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Oxidation of N-Alkylhydroxylamines. V.[1] Anodic Oxidation of N,O-Dialkyl- and N,N,O-Trialkylhydroxylamines

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The anodic oxidation of N,O-dialkyl- and N,N,O-trialkylhydroxylamines in acetonitrile was studied. These hydroxylamines generally showed two waves at a glassy-carbon electrode and the Ep values were larger than those of N-alkyl- and N,N-dialkylhydroxylamines. N,O-Diethyl and N-ethyl-O-*t*-butylhydroxylamine gave O-ethylacetaldoxime and O-*t*-butylacetaldoxime, respectively, as the major oxidation product, which suggests that N-alkoxy-N-alkylamino radical was a transient intermediate in the anodic oxidation.

The nitroxides, $RNH\dot{O}$ and $RRN\dot{O}$, generated in the anodic oxidation of N-alkyl- and N,N-dialkylhydroxylamine, were found to undergo disproportionation to form nitroso compounds and a nitrone, respectively.[1] In earlier studies, Jones[3] and Kothe[4] found that the susceptibility of hydroxylamines to oxidation is significantly depressed by O-substitution and greatly increased by N-substitution. N,O-Dimethyl- and N,O-diethylhydroxylamine are also reported to be inert to several oxidizing reagents.[3,4]

In studies on the effect of O-substitution on the oxidation mechanism, we investigated the electrochemical oxidation of O-alkyl, N,O-dialkyl- and N,N,O-trialkylhydroxylamines.

Results

Cyclic Voltammetry

The values of Ep (peak potential) of O-alkyl-, N,O-dialkyl- and N,N,O-trialkylhydroxylamines at a stationary glassy-carbon electrode in acetonitrile are summarized in Table I.

Table I. Cyclic Voltammetric Data on N,O-Dialkyl and N,N,O-Trialkylhydroxylamines in Acetonitrile at 25°

Compound	E_p V *vs.* SCE	
	1st wave	2nd wave
H_2N-OH	0.80	[a]
H_2N-OMe	1.25	[a]
$H_2N-OtBu$	1.25	
MeNH–OMe	1.10	[a]
EtNH–OEt	1.10	2.30
EtNH–O*t*Bu	1.35	2.40
$(tBu)_2N-OtBu$	1.0	1.60
$\{Me_2C(COOEt)\}_2NO-C(COOEt)Me_2$	1.70	2.55

a) The perchlorate of these hydroxylamines were converted to free hydroxylamines in electrolyte solution by adding excess pyridine. Therefore the appearance of a current caused by electrolysis of pyridine prevented anodic measurements below 1.80 V.

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1) Part IV: H. Sayo, S. Ozaki, and M. Masui, *Chem. Pharm. Bull.* (Tokyo), **21**, 1988 (1973).

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3) L.W. Jones, *Am. Chem. J.*, **20**, 43 (1898).

4) R. Kothe, *Ann.*, **266**, 310 (1891).

N,O-Dialkyl- and N,N,O-trialkylhydroxylamines generally gave two irreversible oxidation waves at a scanning rate of about 0.2—0.05 V $sec.^{-1}$

Only $\{Me_2C(COOEt)\}_2N–OC(COOEt)Me_2$ gave a cathodic wave upon reversal of the scanning direction at 1.7 V, the potential of the first anodic peak. The second wave of N,N,O-tri-*t*-butylhydroxylamine coincided with the oxidation wave of *t*-nitrosobutane, but that of $\{Me_2C(COOEt)\}_2N–OC(COOEt)Me_2$ did not coincide with the oxidation wave of ethyl α-nitroso isobutyrate (1.85 V).

The second wave of N,O-diethylhydroxylamine coincided with the oxidation wave of O-ethylacetaldoxime. Therefore, that of N-ethyl-O-*t*-butylhydroxylamine was expected to coincide with the oxidation wave of O-*t*-butylacetaldoxime. However, O-*t*-butylacetaldoxime was so unstable that its oxidation wave could not be measured.

Controlled Potential Electrolysis

Controlled potential electrolysis of the compounds in Table II was carried out in acetonitrile at a potential near that of the first peak.

TABLE II. Oxidation Products from N,O-Dialkyl and N,N,O-Trialkylhydroxylamines

Compound	Pyridine present	Potential[a] applied	*n*	Product	Yield[b]	
$(t\text{-}Bu)_2NO\text{-}t\text{-}Bu$	no	1.0	0.65	$t\text{-}BuN=O$	28	(33)[c]
				$t\text{-}BuOH$	18	(67)[d]
				$Me_2C=CH_2$	31	
	yes	1.1	2.20	$t\text{-}BuN=O$	90	(100)
				$t\text{-}BuOH$	30	([e])[d]
				$Me_2C=CH_2$	12	
EtNH–OEt	no	1.25	0.67	$(EtN=O)_2$	[f]	(33)[d]
				MeCH=N–OEt	35	
				EtOH	7	(33)[d]
	yes	1.15	2.0	$(EtN=O)_2$	[g]	(100)[d]
				MeCH=N–OEt	70	
				EtOH	trace	([e])[d]
EtNH–O-*t*-Bu	no	1.35	0.63	$(EtN=O)_2$	2	(33)[d]
				MeCH=N–O-*t*-Bu	33	
				t-BuOH	2	(33)[d]
	yes	1.35	2.0	$(EtN=O)_2$	[g]	(100)[d]
				MeCH=N–O-*t*-Bur	50	
				t-BuOH	trace	([e])[d]

[a] volts *vs*. SCE
[b] mole per cent of starting hydroxylamine
[c] The theoretical yields calculated on the basis of the oxidation mechanism are shown in parentheses.
[d] sum of the theoretical yields of the two products
[e] See discussion section.
[f] The absorption of O-ethylacetaldoxime at 256 μm makes it impossible to obtain the exact absorbance of the *cis*-nitrosoethane dimer.
[g] The absorption of the *cis*-nitrosoethane dimer was masked by that of excess pyridine.

N,N,O-Tri-*t*-butylhydroxylamine

Anodic oxidation of N,N,O-tri-*t*-butylhydroxylamine showed an *n* value (the number of coulombs passed per mole of the substrate) of 0.65 and gave *t*-nitrosobutane, *t*-butanol and isobutene in 28, 18 and 31 mole% yields, respectively from the starting material. The total yield of the three products reached 77 mole%, and the sum of the yields of *t*-butanol and isobutene was about twice that of *t*-nitrosobutane. These results suggest that one third of the hydroxylamine was oxidized through two-electron oxidation, while two thirds were not oxidized, probably because of protonation. The yield of *t*-nitrosobutane and the *n* value increased up to 90% and 2.20, respectively, when excess pyridine was added to the solution just before electrolysis as an acceptor of protons generated in the oxidation of the substrate. The sum of the yields of *t*-butanol and isobutene, however, decreased under these conditions.

N,O-Diethylhydroxylamine

In the absence of pyridine, anodic oxidation of N,O-diethylhydroxylamine showed an *n* value of 0.67 and gave O-ethylacetaldoxime and ethanol in 35% and 7% yield, respectively, and a trace of *cis*-nitrosoethane dimer. Addition of excess pyridine increased the *n* value to 2.0 and the yield of O-ethylacetaldoxime to 70%, but decreased the yield of ethanol.

N-Ethyl-O-*t*-butylhydroxylamine

Anodic oxidation of N-ethyl-O-*t*-butylhydroxylamine showed an *n* value of 0.63 and gave acetaldehyde, *cis*-nitrosoethane dimer and ethanol in 33%, 2% and 2% yield, respectively.

The expected product, O-*t*-butylacetaldoxime seemed to be considerably much more unstable than O-ethylacetaldoxime, and was hydrolyzed appreciably to acetaldehyde and O-*t*-butylhydroxylamine during controlled potential electrolysis. The presence of excess pyridine during the oxidation increased the *n* value to 2.0 and the yield of acetaldehyde to 50%, but the yield of *t*-butanol decreased to a negligible amount.

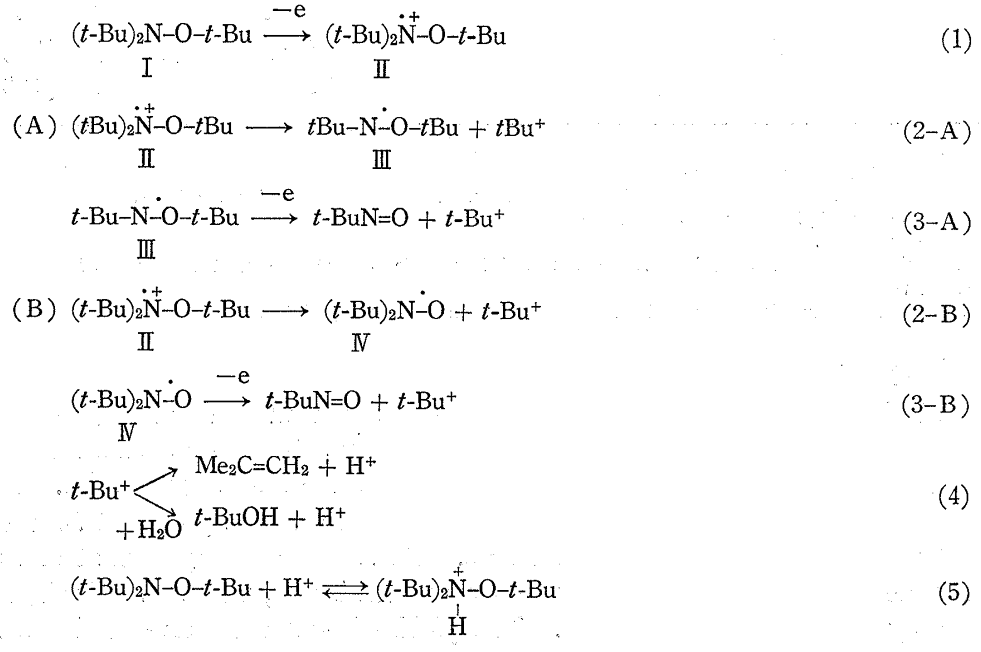
Discussion

The E_p values obtained in this work show that O-substitution in general depresses the susceptibility of hydroxylamines to electrochemical oxidation, whereas N-substitution increases the susceptibility. When the substituent is a methyl group, the E_p value of the first waves decreases in the order $\text{NH}_2\text{OMe} > \text{MeNHOMe} > \text{NH}_2\text{OH} \geqq \text{MeNHOH}$ (0.80 V) $> \text{Me}_2\text{NOH}$ (0.5 V). However, with the bulky *t*-butyl group, the above order is changed as follows; $\text{NH}_2\text{O-}t\text{-Bu} > (t\text{-Bu})_2\text{N–O–}t\text{-Bu} \geqq (t\text{-Bu})_2\text{N–OH}$ (1.0 V) $> t\text{-BuNHOH}$ (0.8 V)

A reaction scheme for the electrochemical oxidation of hydroxylamines was formulated based on the oxidation products and coulometric *n* values of about 0.65 and 2.0 in the absence and presence of pyridine, respectively.

N,N,O-tri-*t*-Butylhydroxylamine

The total yields of *t*-nitrosobutane, *t*-butanol and isobutene was close to that expected from the *n* value. *t*-Nitrosobutane can be generated from either N-*t*-butoxy-N-*t*-butylamino radical (III) or di-*t*-butylnitroxide (IV), so that following two reaction schemes are likely.



$$\underset{\text{I}}{(t\text{-Bu})_2\text{N–O–}t\text{-Bu}} \xrightarrow{-e} \underset{\text{II}}{(t\text{-Bu})_2\overset{\cdot+}{\text{N}}\text{–O–}t\text{-Bu}} \qquad (1)$$

$$(\text{A})\quad \underset{\text{II}}{(t\text{Bu})_2\overset{\cdot+}{\text{N}}\text{–O–}t\text{Bu}} \longrightarrow \underset{\text{III}}{t\text{Bu–}\overset{\cdot}{\text{N}}\text{–O–}t\text{Bu}} + t\text{Bu}^+ \qquad (2\text{–A})$$

$$\underset{\text{III}}{t\text{-Bu–}\overset{\cdot}{\text{N}}\text{–O–}t\text{-Bu}} \xrightarrow{-e} t\text{-BuN=O} + t\text{-Bu}^+ \qquad (3\text{–A})$$

$$(\text{B})\quad \underset{\text{II}}{(t\text{-Bu})_2\overset{\cdot+}{\text{N}}\text{–O–}t\text{-Bu}} \longrightarrow \underset{\text{IV}}{(t\text{-Bu})_2\text{N–}\overset{\cdot}{\text{O}}} + t\text{-Bu}^+ \qquad (2\text{–B})$$

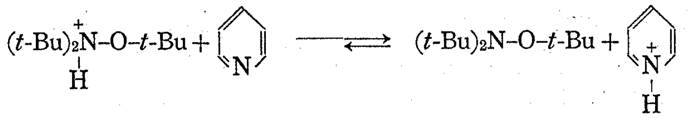
$$\underset{\text{IV}}{(t\text{-Bu})_2\text{N–}\overset{\cdot}{\text{O}}} \xrightarrow{-e} t\text{-BuN=O} + t\text{-Bu}^+ \qquad (3\text{–B})$$

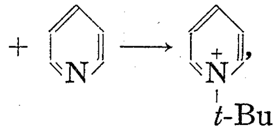
$$t\text{-Bu}^+ \begin{cases} \nearrow \text{Me}_2\text{C=CH}_2 + \text{H}^+ \\ \xrightarrow[+\text{H}_2\text{O}]{} t\text{-BuOH} + \text{H}^+ \end{cases} \qquad (4)$$

$$(t\text{-Bu})_2\text{N–O–}t\text{-Bu} + \text{H}^+ \rightleftarrows (t\text{-Bu})_2\underset{\text{H}}{\overset{+}{\text{N}}}\text{–O–}t\text{-Bu} \qquad (5)$$

Di-*t*-butylnitroxide (IV), which is oxidized at 0.45 V,[1] is easily oxidized at the oxidation potential of N,N,O-tri-*t*-butylhydroxylamine of 1.10 V. However, it is uncertain at present whether path (A) or (B) is predominant.

In the presence of pyridine, there may be an equilibrium

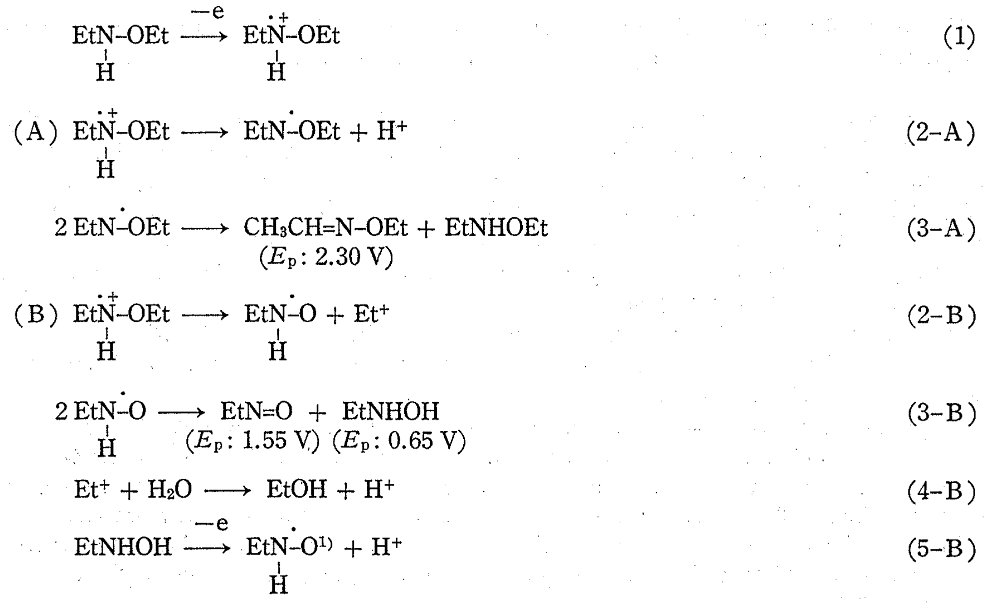


which largely favors formation of the pyridinium ion, so that a substantial amount of N,N,O-tri-*t*-butylhydroxylamine undergoes oxidation without being protonated. The reaction scheme suggests that in the presence of excess pyridine there should be 100% yield of *t*-nitrosobutane from the starting hydroxylamine and that the sum of the yields of isobutene and *t*-butanol formed by reaction of *t*-butyl cation with a trace of water in acetonitrile should be 200%. However, theoretical total yield of *t*-butanol and isobutene could not be obtained in practice, since nucleophilic attack of pyridine on *t*-butyl cation, *t*-Bu$^+$ +  decreased the total yield of *t*-butanol and isobutene.[5] In the absence of pyridine, the yield of *t*-nitrosobutane and the total yields of *t*-butanol and isobutene should be about 33% and 67%, respectively.

N,O-Diethylhydroxylamine

The oxidation products, O-ethylacetaldoxime and nitrosobutane, suggest the presence of an N-ethoxy-N-ethylamine radical, EtṄ–O–Et and ethylnitroxide, respectively, whereas in photolysis of N,O-dialkylhydroxylamines electron spin resonance (ESR) signals were obtained exclusively from N-alkoxy-N-alkylamino radicals.[6]

The possible reaction schemes for anodic oxidation of N,O-diethylhydroxylamine are as follows.



$$\mathrm{Et}\underset{|\atop \mathrm{H}}{\mathrm{N}}\text{-OEt} \xrightarrow{-e} \mathrm{Et}\underset{|\atop \mathrm{H}}{\overset{\cdot +}{\mathrm{N}}}\text{-OEt} \qquad (1)$$

$$(\mathrm{A})\ \mathrm{Et}\underset{|\atop \mathrm{H}}{\overset{\cdot +}{\mathrm{N}}}\text{-OEt} \longrightarrow \mathrm{Et}\dot{\mathrm{N}}\text{-OEt} + \mathrm{H}^+ \qquad (2\text{-A})$$

$$2\,\mathrm{Et}\dot{\mathrm{N}}\text{-OEt} \longrightarrow \underset{(E_\mathrm{p}:\ 2.30\ \mathrm{V})}{\mathrm{CH_3CH{=}N\text{-}OEt}} + \mathrm{EtNHOEt} \qquad (3\text{-A})$$

$$(\mathrm{B})\ \mathrm{Et}\underset{|\atop \mathrm{H}}{\overset{\cdot +}{\mathrm{N}}}\text{-OEt} \longrightarrow \mathrm{Et}\underset{|\atop \mathrm{H}}{\dot{\mathrm{N}}}\text{-O} + \mathrm{Et}^+ \qquad (2\text{-B})$$

$$2\,\mathrm{Et}\underset{|\atop \mathrm{H}}{\dot{\mathrm{N}}}\text{-O} \longrightarrow \underset{(E_\mathrm{p}:\ 1.55\ \mathrm{V})}{\mathrm{EtN{=}O}} + \underset{(E_\mathrm{p}:\ 0.65\ \mathrm{V})}{\mathrm{EtNHOH}} \qquad (3\text{-B})$$

$$\mathrm{Et}^+ + \mathrm{H_2O} \longrightarrow \mathrm{EtOH} + \mathrm{H}^+ \qquad (4\text{-B})$$

$$\mathrm{EtNHOH} \xrightarrow{-e} \mathrm{Et}\underset{|\atop \mathrm{H}}{\dot{\mathrm{N}}}\text{-O}^{1)} + \mathrm{H}^+ \qquad (5\text{-B})$$

These reaction schemes suggest that the sum of the yields of O-ethyacetaldoxime and nitrosobutane, and O-ethylacetaldoxime and ethanol should be about 33%, and the yields of nitrosoethane and ethanol should be nearly equal in the absence of pyridine.

The observed yield of O-ethylacetaldoxime of over 70% shows that most of the N,O-diethylhydroxylamine is oxidized through EtṄ–OEt.

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N-Ethyl-O-*t*-butylhydroxylamine

The *n* value and the products suggest that this hydroxylamine should be oxidized in a similar manner to N,O-diethylhydroxylamine. The O-butylation instead of O-ethylation of N-alkylhydroxylamine appears not to effect formation of the O-alkoxy-N-alkylamino radical relative to that of N-alkylnitroxide on anodic oxidation.

Differences in Anodic Oxidations of N-Alkyl- and (N,N-Dialkyl) hydroxylamines and N,O-Dialkylhydroxylamines

As described in the results section, O-substitution of hydroxylamines depressed their susceptibilities to electrochemical oxidation. It has been reported that O-methylations of NH_2OH, MeNHOH and Me_2NOH decrease their basicities, although the reverse would be expected on the basis of the inductive effect.[7] Therefore, the large values of E_p for O-alkylhydroxylamines may be explained by their weak basicities. From the oxidation products, the major transient intermediate in the anodic oxidation of N,O-dialkylhydroxylamines seems to be the N-alkoxy-N-alkylamino radical and not N-alkylnitroxide, while on anodic oxidation of N-alkyl- and N,N-dialkylhydroxylamines showed ESR signals of only N-alkyl- and N,N-dialkylnitroxides, respectively.

Experimental

Materials——Acetonitrile was purified by the method of Mann.[8] N,N,O-Tri-*t*-butylhydroxylamine,[9] $\{Me_2C(COOEt)\}_2N\text{-}OC(COOEt)Me_2$,[10] N,O-diethylhydroxylamine,[11] N,O-dimethylhydroxylamine,[11] N-ethyl-O-*t*-butylhydroxylamine,[5] and O-ethylacetaldoxime[12] were prepared as described in the literature. Commercial hydroxylammonium hydrochloride and O-methylhydroxylammonium hydrochloride were convered to their perchlorates. *t*-Nitrosobutane and ethyl α-nitrosoisobutyrate were prepared as described previously.[1]

The supporting electrolyte, ethyl-tri-*n*-butylammonium tetrafluoroborate was prepared by the method of House.[13] Sodium perchlorate was recrystallized from ethanol–water, dried and stored *in vacuo* over P_2O_5.

Cyclic Voltammetry——Cyclic voltammetry was done with a three electrode system employing a linear scanning unit (Hokuto Denko Co., Model HB-101) equipped with a potentiostat (Hokuto Denko Co., Model PS-500B). The electrode system consisted of a glassy-carbon indicator electrode (G.C.E.), a glassy-carbon counter electrode, and saturated calomel electrode (S.C.E.). The S.C.E. was separated from the solution (acetonitrile) by a sintered disk and agar plug containing 0.1 M sodium perchlorate.

The G.C.E. was prepared by cutting glassy-carbon (GC-20, Tokai Electrode Manufacturing Co.,) into a cylinder and coating it side with epoxy resin.

Measurements were made at 25° with hydroxylamine concentrations of 2—5 mM and a concentration of supporting electrolyte of about 0.1 M. The scanning rate was 0.05—0.2 V sec^{-1} and current-potential curves were recorded using a Toa Model XYR-2A X-Y recorder.

Controlled Potential Electrolysis——Electrolysis were performed with a potentiostat (Yanagimoto Manufacturing Co., Model V-8) and the current was recorded with a Toa Electronics EPR-10A recorder. The quantity of electricity consumed in the electrolysis was calculated by integration from the current-time curve. An H-cell was used. The electrolysis solution in the anode was separated from the cathode by a sintered disk and a methyl cellulose 400 plug containing 1 M sodium perchlorate. The concentration of substrate was generally $1\text{—}4 \times 10^{-2}$ M and that of supporting electrolyte (ethyl-tri-*n*-butylammonium tetrafluoroborate) was about 0.1 M.

The reactant and pyridine were introduced after pre-electrolysis and the anodic compartment was sealed with a cap. Then electrolysis was carried out with mechanical stirring.

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Product Analysis

a) Monomesic and Dimeric Nitroso Compounds: The monomeric nitroso compound, *t*-nitrosobutane was estimated by measureing the absorption in the visible region, at 680 mμ. The *cis*-nitrosoethane dimer was estimated by measureing the ultraviolet absorption at 267 mμ.

b) Alcohols and Alkene: Ethanol, *t*-butanol and isobutene were measured by gas chromatographic analysis in a JEOL-JGC-750 gas chromatograph using 10 μl of solution after electrolysis. The column was packed with $AgNO_3$–benzylcyanide on 60—80 mesh NEOPAK 1A and maintained at 40°.

c) O-Alkylacetaldoxime: O-Ethylacetaldoxime was estimated by cyclic voltammetric and gas chromatographic analyses. O-Ethylacetaldoxime was hydrolyzed to acetaldehyde and O-ethylhydroxylamine in 2 N HCl and estimated as the 2,4-dinitrophenylhydrazone of acetaldehyde. The hydrazone was recrystallized from ethanol (mp. 149°).

O-*t*-Butylacetaldoxime was estimated as the 2,4-dinitrophenylhydrazone of acetaldehyde in a similar way to O-ethylacetaldoxime.

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