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Abstract

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INTERACTION OF NITRILES WITH HEAVY WATER AND DEUTERIUM CHLORIDE

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The interaction of nitriles with water and hydrogen chloride at low temperatures leads to the formation of iminohydrin chlorides (amide chlorohydrates), free amides, or mixtures of these (1). Treatment of amide chlorohydrates with an excess of water gives amides (1,2).

$$RCN + H_2O + HCl \rightarrow \left[RC\genfrac{}{}{0pt}{}{NH_2}{OH}^{+}\right] Cl^{-} \xrightarrow{H_2O} RC\genfrac{}{}{0pt}{}{O}{NH_2} + HCl \qquad (1)$$

In the present work reaction (1) was studied using heavy water and deuterium chloride. A mixture of 0.01 mole of nitrile and 0.01 mole of deuterium oxide at −5 to −12° was passed through with 0.02-0.03 mole of dry DCl, obtained from NaCl and D_2SO_4. The mixture was left to stand for 24 hours at 0°, and then washed with heavy water until the chloride ion disappeared. The melting points of the amides corresponded to literature values. 94% D_2O and 80% (with respect to deuterium) D_2SO_4 were used. Determination of deuterium in the combustion water of the reaction products was carried out by a refractometric method on an ITR-1 (3). In the reaction products, in addition to determining the number of deuterium atoms, the presence of possible types of bonds (C–H, C–D, N–H, N–D) was determined from infrared spectroscopy data.

The spectra were recorded on a two-beam IR spectrometer IKS-14 (LiF prism). The results of experiments on the interaction of nitriles with D_2O and DCl are presented in Table 1, and the IR spectra of the amides obtained in Table 2. Figure 1 gives—

Table 1

Products of the interaction of nitriles with heavy water and deuterium chloride

Experiment No.	Reaction product	Yield, %	Excess density of combustion water, mol. %	Number of deuterium atoms entering the reaction*
1	Butyramide	42	9.67	1.2
2	Adipamide	93	19.41	3.1
3	Chloroacetamide	60	45.82	2.4
4	Dichloroacetamide	78	51.14	2.1
5	Trichloroacetamide	61	78.08	2.0
6	α, β-Dichloropropionamide	80	40.23	2.7
7	β-Chloropropionamide	80	36.85	3.0
8	Benzamide	64	23.40	2.2

* Calculated for 100% D_2O and DCl.

IR spectra are given of samples of β-chloropropionamide obtained from β-chloropropionitrile using non-deuterated and deuterated reagents.

From the data in the tables it is evident that N-deuteriotrichloroacetamide is obtained from trichloroacetonitrile in high yield. In the case of other aliphatic nitriles having α-hydrogen atoms, in parallel with addition of heavy water to the cyano group (formation of an N—D bond), deuterium exchange occurs at the carbon atom (formation of a C—D bond).

It could be assumed that deuterium exchange occurs at each of the three stages of the reaction: in the interaction of the nitrile with DCl, at the stage of addition of water, and upon treatment of the hydrochloric-acid salt of the amide with heavy water with elimination of DCl and formation of the amide. To clarify this question, additional experiments were carried out. β-Chloropropionitrile was saturated with deuterium chloride in the absence of water under the conditions of amide synthesis. After removal of DCl, β-chloropropionitrile containing no deuterium atoms was obtained. Next, the product of the interaction of β-chloropropionitrile, deuterium chloride, and heavy water was synthesized, but, in contrast to the corresponding experiment given in Table 1, in this case the reaction product was not treated with an excess of D_2O, but was isolated as the hydrochloride. In it were found bond frequencies ν_val, cm^{-1}: N—H 3342, 3168; N—D 2461, 2395; C—H 2973, 2911, 2860. β-Chloropropionamide hydrochloride contained deuterium only at the nitrogen and oxygen atoms, and no C—D bonds were detected in it.

Table 2

IR spectra of the products of the interaction of nitriles with heavy water and deuterium chloride (principal frequencies)

Fig. 1. IR spectrum of β-chloropropionamide (I) and deuterated β-chloropropionamide (II)

Figure 1: Fig. 1. IR spectrum of β-chloropropionamide (I) and deuterated β-chloropropionamide (II)

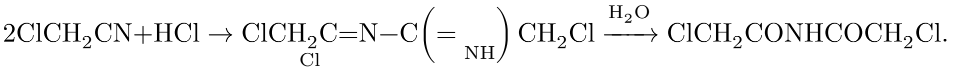
No.	Reaction product	N–H	N–D	C–H	C–D
1	Adipamide	336833413175	254524852406	295129062876	23662341
2	Chloroacetamide	32963180	2500	29532930	2326
3	Trichloroacetamide	33053166	253924802386		
4	α,β-Dichloropropionamide	33263159	2545	29232850	2325
5	β-Chloropropionamide	333332933160	25192455	29162852	2326
6	Benzamide	33533171	2485	30242953	2317
7	β-Chloropropionamide hydrochloride	33423168	24612395	297329112860	

Fig. 1. IR spectrum of β-chloropropionamide (*I*) and deuterated β-chloropropionamide (*II*)

On the basis of these two experiments and taking into account the fact that amide hydrochlorides are unstable in water and readily decompose in it with formation of amides, we came to the conclusion that hydrogen exchange at the carbon atom takes place in the amide–water system. Indeed, in a reverse synthesis, when the iminohydrin chloride synthesized from the nitrile, H_2O, and HCl was dissolved at room temperature in an excess of D_2O, β-chloropropionamide with N–D and C–D bonds was obtained, analogous to that obtained in experiment 7 (Table 1) in the direct synthesis. The easy exchange of hydrogen in amides is also indicated by the fact that, as we found, β-chloropropionamide exchanges with heavy water also in a neutral medium at room temperature, and in the product both N–D and C–D bonds are found. Moreover, in C,N-deuteriated β-chloropropionamide under the same conditions it is possible, by double exchange with an excess of H_2O, to lower the deuterium content from 2.2 atoms to 0.3.

By treating the dimeric hydrochloric-acid salt of chloroaceto-

of the nitrile (the hydrochloride of N-chloromethylenechloroacetamidine)^(4,5) dichloroacetamide is obtained (2).



$$2ClCH_2CN+HCl \rightarrow ClCH_2\underset{Cl}{C}=N-C\left(=_{NH}\right)CH_2Cl \xrightarrow{H_2O} ClCH_2CONHCOCH_2Cl. \qquad (2)$$

When DCl and D_2O were used in this reaction, C,N-deuterated dichloroacetamide containing 1.5 atoms of deuterium was synthesized in 70% yield. IR spectrum, ν_{val}, cm^{-1}: N–D 2412, 2360; N–H 3264, 3194, 3184, 3020; C–D 2274, 2256, 2169; C–H 2986, 2946, 2794, 2732.

The reactions studied, which lead to the formation of deuterated amides and their hydrochlorides, may, owing to their simplicity, be used for the synthesis of labeled compounds.

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