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New Method of Preparation of Alkoxyacetic Acids

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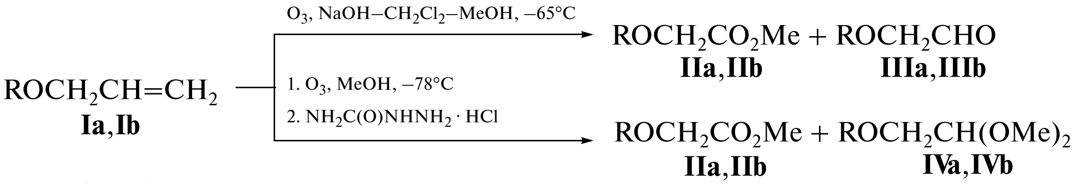
Alkoxyacetic acids and their derivatives are known to be widely used in organic synthesis and as chemical weed and pest killers [1, 2]. Their preparation is based on the transformations of monochloroacetic acid whose manufacture causes a large quantity of toxic byproducts [3].

In this work, we report the results of low-temperature ozonolysis of benzyl and phenyl allyl ethers for the preparation of methyl benzyl- and phenoxyacetates.

The esters of arylacetic acids were prepared by two methods: in the methanol–methylene chloride system in the presence of alkali at –65°C or in methanol at –78°C followed by the treatment of intermediate peroxide products with semicarbazide hydrochloride. The ozonolysis of benzyl and phenyl allyl ethers **Ia** and **Ib** in the presence of NaOH was found to lead in high yield and selectivity to esters **IIa** and **IIb**, respectively. Byproducts formed in small amounts are the corresponding alkoxyacetic aldehydes **IIIa** and **IIIb**. At the same time, the treatment of primary ozonation products (peroxides) with semicarbazide hydrochloride gives a mixture of esters **IIa** and **IIb** and acetals **IVa** and **IVb** (Table 1).



[R = $C_6H_5CH_2$ (**Ia**, **IIa**, **IIIa**),
R = C_6H_5 (**Ib**, **IIb**, **IIIb**)]

As was shown previously [4], the low-temperature ozonolysis of terminal linear olefins leads to acids in yields larger than 90%. Nonetheless, the ozonolysis of allyloxy derivatives was not reported previously, although the products of these reactions may be extremely promising for further chemical transformations and synthesis on their basis of compounds showing biological activity.

Thus, the obtained results allows one to consider the low-temperature ozonolysis of allyl ethers a convenient method for the synthesis of the corresponding alkoxycarbonyl compounds.

EXPERIMENTAL

Equipment of the "Chemistry" Shared Facility Center, Institute of Organic Chemistry, Ufa Research Center, Russian Academy of Sciences was used in the work. ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer operating at 300.13 (^1H) and 75.47 MHz (^{13}C) using Me_4Si as an internal reference. IR spectra were recorded on a Shimadzu IR Prestige-21 spectrometer in thin film. Mass spectra were obtained on a Thermo Finnigan MAT 95 XP high-resolution chromatograph–mass spectrometer at ionizing voltage 70 eV (ionization chamber temperature 250°C, direct injection at 50–270°C, heating rate 10 K/min). GLC study was performed on a

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Table 1. The result of ozonolysis of allyl ethers **Ia** and **Ib**

Compound	Reaction conditions	Product (yield, %)
Ia	O_3/2.5 M NaOH–MeOH–CH_2Cl_2, –65°C	**IIa** (60%) : **IIIa** (32%)
	1. O_3/MeOH, –78°C 2. $NH_2C(O)NHNH_2 \cdot HCl$	**IIa** (42%) : **IVa** (56%)
Ib	O_3/2.5M NaOH–MeOH–CH_2Cl_2, –65°C	**IIb** (80%) : **IIIb** (12%)
	1. O_3/MeOH, –78°C 2. $NH_2C(O)NHNH_2 \cdot HCl$	**IIb** (24%) : **IVb** (63%)

Table 2. Major signals ($CDCl_3$, δ, ppm) and absorption bands (ν, cm^{-1}) in NMR and IR spectra of ozonolysis products of ethers **Ia** and **Ib**

Compound	^{13}C, ppm	^1H, ppm	IR, cm^{-1}	Reference
IIa	170.38; 137.40; 128.03; 127.94; 127.66; 73.01; 71.84; 51.28	3.70 (s); 4.15(s); 4.65 (s); 7.30–7.60 (m)	1739; 1360	[5]
IIb	169.08; 157.43; 129.09; 121.36; 114.23; 65.25; 51.73	3.82 (s); 4.64 (s); 6.95 (m); 7.20–7.40 (m)	1739; 1377	[6]
IIIa	199.96; 137.49; 128.08; 127.56; 127.38; 72.76; 72.04	4.15 (s); 4.65 (s); 7.30–7.40 (m); 10.0 (s)	1754	[7]
IIIb	198.82; 157.43; 128.34; 121.09; 114.23; 69.85	4.51 (s); 6.99 (m); 7.05–7.30 (m); 9.80 (s)	1761	[8]
IVa	137.64; 128.09; 127.72; 127.54; 102.41; 73.10; 69.27; 53.46	3.38 (s); 3.53 (d, $J = 5.3$ Hz); 4.55 (t, $J = 10.4, 5.1$ Hz); 4.59 (s); 7.20–7.40 (m)	1114	[9]
IVb	158.11; 129.10; 120.94; 114.23; 101.78; 67.05; 53.63	3.47 (s); 4.02 (d, $J = 5.2$ Hz); 4.73 (t, $J = 10.4, 5.2$ Hz); 6.95 (m); 7.20–7.40 (m)	1246	This work

Chrom-5 chromatograph (column 1.2 m long), SE-30 (5%) stationary phase on Chromaton N-AW-DMCS (0.16–0.20 mm), working temperature 50–300°C, helium as a carrier gas. TLC monitoring was performed using Sorbfil SiO_2 (Russia), hexane–MTBE (methyl *tert*-butyl ether) as eluent, anisic aldehyde solution in sulfuric acid was used for visualization. Column chromatography was carried out with a Lancaster SiO_2 (70–230) (Great Britain). Ozonator performance was 40 mmol O_3/h.

*Ozonation of Allyl Aryl Ethers **Ia** and **Ib***
(General Procedure)

(1) An ozone–oxygen mixture was bubbled through a solution of 10.00 mmol of ethers **Ia** or **Ib** in a mixture of 20 mL of 2.5 M NaOH in MeOH and 80 mL of CH_2Cl_2 at –65°C until blue color appeared. The reaction mixture was purged with argon, MTBE (70 mL) and water (30 mL) were added, stirred for 1 h at ambient temperature. The organic layer was separated, the aqueous layer was extracted with MTBE. The combined organic extracts were dried with Na_2SO_4. After evaporation, ether **Ia** produced 1.66 g of mixture of compounds **IIa** and **IIIa** in 72 : 28 ratio (according to GLC and NMR data), column chromatography (SiO_2, PE, PE : MTBE = 5 : 1, 4 : 1) gave 1.07 g (60%) of ester **IIa** and 0.47 g (32%) of aldehyde **IIIa**. After evaporation, ether **Ib** produced 1.61 g of a mixture of compound **IIb** and **IIIb** in 88 : 12 ratio (according to GLC and NMR), column chromatography (SiO_2, PE, PE : MTBE = 5 : 1, 4 : 1) resulted in 1.34 g (80%) of ester **IIb** and 0.16 g (12%) of aldehyde **IIIb**.

(2) An ozone–oxygen mixture was bubbled through a solution of 10.00 mmol of ethers **Ia** or **Ib** in 50 mL of MeOH at –78°C until blue color appeared. The reaction mixture was purged with argon, 3.88 g (35.00 mmol) of $NH_2C(O)NHNH_2 \cdot HCl$. HCl was added at –50°C. The mixture was stirred at ambient temperature for 24 h. The reaction mixture was evaporated, the residue was dissolved in 100 mL of $CHCl_3$, washed with H_2O (to pH ≈ 7), and dried with Na_2SO_4. After evaporation, ether **Ia** produced 1.86 g of a mixture of compounds **IIa** and **IVa** in 40 : 60 ratio (according to GLC and NMR), column chromatography (SiO_2, PE, PE : MTBE = 5 : 1, 4 : 1) afforded 0.74 g (42%) of ester **IIa** and 1.09 g (56%) of acetal **IVa**. After evaporation, ether **Ib** produced 1.64 g of a mixture of compounds **IIb** and **IVb** in 25 : 75 ratio (according to GLC and NMR data), column chromatography

(SiO_2, PE, PE : MTBE = 5 : 1, 4 : 1) gave 0.40 g (24%) of ester **IIb** and 1.15 g (63%) of acetal **IVb**.

IR and ^{13}C NMR spectra were the most informative methods to establish the structure of the obtained compounds (**IIa**, **IIb–IVa**, **IVb**) isolated by column chromatography (Table 2). The obtained spectral and physicochemical characteristics of esters **IIa**, **IIb** and aldehydes **IIIa**, **IIIb** agree well with the literature data [5–9].

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