Electrocatalytic Oxidation of Cyclic Ketones

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The oxidation of ketones is a way for preparing carboxylic acids and their derivatives, bifunctional compounds such as α-hydroxyketones, diketones and other useful intermediates in organic synthesis. The formation of adipic acid from cyclohexanone is an important industrial process.

The advance of electrooxidation procedures has provided organic chemists with a synthetic device of great promise. But in the case of the electrooxidation of ketones only some reactions which could provide product-selectivity are known.

The first attempts of the electrochemical oxidation of ketones resulted in the formation of a mixture of acids, saturated and unsaturated hydrocarbons, carbon monoxide and dioxide.[1] The anodic oxidation of cycloalkanones in aqueous alcohols gave mixtures of lactones of different types.[2]

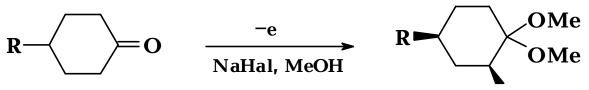
In some oxidative transformations of ketones such as haloform reaction and Favorskii rearrangement the preliminary α-halogenation of ketones is necessary. So for certain cases selective indirect electrooxidation of ketones with the electrochemically generated halides is also known.[3]

Continuing our studies on the electrooxidation of ketones we have accomplished indirect electrochemical oxidation of cyclic ketones in the presence of sodium halides.

It has been found that the result of the electrooxidation of cyclic ketones in methanol in the presence of sodium halides in an undivided cell depends mainly on the ring size of cyclic ketone.

Cyclopentanone affords 2,2-dimethoxycyclopentanone. While cyclohexanone gives rise 2,2-dimethoxycyclohexanol, and cyclic ketones with higher ring size undergo new type of the electrochemically induced Favorskii rearrangement with the formation of methyl cycloalkenecarboxylates containing in the ring on the one carbon atom less than starting ketone. Thus the simple electrocatalytic system can distinguish the ring size of cyclic ketones.

Now we report our results on the new stereoselective indirect electrochemical transformation of 4-substituted cyclohexanones **1** into *cis*-α-hydroxyketals **2,** in methanol, in an undivided cell in the presence of sodium halides as mediators :



1 **2**

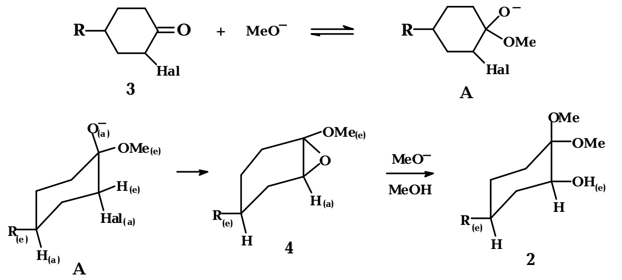
The structures of **2** were established by NMR spectroscopy data using COSY experiments and the CALM program[4] for further analysis of the spin system. Geometry calculations for isomeric structures of **2** were performed in the force field MM2.[5] Comparison of the calculated and experimental spectra of **2** established the equatorial position of the R group and hydroxy substituent in all of the compounds studied, *i. e*., a *cis* (ee) configuration for **2**.

The reactions on electrodes, which take place during the process, are usual for the mediatory system NaI - NaOH in methanol and lead to the formation of iodine or bromine at the anode and methoxide anions at the cathode.

Then α-monohalogenation of the enol form of the ketone takes place.

In the presence of methoxide anions there is an equilibrium between the two possible isomers of α-halogenoketone **3** posessing either an axial or an equatorial halogen.

α-Halogenoketone **3** thus formed, undergoes reversible methoxy anion attack on the carbonyl group with a further intramolecular nucleophilic substitution of the halogen and subsequent cyclization to form epoxide **4**.



It should be mentioned that the substituent **R** in all possible isomers of anion **A** presumably exists in the equatorial position. It has been established earlier that the isomer with both an axial halogen and a hydroxy anion substituent undergoes faster cyclization into the *cis*-epoxide **4**.[6] *cis*-Epoxide **4** exists in the form of a distorted chair with axial and equatorial epoxide C-O bonds.[7] Thus, in the resulting *cis*-epoxide **4** both **R** and **MeO** substituents are equatorial, the **O-C(OMe)** bond is axial and the **O-C(H)** bond is equatorial.[8]

The following attack on *cis*-epoxide **4** by the second methoxide anion resulted in the formation of ketal **2** with both the **R** and **OH** substituents equatorially orientated, *i. e.* leads to *cis*-5-substituted-2,2-dimethoxycyclohexanols **2**. Thus, kinetic and thermodynamic products coincide in the reaction studied.

Under the similar conditions 1-substituted-4-piperidinones were transformed into 1-substituted-4,4-dimethoxy-3-piperidinols in which hydroxy group exists in axial position most probably because of hydrogen bond between hydroxy group and nitrogen atom of the cycle.

Electrolysis of 2,2,6,6-tetramethyl-4-piperidinone led to the mixture methyl 2,2,5,5-tetramethyl-3-pyrrolidinecarboxylate and methyl 2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrolcarboxylate as a result of the electrochemically induced Favorskii rearrangement.

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