CONCLUSIONS

1. The throughgoing electrochemical oxidation of esters of malonic acid in the presence of catalyst carriers – salts of hydriodic acid – in methanol and ethanol leads to esters of ethylenetetracarboxylic acid and the products of the addition to it of alcohols and dialkyl malonates, namely 1-alkoxyethane-1,1,2,2-tetracarboxylic and propane-1,1,2,2,3,3-hexacarboxylic esters.

2. The results of the reaction depends to a significant degree on the temperature and the nature of the cation in the catalyst carrier. Under optimal conditions, each of the enumerated esters can be obtained with the yield of 50-80%.

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OXIDATION OF SECONDARY CYCLOALKANOLS BY THE LEAD TETRAACETATE–METAL HALIDE SYSTEM

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In the oxidation of secondary cyclic alcohols by simultaneous reaction with lead tetraacetate (LTA) and Cu(II) sulfate or acetate, the ω-formylalkyl radicals $HCO(CH_2)_nCH_2$ (n = 3-6) that are generated from the cycloalkanols are converted quantitatively to ω-unsaturated

TABLE 1. Oxidation of Cycloalkanols by the LTA–MCl_m System [80°C, 10-35 min, alcohol:LTA:MCl_m = 1:1:5 (m = 1) and 1:1:3 (m = 2), alcohol 0.01 mole, benzene 20 ml, and LTA conversion 100%]

Alcohol	MCl_m †	Conversion, %	Products, yield, % based on converted alcohol		
			(II)	(III)	(IV)
Cyclopentanol	LiCl	84	96	–	–
	NaCl*	88	47	11	–
	KCl	84	83	11	–
	$ZnCl_2$	73	75	22	–
	$CdCl_2$	80	89	+	–
Cyclohexanol	LiCl	70	64	34	–
	KCl	40	35	58	
Cycloheptanol	LiCl	81	49	23	14
	KCl	56	32	30	29
Cyclooctanol	LiCl	70	50	25	10
	KCl	80	20	24	29

*Reaction time 3 h, ~20% acetoxycyclopentane obtained.
†Solubility of MX in the LTA–benzene system, (mole/liter)·10^{-1}: LiCl 2.5, NaCl 0.4, KCl 0.1, and $CdCl_2$ 1.4.

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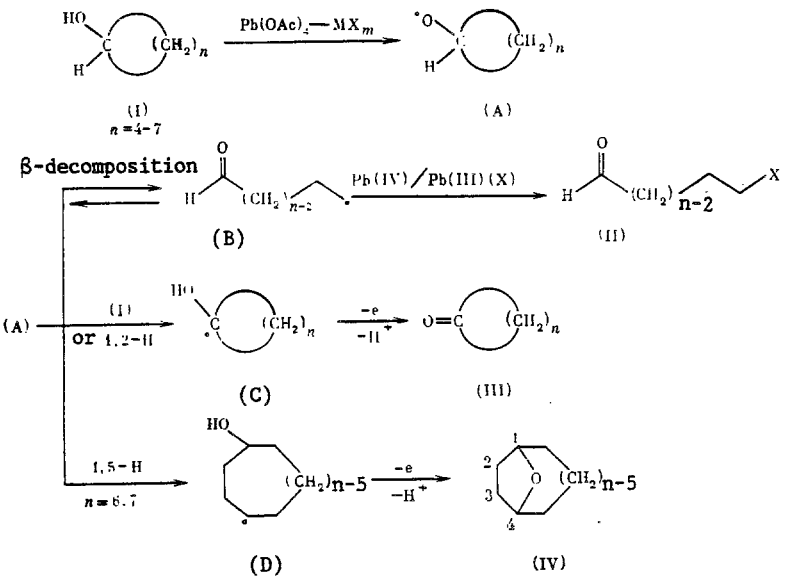
TABLE 2. Oxidation of Secondary Cycloalkanols by the LTA–MBr_m System (80°C, 25-35 min, alcohol:LTA:MBr = 1:1:5, alcohol 0.01 mole, benzene 20 ml, and LTA conversion 100%; with the use of $MgBr_2$, alcohol:LTA:$MgBr_2$ ratio = 1:1:3)

Alcohol	MBr_m	Conversion, %	Products, yield, % based on converted alcohol		
			(II)	(III)	(IV)
Cyclopentanol	KBr	80	64	30	–
	KBr *	78	51	44	–
	KSCN	80	50	15	–
Cyclohexanol	NaBr	28	–	86	–
	KBr	35	54	29	–
	KBr *	28	32	50	–
	$MgBr_2$	37	46	32	–
	KSCN	70	2	73	–
Cycloheptanol	KBr	70	30	28	30
	KBr *	68	25	32	32
Cyclooctanol	KBr	80	6	40	50

*In these runs, pyridine was added, with LTA:C_5H_5N ratio = 1:1.

aldehydes under the reaction conditions [1, 2]. In the reaction of 2-, 3-, and 4-methylcyclohexanols with the LTA–LiCl system, the ω-formalalkyl radicals that are formed are oxidized to ω-chloroalkanals with high selectivity [3].

In the present communication, we give the results of oxidation of secondary cycloalkanols (I) with C_5-C_8 ring size in the presence of the LTA–MX_m system (M = Li, Na, K, Mg, Zn, Cd; X = Cl, Br, SCN; m = 1, 2). The reaction was carried out in benzene at 80°C until complete conversion of LTA with alcohol:LTA:MX_m molar ratios 1:1:5 (m = 1) and 1:1:3 (m = 2). The obtained data are given in Tables 1 and 2. The oxidation of the cycloalkanols can be represented by the scheme



M = Li, Na, K, Mg, Zn, Cd; X = Cl, Br, SCN; $n = 4$–7; $m = 1$–2.

In the first oxidation stage, O-centered radicals (A) are generated, which are isomerized to C-centered radicals by the three indicated routes. In the general case, cycloalkoxy radicals can fragment with ring cleavage to ω-formylalkyl radicals (B), be converted to α-hydroxycycloalkyl radicals (C), and undergo rearrangement, with 1,5 migration of the H atom, to δ-hydroxycycloalkyl radicals (D). The formation of radicals (A)-(C) in the oxidation of secondary cyclic alcohols by LTA was confirmed by an EPR method using spin traps [2]. Radicals (B) are subsequently oxidized quantitatively to ω-haloalkanals (II). Radicals (C) and (D) are oxidized by Pb(IV)/Pb(III) compounds, being converted to cyclic ketone (III) and 1,4-epoxycycloalkane (IV).

Table 1 gives data on the oxidation of cycloalkanols in the presence of the LTA–metal chloride system. Among the chlorides, LiCl is the most efficient in this reaction. One of the reasons for the high efficiency of LiCl as a component of the oxidation system is that it is more soluble in benzene than are other chlorides. Of the investigated secondary cycloalkanols, cyclopentanol is the most reactive in the oxidative decyclization reaction. The β-decomposition of the cyclopentoxy radical is practically the only direction of the cyclopentanol oxidation process. In the case of cyclohexanol, cycloheptanol, and cyclooctanol, the contribution of this process is significantly less. The formation of cyclic ether (IV) was observed in the reaction of the LTA–MCl_m system with C_7-C_8 cycloalkanols, and both in the oxidation of cycloheptanol and in the oxidation of cyclooctanol, only 1,4-epoxycycloheptane and 1,4-epoxycyclooctane were obtained, respectively.

According to the data of Table 2, the best results in the oxidation of the cycloalkanols by the LTA–metal bromide system were obtained when KBr was used. The addition of an amount of pyridine equimolar with respect to LTA led to an increase of the yield of the cyclic ketone. Just as in the oxidation of cycloheptanol and cyclooctanol by the LTA–MCl system, 1,4-epoxycycloalkane was formed as a result of oxidation of these alcohols by the LTA–MBr system.

The LTA–KSCN system is less efficient than the LTA–metal chloride or bromide system in the oxidative decyclization of secondary cyclic alcohols, which was also noted in the oxidation of tertiary cycloalkanols by these systems [4]. Approximately 50% 5-thiocyanopentanal was obtained in the reaction of cyclopentanol with LTA–KSCN, and ~1-2% 6-thiocyanohexanal was obtained in the oxidation of cyclohexanol (Table 2). Isomerization of the SCN group to the isothiocyanate group did not occur. The IR spectrum of the thiocyanoalkanals contained an absorption band at 2160 cm^{-1} belonging to the thiocyanate group and an absorption band at 1720 cm^{-1} belonging to the carbonyl group. The ^{13}C NMR spectrum contained a chemical shift of 111.90 ppm characteristic of the SCN group [5].

EXPERIMENTAL

The GLC analysis was carried out on an LKhM-80 chromatograph with a flame-ionization detector. The columns were 3 m × 3 mm with 5% XE-60, SE-30, and Carbowax-20 on Chromaton NAW-HMDS (0.2-0.25 mm), and the carrier gas was N_2. The ^1H and ^{13}C NMR spectra were recorded on a Bruker WM-250 instrument, and the IR spectra were recorded on UR-20 and Specord-M80 instruments in a thin layer and in a CCl_4 solution.

Cyclopentanol, cycloheptanol, and cyclooctanol were obtained by the reduction of the corresponding ketones, the cyclohexanol was a pure-grade reagent, and the pure-grade $Pb(OAc)_4$ was washed with glacial AcOH and dried in vacuo. The KBr, LiCl, KCl, NaCl, and KSCN were high-purity grade, and the NaBr, LiBr, $CdCl_2$, $ZnCl_2$, and $MgBr_2$ were pure grade. The salts were dried in vacuo over P_2O_5, and the benzene and pyridine were distilled.

Oxidation of Secondary Cycloalkanols by the LTA–MX_m System (General Procedure). A mixture of (I), LTA, and MX_m in benzene was stirred vigorously at 80°C until complete conversion of the LTA (negative iodometric test), cooled, and filtered. The precipitate was washed with ether, and the conversion of (I) and the yield of the reaction products, ω-haloaldehyde (II), cycloalkanone (III), and 1,4-epoxycycloalkane (IV) (Tables 1 and 2), were determined in the combined filtrate by GLC using an internal standard. For recovery of the reaction products, the filtrate was washed successively with a 10% HCl solution, an aqueous $NaHCO_3$ solution, and water, dried with Na_2SO_4, and distilled. The haloaldehydes were identified in the form of 2,4-dinitrophenylhydrazones (2,4-DNPH) or acids, for which air was passed through the reaction mixture for 8-10 h, and the reaction mixture was treated with a 50% aqueous NaOH solution and separated into two layers. The aqueous layer was acidified with dilute H_2SO_4 to pH 2, and the whole was extracted with ether. The extract was dried with $MgSO_4$ and distilled. The cyclic ketones that were formed were identified by GLC by comparison with standard reference samples. The structure of the obtained cyclic ethers was determined by IR and proton and nonproton NMR spectroscopy.

Oxidation of the Cycloalkanols by the LTA–MCl_m System (Table 1). 5-Chloropentanal (IIa), bp 51°C (10 mm), was obtained from cyclopentanol. The IR and proton NMR spectra corresponded to those given in [1]. In addition, (IIa) was identified in the form of 5-chloropentanoic acid. IR spectrum (ν, cm^{-1}): 655 (CH_2Cl), 1730 (C=O), 2950 (OH).

6-Chlorohexanal (IIb), identified in the form of 6-chlorohexanoic acid, was obtained from cyclohexanol. IR spectrum (ν, cm^{-1}): 655 (CH_2Cl), 1730 (C=O), 2950 (OH). Proton NMR

spectrum (δ, ppm): 1.50-1.80 multiplet (6H, CH_2), 2.26 multiplet (2H, CH_2COOH), 3.45 triplet (2H, CH_2Cl), 10.90 singlet (1H, OH).

From cycloheptanol we obtained: a) 7-chloroheptanal (IIc) and (IIc) 2,4-DNPH and b) 1,4-epoxycycloheptane. For a), proton NMR spectrum (δ, ppm): 1.60-1.96 multiplet (8H, CH_2), 2.48 multiplet (2H, $CH_2CH=N$), 3.55 triplet (2H, CH_2Cl), 6.97 triplet, 7.57 triplet (1H, CH=N, syn, anti), 7.95-9.10 multiplet (3H, C_6H_3), 11.00 singlet (1H, NH). In addition, (IIc) was identified in the form of 7-chloroheptanoic acid. IR spectrum (ν, cm^{-1}): 650 (CH_2Cl), 1720 (C=O), 2940 (OH). Proton NMR spectrum (δ, ppm): 1.40-1.80 multiplet (8H, CH_2), 2.30 triplet (2H, CH_2COOH), 3.38 triplet (2H, CH_2Cl), 10.45 singlet (1H, OH). For b), IR spectrum (ν, cm^{-1}): 1060 (CHOCH), Proton NMR spectrum (δ, ppm): 1.50-2.09 multiplet (10H, CH_2), 4.40 multiplet (2H, CHOCH).

From cyclooctanol we obtained: a) 8-chlorooctanal (IId) and (IId) 2,4-DNPH and b) 1,4-epoxycyclooctane. For a), proton NMR spectrum (δ, ppm): 1.58-2.00 multiplet (10H, CH_2), 2.40 multiplet (2H, $CH_2CH=N$), 3.54 triplet (2H, CH_2Cl), 7.00 triplet, 7.55 triplet (1H, CH=N, syn, anti), 7.90-9.10 multiplet (3H, C_6H_3), 11.00 singlet (1H, NH). Additionally, (IId) was identified in the form of 8-chlorooctanoic acid, bp 70°C (0.5 mm). Found: C 53.39; H 8.28; Cl 20.93%. $C_8H_{15}O_2Cl$. Calculated: C 53.63; H 8.37; Cl 20.11%. For b), IR spectrum (ν, cm^{-1}): 1060 (CHOCH). Proton NMR spectrum (δ, ppm): 1.30-2.10 multiplet (12H, CH_2), 4.50 multiplet (2H, CHOCH). Carbon-13 NMR spectrum (δ, ppm): 24.43 (C^6, C^7), 31.54 (C^2, C^3), 36.12 (C^5, C^8), 77.81 (C^1, C^4) [see compound (IV), n = 7, for the notation].

Oxidation of Cycloalkanols by the LTA–MBr_m System (Table 2). 5-Bromopentanal (IIe), bp 70°C (9 mm), was obtained from cyclopentanol. IR spectrum (ν, cm^{-1}): 568 (CH_2Br), 1720 (C=O), 2730 (CHO). Proton NMR spectrum (δ, ppm): 1.70-1.90 multiplet (4H, CH_2), 2.41 multiplet (2H, CH_2CHO), 3.43 triplet (2H, CH_2Br), 9.10 triplet (1H, CHO), (IIe) 2,4-DNPH, mp 115°C (alcohol). Found: C 38.19; H 3.64; Br 23.12; N 16.23%. $C_{11}H_{13}BrO_4N_4$. Calculated: C 38.26; H 3.77; Br 23.19; N 16.23%. Proton NMR spectrum (δ, ppm): 1.80-2.10 multiplet (4H, CH_2), 2.50 multiplet (2H, $CH_2CH=N$), 3.47 triplet (2H, CH_2Br), 6.98 triplet, 7.58 triplet (1H, CH=N, syn, anti), 7.95-9.18 multiplet (3H, C_6H_3), 11.07 singlet (1H, NH).

From cyclohexanol we obtained 6-bromohexanol (IIf) and (IIf) 2,5-DNPH. Proton NMR spectrum (δ, ppm): 1.70-2.00 multiplet (6H, CH_2), 2.48 multiplet (2H, $CH_2CH=N$), 3.46 triplet (2H, CH_2Br), 6.98 triplet, 7.58 triplet (1H, CH=N, syn, anti), 7.95-9.18 multiplet (3H, C_6H_3), 11.02 singlet (1H, NH). Additionally, (IIf) was identified in the form of 6-bromohexanoic acid. IR spectrum (ν, cm^{-1}): 568 (CH_2Br), 1710 (C=O), 2950 (OH). Proton NMR spectrum (δ, ppm): 1.50-1.90 multiplet (6H, CH_2), 2.39 multiplet (2H, CH_2COOH), 3.42 triplet (CH_2Br), 10.00 singlet (1H, OH).

From cycloheptanol we obtained: a) 7-bromoheptanal (IIg) and (IIg) 2,4-DNPH and b) 1,4-epoxycycloheptane. Proton NMR spectrum (δ, ppm): 1.50-2.10 multiplet (8H, CH_2), 2.30 multiplet (2H, $CH_2CH=N$), 3.38 triplet (2H, CH_2Br), 6.88 triplet, 7.60 triplet (1H, CH=N, syn, anti), 7.90-9.20 multiplet (3H, C_6H_3), 11.10 singlet (1H, NH). In addition, (IIg) was identified in the form of 7-bromoheptanoic acid. IR spectrum (ν, cm^{-1}): 570 (CH_2Br), 1710 (C=O), 2950 (OH). Proton NMR spectrum (δ, ppm): 1.20-1.85 multiplet (8H, CH_2), 2.31 triplet (2H, CH_2COOH), 3.38 triplet (2H, CH_2Br), 10.41 singlet (1H, OH).

From cyclooctanol we obtained: a) 8-bromooctanol (IIh) and b) 1,4-epoxycyclooctane. For a), IR spectrum (ν, cm^{-1}): 568 (CH_2Br), 1720 (C=O), 2720 (CHO).

Oxidation of Cycloalkanols by the LTA–KSCN System (Table 2). 5-Thiocyanopentanal (IIi) was obtained from cyclopentanol. IR spectrum (ν, cm^{-1}): 1725 (C=O), 2160 (SCN), 2720 (CHO). Proton NMR spectrum (δ, ppm): 1.62 multiplet (4H, CH_2), 2.45 triplet (2H, CH_2CHO), 2.90 triplet (2H, CH_2SCN), 9.68 triplet (1H, CHO). Carbon-13 NMR spectrum (δ, ppm): 20.20 (CH_2), 29.19 (CH_2), 33.59 (CH_2SCN), 43.81 (CH_2CHO), 111.90 (SCN), 201.07 (CHO), (IIi) 2,4-DNPH, mp 97°C (alcohol). Found: C 44.37; H 4.43; N 21.50; S 9.46%. $C_{12}H_{13}O_4N_5S$. Calculated: C 44.58; H 4.02; N 21.70; S 9.91%.

6-Thiocyanohexanal (IIj) was obtained from cyclohexanol. IR spectrum (ν, cm^{-1}): 1720 (C=O), 2160 (SCN), 2720 (CHO).

CONCLUSIONS

Secondary cyclic alcohols with C_5-C_8 ring size are oxidized by the lead tetraacetate–metal chloride or bromide system in three directions: with ring cleavage and the formation

of ω-haloalkanals and without ring cleavage with the formation of the corresponding ketones and also, for C_7-C_8, 1,4-epoxycycloalkanes.

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NITROSOALKYLUREAS WITH QUATERNARY NITROGEN ATOM.

5.* STUDY OF DECOMPOSITION PRODUCTS OF THE CHOLINE-LIKE NITROSOALKYLUREAS IN AQUEOUS MEDIUM

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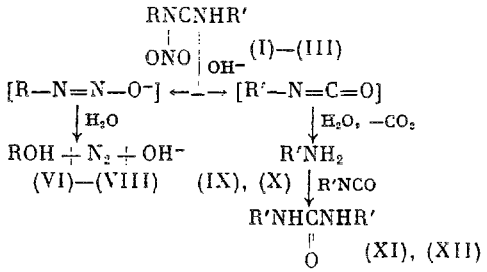
UDC 542.92:547.495.4

The antitumorigenic activity of nitrosoalkylureas (NAU) is based on their ability to decompose with the formation of reactive cytotoxic products, which are diazohydroxides and isocyanates [2]. In the case of nitrosoureido derivatives of biogenic compounds, the biogenic compounds formed during their decomposition may also influence the biological activity to some extent. It was therefore expedient to study the decomposition products of a new group of choline-like NAU (I)-(V), which we have synthesized [3, 4], during the decomposition of which not only cytotoxic compounds, but also the appearance of choline or its analogs, can be expected.

It can be assumed on the basis of the scheme of decomposition of the known dialkyl-substituted NAU, proceeding by the ElcB mechanism [2] that the decomposition of compounds (I)-(III) leads to the formation of alcohols (VI)-(VIII), amines (IX), (X) and (or) symmetric ureas (XI), (XII). In the case of trialkyl-substituted NAU (IV), (V), the decomposition by the BAc2 mechanism with formation of the corresponding alcohols (VI), (VII) as well as of 2-methylaminoethyltrimethylammonium tosylate (XIII) is most probable (see scheme below)



R = Me, R′ = $(CH_2)_2\overset{+}{N}Me_3 \cdot Cl^-$ (I); R = $(CH_2)_2Cl$, R′ = $(CH_2)_2\overset{+}{N}Me_3 \cdot Cl^-$ (II); R = = $(CH_2)_2\overset{+}{N}Me_3 \cdot TsO^-$, R′ = cyclo-$C_6H_{11}$ (III); R = Me (VI); R = $(CH_2)_2Cl$ (VII); R = $(CH_2)_2\overset{+}{N}Me_3 \cdot TsO^-$ (VIII); R′ = $(CH_2)_2\overset{+}{N}Me_3 \cdot Cl^-$ (IX), (XI); R′ = cyclo-C_6H_{11} (X), (XII).

*For previous communication, see [1].

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