921) described C_8- and C_{12}-hydrocarbons obtained by such means from 1 : 4-dibromobutane, and Carothers and his co-workers have since described numerous such reactions and have closely studied the conditions necessary for promoting the polymolecular type of reaction (*J. Amer. Chem. Soc.*, 1929, **51**, 2548; 1930, **52**, 5279; *Chem. Rev.*, 1931, **8**, 353). Attempts, however, to employ an unsaturated dihalide have led so invariably and so completely to the monomeric butadiene by all feasible methods of carrying out the Wurtz and the Grignard reaction that further attempts in this direction have been abandoned.

Rubber Type of Hydrocarbon.—The most promising approach to unit-by-unit synthesis of straight-chain polyisoprenes of the rubber type seemed to be that afforded by Ruzicka's elegant procedure for building up polyterpene alcohols. From geraniol, he passed by the successive action of phosphorus trichloride, acetoacetic ester, acetylene, and nascent hydrogen to a tertiary tri-isoprene alcohol, nerolidol, and thence with phosphorus tribromide to the bromide of its anionotropic (primary alcoholic) counterpart, farnesyl bromide :

$$\underset{\text{Geraniol}}{\text{Ger.}\cdot\text{OH}} \longrightarrow \text{Ger.}\cdot\text{Cl} \longrightarrow \underset{\text{Geranylacetone}}{\text{Ger.}\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CH}_3} \longrightarrow \underset{\text{Dehydronerolidol}}{\text{Ger.}\cdot\text{CH}_2\cdot\text{CMe(OH)}\cdot\text{C}⋮\text{CH}} \longrightarrow$$

$$\underset{\text{Nerolidol}}{\text{Ger.}\cdot\text{CH}_2\cdot\text{CMe(OH)}\cdot\text{CH:CH}_2} \longrightarrow \underset{\text{Farnesyl bromide}}{\text{Ger.}\cdot\text{CH}_2\cdot\text{CMe:CH}\cdot\text{CH}_2\text{Br}}$$

$$[\text{Ger.} = \text{CH}_3\cdot\text{CMe:CH}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CMe:CH}\cdot\text{CH}_2\cdot.]$$

Further, while the present work was in progress he has, by the same method, synthesised the tetra-isoprene alcohol, geranylgeraniol, $C_{20}H_{33}\cdot OH$, from its naturally occurring tri-isoprene analogue, farnesol. Thus it has been demonstrated that it is possible to pass from the C_{10}- to the C_{15}- and thence to the C_{20}-polyisoprene skeleton in the case of alcohols; and further application of the method appears to be limited only by the necessity for using increasingly large quantities of starting material as the series is ascended.

If a ketone of Ruzicka's series, *e.g.*, geranylacetone or farnesylacetone, were to be submitted to the action of a Grignard reagent, a tertiary alcohol might be expected to result, which by dehydration ought to lead to one or more of three hydrocarbons. One of these hydrocarbons should have the correct structure for a member of the straight-chain hydrogen-stabilised (*i.e.*, dihydro) polyisoprene series. We have found that geranylacetone yields smoothly with ethylmagnesium bromide a tertiary alcohol,

$$\text{Ger.}\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CH}_3 \longrightarrow \text{Ger.}\cdot\text{CH}_2\cdot\text{CMe(OH)}\cdot\text{CH}_2\cdot\text{CH}_3 \xrightarrow{-\text{H}_2\text{O}}$$

$$\text{Ger.}\cdot\text{CH}_2\cdot\text{CMe:CH}\cdot\text{CH}_3 \text{ or } \text{Ger.}\cdot\text{CH:CMe}\cdot\text{CH}_2\cdot\text{CH}_3 \text{ or } \text{Ger.}\cdot\text{CH}_2\cdot\text{CEt:CH}_2$$

dihydronerolidol, which by dehydration with potassium bisulphate yields a triolefinic hydrocarbon, $C_{15}H_{26}$. This hydrocarbon gives on ozonolysis acetaldehyde and acetic acid in fairly good yield, but no detectable trace of formaldehyde, formic acid, or methyl ethyl ketone. Furthermore, it gives with dry hydrogen chloride a 93% yield of a homogeneous trihydrochloride. Now, although all the three isomeric hydrocarbons would be likely to yield in large measure, and probably completely, the same form of the trihydrochloride, yet the ozonolysis result points plainly to the fact that the dehydration product of dihydronerolidol is a pure, or at any rate a substantially homogeneous, *dihydrofarnesene*,

$$\text{H}\cdot[\text{CH}_2\cdot\text{CMe:CH}\cdot\text{CH}_2]_3\cdot\text{H},$$

which represents the (hydrogen-stabilised) tri-isoprene member of the rubber series; also there seems little doubt that application of the same procedure to geranylgeraniol will yield the corresponding tetra-isoprene, $\text{H}\cdot[\text{CH}_2\cdot\text{CMe:CH}\cdot\text{CH}_2]_4\cdot\text{H}$—a result which it is hoped to be able to report later.

Soon after the above experiments had been completed, however, it was found that Jones and Haenke (*Proc. Roy. Soc. Queensland*, 1936, **48**, 20, 41) in examining essential oils derived from Queensland flora had isolated a nerolidol fraction, from which in the course of purification by conversion into the sodium salt they had obtained as by-product a hydrocarbon, $C_{15}H_{26}$, having $d^{15\cdot5^\circ}$ 0·8335, $n_D^{20^\circ}$ 1·4700. This hydrocarbon they concluded to be dihydrofarnesene, since linalool under similar treatment gave dihydromyrcene, and they characterised it by forming a solid hexabromide, m. p. 131°. To confirm the constitution assigned they prepared for comparison a reputed dihydrofarnesene by the reduction with sodium and alcohol of farnesene derived by dehydration of nerolidol. This hydrocarbon also gave the hexabromide, m. p. 131°.

This property of giving amongst the various stereoisomeric forms likely to arise from an unconjugated tri-isoprene a *solid* hexabromide, and also the values assigned to the density and refractive index, distinguish the hydrocarbon from that described above, which had $d_{4^\circ}^{20^\circ}$ 0·8202, $n_D^{20^\circ}$ 1·4712, and did not give a solid hexabromide.

We had realised at the outset that farnesene derived by dehydration of farnesol was unlikely ever to be entirely free from its cyclic triene isomeride, bisabolene, since it cyclises so easily with acid reagents, among which must be included the potassium bisulphate probably employed by Jones and Haenke. Kerschbaum (*Ber.*, 1913, **46**, 1732) had dehydrated farnesol by heating it with potassium bisulphate and obtained a hydrocarbon which Ruzicka (*Helv. Chim. Acta*, 1923, **6**, 498) subsequently demonstrated to be not farnesene but bisabolene. Ruzicka, however, obtained a product with better physical constants ($d_{4^\circ}^{18^\circ}$ 0·8385; $n_D^{18^\circ}$ 1·4965), which he concluded to be farnesene, by distilling off the hydrocarbon from the bisulphate as it was formed; he suggested that farnesene must be $C_{10}H_{17}\cdot CH{:}CMe\cdot CH{:}CH_2$, or

$$C_{10}H_{17}\cdot CH_2\cdot C({:}CH_2)\cdot CH{:}CH_2,$$

or a mixture of both. Later, he synthesised bisabolol (*ibid.*, 1932, **15**, 3). Farnesene having either of the (conjugated) structures suggested by Ruzicka should, of course, give the desired dihydrofarnesene on reduction.

Whether farnesene can be obtained entirely free from bisabolene when potassium bisulphate is used as dehydrating agent does not appear from Ruzicka's observations. We have dehydrated farnesol with this reagent, distilling off the hydrocarbon as it was formed, and so obtained a product having rather a higher density ($d_{4^\circ}^{19\cdot5^\circ}$ 0·8469; $n_D^{19^\circ}$ 1·4945) and probably therefore a rather greater bisabolene content than Ruzicka's. Determination of the unsaturation of this hydrocarbon by hydrogenation gave a value, probably somewhat low through incompleteness of reaction, of $|^{=}_{3\cdot5}$ per $C_{15}H_{24}$, indicating the presence therein of at least 50% of farnesene; heating with formic acid (Ruzicka's method) caused complete conversion into bisabolene, as shown by the purity of the derived bisabolene trihydrochloride. Reduction of the hydrocarbon with sodium and alcohol gave a " dihydrofarnesene " having three double bonds (Found, by hydrogenation : $|^{=}_{2\cdot85}$) and physical constants somewhat higher than those of our hydrocarbon from dihydronerolidol, doubtless due to the substantial amount of bisabolene present; but the physical constants of this reduction product agreed closely with those of Jones and Haenke's material. Conversion of this " dihydrofarnesene " into the hydrochloride gave a solid product which was easily separated into two trihydrochlorides, one of bisabolene and one identical with the *trihydrochloride* of our dihydrofarnesene from dihydronerolidol. Nevertheless, we have not yet isolated from the bromide of this " dihydrofarnesene " any crystalline hexabromide. We see no reason, therefore, to doubt the substantial purity of our dihydrofarnesene described above, or the correctness of the constitution assigned to it.

Squalene Type of Hydrocarbon.—With farnesyl bromide as starting point, it is only necessary, as Karrer has shown (*Helv. Chim. Acta*, 1931, **14**, 78) to couple the hydrocarbon radicals of two molecules of halide by a metal such as magnesium to produce a hydrocarbon identical with natural squalene. Starting, however, from the more readily available geraniol, it is necessary to intercalate a centrosymmetrical di-isoprene system between two geranyl radicals. This might be expected to be capable of accomplishment, so far as the carbon framework is concerned, by combining two molecules of geranylacetone with the Grignard reagent derived from 1 : 4-dibromobutane :

$$2\text{Ger.}\cdot CH_2\cdot COMe + MgBr\cdot[CH_2]_4\cdot MgBr \longrightarrow \text{Ger.}\cdot CH_2\cdot CMe(OH)\cdot[CH_2]_4\cdot CMe(OH)\cdot CH_2\cdot\text{Ger.}$$
$$(\text{Ger.} = C_{10}H_{17})$$

As regards the Grignard reagent required, von Braun and Sobecki's experiments (*loc. cit.*) indicated that the metallo-organic derivatives $MgBr\cdot[CH_2]_4\cdot MgBr$, $MgBr\cdot[CH_2]_8\cdot MgBr$, and $MgBr\cdot[CH_2]_{12}\cdot MgBr$ are all formed side by side when magnesium acts on 1 : 4-dibromobutane; also Young, Prater, and Winstein (*J. Amer. Chem. Soc.*, 1933, **55**, 4908) have described optimum conditions for the preparation of the normal Grignard compound from the difficultly reactive crotyl bromide. Since the Grignard product from dibromobutane cannot easily be fractionated before use, we tried to suppress as far as possible the formation of polymeric forms of the metallo-organic compound from 1 : 4-dibromobutane by using the conditions described by Young and his co-workers. This procedure, probably aided by the preferential tendency for the monomeric rather than the polymeric forms of the dimagnesium halide to react with the geranylacetone, has been successful in yielding principally *one* compound—a *glycol* of the expected empirical formula, $C_{30}H_{52}(OH)_2$; there was, however, a residue which probably consisted of the analogous C_{34}-glycol derived from $MgBr{\cdot}[CH_2]_8{\cdot}MgBr$.

The C_{30}-glycol showed a molecular refraction 1·5 units higher than the calculated figure, which recalls the exactly similar experience of Heilbron with non-conjugated natural squalene (J., 1936, 1630; see also Farmer and Sutton, this vol., p. 139) and of Farmer and Van den Heuvel (*J. Soc. Chem. Ind.*, 1938, **57**, 24) with highly unsaturated fish-oil acids. This phenomenon, which is apparently due either to the inaccuracy of the atomic refractivity values (Eisenlohr's) employed in calculating $[R_L]_D$, or to the appearance of conjugation during heating, is being investigated.

By the action of dry hydrogen chloride on the C_{30}-glycol there was obtained a mixture of three isomeric hexahydrochlorides which proved to be identical with the three isomerides first obtained by Heilbron from squalene (*loc. cit.*); and since squalene can easily be regenerated from these hydrochlorides by the action of mildly alkaline reagents, this work constitutes a new synthesis of squalene and also suggests a general method for the synthesis of hydrocarbons of the squalene type. Thus, from farnesylacetone a

$$2Far.{\cdot}CH_2{\cdot}COMe + MgBr{\cdot}[CH_2]_4{\cdot}MgBr \longrightarrow Far.{\cdot}CH_2{\cdot}CMe(OH){\cdot}[CH_2]_4{\cdot}CMe(OH){\cdot}CH_2{\cdot}Far.$$
$$[Far. = C_{15}H_{25}{\cdot}]$$

C_{40}-glycol would be expected to result, from which by direct dehydration, or *via* the derived octahydrochlorides, a C_{40}-polyisoprene hydrocarbon of squalene type might be expected to be formed.

It is on record (Simonsen, " The Terpenes," Vol. 2, 562) that farnesol gives with dry hydrogen chloride the same product as does its dehydration product farnesene :

$$\underset{\text{Farnesol}}{H{\cdot}[CH_2{\cdot}CMe{:}CH{\cdot}CH_2]_3{\cdot}OH} \xrightarrow{HCl} \text{Tetrahydrochloride} \xleftarrow{HCl} \underset{\text{Farnesene}}{H{\cdot}[CH_2{\cdot}CMe{:}CH{\cdot}CH_2]_2{\cdot}CH{:}CMe{\cdot}CH{:}CH_2}$$

The new C_{30}-glycol, as noted above, gives the same mixture of three isomeric hexahydrochlorides as does natural squalene. To this we now add that the dihydronerolidol whose synthesis is described above gives the same trihydrochloride as does its dehydration product dihydrofarnesene. The yield of hydrochloride from the alcohol was quantitative, whereas that from the hydrocarbon at the first attempt was 93%; and it is of considerable interest that the yields of hydrochlorides of polyisoprenes (including rubber with a molecular weight of about 300,000) seem generally to be quantitative, or very nearly so, under suitable conditions of reaction.

EXPERIMENTAL.

Geranylacetone.—Commercial geraniol of good quality was purified by conversion into its calcium chloride compound, essentially the procedure of Bertram and Gildemeister (*J. pr. Chem.*, 1897, **56**, 506) being used. The regenerated geraniol, b. p. 117°/13 mm. (yield 55—60%), was converted into its chloride (yield 60%) and thence into geranylacetone by the method of Ruzicka (*Helv. Chim. Acta*, 1923, **6**, 492). The rectified ketone boiled at 126—128°/10 mm.; yield 70%.

Dihydronerolidol.—To an ethereal solution of ethylmagnesium bromide (6·07 g. of magnesium, 27·2 g. of ethyl bromide, 100 c.c. of ether) contained in a 1-l. flask fitted with condenser, dropping funnel, and a mercury-sealed stirrer, a solution of 48·5 g. of geranylacetone in 50 c.c. of ether was added gradually with good stirring. The reaction product was boiled for 30 mins. and then decomposed by gradual addition of excess of water under good stirring. The stirring was continued whilst sufficient 2N-hydrochloric acid was added to dissolve the magnesium hydroxide, after which the crude dihydronerolidol was extracted with ether, the extract washed in turn with sodium bicarbonate solution and water, and then dried over potassium carbonate. Removal of the solvent gave a product which after suitable fractionation boiled at 137—140°/8 mm.; yield 77%. The *dihydronerolidol* was a colourless, odourless, not very mobile liquid; $d_{4^{\circ}}^{20^{\circ}}$ 0·8693; $n_D^{20^{\circ}}$ 1·4690; $[R_L]_D$ 71·73 (Calc. for $|^{=}_{2}$, 72·06) (Found : C, 80·5; H, 12·7; active H, 0·49. $C_{15}H_{28}O$ requires C, 80·35; H, 12·5; active H, 0·45%).

Dihydrofarnesene.—Dihydronerolidol (20 g.) was refluxed over finely powdered potassium bisulphate for 45 mins. at 18 mm. pressure in a 100 c.c. flask fitted with capillary bubbler (bath temp. 160°). The condenser was replaced by a still-head and the liquid product distilled off. The distillate (b. p. 130—140°/15 mm.) was again refluxed at reduced pressure (for 25 mins.) with 5 g. of fresh potassium bisulphate, and the product distilled off. The distillate was carefully fractionated over sodium in an apparatus based on that described by Schrader and Ritzer (*Ind. Eng. Chem. Anal.*, 1939, **11**, 54), but modified to avoid the strong tendency to evaporative distillation experienced with the apparatus when good oil-pump vacua are employed, and provided with alternative sets of collecting cups. The bulk of the product boiled at 129—131°/11 mm. (yield 65%), leaving a liquid residue of higher b. p. The former was a triolefinic hydrocarbon, *dihydrofarnesene* (Found : C, 86·8; H, 12·7. $C_{15}H_{26}$ requires C, 87·3; H, 12·7%); $d_{4^\circ}^{20^\circ}$ 0·8202, $n_D^{20^\circ}$ 1·4712, unsaturation (iodine value) $|^{=}_{2\cdot99}$, $|^{=}_{2\cdot97}$, $[R_L]_D$ 70·29 (Calc. for $|^{=}_{3}$, 70·07).

Dihydrofarnesene Trihydrochloride.—(i) *From dihydrofarnesene.* The hydrocarbon (3·25 g.), dissolved in dry ether (25 c.c.) and protected against atmospheric moisture, was saturated at 0° during 1 hour with dry hydrogen chloride. The ether and excess hydrogen chloride were evaporated, leaving a thick, oily residue which soon solidified in a vacuum desiccator. The crystals of crude *trihydrochloride* (93% yield) melted at 44—47°, but reached a constant m. p. of 52° after one recrystallisation from methyl alcohol (Found : Cl, 33·75. $C_{15}H_{29}Cl_3$ requires Cl, 33·70%).

(ii) *From dihydronerolidol.* Dihydronerolidol (3 g.), dissolved in dry ether (100 c.c.), when saturated with dry hydrogen chloride as above, gave a white solid (4·2 g.; 100%) of m. p. 44—47°, which after one crystallisation from methyl alcohol melted constantly at 52°. Mixed m. p. with foregoing trihydrochloride, 52°.

Ozonolysis of Dihydrofarnesene.—The hydrocarbon (2·9 g.), dissolved in ethyl acetate (20 c.c.) and cooled in an ice–salt bath, was ozonised (1·44 g. ozone per hour) for 90 mins., after which the solvent was removed under reduced pressure with gentle warming, and the residue decomposed by warming and finally boiling with water. The issuing gases were passed through a liquid-air trap, and the steam distillate fractionated under a short column. The products were : (1) acetone, 0·33 g. (estimated by Messenger's method), identified by 2 : 4-dinitrophenylhydrazone, m. p. 125°; (2) acetone peroxide, m. p. 130°, 50 mg. (total yield of acetone, 47%); (3) acetaldehyde, converted with considerable loss into its dimedon derivative, m. p. 139° (yield 10%); and (4) an aqueous residue containing acetic acid. Half the aqueous residue was neutralised with standard sodium ethoxide solution (3 g./l.), and the neutral solution heated with *p*-bromophenacyl bromide. The titre and the yield of *p*-bromophenacyl acetate (m. p. 83°, mixed m. p. 84—85°) both corresponded to 0·2 g. of acetic acid. The remainder of the aqueous residue gave by extraction with ether a rather viscous liquid which, by reason of its strong iodoform reaction and the formation of a semicarbazone (m. p. 183°, decomp.), was doubtless impure lævulic acid (semicarbazone, m. p. 187°). No formaldehyde could be isolated from, or detected by colour tests in, the condensate in the liquid-air trap or the volatile distillate; and likewise no methyl ethyl ketone could be isolated or detected.

Dehydration of Farnesol.—The farnesol, supplied by C. Naef and Co. of Geneva, was purified by conversion into its hydrogen phthalate and subsequently distilled. The pure alcohol (yield 40%) boiled at 118—120°/1 mm., and was characterised by converting it into farnesal (semicarbazone, m. p. 125°) as recommended by Ruzicka.

Farnesol (10 g.) was heated with finely powdered potassium bisulphate under 12 mm. pressure in a flask placed in a bath maintained at 160—170°, the hydrocarbon being allowed to distil as it was formed. The product was a yellow oil, which on redistillation over sodium boiled at 127—130°/12 mm. and had $d_{4^\circ}^{19\cdot5^\circ}$ 0·8469, $n_D^{19^\circ}$ 1·4945; yield 4·7 g.

A portion of this dehydration product (1 c.c.) was converted into bisabolene by heating it with 90% formic acid (2 c.c.) at 120—130° for 15 mins. The product, when isolated, was an oil, b. p. 130°/15 mm., which when treated with dry hydrogen chloride in ethereal solution gave the hydrochloride. This when once recrystallised from methyl alcohol gave the correct m. p. (79°) for bisabolene trihydrochloride. Another portion (0·1004 g.) was hydrogenated in acetic acid (Adams's catalyst) and took up an amount of hydrogen (37·8 c.c. at N.T.P.) corresponding to $|^{=}_{3\cdot5}$ per $C_{15}H_{24}$.

Reduction, Hydrogenation, and Hydrochlorination of Dehydration Product.—A portion of the dehydration product (3·4 g.) was dissolved in absolute alcohol (30 c.c.) and reduced vigorously with lump sodium (9 g.). When ebullition slackened, the reaction vessel was heated on a water-bath and more alcohol (50 c.c.) was added. The product, isolated in the usual way and distilled over sodium, was an oil; b. p. 120—130°/12 mm., $d_{4^\circ}^{20}$ 0·8348, $n_D^{22^\circ}$ 1·4786. Another portion (0·1854 g.) when hydrogenated as above absorbed hydrogen (58 c.c. at N.T.P.) corresponding to $|^{\equiv}_{2\cdot85}$.

A third portion (1 c.c.) was dissolved in dry ether and saturated with dry hydrogen chloride at 0°. The crude hydrochloride (m. p. 50—56°) was fractionally crystallised from methyl alcohol, and so gave a less soluble hydrochloride, m. p. 77°, and a more soluble one, m. p. 49—41°. The former when mixed with authentic bisabolene trihydrochloride (m. p. 79°) gave m. p. 77°, and the latter when mixed with the trihydrochloride of the hydrocarbon derived by dehydration of dihydronerolidol (see above) gave m. p. 50—51°.

Bromide of Dihydrofarnesene.—Samples of dihydrofarnesene, derived (a) by dehydration of dihydronerolidol and (b) by reduction of the farnesene–bisabolene mixture from farnesol, were dissolved in chloroform and treated with slight excess of bromine in chloroform at 0° and subsequently at room temperature. The bromides were unsolidifiable thick oils.

Synthesis of Squalene Hexahydrochlorides.

Grignard Derivative from 1 : 4-*Dibromobutane.*—1 : 4-Butylene glycol, derived from ethyl succinate (Muller, *Monatsh.*, 1927, **48**, 523, 735; 1928, **49**, 27), was converted by hydrogen bromide into 1 : 4-dibromobutane (Muller, *loc. cit.*) and thence into the corresponding dimagnesium halide under Braun and Sobecki's conditions (*loc. cit.*) as modified by Young (*loc. cit.*) in order to avoid the formation of considerable yields of dimeric and trimeric products.

To magnesium (8·64 g.), covered with dry ether, 1 : 4-dibromobutane (38·4 g.), dissolved in ether (80 c.c.), was very slowly added with rapid stirring. Refluxing occurred, and when it subsided, more ether (150 c.c.) was added, and the whole heated on a water-bath to refluxing for ½ hour. Little of the magnesium remained, and the Grignard complex separated out as a heavy oil.

Dihydroxydihydrosqualene.—Geranylacetone (46 g.; ⅔ of theory), dissolved in ether (50 c.c.), was added gradually with good stirring to the foregoing Grignard derivative. Refluxing set in, and the reaction was completed by maintaining gentle ebullition on a water-bath for ¾ hour. The greenish product was decomposed by cautious addition of water, and the crude glycol so formed extracted from the aqueous liquor (without acidification) with ether. The ethereal extract, dried over potassium carbonate, yielded a light yellow oil (40 g.), which gave by distillation under 1 mm. pressure the fractions: (i) b. p. 80—175°, 13·4 g.; (ii) b. p. 220—250°, 24·1 g.; and (iii) brown, semi-solid residue, 2 g. The fraction (ii) was a nearly colourless, somewhat viscous oil, which on redistillation at 1 mm. pressure gave a colourless oil, b. p. 220—235° (18 g.), and a more viscous liquid, b. p. 240—250°, which was rejected. The former, *dihydroxydihydrosqualene* (Found: C, 80·35; H, 12·3. $C_{30}H_{54}O_2$ requires C, 80·7; H, 12·2%), had $d_{4^\circ}^{20^\circ}$ 0·9079, $n_D^{20^\circ}$ 1·4944, $[R_L]_D$ 143·2 (Calc.: 141·7); active H, 0·42 (Calc.: 0·45%); the latter appeared to be a mixture containing a little dihydroxydihydrosqualene and a similar material probably derived from the C_8-Grignard derivative.

Squalene Hexahydrochlorides.—Through dihydroxydihydrosqualene (5 g.), dissolved in dry ether, cooled in ice-salt and protected from moisture, a slow stream of dry hydrogen chloride was passed until the gas began to escape freely, and then for a further 15 mins. The solvent and excess of hydrogen chloride were removed at reduced pressure, whereupon the residue soon crystallised. The white crystalline mass (m. p. 100—120°), after being washed with ether, had chlorine content 33·8% (Calc. for $C_{30}H_{56}Cl_6$: 33·7%). This was separated into three isomeric hexahydrochlorides, m. p.'s 107°, 112—115°, 144°, by the procedure of Heilbron *et al* (*loc. cit.*): the isomerides (respectively) showed no depression of m. p. when mixed with the corresponding derivatives of similar m. p. obtained for comparison by treatment of genuine squalene from shark oil (*Symnorhinus lichia*) with hydrogen chloride.

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