REDUCTION OF CHLORO- AND BROMONITROACETATE ESTERS

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Esters of nitroacetic acid (NA) are starting reagents in the synthesis of various compounds, in particular, amino acids [1]. However, the methods for the preparation of NA have a number of limitations. The synthesis of NA from readily available esters of chloronitroacetic acid (CA) [2] would seem to hold promise. In a continuation of work on the dehalohydrogenation of CA esters [3], we studied the reaction of these esters and the esters of bromonitroacetic acid (BA) with sodium dithionite and the catalytic hydrogenation of CA esters.

The reaction of CA and BA esters with $Na_2S_2O_4$ in aqueous ethanol rapidly leads to NA esters

$$O_2NCHXCO_2R \xrightarrow{Na_2S_2O_4} O_2NCH_2CO_2R$$

In the case of the reduction of the ethyl esters of CA, an increase in the amount of $Na_2S_2O_4$ introduced increases the content of the NA esters in the product mixture but their total yield is reduced (Table 1, Nos. 3,7,10-12). With other conditions equal, EA esters undergo dehalohydrogenation to a greater extent (Nos. 2 and 4). Extension of the ester alkyl group does not lead to an increase in the conversion (Nos. 1, 3, 5, 6). Use of the ammonium salt of the ethyl ester of CA gave the same result as the starting ester (Nos. 3 and 13). Carrying out the reaction under argon or without argon at 20 ± 1° or 50°C does not have a significant effect on the ratio and yield of the products.

In addition to the two major components, the analyzed ester mixtures contained up to 5% impurities. IR spectra of the reaction products isolated showed doublets at 1770-1750 (C=O), 1580-1550 (NO_2 as) and 1370-1350 cm^{-1} (NO_2 s), which indicates the absorption of CA and NA esters [4]. The mechanism for the reductive dehalogenation of CA and BA esters may be analogous to that proposed for the dehalogenation of α-haloketones [5].

The catalytic hydrogenation of the methyl and ethyl esters of CA at 20-40°C and normal pressure leads to the formation of hydrochloride salts of glycine esters.

EXPERIMENTAL

Esters of chloro- and bromonitroacetic acids were obtained according to our previous procedures [2, 6] and purified by distillation. A sample of $Na_2S_2O_4$ obtained from Fluka and high-purity 96% ethanol were used. The IR spectra were obtained neat or for vaseline mulls on a Specord IR-75 spectrometer. The melting point was determined on a Boetius apparatus using glass plates. High-pressure liquid extrusion chromatography was carried out on a Du Pont model 850 chromatograph with a UV detector at 254 nm using a 25 × 0.46 cm column packed with Zorbax CN (5 μm). The mobile phase was 40% aqueous 2-propanol. The flow rate was 1 ml/min at 20-25°C. Quantitative analysis of the chromatograms was carried out using a Hewlett-Packard model 3380A integrator using the external standard technique.

Reaction of Halonitroacetate Esters with $Na_2S_2O_4$. A sample of $Na_2S_2O_4$ was added to a solution of 50 mmoles halonitroacetate ester in 10 ml ethanol and distilled water was added until the precipitate was fully dissolved (the mixture warmed to 40-50°C and acquired a golden hue). After cooling, ethanol was distilled off and the product was extracted with ether. The extract was dried over Na_2SO_4 and evaporated. Traces of the volatile products were distilled from the residue in vacuum. The results are given in Table 1.

Preparation of Hydrochloride Salt of the Ethyl Ester of Glycine. A sample of 5.3 g ethyl chloronitroacetate in 80 ml ethanol and 1 g 5% Pd/C were placed in a flat-bottomed

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TABLE 1. The Reduction of $O_2NCHXCO_2R$ to $O_2NCH_2CO_2R$

Batch number	Ester to be reduced		Ester/ $Na_2S_2O_4$ mole ratio	Ester mixture isolated, g	Content of NA ester in the ester mixture, %
	X	R			
1	Cl	Me	2 : 1	3,53	41,2±1,3
2	Br	Me	2 : 1	5,19	54,8±2,1
3	Cl	Et	2 : 1	3,82	45,1±1,8
4	Br	Et	2 : 1	5,15	54,3±2,8
5	Cl	Pr	2 : 1	5,52	32,2±1,4
6	Cl	Bu	2 : 1	6,29	33,5±1,1
7	Cl	Et	4 : 1	5,6	27,2±0,8
8	Cl	Et	2,66 : 1	4,83	33,5±1,3
9	Cl	Et	1,33 : 1	2,8	53,7±1,7
10	Cl	Et	1 : 1	2,54	93±3,1
11	Cl	Et	1 : 1,5	2,42	95±2,8
12	Cl	Et	1 : 2	1,56	97±2
13*	Cl	Et	2 : 1	3,82	46±2

*Ammonium salt. The reaction was carried out in water.

flask equipped with a magnetic stirrer, thermometer and three-way stopcock for the introduction of gas and release into a burette. The system was flushed three times with argon and three times with hydrogen. Stirring was initiated and the mixture was heated to 35-40°C. After absorption of H_2, the catalyst was filtered off and the solution was evaporated to dryness. The residue was recrystallized from ethanol and ether to give 2.72 g (65.3%) crystalline product with mp 140-142°C [7].

An analogous procedure was used to obtain the hydrochloride salt of the methyl ester of glycine in 28% yield, mp 172-173°C [7].

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CONCLUSION

The reduction of esters of chloro- and bromonitroacetic acids by sodium dithionite leads to the replacement of the halogen atoms by hydrogen, while the catalytic hydrogenation of chloronitroacetate esters proceeds with the formation of hydrochloride salts of alkyl esters of glycine.

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