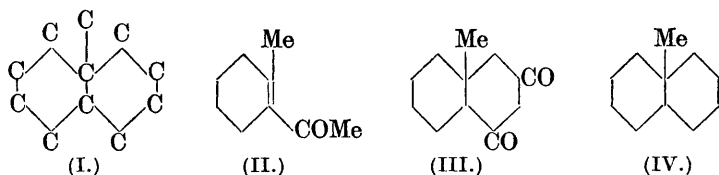


239. *Synthetic Studies in the Decalin Series.* *Part I. The Preparation of 9-Substituted Decalins.*

By GEORGE ROGER CLEMO and JOHN ORMSTON.

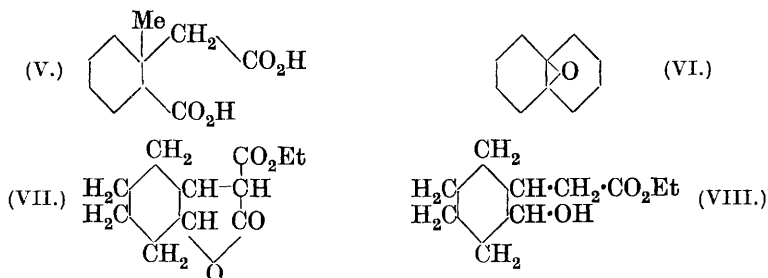
THE work done on santonin (J., 1929, 2368; 1930, 1110, 2579), combined with the fact that many important complex terpenes, the sterols, and certain of the alkaloids are stated to have an alkyl group or a constituent of a ring attached to a carbon atom which is itself a common member of two ring systems such as (I), made it a matter of importance to investigate the synthesis of compounds of this type. The literature appeared not to contain any reference to synthetic work of this nature until Ruzicka and co-workers (*Helv. Chim. Acta*, 1931, **14**, 1151), following a different line from our own, put on record work in this field. The first and simplest case described is the synthesis of 9-methyl-*trans*-decalin (IV) in which



2-acetyl-1-methyl- Δ^1 -cyclohexene (II) and malonic ester are condensed to give (III) and the reduction of this by Clemmensen's method is claimed to give (IV). Oxidation of the diketone-compound (III) is stated to give the acid (V).

We have endeavoured to obtain compounds of the type (I), starting from decalin itself. Nametkin and co-workers (*Ber.*, 1926, **59**, 370; 1929, **62**, 1570) have shown that the nitration of decalin gives 9-nitrodecalin, which on reduction gives the 9-amino-compound (see experimental part), and that this could be converted into Δ^9 : 10 -octalin by long boiling of its hydrochloride with aqueous

sodium nitrite. The octalin thus obtained is the same as that prepared by Hückel and co-workers (*Annalen*, 1929, **474**, 121), since it gives the same derivatives. There is little likelihood of its containing any of the undescribed $\Delta^{1:9}$ -isomeride, since Hückel (*loc. cit.*), in endeavouring to prepare this, always obtained the $\Delta^{9:10}$ -compound. Oxidation of $\Delta^{9:10}$ -octalin by perbenzoic acid in chloroform solution gave the corresponding oxide (VI).



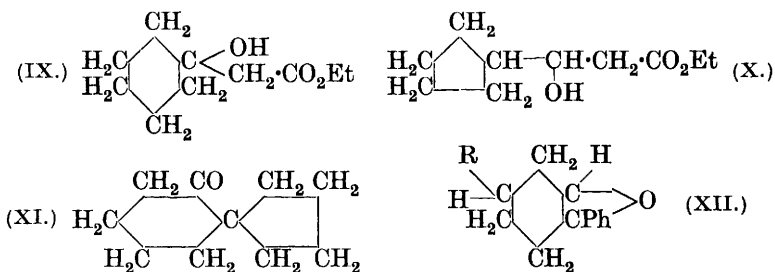
$\Delta^{9:10}$ -Octalin readily adds hydrogen bromide or hydrogen iodide to give 9-bromo- or 9-iodo-decalin. Attempts were made to condense these compounds with ethyl sodio- and potassio-malonates, but in every case hydrogen halide was lost and the octalin regenerated. A similar result was obtained when potassium cyanide was used in an endeavour to replace the halogen by cyanogen. Further, these halogen derivatives gave no Grignard reagents. Likewise attempts to condense $\Delta^{9:10}$ -octalin dibromide with sodiomalonic ester gave only octalin and ethanetetra-carboxylic ester. This result is analogous to the reaction between 1:2-dibromocyclohexane and sodiomalonic ester (Coffey, *Rec. trav. chim.*, 1923, **42**, 387). Coffey showed, however, that cyclohexene oxide and sodiomalonic ester condensed quite smoothly to give 1-carbethoxyhexahydroisocoumaranone (VII). An attempt was therefore made to condense octalin oxide (VI) with sodiomalonic ester, but without success. This agrees with the results of Traube and Lehmann (*Ber.*, 1899, **32**, 720; 1901, **34**, 1971), who, presumably for steric reasons, could not condense sodiomalonic ester with tetrasubstituted ethylene oxides.

The action of methylmagnesium iodide on $\Delta^{9:10}$ -octalin oxide (VI) gave a mixture whose components have not yet been separated and are still under investigation.

The use of oxides in place of ketones in the Reformatsky reaction appears to be novel, and the reaction between cyclohexene oxide and ethyl bromoacetate was investigated in the first instance. The condensation proceeded smoothly, giving a compound which analysis indicated to be ethyl 2-hydroxycyclohexylacetate (VIII). The lactone of the latter has been prepared by Coffey from (VII). It

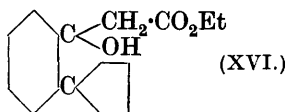
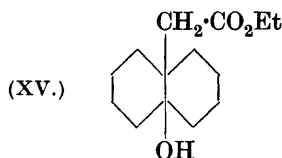
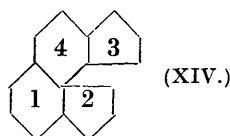
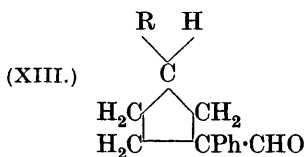
readily forms a hydrazide, m. p. 167.5° , and an amide, m. p. 154° . The compound obtained by us, however, which may be a *trans*-isomeride of (VIII), gave a *hydrazide*, m. p. 154° , but not an amide.

There is a possibility that the *cyclohexene* oxide might first isomerise in the reaction to *cyclohexanone* (compare Kötze and Busch, *J. pr. Chem.*, 1928, 119, 1, who found that $\Delta^{3:4}$ -*p*-menthene oxide with alcoholic hydrogen chloride gave menthone) and that this substance would then undergo the Reformatsky reaction to give ethyl 1-hydroxycyclohexylacetate (IX). This compound was prepared by Wallach and Isaacs (*Annalen*, 1906, 347, 328) and it has now been found to give a *hydrazide*, m. p. 103° . Still another possibility which is being examined is that the *cyclohexene* oxide may isomerise to give *cyclopentanealdehyde* (compare Bedos, *Compt. rend.*, 1929, 189, 255), and this would then yield compound (X) by the Reformatsky reaction.



In the light of the above, $\Delta^{9:10}$ -octalin oxide was treated with zinc and ethyl bromoacetate and two well-defined liquid fractions, A and B, were obtained. The lower-boiling A was 2-ketocyclohexane-*spiro*-cyclopentane (XI), a compound obtained from *cyclopentanone*-pinacol by Meiser (*Ber.*, 1899, 32, 2055), and by Hückel and co-workers by subjecting 9 : 10-dihydroxydecalin to a pinacol-pinacolin transformation. Evidently, therefore, under the very mild conditions used in the Reformatsky reaction the compound (VI) is partly changed to (XI), presumably *via* the pinacol-pinacolin transformation. This result is the more interesting in view of the fact that Tiffeneau and collaborators (*Bull. Soc. chim.*, 1931, 49, 1595) have shown that compounds of the ethylene oxide type can isomerise in a variety of ways, and, in particular, the compound (XII, R = H or Me) can transform to (XIII). This facile change of (VI) to (XI) prompts the suggestion that certain of the more complex compounds such as cholesterol may have *spiro*-structures, at any rate in part, in place of some of the unusual ring systems ascribed to them to-day. Thus it is stated (*Ann. Reports*, 1931, 141) that Wieland's ring system for cholesterol (XIV) needs modifying so that

rings I and IV become seven-membered. This seems most unlikely. Further it appears possible that spiran compounds such as (XI) might, by drastic and prolonged dehydrogenation by sulphur or selenium at 280—340°, form aromatic compounds, in this case naphthalene. Both these points are being investigated.



The fraction B was an *ester*, giving the correct analytical results for (XV) and forming a crystalline *hydrazide*, m. p. 122°. On hydrolysis it gave an acid which, however, has not yet been induced to crystallise. Since some of the ketone (XI) is formed in the reaction, it was thought that B might have been derived from it and have the structure (XVI). With a view to deciding between these two possibilities, (XVI), which should be resolvable, was prepared directly from (XI). It gave a low-melting non-crystallising hydrazide, in marked contrast with the highly crystalline hydrazide from B.

Finally an attempt was made to confirm the structure (XV) for the ester B by dehydrogenating it with selenium: although this reaction did not give a homogeneous product, sufficient naphthalene for identification was isolated from 1.5 g. of B. Amongst the other products of dehydrogenation was a trace of a high-boiling *hydrocarbon*, $C_{18}H_{12}$, m. p. 142—143° (this compound does not appear to be recorded in the literature), and a powerfully smelling liquid (picrate, m. p. 140—141°, depressed to 139° by admixture with 1-methylnaphthalene picrate), whose nature has not yet been elucidated.

This work is being actively extended.

EXPERIMENTAL.

9-Aminodecalin.—Into zinc dust (100 g.) and water (100 c.c.), heated under reflux on the water-bath, 9-nitrodecalin (60 g.) in acetic acid (120 c.c.) was run during 1 hour with vigorous stirring. After 2 hours, the liquid was made alkaline and steam-distilled, giving 9-aminodecalin (37 g.), b. p. 92°/12 mm. The benzoyl

derivative melted at 148° (Found : N, 5.8. Calc. for $C_{17}H_{23}ON$: N, 5.5%).

When 9-aminodecalin was treated with nitrous fumes in the cold, a compound was obtained, m. p. 243° (decomp.), which gave Liebermann's nitroso-reaction (Found : C, 55.4; H, 9.5; N, 13.1. $C_{10}H_{19}N, HNO_3$ requires C, 55.55; H, 9.25; N, 13.0%).

9-Bromodecalin.—Hydrogen bromide was passed into a solution of $\Delta^{9:10}$ -octalin (6 g.) in light petroleum (b. p. $40-60^{\circ}$) at 0° . The residue after removal of the solvent distilled at $80^{\circ}/0.3$ mm. (8.1 g.) and solidified on cooling; m. p. $29-30^{\circ}$ (Found : Br, 37.1. $C_{10}H_{17}Br$ requires Br, 36.9%).

9-Iododecalin, prepared similarly from octalin and hydrogen iodide, had b. p. $100^{\circ}/0.2$ mm. and was too unstable to give accurate analytical data.

Reaction between 9 : 10-Dibromodecalin and Ethyl Sodiomalonate.—The sodio-derivative (sodium 0.2 g., alcohol 3 c.c., malonic ester 1.4 g.) was heated on the water-bath with the dibromide (1.4 g.) in benzene (12 c.c.) for 5 hours. The liquid was then washed with water, separated, and dried, and the solvent removed. On distillation octalin passed over at $72^{\circ}/14$ mm., leaving a residue of ethyl ethanetetetracarboxylate, m. p. 74° .

$\Delta^{9:10}$ -Octalin Oxide (VI).—Octalin (6 g.), when treated with perbenzoic acid as described by Nametkin and also by Hückel, gave 5.8 g. of the oxide, b. p. $84^{\circ}/12$ mm.

The Action of Zinc and Ethyl Bromoacetate on cycloHexene Oxide.—cycloHexene oxide (8.5 g.) ("Organic Syntheses," Vol. 5, p. 33), bromoacetic ester (15 g.), and zinc wool (6 g.) were heated in benzene (30 c.c.) on the water-bath for 4 hours. The benzene solution was then decanted, the residual zinc washed with benzene, and the cold united liquids shaken with dilute sulphuric acid. The benzene layer, dried and fractionated, yielded 4.1 g., b. p. $114^{\circ}/13$ mm. (Found : C, 64.4; H, 9.7. $C_{10}H_{18}O_3$ requires C, 64.5; H, 9.7%). The ester, heated on the water-bath with hydrazine hydrate (90–95%) for a few minutes, gave the *hydrazide*, which crystallised from water in needles, m. p. 154° [Found : C, 55.2; H, 9.3; N, 16.5; *M* (Rast), 178. $C_8H_{16}O_2N_2$ requires C, 55.8; H, 9.3; N, 16.3%; *M*, 172].

The *hydrazide* of 1-hydroxycyclohexylacetic acid forms plates, m. p. 103° (Found : N, 16.8. $C_8H_{16}O_2N_2$ requires N, 16.3%).

The Action of Ethyl Bromoacetate and Zinc on $\Delta^{9:10}$ -Octalin Oxide.—The oxide (6 g.), bromoacetic ester (8 g.), and zinc wool (3.5 g.) in dry benzene (30 c.c.) were heated in the water-bath for 6–7 hours and the product was worked up as described in the previous experiment. Fractionation after removal of the solvent gave 2 g. of 2-ketocyclohexane-*spiro-cyclopentane* (XI), b. p. $95^{\circ}/14$ mm. (Found :

C, 78.9; H, 10.9. Calc. for $C_{10}H_{16}O$: C, 78.95; H, 10.5%, and 3 g. of B (XV), b. p. $125^{\circ}/0.1$ mm. (Found: C, 70.1; H, 9.65. $C_{14}H_{24}O_3$ requires C, 70.0; H, 10.0%). The ester (XV) is a viscous liquid with a peculiar sweetish smell. When it is mixed with hydrazine hydrate (90–95%), a *hydrazide* is obtained after 1 day; this forms prisms, m. p. 122° , from ether [Found: C, 63.4; H, 9.95; N, 12.4; *M* (Rast), 219. $C_{12}H_{22}O_2N_2$ requires C, 63.7; H, 9.7; N, 12.6%; *M*, 226].

The Action of Ethyl Bromoacetate and Zinc on 2-Ketocyclohexane-spiro-cyclopentane (XI).—The ketone (XI) (1.5 g.), bromoacetic ester (2 g.), and zinc wool (1 g.) were heated in benzene (7 c.c.) for 5 hours. The usual procedure then gave (1) 0.5 g. of unchanged ketone, b. p. 80 – $100^{\circ}/12$ mm., and (2) 0.7 g., b. p. $135^{\circ}/0.25$ mm. (Found: C, 70.5; H, 10.1. $C_{14}H_{24}O_3$ requires C, 70.0; H, 10.0%). The latter when treated with hydrazine hydrate gave a solid hydrazide only after standing for 2 weeks.

Dehydrogenation of (XV) with Selenium.—The ester (XV) (1.5 g.) and powdered selenium (3 g.) were heated at 280 – 290° for 24 hours and then at 330 – 340° for 8–10 hours. The product was extracted four times with light petroleum (b. p. 40 – 60°), and the extract refluxed for $\frac{1}{2}$ hour over sodium. Distillation then gave a liquid (0.25 g.), b. p. $110^{\circ}/17$ mm., and a small quantity of a higher-boiling substance. The first portion was refractionated over sodium into approximately equal head and tail fractions. The head fraction solidified to a buttery mass, which was pressed on a porous plate and recrystallised from methyl alcohol and water (4:1); it then melted at 79 – 80° , alone or mixed with naphthalene (the styphnates also were identical).

The small amount of high-boiling substance formed in light petroleum (b. p. 40 – 60°) a blue fluorescent solution, from which colourless crystals separated, m. p. 142 – 143° (Found: C, 94.5; H, 5.6. $C_{18}H_{12}$ requires C, 94.7; H, 5.3%).

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