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# Some Transformations of Aliphatic Polychlorinated Ketones Mediated by Lewis Acids

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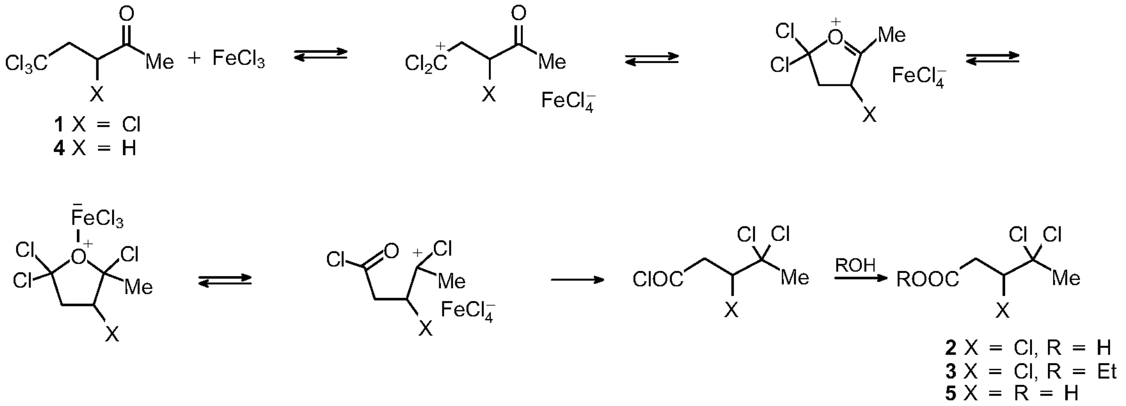
3,5,5,5-Tetrachloropentan-2-one and 5,5,5-trichloropentan-2-one are transformed into the respective carboxylic acids under the action of $FeCl_3$, while $SnCl_4$ and $AlCl_3$ are not effective in the reactions mentioned.

Selective transformation of the trichloromethyl group into a carboxylic group is an important synthetic problem since polyhalogenated adducts of carbon tetrachloride with various unsaturated compounds appear to be good precursors in heterocyclic synthesis.[1] In particular, 3,5,5,5-tetrachloropentan-2-one **1** was used for the synthesis of various compounds of the thiazole, furan and furo[2,3-*d*]pyrimidine series containing a 2,2,2-trichloroethyl moiety.[2] Selective hydrolysis to the related acids with transformation of the trichloromethyl group into a carboxylic group, either in the starting α-chloroketone or in the final heterocyclic compound, could lead to heteroarylacetic acids. Here we present the first results of an investigation of a transformation of tetrachloropentanone **1** into related acids under the action of Lewis acids.

Such an approach is based on the procedure proposed for the transformation of $C_4$–$C_6$ carboxylic acids and their esters, containing a trichloromethyl group, into the corresponding dicarboxylic acids as a result of the action of catalytic amounts of Lewis acids under mild conditions,[3] $FeCl_3$ being shown to be the best catalyst for the reaction. However, the ketone **1** suffered a transformation only when an equimolar amount of iron(III) chloride was used in methylene dichloride as a solvent, but the final product after hydrolysis of the reaction mixture unexpectedly appeared to be 3,4,4-trichlorovaleric acid **2**, alcoholysis of the mixture giving the respective ester **3**. The presence of a chlorine atom at the C-atom adjacent to the keto function exerts no influence on the reaction: 5,5,5-trichloropentan-2-one **4**[4] yields the corresponding *gem*-dichlorinated acid **5**.†



Scheme 1

The direct products of these interactions are the corresponding acid chlorides formed by formal exchange of carbonyl oxygen for chlorine atoms of the trichloromethyl

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† *Typical procedure.* To a stirred solution of ketone **1** (4.5 mmol in 15 ml of dry $CH_2Cl_2$) an equivalent amount of anhydrous $FeCl_3$ was added at ~ 0 °C. The reaction mixture was allowed to stand for 4 h at room temperature, then the mixture with an acid chloride odour was poured into 100 ml of water or ethanol and boiled for 2 h. The resulting solution was filtered and extracted with ether and the ether layer was washed with water, dried with magnesium sulfate and evaporated. Products, *i.e.* acid **2** or ester **3**, were distilled *in vacuo* or recrystallized from an ether–hexane mixture.

3,4,4-*Trichlorovaleric acid* **2**. White crystals (yield 68%), m.p. 106 °C. $M^+$ = 205 (17 eV); $^1$H NMR ($CDCl_3$, δ ppm): 10.3 (br., 1H, COOH), 4.65 [dd, 1H ($H^3_X$)], 3.54 [dd, 1H ($H^4_M$)], 3.03 [dd, 1H ($H^4_A$)], 2.30 (s, 3H, Me, AMX-system: $J_{MX}$ = 17.1 Hz, $J_{AX}$ = 10.2 Hz, $J_{AM}$ = 2.2 Hz); $^{13}$C NMR ($CDCl_3$, δ ppm): 175.9 (COOH), 89.7 ($CCl_2$), 65.1 (CHCl), 40.3 ($CH_2$), 35.1 (Me); IR (KBr, ν/cm$^{-1}$): 1725 (CO), 3000 (OH). (Found: C 29.40, H 3.48, Cl 51.72%. Calc. for $C_5H_7C1_3O_2$: C 29.22, H 3.43, Cl 51.76%).

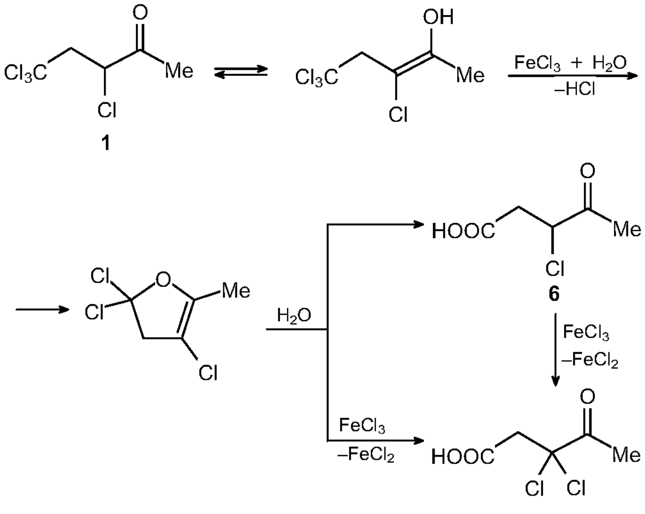
*Ethyl* 3,4,4-*trichlorovalerate* **3**. B.p. 105–110 °C/10 mmHg, $M^+$ = 232, $^1$H NMR ($CDCl_3$, δ ppm): 4.15 (q, 2H, $CH_2$), 4.60 [dd, 1H ($H^3_X$)], 3.36 [dd, 1H ($H^4_M$)], 2.87 [dd, 1H ($H^4_A$)], 2.01 (s, 3H, Me), 1.23 (t, 3H, $CH_3CH_2$, $J_{Me,CH_2}$ = 7 Hz, AMX-system: $J_{AM}$ = 2.3 Hz, $J_{AX}$ = 10.5 Hz, $J_{MX}$ = 16.5 Hz).

4,4-*Dichlorovaleric acid* **5** was obtained from ketone **3**. Oil (yield 57%), b.p. 95–100 °C/20 mmHg, $M^+$ = 170 (CI); $^1$H NMR ($CDCl_3$, δ ppm): 8.3 (br., 1H, COOH), 2.18 (s, 3H, Me), 2.74 (m, 2H, 2-$CH_2$), 2.6 (m, 2H, 3-$CH_2$); IR ($CHCl_3$, ν/cm$^{-1}$): 1710 (CO), 3000 (OH).

group. The transformation observed is reminiscent of known reactions of carbon tetrachloride[5] or trichloromethylarenes[6] with aldehydes in the presence of equimolar quantities of Lewis acids leading to the corresponding acid chlorides and alkylidene (arylidene) dichlorides, ketones and aliphatic trichloromethyl-substituted compounds being known to be unreactive under such conditions.[6] In our case the process is probably facilitated by its intramolecular character (Scheme 1).

Attempts to use other Lewis acids were not successful in obtaining any acidic products. No transformation occurred with $SnCl_4$ even after prolonged heating in the absence of a solvent while the main product of the reaction with $AlCl_3$ was 5,5,5-trichloropent-3-en-2-one identical, according to NMR spectroscopy, to the sample prepared by an independent route.[7] The result could be explained by the insufficient activity of $SnCl_4$ to generate a carbocation from the trichloromethyl group while for a much stronger Lewis acid, *i.e.* $AlCl_3$, only the process of dehydrohalogenation is allowed.

The target product of hydrolysis, β-chlorolevulinic acid **6**, was formed under conditions similar to those described for hydrolysis of 1,1,1-trichloroethane to acetic acid,[8] *i.e.* when anhydrous $FeCl_3$ in methylene dichloride was used together with 2–4 equiv. of water and the reaction mixture was boiled for *ca.* 10 h.[‡] β,β-Dichlorolevulinic acid **7** was identified as a by-product in the reaction. Its formation could be explained by the action of $FeCl_3$ as chlorinating agent, since $FeCl_2$ was found in the reaction mixture. The change of the reaction route is probably connected with enolization of the starting ketone in the presence of water which could hinder the transformation, according to Scheme 1. A mechanism proposed for the process is shown in Scheme 2. The hexahydrate of $FeCl_3$ was inert in the reaction.



**Scheme 2**

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[‡] *Typical procedure.* To anhydrous $FeCl_3$ (5 g, 31 mmol) in dry methylene dichloride (15 ml) was added water (0.1 ml, 2 equiv.) and the mixture was boiled for 10 min. Tetrachloropentanone **1** (6 g) was then added and the reaction mixture was boiled under reflux for 10–12 h. Hydrogen chloride was liberated during the reaction and a greeny-white powder of $FeCl_2$ (0.78 g) precipitated. The reaction mixture was filtered off, treated with water and evaporated under reduced pressure. Distillation of the residue gave a mixture of β-chlorolevulinic **6** and β,β-dichlorolevulinic **7** acids, b.p. 150–170 °C/8–10 mmHg, containing 70% of the acid **6** (yield ~23%).

β-*Chlorolevulinic acid* **6**. $^1$H NMR ($CDCl_3$, δ ppm): 9.5 (br., 1H, COOH), 4.59 [dd, 1H ($H^2_X$)], 3.19 [dd, 1H ($H^3_M$)], 2.89 [dd, 1H ($H^3_A$)], 2.4 (s, 3H, Me, $J_{AX}$ = 6.25 Hz, $J_{AM}$ = 17.5 Hz, $J_{MX}$ = 7.5 Hz).
When the reaction mixture was treated with methanol and then boiled for 4 h, a mixture, b.p. 100–120 °/15 mmHg, containing the methyl esters of the acids **6** and **7** in the ratio 70:30 (according to GLC and $^1$H NMR) was formed.

*Methyl* β-*chlorolevulinate.* $M^+$ = 164.0237 (high resolution mass spectrum, $C_6H_9ClO_3$); $^1$H NMR ($CDCl_3$, δ ppm): 4.59 [dd, 1H ($H^2_X$)], 3.70 (s, 3H, OMe), 3.19 [dd, 1H ($H^3_M$)], 2.82 [dd, 1H ($H^3_A$)], 2.37 (s, 3H, Me, $J_{AM}$ = 17.0, $J_{MX}$ = 7.38, $J_{AX}$ = 6.31); $^{13}$C NMR ($CDCl_3$, δ ppm): 200.9 (CO), 169.9 (COO), 56.7 (CHCl), 51.8 (MeO), 37.8 ($CH_2$), 26.7 (Me).

*Methyl* β,β-*dichlorolevulinate.* $M^+$ = 198; $^1$H NMR ($CDCl_3$, δ ppm): 2.56 (s, 3H, Me), 3.56 (s, 2H, $CH_2$), 3.71 (s, 3H, OMe); $^{13}$C NMR ($CDCl_3$, δ ppm): 195.0 (CO), 167.4 (COO), 82.6 ($CCl_2$), 52.0 (MeO), 47.5 ($CH_2$), 23.2 (Me).