SUBSTITUTION OF THE HALOGEN ATOMS IN α -HALOGENONITRO COMPOUNDS OF THE ALIPHATIC SERIES. 4. INTERACTION OF CARBONYL COMPOUNDS WITH ETHYL CHLORONITROACETATE

UNDER THE CONDITIONS OF THE REFORMATSKY REACTION

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The reaction of ethyl chloronitroacetate with carbonyl compounds of the aliphatic series under the conditions of the Reformatsky reaction in ether, THF, or benzene does not proceed with the substitution of the chlorine atom, but by the scheme of the Anri reaction with the formation of ethyl α -nitro- α chloro- β -hydroxycarboxylates. The reaction proceeds via the intermediate formation of the zinc salt of ethyl chloronitroacetate.

In the preceding communication [1], the oxidation-reduction substitution of the halogen atoms of bromo- and chloronitroacetic esters by the sodium sulfo group was described and the unsuccessful attempt to substitute the halogens of the same compounds under the conditions of the Grignard and Friedel-Grafts reactions was noted. The Reformatsky reaction is one of the most studied reactions for the substitution of halogens in esters of halogenocarboxylic acids [2]. Since the expected products of the named reaction with readily available alkyl halogenonitroacetates - esters of α -nitro- β -hydroxycarboxylic acids - serve as intermediates in the synthesis of α -amino- β -hydroxycarboxylic acids [3], we undertook the investigation of this reaction.

Notwithstanding the external features inherent to the Reformatsky reaction (the boiling of the reaction mixture, the dissolving of the zinc, etc.), the reaction of the aliphatic carbonyl compounds (IIa)-(IIe) with ethyl chloronitroacetate (I) does not lead to the expected ethyl α -nitro- β -hydroxycarboxylates (III) but to the ethyl α -nitro- α -chloro- β -hydroxycarboxylates (IV).

 $\begin{array}{c} O_2 \text{NCHClCO}_2 \text{Et} + \text{RR'CO} & \frac{\text{zinc}}{\text{solvent}} \\ (I) & (II_a - e) \end{array} \xrightarrow[]{} O_2 \text{NCHCO}_2 \text{Et} \\ & \text{RR'COH} & (III) \\ & & O_2 \text{NCClCO}_2 \text{Et} \\ & \text{RR'COH} & (IVa - e) \\ & & \text{R'COH} & (IVa - e) \\ & & \text{R'COH} & (IVa - e) \\ \end{array}$

The readily volatile and low-boiling fractions besides the unreacted carbonyl compounds and (I) contained ethyl nitroacetate (V), the percentage content of which was determined from the ratio of the α -CH protons in the PMR spectra [6.7 ppm (CHC1) and 5.3 ppm (CH₂), Table 1]. The highest yields of (IV) were obtained in the cases of the application of the acetic (IIa) and propionic (IIb) aldehydes. The optimal conditions of these reactions were as follows: the boiling of the reaction mixture for 5 h and the application of diethyl ether as the solvent (Table 1, Experiments 1, 4, 5). The decrease in the reaction time reduces the yield of (IV). The lengthening of the time of the process gives a lower yield of (IV), just as when benzene is applied as the solvent. The utilization of (IIc)-(IIe) leads to worse results. When (IIc)-(IId) are applied, the reaction is accompanied by significant decomposition and no high-boiling product could be isolated in the individual form. In sev-

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Reforma	tsky Re	action								
No. of		4	Time of boiling, h	Fraction	(A) + (I)	Residue after the distilla-	High-boiling	Bp, °C (p, mm	20	Vield %*
experi- ment	(11)	Solvent	(room tem- perature)	weight, g	(V), mole %	tion of (I) + (V), g	products	of Hg stem), cf. [4]	ď.	e (htott
1	ta	Ether	5(1)	4,52	6	7,8	(IVa)	92-94(1,5)	1,4505	47
5	¢	*	8(10)	2,7	15	4,3	(IVa)	92 - 94(1,5)	1.4505	28
e	đ	Benzene	3(1)	5,54	5	2,6	(IVa)	92 - 94(1,5)	1.4505	10
4	ф	Ether	5(20)	7,06	40	9,05	(IVb)	100 - 102(1,5)	1,4500	72
5 C	Ą	*	8(40)	3,91	42	8,0	(9/1)	100 - 102(1,5)	1,4500	11
9	Ą	Benzene	2(20)	4,66	25	2,3	(IVb)	100 - 102(1,5)	1,4500	10
L	υ	Ether	2	12,94	17	0,3	I .	.1	1	1
x	υ	THF	ر م	1,7	47,6	1,3	(IVc) + (VIIc)	100-115(1)	1,4585	1,05 †
6	q	Ether	2,5 (20)	2,16	37	0,3	ł	ļ	!	I
10	đ	Benzene	1,5 (20)	3,43	20	1,5 #	I	I	I	I
11	đ	THF	3(20)	3,12	31	2,6	(\$\D\$ \U_1 \U_1 \U_1 \U_1 \U_1 \U_1 \U_1 \U_1	92-124(1)	1,4600	2,36†
12	J.	Ether	1,5(72)	6,83	5	4,22	(IVe) + (VIIe)	96 - 102(1)	1,4640	3,42 †
13	Ð	Ether	9(20)	10,87	ۍ	1,1	(IVe) + (VIIe)	97(1)	1.4634	0.73 †
14	U	Benzene	2(20)	7,52	14,3	1 #	I	l	l	1

TABLE 1. Reaction of (IIa)-(IIe) (0.1 mole) with (I) (16.8 g, 0.1 mole) under the Conditions of the

*Based on the (I) entering into the reaction. \pm The oil of yellow color, g. The test for halogen was positive. The IR spectra (a film, v, cm⁻¹) were as follows: 3400 broad strong (OH), ~170 very strong, ~1730 shoulder (C=O), ~1610 weak (C=C), ~1560 strong, and ~1540 shoulder (NO₂ asym.). \pm The product was not distilled in vacuo at $3 \cdot 10^{-3}$ torr. Other methods of purification were not ap-

plied.

eral cases mixtures of two substances were obtained (Experiments δ , 11-13). These results agree with the previously obtained data on the condensation of the aldehydes (IIc), (IId) with alkyl chloronitroacetates, where mixtures of the condensation products were also obtained [4].

The unusual course of the condensation reaction may be explained by the formation of the zinc salt of ethyl chloronitroacetate (VI) and its subsequent reaction with carbonyl compounds leading to (IV) (the Anri reaction).

$$2(1) \xrightarrow[-H_2]{Zn} [Zn (O_2NCCICO_2Et)_2] \xrightarrow{(IIa-e)} (IVa-e)$$
(VI)

The hydrogen formed in the reaction can reduce (I) to (V). Such a conclusion is confirmed by a special experiment where (I) was converted by 5-10% to (V) by the interaction with zinc and concentrated hydrochloric acid. The isolation of the analogous salts of copper and chloronitroacetamide in a dry medium indicates the possibility of the formation of the salt (VI) [5]. The formation of the salt (VI) is in agreement with the data presented in Table 1. The salt (VI) is evidently solvated better by ether and THF than by benzene; the yield of (IV) and (V) is consequently higher in the first solvents. The increase in the reaction time as well as in the lipophilicity of the reaction mixture [in the cases of the utilization of (IIc)-(IId) and benzene] favors the decomposition of (VI) and other intermediate products of the reaction. The presence of the admixtures of the ethyl 2-nitrohex-2enolate O₂NC(CO₂Et)=CHCH₂CH₂CH₃ (VIIc) and ethyl 2-nitro-4-methylhept-2-enoate O₂NC(CO₂Et)=CH-CH(CH₃)₂ (VIId) correspondingly in the compounds (IVc) and (IVd) was shown by the identification of the IR spectra of the products obtained and of the known mixtures of (IVc) and (VIIc), and (IVd) and (VIId) synthesized according to [3, 4]. Their formation may be explained by the reaction of the aldehydes (IIc), (IId) with (V) according to the scheme of the Anri reaction and the subsequent dehydration of the products (III) (Experiments 8, 11). The IR spectrum of the mixture of the products (IVe) and ethyl 2-nitro-3-methylpent-2-enoate $O_{2NC}(CO_{2E}) = C(CH_{3})C_{2}H_{5}$ (VIIe) is similar to the IR spectra of the mixtures of (IVc) and (VIIc) as well as (IVd) and (VIId) (Table 1, Experiments 12, 13).

Therefore, the Reformatsky reaction does not proceed with the substitution of chlorine by the hydroxyalkyl group under the conditions utilized. Such an effect may be explained by the low negative discharge on the Cl atom in (I). The determination of the charges on the chlorine for some derivatives of chloronitroacetic acid with the application of 35 Cl NQR and quantum-chemical calculations [6] confirms such a conclusion.

It should be noted that there are no data in the literature on the carrying out of the Anri reaction with the utilization of zinc and aprotic solvents.

EXPERIMENTAL

The reagents utilized were purified by distillation immediately before application. The solvents were rendered absolute by boiling them with sodium. Ethyl chloronitroacetate was obtained according to [7]. The zinc dust was washed with 10% HCl, distilled water until a neutral reaction was obtained, acetone, and ether, and dried in vacuo. The IR spectra of the substances in the form of films were obtained on a "Specord IR-75" instrument. The PMR spectra were registered on a "Bruker CXP-200" spectrometer using TMS as the standard.

Interaction of (I) with (IIb) in the Presence of Zinc in Absolute Ether (Standard Experiment). The mixture of 12.5 ml (0.1 mole) of (I) and 7 ml (0.1 mole) of (IIb) was added dropwise to the stirred suspension of 6.7 g of Zn in 50 ml of abs. ether at a rate which maintained the even boiling of the reaction mixture (20 min). After the mixing of the reagents, several iodine crystals were added to activate the reaction. The reaction mixture was boiled with stirring for 5 h and was processed after 20 h. The solution was decanted; the unreacted Zn was washed with ether (2 × 20 ml). The ether extracts were shaken with 50 ml of 10% HCl and the acid layer was extracted with 40 ml of ether. The combined ether extracts were washed with water (5 × 30 ml) until a neutral reaction was obtained, dried with CaCl₂, and filtered. The solvent and the readily volatile substances were evaporated in vacuo and the residue was distilled in vacuo. The first fraction was characterized as follows: 7.06 g, 55-58°C (1 mm), $nD^{2^{\circ}}$ 1.4425. The second fraction was characterized as follows: 8.95 g, 100-102°C (1 mm), $nD^{2^{\circ}}$ 1.4500 (Experiment 4). The Beilstein test for halogen was positive. The IR spectra of the first product were identical with the spectra of the

known mixtures of (I) and (V) and the second product had a spectrum identical to that of the known (IVb), obtained according to [4].

Interaction of (I) with Zinc and Hydrochloric Acid. To the mixture of 12.5 ml (0.1 mole) of (I), 6.7 g of zinc, and 20 ml of abs. benzene were added, with stirring at ~20°C, 8 ml (0.1 mole) of concentrated HCl in the course of 20 min. The temperature was thereby raised to the boiling point. The reaction mixture was stirred for 1 h and was left at ~20°C for 2 days. To the mixture were added 30 ml of 10% HCl in portions. The solution obtained was extracted with ether (3 × 50 ml) and the ether extracts were washed with water until a neutral pH was obtained. The extracts were dried with MgSO₄ and the solvent was evaporated in vacuo prior to distillation. The yield of 6.85 g of the product was obtained; it had the bp 75-73°C (10 mm) and the np²⁰ 1.4358. According to the PMR data, the ratio of (I) : (V) is 23:4.

LITERATURE CITED

- 1. A. I. Yurtanov, A. V. Yarkov, T. I. Ignat'eva, et al., Izv. Akad. Nauk SSSR, Ser. Khim., 2549 (1988).
- 2. N. S. Vul'fson and L. Kh. Vinograd, Reactions and Methods of the Investigation of Organic Compounds [in Russian], Vol. 17, Khimiya, Moscow (1967), p. 5.
- 3. S. Umezawa and S. Zen, Bull. Chem. Jpn., <u>36</u>, 1143 (1963).
- 4. I. V. Martynov, E. V. Stoyankova, and A. I. Yurtanov, Zh. Org. Khim., <u>18</u>, 1849 (1982).
- 5. A. I. Yurtanov, A. N. Chekhlov, and I. V. Martynov, Izv. Akad. Nauk SSSR, Ser. Khim., 214 (1987).
- 6. V. I. Shestov, I. V. Martynov, A. I. Yurtanov, et al., Izv. Akad. Nauk SSSR, Ser. Khim., 1998 (1987).
- 7. I. V. Martynov, Yu. L. Kruglyak, and S. P. Makarov, Zh. Obshch. Khim., 33, 3382 (1963).

NITRATION OF FLUOROETHYLENES BY NITRATING MIXTURE (HNO3 + H2SO4 + SO3)

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The nitration of fluoroethylenes with sulfuric-nitric mixtures and added sulfuric anhydride was studied. It was shown that acid fluorides of halogenonitroacetic acids are formed in the nitration of fluoroethylenes containing the fluorochloromethylene fragment, whereas nitroethylfluorosulfates are the main reaction product in the nitration of ethylenes having the difluoromethylene grouping. The structure of the compounds obtained was shown by the data of ¹⁹F and ¹H NMR and IR spectroscopy.

The nitration of fluorinated ethylenes has been studied in detail. Two most practicable methods of nitration are known: the radical nitration with oxides of nitrogen [1] and the ionic nitration with nitrating mixture [2]. The ionic nitration is the most convenient for the synthesis of halogenonitrocarbonyl compounds. The mechanism of the nitration of halogenoethylenes, assuming the formation of acid fluorides of halogenonitrocarboxylic acids as the intermediate compounds, was proposed; however they could not be isolated or detected [3].

With the object of widening the synthetic possibilities of ionic nitration, as well as specifying the mechanism of the reaction, we developed a method for the nitration of fluoro-olefins using the mixture of HNO_3 , H_2SO_4 , and SO_3 . The addition of SO_3 to the nitrating mixture leads to the binding of water and prevents the hydrolysis of the resulting acid

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