SYNTHESIS OF 1,3-DIOXOLANE DERIVATIVES

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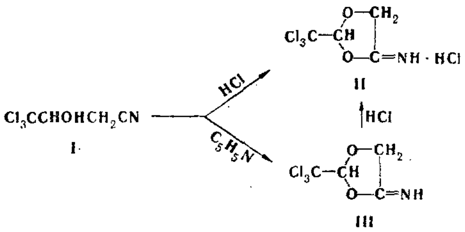
Chloral cyanomethylhemiacetal is converted to 2-trichloromethyl-4-imino-1,3-dioxolane under the influence of hydrogen chloride or pyridine. Acetone cyanohydrin reacts with chloral to give 2-trichloromethyl-4-imino-5,5-dimethyl-1,3-dioxolane, the hydrochloride of which in water gives 2-trichloromethyl-4-oxo-5,5-dimethyl-1,3-dioxolane.

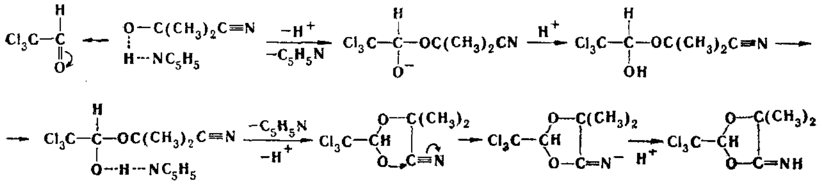
The reaction of hydroxynitriles with chloral has not been studied. We have found that formaldehyde cyanohydrin reacts with chloral to give cyanomethylhemiacetal I [1], which decomposes during vacuum distillation.

Compound I reacts with hydrogen chloride to give 2-trichloromethyl-4-imino-1,3-dioxolane hydrochloride (II), but is converted to base III, the hydrochloride of which is identical to II, in the presence of catalytic amounts of pyridine.



Compound II is readily hydrolyzed to give a viscous syrupy liquid, which decomposes even at the temperature of a boiling-water bath with chloral liberation.

Ketone cyanohydrins react very sluggishly with chloral. Heating of a mixture of the starting substances for many hours did not give any positive results. However, if an equimolecular mixture of acetone cyanohydrin and chloral is allowed to stand at room temperature for 2.5-3 months, the liquid solidifies almost completely because of the formation of crystalline 2-trichloromethyl-4-imino-5,5-dimethyl-1,3-dioxolane (IV). Cyclization can be sharply accelerated by the addition of traces of pyridine [2].



The catalytic action of pyridine is apparently due to the formation of a pyridine–cyanohydrin activated complex in which the oxygen atom of the cyanohydrin is more nucleophilic owing to the development of a hydrogen bond and therefore readily attacks the carbonyl group of chloral. The adduct that forms in this manner undergoes subsequent heterocyclization, probably also through a step involving the formation of an activated complex.

The catalytic action of hydrogen chloride is apparently due to protonation of the nitrile group and conversion of it to a nitrile cation, which also attacks the free pair of electrons of the hydroxyl group:

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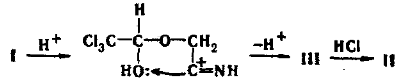
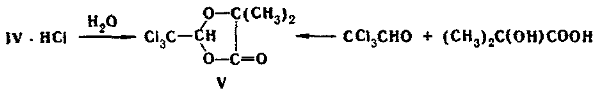


Bands of stretching vibrations of OH and C ≡ N groups are absent in the IR spectra of II, III, and IV, but the spectra do contain intense absorption at 1100-1130 (C–O), 1705-1714 (O–C =N), and 3210-3260 cm^{-1} (NH).

The hydrochloride of IV is hydrolyzed on dissolving in water to give the completely stable 2-trichloromethyl-4-oxo-5,5-dimethyl-1,3-dioxolane (V); bands of C–O stretching vibrations (1100-1130 cm^{-1}) and of C =O groups in five-membered lactones at 1775-1785 cm^{-1} are displayed distinctly in the IR spectrum of V.



Compound V was also obtained by condensation of chloral with α-hydroxyisobutyric acid.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-10 spectrometer.

2-Trichloromethyl-4-imino-1,3-dioxolane Hydrochloride (II). A mixture of 14.8 g (0.1 mole) of chloral and 5.7 g (0.1 mole) of formaldehyde cyanohydrin [bp 81-83° (5 mm)] was heated on a water bath for 1 h and allowed to stand at room temperature for 2 days. Absolute ether (50 ml) was added to the resulting I, and the mixture was cooled to –10° with stirring and saturated with dry hydrogen chloride. After 2 h, the precipitate was removed by filtration, washed with absolute ether, and dried in a desiccator over concentrated sulfuric acid to give 16.8 g (70%) of a product with mp 112-113° (dec.). Found, %: Cl 14.7; Cl 68.0; N 6.9. $C_4H_5Cl_4N$. Calculated, %: Cl 14.8; Cl 67.9; N 6.7.

2-Trichloromethyl-4-imino-1,3-dioxolane (III). A 0.05 g sample of pyridine was added with stirring at –10° to a mixture of 7.4 g (0.05 mole) of chloral, 2.9 g (0.05 mole) of formaldehyde cyanohydrin, and 25 ml of dry petroleum ether. The mixture was allowed to stand in a refrigerator overnight. The next day, the petroleum ether was decanted, and the solid was treated several times with new portions of dry petroleum ether. The mixture was then filtered, and the solid was air dried to give 9.8 g (96%) of a product with mp 95-96°. Found, %: Cl 52.3; N 6.9. $C_4H_4Cl_3NO_2$. Calculated, %: Cl 52.0; N 6.8. The hydrochloride had mp 112-113°. No melting-point depression was observed for a mixture of the product with a sample of II.

Hydrolysis of 2-Trichloromethyl-4-imino-1,3-dioxolane Hydrochloride. Water (10 ml) was added dropwise with stirring and cooling to a mixture of 10 g of II and 25 ml of diethyl ether, after which stirring was continued for another 30 min. The aqueous layer was then separated and extracted with ether. The ether was removed, and the residue was distilled at 95-97° to give 5 g of chloral hydrate with mp 56-57° (mp 57-58°, according to the literature). No melting-point depression was observed for a mixture of this product with a sample of chloral hydrate.

2-Trichloromethyl-4-imino-5,5-dimethyl-1,3-dioxolane (IV). A 0.05 g sample of pyridine was added to a water-cooled mixture of 6.9 g (0.047 mole) of chloral, 3.8 g (0.047 mole) of acetone cyanohydrin, and 25 ml of dry petroleum ether. A copious precipitate began to form immediately. The reaction mixture was allowed to stand overnight and was filtered the following day. The solid was washed with petroleum ether and air dried to give 9.5 g (88%) of a product with mp 133° (after reprecipitation from acetone by the addition of water). Found, %: Cl 46.2; N 6.3. $C_6H_3Cl_3NO_2$. Calculated, %: Cl 45.8; N 6.0. The compound had R_f 0.4 [activity II Al_2O_3, hexane–acetone (60 :40), development with 2% $AgNO_3$ and 0.4% bromphenol blue]. The hydrochloride had mp 172-173°.

2-Trichloromethyl-4-oxo-5,5-dimethyl-1,3-dioxolane (V). A. A 3.5 g sample of the hydrochloride of IV was dissolved in a small amount of water and stirred thoroughly for 1 h. The resulting precipitate was removed by filtration and air dried to give 3.2 g (98.6%) of colorless crystals with mp 72°. Found, %: C 31.1; H 3.2; Cl 45.8. $C_6H_7Cl_3O_3$. Calculated, %: C 30.8; H 3.0; Cl 45.6. The product had R_f 0.7 [activity II Al_2O_3, hexane–acetone (98 : 2), development with 2% $AgNO_2$ and 0.4% bromphenol blue].

B. A mixture of 2.21 g (0.015 mole) of chloral and 1.56 g (0.015 mole) of hydroxylisobutyric acid (mp 78-79°) was heated at 120° on an oil bath for 3 h. The mixture was cooled, and the reaction product was treated with water. The precipitate was removed by filtration, dissolved in acetone, and precipitated with water to give 2.6 g (74%) of a product with mp 72°. No melting-point depression was observed for a mixture of this product with a sample of the material described above.

LITERATURE CITED

1. V. V. Dovlatyan and D. A. Kostanyan, Arm. Khim. Zh., 22, 598 (1969).
2. V. V. Dovlatyan and D. A. Kostanyan, USSR Author's Certificate No. 266,776 (1968); Byul. Izobret., No. 3, 140 (1973).