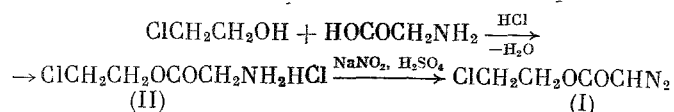


SYNTHESIS OF 2-CHLOROETHYL DIAZOACETATE
AND STUDY OF ITS CARBENIC DECOMPOSITIONE. A. Shapiro, G. V. Lun'kova,
I. E. Dol'gii, and O. M. Nefedov

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We have already reported on the formation of the 2-chloroethyl ester of diazoacetic acid (I) and a side product in the synthesis of the 2-hydroxyethyl ester of this acid [1]. In the present work we synthesized (I) directly and studied its carbenic decomposition in the presence of different carbene acceptors.

Ester (I) is obtained in a yield of 80% yield by diazotization of 2-chloroethyl aminoacetate hydrochloride (II), which, in turn, is prepared in a 95% yield by the esterification of glycine by ethylene chlorohydrin in the presence of anhydrous HCl with distillation of the water formed.



The diazoester (I) was purified by distillation in vacuo and characterized by IR and PMR spectra. It is readily soluble in organic solvents and stable on heating to 80°C. The thermal and thermocatalytic decomposition of (I) at higher temperatures leads to the formation of products of intermolecular interaction of 2-chloroethoxycarbonylcarbene (CEC) formed under these conditions with the corresponding acceptors. Products of intramolecular transformation of this carbene have not been detected in any of these cases.

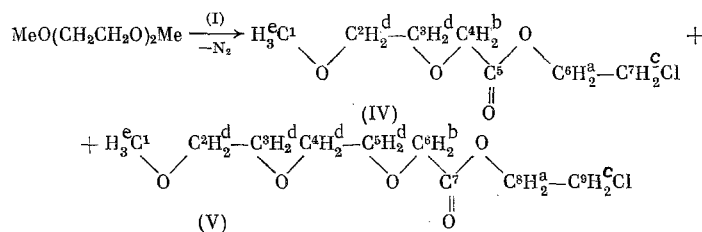
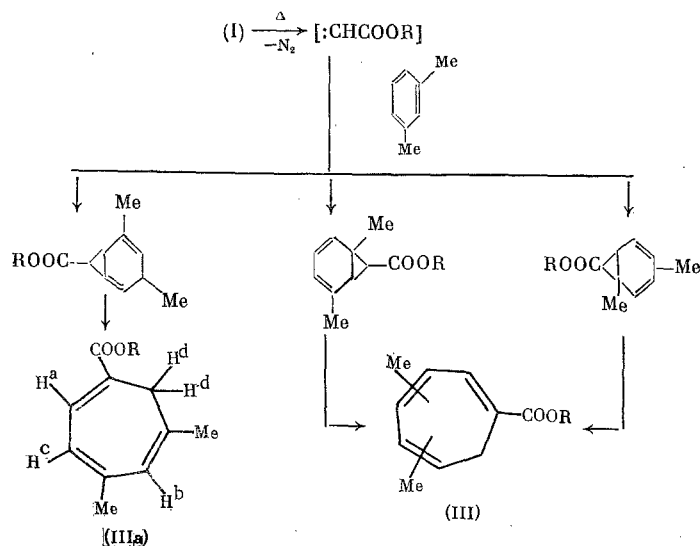
According to GLC and PMR data, in the thermal decomposition of the diazoester (I) in m-xylene at 144°C, a mixture of six to seven isomeric 2-chloroethyl esters of cycloheptatrienecarboxylic acids (III) was obtained in a 37% yield, with the 2-chloroethyl ester of 3,5-dimethyl-2H-cyclohepta-3,5,7-trienecarboxylic acid (IIIa) predominating (55% content in the mixture).

Present in the weak field region of the spectrum of the mixture of (III) are a singlet, broadened by a long-range spin-spin interaction at δ 6.32 ppm, attributed to the H^b proton, and signals of H^a and H^c protons at 7.36 and 5.77 ppm split into doublets with J = 6 Hz. The megnetoequivalent H^d protons give a singlet at δ 2.19 ppm. The protons of the methyl groups with similar values of δ appear in the form of a broadened singlet with δ 1.93 ppm.

The formation of a mixture of isomeric methyl esters of dimethylcycloheptatrienecarboxylic acids, analogous to (III), has already been observed in the photolytic decomposition of methyl diazoacetate in m-xylene as the result of the addition of methoxycarbonylcarbene to aromatic multiple bonds, followed by isomerization of the esters of the bicyclic acids formed [2]. It is possible that the reaction of (I) with m-xylene takes place by the same scheme. Thus, the preferential formation of (IIIa) indicates a selective attack by carbene of bonds removed from the methyl substituents, which also agrees with the data in [2].

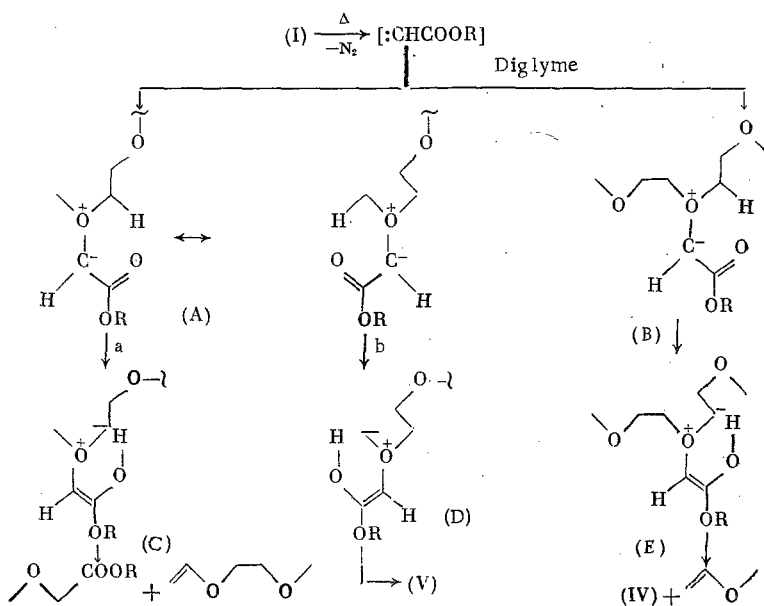
The thermal decomposition of (I) in an excess of diglyme at 140°C led to a mixture (1:3) of 2-chloroethyl esters of 2-methoxyethoxyacetic acid (IV) and 2-[2-(2-methoxyethoxy)ethoxy]acetic acid (V) in an overall yield of 24%.

The structure of esters (IV) and (V) isolated in an individual state by preparative TLC was confirmed by PMR and ¹³C NMR spectra. Despite a certain difference in the structure of these esters, their PMR spectra scarcely differ. The H^a protons give triplets at δ 4.28 ppm, H^b protons give singlets at δ 4.03 ppm for ester (IV) at δ 4.05 ppm for ester (V), H^c protons give triplets at δ 3.60 ppm for (IV) and 3.62 ppm for (V). The H^d protons of the methylene groups of the two esters form complex multiplets in the region of



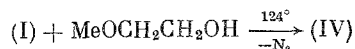
3.3–3.7 ppm. The H^{e} protons give singlets at δ 3.24 ppm for ester (IV) and δ 3.25 ppm for ester (V). The ^{13}C NMR signals were assigned according to their multiplicity, due to the ^{13}C –H interaction. In the mass spectrum of (IV) there are two peaks of molecular ions, due to ^{35}Cl and ^{37}Cl isotopes. The mass spectrum of (V) does not contain molecular ion peaks.

According to [3], the formation of esters (IV) and (V) can be obtained by the β -elimination of H atoms in the oxonium ylides A and B, formed in the attack of CEC on different O atoms of diglyme, and by dissociation of new ylides C–E formed. We can deduce from the reaction products that the preferential, if not the only direction of β -elimination for ylide is path b, leading to ester (V), which agrees with the data on [3] on the selectivity of the reaction of alkyl diazoacetates with methyl alkyl ethers



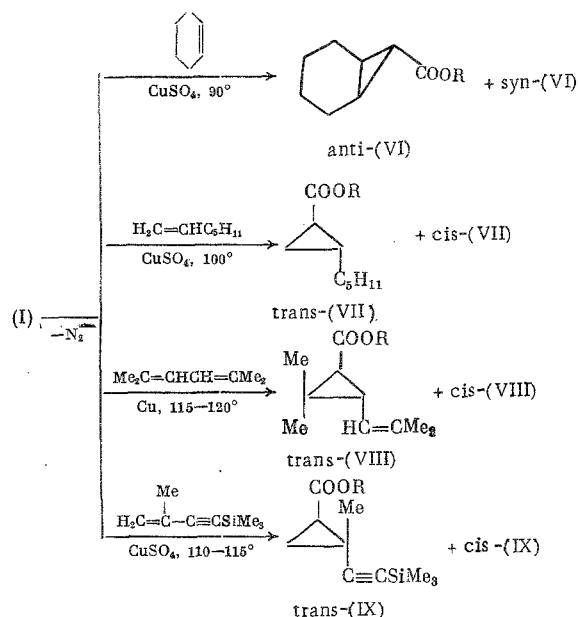
The possible existence of oxonium ylides follows, in particular, from the calculated data of $^1\text{CH}_2$ complexes with water [4].

We observed the formation of (IV) in a 25% yield in the thermal reaction of diazoester (I) with ethylene glycol monomethyl ether



The products of splitting the ether at the C-O bond were not detected. Previously, the introduction of alkoxy-carbonyl-carbenes at the O-H bond of alcohols had only been observed in the photolytic and thermocatalytic decomposition of alkyl diazoacetates [5, 6].

To synthesize 2-chloroethyl esters of cyclopropane- and cyclopropenecarboxylic acids, we studied the thermocatalytic decomposition of (I) in the presence of unsaturated compounds. The decomposition of (I) by the action of CuSO_4 in excess of cyclohexene at 90°C led to the formation of 2-chloroethyl esters of syn- and anti-isomers of bicyclo[4,1,0]heptane-7-carboxylic acid (VI) in an overall yield of 80%. The reaction of (I) with a tenfold excess of 1-heptene in the presence of CuSO_4 at 100°C was accompanied by considerable resinification, and gave 2-chloroethyl esters of trans- and cis-isomers of 2-amylcyclopropanecarboxylic acid in an overall yield of 15% only.



$\text{R} = \text{CH}_2\text{CH}_2\text{Cl}$.

In the presence of copper catalysts, at $115\text{--}120^\circ\text{C}$, the diazoester (I) reacts with a tenfold excess of 2,5-dimethyl-2,4-hexadiene to form a mixture (55:45) of 2-chloroethyl esters of trans- and cis-isomers of chrysanthemic acid (VIII). The highest overall yield of esters (53%) was achieved when copper bronze was used as the catalyst. In the presence of CuCl or CuSO_4 , the reaction was accompanied by considerable resinification of the initial diene, which led to a decrease in the yield of ester (VIII) to 20-35%.

The thermocatalytic reaction of (I) with a threefold excess of 1-trimethylsilyl-2-isopropylacetylene in the presence of anhydrous CuSO_4 at $110\text{--}115^\circ\text{C}$ proceeds regioselectively at the double bond only to give a mixture (55:45) of 2-chloroethyl esters of trans- and cis-isomers of 2-methyl-2-trimethylsilylethynylcyclopropanecarboxylic acid (IX) in a 45% yield.

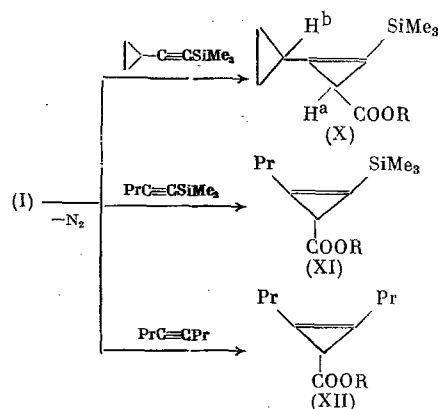
Esters (VI)-(IX) were characterized by IR, PMR, and mass spectra. The spectral data and also certain constants of these esters are given in Table 1. The protons of the OCH_2 and CH_2Cl fragments appear in the PMR spectra in the form of multiplets at δ 4.2-4.4 and 3.57-3.60 ppm, respectively. In the mass spectra of all the esters there are signals of two molecular ions due to ^{35}Cl and ^{37}Cl isotopes.

The reaction of diazoester (I) with a threefold excess of acetylenic compounds, 1-trimethylsilyl-2-cyclopropylacetylene, 1-trimethylsilyl-2-propylacetylene, and 1,2-dipropylacetylene leads at $110\text{--}120^\circ\text{C}$ and in the

TABLE 1. Properties of 2-Chloroethyl Esters of Cyclopropanecarboxylic- and Cyclopropene-3-carboxylic Acids

Compound	Yield, %	Bp, °C (mm)	n_D^{20}	IR-spectrum ν , cm^{-1}	PMR spectrum, δ , ppm			Mass spectrum, M^+ , m/z
					OCH ₂	CH ₂ Cl	other protons	
(VI)	80	101 (2)	1,4925	1725 (C=O)	4,20	3,57	1,0-2,0 (11 H)	202 and 204
(VII)	15	81 (3)	1,4580	1725 (C=O)	4,26	3,60	1,3 m (4 CH ₂), 0,85 m (CH ₃)	218 and 220
(VIII)	53	106-109 (1,5)	1,4806	1730 (C=O)	4,40	3,58	5,28 and 4,84 d (HC=, trans- and cis-isomers), 1,68 m ((CH ₃) ₂ C=), 1,22 s, 1,18 s, 1,10 s (2 CH ₃ trans- and cis-isomers)	230 and 232
(IX)	45	116 (3)	1,4770	1730 (C=O) 2170 (C=C)	4,28	3,60	2,02 d, d (H ^a trans-isomer), 1,5-1,7 (H ^a + H ^b of cis-isomer), 1,34 br. s (CH ₃), 1,16-1,40 (H ^b + H ^c trans-isomer), 1,0 d, d (H ^c cis-isomer), 0,03 s (Si(CH ₃) ₃)	258 and 260
(X)	20	101 (3)	1,4840	1725 (C=O) 1830 (C=C)	4,17	3,52	1,84 s (H ^a), 1,72 m (H ^b), 0,2-1,3 (2 CH ₃), 0,05 s (Si(CH ₃) ₃)	258 and 260
(XI)	19	80 (2)	1,4487	1720 (C=O) 1830 (C=C)	4,15	3,61	2,40 (CH ₂ C=C), 1,93 s (CH), 2,53 m (CH ₂), 0,87 t (CH ₃), 0,12 s (Si(CH ₃) ₃)	260 and 262
(XII)	50	89 (2)	1,4635	1725 (C=O) 1900 (C=C)	4,20	3,57	2,38 t (CH ₂ C=C), 1,97 s (CH), 1,57 m (CH ₂), 0,97 t (CH ₃)	230 and 232

presence of CuSO₄ to 2-chloroethyl esters of 1-cyclopropyl-2-trimethylsilylcyclopropene-2-carboxylic acid (X), 1-propyl-2-trimethylsilylcyclopropene-3-carboxylic acid (XI), and 1,2-dipropylcyclopropene-3-carboxylic acid (XII), respectively. All the experiments were accompanied by the formation of an appreciable amount of high-molecular-weight products, and the yields of esters (X)-(XII) were determined by the nature of the substituent in the acetylene. As in reactions with alkyl diazoacetates [7], the silylated acetylenes were found to be less reactive than their hydrocarbyl analogs. The nonsilylated ester (XII) was obtained in a yield of 50%, based on (I) used in the reaction, while the silylated esters (X) and (XI) were obtained in yields of 20 and 19%, respectively.



R = CH₂CH₂Cl.

The structure of esters (X)-(XII) was confirmed by the data of IR, PMR and mass spectroscopy. The proton signals of the OCH₂ (4.15-4.20 ppm) and CH₂Cl (3.52-3.61 ppm) fragments are observed in the PMR spectra of the compounds in the same region as the proton signals of these groups in cyclopropanecarboxylic esters (VI)-(IX). In the mass spectra of esters (X)-(XII) signals of two molecular ions are observed, due to ³⁵Cl and ³⁷Cl isotopes. In the IR spectra, the band at 1830 cm⁻¹ for esters (X) and (XI) and at 1900 cm⁻¹ for ester (XII) corresponds to the intracyclic multiple bond.

EXPERIMENTAL

The GLC analysis was carried out on the LKhM-8MD apparatus with a catharometer on a 2 m × 2 mm column with 15% Carbowax 20, on N-AW-DMCS chromatone (column 1) and with 5% silicone SE-30 on N-AW-DMCS chromatone (column 2), carrier gas He, 30 ml/min. The PMR spectra of 20% solutions in CCl₄ and CHCl₃ were recorded on the Tesla BS-467 (60 MHz) and Tesla BS-497 (100 MHz) spectrometers with TMS as internal standard. The ¹³C NMR spectra of the solutions in CDCl₃ were run on the Bruker-WP-60 apparatus (15.08 MHz) with TMS as internal standard. The IR spectra were run on the UR-10 and Specord IR-75 spectrophotometers, and the mass spectra were taken on the Varian MAT CH-6 apparatus.

2-Chloroethyl Aminoacetate Hydrochloride (II). A boiling mixture of 97.5 g (1.3 mole) of glycine, 326 g (4.0 moles) of ethylene chlorohydrin in 200 ml of benzene was saturated for 24 h with anhydrous hydrogen chloride. Water was removed as an azeotrope with benzene. The mass was cooled, and the precipitate was filtered. Yield, 215 g (95%) of (II), mp 155-156°C (from EtOH). IR spectrum (KBr, ν , cm⁻¹): 1750 (C=O), 3000 br (NH).

2-Chloroethyl Diazoacetate (I). A solution of 36.5 g (0.5 mole) of NaNO₂ in 100 ml of water was added in the course of 10 min to a cooled mixture (-5°C) of 69.6 g (0.4 mole) of (II) in 100 ml of water and 250 ml of CH₂Cl₂. The mixture was cooled to -10°C, and 38 ml of 5% H₂SO₄ were added in the course of 5 min. The mixture was heated to 20°C and left to stand for 15 min. The organic layer was separated, neutralized by 500 ml of a 5% solution of NaHCO₃, dried over MgSO₄, and evaporated at < 80°C. The residue was distilled in vacuo. Yield, 48.4 g (80%) of (I), bp 52°C (4 mm), n_D^{20} 1.5013. IR spectrum (ν , cm⁻¹): 1705 (C=O), 2120 (CN₂). PMR spectrum (in CHCl₃, δ , ppm): 4.76 s (CH), 4.28 m (OCH₂), 3.57 m (CH₂Cl), $J_{1,2} = 5.7$ Hz.

2-Chloroethyl Esters of Isomeric Dimethylcycloheptatrienecarboxylic Acids (III). A solution of 4.5 g (0.03 mole) of (I) in 10 g of *m*-xylene was added in the course of 10 h to 32 g of boiling xylene. The mixture was heated for another hour until no more N₂ was evolved, and was distilled. Yield, 2.5 g (37%) of a mixture of isomeric (III), bp 105-111°C (2 mm), n_D^{20} 1.5383, containing, according to GLC data (column 1, 190°C) 55% of (IIIa). IR spectrum (ν , cm⁻¹): 1550, 1630 and 1680 (C=C), 1720 (C=O). PMR spectrum (δ , ppm in CCl₄): 7.36 d (H^a), 6.32 s (H^b), 5.77 d (H^c), 4.30 t (OCH₂), 3.62 t (CH₂Cl), 2.19 s (H^d), 1.98 s (CH₃). In the PMR spectrum there are also low-intensity signals due to isomers of (III). The mass spectrum of the mixture of (III) contains peaks of molecular ions with *m/z* 226 and 228, due to ³⁵Cl and ³⁷Cl isotopes.

2-Chloroethyl Esters of 2-Methoxyethoxyacetic Acid (IV) and 2-[(2-Methoxyethoxy)ethoxy]acetic Acid (V). A solution of 4.5 g (0.03 mole) of (I) in 10 g of diglyme was added in the course of 10 h to 40 g of diglyme heated to 140°C. The mixture was heated for 1 h until no more N₂ was evolved, the excess of diglyme was distilled, and the residue was distilled in vacuo. Yield, 1.8 g of a mixture of products, bp 95-115°C (2 mm), from which ester (IV), *R_f* 0.63 and ester (V), *R_f* 0.24, were isolated by preparative chromatography on silica gel (eluent, a benzene-ether mixture (1:1)).

Ester (IV). IR spectrum (ν , cm⁻¹): 1755 (C=O). PMR spectrum (in CCl₄, δ , ppm): 4.28 t (2H^a), 4.03 s (2H^b), 3.60 t (2H^c), 3.3-3.7 m (4H^d), 3.24 (3H^e). ¹³C NMR spectrum (δ , ppm): 170.17 s (C⁵), 71.94 s (C⁴), 71.10 t (C⁶), 68.60 t (C³), 64.29 t (C²), 59.07 q (C¹), 41.41 t (C⁷). The mass spectrum contains peaks of molecular ions with *m/z* 196 and 198.

Ester (V). IR spectrum (ν , cm⁻¹): 1755 (C=O). PMR spectrum (in CCl₄, δ , ppm): 4.28 t (2H^a), 4.05 s (2H^b), 3.62 t (2H^c), 3.3-3.7 (8H^d), 3.25 s (3H^e). ¹³C NMR spectrum (δ , ppm): 170.17 s (C⁷), 71.94 t (C⁶), 71.03 t (C⁸), 70.55 t (C² and C³), 68.42 t (C⁵), 64.23 t (C⁴), 58.89 q (C¹), 41.47 (C⁹).

Ester (IV) was also obtained as follows. A solution of 2.97 g (0.02 mole) of (I) in 1.9 g of ethylene glycol monomethyl ether was added in the course of 6 h to 4.2 g of ethylene glycol monomethyl ether heated to 124°C (total amount of ethylene glycol monomethyl ether 6.1 g (0.08 mole)). The mixture was heated for another 40 min until no more N₂ was evolved, and was distilled. Yield, 0.96 g (24.5%) of (IV), bp 117-122°C, n_D^{20} 1.4470.

2-Chloroethyl Ester of Bicyclo[4.1.0]heptanecarboxylic Acid (VI). A solution of 2.97 g (0.02 mole) of (I) in 3 g of cyclohexene was added in the course of 7 h to a boiling suspension of 0.02 g (0.1 mmole) of anhydrous CuSO₄ in 13.4 g of cyclohexene (total amount of cyclohexene 16.4 g (0.2 mole)). The mixture was boiled for 40 min until no more N₂ was evolved, excess cyclohexene was distilled, and the residue was distilled in vacuo. Yield, 3.25 g (80%) of (VI), bp 101°C (2 mm), n_D^{20} 1.4925.

2-Chloroethyl esters of 2-amylcyclopropanecarboxylic acid (VII), chrysanthemumic acid (VIII), and 2-methyl-2-trimethylsilyl ethynylcyclopropanecarboxylic acid (IX) were obtained in a similar way. In the pre-

paration of (VIII), copper bronze was used as the catalyst. The properties of esters (VI)-(IX) are listed in Table 1.

2-Chloroethyl Ester of 1,2-Dipropylcyclopropene-3-carboxylic Acid (XII). A 2.97-g portion (0.02 mole) of (I) was added in the course of 2 h to a hot (120°C) suspension of 0.01 g (0.1 mmole) of anhydrous CuSO_4 and 6.6 g (0.06 mole) of dipropylacetylene. The reaction mixture was stirred for 30 min until no more N_2 was evolved, and was distilled. Yield, 2.28 g (50%) of (XII), bp 89°C (2 mm), n_D^{20} 1.4635.

2-Chloroethyl esters of 1-cyclopropyl-2-trimethylsilylcyclopropene-3-carboxylic acid (X) and 1-propyl-2-trimethylsilylcyclopropene-3-carboxylic acid (XI) were obtained in a similar way. The properties of esters (X)-(XII) are listed in Table 1.

CONCLUSIONS

1. 2-Chloroethyl diazoacetate was obtained in an overall yield of 75% by esterification of glycine with ethylene chlorohydrin by the action of gaseous HCl, followed by diazotization of the 2-chloroethyl aminoacetate formed.

2. Thermal and thermocatalytic decomposition of 2-chloroethyl diazoacetate at $> 80^\circ\text{C}$ is carbenic in character and in the presence of olefinic and acetylenic acceptors of *m*-xylene leads with preparative yields to 2-chloroethyl esters of cyclopropanecarboxylic, cyclopropenecarboxylic, and cycloheptatrienecarboxylic acids, respectively.

3. Thermal decomposition of 2-chloroethyl diazoacetate in the presence of diglyme is accompanied by splitting of the ether bonds with the formation of 2-chloroethyl esters of alkoxyacetic acids in a 24% yield. Under the same conditions, the reaction of this diazoester with ethylene glycol monomethyl ether leads to 2-chloroethyl ester of 2-methoxyethoxyacetic acid (in a 25% yield), the product of formal introduction of 2-chloroethoxycarbonylcarbene at the O-H bond.

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