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Salt Effects in the Reaction of Alcohols Oxidation with a Nitroxyl Radical–Iodine Catalytic System

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Abstract—Influence of tetraethyl- and tetrabutylammonium salts on alcohols oxidation with the 4-acetylamino-2,2,6,6-tetramethylpiperidine-1-oxyl–iodine catalytic system has been studied. Addition of these salts inhibits the reaction and reduces the conversion.

Keywords: nitroxyl radical, iodine, alcohol oxidation, tetraalkylammonium salt, salt effect

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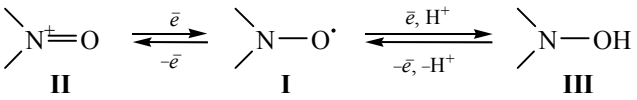
Application of nitroxyl radicals **I** for oxidation of alcohols is based on their redox properties [1].



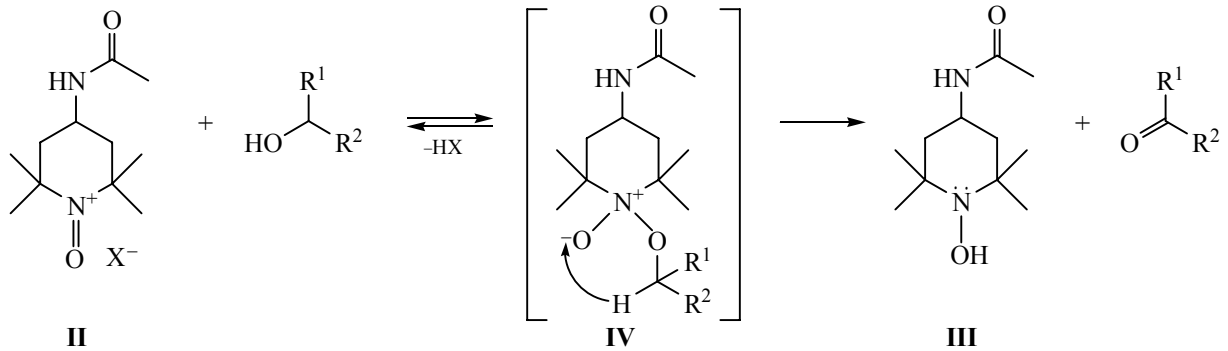
II **I** **III**

The preliminary prepared oxoammonium salt **II** can be used for alcohols oxidation [2–4]. However, salt **II** is often generated via oxidation of radical **I** with a primary oxidizer (NaOCl [5], NaOBr [6], I_2 [7], oxone [8], anode [9, 10], or *m*-chloroperbenzoic acid [11]).

A number of the oxidation reaction mechanisms have been discussed [10, 12–15]; however, it is generally assumed that the first stage of the catalytic oxidation of alcohols in a nonaqueous solution involved addition of the alcohol to the oxoammonium cation **II** to form intermediate **IV** (catalysis via approaching). The rate-limiting reaction stage is a proton elimination [10–16] to form the carbonyl compound and hydroxylamine **III** (Scheme 1).

It has been suggested that oxoammonium salts, similar to other charged compounds, exist in the form of ion pairs in equilibrium with the counterions in nonaqueous solutions [17]. Reactivity of the ion pairs is significantly different from that of the free ions. This has never been considered in the discussion of the mechanism of alcohols oxidation with oxoammonium salts; however, it can explain many of the reaction features. The reactivity of ion pairs is significantly

Scheme 1.



II **IV** **III**

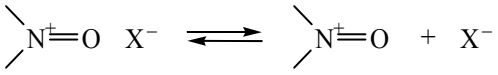
The influence of quaternary ammonium salts on the alcohols oxidation with the 4-acetylamino-2,2,6,6-tetramethylpiperidine-1-oxyl (**I**)–iodine catalytic system

Alcohol	Salt	Salt : radical **I** molar ratio	Alcohol conversion, %	Reaction products (selectivity, %)
Cyclohexanol	–	–	92.4	Cyclohexanone (100)
Heptanol-1	–	–	46.4	Heptanal (84)
Hexanol-2	–	–	43.0	Hexanone-2 (100)
Benzyl alcohol	–	–	100	Benzaldehyde (100)
Cyclohexanol	$N(C_2H_5)_4I$	10	2.3	Cyclohexanone (100)
Cyclohexanol	$N(C_2H_5)_4Cl$	10	4.0	Cyclohexanone (100)
Heptanol-1	$N(C_2H_5)_4I$	10	6.8	Heptanal (91)
Hexanol-2	$N(C_2H_5)_4I$	10	0.6	Hexanone-2 (100)
Benzyl alcohol	$N(C_2H_5)_4I$	10	6.4	Benzaldehyde (100)
Cyclohexanol	$N(C_2H_5)_4I$	1	70.7	Cyclohexanone (100)
Cyclohexanol	$N(C_4H_9)_4Cl$	1	67.5	Cyclohexanone (100)
Heptanol-1	$N(C_2H_5)_4I$	1	43.5	Heptanal (95)
Heptanol-1	$N(C_4H_9)_4Cl$	1	44.7	Heptanal (92)
Hexanol-2	$N(C_4H_9)_4Cl$	1	38.8	Hexanone-2 (91)

influenced by the inert salts that can accelerate as well as slow down the oxidation reaction [17, 18].

In this work we studied the influence of quaternary ammonium salts on the course of alcohols oxidation with a 4-acetylamino-2,2,6,6-tetramethylpiperidine-1-oxyl–iodine catalytic system. Iodine and certain organic compounds oxidize primary and secondary alcohols in the presence of nitroxyl radicals to yield the corresponding aldehydes and ketones. Either elemental iodine can be used [7] or it can be generated electrochemically via oxidation of iodide ion [19]. The reaction is relatively slow, allowing for the study of its kinetics. In this work we oxidized the alcohols with iodine at room temperature in the two-phase CH_2Cl_2–water system.

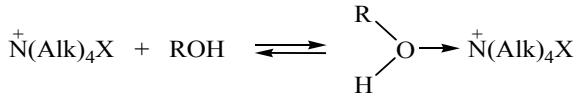
We observed remarkable deceleration of the oxidation of primary and secondary alcohols upon introduction of chloride or iodide of tetraethyl- or tetrabutylammonium into the reaction mixture (see table). At the alcohol : radical **I** : quaternary salt ratio of 1 : 0.1 : 1 the reaction was practically blocked, and its conversion did not exceed 0.6–6.8%. The tenfold decrease in the salt concentration resulted in the decrease in the conversion by 2–20% as compared to the reference experiment in the salt-free solutions. The effect could be explained by the reactivity of the oxoammonium salts depending on the position of equilibrium between the ion pairs and free ions. Addition of the highly dissociated [20] quaternary ammonium salts resulted in the equilibrium shift towards the ion pairs, decrease in the oxoammonium ion concentration, and reduced reactivity of the oxidizing system.



The similar considerations explained the influence of the counterion and the solvent on the oxoammonium salts reactivity [7, 14, 15]. The oxidation of alcohols with oxoammonium chloride occurred within seconds, whereas the reaction time was up to 60 min when using the corresponding bromides [21]. Oxoammonium perchlorates and tetrafluoroborates were the weakest oxidizers as compared to the salts with other anions [2]. That was likely due to the basicity of the anions and the resulting differences in the oxoammonium–anion bonding [17].

Another factor affecting the rate of alcohols oxidation with oxoammonium salts could be competitive interaction of tetraalkylammonium salts with

the alcohol resulting in the decrease of nucleophilicity of the latter and, hence, slowing down the oxidation reaction [22].



Chlorides, bromides, and iodides of tetraalkylammonum produced approximately equal effects on the rate of alcohols oxidation (see table). That was due to the generation of iodide ions in the course of the oxidation. Tetraalkylammonium iodides are better extracted from aqueous phase as compared to the bromides and chlorides.

The obtained data should be considered in studies of mechanism of alcohols oxidation with oxoammonium salts and in development of preparative methods of alcohols oxidation, especially when quaternary ammonium salts are used as source of halide ions.

EXPERIMENTAL

4-Acetylamino-2,2,6,6-tetramethylpiperidine-1-oxyl was prepared as described elsewhere [23] via oxidation of the corresponding spatially hindered amine; other chemicals were supplied by Aldrich and used as received.

Gas chromatography–mass spectroscopy experiments were run using an Agilent 7890A chromatograph equipped with an Agilent 5975C mass-selective detector (EI, 70 eV) and an HP-5MS capillary column. The peaks were identified via comparison with the reference spectra from NIST database. The equipment control and the data acquisition and processing were performed using MSD ChemStation software package. Quantitative analysis of the peaks area was performed using the auto-integration in the MSD ChemStation software.

Oxidation of alcohols with a 4-acetylamino-2,2,6,6-tetramethylpiperidine-1-oxyl–iodine system (general procedure). A solution of 4 mmol of the alcohol in 12 mL of CH_2Cl_2 was added to a mixture of 12 mL of 0.1 mol/L sodium hydrogen carbonate solution, 2 g (8 mmol) of crystalline iodine, and 0.085 g (0.4 mmol) of 4-acetylamino-2,2,6,6-tetramethylpiperidine-1-oxyl (**I**) (alcohol–nitroxyl radical molar ratio of 10 : 1). The mixture was stirred during 1 h at 20°C, extracted with CH_2Cl_2 (2 × 15 mL), treated with 20 wt % solution of sodium thiosulfate (to remove iodine), and analyzed.

The reaction in the presence of tetraalkylammonium salts was performed similarly adding 4 or 0.4 mmol of the salt to the reaction mixture; the components molar ratios are given in the table.

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