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TERTIARY ALKYL AMINES: AN AUTOXIDATION-DEALKYLATION PROCESS. II.*

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Autoxidation of tertiary alkyl amines is not a common process: E.S.R. evidences support a base-catalyzed process. Several tertiary alkyl amines/water systems have been investigated in order to verify the generality of such a process, if some requests are satisfied.

KEY WORDS: Autoxidation, amines, aminoxyl-radicals, E.S.R.

The study of tertiary alkyl amines[1,2] oxidation is of considerable interest for organic chemists, as a current approach to the problem of reaction mechanism, and to biochemists[3] as well, in view of the biological importance of aliphatic amines. In the present work, several tertiary alkyl amines/water systems have been investigated in order to verify if, under certain conditions, trialkylamines can be readily oxidized by molecular oxygen in basic aqueous solution. In particular, trialkylamines with -OH or -CN substituents, into alkyl chains, were selected. Comparison with results obtained[4] with unsubstituted tertiary alkyl amines, let to conclude that the dealkylation trend seems unaffected by the presence of such groups.

EXPERIMENTAL

All the amines were commercial products except $Me_2N\text{-}Bu^t$ and $Me_2N\text{-}CH_2CH(CH_3)_2$ that were synthesized as reported in the literature.[10] The experiments were carried out at room temperature and the samples were prepared by mixing the freshly distilled[a] amine with distilled water in the presence of atmospheric oxygen. The reaction can be considered to take place almost immediately, in fact the intensity of the E.S.R. signal is yet at is highest intensity when the sample is introduced in the spectrometer cavity, roughly 40 seconds after mixing. It can be unambiguously attributed to a secondary alkyl nitroxide; its structure was confirmed comparing the ESR parameters with those of the radical obtained from the corresponding secondary alkyl amine with hydrogen peroxide. The pH measurements have been done at room temperature using a combined electrode.

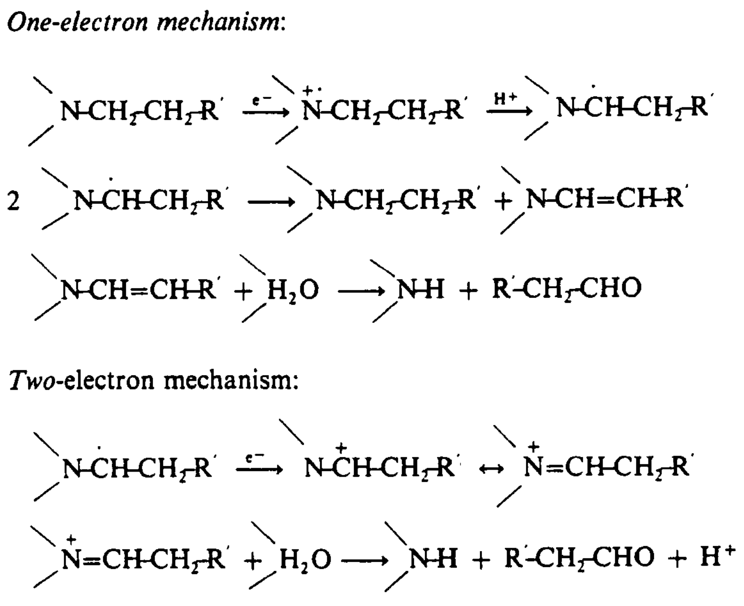
(*) Part. I is Ref.[4].

(a) An indirect test of the purity of amine, was the impossibility to succeed in the E.S.R. experiments when non distilled amines were used.

RESULTS AND DISCUSSION

In a previous paper[4] it was reported that when a freshly distilled tertiary alkyl amine is mixed with water in the presence of oxygen, at room temperature, a rapid reaction takes place leading to the formation of an alkene and/or a carbonyl-containing compound and a nitroxyl radical detectable by E.S.R.

It is known that amines can be oxidized either in the presence of a catalyst,[5] or electrochemically[6] or photochemically[7] and in particular it has been suggested that tertiary alkyl amines undergo dealkylation[6a] either by hydrolysis of the enamine formed in a *one*-electron process, or by hydrolysis of the iminium salt formed in a *two*-electron process, Scheme 1;



One-electron mechanism:

Two-electron mechanism:

SCHEME 1

however oxidation of amines by molecular oxygen is not very common. Studies performed in solution[11] report that the oxidation mechanism induced by oxygen could be similar to that involved in the autoxidation of an hydrocarbon, i.e. through a peroxyl radicals intermediate[3a,8] (Scheme 2).

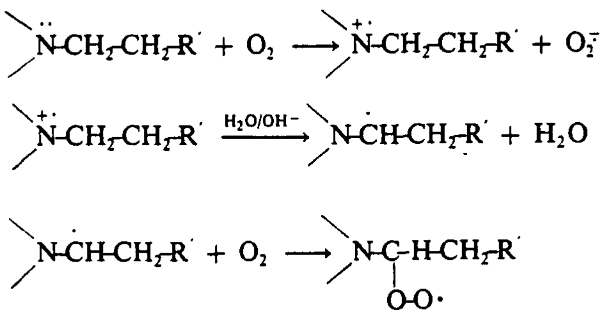
Following this mechanism, although the rate of the reaction is controlled by the redox process[b] between molecular oxygen and the amine, the product dermining step is an α-proton abstraction. Because tertiary alkyl amines have different alkyl chains, from which chain the α-proton will be abstracted is controlled by the acidity[c] and statistical abundance of the proton itself. However, for substrates containing methyl groups (Table I), no evidence of such a process was obtained, and yet proton abstraction should favored with such a group.

(b) It needs to be pointed out that the redox process (first reaction), seems poorly probable because of the redox potentials of the species involved.

TABLE I
Hyperfine Splitting Constants of Nitroxyl Radicals.

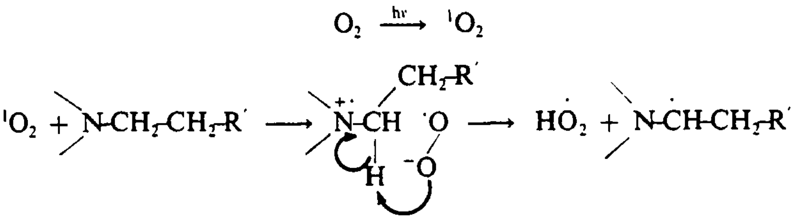
Amine	Nitroxide[a]	h.f.c. (Gauss)	Amine	Nitroxide[a]	h.f.c (Gauss)
$\begin{matrix}Et\\Et\end{matrix}\!>\!N{-}CH_2{-}CH_2{-}OH$	$\begin{matrix}Et\\HO{-}CH_2{-}CH_2\end{matrix}\!>\!N{-}O\cdot$	$a_N = 16.10$ $a_H(4H) = 11.40$	$\begin{matrix}Me\\Me\end{matrix}\!>\!N{-}CH_2{-}CH_2{-}OH$	$\begin{matrix}Me\\Me\end{matrix}\!>\!N{-}O\cdot$	$a_N = 17.00$ $a_H(CH_3) = 14.75$
$\begin{matrix}Et\\Et\end{matrix}\!>\!N{-}(CH_2)_2{-}\underset{OH}{CH_2}$	$\begin{matrix}Et\\Et\end{matrix}\!>\!N{-}O\cdot$	$a_N = 16.63$ $a_H(4H) = 11.50$	$\begin{matrix}Me\\Me\end{matrix}\!>\!N{-}CH_2{-}CH_2{-}\underset{OH}{CH_2}$	$\begin{matrix}Me\\Me\end{matrix}\!>\!N{-}O\cdot$	$a_N = 17.00$ $a_H(CH_3) = 14.75$
$\begin{matrix}Et\\Et\end{matrix}\!>\!N{-}CH_2{-}\underset{OH}{CH}{-}CH_3$	$\begin{matrix}CH_3{-}\underset{OH}{CH}{-}CH_2\\Et\end{matrix}\!>\!N{-}O\cdot$	$a_N = 16.00$ $a_{3H}(CH_2 = 1H) = 11.75$ $a_{1H} = 7.50$	$\begin{matrix}Me\\Me\end{matrix}\!>\!N{-}CH_2{-}\underset{OH}{CH}{-}CH_3$	No Radical[c]	
$\begin{matrix}i\text{-}Pr\\i\text{-}Pr\end{matrix}\!>\!N{-}(CH_2)_2{-}OH$	$\begin{matrix}i\text{-}Pr\\i\text{-}Pr\end{matrix}\!>\!N{-}O\cdot$ and $\begin{matrix}HO{-}(CH_2)_2\\i\text{-}Pr\end{matrix}\!>\!N{-}O\cdot$	$a_N = 16.75$ $a_N = 16.40$ and $a_H(CH_2) = 11.75$ $a_H(CH) = 4.75$ $a_H(CH) = 5.30$	$\begin{matrix}Me\\Me\end{matrix}\;N{-}CH_2{-}\overset{CH_3}{\underset{CH_3}{CH_2}}$	No Radical[c]	
$(HO{-}CH_2{-}CH_2)_3N$	$\begin{matrix}HO{-}CH_2{-}CH_2\\HO{-}CH_2{-}CH_2\end{matrix}\!>\!N{-}O\cdot$	$a_N = 15.50$ $a_H(4H) = 10.65$	$\begin{matrix}Me\\Me\end{matrix}\;N{-}\overset{CH_3}{\underset{CH_3}{C}}{-}CH_3$ (d)	$\begin{matrix}Me\\Me\end{matrix}\!>\!N{-}O\cdot$	$a_N = 17.00$ $a_H(CH_3) = 14.75$
$\begin{matrix}Et\\Et\end{matrix}\!>\!N{-}CH_2{-}CN$	No radical[b]		$\begin{matrix}Me\\Me\end{matrix}\!>\!N{-}CH_2{-}CH_2{-}CN$	$\begin{matrix}Me\\Me\end{matrix}\!>\!N{-}O\cdot$	$a_N = 17.00$ $a_H(CH_3) = 14.75$

(a). The "g" value of all nitroxides is 2.0055 ± 0.0001. (b) The pH of a saturated solution of this amine in water is less than 8 pH units, see Table II. (c) Only one hydrogen is present in β-position. (d) See ref.[4]



SCHEME 2

The reaction proceed equally well in the dark; in fact in one experiment with Et_3N/H_2O the same radical species (Et_2N-O•) was obtained. Thus, the possiblity of any photosensitized oxidation can be excluded, Scheme 3.



SCHEME 3

To point out the role played by the structure of the alkyl chain and in particular the presence of β-hydrogens, substrates with alkyl groups having one, or two, or three β-hydrogens were chosen. It has been found that the alkyl chain involved in the dealkylation process has to have at least two hydrogens in that position (Table I). In fact, comparing Et_2N-CH_2-CH(OH)-CH_3 and Me_2N-CH_2-CH(OH)-CH_3 it becomes evident that with the former amine, which has two different alkyl chains both with β-hydrogens, a mixture of two nitroxyl radicals should have been detected. The E.S.R. spectrum shows only the signal due to EtN(O•)CH_2-CH(OH)-CH_3; i.e. only the group with two β-hydrogens undergoes dealkylation. When Me_2N-CH_2-CH(OH)-CH_3

TABLE II
pH of water saturated solutions of amines.

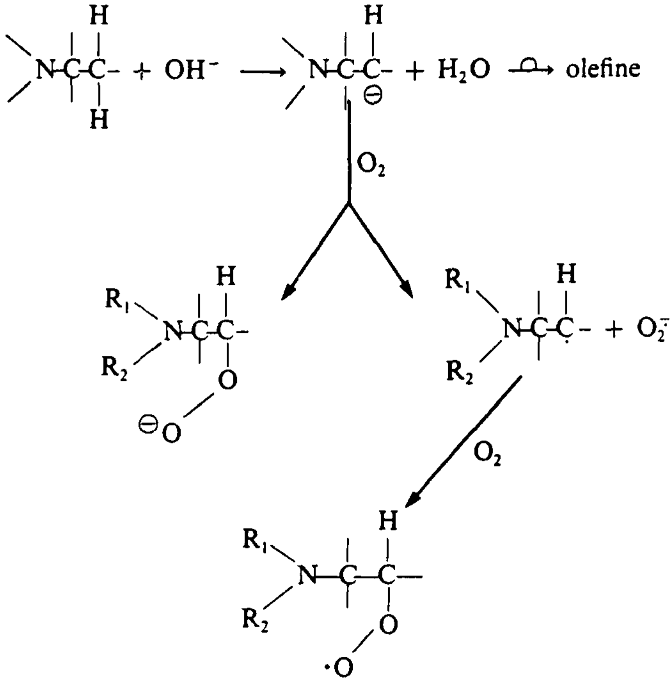
Amine	pH	Amine	pH
Et_2N CH_2CH_2OH	12.17	Me_2N CH_2CH_2OH	12.13
Et_2N $(CH_2)_2CH_2OH$	12.20	Me_2N $(CH_2)_2CH_2OH$	12.15
Et_2N CH_2 CH(OH)CH_3	12.28	Me_2N (CH_2 CH(OH)CH_3	11.88
(i-Pr)$_2$N CH_2CH_2OH	11.79	Me_2N CH_2 CH$(CH_3)_2$	10.20
(HO $CH_2CH_2)_3N$	11.22	Me_2N Bu^t	12.35
Et_2N CH_2CN	7.99	Me_2N CH_2CN	10.83

(c) The order of acidity based on inductive effects should be methyl > n-butyl > isobutyl > s-butyl ⩾ cycloexyl.

is used (only one alkyl chain has β-hydrogens), in agreement with the request of the presence of at least two β-hydrogens, no radical species was detected.

The compulsory presence of β-hydrogens could suggest that the enamine formation is involved in the dealkylation of simple aliphatic amines, but enamine formation should be independent from the number of hydrogens. Finally, the request of a basic media with pH > 9 is easily satisfied (Table II) except for 2(Ethylamino)acetonitrile (pH = 7.99) which, in fact, does not show evidence of radical species.

The reaction mechamism previously suggested[4] still appears to hold;



SCHEME 4

this concerted mechanism involves the formation of a carbanion, undergoing reaction with molecular oxygen (Scheme 4).

Attempts have been made to distinguish between the two possible routes, ionic and radical, but no clear results have been obtained at this stage of the research.

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