CCIV.—*The Preparation of Unsaturated Ketones from the Chlorides of Hydroxy-acids.*

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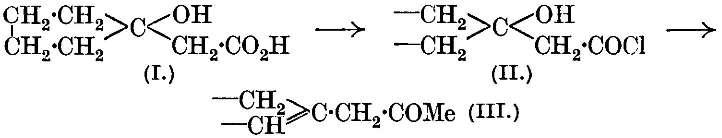
In seeking to extend the methods by which ketones of the type of *cyclo*hexenylacetone are obtained, we were led to examine the action of zinc methyl iodide and of zinc ethyl iodide on the chlorides produced directly from hydroxy-acids, without previously converting these into unsaturated acids. This object had already been partly achieved by Blaise and Maire (*Ann. Chim. Phys.*, 1908, **15**, 556), who acetylated the hydroxy-acids before converting them into their chlorides; they found, however, that this method failed when applied to β-disubstituted acids, as these, instead of being acetylated, were dehydrated to a mixture of unsaturated acids. The work of Darzens (*Compt. rend.*, 1911, **152**, 1314, 1601) also made it appear probable that the action of thionyl chloride or phosphorus pentachloride on hydroxy-acids would lead to dehydration. Actually, it was found that cyclic β-hydroxy-acids gave each a mixture containing, in addition to varying quantities of the chlorides of the two possible unsaturated acids, a considerable proportion of its own chloride, from which it could be regenerated. These chlorides, on treatment with zinc methyl iodide, gave ketones identical with those obtainable from the chlorides of the unsaturated acids. Thus, *cyclo*pentanolacetic acid (I) gave a chloride (II) from which, on treatment with zinc methyl iodide, a fair yield of *cyclo*pentenylacetone (III) was obtained. This ketone is probably best prepared by the process now described. The corresponding ethyl ketones were obtained only in very poor yield, owing to the simul-



$$\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad\\ CH_2\cdot CH_2\end{matrix}\!>\!C\!<\!\begin{matrix}OH\\ CH_2\cdot CO_2H\end{matrix} \longrightarrow \begin{matrix}-CH_2\\ -CH_2\end{matrix}\!>\!C\!<\!\begin{matrix}OH\\ CH_2\cdot COCl\end{matrix} \longrightarrow$$

(I.) (II.)

$$\begin{matrix}-CH_2\\ -CH\end{matrix}\!\geqslant\! C\cdot CH_2\cdot COMe$$

(III.)

taneous formation of the ethyl ester of the βγ-unsaturated acid. The production of this ester is at present unexplained. Experiments carried out with a few α-hydroxy-acids sufficed to show that the chlorides were highly unstable and had no practical value for the synthesis of ketones; a small quantity of tetrahydroacetophenone was, however, prepared from *cyclo*hexanolcarboxylic acid.

EXPERIMENTAL.

1-Hydroxy*cyclo*pentane-1-carboxylic acid (43 g.) was treated with excess of thionyl chloride in the cold. When the frothing had subsided, the mixture was warmed for 20 minutes, and the excess of reagent removed in a vacuum. The chloride decomposed during distillation even under 3·5 mm.

In another experiment the acid (43 g.) was gradually added to 69 g. of phosphorus pentachloride and the mixture was warmed for 30 minutes, but no attempt was made to purify the chloride. A portion of it gave, on treatment with formic acid, the original acid, m. p. 103°. The crude chloride was then treated with zinc methyl iodide, but only a very small amount of a disagreeable-smelling, non-ketonic liquid was obtained.

1-Hydroxy*cyclo*hexane-1-carboxylic acid behaved exactly like the lower homologue both with phosphorus pentachloride and with thionyl chloride. The action of zinc methyl iodide on the crude chloride gave a very poor yield of a substance which combined with semicarbazide, giving tetrahydroacetophenone semicarbazone (m. p. and mixed m. p. 216—217°). The action of zinc ethyl iodide gave no ketonic product, but a small amount of an oil, b. p. 110—114°/20 mm., which appeared to be ethyl tetrahydrobenzoate.

A chloride could not be obtained from hexahydromandelic acid.

1-Hydroxy*cyclo*pentane-1-acetic acid (48 g.), after treatment with excess of thionyl chloride, gave on distillation 5 g. of a chloride, b. p. 85—87°/17 mm., and 16 g. (30%) of another chloride, b. p. 98—110°/17 mm. The former gave, when poured into formic acid, *cyclo*pentenylacetic acid, m. p. 51—52°, and when treated with aniline, cyclo*pentenylacetanilide*, which crystallised from methyl alcohol in silky needles, m. p. 98° (Found: C, 77·3; H, 7·9. $C_{13}H_{15}ON$ requires C, 77·6; H, 7·5%). The higher-boiling chloride gave a mixture of anilides from which cyclo*pentylideneacetanilide* could be isolated in nodules, m. p. 152—153°, after several crystallisations (Found: C, 77·2; H, 7·6. $C_{13}H_{15}ON$ requires C, 77·6; H, 7·5%). On pouring the chloride into formic acid, a gummy acid was obtained from which the original acid, m. p. 77°, was isolated after repeated treatment with benzene–petroleum.

The action of zinc methyl iodide (1/3 mol.) on the higher-boiling chloride prepared from 48 g. of the hydroxy-acid gave 8 g. of a ketone. The semicarbazone prepared from this was separated by crystallisation into three forms, m. p. 138°, 189°, and 121—122°, respectively, the last being apparently a constant-melting mixture of the other two. These were the two semicarbazones of *cyclo*pentenylacetone (Kon, J., 1921, **119**, 823); the one of m. p. 138° was formed in greater quantity.

The action of zinc ethyl iodide on the same chloride gave an ester, probably ethyl *cyclo*pentenylacetate; no ketone appeared to be formed.

The action of thionyl chloride on 1-hydroxy*cyclo*hexane-1-acetic acid (53 g.) gave 35 g. of a product, b. p. 95—98°/15—17 mm., consisting mainly of the chloride of the hydroxy-acid, as it gave the original acid on being poured into formic acid. The action of aniline on it gave a mixture from which the *anilides* of *cyclo*hexenylacetic acid, needles, m. p. 117° (Found : C, 77·9; H, 8·2%) and of *cyclo*hexylideneacetic acid, m. p. 138—139° (Found : C, 78·4; H, 7·8. $C_{14}H_{17}ON$ requires C, 78·1; H, 7·9%), were obtained. The anilide of the hydroxy-acid appears to be indefinite.

The acid chloride from 53 g. of the acid was treated with zinc methyl iodide; 17 g. of *cyclo*hexenylacetone, b. p. 102—104°/20 mm., identified by means of the semicarbazone, were obtained.

The reaction was repeated with zinc ethyl iodide, but the yield of ketone was very much less, partly owing to the formation of ethyl *cyclo*hexenylacetate in some quantity. The ketone gave two semicarbazones, m. p. 153° and 184—185° respectively. The former is identical with the semicarbazone of Δ^1-*cyclo*hexenylmethyl ethyl ketone (Kon, J., 1926, 1797), whilst the latter is isomeric with it and is probably the semicarbazone of the αβ-form [Found : (for the form of low m. p.) C, 63·2; H, 9·2; (for the form of high m. p.) C, 62·9; H, 9·5. $C_{10}H_{17}ON_3$ requires C, 63·2; H, 9·0%].

1-Hydroxy-α-ethyl*cyclo*pentane-1-acetic acid (see preceding paper) (29 g.) gave 17 g. of a chloride, b. p. 99—102°/25 mm. The chloride gave with ammonia a mixture of the αβ- and the βγ-unsaturated amide, in the proportion of 1 : 2; a third amide, melting indefinitely at about 70°, was also obtained but could not be purified. The action of zinc methyl iodide (1/6 mol.) on 15 g. of the acid chloride gave 8·5 g. of a liquid, b. p. 103—105°/25—27 mm., from which the semicarbazone of α-ethyl-Δ^1-*cyclo*pentenylacetone, m. p. 166—167° after crystallisation, was readily obtained.

1-Hydroxy-α-ethyl*cyclo*hexane-1-acetic acid (see preceding paper) (30 g.) gave 22 g. of a chloride, b. p. 122—127°/20 mm. This, on treatment with ammonia, gave an amide, m. p. 108—110°, which, on repeated crystallisation, melted at 113—114° and proved identical with the βγ-unsaturated amide; a trace of another amide, m. p. 108—109°, distinct from both the αβ- and the βγ-amide, was also obtained. By the action of zinc methyl iodide (1/6 mol.) on the acid chloride (20 g.), 9 grams of a liquid, b. p. 122—124°/20 mm., were obtained. This contained a considerable amount of unsaturated ester in addition to α-ethyl*cyclo*hexenylacetone, which was isolated in the form of its semicarbazone, m. p. 185°.

β-Hydroxy-β-methyl-α-ethylpentanoic acid gave a 70% yield of chloride, b. p. 75—90°/20—25 mm., on treatment with thionyl chloride. It consisted mainly of the chlorides of the two unsaturated acids, as evidenced by the *p*-toluidides obtained from it, but a third, indefinite, product was also formed, probably derived from the hydroxy-acid. The yield of ketone, b. p. 78—82°/25 mm., from the acid chloride was poor; it readily gave the characteristic semicarbazone, m. p. 163—164°, identical with that previously obtained from the unsaturated acids.

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