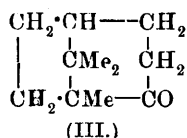
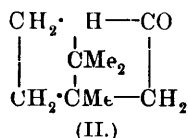
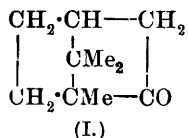


LXXIX.—*Homocamphor*.

By ARTHUR LAPWORTH and FRANK ALBERT ROYLE.

CAMPHOR (I) and the large group of compounds closely related to it have attracted an unusual amount of interest, owing to the difficulty with which they yielded up the secrets of their exact structures. The varied changes to which the molecules of these substances are prone are not less remarkable because the gross results of such transformations can now be represented graphically; and although analogies may be drawn between their transformations and those in some other series, little is yet known of their mechanism. Again, although several ketones nearly allied to camphor have been prepared, these have not, for the most part, been very closely investigated, and therefore peculiarities in the behaviour of camphor have not yet been clearly associated with irregularities in structure; it is not clear, for instance, what is the precise influence exerted by the methyl groups, or what would be the effect of a change in the size of the carbon rings. Epicamphor (II) is unique as an instance of a compound which is very closely related to camphor, and has been experimentally compared with camphor in nearly all interesting particulars (Bredt and Perkin, T., 1913, **103**, 2182).

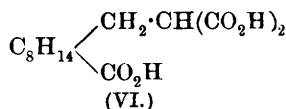
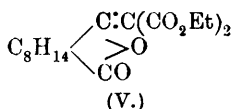
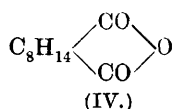
In 1913, the authors had in view the desirability of studying a substance differing from camphor in one particular only, namely, in the inclusion of an additional  $\cdot\text{CH}_2\cdot$  group in the ketone ring. This substance they have prepared, and propose to term *homocamphor* (III). It was originally hoped to make the research a



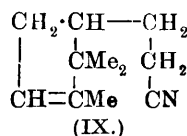
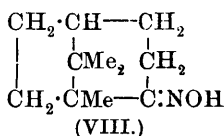
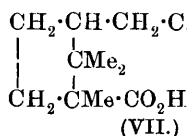
fairly exhaustive one, but it was found that the preparation of homocamphor in sufficient quantity would be a very lengthy and costly undertaking, and the conditions which have succeeded the outbreak of war, when the work was interrupted, have made the project impracticable for the present. It has therefore been decided to describe the results which have already been obtained.

The first step in the synthesis of homocamphor consisted in the preparation of camphorylmalonic ester (V) from camphoric

anhydride (IV) and diethyl sodiomalonate by Winzer's method (*Annalen*, 1890, **257**, 298).



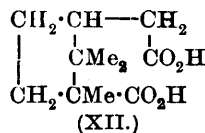
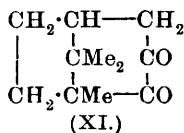
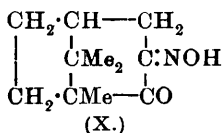
By reduction of (V) (best carried out electrolytically under the conditions referred to in the experimental part) and subsequent hydrolysis, hydrocamphorylmalonic acid (VI) is obtained, and this is readily converted, on distillation, into carbon dioxide and Winzer's hydrocamphorylacetic acid (VII). The latter can be converted into homocamphor either by heating its lead salt in a current of carbon dioxide or by prolonged action of acetic anhydride, followed by distillation in a vacuum. Homocamphor



forms a colourless, indefinitely crystalline mass closely resembling camphor in odour, taste, and in general behaviour towards solvents. Its optical rotatory power is, however, in the opposite sense to that of the camphor from which, through camphoric anhydride and the above series of reactions, it is prepared; it has  $[\alpha]_D -112.9^\circ$  in benzene, whilst camphor has  $[\alpha]_D +39.1^\circ$ .

Homocamphor readily yields a *semicarbazone* and an *oxime* (VIII). The latter closely resembles camphoroxime, and has much the same peculiar odour as that substance; like camphoroxime, it develops a perfume resembling that of raspberries when heated with sulphuric acid, and this is doubtless due to the formation of homocampholenonitrile (IX). This product does not appear to be formed so readily as is campholenonitrile from camphoroxime, which fact seems to indicate a greater stability of the six-carbon ring as compared with the five-carbon ring in camphoroxime.

An *isonitroso*-derivative (X) may be obtained from homocamphor under conditions similar to those used in converting camphor into its *isonitroso*-derivative, and closely resembles the latter in properties. By the action of acid formaldehyde on *isonitroso*homocamphor



(compare Lapworth, T., 1896, **69**, 323), a small quantity of a volatile, yellow compound is obtained, and this much resembles camphorquinone, although it appears to be less intensely coloured; it is doubtless *homocamphorquinone* (XI).

In order to establish the structure of homocamphor, which in the absence of further data would have rested on the assumptions that Winzer's hydrocamphorylacetic acid has the structure (VII), and that no change of structure had attended the ring-closure at the succeeding step in the synthesis, advantage was taken of the ease with which cyclic *isonitroso*-ketones, like *isonitrosocamphor*, undergo the Beckmann change, becoming converted into amides or imides of the open-chain dicarboxylic acids. *isoNitrosohomo*-camphor was warmed with acetyl chloride, and the product hydrolysed with alkali; as was anticipated, *homocamphoric acid* (XII) was precipitated on addition of acid, so that there can be no question that the structures assumed for homocamphor (III) and its *isonitroso*-derivative (X) are correct.

#### EXPERIMENTAL.

Camphorylmalonic ester was prepared by the condensation of ethyl sodiomalonate with camphoric anhydride in benzene, in accordance with Winzer's method (*loc. cit.*). It was obtained as a viscid, colourless liquid distilling at 218°/20 mm., and ultimately setting to a solid, which melted at 81° after recrystallisation from benzene. The yield fluctuated between 70 and 75 per cent. Attempts to shorten the time required for the condensation process by substituting toluene for benzene as solvent were not successful, and a trial of substituting camphoryl chloride for camphoric anhydride (Winzer, *loc. cit.*) did not give encouraging results.

For the reduction of camphorylmalonic ester, comparative tests of several methods were made. Winzer used sodium amalgam, allowing this to act on an alcoholic solution of the unsaturated ester, with such intermittent additions of sulphuric acid as were required to maintain a slightly acid reaction in the solution. He does not give the yield. In using this method, the present authors found that a decided improvement was effected by omitting the additions of sulphuric acid and employing instead a constant stream of carbon dioxide.

Much trouble was at first experienced in obtaining the hydrocamphorylmalonic acid in crystalline form, and the cause of this was ultimately traced to the fact that during the reduction the hydrolysis of the ester is not by any means so complete as Winzer's description would lead one to infer, and appreciable quantities of

the mono- and di-ethyl esters of hydrocamphorylmalonic acid are invariably left. It is therefore necessary, after the reduction itself is complete, to add to the solution a considerable excess of alkali and to heat for some time; when a portion of the liquid on acidification yields an acid which solidifies at once, the whole may be worked up in the usual manner. With these precautions, the authors were able to obtain yields of pure hydrocamphorylmalonic acid corresponding with 66 per cent. of that theoretically possible.

Many experiments were also made with the view of effecting the reduction electrolytically. A pure lead sheet,  $20 \times 30$  cm., carefully polished, cleaned, and then covered with a deposit of spongy metal, was employed as cathode, and a sheet of platinum foil  $5 \times 2.5$  cm. as anode. A clean, porous porcelain cell was used to contain the anode liquid (dilute sulphuric acid), and this was immersed in a beaker containing the cathode liquid. Glass spirals, through which cold water circulated, were immersed in the electrode chambers, and served for cooling purposes. The cathode liquid contained the unsaturated ester (20 grams) dissolved in a mixture of spirit (1500 grams) and concentrated sulphuric acid (150 grams). A current of 2 amperes at 10 volts was employed until reduction was complete, when the cathode liquor was completely hydrolysed with excess of alkali and worked up for hydrocamphorylmalonic acid. By this process, yields of 85 per cent. of the theoretical were normally obtained, but, like other similar reduction processes, success is uncertain unless the utmost care is exercised to ensure the purity of the fluids, electrodes, and cells.

Aluminium amalgam, used as reducing agent in diluted alcohol, gave yields of hydrocamphorylmalonic acid amounting to only 57 per cent. of the theoretical. Other methods of reduction, including the use of gaseous hydrogen and colloidal palladium, proved even less satisfactory.

The crude hydrocamphorylmalonic acid obtained by any of the above processes was converted into hydrocamphorylacetic acid by heating for an hour in an oil-bath at  $180^{\circ}$ , and then distilling in a vacuum; the fraction boiling at  $260\text{--}270^{\circ}/20$  mm. yielded, as a rule, the pure hydrocamphorylacetic acid, melting at  $142^{\circ}$ , on recrystallisation from water. Occasionally, however, the product contained an impurity of an unsaturated character, in which case it was dissolved in sodium carbonate and left in contact with excess of permanganate for an hour, when it was subsequently recovered in satisfactory condition.

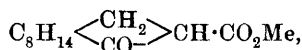
*Dimethyl Hydrocamphorylacetate.*

As one of the carboxyl groups of hydrocamphorylacetic acid is attached to a quaternary carbon atom, and is therefore resistant to the ordinary esterification processes, the dimethyl ester of the acid was prepared through the normal silver salt. The latter was readily obtained as an insoluble precipitate on addition of silver nitrate to the aqueous solution of the neutral sodium salt. The washed salt, dried at  $110^{\circ}$ , was boiled for three hours with methyl iodide dissolved in dry ether. The resulting ester was worked up in the usual manner, the main fraction being obtained as a colourless, viscid oil boiling at  $175^{\circ}/20$  mm. Found:  $C=65.5$ ;  $H=9.6$ .  $C_{14}H_{24}O_4$  requires  $C=65.6$ ;  $H=9.4$  per cent.).

By cooling in liquid air and allowing the temperature slowly to rise, the oil set to a crystalline mass melting at about  $25^{\circ}$ .

An acid by-product, doubtless the *monomethyl* ester, was isolated during the working up of the diethyl ester; it distilled at  $202-212^{\circ}/19$  mm. as a viscid, colourless oil which, when the interior of the containing tube was scratched with a glass rod, solidified to a mass of small needles.

When the above dimethyl ester is heated with excess of sodium methoxide at about  $100^{\circ}$ , the whole becomes brownish-red. On subsequently acidifying the solution, there is obtained a product which with ferric chloride gives a red coloration, soluble in amyl alcohol, and a copper derivative which is insoluble in water but soluble in alcohol. These facts point to the presence in this product of methyl homocamphorcarboxylate,



but this substance, from which it was hoped to prepare homocamphor, has not been closely examined, as the desired end was ultimately attained by a shorter route.

*Homocamphor* (III, p. 743).

This substance was obtained from hydrocamphorylacetic acid by the following processes:

(1) The acid was converted into its neutral sodium salt, and this, by double decomposition in aqueous solution with lead acetate, into the lead salt, which forms a heavy, white precipitate, and may be collected, washed with water and alcohol successively, and dried at  $100^{\circ}$ .

Ten grams of this salt were placed in a wide, hard-glass tube, which was slowly heated in an inclined position while a current of carbon dioxide was led through it from the higher end. The lower end of the tube was connected by means of an adapter to a flask, which served as a receiver, the issuing gases from the latter being passed through ether in order to retain the last traces of homocamphor. The crude product, after carefully evaporating off the ether used to collect it all, was a pale brown solid, and was purified by distillation in a current of steam.

(2) Homocamphorylacetic acid (8 grams) was boiled with acetic anhydride (20 grams) for several hours, and then allowed to remain at the ordinary temperature for some days. The acetic anhydride was subsequently removed by distillation, and the residue slowly heated under diminished pressure (12—20 mm.), the semi-solid distillate being warmed with aqueous sodium carbonate and distilled in a current of steam.

*Homocamphor* forms a white, indistinctly crystalline mass. In appearance, odour, and behaviour towards the usual media, it very closely resembles ordinary camphor, and, like that compound, is appreciably soluble in water, to which it communicates a camphoraceous odour. It was analysed after exposure in a vacuum desiccator over sulphuric acid (Found: C=79.3; H=10.9.  $C_{11}H_{18}O$  requires C=79.5; H=10.9 per cent.).

Homocamphor melts at 189—190°, and sublimes readily far below this temperature. It is laevorotatory, and has  $[\alpha]_D -112.9^\circ$  in 4 per cent. solution in benzene.

*Homocamphorsemicarbazone*,  $C_{11}H_{18}:N \cdot NH \cdot CO \cdot NH_2$ .

This is readily obtained by boiling homocamphor in alcoholic solution with semicarbazide hydrochloride and sodium acetate for three hours. It crystallises from alcohol in slender, colourless needles melting and decomposing at 250—252°. The substance is very sparingly soluble in water, but dissolves readily in methyl or ethyl alcohol. Cold concentrated hydrochloric acid dissolves it, and, on adding water, the semicarbazone is precipitated unchanged; but, if steam is passed through the solution, pure homocamphor passes over.

*Homocamphoroxime* (VIII, p. 744).

This is prepared by dissolving homocamphor (1 gram) in alcohol, adding solid hydroxylamine hydrochloride (0.8 gram) and sodium acetate (2—5 grams), and boiling the whole for two hours on the

water-bath. On cooling and diluting with water, the oxime is slowly deposited in crystals, which are collected and recrystallised from dilute methyl alcohol (Found: C=73·3; H=10·7; N=7·9.  $C_{11}H_{19}ON$  requires C=72·9; H=10·5; N=7·7 per cent.).

This oxime much resembles camphoroxime in general behaviour towards organic solvent media, and has much the same peculiar odour as that substance. It crystallises from dilute methyl alcohol in long needles melting at 167—168°. When a small quantity of the oxime is heated with a drop of concentrated sulphuric acid, an odour very similar to that of campholenonitrile becomes perceptible: the quantities of material available did not admit of the product being isolated.

*isoNitrosohomocamphor* (X, p. 744).

Homocamphor (3 grams) is dissolved in anhydrous ether (100 c.c.), and finely powdered sodamide (2 grams) is then added. The whole is stirred mechanically for two hours, then cooled to 0°, and maintained at this temperature while freshly distilled amyl nitrite (4·5 c.c.) is gradually introduced. After remaining overnight, the product is poured into ice-water, the aqueous layer separated, extracted repeatedly with ether, and then acidified with acetic acid. The precipitated solid (2 grams) is collected, washed with water, dried, and crystallised from a mixture of benzene and light petroleum.

The substance dissolves in all the usual organic media, and crystallises from water in long, slender needles, and from benzene and petroleum in small, flat plates. It melts at 167—168°.

It dissolves in formaldehyde (40 per cent.), and if the solution is warmed on the water-bath for two hours and then heated with excess of hydrochloric acid under a reflux condenser, minute, pale yellow crystals, which have a sweet, camphoraceous odour, collect in the condenser tube; these crystals doubtless consist of *homocamphorquinone* (XI, p. 744). The rate of formation of this compound is not so rapid as that of ordinary camphorquinone from *isonitrosocamphor* in similar circumstances (compare Lapworth, *loc. cit.*), and as the yield was very small, sufficient could not be obtained for accurate characterisation or analysis.

*Conversion of isoNitrosohomocamphor into Homocamphoric Acid.*

*isoNitrosohomocamphor* (0·5 gram) was boiled with acetyl chloride for five hours, the solution then evaporated to dryness, and the solid residue boiled with 40 per cent. aqueous potassium hydroxide

for ten hours, during which time ammonia was slowly evolved. After a preliminary extraction with ether to remove neutral material, the alkaline liquid was acidified with sulphuric acid. The resulting brown acid which was precipitated proved to be highly insoluble in most of the ordinary organic media, but dissolved freely in boiling nitrobenzene, and, on cooling, separated in microscopic needles melting at  $233^{\circ}$ ; its equivalent, determined by titration against  $N/10$ -sodium hydroxide, using phenolphthalein as indicator, was 106. The characters described are precisely those of *homocamphoric acid* (XII, p. 744), the calculated equivalent of which is 107.

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