Hydroperoxide Oxidations Catalyzed by Metals. II. The Oxidation of Tertiary Amines to Amine Oxides

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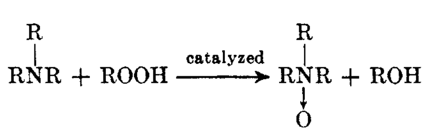
A novel reaction of tertiary amines with organic hydroperoxides in the presence of group VB and VIB transition metals has been found. This oxidation reaction gives excellent yields of amine oxides. The amines studied were N,N-dimethyldodecylamine, tri-*n*-butylamine, triethylamine, 1-dimethylamino-2-propanol, and pyridine. The hydroperoxides studied were *t*-butyl hydroperoxide, cumene hydroperoxide, and a mixture of 2-(2-methylbuten-3-yl) hydroperoxide and 2-(3-methylbuten-3-yl) hydroperoxide. Compounds of vanadium and molybdenum are catalysts for this reaction. Vanadium compounds are the superior catalyst. The results support an ionic mechanism for this reaction.

Tertiary amines have been found to react with organic hydroperoxides in the presence of group VB and VIB transition metals, and to give excellent yields of amine oxides (eq 1). This reaction was studied as an extension of the work done in this laboratory on the organic hydroperoxides epoxidation of olefins in the presence of catalytic amounts of these transition elements.[1] After our work was completed, the same reaction was reported by Kuhnen.[2] His paper states that the reaction is catalyzed by vanadium, molybdenum, and titanium compounds and occurs in a few hours at temperatures between 20 and 80° in a suitable solvent but gave few further details. Our work shows that there are four parameters which affect this reaction. They are the transition element chosen as catalyst, the reactivity and stability of the hydroperoxide, the solvent, and the steric effect of the amine.



$$\mathrm{R}\overset{\overset{\mathrm{R}}{|}}{\mathrm{N}}\mathrm{R} + \mathrm{ROOH} \xrightarrow{\text{catalyzed}} \mathrm{R}\underset{\underset{\mathrm{O}}{\downarrow}}{\overset{\overset{\mathrm{R}}{|}}{\mathrm{N}}}\mathrm{R} + \mathrm{ROH} \qquad (1)$$

Results

In Table I, experiments with N,N-dimethyldodecylamine and *t*-butyl hydroperoxide in refluxing *t*-butyl alcohol are listed. These experiments were followed by periodic titration of the hydroperoxide.[3] These data show that vanadium compounds are the most active catalysts for the oxidation of aliphatic amines to amine oxides. Molybdenum compounds catalyze the oxidation, but the rate of the reaction is slower. Tungsten, niobium, and tantalum compounds were poorer catalysts, whereas chromium, cobalt, manganese, and iron compounds did not catalyze the reaction. Experiments with these last four elements were carried out at lower temperatures with the same results.

TABLE I

THE REACTION OF N,N-DIMETHYLDODECYLAMINE AND *t*-BUTYL HYDROPEROXIDE[a] WITH VARIOUS CATALYSTS

Catalyst[b]	Time, hr	Conversion, %[c]	Yield, %[d]
None	3	71	33
$Mo(CO)_6$	2	79	86
$VO(acac)_2$[e]	0.3	100	86
$V(acac)_3$	0.3	100	81
$VOSO_4$	0.3	100	82
$V(C_8H_{15}O_2)_x$[f]	0.25	100	89
VCl_3	0.16	100	88
V_2O_3	0.16	100	92
V_2O_5	0.25	90	96
V powder	1	90	54
$W(CO)_6$	5	69	51
$Cr(acac)_3$	5	85	17
Nb_2O_5	7	71	49
Ta_2O_5	10	79	44
$Co(C_8H_{15}O_2)_x$[f]	1	100	3
$Mn(acac)_3$	2.5	90	6
$Fe(acac)_3$	3	90	10

[a] Reagents were 0.09 mole of amine, 0.048 mole of *t*-butyl hydroperoxide, and 35 ml of *t*-butyl alcohol; reflux temperature for this mixture is 86°. [b] Catalyst concentration was 0.05 g except tungsten hexacarbonyl which was 0.02 g. [c] Conversion of hydroperoxide. [d] The yield of amine oxide is based on conversion of hydroperoxide. [e] (acac) = acetylacetonate. [f] Vanadium and cobalt octoate are a solution in heavy oil. They analyzed as 3% vanadium and 6% cobalt.

TABLE II

OXIDATION OF N,N-DIMETHYLDODECYLAMINE WITH CUMENE AND AMYLENE HYDROPEROXIDE REACTIONS

Hydroperoxide[a]	Solvent	Catalyst[b]	Time, hr	Temp, °C	Conversion, %[c]	Yield, %[d]
Cumene	*t*-BuOH	Mo	1	86	100	73
Cumene	THF	V	0.25	74	90	88
Cumene	MeOH	V	1.5	66	85	87
Cumene	$(Me)_2CO$	V	0.75	61	86	96
Cumene	Et_2O	V	2	41	67	100
Amylene	*t*-BuOH (17)	Mo	0.75	86	92	77
Amylene	*t*-BuOH (17)	V	0.25	86	100	63
Amylene	*t*-BuOH	V	2.25	60	88	87
Amylene	THF	V	0.5	74	92	84
Amylene	THF	Mo	2	74	60	85
Amylene	$(Me)_2CO$	V	0.75	60	89	91
Amylene	$(Me)_2CO$	Mo	8.83	60	72	93
Amylene	Et_2O	V	2.75	41	80	90
Amylene	Et_2O	Mo	8.83	41	42	100

[a] Reagent concentrations were 0.045 mole of amine, 0.025 mole of hydroperoxide, and 35 ml of solvent unless indicated in parentheses, and 0.02 g of catalyst was used. [b] Molybdenum was the hexacarbonyl and vanadium the oxyacetylacetonate. [c] Conversion of hydroperoxide. [d] Based on hydroperoxide conversion.

In Table II, experiments with N,N-dimethyldodecylamine and various organic hydroperoxides are listed. This data and the experiments listed in Tables I and III show a difference in the reactivity of the hydroperoxides. The reactivity of the hydroperoxides increases in the order *t*-butyl < cumene ≤ amylene

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[1] International Oxidation Symposium, San Francisco, Calif., Aug 1967.

[2] L. Kuhnen, *Chem. Ber.*, **99**, 3384 (1966).

[3] D. H. Wheeler, *Oil & Soap*, **1**, 89 (1932).

TABLE III

STERIC EFFECT IN THE AMINE HYDROPEROXIDE REACTION[a]

Amine, (mole)	Hydroperoxide (mole)	Solvent, 35 ml	Catalyst (g)	Time, hr	Conversion, %	Yield, %
Tri-*n*-butyl (0.05)	Amylene (0.025)	(Me)$_2$CO	VO(acac)$_2$ (0.02)	1.5	84	50
Tri-*n*-butyl (0.05)	Amylene (0.025)	(Me)$_2$CO	VO(acac)$_2$ (0.02)	5	67	75
Tri-*n*-butyl (0.10)	Amylene (0.05)	(Me)$_2$CO	VO(acac)$_2$ (0.02)	3.25	67	91
Tri-*n*-butyl (0.10)	*t*-Butyl (0.05)	(Me)$_2$CO	Mo(CO)$_6$ (0.02)	3.16	23	100
Tri-*n*-butyl (0.10)	*t*-Butyl (0.05)	*t*-BuOH	VO(acac)$_2$ (0.05)	1	96	39
Tri-*n*-butyl (0.10)	*t*-Butyl (0.05)	*t*-BuOH	Mo(CO)$_6$ (0.05)	2	84	39
Triethyl (0.05)	Amylene (0.025)	(Me)$_2$CO	VO(acac)$_2$ (0.02)	0.75	80	93
Triethyl (0.05)	Amylene (0.025)	(Me)$_2$CO	Mo(CO)$_6$ (0.02)	4.75	60	85
Triethyl (0.10)	*t*-Butyl (0.05)	(Me)$_2$CO	VO(acac)$_2$ (0.02)	2.3	83	100
Triethyl (0.10)	*t*-Butyl (0.05)	*t*-BuOH	VO(acac)$_2$ (0.05)	0.75	94	68
Triethyl (0.10)	*t*-Butyl (0.105)	*t*-BuOH	Mo(CO)$_6$ (0.05)	3.25	84	71
1-Dimethylamino-2-propanol (0.05)	Amylene (0.025)	(Me)$_2$CO	VO(acac)$_2$ (0.02)	0.5	86	100
1-Dimethylamino-2-propanol (0.05)	Amylene (0.025)	(Me)$_2$CO	Mo(CO)$_6$ (0.02)	3	52	100
1-Dimethylamino-2-propanol (0.05)	*t*-Butyl (0.025)	*t*-BuOH	VO(acac)$_2$ (0.02)	0.5	100	24
1-Dimethylamino-2-propanol (0.05)	*t*-Butyl (0.025)	*t*-BuOH	Mo(CO)$_6$ (0.02)	3.5	88	92
1-Dimethylamino-2-propanol (0.05)	*t*-Butyl (0.025)	(Me)$_2$CO	Mo(CO)$_6$ (0.02)	3.75	58	100
1-Dimethylamino-2-propanol (0.05)	*t*-Butyl (0.025)	(Me)$_2$CO	VO(acac)$_2$ (0.02)	0.75	84	80

[a] The temperature was the reflux temperature of the reaction mixture.

hydroperoxide.[4] The more reactive hydroperoxides allow the oxidation reaction to be run at lower temperatures. The reactions at these lower temperatures show again the great difference in the catalytic ability of molybdenum and vanadium.

These runs also show that the stability of the hydroperoxide in the presence of the amine affect the yield of the amine oxide. Two reactions must occur. One decomposes the hydroperoxide[5,6] and does not give amine oxide; the other, the catalytic oxidation, gives the amine oxide. The decomposition reaction is very temperature dependent, and the stability of the hydroperoxide to this reaction determines the limiting temperature for optimum yields of the amine oxide. The stability of the hydroperoxides to the decomposition reaction and their reactivity in the catalyzed oxidation seems to be related, although they do not have to occur by the same mechanism. Thus, the hydroperoxides that are less stable to the decomposition reaction are also more reactive in the catalytic oxidation. The stability of the studied hydroperoxides in this reaction media decreases in the order *t*-butyl > cumene ≥ amylene hydroperoxide. Thus, in refluxing *t*-butyl alcohol, the yield of the amine oxide is lower when cumene and amylene hydroperoxides are the oxidizing agents. In lower boiling solvents, high yields of the oxide are obtained with these hydroperoxides.

TABLE IV

THE EFFECT OF SOLVENT ON THE OXIDATION OF AMINE

Solvent[a]	Catalyst[b]	Temp, °C	Time, hr	Conversion, %[c]	Yield, %[d]
None	VO(acac)$_2$	51	6.5	28	100
None	VO(acac)$_2$	65	3.6	88	72
None	VO(acac)$_2$	75	2.3	92	67
t-BuOH	VO(acac)$_2$	60	5.3	80	87
t-BuOH	V$_2$O$_5$	60	5.3	80	87
t-BuOH	V$_2$O$_3$	60	8.75	88	80
MeOH	VO(acac)$_2$	66	1.5	84	90
MeOH	V$_2$O$_5$	66	1	89	87
MeOH	V$_2$O$_3$	66	0.75	77	90
THF	VO(acac)$_2$	72	0.5	92	84
THF	V$_2$O$_5$	72	0.75	84	91
THF	V$_2$O$_3$	72	0.75	91	91
(Me)$_2$CO	VO(acac)$_2$	60	0.75	88	94
(Me)$_2$CO	V$_2$O$_5$	60	3	87	82
(Me)$_2$CO	V$_2$O$_3$	60	0.75	86	89
Et$_2$O	VO(acac)$_2$	41	2.75	80	90
Et$_2$O	V$_2$O$_5$	41	14.25	74	87
Et$_2$O	V$_2$O$_3$	41	5.25	76	96

[a] Without solvent, the reagents were 0.09 mole of N,N-dimethyldodecylamine and 0.05 mole of amylene hydroperoxide; with solvent, the reagents were 0.045 mole of N,N-dimethyldodecylamine and 0.025 mole of amylene hydroperoxide. [b] Catalyst was 0.02 g. [c] Conversion is the hydroperoxide. [d] Yield is based on hydroperoxide conversion.

TABLE V

OXIDATION OF PYRIDINE WITH *t*-BUTYL HYDROPEROXIDE

Pyridine, mole	*t*-BuOOH, mole	*t*-BuOH, ml	Mo(CO)$_6$, g	Temp, °C	Time, hr	Conversion, %	Yield, %
0.05	0.048	35	0.05	86	1	44	
					2	56	
					5	63	83
0.05	0.048	70	0.05	86	1.75	66	
					2.75	69	76
0.05	0.10	35	0.05	86	1	90	100

The effect of solvent on the reaction is shown in Table IV. The absence of solvent retards the reaction rate and lowers the amine oxide yield. Therefore, for optimum yields, a solvent is necessary. Amines and amine oxides are known to form complexes with metals.[7,8] They can compete with the hydroperoxide in complexing the catalyst. In Table V, this effect is shown with pyridine. The initial conversion of hydroperoxide is very rapid. Thus the pyridine does not seem to be complexing with the catalyst. As the amine oxide concentration increases, the rate of the reaction is retarded. Simultaneously a white solid precipitates from the refluxing solution. Elemental analysis showed there is a 1:2:4 ratio of molybdenum, pyridine oxide, and carbon monoxide in this molecule. The structural determination of this compound is being attempted. If a 2:1 hydroperoxide–pyridine ratio is used, a high conversion and yield of the pyri-

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[4] D. B. Sharp and J. R. LeBlanc, Abstracts, 142nd National Meeting of the American Chemical Society, Cleveland, Ohio, April 1962, p 47C. Amylene hydroperoxide is a mixture of 2-(2-methylbutene-3-yl) hydroperoxide (58%) and 2-(3-methylbutene-3-yl) hydroperoxide (42%).

[5] C. W. Capp and E. G. E. Hawkins, *J. Chem. Soc.*, 4106 (1953).

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

[7] W. E. Hatfield and J. T. Yoke, *Inorg. Chem.*, **1**, 463 (1962).

[8] R. L. Carlin, *J. Am. Chem. Soc.*, **83**, 3773 (1961).

dine N-oxide is obtained in a short reaction time. The higher hydroperoxide concentration allows it to compete with the amine oxide for the catalyst. Vanadium compounds do not catalyze the pyridine oxidation. The vanadium catalyst probably forms a stronger complex with pyridine N-oxide than molybdenum.

Alcohol solvents retard the reaction rate. This is best seen in the case of vanadium oxyacetylacetonate which is soluble in organic solvent. Reactions catalyzed by this compound show that the rate is faster in tetrahydrofuran, acetone, and diethyl ether than in *t*-butyl alcohol and methanol. A comparison is not possible with vanadium pentoxide and vanadium trioxide, because these compounds are not completely dissolved in the reaction mixture. There are two possible explanations for the rate retardation in alcohol solvents. The alcohols could compete directly with the hydroperoxide in complexing the catalyst. The alcohols could also hydrogen bond with the hydroperoxide. This effect would make the electrons less available for complexing with the metal and retard the reaction rate. This last reason has been proposed to explain the difference in the kinetics observed in hydrocarbon and alcohol solvents for the reaction of cyclohexyl methyl sulfide with *t*-butyl hydroperoxide to give sulfoxides.[9]

A comparison of vanadium oxyacetylacetonate, vanadium trioxide, and vanadium pentoxide in the same solvent shows that there is a difference in catalytic ability of these compounds. This difference results from the solubility of the initial vanadium compounds in the reaction mixture and also its rate of conversion by the hydroperoxide to the catalyst. In general, organic soluble vanadium complexes are preferred catalysts for this reaction.

The steric effect of the groups on the nitrogen is important in selecting the reaction conditions. This is shown in Table III. With proper choice of hydroperoxide, temperature, and catalyst, high yields of the amine oxide can be obtained. The poor yield in the oxidation of 1-dimethylamino-2-propanol by *t*-butyl hydroperoxide–vanadium oxyacetylacetonate in refluxing *t*-butyl alcohol is a good example of the criticality of the reaction conditions. This same reaction in acetone gives a high yield of the amine oxide.

The mechanism of the oxidation of tertiary amines by hydroperoxides in the presence of VB and VIB transition elements appears to be ionic. Compared with olefins the faster rate and the lower temperatures required for the oxidation of the amines would be expected because of the greater availability of the unshared pair of electrons on the nitrogen. A free-radical reaction mechanism does not appear likely. Metal complexes such as cobalt, manganese, and iron, which are most effective in converting peroxides[10,11] to radicals are not catalysts for this reaction. The reaction of tertiary amines and *t*-butyl hydroperoxide under free-radical conditions has been studied and gave either the secondary amine[6] or small yields of the hydroxylamine[12] as the products but not the amine oxide.

Experimental Section

Materials.—*t*-Butyl hydroperoxide (94% purity) was purchased from the Lucidol Division, Wallace and Tiernan, Inc. Cumene hydroperoxide (79% purity), tri-*n*-butylamine, and triethylamine were purchased from Matheson Coleman and Bell. N,N-Dimethyldodecylamine (practical grade) was purchased from Eastman Organic Chemicals. 1-Dimethylamino-2-propanol was purchased from Aldrich Chemical Co. Cobalt octoate and vanadium octoate were purchased from Nuodex Products Co. The other inorganic compounds were purchased from various sources. All these reagents were used without further purification. Solvents were reagent grade. Amylene hydroperoxide was made according to the literature procedure.[4]

N,N-Dimethyldecylamine. Procedure A.—A solution of 21 g (0.1 mole) of practical grade N,N-dimethyldodecylamine, 4.6 g (0.05 mole) of *t*-butyl hydroperoxide (94% purity), 0.05 g of vanadium oxyacetylacetonate, and 27 g of *t*-butyl alcohol was added to a round-bottom flask equipped with a thermometer and reflux condensor. The reaction was refluxed at 90° for 15 min and cooled. The hydroperoxide was determined by iodometric titration.[3] There was complete conversion of the hydroperoxide. The amine oxide was determined by standard hydrochloric acid titration after reaction of the excess amine with methyl iodide.[13] The titration analysis showed an 86% yield of amine oxide. The titration was confirmed by nmr analysis. For the nmr analysis, methylene chloride was used as an internal standard and TMS as the reference compound. The methyl groups on the nitrogen of the amine and the oxide appeared at τ 7.87 and 6.8. The amine oxide was isolated by flash evaporating of the solvent, dissolving the residue in ether, and extracting the amine oxide into water. The water was flash evaporated. The resulting gel was dissolved in a minimum of acetone and cooled. This yielded 6.3 g (57% yield) of crystals, mp 120–122° (lit.[14] mp 117–123°). Alternatively, 30 ml of pentane was added to the residue after flash evaporation of the solvent. This precipitated the amine oxide (6.4 g, 58% yield), mp 120–124°.

Procedure B.—A solution of 21 g (0.1 mole) of practical grade N,N-dimethyldodecylamine, 9.2 g (0.1 mole) of *t*-butyl hydroperoxide (94% purity), 0.05 g of vanadium oxyacetylacetonate, and 27 g of *t*-butyl alcohol was treated as above. The hydrochloric acid–methyl iodide titration showed a 97% yield of amine oxide. The solvent was flash evaporated and gave 21 g of solid, mp 123–125°. The solid was triturated with 50 ml of pentane, filtered, and dried under vacuum. This yielded 17.7 g (80% yield) of anhydrous amine oxide, mp 128–130°. The infrared and nmr spectra were identical with those of an authentic sample.

Pyridine.—A solution of 3.9 g (0.05 mole) of pyridine, 9.2 g (0.1 mole) of *t*-butyl hydroperoxide (94% purity), 0.05 g of molybdenum hexacarbonyl, and 27 g of *t*-butyl alcohol was refluxed at 86° for 1 hr. There was a 90% conversion of the hydroperoxide based on the amine. Nmr analysis showed a 100% yield of the amine oxide. The pyridine oxide yield could not be obtained by the hydrochloric acid–methyl iodide method. The nmr spectrum of pyridine oxide was of the ABB′CC′ type with broad bands centered at τ 1.4, 1.6, and 2.5. The pyridine spectrum was the same type with bands at τ 2.4 and 2.8. Although the resonances overlap, an integral yielded the relative ratios of the two compounds. The addition of an internal standard, methylene chloride, to the sample permitted calculation of the amine oxide yield. The product was not isolated.

Registry No.—N,N-dimethyldodecylamine, 112-18-5; tri-*n*-butylamine, 102-82-9; triethylamine, 121-44-8; 1-dimethylamino-2-propanol, 108-16-7; pyridine, 110-86-1; *t*-butyl hydroperoxide, 75-91-2; cumene hydroperoxide, 80-15-9; 2-(2-methylbuten-3-yl) hydroperoxide, 15315-29-4; 2-(3-methylbuten-3-yl) hydroperoxide, 15315-30-7.

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(9) L. Bateman and K. R. Hargrave, *Proc. Roy. Soc.* (London), **A224**, 389, 399 (1954).

(10) W. H. Richardson, *J. Am. Chem. Soc.*, **87**, 247, 1096 (1965).

(11) E. G. E. Hawkins, "Organic Peroxides," D. Van Nostrand Co., Inc., New York, N. Y., 1961, p 17.

(12) L. A. Harris and H. S. Olcott, *J. Am. Oil Chemists' Soc.*, **43**, 11 (1966).

(13) L. D. Metcalfe, *Anal. Chem.*, **34**, 1849 (1962).

(14) G. L. K. Hoh, *et al.*, *J. Am. Oil Chemists' Soc.*, **40**, 268 (1963).