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CATION RADICALS OF HETEROCYCLIC N-OXIDES AND THEIR REACTIONS

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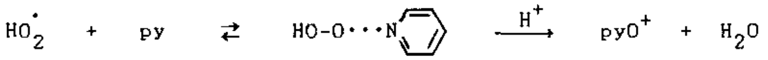
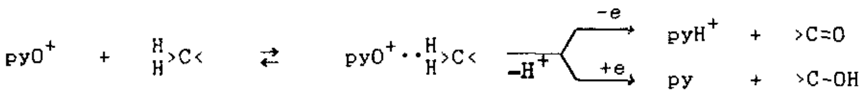
Abstract-Cation radicals of heterocyclic N-oxides were generated by electro- and photochemical one-electron oxidation of corresponding N-oxides. In their interaction with cyclohexane and toluene an intermediate complex was found to be produced which reacted with dioxygen to form oxidation products. One of the ways of cation radicals transformation is their deoxygenation producing corresponding amines. A hypothesis was put forward that cation radicals could be intermediates in hydrocarbon oxidation in pyridine solution.

Recently the problems of selective functionalization of alkanes aroused much interest[1]. Though alkane oxidation coupled with that of other compounds was known for many years[2] Barton et al. proposed an interesting new way of hydrocarbon oxidation by dioxygen based on the coupled process in pyridine[3]. The systems are known at present as GIF- and GIF-ORSAY systems[4,5] and involve an iron complex as the catalyst together with metallic iron, zinc or mercury cathode as reductants. Coupled hydrocarbon oxidation takes place in the presence of dioxygen. Ketones usually are the main products for compounds containing CH_2 groups but they are not formed via alcohols and there is much evidence that alkyl radicals are not the intermediates in the process[4]. The latter fact is very unusual for the mechanism of alkane oxidation by dioxygen Barton et al. proposed a hypothetical carbene iron complex as the key intermediate which reacts further to form the observed products[4].

An alternative hypothesis was put forward in the papers[6,7] with three-electron mechanism of C-H oxidation not involving transition metals. The hypothesis is base on the weak sensitivity of the reaction selectivity to the nature of the ligands and even of the metals used. GIF-like selectivity was observed also in hydrocarbon oxidation by hydrogen peroxide catalyzed by copper and iron salts[7-9]. Pyridine is again essential as the solvent and free radicals are not the intermediates for the main part of the reaction. These common features for the oxidation reactions (the necessity of pyridine and weak sensitivity to the nature of the catalyst) have led to the suggestion of the following hypothesis for the possible reaction mechanism[7] $HO_2^{\bullet}$ radicals formed in dioxygen reaction with a metal were postulated to react with pyridine and acid producing cation radicals pyO^+:


(1)

Simple estimates show this reaction to be thermodynamically allowed. Other molecules may in principle replace pyridine in *solvating* O^+ *and therefore* LO^+ may be called "solvated oxygen cation"[7] At the same time pyO^+ may be obtained *from pyridine N-oxide and* therefore represents the N-oxide cation radical (though some differences may arise due to different solvating molecules, e.g. in pyridine pyO^+ may be solvated by another pyridine molecule to form py_2O^+). PyO^+ is potentially a three-electron oxidant provided it can transfer O^+ to a substrate molecule. N-oxides are known to oxidize alkanes and to be deoxygenated when they are photochemically excited[10]. In conditions of mass-spectral analysis N-oxide cation radicals usually lose oxygen[11]. The following reactions may be suggested for pyO^+ interaction with a hydrocarbon molecule in solution:



$$pyO^+ + \overset{H}{\underset{H}{}}{>}C{<} \rightleftarrows pyO^+\cdot\cdot\overset{H}{\underset{H}{}}{>}C{<} \xrightarrow{-H^+} \begin{cases} \xrightarrow{-e} pyH^+ + {>}C{=}O \\ \xrightarrow{+e} py + {>}C{-}OH \end{cases} \qquad (2)$$

One-electron oxidation or reduction of the intermediate complex would lead to the formation of ketone or alcohol respectively without free alkyl radicals as intermediates.

At the same time pyO^+ is a strong one-electron oxidant ($E_{1/2}$ = 1.75 v, SCE[12]) and therefore may react with alkane or other organic molecules to form free radicals[13]:

$$pyO^+ + RH \longrightarrow pyO + R^{\cdot} + H^+ \qquad (3)$$

The latter reaction may proceed through H atom transfer:

$$pyO^{+} + RH \longrightarrow pyOH^{+} + R^{\cdot} \qquad (4)$$

$$pyOH^{+} \longrightarrow pyO + H^{+} \qquad (5)$$

To investigate the chemistry of N-oxides cation radicals they can be obtained by anodic oxidation of corresponding N-oxides[12]. Some of the cation radicals are sufficiently stable (e.g. those of phenazine di-N-oxide) to be characterized by their EPR spectra[14].

We have found[15] that pyO^{+} obtained by anodic oxidation of pyridine N-oxide is able to react with cyclohexane producing alcohol and ketone in the presence of dioxygen with the products ratio close to 1.2. Cyclic voltammetric study of various N-oxides at platinum electrode in acetonitrile has shown that the oxidation is diffusion-controlled and that the N-oxides studied undergo one-electron oxidation at potentials listed in Table 1

Table 1

Anodic peak potentials (E) of N-oxides in $CH_3CN/0.05M\ Et_4NClO_4$, Pt anode, $C_o = 2\cdot10^{-3}M$, scan rate = 0 2v/sec

N°	N-oxide	E,v,SCE
I	pyridine N-oxide	1.89
II	4-methoxypyridine N-oxide	1.50
III	4-nitropyridine N-oxide	2 30
IV	quinoxaline N-oxide	2 23
V	quinoxaline di-N-oxide	1.72
VI	α,α-dipyridyl di-N-oxide	1.88
VII	phenazine N-oxide	1.88
VIII	phenazine di-N-oxide	1.48

Whereas the heights of anodic peaks for compounds I-VIII are virtually equal, the corresponding cathodic peaks are observed only for the compounds II, V and VIII. For the latters the anodic and cathodic peak separation ($\Delta E = E_{ap} - E_{cp}$) is equal to 60mv, indicating reversible character of the electrode reaction. For all the other N-oxides cathodic response is absent even for the scan rates up to 1000v/sec. It shows the corresponding cation radicals to be very unstable.

For the cation radicals II, V, VIII their reactivities towards cyclohexane, toluene and benzene were investigated. The life-time (τ) of V cation radical does not change in the presencs of benzene even for the concentrations up to 1M, whereas τ decreases in the presence of 0.1M cyclohexane. Similar decrease of τ was observed in the presence of toluene even when its concentration was one order of magnitude lower than that of cyclohexane. Thus toluene is more active than cyclohexane probably because of weak C-H bond in methyl group since benzene is not active. It is essential that the introduction of dioxygen together with cyclohexane decreases τ further and the removal of O_2 returns τ to its initial value (without dioxygen). Since O_2 does not influence τ without hydrocarbon the effect of dioxygen may be attributed to its reaction with the complex formed in the N-oxide cation radical interaction with the hydrocarbon molecule:

$$LO^{+} + RH \rightleftarrows [LO\cdots RH]^{+\cdot} \genfrac{}{}{0pt}{}{\nearrow \text{products}}{\searrow \text{products}} \qquad (6)$$

No shift in redox pair LO/LO^{+} peak potential was observed at the addition of a hydrocarbon for cation radicals V and VIII, thus the complex formation apparently does not change LO^{+} redox properties.

To investigate the reactivity of short-life cation radicals, particularly of pyO^{+} we have worked out the method of their generation in conditions of flash-photolysis[16]. PyO^{+} cation radicals were generated in acetonitrile solution in reaction of pyO with excited chloranil molecule (λ = 360nm) with a high redox potential for the triplet state ^{3}CQ (E° = 2.15v,SCE[17]). The latter reacts readily with pyO:

$$^{3}CQ + pyO \longrightarrow CQ^{\cdot -} + pyO^{+} \quad (k_7 = 7\cdot 10^{9}\ M^{-1}sec^{-1}) \quad (7)$$

Both ion radicals quickly recombine:

$$CQ^{\cdot -} + pyO^{+} \longrightarrow CQ + pyO \quad (k_8 = 2.5\cdot 10^{9}\ M^{-1}sec^{-1}) \quad (8)$$

Optical absorption of pyO^{+} in the visible light turned out to be weak and in the same region as the absorption of CQ^-. To separate the absorption spectrum of pyO^+ one has to prevent the fast reaction 8. This was achieved by addition of cupric salt readily reacting with $CQ^{\bar{\cdot}}$.

$$CQ^{\bar{\cdot}} \quad + \quad Cu^{2+} \quad \longrightarrow \quad CQ \quad + \quad Cu^{2+} \qquad (k_9 = 1\ 5 \cdot 10^9 M^{-1} sec^{-1}) \qquad (9)$$

In the range of Cu^{2+} concentrations $(1\text{-}10)\ 10^{-4}M$ virtually all CQ^- is oxidized by Cu^{2+} during the flash, therefore the short-living intermediate observed may be only pyO^+ In the spectrum of the intermediate a broad line is observed with the maximum in the region 430-460 nm (Fig.1) and $\varepsilon = 7\ 10^2 M^{-1} cm^{-1}$.

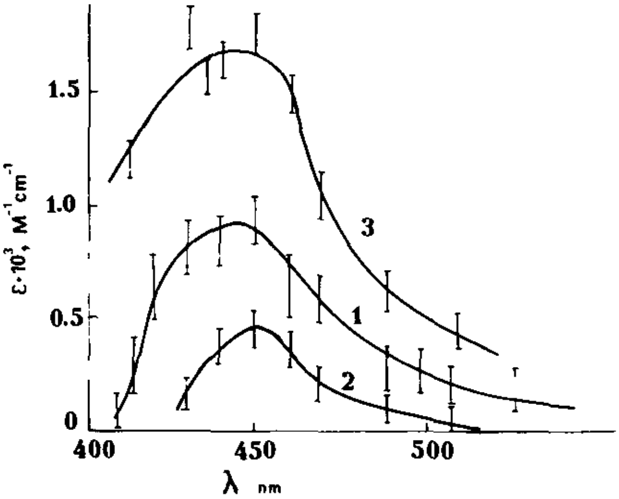


Fig 1 Absorption spectra of the intermediates formed in quenching of ^3CQ by pyO in CH_3CN $[CQ] = 4\ 10^{-4}M$; $[Cu(ClO_4)_2] = 4 \cdot 10^{-4}M$; $[pyO] = 1\ 10^{-2}M$, 1: without RH: 2. with toluene ($[PhCH_3] = 4\ 10^{-2}M$);3: with cyclohexane ($[C_6H_{12}] = 0\ 8M$)

PyO^+ disappears in reactions with Cu^+ formed ($k \approx 10^9 M^{-1} sec^{-1}$) and with the solvent ($k < 10^3 sec^{-1}$) Introduction of hydrocarbons decreases the life-time of pyO^+. At the increase of toluene concentration τ first decreases and then stops changing with $[PhCH_3]$ in the range $(1\text{-}3) \cdot 10^{-2}M$, the effective rate constant being $2\ 10^3 sec^{-1}$ for this range

The kinetics supports the suggestion that an intermediate complex forms reversibly in the process

$$\mathrm{pyO^+} \quad + \quad \mathrm{RH} \quad \overset{K_{10}}{\rightleftarrows} \quad [\mathrm{pyO\cdots RH}]^{+\cdot} \quad \xrightarrow{k_{10}} \quad \text{products} \qquad (10)$$

K_{10} may be easily estimated from the kinetic data (Table 2) and it is seen that at toluene concentrations higher than $1\cdot10^{-2}$M almost all $\mathrm{pyO^+}$ must be in the form of the complex with toluene. The spectrum of the complex does not differ much from that of $\mathrm{pyO^+}$ itself. The band is more narrow, the maximum is shifted to the longer wave region and the extinction coefficient is smaller (Fig.1)

Table 2

Thermodynamic and kinetic parameters[16] of the reactions 10 and 11

Constant	$PhCH_3$	CH_3OH	C_6H_{12}
K_{10}, M^{-1}	$2\cdot10^2$	$1\cdot10^2$	$1\cdot10$
$k_{10}\cdot10^{-3}, sec^{-1}$	2.0	1.7	1.2
$k_{11} M^{-1} sec^{-1}$	$5\cdot10^8$	$5\cdot10^7$	$5\cdot10^6$

Similar picture was observed in the case of cyclohexane which was again less reactive. Because of smaller K_{10} and limited solubility of C_6H_{12} the life-time of $\mathrm{pyO^+}$ does not reach independence on C_6H_{12} concentration. The spectrum obtained at $[C_6H_{12}] = 0.8M$ has a maximum somewhat shifted to the longer wave region with the extinction coefficient about twice higher than that for $\mathrm{pyO^+}$ (Fig.1). In the same way as in the conditions of electrochemical generation benzene does not influence the $\mathrm{pyO^+}$ life-time, whereas methanol was found to behave similarly to toluene and cyclohexane (Table 2). Weak sensitivity of K_{10} to the hydrocarbon nature is noteworthy: perhaps the rate of the reaction 10 is determined by N-O bond cleavage in the complex.

Similarly to the electrochemical experiments the life-time of $\mathrm{pyO^+}$ falls down when a hydrocarbon and dioxygen are present together. Since dioxygen alone does not influence the kinetics of $\mathrm{pyO^+}$ reaction, the suggestion may be put forward that O_2 reacts with the complex $[\mathrm{pyO\cdots RH}]^+$, e g.:

$$[\mathrm{pyO\cdots RH}]^{+\cdot} \quad + \quad O_2 \quad \xrightarrow{k_{11}} \quad HO_2 \quad + \quad \text{products} \qquad (11)$$

The k_{11} values are given in the Table 2. It is seen that k_{11} increases with the decrease of the hydrocarbon C-H bond energy: for toluene k_{11} is close to the rate constant of O_2 reaction with benzyl radical[18].

Thus N-oxides cation radicals definitely react with hydrocarbons, O_2 participating in the reaction. It is essential to prove that O^+ can be transferred from the cation radical to a substrate molecule and to find out the way of O_2 participation.

To determine the reaction products the electrolysis of phenazine di-N-oxide was carried out at controlled potential (E = 1 55v,SCE). In the course of the elecrtolysis di-N-oxide disappears, current-yeald (η) of the reaction approaching 50%. Corresponding mono-N-oxide is accumulating during the process, the yield being about 50% with respect to the di-N-oxide consumed. The presence of O_2 does not influence the reaction. When the electrolysis is carried out in the presence of cyclohexane (without O_2) di-N-oxide also disappears (η = 25%), however, instead of mono-N-oxide a new product is observed which has not yet been identified No cyclohexanone and cyclohexanol were detected in the products of the reaction

In the presence of O_2 mono-N-oxide is again formed with the yield about 50% and η close to 10% with respect to di-N-oxide consumed. Cyclohexanone is the main product of C_6H_{12} oxidation, cyclohexanol yield being less than 10%. The concentration of cyclohexanone formed is twice as large as that of di N-oxide consumed.

It may be concluded that O^+ transfer to a substrate is a possible reaction of heterocyclic N-oxide cation radicals Cation radicals may be suggested to be intermediates in the well-known "oxidative deoxygenation" of N-oxides.

In the case of phenazine di-N-oxide solution without a hydrocarbon the cation radical presumably attacks another di-N-oxide molecule transferring O^+ and producing some oxidation products This explains the reaction stoichiometry (half mole of mono-N-oxide per one mole of initial di-N-oxide).

In the presence of a hydrocarbon but without O_2 the complex of the cation radical with RH reacts further to form some kind of condensation product. When O_2 is present it reacts with the complex (possibly abstracting H atom) and produces mono-N-oxide again with hydrocarbon oxidation products:

$$LO^+ + RH \rightleftarrows [LO\cdots RH]^{+\cdot} \xrightarrow{O_2} LH^+ + {>}C{=}O + HO_2^{\cdot} \qquad (12)$$

The reaction 12, *however, does not represent* the observed stoichiometry quantitatively. Thus the ketone actual yield is higher than according to 12. This may be due to short chains, e.g. $HO_2^{\bullet}$ formed might again produce LO^+ in a reaction of the type 1, or the reaction 12 and one-electron reaction of the type 3 may develop in parallel We hope to find more precise picture of LO^+ reactions in our *future investigations*.

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REFERENCES

1. A E. Shilov, "Activation of Saturated Hydrocarbons by Transition Metal Complexes", Reidel, Dordrecht, 1984.
2. Yu.V. Geletii, E.I. Karasevich, and A.A. Shteinman, Neftekhimiya, 1978, 18, 673.
3. D.H.R. Barton, M.J. Gastiger, and W.B. Motherwell, J.Chem.Soc., Chem. Commun., 1983, 41.
4. D.H.R. Barton, J. Boivin, M. Gastiger, J.Morszycki, R.S Hay-Motherwell, N. Ozbalik, and K.M. Schwartzentruber, J.Chem.Soc., Perkin Trans.1, 1986, 947; D.H.R. Barton, J Boivin, W.B. Motherwell, N. Ozbalik, and K.M. Schartzentruber, Nouv.J.Chim, 1988, 10, 387, and refs.therein.
5. G. Balavoine, D.H.R Barton, J.Boivin, A. Gref, N. Ozbalik, and H. Rivier, Tetrahedron Lett., 1986, 27, 2849; G. Balavoine, D.H.R. Barton, J. Boivin, A. Gref, N Ozbalik, and H. Rivier, J.Chem.Soc., Chem.Commun., 1986, 1727.
6. Yu.V. Geletii, G.V. Lubimova, and A.E. Shilov. Kinetika i Kataliz, 1985, 26, 1023.
7. Yu.V Geletii, V.V Lavrushko, and A E. Shilov, Dokl.Akad.Nauk SSSR, 1986, 288, 139
8. Yu.V. Geletii. in: Proc. 7th French-Soviet Seminar on Catalysis, Univ. Louis Pasteur, Strasbourg, 21-26 September 1986, p 72; Yu.V.Geletii, and A.E. Shilov, "The Role of Oxygen in Chemistry and Biochemistry", W. Ando, ed.,Elsevier·Amsterdam, 1988, p.293.
9. Yu.V. Geletii, V.V. Lavrushko, and G.V. Lubimova, J.Chem.Soc., Chem.

Commun., 1988, 936.

10. A Albini and M. Alpegiani, *Chem.Rev.*, 1984, **84**, 43.
11. R. Grigg and B.G. Odell, *J.Chem.Soc., B*, 1966, 218
12. H. Miyazaki, T. Kubota, and M.Yamakawa, *Bull.Chem.Soc.Japan*, 1972, **45**, 780.
13. S I Kulakovskaya, S.N. Shamaev, and V.M. Berdnikov, *Izv.AN SSSR, Ser. Khim.*, (in press)
14. K. Nishikida, T. Kubota, N. Miyazaki, and Sh. Sakata, *J.Mag.Res.*, 1972, **7**, 280.
15. S I Kulakovskaya, Yu.V. Geletii, L.A. Kushch, S.N. Shamaev, and A E. Shilov, *Kinetika i Kataliz*, 1987, **28**, 1013.
16. Yu.G.Geletii, V.A. Kuzmin, P.P. Levin, and V Ya Shafirovich, *React. Kinet.Catal.Lett.*, 1988, **37**, 307.
17. N.A. Shcheglova, D.V Shigorin, G G. Yababson, and L.Sh. Tushishvili, *Zh. Fiz.Khim.*, 1969, **43**, 1984.
18. E.T. Denisov, "Rate Constants of Homolytic Liquid-Phase Reactions", Nauka, Moscow, 1977

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