112. *The Synthesis of Polyterpenoid Compounds. Part I. Preliminary Experiments.*

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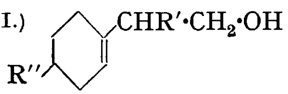
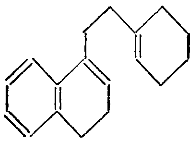
Methods recently developed in this and other laboratories for the synthesis of hydrogenated phenanthrene derivatives necessarily give products which contain at least one aromatic ring, a circumstance which precludes the general extension of such methods to the synthesis of many of the naturally occurring polycyclic compounds. However, it is well known that terpenoid compounds often readily undergo cyclisation by interaction of pairs of ethylenic bonds within the molecule. The purpose of this series of memoirs is to present methods of synthesis of compounds containing two double bonds suitably disposed for cyclisation to polycyclic hydroaromatic compounds. The outcome of the experiments now described has not been very satisfactory, partly on account of the difficulty of isolating homogeneous substances in the later stages of the syntheses, and partly on account of the unexpected resistance to cyclisation shown by the synthetic dienes. Nevertheless, it is desired to place on record the procedure adopted in the synthesis of such dienes, and it is proposed to extend these methods to compounds in which a methyl group is attached to one of the unsaturated carbon atoms at which cyclisation should occur. Experience with other types of compound (Cook, Hewett, Mayneord, and Roe, J., 1934, 1727) encourages the belief that the presence of such methyl groups will facilitate cyclisation. This is also suggested by the presence of similarly disposed methyl groups in the terpenes which so readily undergo cyclisation, even by boiling with formic acid; for example, α-camphorene (Ruzicka and Stoll, *Helv. Chim. Acta*, 1924, **7**, 271) and squalene (Heilbron, Kamm, and Owens, J., 1926, 1641).

Bouveault reduction of ethyl Δ^1-*cyclo*hexenylacetate led to the anticipated β-Δ^1-cyclo*hexenylethyl alcohol* (I; $R' = R'' = H$), the βγ-double bond being unattacked by sodium and alcohol. The Grignard compound of the corresponding *bromide* was treated with (a) *cyclo*hexanone and (b) α-tetralone. The resulting crude carbinols were dehydrated to the corresponding dienes, that from α-tetralone, for example, being represented in all probability by structure (II), for it is well known that dehydration of cyclic carbinols leads to an endocyclic rather than an exocyclic double bond.

(I.)





(II.)

Attempts to cyclise (II) to a decahydrochrysene by prolonged heating with 98% formic acid were unsuccessful, and the bromine absorption value of the analogous diene obtained from *cyclo*hexanone was not appreciably diminished by 24 hours' boiling with formic acid. Partial cyclisation of (II) was effected by boiling acetic acid containing sulphuric acid, the reaction being accompanied by much resinification. The unpolymerised product gave chrysene when dehydrogenated with selenium.

Bouveault reduction of ethyl α-(4-methyl-Δ^1-*cyclo*hexenyl)propionate gave β-(4-methyl-Δ^1-*cyclo*hexenyl)-*n*-propyl alcohol (I; $R' = R'' = Me$). No sesquiterpenoid hydrocarbon could be obtained from the products of interaction of *iso*valeraldehyde with the Grignard solution prepared from the bromide of this alcohol.

EXPERIMENTAL.

β-Δ^1-cyclo*Hexenylethyl Alcohol* (I; $R' = R'' = H$).—The Reformatsky reaction with *cyclo*hexanone was carried out in benzene solution (Wallach, *Annalen*, 1905, **343**, 51; 1906, **347**, 328), Kahlbaum's ethyl bromoacetate being used. In spite of many attempts we were unable to effect any condensation with ethyl bromoacetate supplied by British Drug Houses, Ltd. Dehydration of ethyl *cyclo*hexanol-1-acetate to ethyl Δ^1-*cyclo*hexenylacetate was only partially effected with potassium hydrogen sulphate (contrast Auwers and Ellinger, *Annalen*, 1912, **387**, 228). The incompleteness of the dehydration was probably due to some peculiarity of the potassium hydrogen sulphate with which we were unfortunate enough to be supplied, for one of us (J. W. C.) has repeatedly failed to effect complete dehydration with this material (which was well fused immediately before use) of divers carbinols for which the successful use of potassium hydrogen sulphate had been claimed in the literature. Dehydration of ethyl *cyclo*hexanol-1-acetate (36 g.) was successfully accomplished by 2½ hours' heating on the water-bath with phosphoric oxide (50 g.) in benzene (150 g.).

Sodium (66 g.) was gradually added to a boiling solution of ethyl Δ^1-*cyclo*hexenylacetate (80 g.) in ethyl alcohol (380 g.), the temperature of the bath being gradually raised to 130° during addition, and maintained at this point for 7 hours. Water was cautiously added until the excess of sodium was destroyed. A large volume of water was then added, and the cold liquid repeatedly extracted with ether. The extract was dried (sodium sulphate), the ether and most of the ethyl alcohol distilled through a fractionating column, and the residue cautiously distilled in steam until the last traces of ethyl alcohol had been removed. The *cyclo*hexenylethyl alcohol was then again extracted with ether and distilled in a vacuum. It formed a colourless pleasant-smelling liquid, b. p. 85—90°/8 mm. (yield, 55%), and absorbed the amount of bromine required for one double bond (method of Rosenmund and Kuhnhenn, *Z. Unters. Nahr. Genussm.*, 1923, **46**, 154).

β-Δ^1-cyclo*Hexenylethyl* 3 : 5-*dinitrobenzoate*, formed by brief warming at 100° with 3 : 5-dinitrobenzoyl chloride in pyridine, formed colourless needles (from alcohol), m. p. 80° (Found : C, 56·1; H, 5·0. $C_{15}H_{16}O_6N_2$ requires C, 56·2; H, 5·0%). β-Δ^1-cyclo*Hexenylethyl alcohol*, obtained by hydrolysis of the pure dinitrobenzoate, gave low values for carbon, probably on account of oxidation at the expense of the potassium dinitrobenzoate (compare Hückel and Kumetat, *Ber.*, 1934, **67**, 1890) (Found: C, 75·3; H, 11·7. $C_8H_{14}O$ requires C, 76·2; H, 11·2%).

β-Δ^1-cyclo*Hexenylethyl Bromide*.—Phosphorus tribromide (14 g.) was slowly added to an ice-cold mixture of the alcohol (17 g.), ligroin (20 g.), and pyridine (1 c.c.). After being kept at 0° for 2 hours, the whole was treated with water, and the oily layer separated, washed with water and dilute sodium carbonate solution, dried (calcium chloride), and distilled in a vacuum. The *bromide* (yield, 50%) formed an unstable colourless liquid, b. p. 90°/7 mm. (Found : C, 50·3; H, 7·3. $C_8H_{13}Br$ requires C, 50·8; H, 6·9%).

β-(4-Methyl-Δ^1-*cyclo*hexenyl)-*n*-propyl alcohol was obtained by reduction with sodium and ethyl alcohol of ethyl α-(4-methyl-Δ^1-*cyclo*hexenyl)propionate (Wallach, *Annalen*, 1908, **360**, 52), exactly as in the case of the lower homologue. It formed a colourless, viscous, pleasant-smelling liquid, b. p. 105—109°/10 mm. (yield, 35%), and gave a 3 : 5-*dinitrobenzoate*, which crystallised from alcohol in colourless needles, m. p. 71° (Found : C, 58·4; H, 5·9. $C_{17}H_{20}O_6N_2$ requires C, 58·6; H, 5·8%). The free alcohol absorbed the amount of bromine required for one double bond. The *bromide*, prepared by the method described above, was a very unstable, colourless liquid, b. p. 95—100°/10 mm., having a camphor-like smell (Found : C, 57·1; H, 8·3. $C_{10}H_{17}Br$ requires C, 55·3; H, 7·9%).

Attempted Synthesis of Dodecahydrophenanthrene.—A mixture of β-Δ^1-*cyclo*hexenylethyl bromide (16 g.) and anhydrous ether (50 c.c.) was added during an hour to a large excess of magnesium (5 g.), the liquid being kept vigorously boiling. Under other conditions very poor yields of Grignard compound were obtained. The clear solution was decanted from the excess of magnesium, cooled in ice, and treated dropwise with *cyclo*hexanone (8·5 g.). After being kept at room temperature over-night, the product was decomposed (ice and ammonium chloride), washed, dried (sodium sulphate), and distilled at 5 mm. β-Δ^1-cyclo*Hexenylethyl*cyclo*hexanol*, which could not be obtained analytically pure, formed a colourless, somewhat viscous liquid, b. p. 89—91°/0·3 mm., with a faint orange-like smell (Found : C, 82·8; H, 11·5. $C_{14}H_{24}O$ requires C, 80·7; H, 11·6%). Dehydration with potassium hydrogen sulphate was incomplete; the resulting colourless liquid, after distillation over sodium, had b. p. 97—98°/4—5 mm. (Found : C, 86·7; H, 12·1. $C_{14}H_{22}$ requires C, 88·3; H, 11·7%). No change in the bromine absorption value was brought about by 24 hours' boiling with 98% formic acid (4 parts), and subsequent heating with selenium at 300—310° for 16 hours did not result in dehydrogenation (Found, after redistillation over sodium : C, 88·5; H, 11·2%). The significance of the latter observation need not be discussed at present, as an investigation of other hydroaromatic compounds resistant to the dehydrogenating action of selenium is in progress.

Formation of Chrysene.—A Grignard solution prepared from β-Δ^1-*cyclo*hexenylethyl bromide (9·4 g.) was treated with α-tetralone (7·25 g.) and then boiled for 2 hours. After decomposition with ice and ammonium chloride the ethereal solution was washed, dried, and distilled. The crude carbinol fraction (3·5 g.; b. p. 140—175°/6 mm.) was heated at 160—170° for 2 hours with potassium hydrogen sulphate, and the product redistilled in a vacuum. The bromine absorption value was in agreement with formula (II). Attempted cyclisation with formic acid under various conditions (*e.g.*, by heating on the water-bath for 24 hours with 98% acid) led to no change in the bromine absorption value, and subsequent dehydrogenation with selenium gave no more than a trace of chrysene. When the hydrocarbon (II) (1 g.) was boiled for 5 hours with concentrated sulphuric acid (1 c.c.) in acetic acid (10 c.c.), much resinification took place. After extraction with ether and distillation in a vacuum, 0·2 g. of an oil was obtained, and this gave 20 mg. of pure chrysene (identified by comparison with an authentic sample) after dehydrogenation with selenium.

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