REACTIONS OF CARBOXYLIC ACID CHLORIDES WITH DIMETHYLFORMAMIDE

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The reactions of dimethylformamide (DMFA) with organic acid chlorides have received little study. It is known only that benzoyl chloride (Ia) reacts with DMFA under relatively severe conditions (at the boil) with formation of N,N-dimethylbenzamide (IIa) [1]. This reaction really amounts to transamidation, which in principle can be effected as an equilibrium reaction for any pair made up of a disubstituted amide and a carboxylic acid chloride [2].

When DMFA (R' = H) is taken as the disubstituted amide, one of the partners in the equilibrium becomes the unstable formyl chloride, which decomposes irreversibly into carbon monoxide and hydrogen chloride; the reaction therefore goes in the forward direction to completion. In scheme 1 the first act of the reaction is attack by the electrophilic carbon atom of the carbonyl group of the acid chloride on the nitrogen atom of DMFA.

It is known that in the first stage of the Vilsmeier-Haack reaction [3] phosgene [4], carbonyl fluoride [5], and oxaly chloride [6] react with DMFA in such a way that attack by the electrophilic species RCO (in which R = Cl, F, COCl) is directed on the oxygen atom of DMFA. An unstable adduct is formed, and its decarboxylation leads to the corresponding methyleneammonium salt:

\[
\text{Cl}_2\text{CO} + \text{OCHN(CH}_3)_2 \rightarrow \text{Cl} = \text{C} = \text{N} \text{(CH}_3)_2 + \text{Cl} \text{CO} \text{N} \text{(CH}_3)_2 + \text{Cl} \text{CO} \text{N} \text{(CH}_3)_2 + \text{Cl} \text{CO} \text{N} \text{(CH}_3)_2 + \text{Cl} \text{CO} \text{N} \text{(CH}_3)_2
\]

We have investigated the reactions of carboxylic acid chlorides with DMFA, and we have found a number of examples which enable us to propose a general scheme for the reactions of organic acid chlorides with DMFA. It was found that, like benzoyl chloride (Ia), acetyl (Ib), trifluoroacetyl (Ic), isobutyryl (Id), and heptafluorobutyril (Ie) chlorides react with DMFA with formation of the corresponding N,N-dimethylalkanamides (IIb)-(IIe) (see scheme 1). In the case of heptafluorobutyryl chloride (Ie), as well as the main product (IIe), heptafluoro-N,N-dimethyl-2-oxoalvaramide (III) is formed:

\[
\text{C}_3\text{F}_7\text{COCl} + \text{DMFA} \rightarrow \text{C}_3\text{F}_7\text{CON} \text{(CH}_3)_2 + \text{C}_3\text{F}_7\text{COCON} \text{(CH}_3)_2 \rightarrow \text{C}_3\text{F}_7\text{CON} \text{(CH}_3)_2 + \text{C}_3\text{F}_7\text{COCON} \text{(CH}_3)_2 \rightarrow \text{C}_3\text{F}_7\text{CON} \text{(CH}_3)_2 + \text{C}_3\text{F}_7\text{COCON} \text{(CH}_3)_2
\]

The structure of (III) was confirmed by its IR spectrum (two carbonyl absorption bands) and its F\text{^19} NMR spectrum, in which the signal from the CF$_3$ group is split into a triplet as a result of the spin-spin interaction between the fluorine atoms of the CF$_3$ and $\beta$-CF$_2$ groups. Such a character in the spin-spin interaction is in accord with the F\text{^19} NMR spectrum of the CF$_3$ group [7] and is analogous to that found in the...
spectrum of the dimethylamide (IIe). The structure (III) was also confirmed by the formation of the hydrate
(IV). The mechanism of the formation of (III) will be investigated. Unlike the acid chlorides enumerated
above, which react in accordance with scheme 1, 3,3,3-trifluoro-2-(trifluoromethyl)propionyl chloride (II)
reacts with DMFA under mild conditions with liberation of carbon dioxide and formation of an unstable
crystalline substance, which is readily hydrolyzed into the known [8] 3,3,3-trifluoro-2-(trifluoromethyl)-
propionaldehyde (VII) (scheme 2). This result is readily explained if we assume that in this reaction, as
in the above-cited reaction for phosgene, the initial attack of the electrophilic carbon atom of the carbonyl
group of the acid chloride is directed onto the oxygen atom of DMFA, which leads to the formation of a salt
which is decarboxylated into dimethyl[3,3,3-trifluoro-2-(trifluoromethyl)propylidene]ammonium chloride
(Vf), which is hydrolyzed to the aldehyde (VII).

Scheme 2

\[
\begin{align*}
\text{R} & \text{--COCl} + \text{OCHN (CH}_3\text{)}_2 \rightleftharpoons \left[ \text{R} \text{--CO} \text{--O} \text{--CH} = \text{N} \text{.CH}_3\text{ + Cl} \right] \rightarrow \text{CO} \\
\text{R} & \text{--CH} = \text{N} \text{.CH}_3\text{ + Cl} \overset{\text{H}_2\text{O}}{\longrightarrow} \text{R} \text{--CHO} + \text{NH} \text{.(CH}_3\text{)}_2 \cdot \text{HCl}
\end{align*}
\]

Further confirmation of this reaction mechanism was provided by the investigation of the IR spec-
trum of the alkylideneammonium salt (Vg); we succeeded in isolating this intermediate product by conduct-
ing the reaction between 2-chloro-3,3,3-trifluoro-2-(trifluoromethyl)propionyl chloride (Ig) and DMFA in
diethyl ether solution. Although it was not found possible to obtain the salt (Vg) in a pure state because of
the occurrence of the side processes considered below, the absorption band of the carbonyl group of the
original acid chloride at 1760 cm\(^{-1}\) was quite clearly absent from its IR spectrum, and a new band appeared
at 1691 cm\(^{-1}\), characteristic for the \(\text{> C = N <}\) group. A product of similar structure was isolated earlier
by Arnold [4] in the reaction of phosgene with DMFA.

Acid chlorides which react with DMFA in an analogous way to 3,3,3-trifluoro-2-(trifluoromethyl)-
propionyl chloride (II), i.e., through the stage of decarboxylation and formation of an alkylideneammonium
salt (V), are 2-chloro- (Ig) and 2-bromo- (Ih) -3,3,3-trifluoro-2-(trifluoromethyl)propionyl chlorides,
3,3,3-trifluoro-2-methyl-2-(trifluoromethyl)propionyl chloride (II), perfluoropivaloyl chloride (Ij), and
trichloroacetyl chloride (Ik). However, the reaction is often complicated by side processes (see below),
as a result of which it is not always possible to isolate the aldehyde (VI), but only its transformation products.

Apart from aldehydes, the products of the reactions of 3,3,3-trifluoro-2-(trifluoromethyl)propionyl
chlorides (II), (Ig), and (Ih) and of trichloroacetyl chloride (Ik) with DMFA include the corresponding
chloroalkanes (VII) and carbon monoxide — products of the decarbonylation of the original acid chlorides.

Scheme 3

\[
\begin{align*}
\text{R} & \text{--COCl} \overset{\text{DMFA}}{\longrightarrow} \text{R} \text{--Cl} + \text{CO} \\
\text{R} & \text{: } f = (\text{CF}_3)_2\text{CH}; g = (\text{CF}_3)_2\text{CCl}; h = (\text{CF}_3)_2\text{CBr}; i = (\text{CF}_3)_2\text{C(CH}_3\text{)}; \\
& j = (\text{CF}_3)_2\text{C}; k = \text{CCl}_3
\end{align*}
\]

Trichloroacetyl chloride (Ik) is the only one of the acid chlorides which we investigated which reacts
with DMFA in accordance with Schemes 1, 2, and 3 simultaneously, which leads to the formation of
2,2,2-trichloro-N,N-dimethylacetamide (Ik), chloral (VIIk), and carbon tetrachloride (VIIk). Perfluoro-
pivaloyl chloride (Ij) reacts with DMFA with liberation of one molecular proportion of carbon dioxide and
formation of a saltlike product, which on hydrolysis gives 2H-hexafluoro-2-(trifluoromethyl)propane (VIII).
This can be explained on the assumption that, under the conditions of the hydrolysis of the alkylidene-
ammonium salt (Vj) (i.e., in aqueous DMFA at 0\(^\circ\)), perfluoropivalaldehyde (VIIj) (perfluoropivalaldehyde is
unknown) is unstable and is quickly decarboxylated (see scheme on following page).

The course of the reaction of DMFA with 3,3,3-trifluoro-2-methyl-2-methyl-2-(trifluoromethyl)-
propionyl chloride (II) is more complex. By conducting the reaction under mild conditions we were able