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Oxidation of N-Alkylhydroxylamines. II.[1] Reaction of N-Alkylhydroxylamines with *tert*-Butylhydroperoxide

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The title reaction in benzene gives a C-nitroso compound, *tert*-butanol and presumably water according to the equation:

$$\text{RNHOH}+\textit{tert}\text{-BuOOH}\longrightarrow \text{R–N=O}+\textit{tert}\text{-BuOH}+\text{H}_2\text{O}$$

During the reaction electron spin resonance (ESR) spectra due to $\underset{\substack{| \\ \text{H}}}{\text{RNO}}\cdot$ is observed.

In the presence of a large excess of N-alkylhydroxylamine, *tert*-butylhydroperoxide decomposes through a 1:2 complex with N-alkylhydroxylamine and the activation energy of the reaction is about 12 kcal.

Unless N-alkylhydroxylamine is present in fairly large excess, *tert*-butylhydroperoxide decomposes by direct homolysis:

$$\textit{tert}\text{-BuOOH}\longrightarrow \textit{tert}\text{-BuO}\cdot+\text{HO}\cdot$$

and the activation energy is about 33 kcal.

There are few reports of kinetic studies on the oxidation of hydroxylamine derivatives, unlike amines, and these studies have been insufficient to clarify oxidation mechanism. Moreover it seems probable that instability of hydroxylamine derivatives and their oxidation products, such as nitroso compounds or nitrones[3)] would make kinetic studies on the mechanism very difficult.

While investigating the oxidation of hydroxylamines, we found that *tert*-butylhydroperoxide oxidized N-alkylhydroxylamines in benzene at about 50° at an appropriate rate for kinetic studies.

tert-Butylhydroperoxide (*t*-BHPO) has been widely used to initiate chain reactions and convert alkenes to epoxides,[4)] but its kinetic and thermodynamic behaviours do not appear to have been studied in detail. For example, attempts to measure the rate of thermal homolysis of the O–O bond have not been successful,[5)] probably due to induced decomposition of *t*-BHPO, in which radicals arising from its spontaneous homolysis of O–O bond and from other sources should attack *t*-BHPO.

In the present paper, we propose a mechanism for the title reaction and also report results on the kinetic behaviour of *t*-BHPO.

Result and Discussion

When *t*-BHPO was mixed with N-alkylhydroxylamines of the type $\text{R(Me)}_2\text{CNHOH}$ where R was Me, Et, or CH_2OAc in benzene at 50° in the dark, slow development of the characteristic blue colour of a C-nitroso compound was observed.[1)] However, when R was CN, COOEt or CH_2OH no blue colour was observed, because of the instability of C-nitroso compounds produced from these N-alkylhydroxylamines.

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1) Part I: S. Ozaki, H. Sayo, and M. Masui, *Chem. Pharm. Bull.* (Tokyo), **19**, 2389 (1971).
2) Location: *1, Toneyama-6-chome, Toyonaka.*
3) H.E. De La Mare and G.M. Coppinger, *J. Org. Chem.*, **28**, 1068 (1963).
4) W.F. Brill and N. Indictor, *J. Org. Chem.*, **29**, 710 (1964).
5) *a*) R.R. Hiatt and W.M. Strachan, *J. Org. Chem.*, **28**, 1893 (1963); *b*) R.R. Hiatt and K.C. Irvin, *ibid.*, **33**, 1436 (1968).

Hence, we investigated the kinetics of the reaction using N-alkylhydroxylamines which gave stable C-nitroso compounds. The N-alkylhydroxylamines used were *tert*-butylhydroxylamine (*t*-BHA), *tert*-amylhydroxylamine and 1,1-dimethyl-2-acetoxyethylhydroxylamine $Me_2C(CH_2OAc)NHOH$.

The appearance of the C-nitroso compound was followed by observing the absorption at 680 mμ and the absorbance at infinite time was taken as a measure of the amount of C-nitroso compound formed in a particular kinetic run. The yields of the C-nitroso compounds are shown in Table I, which shows that the yields were essentially quantitative ($\geqq 90\%$).

Table I. Reactions of N-Alkylhydroxylamines and *t*-BHPO in Benzene at 50°

N-Alkylhydroxylamine 10^{-2}M	*t*-BHPO 10^{-2}M	Products (C-Nitrosocompound) 10^{-2}M
t-BHA		
3.28	1.98	1.96
1.61	1.98	1.44
1.87	2.99	1.68
t-AHA		
1.50	1.98	1.34

t-BHA: *tert*-butylhydroxylamine *t*-AHA: *tert*-amylhydroxylamine

Thus the stoichiometry of the reaction can be written:

$$R(Me)_2CNHOH + (Me)_3COOH \longrightarrow R(Me)_2CN{=}O + (Me)_3COH + H_2O$$

tert-Butanol, another product of the reaction was detected by gas liquid partition chromatography, but its rate of appearance could not be measured, because decomposition of *t*-BHPO during the analysis also gave *tert*-butanol.

In the reactions with *t*-BHA (2.5—5×10^{-1}M) and *t*-BHPO (2—3×10^{-2}M) at 50°, the pseudo first-order plots were linear for over 70% of the reaction. The pseudo first-order rate constant was independent of both the initial concentration of *t*-BHPO and the concentration of *t*-BHA, which was present in excess. This means that the reaction was zero-order with respect to *t*-BHA under these conditions.

An Arrhenius plot of the first-order rate constants gave an activation energy of about12 kcal. This value for the activation energy is like that for the reaction of diphenylhydroxylamine with benzoylperoxide,[6] in which the activation energy has been reported to be 12±0.7 kcal.

Thus, it is concluded that the oxidation of *t*-BHA with *t*-BHPO produces *tert*-nitrosobutane through molecule-induced homolysis of *t*-BHPO. Moreover the zero-order dependence on *t*-BHA concentration suggests that *t*-BHA reversibly forms a complex with *t*-BHPO and equilibrium of the reaction strongly favours complex formation.

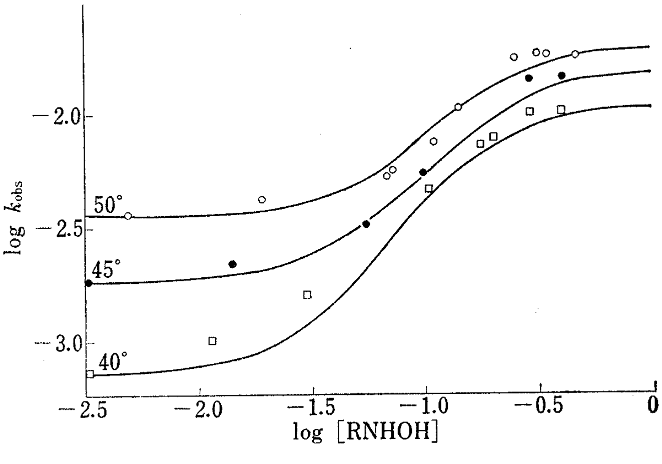

Fig. 1. Experimental and calculated Values of k_{obs} in Reactions with Various Initial Concentrations of *t*-BHA and a Constant Initial Concentration of *t*-BHPO (1.98×10^{-2}M)

solid lines,——: calculated values; ○, ●, □——: experimental values

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[6] G.R. Chalfont and M.J. Perkins, *J. Chem. Soc.* (*B*), **1971**, 245.

Next, reactions were carried out with initial concentration of 3.1×10^{-3}M to 5.0×10^{-1}M *t*-BHA and a constant initial concentration of *t*-BHPO (1.98×10^{-2}M) at 40°, 45°, and 50°. The effect of the initial concentration of *t*-BHA on the rate of the reaction is shown in Fig. 1. With concentration of 6.3×10^{-2}—2.5×10^{-1}M *t*-BHA, the reaction was initially approximately pseudo first-order with respect to *t*-BHPO and the rate constant decreased with decrease in *t*-BHA concentration.

On the other hand, at initial concentrations of *t*-BHA, $[t\text{-BHA}]_0$, below 6.3×10^{-2}M at 50° the reaction was first-order with respect to *t*-BHPO concentration and the rate constant was essentially independent of the initial concentration of *t*-BHA.

When the concentration of *t*-BHA was below 3.1×10^{-3}M, the activation energy was calculated to be about 33 kcal.

With *tert*-amylhydroxylamine the same activation energy was observed.

The results imply that induced homolysis of *t*-BHPO through complex formation contributes to the over-all rate at $[t\text{-BHA}]_0$ above 2.5×10^{-1}M, while direct homolysis of *t*-BHPO becomes rate-determining at $[t\text{-BHA}]_0$ below 6.3×10^{-2}M.

The formation of the complex was established as follows.

It has been thought that *t*-BHPO formed a 1: 1 complex with *t*-BHA.⁷⁾ Thus the reaction should involve parallel reactions in which *t*-BHPO decomposes both through the 1: 1 complex and by direct homolysis.

However, it was found that the rate constants evaluated from the above reaction mechanism were not in good agreement with the observed rate constants.

Another possibility is the following parallel reactions:

$$\mathrm{A} \xrightarrow{k_1} \mathrm{C}$$

$$\mathrm{A} + 2\mathrm{B} \overset{K}{\rightleftarrows} (\mathrm{AB}^2)$$

$$(\mathrm{AB}^2) \xrightarrow{k_1'} \mathrm{C} + 2\mathrm{B}$$

$$\mathrm{C} + \mathrm{B} \xrightarrow{\text{fast}} \mathrm{D}\ (\text{product})$$

for which the rate of the reaction can be written as:

$$d[\mathrm{D}]/dt = d[\mathrm{C}]/dt = k_1[\mathrm{A}] + k_1'K[\mathrm{A}][\mathrm{B}]^2 = (k_1+k_1'K[\mathrm{B}]^2)[\mathrm{A}]_{\text{tot.}}/(1+K[\mathrm{B}]^2) \qquad (1)$$

where [A], [B], [C], and [D] are the concentrations of *t*-BHPO, *t*-BHA, the radicals arising from homolysis of *t*-BHPO and the product (C-nitroso compound), respectively, and $[\mathrm{A}]_{\text{tot.}}$ is the total concentration of *t*-BHPO. (A B²) represents a 1:2 complex of *t*-BHPO with *t*-BHA and $K=[\mathrm{A\ B}^2]/[\mathrm{A}][\mathrm{B}]^2$.

When the concentration of *t*-BHA is such that $K[\mathrm{B}]^2\gg1$ or $(k_1'/k)K[\mathrm{B}]^2\ll1$, the reaction should be first-order.

If either of the above conditions is not satisfied, the rate constant of the reaction is not a simple term.

However, the initial rate of each reaction will be expressed as:

$$d[\mathrm{D}]/dt = d[\mathrm{C}]/dt \fallingdotseq (k_1+k_1'K[\mathrm{B}]_0^2)[\mathrm{A}]_{\text{tot.}}/(1+K[\mathrm{B}]_0^2) = k_{\text{obs.}}[\mathrm{A}]_{\text{tot.}} \qquad (2)$$

where $[\mathrm{B}]_0$ is the initial concentration of *t*-BHA.

The rate constants evaluated experimentally at $[\mathrm{B}]_0=3.1\times10^{-3}$M and at $[\mathrm{B}]_0=0.5$M were used as the values of k_1 and k_1' respectively (Table II).

Values of the equilibrium constant, *K*, were determined as 43.7, 47.8, and 60.2 at 50°, 45° and 40°, respectively, from Eq. (2) using the values of $[\mathrm{B}]_0$ at $k_{\text{obs}}=(k_1+k_1')/2$ in Fig. 1.

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7) H.E. De La Mare, *J. Org. Chem.*, **25**, 2114 (1960).

Table II. The Rate Constant evaluated experimentally at $[B]_0=3.1\times10^{-3}\,\mathrm{M}$ (k_1) and $[B]_0=0.5\,\mathrm{M}$ (k_1')

Temp. (°C)	$k_1\times10^3$ min^{-1}	$k_1'\times10^3$ min^{-1}
50	3.55	18.6
45	1.82	14.5
40	0.7	10.3

The plot of $k_{\mathrm{obs.}}$ against $[B]_0$ calculated using Eq. (2) is in close agreement with that obtained experimentally (Fig. 1).

Thus under the present conditions the decomposition of *t*-BHPO takes place in two ways: by direct homolysis and by induced homolysis through a 1:2 complex of *t*-BHPO and *t*-BHA.

However, values of $k_{\mathrm{obs.}}$ calculated based on a 1:3 complex and a 1:1 complex seem to show better agreement in the region of $[B]_0> 2.1\times10^{-1}\,\mathrm{M}$ and $[B]_0 <5\times10^{-3}\,\mathrm{M}$, respectively.

The observation that the reaction is first-order with respect to *t*-BHPO excludes the possibility of a chain reaction in which radicals such as HO· or $Me_3CO\cdot$ formed by homolysis of *t*-BHPO attack *t*-BHPO. Hence, HO· or $Me_3CO\cdot$ mainly attacks *t*-BHA forming $Me_3C\underset{\mathrm{H}}{\underset{|}{\mathrm{N}}}O\cdot$.

Figure 2 shows that two nitroxides, concluded to be $Me_3C\underset{\mathrm{H}}{\underset{|}{\mathrm{N}}}O\cdot$ and $(Me_3C)_2NO\cdot$, were detected during the reaction of *t*-BHA with *t*-BHPO at 70°.

As described previously,[6] the nitroxide $(Me_3C)_2NO\cdot$ is generated by photolysis of *tert*-nitrosobutane, one of the reaction products.

From the experimental observation it is concluded that, (a) the reaction obeys first-order kinetics in the regions $[t\text{-BHA}]_0 <6.2\times10^{-2}\,\mathrm{M}$ and $[t\text{-BHA}]_0>2\times10^{-1}\,\mathrm{M}$ (50°), (b) the value of activation energy for the reaction in which the direct homolysis of *t*-BHPO, $Me_3COOH\rightarrow Me_3CO\cdot+HO\cdot$, is major importance to the reaction is about 33 kcal, and that of induced homolysis through a 1:2 complex is about 12 kcal., and (c) a nitroxide, $Me_3C\underset{\mathrm{H}}{\underset{|}{\mathrm{N}}}O\cdot$, is generated in the reaction.

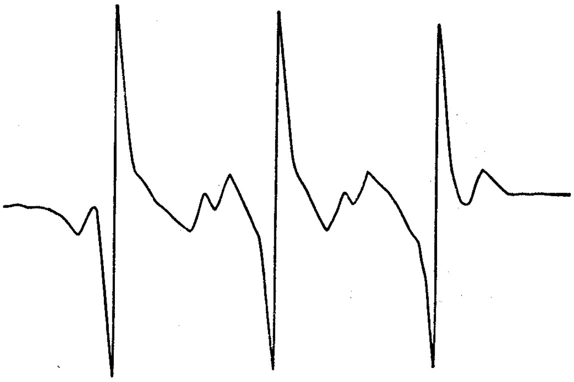


Fig. 2. ESR Spectrum of Paramagnetic Intermediate formed from *tert*-Butylhydroxylamine

mixture of radicals responsible for *tert*-butylnitroxide (A_N = 13.3 G A_{NH}=11.0 G) and di-*tert*-butylnitroxide (A_N = 15.4 G)

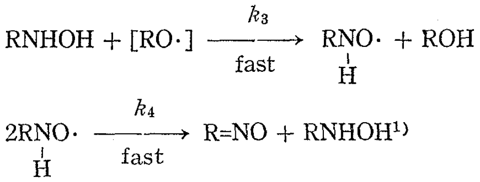
Accordingly the following mechanism is proposed:

$$2\mathrm{RNHOH} + \mathrm{ROOH} \overset{K}{\rightleftarrows} [\text{complex}]$$

$$[\text{complex}] \xrightarrow[\text{slow}]{k_1'} 2\mathrm{RNHOH} + [\mathrm{RO}\cdot] + [\mathrm{HO}\cdot]$$

$$\mathrm{ROOH} \xrightarrow[\text{slow}]{k_1} [\mathrm{RO}\cdot] + [\mathrm{HO}\cdot]$$

$$\mathrm{RNHOH} + [\mathrm{HO}\cdot] \xrightarrow[\text{fast}]{k_2} \mathrm{R}\underset{\mathrm{H}}{\underset{|}{\mathrm{N}}}\mathrm{O}\cdot + \mathrm{H_2O}$$



$$\mathrm{RNHOH} + [\mathrm{RO}\cdot] \xrightarrow[\text{fast}]{k_3} \mathrm{R}\underset{\mathrm{H}}{\underset{|}{\mathrm{N}}}\mathrm{O}\cdot + \mathrm{ROH}$$

$$2\mathrm{R}\underset{\mathrm{H}}{\underset{|}{\mathrm{N}}}\mathrm{O}\cdot \xrightarrow[\text{fast}]{k_4} \mathrm{R{=}NO} + \mathrm{RNHOH}^{1)}$$

This mechanism included formation of the complex which is responsible for the upper limit for the value of k_{obs}.

A similar example of formation of a complex preceding molecule-induced homolysis has been reported, but no evidence was given for formation of the complex.[6]

t-BHA reacts rapidly with $\mathrm{Me_3CO\cdot}$ or $\mathrm{HO\cdot}$, and so it inhibits radical-induced homolysis of *t*-BHPO. Accordingly, the activation energy of the reaction may show the homolytic dissociation energy of *t*-BHPO, $\mathrm{D(Me_3CO\text{-}OH)}$, when the first-order rate constants are extrapolated to zero concentration of *t*-BHA. Indeed the value of 33 kcal. for the activation energy at $[t\text{-BHA}]_0 = 3.1\times10^{-3}\,\mathrm{M}$ falls in the range of experimental values quoted previously.

However, the reaction at $[t\text{-BHA}]_0 < 3\times10^{-3}\,\mathrm{M}$, where direct homolysis of *t*-BHPO has a major effect on the over-all rate, showed poor reproducibility, since the surface condition of the quartz reactor, cell, markedly affected the reaction rate. Hence, there was no significance in extrapolating to zero concentration of *t*-BHA.

As shown in the reaction scheme, the rate-determining step of the reaction is the homolysis of *t*-BHPO in the complex or of free *t*-BHPO, not the formation of the complex or generation of the nitroxide. Therefore, detailed information on the mechanism of formation of the complex or generation of nitroxide can not be obtained kinetically with this system. To investigate these problems further studies are required on oxidation of hydroxylamines with radicals.

Experimental

Materials——N-Alkylhydroxylamines and the corresponding C-nitroso compounds were prepared as described previously.[1]

Commercial *tert*-butylhydroperoxide was purified by distilation under reduced pressure (bp 35° 20 mmHg), and analysed using the method described by Wagner and Smith.[8]

Benzene was purified as described previously.[1]

Kinetic Measurements——The reactions were carried out using 6 ml of N-alkylhydroxylamine solution and 1 ml of *t*-BHPO solution both in deoxygenated benzene.

The solutions were adjusted to the desired temperature thermostatically and then mixed in a cell of 2 cm light path.

The reactions were followed by observing the appearance of C-nitroso compounds in a Hitachi 139 model spectrophotometer equipped with a thermostatically regulated cell.

The molar absorption coefficients of C-nitroso compounds ($\mathrm{R(Me)_2CN{=}O}$, where R was Me, Et or $\mathrm{CH_2OAc}$) were 24.8 at 680 mμ.

For analysis of *tert*-butanol a JEOL–JEC 750 gas chromatograph with a flame ionization detector was used. The column was packed with PEG 20 M.

Detection of the Radical——Benzene solution containing $4.5\times10^{-1}\,\mathrm{M}$ *t*-BHA and $2.9\times10^{-1}\,\mathrm{M}$ *t*-BHPO was placed in a 5 mm OD sample tube and maintained at 70—72° by passage of hot nitrogen gas through the cavity of a JEOL P-10 spectrometer. The reaction continued for more than 30 min. and during the reaction ESR spectra due to *tert*-butylnitroxide and di-*tert*-butylnitroxide were recorded.

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8) C.D. Wagner, R.H. Smith, and E.D. Peters, *Anal. Chem.*, **19**, 976 (1947).