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THE REACTION OF ETHYL ISOCYANIDE WITH METHANOL, ETHANOL, AND ETHYL MERCAPTAN AT HIGH PRESSURE

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p-Tolyl isocyanide is reported to combine with ethyl mercaptan at 100° to give a formimido thioester, *p*-$CH_3C_6H_4N{=}CHSC_2H_5$, and to combine with ethanol in the presence of sodium ethoxide at 120° to give a formimido ester, *p*-$CH_3C_6H_4N{=}CHOC_2H_5$ (1). Alcohols have sometimes been used as solvents in reactions involving isocyanides, suggesting that alcohols do not react readily with isocyanides. Otherwise, the action of alcohols or mercaptans on isocyanides seems to have been little studied. This paper reports such a study at high pressure.

When methanol and ethyl isocyanide were heated together at 125° under a pressure of 8500 atmospheres, a product built up from two molecules of ethyl isocyanide and two molecules of methanol was formed in 64% yield. Analogous products were obtained when methanol was replaced by ethanol (40% yield) or ethyl mercaptan (78% yield), but replacement of methanol by water gave N-ethylformamide. The pressure of 8500 atmospheres probably favored the observed reactions. However, it was not essential to them, for in an experiment at 1070 atmospheres the yield of product from ethyl isocyanide and ethyl mercaptan was 57%, only a little less than that (78%) at 8500 atmospheres.

Only one of the nitrogen atoms in these compounds is basic enough to be titrated by perchloric acid in acetic acid. Acid hydrolysis of the methanol product liberated methanol, which indicates at least one methoxyl group per molecule. That the alcohol products actually contain two alkoxyl groups per molecule is shown by results of Zeisel analyses. The infrared absorption spectrum of the methanol product and of the ethyl mercaptan product both have a strong band at 6.0μ, which is in the region of C=N absorption.

The ethyl isocyanide used in these experiments was basic, perhaps due to a small amount of ethylamine or ammonia. This suggests that the products may have been formed by a base-catalyzed mechanism. Any sort of free-radical mechanism seems unlikely because of the fact that alcohols and ethyl mercaptan gave analogous products.[1] A formamidine structure (V) is consistent with the experimental data summarized above and can be accounted for by a base-catalyzed mechanism as follows. Attack of ethyl isocyanide by an alkoxide or alkylthio ion (I) would lead to a formimido ester or thioester (II). As mentioned

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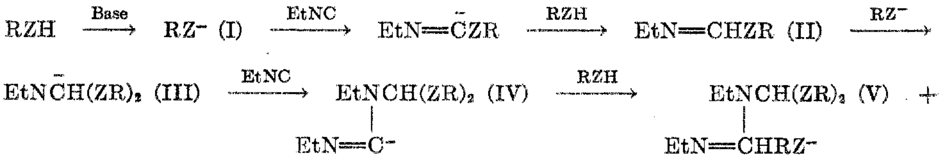
[1] A mercaptan, RSH, gives products containing RS— groups in both base-catalyzed and free-radical-initated reactions, the reactive intermediate being RS^- and $RS\cdot$, respectively (12). An alcohol, ROH, gives products with RO— groups in base-catalyzed reactions, the reactive intermediate being RO^-. However, ROH generally gives other types of products in free-radical-initated reactions because the reactive intermediate usually is not $RO\cdot$, but a free radical formed by loss of hydrogen from a carbon atom (13).

above, such reactions of isocyanides have been reported before (1); they are analogous to the base-catalyzed formation of alkyl formates from carbon monoxide and alcohols (11). Subsequent attack of II by an alkoxide or alkylthio ion would give an ionic intermediate (III) that, by addition to ethyl isocyanide, would give the ionic intermediate, IV. Abstraction of a proton from an alcohol or mercaptan by IV would then give the formamidine, V. Since no formimido ester (II) was ever isolated from a reaction mixture, this mechanism implies that imido esters are more susceptible to attack by basic reagents than are isocyanides. From what is known of the chemistry of isocyanides (3) and imido esters (4), this seems reasonable. Although the formamidine structure (V) certainly cannot be considered established, it does seem a useful working hypothesis.



$$\mathrm{RZH} \xrightarrow{\text{Base}} \mathrm{RZ^-}\ (\mathrm{I}) \xrightarrow{\text{EtNC}} \mathrm{EtN{=}\overset{-}{C}ZR} \xrightarrow{\text{RZH}} \mathrm{EtN{=}CHZR}\ (\mathrm{II}) \xrightarrow{\mathrm{RZ^-}}$$

$$\mathrm{EtN\overset{-}{C}H(ZR)_2}\ (\mathrm{III}) \xrightarrow{\text{EtNC}} \begin{array}{c}\mathrm{EtNCH(ZR)_2}\ (\mathrm{IV})\\ \vert \\ \mathrm{EtN{=}C^-}\end{array} \xrightarrow{\text{RZH}} \begin{array}{c}\mathrm{EtNCH(ZR)_2}\ (\mathrm{V})\\ \vert \\ \mathrm{EtN{=}CHRZ^-}\end{array} +$$

(RZ = MeO, EtO, or EtS)

EXPERIMENTAL

Ethyl isocyanide was prepared at atmospheric pressure by the procedure of Lowry and Henderson (5) modified in that the cake formed from silver cyanide and ethyl iodide was crushed and dried at 25° for 15 hours in order to remove all traces of ethyl iodide (2, 10). The product was purified by distillation through a 12-inch column of glass helices. The ethyl isocyanide (yield 67%; b.p. 75–78°; n_{D}^{25} 1.3597) turned indicator paper a color corresponding to *p*H 8.

The reactions of ethyl isocyanide. All experiments with ethyl isocyanide were done at 125° for 18 hours under an initial pressure of 8500 atmospheres unless otherwise stated. The procedure was in each case similar to that given below for the reaction of ethyl isocyanide with methanol. Molecular weights were determined ebullioscopically in benzene. Neutral equivalents were determined in acetic acid by titration with perchloric acid.

The reaction of ethyl isocyanide with methanol. A homogeneous mixture of 3.33 g. of ethyl isocyanide and 3.33 g. of methanol was placed in a collapsible lead tube about 0.5″ in diameter and 0.005″ in wall thickness with a lead disc soldered onto its bottom. A standard gasketed cap proved an unreliable means of closing the top and was replaced by a steel nut fitted with a short valve stem; a tight closure was obtained by forcing the point of the valve stem into the top of the lead tube. The tube was placed in a Bridgman-type apparatus (6). The chambers of the apparatus were filled with kerosene and the tube was subjected to a pressure of 8500 atm. The chamber of the apparatus holding the tube was then heated electrically to 125° and held at this temperature for 18 hours, during which time the pressure gradually fell (a usual phenomenon). The final pressure was 7300 atm. The apparatus was cooled to 25° and the pressure was released. The lead tube had become partially collapsed, indicating that a reaction accompanied by a diminution of volume had taken place. The contents of the lead tube were transferred to a small Claisen flask. The lead tube was rinsed with ether and the rinsings were added to the Claisen flask. By distillation, 3.3 g. (64% yield) of crude 2EtNC–2MeOH, b.p. 26–33° (0.4 mm.), was separated from 1.00 g. of dark, viscous material not volatile at a pot temperature of 82° (0.4 mm.). The 2EtNC–2MeOH was redistilled at a pressure of 11 mm. through a 13 cm. × 0.6 cm. vacuum-jacketed glass tube containing a glass spiral. A middle portion, b.p. 79–80° (11 mm.), b.p. 196–197° (760 mm.),[2] n_D^{25} 1.4883, was analyzed.

Anal. Calc'd for $C_8H_{18}N_2O_2$: C, 55.1; H, 10.4; N, 18.4; CH_3O, 35.6; Mol. wt., 174.

Found: C, 55.05; H, 10.55; N, 17.5; CH_3O, 27.5; Mol. wt., 170; Neut. equiv., 165

The compound is easily soluble in water and the common organic solvents, including cyclohexane. It rapidly decolorizes bromine in carbon tetrachloride or water, a heavy oil forming in the latter case. It does not decolorize potassium permanganate in cold acetone. Hydrolysis with 3 *N* sulfuric acid at 100° followed by distillation gave an aqueous distillate containing methanol, identified by the chromotropic acid test (8).

There was very little reaction when the experiment was repeated at 60°.

The reaction of ethyl isocyanide with ethanol. A mixture of 3.52 g. of ethyl isocyanide and 3.52 g. of absolute ethanol gave A, 0.83 g. of tar, and B, 2.60 g. (40% yield) of crude 2EtNC–2EtOH, b.p. 87–95° (11 mm.), n_D^{25} 1.4431. Redistillation of B gave 2EtNC–2EtOH of b.p. 93° (11 mm.), b.p. 213° (760 mm.), n_D^{25} 1.4409. The compound is almost insoluble in water, but is easily soluble in 5% hydrochloric acid or the common organic solvents.

Anal. Calc'd for $C_{10}H_{22}N_2O_2$: C, 59.4; H, 11.0; N, 13.85; C_2H_5O, 44.55; Mol. wt., 202.

Found: C, 59.1; H, 11.2; N, 14.0; C_2H_5O, 42.5; Mol. wt., 190; Neut. equiv., 197.

The reaction of ethyl isocyanide with ethyl mercaptan. A mixture of 3.60 g. of ethyl isocyanide and 3.60 g. of ethyl mercaptan gave A, 1.17 g., b.p. 40–66° (5 mm.), n_D^{25} 1.4814; B, 5.34 g. (78% yield) of crude 2EtNC–2EtSH, b.p. 120–131° (5 mm.), n_D^{25} 1.5142; and C, 0.18 g. of tar. Redistillation of B gave 2EtNC–2EtSH of b.p. 85–88° (0.6 mm.) and n_D^{25} 1.5180. It is soluble in the common organic solvents but insoluble in water.

Anal. Calc'd for $C_{10}H_{22}N_2S_2$: C, 51.2; H, 9.5; N, 11.95; S, 27.35; Mol. wt., 234.

Found: C, 51.2; H, 9.7; N, 11.9; S, 27.6; Mol. wt., 190; Neut. equiv., 250.

When the experiment was repeated at an initial pressure of 1070 atm., the yield of 2EtNC–2EtSH was 57%.

The reaction of ethyl isocyanide with water. A mixture of 3.43 g. of ethyl isocyanide and 1.14 g. of water, dissolved in sufficient dioxane (3.69 g.) to make a homogeneous solution, gave as the principal product 1.87 g. (41% yield) of N-ethylformamide, b.p. 86–89° (10 mm.), n_D^{25} 1.4291. Its properties, including infrared absorption spectrum, are in agreement with those of an authentic sample of N-ethylformamide (2, 9), b.p. 86–87° (11 mm.), n_D^{25} 1.4298, prepared in 45% yield by adding methyl formate to 33% aqueous ethylamine at 25°. Hydration of ethyl isocyanide to N-ethylformamide has been observed under other conditions (2).

SUMMARY

Two molecules of ethyl isocyanide react with two molecules of methanol, ethanol, or ethyl mercaptan at 125° and a pressure of 8500 atmospheres to give products for which the formamidine structure, $EtN(CH{=}NEt)CH(ZR)_2$ (ZR = OMe, OEt, or SEt), has been suggested.

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[2] The boiling point is further evidence that the product is $C_8H_{18}N_2O_2$, not C_4H_9NO. In particular, it is probably not $C_2H_5N{=}CHOCH_3$, for an isomeric imido ester, $HN{=}C(CH_3)$-OC_2H_5, boils at 97° (760 mm.) (7).

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