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FUNCTIONALIZATION OF THE δ-CARBON ATOM BY THE FERROUS ION INDUCED DECOMPOSITION OF ALKYL HYDROPEROXIDES IN THE PRESENCE OF CUPRIC SALTS

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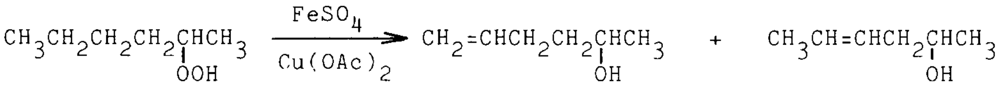
Abstract.- In the ferrous ion induced decomposition of alkyl hydroperoxides in the presence of cupric halides or pseudohalides, intramolecular functionalization, with ligand transfer from cupric salts to δ-carbon atom, is achieved.

Alkoxy radicals containing more than four carbon atoms in an alkyl chain, generated from different type of precursors[1], inculding alkyl hydroperoxides[2] and dialkyl peroxides[3], undergo intramolecular 1,5-hydrogen abstraction thus generating δ-carbon centered radicals. The stabilization of δ-alkyl radicals and functionality on the δ-carbon atom are determined by the precursors of the alkoxy radicals and reaction conditions[1]. By each of the reactions of this type only certain functional groups could be introduced at the nonactivated δ-carbon atom[1-4]. In the ferrous ion induced decomposition of alkyl hydroperoxides and dialkyl peroxides in the presence of cupric acetate, an electron-transfer oxidation of δ-alkyl radical occurs and δ-olefinic alcohols are the principal reaction products, in addition to small amounts of γ-olefinic alcohols[2-5].

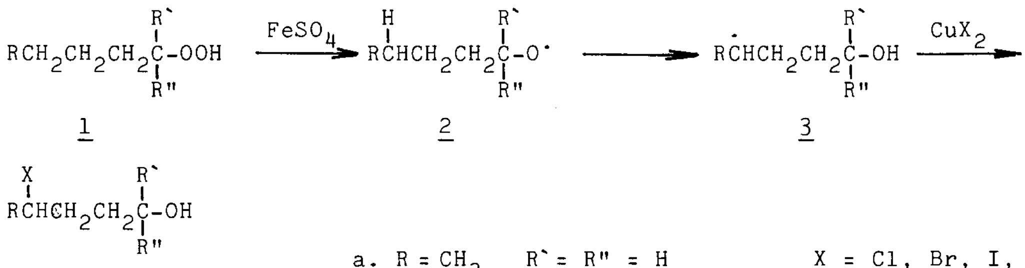


$$CH_3CH_2CH_2CH_2\underset{OOH}{CH}CH_3 \xrightarrow[Cu(OAc)_2]{FeSO_4} CH_2{=}CHCH_2CH_2\underset{OH}{CH}CH_3 + CH_3CH{=}CHCH_2\underset{OH}{CH}CH_3$$

60% 10%

As it had been established that a δ-alkyl radical is certainly an intermediate in the ferrous ion reduction of alkyl hydroperoxides[4-8], it was intriguing for us to investigate the ligand transfer oxidations of δ-carbon centered radicals in order to introduce different functional groups at the nonactivated carbon atom starting from an alkyl hydroperoxides. The oxidative ligand transfer of halides and pseudohalides from a metal ion to alkyl radicals generated in the fragmentation of alkoxy radicals[9], decarboxylation of acyloxy radicals[10] or by addition reactions[11], have been widely investigated[6,7,12]. The decomposition of 2-hexyl hydroperoxides in the presence of ferrous ion and cupric chloride is the only example of the ligand transfer oxidation of δ-alkyl radical generated by intramolecular hydrogen abstration[4].

In the ferrous ion induced decomposition of the primary 1a and 1b, secondary 1c and tertiary alkyl hydroperoxides 1d and 1e, the alkoxy radical 2 is generated which by subsequent intramolecular hydrogen abstraction affords the δ-carbon centered radical 3. The alkoxy radical 2 as well as the δ-alkyl radical 3 are not in radical pair system and they are sufficiently free that carbon centered radical 3 can be oxidatively intercepted by means of appropriate ligand transfer reagents such as cupric salts. Thus, when ferrous ion induced decompositions of alkyl hydroperoxides were performed in the presence of cupric halides or pseudohalides, such as chloride, bromide, iodide, thiocyanate and azide, oxidative interception of δ-alkyl radical 3 occurs and ligand transfer from cupric ion to the alkyl radical takes place and the corresponding halides and pseudohalides were introduced at the radicalic δ-carbon atom, furnishing δ-substituted alcohols 4, Table 1.



$$\underset{\mathbf{1}}{RCH_2CH_2CH_2\overset{R'}{\underset{R''}{C}}\text{-}OOH} \xrightarrow{FeSO_4} \underset{\mathbf{2}}{R\overset{H}{C}HCH_2CH_2\overset{R'}{\underset{R''}{C}}\text{-}O^{\bullet}} \longrightarrow \underset{\mathbf{3}}{R\dot{C}HCH_2CH_2\overset{R'}{\underset{R''}{C}}\text{-}OH} \xrightarrow{CuX_2} \underset{\mathbf{4}}{R\overset{X}{C}HCH_2CH_2\overset{R'}{\underset{R''}{C}}\text{-}OH}$$

4

a. $R = CH_3$ $R' = R'' = H$
b. $R = C_2H_5$ $R' = R'' = H$
c. $R = R' = CH_3$ $R'' = H$
d. $R = R' = R'' = CH_3$
e. $R = C_2H_5$ $R' = R'' = CH_3$

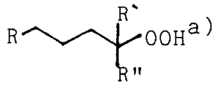
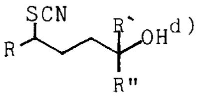
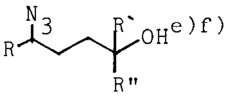
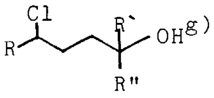
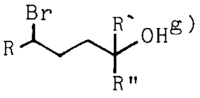
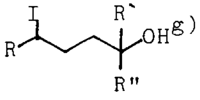
X = Cl, Br, I, SCN, N_3

As it was proposed that the ligand transfer oxidation of alkyl radicals generated from the other precursors by using cupric pseudohalides as a ligand transfer reagents the oxidation proceeds by an inner-sphere mechanism[12]. Since isothiocyanate derivatives were not obtained[13] in the ferrous ion decomposition of alkyl hydroperoxides in the presence of cupric thiocyanate, we belive that inner-sphere oxidation of δ-alkyl radical 3 involves attack of SOMO of alkyl radical on the sulfur site of the thiocyanate ligand[14]. If outer-sphere mechanism is involved the mixture of isothiocyanate and thiocyanate derivatives should be obtained[13].

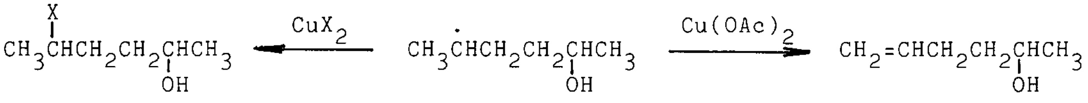
By using $Cu_3(en)_2(CN)_4$ as a ligand transfer oxidans for δ-alkyl radical 3 poor yields (up to 8%) of the corresponding δ-cyano alcohols were obtained.

As it has been pointed out, in the other well known reactions for intramolecular functionalization of the nonactivated δ-carbon atom, the functionality is determined by the precursor of the alkoxy radical[1]. However, when δ-carbon radicals are generated by the ferrous ion induced decomposition of alkyl hydroperoxides, they can be oxidatively intercepted either by cupric halides and pseudohalides as ligand transfer oxidans affording the corresponding δ-functionalized alcohols 4

Table 1. Ferrous ion induced decomposition of alkyl hydroperoxides in the presence of cupric halides and pseudohalides. Products and their yields (%).

 [a]	CuX_2				
	X = SCN[b]	X = N_3[c]	X = Cl	X = Br	X = I
R = CH_3, R\`=R"= H	 [d] (52)	 [e][f] (60)	 [g] (67)	 [g] (58)	 [g] (62)
R = C_2H_5, R\`=R"= H	(55)	(58)[e][h]	(68)	(55)	
R = R\`= CH_3, R"= H	(48)	(62)[e]	(65)		
R = R\`= R" = CH_3	(44)	(51)[e][i]			
R = C_2H_5, R\`= R"= CH_3	(45)	(47)[e][j]			

a) Primary and secondary alkyl hydroperoxides prepared as discribed by H. R. Williams and H. S. Mosher, J. Am. Chem. Soc., 76, 2984 (1954), while tertiary peroxides were made following ref. 5. Alkyl hydroperoxides were 93-97% purity. b) Prepared from cupric sulfate hydrate and potassium thiocyanate (1 : 2 molar ratio) in aqueous solution in inert atmosphere as it was discribed in ref. 10. c) Cupric azide was prepared by reaction of cupric sulfate hydrate with 2 mole of sodium azide in aqueous solution; precipitated cupric azide was filtered of and wet precipitate was dissolved in acetonitrile/acetic acid (6 : 4 v/v) to prepare 20% solution used in the reactions. d) δ-Hydroxy thiocyanates were identified, after glc separation, by ir (2160 cm^{-1}), mass spectra and elemental microanalysis, and obtained results are in full aggreement with the proposed structures. e) The structures of the δ-azido-alcohols were determined by ir spectra (2110 cm^{-1}) of crude reaction mixture and by reduction of δ-azido-alcohols by $LiAlH_4$ to the corresponding δ-amino-alcohols which have been characterized by ir and mass spectra and elemental analysis of their dibenzoyl derivatives. f) Dibenzoyl derivative, mp. 102°C. g) 1,4-Halogenhydrines were treated with methanolic potassium hydroxide and the corresponding cyclic ethers were analyzed by glc and compared with authentic samples. h) By using 0.5 eq. of cupric azide and 1 eq. of sodium azide almost same yield of δ-azido-alcohol was obtained. i) Dibenzoyl derivative, mp. 112°C. j) Dibenzoyl derivative, mp. 108°C.



$$CH_3\overset{X}{\overset{|}{C}}HCH_2CH_2\underset{OH}{\underset{|}{C}}HCH_3 \xleftarrow{CuX_2} CH_3\dot{C}HCH_2CH_2\underset{OH}{\underset{|}{C}}HCH_3 \xrightarrow{Cu(OAc)_2} CH_2{=}CHCH_2CH_2\underset{OH}{\underset{|}{C}}HCH_3$$

4c 3c

or by cupric acetate as an electron-transfer reagent yielding δ-unsaturated alcohols[2,4].

In a typical experiment: to a solution of 2.76 g of ferrous sulfate hydrate and 10 mmole of cupric halides or pseudohalides in 30 ml of acetonitrile/acetic acid (60/40 v/v) and 1 ml of water, 10 mmole of alkyl hydroperoxide was added over 0.5 hr period. The heterogenous reaction mixture was stirred under N_2 at room temperture for 5 to 8 hrs. The mixture was diluted with water and extracted with ether; the etheral solution was washed with aqueous $NaHCO_3$ and water. After removing of the solvent the reaction products were characterized as it is described in footnotes in Table 1.

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13. The reaction mixture obtained by ferrous ion decomposition of alkyl hydroperoxides in the presence of cupric thiocyanete was reduced by $LiAlH_4$ and only δ-mercapto alcohols were obtained and no traces of δ-amino alcohols were detected.
14. It was observed that thiocyanate ligand in cupric complexes is attached to copper (II) through nitrogen atom. R. N. Raymon and F. Basolo, Inorg. Chem., 7, 617 (1968); S. E. Livingstone, Quart. Rev., 19, 386 (1965).

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