REACTIONS OF HALONITROACETATE ESTERS WITH AMINE-TYPE REAGENTS

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By the action of ammonia and amines the esters of α-chloro-α-nitrocarboxylic acids undergo haloform cleavage [1]. Thus, when NH_3 is passed into an ether solution of methyl α-chloro-α-nitrofluoropropionate at −30°, an unstable amide and methylurethan are obtained:

$$CF_3CCl(NO_2)CO_2CH_3 + NH_3 \rightarrow CF_3CCl(NO_2)CONH_2 + H_2NCO_2CH_3$$

Moreover, it is known [2] that the CH-acidic ethyl esters of chloro- and bromonitroacetic acids (EECA and EEBA) under similar conditions form ammonium salts. It has also been shown that in contrast to EECA, EEBA is reduced by hydrazine hydrate [2].

The existing data are insufficient for a confident judgment concerning the behavior of these esters toward amine-type reagents. Therefore, the present work presents a further study of their reactions with ammonia, amines, and hydrazine hydrate.

It has turned out that with aqueous ammonia at 50-60° EECA and EEBA form the ammonium salts of the amides, the oxidation of which gives the respective amides [3, 4]. Hydrazinolysis of EECA was carried out for 24 h at 20° (Table 1):

$$O_2NCH(Hal)CO_2C_2H_5 + H_2NR \rightarrow H_3\overset{+}{N}R\ \ \overline{O}_2NC(Hal)CONHR \xrightarrow{H^+} O_2NCH(Hal)CONHR$$

where Hal = Br, Cl; and R = H, CH_3, NH_2.

When the temperature is raised to 80-100°, along with the aminolysis products the amine and hydrazine hydrohalides also form.

Brief treatment of EECA with aqueous dimethylamine and diethylamine gives the ammonium salts, while upon prolonged retention they decompose to the respective amine hydrochlorides (Table 2). Thus, the dimethylammonium salt of EECA is obtained in 97% yield when it is separated within 10 min after the reagents are mixed (cf. Table 1). The aminolysis of the ester group by aqueous ammonia, hydrazine, and methylamine under relatively mild conditions and the absence of aminolysis by secondary amines are explainable by steric effects and the degree of hydration of the intermediate and final reaction products.

Except for the methylammonium salt of the methylamide of chloronitroacetic acid, all the synthesized compounds are quite stable. The ammonium salts of chloronitroacetamide and the dimethylammonium salts of EECA do not change after 1-2 months at 20-25°, whereas for most of the salts of the nitro compounds, poor stability is typical. This is probably related to the crystal structure of the compounds. The solid-state IR spectra (suspension in Nujol or hexachlorobenzene) show broadened bands in the 3500-3180 cm^{-1} region that correspond to the NH stretching vibrations (free and bonded) [5].

In the retention of chloronitroacetate esters [2, 6-8] with primary, secondary, and tertiary amines and ammonia in absolute ether and 96% alcohol with reaction times of 0.3 h and longer, the amine hydrochlorides form (cf. Table 2):

$$O_2NCHClCO_2R + R^1R^2R^3N \rightarrow R^1R^2R^3N \cdot HCl$$

where $R^1R^2R^3N$ is ammonia, aniline, diethylamine, triethylamine, or gramine.

In ether the reaction proceeds so vigorously that it requires cooling; in alcohol it goes more quietly. The filtrates are viscous liquids that according to GLC and TLC data contain five to nine components. Attempts to separate them by vacuum distillation were unsuccessful.

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TABLE 1. Properties of Synthesized Compounds

Compound	Yield %	mp °C	Found, %				Empirical formula	Calculated, %			
			C	H	N	Cl		C	H	N	Cl
$\overset{+}{N}H_4\bar{O}_2NCClCONH_2$	88	117	15,32	3,86	28,01	24,99	$C_2H_2ClN_3O_3$	15,44	3,89	27,01	22,79
$O_2NCHClCONH_2$	97,5	67,5	17,02	1,86	19,61	25,75	$C_2H_3ClN_2O_3$	17,34	2,18	20,23	25,6
$\overset{+}{N}H_4\bar{O}_2NCBrCONH_2$	64	131	12,71	3,03	21,52	40,72	$C_2H_6BrN_3O_3$	12,01	3,02	21,01	39,96 *
$O_2NCHBrCONH_2$	97	73	13,52	1,86	15,17	44,73	$C_2H_3BrN_2O_3$	13,14	1,64	15,31	43,7 *
$NH_2\overset{+}{N}H_3\bar{O}_2NCClCONHNH_2$	42	120–121	12,51	4,09	35,79	18,62	$C_2H_5ClN_5O_3$	12,94	4,32	37,74	19,11
$(CH_3)_2\overset{+}{N}H_2\bar{O}_2NCClCO_2C_2H_5$	97	133–134	34,25	6,25	12,67	17,3	$C_6H_{13}ClN_2O_4$	33,89	6,16	13,18	16,68

*Br; cf. [4].

TABLE 2. Yields and Conditions for Synthesis of Amine Hydrochlorides from α-Chloro-α-nitrocarboxylic Esters

Starting ester	Amine (no. of equiv. per ester)	T., deg C, time, h; solvent	Yield of amine hydrochloride, %
$O_2NCHClCO_2CH_2C_6H_5$	Et_3N (2,5)	20, then 60, then 30; 0,5; 96 % ethanol	87
$O_2NCCl(CH_2OH)CO_2C_2H_5$	EtN (1)	29; 0,3: 96 % ethanol	94
$O_2NCCl(CH_2OCOCH_3)CO_2C_2H_5$	Same	20; 0,5; 96 % ethanol	78
$O_2NCHClCO_2C_2H_5$	Et_3N (1)	15–20; abs. ether	91
Same	Gramine(1)	20; 0,5; abs. ether	66
»	33 % aqueous Me_2NH (6)	20; 120	89
»	25 % aqueous Et_2NH (3)	75, 9, then 20; 72	91

With amine-type reagents the halonitroacetate esters form for the first time the ammonium salts of the aci-nitro compounds, which were isolated. In aqueous solution such compounds are relatively stable due to hydration of the anion, in which the negative charge is shifted to the nitro oxygen [9, 10]. In aprotic medium there is evidently a leveling of electron density in the O–N–C–Cl segment; the chlorine acquires a negative charge and can be removed by an ammonium ion. The product undergoes further chemical change.

The decomposition of ethyl α-chloro-α-nitro-β-hydroxypropionate (cf. Table 2) can be explained similarly [7]. In 96% alcohol its acetyl derivative first hydrolyzes at the acetyl group, and is then converted as described before.

EXPERIMENTAL

The purity of reagents and products was established by GLC on an LKhM-8MD-5 apparatus (stainless steel column 3 × 3000 mm, Chromosorb G-AW-DMCS 60-80 mesh + 1% OV-101, helium, katharometer, 100-230°); by TLC on Silufol UV-254 plates in heptane–ethyl acetate (1:1 by volume); and by chromatography mass spectrometry on a Finnigan 4021 apparatus. The IR spectra were obtained on a Specord IR-75 apparatus.

Ammonium Salt of Chloronitroacetamide. EECA, 0.05 mole, was added in 5-7 portions to 50 ml of stirred 25% aqueous ammonia. The mixture was heated for 1-2 h at 55-60°, then transferred to a crystallizer. After 20 h the golden yellow crystalline precipitate was separated, washed with 10 ml of abs. ethanol and ether, and dried in vacuum. An additional amount of crystals was separated from the filtrate. IR spectrum (ν, cm^{-1}): 3500-3180 (NH), 1620 (C=O, amide). Mass spectrum (m/z): 156, 139, 92, 64, 44. Other salts were obtained by a similar procedure (see Table 1).

Chloronitroacetamide. To 10 mmoles of the ammonium salt of chloronitroacetamide was added 25 mmoles of HCl in abs. ether. The color changed from golden yellow to white and the crystal volume decreased. After 15 min the crystals were filtered off, washed with ether, and dried in vacuum. There was obtained 535 mg (100%) NH_4Cl (identified by comparison of its IR spectrum with that of an authentic sample). The filtrate was evaporated, and the white crystalline residue was dried in vacuum. To obtain macrocrystals, the product was recrystallized from $CHCl_3$. IR spectrum (ν, cm^{-1}): 3360-3160 (NH, bonded and unbonded), 1680 (C=O, amide), 1560 (NO_2), mass spectrum (m/z): 138, 92, 64, 44. The other amides were obtained similarly.

Reaction of EECA with Triethylamine in Abs. Ether. To a solution of 50 mmoles of EECA in 15 ml of abs. ether at 150-20° was added 50 mmoles of triethylamine in 10 ml of ether over 1 h with vigorous stirring. The reaction mixture turned red, and a precipitate formed. After 0.5 h the precipitate was filtered off, washed with 5 ml of abs. ethanol and 10 ml of ether, and dried in vacuum. The IR spectrum of the crystalline product was identical with that of an authentic sample of triethylamine hydrochloride.

Reaction of EECA with Gramine in Abs. Ether. To 20 mmoles of gramine in 100 ml of abs. ether was added a solution of 20 mmoles of EECA in 15 ml of abs. ether in several portions. The mixture warmed up slightly. After 0.5 h the mixture was evaporated. To the viscous residue was added 10 ml of acetone; the crystalline precipitate was filtered off, washed with 5 ml of acetone, and dried in vacuum. There was obtained 2.8 g (66%) of gramine hydrochloride. Recrystallization from a water–acetone–ether mixture gave coarse colorless crystals, mp 191-192°. Found: C 62.73; H 7.12, Cl 15.84; N 12.83%. $C_{15}H_{20}ClNO_4$. Calculated: C 62.69; H 7.18; Cl 16.83; N 13.3%.

Reaction of EECA with Aqueous Methylamine. A mixture of 50 mmoles of EECA and 20 ml (0.3 mmole) of 48% aqueous methylamine was heated for 2 h at 50-60° until the precipitate had completely dissolved, and was then left at 20°. After 72 h the solution was evaporated in vacuum (15 mm). The viscous residue was dissolved in 15 ml of abs. ethanol, and ether was added until the turbidity was permanent. The material quickly crystallized throughout the whole volume. The precipitate was filtered off, washed with ether, and dried in vacuum. After drying, the product decomposes.

CONCLUSIONS

The reactions of halonitroacetate esters with amines, ammonia, and hydrazine yield halonitroacetamides in high yield.

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REARRANGEMENT OF SULFONAMIDYL RADICALS WITH HYDROGEN MIGRATION

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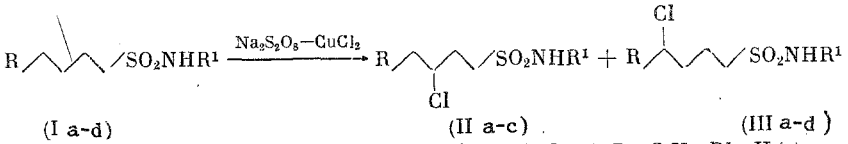
The nitrogen-centered sulfonamidyl radicals (NSRs) have been the object of detailed investigation [1-4]. The methods by which they are generated are based predominantly on the photolysis of N-halosulfonamides [1-4]. The electron configuration of NSRs has been studied by EPR [4-6]. The electron configuration of NSRs has been studied by EPR [4-6] and also quantum-chemically [7]. The photolytic rearrangements of these radicals with migration of an H atom from C to N have been discussed [1-3, 8], as well as some other chemical reactions, viz., intramolecular cyclization to sultams by addition of radicals at the aromatic ring [9], and ring cleavage to N-(cycloalkyl)tosylamidyl radicals [10].

Such attention to NSRs is the result of their relative accessibility and ease of use in organic synthesis, and by their possible use as model systems for comparing the reactivities of various types of nitrogen-centered radicals.

In continuation of our investigation of reactions of N-centered aminyl [11] and carboxamidyl [12] radicals in redox systems we recently established that N-(methanesulfonyl)alkylamidyl radicals generated by oxidation of N-methanesulfonylalkylamines in the $Na_2S_2O_8$–$CuCl_2$ system cyclize to N-methanesulfonylpyrrolidines [13] by a regiospecific outlying oxidative functionalization of the amide segment.

The present work is a study of the one-step outlying functionalization of NSRs at the alkylsulfonyl segment. We have established that alkanesulfonamides (Ia-d) under the influence of the $Na_2S_2O_8$–$CuCl_2$ system in water, when equimolar amounts of substrate and oxidant system components are used, are converted by one-step oxidative chlorination to 3- and 4-chloroalkanesulfonamides II and III*:



(I a-d) (II a-c) (III a-d)

R = R¹ = H(a); R=H, R¹=CH₃ (b); R=CH₃, R¹=H (c); R=C₂H₅, R¹=H (d).

*For the preceding communication see [14].

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