January, 1982] © 1982 The Chemical Society of Japan Bull. Chem. Soc. Jpn., 55, 33—35 (1982) 33

The Ammonolysis of Trichloroethylene to Glycine

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(Received April 13, 1981)

Glycine was obtained by the ammonolysis of trichloroethylene with aqueous ammonia. Various alkalines, such as alkaline metal hydroxides, carbonates, and hydrogencarbonates, accelerated the reaction; the yield of glycine was 40—70% after a 4 h reaction at 180 °C. Our results on the effect of alkalines indicate that ammonolysis proceeded sequentially *via* the formation of aminoacetonitrile. A good yield of the intermediate compound, aminoacetonitrile, was obtained by heating trichloroethylene at 70 °C with anhydrous ammonia under reaction conditions.

Glycine and its derivatives are widely used in the pharmaceutical industry as materials for drugs and food additives. In the synthesis of glycine, the ammonolysis of chloroacetic acid, the Strecker reaction, and the hydrolysis of hydantoin are performed. As the Strecker reaction involves the hydrolysis of aminoacetonitrile, several method have been developed for the synthesis of aminoacetonitrile, *e.g.*, the ammonolysis of chloroacetonitrile[1)] and hydroxyacetonitrile.[2)] The use of cyanides as a raw material is now considered impractical by the chemical industry because it requires the laborious removal of cyanide ions from the waste solution.

We ourselves have previously reported that tetrachloroethanes and trichloroethylene, which are commercially used nonflammable solvents, readily react with aqueous ammonia to yield glycine selectively; the yield can be increased by adding various alkalines.[3)] In our continuing investigations of the mechanism of ammonolysis, we obtained aminoacetonitrile, a possible intermediate compound, in a good yield with anhydrous ammonia under mild reaction conditions. We wish now to present details of the ammonolysis of trichloroethylene and the effect of alkalines.

Experimental

Ammonolysis of Trichloroethylene with Aqueous Ammonia. A mixture consisting of 20 ml of aqueous ammonia, 1 ml (11.15 mmol) of trichloroethylene, and alkaline catalysts was placed in a stainless steel autoclave (100 ml volume; SUS 32). The autoclave was then heated under a nitrogen atmosphere(30 kg/cm^2), and the mixture was stirred magnetically. After the reaction, glycine was analyzed by means of an amino-acid analyzer(KLA-5, Hitachi, Ltd.) using a Type #2661 column (10 mm i.d., ×250 mm in length).

Table 1. Ammonolysis of chloroethanes and trichloroethylene with aqueous ammonia

Compound (mmol)	Yield/mmol
1,1-Dichloroethane(11.86)	0
1,2-Dichloroethane(12.66)	0
1,1,1-Trichloroethane(10.03)	0
1,1,2-Trichloroethane(10.80)	0
1,1,1,2-Tetrachloroethane(9.18)	1.54
1,1,2,2-Tetrachloroethane(9.50)	1.97
1,1,2,2-Tetrabromoethane(4.46)	1.82
Pentachloroethane(8.34)	0
Hexachloroethane(4.22)	0
Trichloroethylene(11.15)	3.05

14% Aq ammonia 20 ml, N_2 30 kg/cm^2, 180 °C for 2 h.

Ammonolysis of Trichloroethylene with Anhydrous Ammonia. A test tube (30 mm i.d., ×150 mm in length) containing 1 ml of trichloroethylene and 10 ml of liquid ammonia, trapped by cooling with liquid nitrogen, was placed into the autoclave immediately after the introduction of the materials. The autoclave was then heated at 70 °C for 20 h under the conditions described above. Then, the unreacted ammonia was evaporated at room temperature, and the reaction products were diluted with distilled water. The aminoacetonitrile thus formed was analyzed using the above amino-acid analyzer and a Type #2663 column (6 mm i.d., ×70 mm in length).

Results and Discussion

Ammonolysis of Trichloroethylene with Aqueous Ammonia. The ammonolyses of various halogenoethanes were carried out as is shown in Table 1. Tetrachloroethanes yield glycine exclusively; from 1,1,1,2- and 1,1,2,2-tetrachloroethanes, 16.3 and 21.2% glycine were yielded respectively when they were treated at 180 °C for 2 h with 14% aqueous ammonia. The ammonolysis was similar with trichloroethylene; the glycine yield was 27.4%. The dehydrochlorination of tetrachloroethane to trichloroethylene in an aqueous ammonia solution is a known process.[4)] On the basis of these observations, we examined the ammonolysis of trichloroethylene to glycine under various conditions. As is shown in Fig. 1, the glycine yield increased with an increase in the ammonia concentrations; saturation was reached at 15% aqueous ammonia. The addition of Na_2CO_3 increased the yield almost two-fold, irrespective of the ammonia concentration used. Fig. 2 shows the effect of the reaction temperature on the glycine yield. In the presence of Na_2CO_3, ammonolysis took place from 80 °C; the maximum yield (*ca.* 60%) was obtained at 180 °C for 2 h. In the absence of Na_2CO_3, the yields were poor throughout the temperature range examined. The observations that apparently all trichloroethylene was consumed upon 180 °C, 2-h heating with aqueous ammonia, and that the glycine yield was remarkably increased by the addition of Na_2CO_3 to the reaction solution, suggests the formation of a precursor of glycine.

Judging from the comparison of glycine yields from chloroacetic acid, glycinamide, and aminoacetonitrile

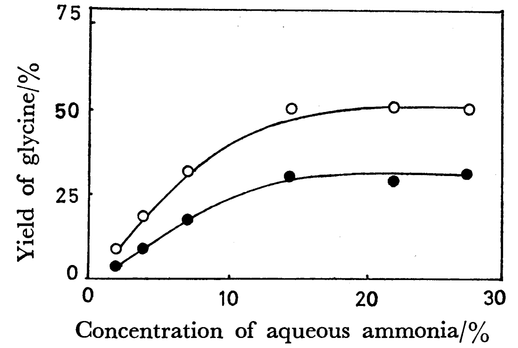


Fig. 1. Effect of the ammonia concentration on the ammonolysis of trichloroethylene to glycine.
Trichloroethylene 11.15 mmol, N_2 30 kg/cm^2, 180 °C for 2 h.
●: Ammonolysis in aq ammonia (20 ml), ○: ammonolysis in aq ammonia (20 ml) + Na_2CO_3 (1 g).

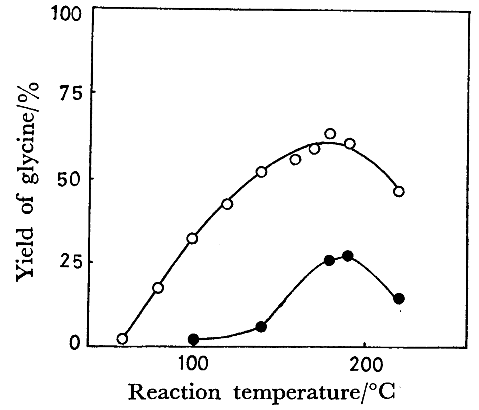


Fig. 2. Effect of the reaction temperature on the ammonolysis of trichloroethylene to glycine.
Trichloroethylene 11.15 mmol, N_2 30 kg/cm^2, 180 °C for 2 h.
●: Ammonolysis in 28% aq ammonia (20 ml), ○: ammonolysis in 28% aq ammonia (30 ml) + Na_2CO_3 (5 g).

TABLE 2. HYDROLYSIS AND AMMONOLYSIS OF POSSIBLE INTERMEDIATES IN THE PRESENCE AND ABSENCE OF VARIOUS ALKALINES

Compound (mmol)	Alkaline(mmol)	Yield/mmol
$ClCH_2COOH$(10.58)a)	None	5.65
$ClCH_2COOH$(10.58)a)	Na_2CO_3(9.4)	7.18
$NH_2CH_2CONH_2\cdot HCl$(9.13)a)	None	4.89
$NH_2CH_2CONH_2\cdot HCl$(9.13)a)	Na_2CO_3(9.4)	7.36
$NH_2CH_2CN\cdot H_2SO_4$(10.82)a)	None	2.85
$NH_2CH_2CN\cdot H_2SO_4$(10.82)a)	Na_2CO_3(14.1)	6.97
$NH_2CH_2CN\cdot H_2SO_4$(10.82)b)	NaOH(35.0)	8.80
$NH_2CH_2CN\cdot H_2SO_4$(10.82)b)	Na_2CO_3(17.5)	7.31
$NH_2CH_2CN\cdot H_2SO_4$(10.82)b)	$NaHCO_3$(35.0)	6.63

28% Aq ammonia 20 ml, N_2 30 kg/cm^2, 180 °C for a) 4 h and b) 2 h.

TABLE 3. AMMONOLYSIS OF TRICHLOROETHYLENE IN THE PRESENCE OF VARIOUS ALKALINES

Alkaline (mmol)	28% Aq ammonia (ml)	Yield/mmol
None	20	3.13
LiOH(35.0)	20	4.62
NaOH(35.0)	20	4.01
KOH(35.0)	20	3.55
Li_2CO_3(17.5)	20	6.03
Na_2CO_3(17.5)	20	5.60
K_2CO_3(17.5)	20	5.35
$NaHCO_3$(35.0)	20	6.59
$NaHCO_3$(35.0)	40	6.93
$NaHCO_3$(35.0)	60	7.98
$KHCO_3$(35.0)	20	6.33

Trichloroethylene 11.15 mmol, N_2 30 kg/cm^2, 180 °C for 4 h.

in the presence and absence of Na_2CO_3 in 7% aqueous ammonia, aminoacetonitrile has been thought to be the most likely intermediate compound for this reaction.[3] As is shown in Table 2, the same tendency was observed in 28% aqueous ammonia. The glycine yields from glycinamide and chloroacetic acid were strikingly higher than from trichloroethylene. On the other hand, aminoacetonitrile gave a glycine yield similar to that in the ammonolysis of trichloroethylene. In fact, the initial step is a rapid intermediate formation process; about 90% of trichloroethylene was consumed in a reaction at 180 °C for 30 min in 28% aqueous ammonia. However, from trichloroethylene, we obtained glycine in a 15.0% yield, together with a small amount of aminoacetonitrile (3.7%). The other was a methanol-soluble resinous product (0.5 g) supposed to originate from aminoacetonitrile, since the same product was obtained by heating aminoacetonitrile in aqueous ammonia. The polymer was not hydrolyzed to glycine when treated with Na_2CO_3 and NaOH. On the other hand, there was no detectable formation of chloroacetic acid. Therefore, it is considered that, in aqueous ammonia, the ammonolysis to aminoacetonitrile proceeds faster than in the second step of the hydrolysis to glycine, and that aminoacetonitrile, once formed, is then polymerized to an undesirable product. In the presence of alkalines, the hydrolysis is also accelerated. The effectiveness of alkalines may be attributable to their catalytic action on the hydrolysis of the intermediate compound, such as aminoacetonitrile. The change from aminoacetonitrile to glycine has been achieved by using $Ba(OH)_2$.[5]

The use of different types of alkalines significantly affected the glycine yield (Table 3). The effect of alkaline metal compounds on the yields was on the order of: hydrogencarbonates > carbonates > hydroxides. The most effective catalyst was $NaHCO_3$; the yield reached 71.6% at 180 °C for 4 h at a 1:88 molar ratio of trichloroethylene to ammonia. The tendencies observed in the series of alkaline catalysts could not be recognized from their activity in the hydrolysis of aminoacetonitrile, because the glycine yields obtained in the hydrolysis of aminoacetonitrile were in the reverse order: $NaOH > Na_2CO_3 > NaHCO_3$. Since the decomposition of glycine in the presence of NaOH and Na_2CO_3 is essentially negligible under our reaction conditions at 180 °C, the difference in yield may be due to other factors; possibly, a facile abstraction of halogen atoms from trichloroethylene by strong alkalines results in the formation of polymerized prod-

TABLE 4. COMPOSITION OF PRODUCTS IN THE AMMONOLYSIS OF TRICHLOROETHYLENE

Concentration of ammonia	Products		
	Glycine (mmol)	Iminodiacetic acid (mmol)	Nitrilotriacetic acid (mmol)
7%	3.17	0.24	0.04
28%	7.45	0.18	0.05

Trichloroethylene 11.15 mmol, aq ammonia 30 ml, Na_2CO_3 1.9 g, N_2 30 kg/cm², 180 °C for 4 h.

TABLE 5. AMMONOLYSIS OF TRICHLOROETHYLENE WITH ANHYDROUS AMMONIA

Alkaline (mmol)	Temp °C	Time h	Yield mmol
None	50	20	1.47
None	70	20	4.77
None	70	20	6.81
NaOH(35.0)	70	20	1.97
Na_2CO_3(17.5)	70	20	5.16

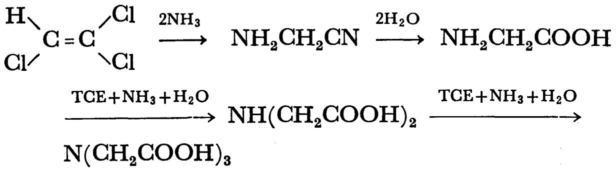
Trichloroethylene 11.15 mmol, liquid ammonia 10 ml.

ucts.

Reaction Products and Mechanism. In the ammonolysis of trichloroethylene, glycine is the only amino-acid species detected by means of an amino-acid analyzer. However, the elementary analysis of the reaction products obtained with 7% aqueous ammonia gave a nitrogen atomic ratio lower than that of glycine. For example, trichloroethylene (11.15 mmol) was heated at 180 °C for 4 h with 7% or 28% aqueous ammonia (30 ml) in the presence of Na_2CO_3 (1.9 g). Then, unreacted ammonia was removed by evaporation, and the amino-acid species were separated from NH_4Cl by treatment with an anion-exchange-resin (IRA-400, Roam & Haas Co.), followed by a cation-exchange-resin (IR-120B): (A) with 7% aqueous ammonia, yield, 0.4 g, Found: C, 30.68; H, 6.18; N, 16.26%; Calcd for $C_2H_5NO_2$: C, 32.00; H, 6.71; N, 18.66%; and (B) with 28% aqueous ammonia, yield, 0.6 g; Found: C, 31.78; H, 6.52; N, 18.04%. These results suggest the formation of undesired amino acids, *e.g.*, *N*-substituted amino acids, in addition to glycine.

High-power liquid chromatography, using a Shodex OHpak M-614 column (6 mm i.d., ×250 mm in length; Showa Denko K.K.) and 0.002 M H_3PO_4 as the eluent, identified glycine, iminodiacetic acid, and nitrilotriacetic acid by means of their retention times (Table 4). The ratios of these by-products to glycine was higher in the case of ammonolysis using 7% rather than 28% aqueous ammonia. Therefore, the amount of undesirable side products, such as iminodiacetic and nitrilotriacetic acid, can be decreased by increasing the molar ratio of ammonia to trichloroethylene.

Based on the present findings, we suggest that the reaction path for ammonolysis is:



$$HClC{=}CCl_2 \xrightarrow{2NH_3} NH_2CH_2CN \xrightarrow{2H_2O} NH_2CH_2COOH \xrightarrow{TCE+NH_3+H_2O} NH(CH_2COOH)_2 \xrightarrow{TCE+NH_3+H_2O} N(CH_2COOH)_3$$

TCE: trichloroethylene.

On the basis of the proposed mechanism, we expected that aminoacetonitrile could be obtained by treating trichloroethylene with ammonia under mild reaction conditions. When trichloroethylene was heated in 28% aqueous ammonia at 80 °C for 24 h, almost all the trichloroethylene was recovered, while aminoacetonitrile and glycine were obtained only in 1.8% and 0.1% yields respectively. The aminoacetonitrile yield increased with increase in the ammonia concentration; in ammonia–water (7:3) media, aminoacetonitrile (30.7% yield) and a trace amount of glycine were obtained at 70 °C for 20 h. Anhydrous ammonia gave high yields (Table 5). At temperatures from 50 °C in the presence of excess ammonia (the volume of liquid ammonia was 10 times that of trichloroethylene), ammonolysis occurred, yielding aminoacetonitrile selectively. A yield of 61% was obtained at 70 °C for 30 h. At higher temperatures, the product decomposed, resulting in brown products. Due to the observed effect of alkalines in aqueous ammonia, we added NaOH of Na_2CO_3 to the system. The presence of NaOH induced the formation of a water-insoluble black polymer. The yield decreased far below that obtained in non-catalyzed reactions. On the other hand, the addition of Na_2CO_3 had little effect on the yield. Therefore, the difference in the catalytic activities of strong and weak alkalines in aqueous ammonia may be explicable in terms of instability of trichloroethylene with strong alkalines.

The authors wish to express their thanks to Dr. Shunichi Hirokami for his valuable Discussions.

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