REACTIONS OF ω -CHLORO CARBONITRILES

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 ω -Chloro carbinitriles have become accessible substances, being obtained by the telomerization of ethylene with cyanogen chloride, but their reactions have been little studied. Particular interest is presented by the finding of reactions in which both functional groups of chloro nitriles take part, for these reactions can be regarded as specific for this class of compounds.

In the present work we studied the action of nucleophilic reagents — ammonia, amines and alkoxides — on 5-chlorovaleronitrile and 7-chloroheptanenitrile. It is known from the literature that in the action of ammonia [1], primary amines [1, 2], and secondary amines [3-6] on ω -chloro carbonitriles the chlorine atom is replaced by an amino group, whereas tertiary amines usually bring about the dehydrochlorination of these chloroalkanenitriles [5]. A peculiar feature of the behavior of 4-chlorobutyronitrile and 5-chlorovaleronitrile in their reactions with ammonia and primary amines is the ease with which cyclization occurs with formation of five- and six-membered heterocycles [6-8]. The reactions of 5-chlorovaleronitrile with ammonia and methylamine are described only in patents [2, 6, 7], and the products have been characterized inadequately.

In the performance of the reaction of 5-chlorovaleronitrile with liquid ammonia at 100°C, together with 5-aminovaleronitrile we isolated 5,5'-iminodivaleronitrile, the amount of which depends appreciably on the proportions of the reactants: with increase in the amount of liquid ammonia the yield of the imino derivative diminishes. Under the same conditions with alcoholic ammonia about 13% of 2-piperidone is formed. With rise in the reaction temperature to 150° the piperidone becomes the main reaction product, and the formation also of considerable amounts of 5-(2-oxopiperidino)valeronitrile is observed.



The reaction of 5-chlorovaleronitrile with anhydrous methylamine in benzene leads to the formation of 5-(methylamino)valeronitrile; whereas in alcohol in presence of water, reaction goes with cyclization and formation of a considerable amount of 1-methyl-2-piperidone. 5,5'- (Methylimino)divaleronitrile was isolated in low yield, and this was hydrolyzed with concentrated hydrochloric acid into the corresponding dicarboxylic acid.



We also considered that it would be of interest to find a convenient method to pass from chloroalkanenitriles to unsaturated nitriles and so to unsaturated acids. The literature described only the catalytic method for the dehydrochlorination of 5-chlorovaleronitrile [8, 9] and the dehydrochlorination of 3-chloro-

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propionitrile and 4-chlorobutyronitrile with triethylamine, pyridine, and quinoline [5]. We showed that 5chlorovaleronitrile and 7-chloroheptanenitrile are not dehydrochlorinated under the action of N,N-diethylaniline or pyridine at 150-180° (in the second case a 2.8% yield of 6-heptenenitrile was isolated). The course of the reactions of these nitriles with triethylamine at 150-180° was interesting; under these conditions the formation of the unsaturated nitriles, the yields of which attained 50%, was accompanied by the formation of the ω - (diethylamino)alkanenitriles (C₂H₅)₂N(CH₂)_nCN, n = 4 and 6.

The formation of unsaturated nitriles and (diethylamino)alkanenitriles can be represented by a scheme in which the intermediately formed quaternary ammonium salt formed from the chloroalkanenitriles and triethylamine undergoes thermal decomposition in two directions:

 $(C_{2}H_{5})_{3}\overset{+}{\underset{C1}{\overset{+}{N}}}(CH_{2})_{n}CN - \bigcup_{(C_{2}H_{5})_{2}}^{\overset{+}{O}}(CH_{2})_{n-2}CN + (C_{2}H_{5})_{3}N \cdot HCl$

5- (Diethylamino)valeronitrile was characterized in the form of the picrate. The structure of 7- (diethylamino)heptanenitrile was proved by independent synthesis and also by its hydrolysis to 7- (diethylamino)heptanoic acid which was isolated as its ethyl ester. The reactions of the ω -chloro nitriles under investigation with sodium ethoxide led to the formation of 5-ethoxyvaleronitrile and 7-ethoxyheptanenitrile; unsaturated nitriles were formed in only 5-6% yield.

EXPERIMENTAL

<u>Ammonolysis of 5-Chlorovaleronitrile with Liquid Ammonia</u>. A mixture of 41.1g of 5-chlorovaleronitrile and 400 ml of liquid ammonia was heated in an autoclave at 100° for 2 h. Ammonia was driven off, and the reaction mixture was diluted with water, extracted with ether (to remove unchanged chloro nitrile), and treated with excess of 40% sodium hydroxide solution. The amines liberated were extracted with ether several times, and the residue remaining after the removal of ether was vacuum-distilled. We obtained 22.0 g (64%) of 5-aminovaleronitrile; b.p. 80° (5 mm); n_D^{20} 1.4457; d_4^{20} 0.9187; found MR 28.47; calculated MR 28.53. The literature [10] gives b.p. 92-93° (12 mm). Benzoyl derivative, m.p. 57.5° (from benzene); the literature [10] gives m.p. 57-59°. We also obtained 6.9 g (22%) of 5,5'-iminodivaleronitrile; b.p. 172-174° (2 mm); n_D^{20} 1.4808; d_4^{20} 0.9790. Found %: C 66.24, 66.46; H 9.57, 9.51; N 23.21, 22.92. MR 52.08. $C_{10}H_{17}N_{3}$. Calculated %: C 67.00; H 9.56; N 23.44. MR 51.62.

<u>Ammonolysis of 5-Chlorovaleronitrile with Alcoholic-Aqueous Ammonia</u>. A mixture of 34.2 g of 5-chlorovaleronitrile and 280 ml of ethanol containing 40 g of NH₃ and 20 ml of water was heated in an autoclave for 4 h at 140-150°. Alcohol and water were driven off, the residue was treated with dichloroethane, precipitated ammonium chloride was filtered off, dichloroethane was driven off, and the residue was vacuum-distilled. We obtained 15.8 g (55%) of crystalline 2-piperidone, b.p. 100-102° (2 mm), and 3.0 g of 5-(2-oxopiperidino)valeronitrile, b.p. 165-166° (3 mm) and n_D^{20} 1.4932, which after redistillation had the constants: n_D^{20} 1.4930; d_4^{20} 1.0522. Found %: C 66.55, 66.50; H 9.41, 9.30; N 15.65, 15.38. MR 49.78. $C_{10}H_{16}N_2O$. Calculated %: C 66.63; H 8.95; N 15.54. MR 49.95.

The residue, which had crystallized in the distilling flask, was dissolved in alcohol and reprecipitated with ether, and we isolated 2.8 g (2.9%) of a substance of m.p. 217°, raised by recrystallization from alcohol to 229°. Found %: C 18.00, 18.27; H 8.96, 8.87; Cl 53.42, 53.07; N 21.81. $C_5H_{10}N_2 \cdot 2HCl \cdot 3NH_4Cl$. Calculated %: C 18.11; H 7.30; N 21.12; Cl 53.47 (it is probable that a complex of 2-iminopiperidine hydrochloride with ammonium chloride was obtained; its structure was not proved). From the filtrate, after removal of alcohol and ether, treatment with 40% NaOH solution, and extraction with ether, by vacuum distillation we obtained 1.7 g (5.9%) of 5-aminovaleronitrile contaminated with 2-piperidone and 2.8 g (22.2%) of 5- (2-oxopiperidino)valeronitrile.

Reaction of 5-Chlorovaleronitrile with Methylamine in Benzene. A mixture of 25.2 g of 5-chlorovaleronitrile and 70 ml of benzene containing 4.2 g of methylamine was introduced into an autoclave and heated at 100° for 5 h. The benzene solution was washed with 1 : 1 hydrochloric acid and dried, benzene was driven off, and the residue was vacuum-distilled. We obtained 12.5 g of unchanged 5-chlorovaleronitrile. The hydrochloric acid solution was treated with 40% NaOH solution, the oil formed was separated, and the solution was extracted repeatedly with ether. After vacuum distillation we obtained 4.1 g (34.1% on the chloro nitrile that reacted) of 5-(methylamino)valeronitrile, b.p. 56-59° (2 mm), and

2.4 g (22.7% on the chloro nitrile that reacted) of 5,5'- (methylimino)divaleronitrile, b.p. 143-146° (2 mm). After redistillation 5- (methylamino)valeronitrile had the constants: n_D^{20} 1.4450; d_4^{20} 0.8962; found MR 33.48; calculated MR 33.32. According to gas-liquid chromatography the 5- (methylamino)valeronitrile contained about 2% of 1-methyl-2-piperidone. From the high-boiling fractions accumulated from several experiments we isolated 5,5'- (methylimino)divaleronitrile with the constants: b.p. 170° (4 mm); n_D^{20} 1.4600; d_4^{20} 0.9388. Found %: C 68.55, 68.71; H 10.05, 10.02. MR 56.39. $C_{11}H_{19}N_3$. Calculated %: C 68.35; H 9.91. MR 56.57.

By the hydrolysis of 2.0 g of 5,5'- (methylimino)divaleronitrile with concentrated HCl and isolation of the reaction product with the aid of the cation-exchanger KU-2, we obtained 2.2 g (93% of 5,5'- (methyl-imino)divaleric acid, m.p. 152-153° (from alcohol). Found %: C 57.10, 57.26; H 9.22, 9.38; N 6.30, 6.17. $C_{11}H_{21}NO_4$. Calculated %: C 57.12; H 9.15; N 6.06.

<u>Reaction of 5-Chlorovaleronitrile with Methylamine in Alcohol</u>. Under the same conditions from 21.1 g of 5-chlorovaleronitrile and 15 g of methylamine in 100 ml of alcohol, after removing alcohol, treating the residue with 40% NaOH solution, and extracting with ether, we obtained 12.4 g (61.2%) of a mixture of 1-methyl-2-piperidone and 5- (methylamino)valeronitrile, b.p. 59-62° (1 mm), n_D^{20} 1.4765; d_4^{20} 1.0171 (for 1-methyl-2-piperidone the literature [11] gives: n_D^{20} 1.4818; d_{20}^{20} 1.0331), and 4.0 g of a fraction with b.p. 133-145° (1 mm) and n_D^{20} 1.4625, consisting mainly of 5,5'- (methylimino)divaleronitrile.

<u>Reaction of 5-Chlorovaleronitrile with Triethylamine</u>. A small autoclave containing 23.5 g of 5-chlorovaleronitrile and 23.0 g of triethylamine was heated at 170-180° for 7 h. The reaction product — a solid mass — was extracted with water, and the reaction mixture was treated with 1 : 1 hydrochloric acid until weakly acid. Neutral products were extracted with ether, the extract was dried, ether was driven off, and the residue was vacuum-distilled. We obtained 7.7 g (47.5%) of 4-pentenenitrile; b.p. 52° (25 mm); n_D^{20} 1.4210; d_4^{20} 0.8394; found MR 24.50; calculated MR 24.64. The literature [12] gives: n_D^{19} 1.4210; d_4^{19} 0.8379.

The acidic solution was vacuum-evaporated, treated with 40% NaOH solution, and extracted repeatedly with ether. We obtained 6.9 g (22.4%) of 5- (diethylamino)valeronitrile; b.p. 87° (5 mm); n_D^{20} 1.4410; d_4^{20} 0.8615. Found %: C 70.21, 70.09; H 11.74, 11.61; N 18.33, 18.11. MR 47.28. $C_3H_{18}N_2$. Calculated %: C 70.08; H 11.76; N 18.16. MR 47.52. Picrate, m.p. 87-88° (from alcobol). The literature [4] gives: n_D^{22} 1.4382; d_4^{22} 0.857; picrate, m.p. 85°.

 $\begin{array}{c} \underline{\text{Reaction of 7-Chloroheptanenitrile with Triethylamine.}} \\ \underline{\text{Reaction of 7-Chloroheptanenitrile with Triethylamine.}} \\ \underline{\text{Conditions of the preceding experiment, from 29.0 g of 7-chloroheptanenitrile we obtained 9.6 g (44.4%) of the unsaturated nitrile; b.p. 82° (20 mm); n_D^{20} 1.4332; d_4^{20} 0.8390. \\ \underline{\text{Found \%: C 76.62, 76.56; H 10.41, 10.20; N 13.19, 13.32.} \\ \underline{\text{MR 33.83. C_7H_{11}N. Calculated \%: C 77.01; H 10.16; N 12.83.} \\ \underline{\text{MR 33.88}} \\ \underline{\text{the literature [13] gives: b.p. 75 to} \\ \underline{\text{78° (13 mm)}} \\ \underline{\text{and 8.2 g (22.6\%) of 7- (diethylamino)heptanenitrile; b.p. 139° (14 mm); n_D^{20} 1.4460; d_4^{20} 0.8623.} \\ \underline{\text{Found \%: C 72.49, 72.54; H 12.30, 12.37; N 15.83, 15.65.} \\ \underline{\text{MR 56.38. C_{11}H_{22}N_2}. \\ \underline{\text{Calculated \%: C 72.47; H} \\ \underline{\text{12.16; N 15.37.} \\ \underline{\text{MR 56.76.} \\ \underline{\text{Hydrochloride, m.p. 99° (in a sealed capillary).} \\ \underline{\text{Found \%: C 60.67; H 10.20; Cl 15.91.} \\ \underline{\text{C}_{11}H_{22}N_2 \\ \underline{\text{HCl. Calculated \%: C 60.39; H 10.60; Cl 16.21.} \\ \end{array}}$

By gas-liquid chromatography we proved the identity of the substance obtained with the known 7- (diethylamino)heptanenitrile obtained in the next experiment. After the hydrolysis of the 7- (diethylamino)heptanenitrile and isolation of the product with the aid of the cation-exchanger KU-2, we obtained liquid 7- (diethylamino)heptanoic acid, which was converted into its ethyl ester in good yield; b.p. 87° (1 mm); n_D^{20} 1.4386; d_4^{20} 0.8889. Found %: C 68.14, 68.28; H 12.43, 12.65; N 6.40, 6.41. MR 67.81. $C_{13}H_{27}NO_2$. Calculated %: C 68.07; H 11.87; N 6.11. MR 67.83. Hydrochloride, m. p. 68-69°. Found %: C 58.49; H 10.87; Cl 13.43. $C_{13}H_{27}NO_2 \cdot HCl$. Calculated %: C 58.74; H 10.62; Cl 13.34.

<u>Reaction of 7-Chloroheptanenitrile with Diethylamine</u>. By heating 14.5 g of 7chloroheptanenitrile with 22.0 g of diethylamine in 20 ml of alcohol in an autoclave at 100° for 5 h and treating the reaction mixture as described for the experiment with methylamine (in benzene), we obtained 14.3 g (87.7% on the chloro nitrile that reacted) of 7-(diethylamino)heptanenitrile; b.p. 86° (1 mm); n_D^{20} 1.4453; d_4^{20} 0.8552. Found %: C 72.11, 72.17; H 11.96, 12.06. MR 56.78. $C_{11}H_{22}N_2$. Calculated %: C 72.47; H 12.16. MR 56.76. By hydrolyzing 7-(diethylamino)heptanenitrile with concentrated HCl and subsequent esterification we obtained ethyl 7-(diethylamino)heptanoate; n_D^{20} 1.4390; d_4^{20} 0.8918. It was shown by gas-liquid chromatography that the ethyl esters obtained in this and the preceding experiment were identical. Reaction of 7-Chloroheptanenitrile with Sodium Ethoxide. 29 g of 7-chloroheptanenitrile was added to sodium ethoxide solution prepared from 5 g of sodium and 65 ml of absolute ethanol, and the solution was heated at the boiling point of alcohol for 5 h. The reaction mixture was decomposed with water and extracted several times with ether; the extract was dried with Na₂SO₄, ether was driven off, and the residue was vacuum-distilled. We obtained 1.2 g (5.5%) of 6-heptenenitrile, b.p. 53° (2 mm), n_D^{20} 1.4312, and d_4^{20} 0.8493, and 19.1 g (61.9%) of 7-ethoxyheptanenitrile, b.p. 78-81° (2mm), which after redistillation had the constants: b.p. 108° (7 mm); n_D^{20} 1.4303; d_4^{20} 0.8829. Found %: C 69.16, 69.10; H 11.02, 10.96; N 9.46, 9.33. MR 45.45. C₉H₁₇NO. Calculated %: C 69.63; H 11.04; N 9.02. MR 45.22.

When the solution of sodium ethoxide was added to an alcoholic solution of the chloro nitrile heated to 60-70° in the course of 3 h, from the same amounts of the reactants we obtained a 4% yield of the unsaturated nitrile, 70.2% of 7-ethoxyheptanenitrile, and 3.8% of 7-ethoxyheptanamide, m.p. 76-77° (from benzene). Found %: C 62.83, 62.78; H 11.07, 11.02; N 8.06, 8.27. $C_9H_{19}NO_2$. Calculated %: C 62.39; H 11.05; N 8.09.

 $\frac{\text{Reaction of 5-Chlorovaleronitrile with Sodium Ethoxide.}}{\text{of the preceding experiment, from 23.5 g of 5-chlorovaleronitrile, we obtained 1.0 g (6.2%) of 4-pentenenitrile, np²⁰ 1.4200; d₄²⁰ 0.8388, and 13.4 g (59.8%) of 5-ethoxyvaleronitrile; b.p. 100° (23 mm); np²⁰ 1.4200; d₄²⁰ 0.8921; found MR 36.07; calculated MR 35.99. The literature [4] gives: b.p. 83° (11 m*); np¹⁸ 1.4209; d₄¹⁸ 0.897.$

CONCLUSIONS

1. A study was made of the action of nucleophilic reagents — ammonia, amines, and alkoxides — on 5-chlorovaleronitrile and 7-chloroheptanenitrile.

2. The reaction of 5-chlorovaleronitrile with ammonia and methylamine goes with formation both of the usual products of the replacement of the chlorine atom and also of cyclic compounds. In the case of ammonia 5-aminovaleronitrile, 2-piperidone, 5,5'-iminodivaleronitrile, and 5-(2-oxopiperidino)valeronitrile were isolated. In the case of methylamine 5-(methylamino)valeronitrile, 1-methyl-2-piperidone, and 5,5'-(methylimino)divaleronitrile were isolated.

3. In the action of triethylamine on 5-chlorovaleronitrile and 7-chloroheptanenitrile at 150-180°, as well as dehydrochlorination with formation of unsaturated nitriles, the formation of ω -(diethylamino)alkanenitriles occurs.

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