III.—*Synthesis of an Isomeride of Camphoronic Acid.*

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SOME years ago, Wreden (*Ann.*, 1877, 187, 156) showed that when camphoronic acid was heated with concentrated hydriodic acid, it yielded a tetrahydroisoxylene. Again, oxycamphoric acid, when distilled, gives a hydrocarbon isomeric with this and having similar properties, although it is not identical with it, as Aschan, who called it laurene (*Ann.*, 1896, 290, 185), subsequently proved.

These facts, together with others since observed by myself, and which I hope soon to communicate to the Society, led me to the conclusion that camphoric acid was a derivative of metadimethylhexamethylene; and on this assumption the formula for this acid most in agreement with its reaction seemed to be

This constitution would explain the following facts.

a. That when brominated by the action of phosphorus and bromine only a monobromo-derivative is obtainable, for more than one bromine atom has not, as yet, been introduced into the molecule by these means. In accordance with the researches of Hell, Auwers, and others, the bromine always enters in the α -position relatively to the carboxyl group, and in the above formula only one replaceable hydrogen atom exists in such a position.

b. When a hydroxyl group is substituted for the bromine atom, a lactonic acid is produced, hence the bromine atom must be in the γ -position relatively to the second carboxyl group.

Moreover, Reyter (*Inaug. Dissert. Leipzig*, 1891) has shown that this lactonic acid (camphanic acid), on oxidation, yields camphoronic acid.

On these assumptions, a formula for camphoronic acid would be derived as follows:

The latter substance was synthesised in the following way.

Ethyl methacrylate was heated with ethyl sodiomethylmalonate according to the method of Auwers, Köbner, and v. Meyenburg (*Ber.*, 1891, **24**, 2887), and the sodio-additive product, without being isolated, was treated directly with ethyl sodacetate and then hydrolysed.

Ethyl Methacrylate.

Ethyl methacrylate is most conveniently prepared by a modification of Frankland and Duppa's method (*Ann.*, 1865, **136**, 12), namely, by the action of phosphorus trichloride on ethyl hydroxyisobutyrate.

Preparation of Ethyl Hydroxyisobutyrate.—Hydroxyisobutyric acid dissolved in twice its weight of absolute alcohol containing 3 per cent. of hydrogen chloride is left for a couple of days over fused sodium sulphate, and then heated for 2 hours on a water bath. After fractionation, a portion boiling between 145° and 155° was obtained and used for subsequent operations. The yield is about 50 per cent. of the theoretical.

Preparation of Ethyl Methacrylate.—To the ethyl hydroxyisobutyrate prepared as above, about twice the theoretical quantity of phosphorus trichloride is added drop by drop; the mixture is then heated gently for a few minutes on a sand bath, using a reflux condenser, until it begins to get turbid owing to the separation of phosphorus; it is then distilled, &c., one fractionation being sufficient to separate the ethyl methacrylate from the phosphorus compounds. In order to remove the last traces of the latter, the distillate is shaken with a dilute

solution of potassium carbonate. It is advisable to avoid frequent fractionation owing to the ease with which the methacrylate polymerises.

Synthesis of the Isomeride of Camphoronic acid.

For this purpose, the ethylic methacrylate is treated with ethylic sodiomethylmalonate, according to the method employed by Auwers and others (*loc. cit.*) in the preparation of dimethylglutaric acid. Instead of decomposing the sodium additive product, however, ethylic iodacetate is added directly to the alcoholic solution; the mixture becomes hot, and the reaction is completed by heating it in a corked soda water bottle at 100° until it is nearly neutral. The alcohol is then distilled off, and the oily residue washed with water. As the molecular weight of the ethylic salt thus obtained is so high that it cannot be advantageously submitted to fractional distillation, it is hydrolysed directly with twice its volume of hydrochloric acid (1 water : 1 acid), as recommended by Auwers in similar cases.

The product, after being filtered and distilled with steam, to separate the propionic and other volatile acids formed, is extracted several times with ether. It is advisable to put a little animal charcoal into the flask during the steam distillation, so as to decolorise the liquid. The ethereal extract contains much methylsuccinic acid formed by the action of the ethylic iodacetate on unchanged ethylic methylmalonate; there is, however, another acid present, which can be separated from the rest owing to the fact that, *like camphoronic acid, it forms a lead salt insoluble in acetic acid*. Accordingly, the residue left on evaporating the ethereal extract is dissolved in water, and lead acetate is added *without previously neutralising the solution*; the precipitate of lead salt, after being washed with water, alcohol, and ether, is dried, suspended in ether, and decomposed by dry hydrogen sulphide. On evaporating the filtrate from the lead sulphide, an almost colourless syrup is left, which does not crystallise even after standing for several months in a desiccator.

Attempts were made to prepare a crystalline anhydride from it on the assumption that the syrup was a mixture of geometrical isomerides and therefore not easily crystallisable. For this purpose, it was treated with acetyl chloride, when a minute quantity of crystals separated; water was then added to the acetyl chloride solution, the acetic acid removed by evaporation, and a silver salt prepared by precipitation. This, after being washed and dried, was suspended in ether and decomposed by hydrogen sulphide, but on evaporating the ether a syrup was again obtained. This was dissolved in strong nitric acid, when a slight oxidation took place, and the solution was immediately diluted with an equal bulk of water. After some time, crystals

of the hydroxy-acid began to separate in hard, indistinct crusts, and these, after being separated from the mother liquor, and dried over sulphuric acid and caustic soda in a vacuum, so as to free them from the last traces of water and nitric acid, were recrystallised once or twice from ether which had been distilled over sodium. The substance was thus obtained in snow white, microscopic crystals melting sharply at 137° .

0.1448 gave 0.2452 CO_2 and 0.794 H_2O . $\text{C} = 46.18$; $\text{H} = 6.09$.

$\text{C}_9\text{H}_{14}\text{O}_7$ requires $\text{C} = 46.15$; $\text{H} = 5.98$ per cent.

It may be remarked that camphoronic acid, when treated with nitrohydrochloric acid, is also oxidised to oxycamphoronic acid.

It had been my intention to prepare this acid in larger quantities and investigate its salts, but the synthesis takes a long time to carry out and is costly. As, moreover, Drs. W. H. Perkin, jun., and J. T. Thorpe published their synthesis of the true camphoronic acid at the time my work had reached the stage described, the main object with which it had been undertaken was accomplished, and I have therefore been compelled to relinquish any further investigations in this direction.