Organic Chemistry

Oxidation of aliphatic alcohols with the lead tetraacetate—metal halide system under mechanical activation

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The mechanochemical oxidation of *n*-pentanol, *n*-hexanol, and *n*-octanol with the $Pb(OAc)_4$—MHal system (M = Li, K; Hal = Cl, Br) in the absence of a solvent affords esters, and secondary alcohols with the composition $C_8H_{17}OH$ and $C_9H_{19}OH$ give ketones.

Key words: mechanical activation, oxidation, aliphatic alcohols, lead tetraacetate, metal halide, esters, ketones.

Lead tetraacetate is one of the most widely used oxidants in organic chemistry. Substances of many classes enter into processes involving $Pb(OAc)_4$. The reactions of aliphatic alcohols with $Pb(OAc)_4$ in solutions[1] have been studied in detail. Unbranched primary alcohols with the composition $\geq C_5$ in non-polar solvents (benzene, heptane, and cyclohexane) are oxidized to form mainly 2-alkyltetrahydrofurans; their cyclization to 2-alkyltetrahydropyrans occurs in parallel with a very insignificant contribution. Secondary *n*-alkanols with the same composition are mainly transformed into cyclic ethers under the same conditions. The oxidation of primary and secondary *n*-alkanols in pyridine or in a neutral solvent containing pyridine affords carbonyl compounds, *viz.*, aldehydes and ketones.

The oxidation of primary and secondary higher alkanols with the systems $Pb(OAc)_4$—Group I or II metal chlorides in benzene at 80 °C occurs in a different way.[2] Such systems oxidize alcohols to form δ-chloroalkanols, and minor products are ε-chloroalkanols and 2-alkyltetrahydrofurans. In the case of secondary alkanols bearing branching at the C_β atom, the oxidation occurs with C_α—C_β bond cleavage. It follows from these data that, in the absence of pyridine, in the first step of oxidation involving $Pb(OAc)_4$ or the $Pb(OAc)_4$—metal chloride system, alcohols generate alkoxyl radicals, which are rearranged in a solution with 1,5- and 1,6-hydrogen shift. The formation of alkoxyl radicals is confirmed by their trapping with the spin trap, *C*-phenyl-*N*-*tert*-butylnitrone, and the spin-adducts were identified[2] by ESR. The carbon-centered radicals that appeared due to rearrangement and whose formation was also confirmed[2] by ESR, are oxidized with the transfer of an electron or the ligand to form cyclic ethers

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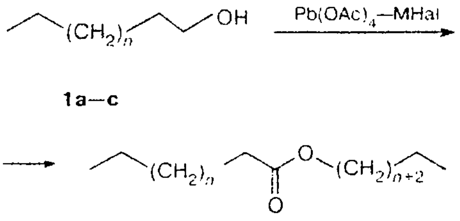
Published in *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 11, pp. 1870—1873, November, 2000.

1066-5285/00/4911-1842 $25.00

and chloroalkanols, respectively. The alkoxyl radicals generated from β-branched secondary alcohols undergo β-fragmentation to be transformed into alkyl radicals and aldehydes; the latter were identified in the reaction products.[2]

In the present work, in a continuation of studies of the reactions of lead tetraacetate with organic compounds under mechanical activation without a solvent,[3] we oxidized primary (**1a—c**) and secondary (**2a—c**) alkanols with the $Pb(OAc)_4$—MHal system (M = Li, K; Hal = Cl, Br). Experiments were carried out at 20 °C on vibrational mills in closed steel reactors filled with steel balls.

We obtained an unexpected result: under these conditions, alkanols **1** are transformed into esters **3** (Table 1; the results of previous studies[2] (entries *4*, *9*, and *12*) are presented for comparison).

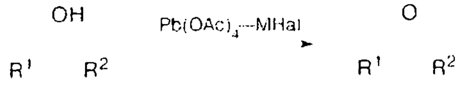


1a—c

3a—c

n = 1 (**a**), 2 (**b**), 4 (**c**)

Secondary alkanols **2** give only ketones **4**, and the branching at the $C_β$ atom in 2-methyloctan-3-ol (**2b**) has no effect on the oxidation that occurs without $C_α$—$C_β$ bond cleavage (Table 2; the results of previous studies[2] (entries *3*, *7*, *8*, and *12*) are presented for comparison).



2a—c **4a—c**

	a	**b**	**c**
R^1	Me	Pr^i	*iso*-C_5H_{11}
R^2	*n*-C_6H_{13}	*n*-C_5H_{11}	Pr^n

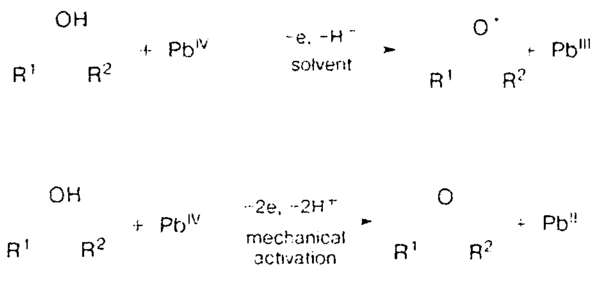
Unlike transformations of primary and secondary aliphatic alcohols induced by $Pb(OAc)_4$ and in the $Pb(OAc)_4$—MHal system in the presence of a solvent, under mechanical activation, cyclic ethers and δ-haloalkanols are virtually not formed. This is the more so unexpected that the oxidation of tertiary cycloalkanols with the $Pb(OAc)_4$—MHal system both in a solution and under mechanical activation in the absence of a solvent results in ring opening and formation of ω-haloalkanones[3]; therefore, the oxidation follows the homolytic mechanism including the step of alkoxyl radical generation.

Based on the previous and newer data, we may conclude that mechanical activation brings about changes in the mechanism of the oxidation of primary and secondary alcohols with the $Pb(OAc)_4$—MHal system. In a solution (non-polar solvent, MHal = LiCl), the one-electron process with the generation of alkoxyl radicals occurs in the first step. Under mechanical activation in the absence of a solvent, the reaction follows the two-electron heterolytic mechanism to afford aldehydes and ketones.

Table 1. Oxidation of primary alkanols **1a—c** with the $Pb(OAc)_4$—MHal system under mechanical activation

Alkanol	Entry	Molar ratio **1** : $Pb(OAc)_4$: MHal	MHal	Conversion of **1** (%)	Product	Yield of product[a] (%)
1a	*1*	1 : 1.2 : 5	LiCl	55	**3a**	38/69
	2[b]	1 : 1.2 : 5	LiCl	60	**3a**	40/67
	3	1 : 2 : 5	LiCl	66	**3a**	42/64
	4[c]	1 : 2 : 5	LiCl	67	4-Chloropentan-1-ol	65/97
	5	1 : 1.2 : 5	LiBr	65	**3a**	41/63
	6[b]	1 : 1.2 : 5	LiBr	84	**3a**	64/76
	7	1 : 1.2 : 5	KBr	86	**3a**	67/78
	8	1 : 2 : 5	KBr	83	**3a**	71/86
	9[c]	1 : 2 : 5	KBr	10	**3a**	3/3
	10	1 : 1.2 : 0	—	5	**3a**	3/60
1b	*11*	1 : 2 : 5	LiCl	72	**3b**	49/68
	12[c]	1 : 2 : 5	LiCl	70	5-Chlorohexan-1-ol	67/96
	13	1 : 2 : 5	KBr	87	**3b**	72/83
	14	1 : 1.2 : 0	—	4	**3b**	2/50
1c	*15*	1 : 2 : 5	LiCl	72	**3c**	48/67
	16	1 : 1.2 : 5	KBr	60	**3c**	50/83
	17	1 : 2 : 5	KBr	85	**3c**	64/75
	18	1 : 1.2 : 0	—	5	**3c**	4/80

[a] The yield was calculated with respect to the starting/converted alkanol.
[b] The frequency of vibrations was 19 Hz.
[c] Liquid-phase reaction in benzene at 80 °C without mechanical activation.[2]



R¹ = Alkyl, R² = H, Alkyl

Ketones are the final products and are not involved in subsequent transformations, whereas aldehydes are rapidly oxidized under the reaction conditions to form esters **3**. This process was simulated in a glass reactor without using a vibrational mill. *n*-Pentanol, *n*-pentanal, $Pb(OAc)_4$, and KBr were mixed in a molar ratio of 1 : 1 : 3 : 6, and after 10 min the conversion of the aldehyde and the alcohol was 88% and the yield of pentyl pentanoate was 86%. At longer reaction time, the conversion of the alcohol and the aldehyde and the yield of the ester increased in equal proportions, *i.e.*, the alcohol was virtually not oxidized in the presence of the aldehyde and only participated as the esterification agent. Probably, the aldehyde and lead tetraacetate form an oxallyl complex,[4] whose decomposition affords the ester.

Metal halide is a necessary reactant in the oxidation of alkanols **1** to esters **3** and in the oxidation of alkanols **2** to ketones **4**. In the absence of metal halide, other conditions being the same, the conversion of alkanols **1** and **2** and the yield of products **3** and **4** decrease 10—30-fold, being only 2—5% (see Table 1, entries *10*, *14*, and *18*; Table 2, entries *4*, *9*, and *13*). There are strong grounds to believe that under mechanical activation, as has been mentioned previously,[5,6] metal halide and $Pb(OAc)_4$ afford the salt $[Pb(OAc)_4Hal_2]M_2$, which efficiently conducts the oxidation process, being a stronger oxidant than $Pb(OAc)_4$. The conversion of $Pb(OAc)_4$ over the reaction time was 100%. The conversion of alkanols **1** and **2** ranges from 55 to 98% depending on the nature of the metal halide, the amount of the oxidant, and the operating regime of the vibrational mill. The selectivity of the reactions with respect to the alkanol is 70—80%.

Table 2. Oxidation of secondary alkanols **2a—c** with the $Pb(OAc)_4$—MHal system under mechanical activation at the molar ratio alkanol : $Pb(OAc)_4$: MHal = 1 : 2 : 5

Alkanol	Entry	MHal	Conversion of **2** (%)	Product	Yield[a] (%)
2a	*1*	LiCl	54	**4a**	42/78
	2	KBr	78	**4a**	63/81
	3[b]	LiCl	69	5-Chloro-octan-2-ol	65/94
	4	—	6	**4a**	3/50
2b	*5*	LiCl	72	**4b**	51/71
	6	KBr	95	**4b**	79/83
	7[b]	LiCl	63	*n*-Hexanal	60/95
	8[b]	KBr	8	**4b**	4/5
	9	—	4	**4b**	2/50
2c	*10*	LiCl	60	**4c**	43/72
	11	KBr	98	**4c**	88/90
	12[b]	LiCl	27	7-Methyl-7-chlorooctan-4-ol	23/85
	13	—	5	**4c**	4/80

[a] The yield was calculated with respect to the starting/converted alkanol.

[b] Liquid-phase reaction in benzene at 80 °C without mechanical activation.[2]

When the content of $Pb(OAc)_4$ is increased from 1.2 to 2.0 moles per mole of alkanols **1a** and **1c**, the conversion of alkanols and the yield of esters **3a** and **3c** increased. However, the theoretical yield of ester **3** and ketone **4** requires only 1 mole of $Pb(OAc)_4$. It thus follows that a portion of the oxidant is consumed in side intra- and intermolecular reactions. An increase in the frequency of vibrations of the vibrational mill from 12 to 19 Hz also increases the efficiency of the oxidation process (see Table 1, entries *1* and *2*, *5* and *6*).

Under mechanical activation, the oxidation of alkanols **1** and **2** with the $Pb(OAc)_4$—MHal system involving LiBr and KBr is more efficient than that with LiCl (see Table 1, entries *1* and *5*, *2* and *6*, *3* and *8*, *11* and *13*, *15* and *17*; Table 2, entries *1* and *2*, *5* and *6*, *10* and *11*). However, $Pb(OAc)_4$ in combination with KBr is not efficient in the liquid-phase reaction without mechanical activation (see Table 1, entry *9*; Table 2, entry *8*). The $Pb(OAc)_4$—LiCl system actively oxidizes alkanols **1** and **2** under mechanical activation both without a solvent and in the liquid-phase reaction, but these processes, as has been mentioned above, give different products (see Table 1, entries *3* and *4*, *11* and *12*; Table 2, entries *1* and *3*, *5* and *7*). Thus, mecahnical activation changes the mechanism of the oxidation of alkanols with the composition $\geq C_5$ by the system mentioned. As a result, primary alkanols afford esters and secondary alkanols give ketones, whereas in the liquid-phase process primary and secondary alkanols afford δ-chloroalkanols.

Experimental

GLC was performed on an LKhM-80 chromatograph using a flame-ionization detector and analytical glass columns 3 m × 3 mm packed with 5% SE-30 and 5% XE-60 on Chromaton N-AW-HDMS (0.16—0.20 mm). IR spectra were recorded on a Perkin—Elmer 577 spectrometer in a thin layer. ^1H and ^{13}C NMR spectra were obtained on a Bruker AC-250P spectrometer under standard conditions in $CDCl_3$. The starting primary (**1**) and secondary (**2**) aliphatic alcohols (*n*-pentanol, *n*-hexanol, *n*-octanol, octan-2-ol, 2-methyloctan-3-ol, and 7-methyloctan-4-ol) are commercially available; they were distilled before use. Lead tetraacetate (pure grade) was washed with glacial AcOH and dried *in vacuo* over KOH. Commercially available LiCl, LiBr, and KBr were dried in a desiccator before use.

Oxidation of primary and secondary aliphatic alcohols with the $Pb(OAc)_4$—MHal system (general procedure). Mechanical activation of a reaction mixture comprising an aliphatic alcohol (4.0 mmol), $Pb(OAc)_4$, and metal halide (total weight ~1—2 g) was performed at an initial temperature of −20 °C on a vibration mill with a frequency of vibrations of 12 Hz and an amplitude of 11 mm in a hermetically sealed steel ~80-cm^3 reactor. Steel balls with a diameter of 12.3 mm and a total weight of ~150 g were used as the activating packing. The duration of the mechanical treatment was 4 h. During this time, the reaction temperature increased by 10—15 °C. After mechanical treatment, the reaction mixture (a baked gray mass) was extracted from the reactor with diethyl ether (2×25 mL) and chloroform (2×25 mL). To isolate the reaction products, the combined extracts were washed with 3% HCl and an aqueous solution of $NaHCO_3$, dried with Na_2SO_4, and distilled. The structure of the synthesized compounds was established using IR and ^{1}H and ^{13}C NMR spectroscopy. The conversion of alkanols and the yield of the reaction products were determined by GLC using an internal standard (see Tables 1 and 2). The conversion of Pb^{IV} was found iodometrically[7] to be 100%.

***n*-Pentyl pentanoate (3a).** b.p. 202—204 °C (*cf.* Ref. 8: b.p. 204 °C). ^{1}H NMR ($CDCl_3$), δ: 0.90 (t, 6 H, CH_3, J = 6.6 Hz); 1.35 (m, 6 H, CH_2); 1.63 (m, 4 H, CH_2); 2.37 (t, 2 H, CH_2COO, J = 7.4 Hz); 4.09 (t, 2 H, CH_2OCO, J = 6.6 Hz). ^{13}C NMR ($CDCl_3$), δ: 13.65, 13.91 (CH_3); 22.25, 22.48, 27.04, 28.03, 28.28 (CH_2); 34.08 ($\underline{C}H_2COO$); 64.42 ($\underline{C}H_2OCO$); 174.17 (CO).

***n*-Hexyl hexanoate (3b).** b.p. 125—126 °C (20 Torr) (*cf.* Ref. 9: b.p. 246 °C). IR, ν/cm^{-1}: 1740 (O—C=O). ^{1}H NMR ($CDCl_3$), δ: 0.88 (t, 6 H, CH_3, J = 6.7 Hz); 1.28 (m, 10 H, CH_2); 1.61 (m, 4 H, CH_2); 2.30 (t, 2 H, CH_2COO, J = 7.5 Hz); 4.06 (t, 2 H, CH_2OCO, J = 6.7 Hz). ^{13}C NMR ($CDCl_3$), δ: 13.94 (CH_3); 22.33, 22.54, 24.71, 25.60, 28.60, 31.32, 31.42 (CH_2); 34.38 ($\underline{C}H_2COO$); 64.41 ($\underline{C}H_2OCO$); 174.06 (CO).

***n*-Octyl octanoate (3c).** b.p. 304—305 °C (*cf.* Ref. 10: b.p. 306 °C). IR, ν/cm^{-1}: 1745 (O—C=O). ^{1}H NMR ($CDCl_3$), δ: 0.88 (t, 6 H, CH_3, J = 6.5 Hz); 1.29 (m, 18 H, CH_2); 1.62 (m, 4 H, CH_2); 2.30 (t, 2 H, CH_2COO, J = 7.5 Hz); 4.06 (t, 2 H, CH_2OCO, J = 6.7 Hz). ^{13}C NMR ($CDCl_3$), δ: 14.07 (CH_3); 22.62, 25.02, 25.92, 28.63, 28.92, 29.04, 29.19, 29.38, 29.69, 31.65, 31.77 (CH_2); 34.39 ($\underline{C}H_2COO$); 64.40 ($\underline{C}H_2OCO$); 174.07 (CO).

Octan-2-one (4a). b.p. 173 °C (*cf.* Ref. 11: b.p. 171 °C). IR, ν/cm^{-1}: 1715 (C=O). ^{1}H NMR ($CDCl_3$), δ: 0.81 (t, 3 H, CH_3, J = 6.3 Hz); 1.20 (m, 6 H, CH_2); 1.49 (m, 2 H, $C\underline{H}_2CH_2CO$); 2.06 (s, 3 H, CH_3CO); 2.35 (t, 2 H, CH_2CO, J = 7.4 Hz). ^{13}C NMR ($CDCl_3$), δ: 13.99 (CH_3); 22.46, 23.79, 28.82, 31.56, 43.80 (CH_2); 29.82 ($\underline{C}H_3CO$); 209.44 (C=O).

2-Methyloctan-3-one (4b). b.p. 183 °C (*cf.* Ref. 12: b.p. 184 °C). IR, ν/cm^{-1}: 1710 (C=O). ^{1}H NMR ($CDCl_3$), δ: 0.89 (t, 3 H, CH_3, J = 6.7 Hz); 1.09 (d, 6 H, CH_3, J = 6.9 Hz); 1.26 (m, 4 H, CH_2); 1.57 (m, 2 H, $C\underline{H}_2CH_2CO$); 2.44 (t, 2 H, CH_2CO, J = 7.3 Hz); 2.60 (m, 1 H, CH). ^{13}C NMR ($CDCl_3$), δ: 13.89 (CH_3); 18.22 ($\underline{C}H_3CH\underline{C}H_3$); 22.44, 23.44, 31.45, 40.73 (CH_2); 40.28 (CH); 215.20 (C=O).

7-Methyloctan-4-one (4c). b.p. 175 °C (*cf.* Ref. 13: b.p. 177 °C). IR, ν/cm^{-1}: 1705 (C=O). ^{1}H NMR ($CDCl_3$), δ: 0.90 (m, 9 H, CH_3); 1.53 (m, 5 H, $C\underline{H}C\underline{H}_2CH_2COCH_2C\underline{H}_2$); 2.38 (t, 4 H, CH_2COCH_2, J = 7.4 Hz). ^{13}C NMR ($CDCl_3$), δ: 13.77 (CH_3); 17.32, 32.66, 40.86, 44.68 (CH_2); 22.34 ($\underline{C}H_3CH\underline{C}H_3$); 27.73 (CH); 211.72 (C=O).

This work was financially supported by the Russian Foundation for Basic Research (Project No. 97-03-32921a).

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Received June 19, 2000