

# Reaction of Aliphatic Tertiary Amines with Hydroperoxides

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## Abstract

Triethylamine acts as an antioxidant in fats at 70C but not at lower temperatures. A reactive antioxidant intermediate was sought. Diethylhydroxylamine was obtained from the reaction of triethylamine and *t*-butyl peroxide at 70C. The recrystallized product had antioxidant properties. About 0.1% existed as stable free radical by electron-spin resonance. Didecyl- and didodecylhydroxylamines were also synthesized from the corresponding tertiary amines. These and a sample of commercial diethylhydroxylamine also contained free radicals and possessed antioxidant activity.

## Introduction

ALIPHATIC AMINES ACT as synergists for phenolic-type antioxidants in unsaturated lipid systems (1). When octyl-, dioctyl- and trioctylamines were tested alone as antioxidants, inhibition of oxidation was not striking, except for the tertiary amine. At room temperature, and at 50C and 60C the tertiary amine was ineffective; but at 70C menhaden oil was protected from oxidation for over a month at a level of 50  $\mu$ M amine/g of oil (1.8%) (2). This unusual temperature effect was assumed to be due to the formation of an antioxidant by reaction of the tertiary amine with hydroperoxides produced in the initial stages of lipid oxidation. The work described in this paper was undertaken to investigate this hypothesis.

Cullis and Waddington (3) observed that aliphatic amines had an inhibitory influence on the gaseous oxidation of acetaldehyde. Thomas (4) used trimethyl and tri-*n*-butylamines as inhibitors for the oxidation of *p*-cumene in the presence of azoisobutyronitrile (AIBN) as an initiator at 70C. De La Mare et al. (5,6) and Coppinger and Swalen (7) studied the reaction of aliphatic amines with tertiary butyl hydroperoxide. These reactions were followed by electron-spin resonance (ESR) spectroscopy.

## Experimental

### Methods and Material

Tri-*n*-octylamine (Eastman Organic Chemicals, Distillation Products Industries), *p*-menthane hydroperoxide (Lucidol Division, Wallace and Tiernan, Inc.), and tert-butyl hydroperoxide and *N,N'* diethylhydroxylamine (K and K Laboratories, Inc.) were used without further purification. The substrate for antioxidant analyses was squalene (Sigma, Grade 1). It was purified on silicic acid columns as follows (8): The column was prepared from Mallinkrodt No. 2874 silicic acid slurried with petroleum ether. The sample (approximately 0.5 g per g silicic acid) was added in petroleum ether solution and eluted with petroleum ether. Eluate containing the first 10% was discarded. The remaining sample was collected as one fraction until 70–80% of the original material was recovered. The peroxide value of this fraction was below the limit of measurement.

The weighing method for determination of induction periods was that described by Olcott and Einset (9).

The ESR spectra were obtained with a Varian 4502 EPR spectrometer. Chloroform or carbon tetrachloride was used as solvent. Diethylhydroxylamine was not diluted. A Beckman IR7 spectrometer was used for the determination of infrared spectra. Molecular weights were estimated with a Mechrolab Vapor Pressure Osmometer, Model 301.

For thin-layer chromatography, the adsorbant was Silica Gel G according to Stahl, No. 7731, obtained from Brinkman Instruments, Inc. The developing solvent used was prepared by equilibrating chloroform with 1*N* ammonium hydroxide (10:1 v/v), discarding the ammonia layer, and adding methanol to a ratio of 3:97 v/v. Plates were developed with dichlorofluorescein or iodine vapor. Good separation of mono-, di-, and triamines was accomplished, but isomeric species could not be separated with this system.

Triethylamine oxide was prepared by the method described by Hoh et al. (10) and used without further purification. Absolute ethanol was used as the diluting solvent instead of water. The oxide was identified by its infrared absorption spectra at 950–970  $\text{cm}^{-1}$  (11).

### Reaction Conditions

Tert-butyl hydroperoxide and tri-*n*-octylamine were mixed in 5:1 molar ratio at room temperature. The mixture was held at 70C for 48 hr. Mixtures of *p*-menthane hydroperoxide and tri-*n*-octylamine (2:1 molar ratio) were treated similarly.

Silicic acid column chromatography of the reaction product of *t*-butyl hydroperoxide and tri-*n*-octylamine was carried out as follows: Bio-Rad Silicic Acid, minus 325 mesh, was washed with chloroform, then dried under nitrogen and held at 105C for 24 hr for activation. The activated silicic acid was slurried with chloroform, and a 24  $\times$  2.5 cm column was packed under 2 lb nitrogen pressure. The amine-peroxide reaction mixture was introduced on to the column with chloroform and eluted with chloroform.

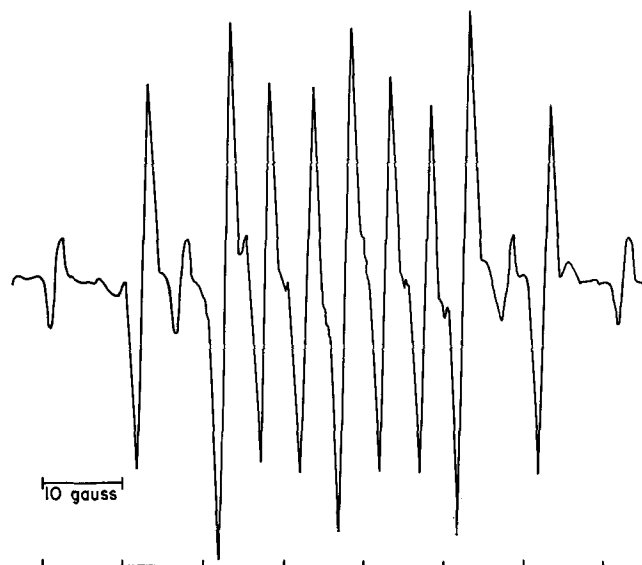


FIG. 1. Derivative plot of ESR spectrum, diethylhydroxylamine in carbon tetrachloride.

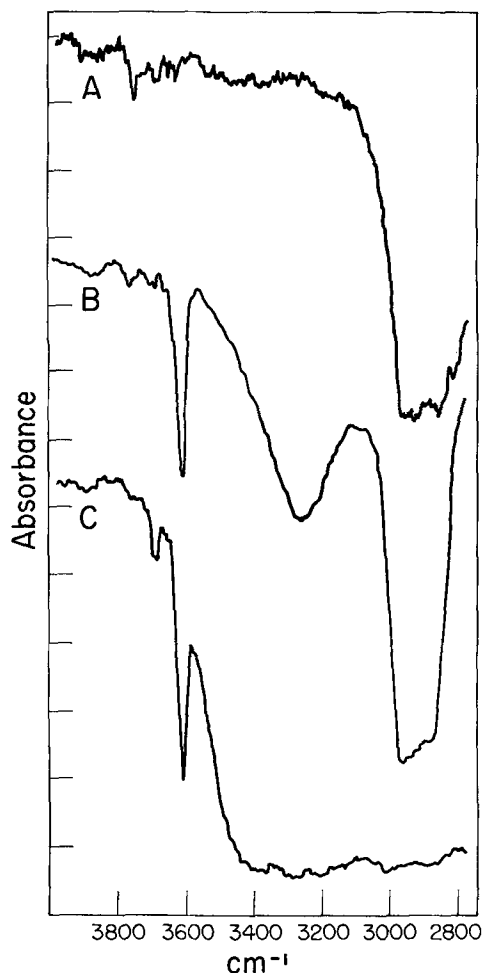


FIG. 2. Infrared absorption spectra of dioctyl amine (A), dioctylhydroxylamine (B), and diethylhydroxylamine (C), all in carbon tetrachloride.

When no further product was obtained, the solvent system was changed to 97:3 chloroform-methanol and more fractions were collected. Each fraction was analyzed for total solid content and antioxidant activity. Those fractions that showed antioxidant properties were then further examined for the presence of the free radical.

## Results

### Tri-n-octyl Amine and t-butyl Hydroperoxide

The reaction of tri-n-octyl amine with t-butyl hydroperoxide for 48 hr at 70°C yielded a clear yellow oil. This product contained a free radical by ESR spectroscopy. The spectrum was split into three lines of equal intensity interpreted as due to spin coupling of a free electron with a nitrogen nucleus. Hyperfine

splitting was also observed due to interaction with four  $\alpha$ -protons. Coupling constants were  $A_N = 15.6$  gauss,  $A_H = 10.6$  gauss (12). These are in good agreement with those reported by Coppinger and Swalen (8) for dialkylamine nitroxide radicals generated by the reaction of short chain aliphatic amines with t-butyl hydroperoxide.

Tri-n-octylamine and t-butyl hydroperoxide were mixed and examined at room temperature; only a faint unresolved ESR signal was observed. However, when the temperature in the cavity was raised to 70°C, a 15 line free radical signal appeared at once.

A white crystalline precipitate formed in the tri-n-octylamine-t-butyl hydroperoxide reaction mixture after standing for an additional day at room temperature. The precipitate was separated and recrystallized as colorless needles from hot ethanol to a constant melting point of 77.5–78.5°C. The yield was approximately 1%. The nitroxide free radical signal (8) was concentrated in the crystals as compared to the oily residue, and was estimated to be equivalent to  $10^{-3}$  M. Figure 1 shows the derivative plot of the ESR spectrum of the crystals in carbon tetrachloride.

The compound had the following composition: C, 74.4; H, 13.9; N, 5.4; (theor. for dioctylhydroxylamine,  $C_{16}H_{35}NO$ : C, 74.4; H, 13.6; N, 5.45). Determinations of molecular weight by vapor pressure lowering gave values between 230 and 300 (theor.  $C_{16}H_{35}NO = 257$ ).

Infrared absorption spectra of this product, of diethylhydroxylamine and of dioctylamine are shown in Figure 2. The hydroxyl peak of diethylhydroxylamine falls at  $3616\text{ cm}^{-1}$ . An absorption peak occurs also at this wavelength in the spectrum of the new compound.

### Tri-n-Decylamine and Tri-n-Dodecylamine with t-Butyl Hydroperoxide

Tri-n-decylamine and tri-n-dodecylamine were reacted with t-butyl hydroperoxide under the same conditions as were used with tri-n-octylamine. The white crystalline products melted at 85–86°C and 92.5–93.5°C, respectively. Each product gave a free radical signal of the same form and approximately the same strength as that observed with the product from tri-octylamine.

### Tri-n-Octylamine and p-Menthane Hydroperoxide

Reaction of tri-n-octylamine with p-menthane hydroperoxide at 70°C for 48 hr yielded a dark brown viscous oil. The crude reaction mixture showed an asymmetrical ESR spectrum resulting from the spectra of two free radical species superimposed upon each other. One of the two species was the nitroxide radical observed before. This signal disappeared in 10 min at 145°C when the sample was heated in the cavity of the instrument so that it was possible to isolate the spectrum of the second free radical species. The second signal contained 16 observable lines. There was no evidence for a nitrogen atom from the hyperfine pattern. Since hydrocarbon radicals are not usually stable at such high temperatures, it was probably a peroxy radical. Only a small amount of crystalline product could be isolated from this system.

### Oxidized Squalene-Amine System

Tri-n-octylamine and squalene were mixed and allowed to stand in contact with air at room temperature

TABLE I

Antioxidant Activity of Tertiary Amines and Dialkylhydroxylamines in Squalene at 50°C

| Additive <sup>a</sup> | Induction period (days) |     |      |      |      |       |
|-----------------------|-------------------------|-----|------|------|------|-------|
|                       | TOA                     | TDA | TDDA | DOHA | DDHA | DDDHA |
| 0.5                   |                         |     |      | 3    | 4    | 3     |
| 2.5                   |                         |     |      | 9+   | 10+  | 9     |
| 3.5                   |                         |     |      | 16   | .... | ....  |
| 5                     |                         |     |      | .... | 15   | 14    |
| 25                    | 1                       | 1   | 1    |      |      |       |
| 50                    | 1                       | 1   | 1    |      |      |       |

<sup>a</sup> In  $\mu\text{M}$  per g  
TOA indicates trioctylamine; TDA, tridecylamine; TDDA, tridodecylamine; DOHA, dioctyl hydroxylamine; DDHA, didecyl hydroxylamine; DDDHA, didodecyl hydroxylamine.

overnight. Only a faint signal was observed by ESR analysis. The sample was then heated to 70–75°C in the cavity and the 15-line spectrum of the nitroxide appeared. Although there was some contaminating radical present in the sample, the major signal was identical to that obtained from the isolated product of the model system (Fig. 3).

#### Antioxidant Activity

The antioxidant activities of the tertiary alkyl amines and of the corresponding dialkyl hydroxylamines in squalene are shown in Table I.

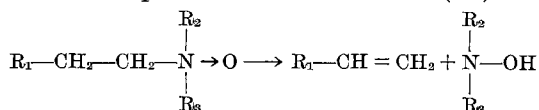
#### Discussion

Tri-*n*-octylamine and its analogues react with *t*-butyl hydroperoxide at 70°C to form crystalline products with antioxidant properties. Elemental analysis and infrared absorption spectra indicate that the crystals are dialkyl hydroxylamines.

De La Mare (6) proposed a mechanism for the conversion of tertiary alkyl amines to nitroxides by reaction with *t*-butyl hydroperoxide. The mechanism, later modified by Coppinger and Swalen (7), predicted that the reaction proceeded through the formation of a substituted hydroxylamine. However, no hydroxylamines were isolated in their work.

Other studies of amine-hydroperoxide reactions suggest an alternate route. Oswald et al. (13) found that trialkyl amines and hydroperoxides react at room temperature to form alkylammonium peroxide salts. The same peroxides form when tertiary aliphatic amines react with hydrogen peroxide at low temperature (–50°C). These compounds decompose at 50°C to trialkylamine oxides (14). Hoh et al. (10) also studied the oxidation of tertiary amines with hydrogen peroxide. When dimethyldodecylamine was treated with 35% hydrogen peroxide solution (1:1 molar ratio) at 60–65°C, the product was the tertiary amine oxide. At higher temperatures yields were reduced.

Thermal decomposition of tertiary amine oxides results in the Cope elimination reaction (15):



Although this reaction is usually carried out at temperatures above 90°C, some conversion to the disubstituted hydroxylamine could occur at 70°C.

The pathway to formation of the hydroxylamine might therefore be:

1.  $\text{R}_3\text{N} + \text{R}'\text{OOH} \longrightarrow (\text{R}_3\text{N} - \text{R}'\text{OOH})$  (13)
2.  $(\text{R}_3\text{N} - \text{R}'\text{OOH}) \longrightarrow \text{R}_3\text{NO} + \text{R}'\text{OH}$
3.  $\text{R}_3\text{N} \rightarrow \text{O} \xrightarrow{\Delta} \text{R} = \text{CH}_2 + \text{R}_2\text{NOH}$

In order to obtain further information concerning the possibility that a tertiary amine oxide may be an intermediate, trioctylamine oxide was prepared according to the method of Hoh et al. (10) and examined for the presence of a free radical species. None was observed. However, when trioctylamine oxide was heated at 70°C for 24 hr, approximately 0.1% of the sample was converted to the nitroxide. Although this does not necessarily indicate that the major pathway to dialkyl hydroxylamine is through tertiary amine oxide formation, the evidence lends some credence to this mechanism. A recent study of the heat decomposition of dimethyl-laurylamine oxide indicates that dimethylhydroxylamine is only a

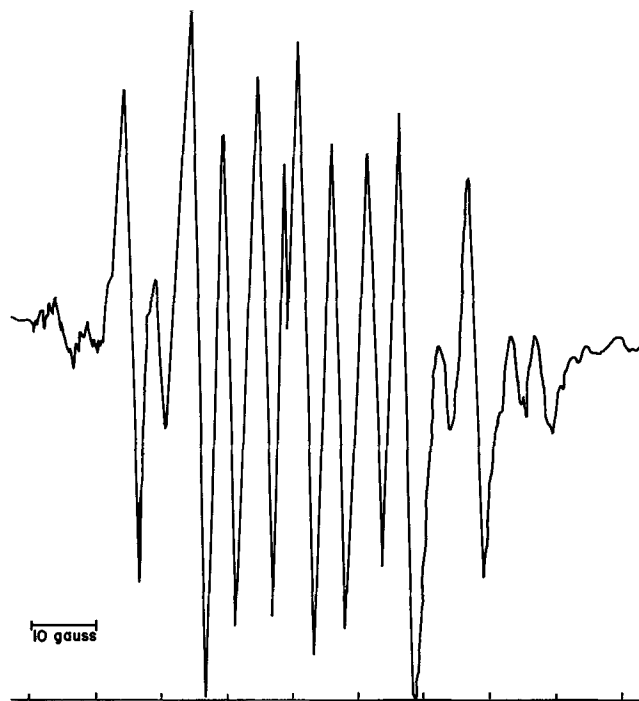


FIG. 3. Derivative plot of ESR spectrum, tri-*n*-octyl amine in oxidizing squalene.

minor component of this reaction (16). Trimethylamine oxide had no antioxidant activity under the conditions used in these experiments.

The nitroxide ESR signal was also observed with a commercial preparation of diethylhydroxylamine. The concentration of the free radical was approximately  $10^{-6}$  M. When *t*-butyl hydroperoxide was added to the sample at room temperature in a molar ratio of 3:1 hydroxylamine to hydroperoxide, the concentration of nitroxide increased to  $10^{-4}$  M within 10 min.

The sample of commercial diethylhydroxylamine was compared with dioctylhydroxylamine as an antioxidant for squalene. The two were approximately equivalent (Table II).

The chain terminating step with the hydroxylamine as antioxidant might be:



The nitroxide radical may also contribute to oxidation inhibition. Hoffmann et al. (17) prepared di-*t*-butyl nitroxide by the reduction of tertiary-nitrobutane with sodium and stated that it was an effective antioxidant, polymerization inhibitor and radical trap. An attempt by us to oxidize dioctylhydroxylamine quantitatively to the nitroxide with lead dioxide was unsuccessful. Free radicals were destroyed rather than synthesized in the process, suggesting that the oxidation was too vigorous for dialkyl hydroxylamines.

The observations in this paper add to the growing list of syntheses of antioxidants by oxidation reac-

TABLE II  
Comparison of Antioxidant Activity of Diethylhydroxylamine (DEHA) and Dioctyl Hydroxylamine (DOHA) in Squalene

|      | Temp. | Conc. ( $\mu\text{M/g}$ ) | Induction period (days) |
|------|-------|---------------------------|-------------------------|
| DEHA | 23C   | 1.0                       | 90                      |
|      | 50C   | 1.0                       | 5                       |
| DOHA | 23C   | 1.0                       | 90                      |
|      | 50C   | 1.0                       | 5                       |

tions. For example, Pedersen (18) showed that, of the oxidation products of N, N' diphenyl-p-phenylene diamine, the quinone diimine N, N' dioxide was a more effective antioxidant than the quinone diimine.

Similarly the active species formed when thio- and dithio-compounds are used as antioxidants, are considered to be sulfoxides and thiosulfates by Barnard et al. (19). The antioxidant effectiveness of seleno-compounds is similarly thought to be due to the synthesis of oxidized intermediates (20,21).

Whether substituted hydroxylamines are of practical significance as antioxidants for edible oils remains to be determined. Very little is known about their toxicological properties. Also it is not yet known whether a mechanism related to that described here may explain the synergistic effects of phospholipids (22) and other nitrogenous food constituents. Experiments designed to pursue these topics are in progress.

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# Homogeneous Catalytic Hydrogenation of Unsaturated Fats: Metal Acetylacetonates<sup>1</sup>

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#### Abstract

Hydrogenation of linseed and soybean methyl esters was achieved at 100–180°C, 100–1000 psi H<sub>2</sub> and 0.05–0.25 moles catalyst per mole of ester. The relative activity of metal acetylacetonates in decreasing order was: nickel(III), cobalt(III), copper(II) and iron(III). Reduction occurred readily in methanol solution but only slowly in dimethylformamide and acetic acid. No reduction occurred in the absence of solvents. Soybean oil was also hydrogenated rapidly with nickel(III) acetylacetonate in methanol, but in this system the triglycerides were converted to methyl esters. Nickel(III) acetylacetonate was the most selective catalyst toward linolenate hydrogenation. Methyl linoleate and linolenate hydrogenated with nickel(III) acetylacetonate were fractionated into monoenes, dienes and trienes. The *cis* monoenes separated in 62 to 68% yield had double bonds in the original position. The remaining *trans* monoenes had extensively scattered unsaturation. The dienes and trienes showed no conjugation, but some of the double bonds in the dienes were not conjugatable with alkali. Little stearate was formed.

#### Introduction

IN A PROGRAM at this Laboratory to find selective catalysts for the hydrogenation of linolenate in soybean oil, bis- and tris (2,4-pentanedione) metal complexes were investigated. These complexes, com-

monly known as metal acetylacetonates, are soluble hydrogenation catalysts rather than heterogeneous as normally used in commercial operations. In the past, olefinic compounds have been successfully reduced by soluble hydrogenation catalysts (11–13). Soluble metal complexes previously used to hydrogenate polyunsaturated fats include iron and cobalt carbonyls (8–10), pentacyanocobaltate (17,18) and triphenylphosphine derivatives of platinum(II) and tin(II), (1).

#### Experimental

##### Materials

Methyl esters of fatty acids of commercially refined and bleached soybean and linseed oils were obtained by transesterification with methanol and potassium hydroxide and were distilled under vacuum (soybean methyl esters IV 135; linseed methyl esters IV 183). Methyl linoleate (IV 172.4) was obtained from The Hormel Institute. Methyl linolenate (IV 260.1) was prepared by countercurrent distribution (CCD) of distilled linseed methyl esters (21). Gas-liquid chromatography (GLC) showed the methyl linoleate and linolenate to be 100% pure. Nickel(III), cobalt(III), copper(II) and iron(III) acetylacetonates were obtained from the Pearsal Company and used without purification. Small amounts of methanol-insoluble impurities were present, but they exhibited no catalytic activity.

*Hydrogenations* were carried out in a Magne-Dash high-pressure 150-ml, or 300-ml, stainless steel autoclave or a rocking autoclave fitted with a six 10-ml compartment stainless steel insert (6). The catalyst was decomposed after hydrogenation with dilute HCl (2:1) as described previously (10).

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<sup>2</sup> No. Util. Res. and Dev. Div., ARS, USDA.