is estimated as 5.0, whereas for $Cu(HL)_2^{4+}$ the value is 7.6. Therefore, we can expect that the association constants for reaction 22 and also for reaction 24 include approximately 2.5 log units of stability which are provided by this energetically favored proton transfer, in addition to the stability due to the association of the species in the reaction. This effect is seen more dramatically, perhaps, in the comparison of the corresponding pairs of reactions, (17) with (20), (18) with (21), and (19) with (22). In the first two pairs, the stabilities show the expected decrease between the addition of the first and second ligand, whereas in going from reaction 19 to reaction 22 the constant for Cu actually increases because the added stability caused by the proton transfer is larger than the normal decrease between the addition of the second and third ligands.

Many other trends are apparent and will be discussed briefly. The end products formed in the sequence (20), (21), (22) are the same as those formed in (20), (25), (24), respectively, but whereas the constants follow the order (20) > (21) > (22) in the first series, we find that in the second series (20) < (25) < (24) because in this case the increasing positive charge resides not on the ligand but on the metal complex and thus facilitates association with the nucleophilic ligand. Likewise, in the series (22), (23), (24), the same end product, $M(HL)_2^{4+}$, is formed in each case, but the constants follow the order (22) < (23) < (24), because in this order, the extra positive charges are switched from the ligand to the metal complex. This again favors stronger association. In addition if we allow for the (approximately) 2.5 log units of extra stability in the values for (22) and (24), the increase obtained is quite regular, being 3.3, 6.1 for Ni and 3.8, 6.3, 9.4 for Cu.

Finally, Anderegg[5] did not report the formation constant for the tricoordinated complex $Zn(adap)^{2+}$, apparently because of the formation of hydrolysis products in an overlapping step as the bidentate $ZnH(adap)^{3+}$ was being converted to $Zn(adap)^{2+}$. In this study, we were able to obtain a formation constant for the tricoordinated complex $ZnH(tam)^{3+}$ but unable to obtain a constant for $Zn(tam)^{2+}$ because of hydrolytic polynucleation which resulted in precipitate formation. Thus the appearance of hydrolysis in these Zn complexes seems to depend more on the charge of the complex than on the number of ligand donor groups bound.

Acknowledgment. Part of this research was supported by the Public Health Service under Research Grant No. GM 10883 from National Institute of General Medical Sciences. One of us (L. J. Z.) thanks the University of Massachusetts for a Faculty Research Grant.

Metal Ion Catalysis of Oxygen Transfer Reactions. I. Vanadium Catalysis of the Epoxidation of Cyclohexene[1]

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Contribution from the Department of Chemistry at Kent State University, Kent, Ohio, and the Department of Physical Organic Chemistry, Stanford Research Institute, Menlo Park, California. *Received February 28, 1968*

Abstract: The reaction of *t*-butyl hydroperoxide with cyclohexene, in the presence of catalytic quantities of the vanadium acetylacetonates $VO(acac)_2$ and $V(acac)_3$ or the octoate $V(oct)_3$, gives quantitative yields of cyclohexene oxide at temperatures up to 84°, but this epoxidation is not catalyzed by the corresponding cobalt(II) derivatives or by di-*t*-butyl peroxalate. The reaction, as catalyzed by $VO(acac)_2$, is first order in catalyst (in the range 6×10^{-5} to 1.2×10^{-3} *M* chelate), and, with cyclohexane as the major solvent component, is first order also in olefin (in the range 0.088–1.8 *M*). The epoxidation is strongly inhibited by *t*-butyl alcohol, a reaction product. Initial rates (extrapolated values) in cyclohexene conform to the rate law, rate $= k[V_0]/\{(1/[P]K_p) + 1\}$, where $[V_0]$ is the concentration of added vanadium and [P] is the concentration of hydroperoxide. This is consistent with reaction *via* a hydroperoxide–vanadium complex (VP) having an association constant K_p and a specific rate k. Values of k lie between 7.3 min^{-1} (24.1°) and 39.3 min^{-1} (50.6°); activation parameters are $\Delta H^{\ddagger} = 12.7$ kcal/mole and $\Delta S^{\ddagger} = -19.8$ eu. Values of K_p are 15.3 M^{-1} at 24.1° and 10.3 M^{-1} at 50.6°. Rates in the presence of *t*-BuOH follow a more complex rate law (eq 3 in the text) of the type which indicates competitive inhibition by alcohol through two alcohol–vanadium complexes, VA and VA_2, having association constants 119 M^{-1} and 2.1×10^4 M^{-2} at 41.3°. The proposed mechanism involves neither a free-radical chain process nor a recycling of the metal between two oxidation states, but rather a rate-determining heterolysis of the O–O bond in a vanadium(V)–hydroperoxide complex. The structural requirements for this type of metal catalysis are considered.

It is widely recognized that the reactions of hydrogen peroxide and alkyl hydroperoxides may be strongly influenced by catalytic quantities of compounds of the transition metals; decomposition rates may increase dramatically, and the manner in which these oxidants react with oxidizable substrates may be seriously

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(1) Initial stages of this research were carried out by the three authors at Stanford Research Institute under multiple industrial sponsorship. Kinetic studies, at Kent State University, were supported jointly by the Petroleum Research Fund of the American Chemical Society (Grant 2868-A3) and the Federal Water Pollution Control Administration (Grant WP-01209-01).

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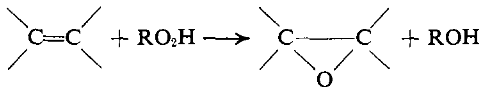
modified.[3] Transition metal catalysts for peroxide reactions fall mainly into two distinct classes: on one hand, metals such as iron and cobalt having two comparably accessible oxidation states differing by a single unit tend to promote homolysis of the peroxy linkage and subsequent reaction of the resulting free radicals; in contrast, higher oxidation states of elements in the vanadium and chromium groups may assist heterolytic cleavage of the O–O bond and lead to reactions of what is, formalistically speaking, electron-deficient oxygen. The highly selective epoxidation of olefins using hydroperoxides or H_2O_2 in the presence of certain transition metal catalysts[4]



appears to belong to the second of these classes, for Indictor and Brill,[5] working with metal acetylacetonates, have shown that metal ions which are most effective in converting peroxides to radicals are not suitable catalysts in this case, whereas with derivatives of VO^{2+}, V^{3+}, and MoO_2^{2+}, yields of epoxide may, under favorable circumstances, be quantitative. The same authors report that epoxidation of octene-1 with *t*-butyl hydroperoxide in the presence of these three catalysts proceeds according to the rate law

$$\text{rate} = -d(t\text{-BuO}_2\text{H})/dt = k(t\text{-BuO}_2\text{H})(\text{catalyst})^{0.5} \quad (1)$$

and suggest that the reactions proceed through complexes of the hydroperoxide with the metal chelate; it is, however, not immediately evident how the intervention of such a complex is implied from the rate law given. The present report describes a more detailed kinetic study of a single example of this oxidation, *i.e.*, the epoxidation of cyclohexene with *t*-BuO_2H and $VO(acac)_2$. We find the dependency, both on hydroperoxide and on catalyst, to be different from that reported by Brill and Indictor, although, somewhat paradoxically, our rate expression is consistent with reaction through an intermediate of the type which they propose.

Experimental Section

Materials. *t*-Butyl hydroperoxide (Matheson, Practical grade) was purified by vacuum distillation, bp 32° at 15 mm; a number of cuts of the distillate were taken, and each was analyzed iodimetrically for hydroperoxide (see below). Only those portions having a *t*-BuO_2H content greater than 99.8% were used in kinetic runs. Samples were stored at −40°, at which temperature there was no detectable decomposition on standing for 6 months.

Vanadyl acetylacetonate, $VO(acac)_2$ (J. T. Baker), was recrystallized from anhydrous acetone. Unlike the bottled material, the purified chelate dissolved readily in benzene and chlorobenzene without leaving a residue. The resulting vanadium(IV) solutions showed some deterioration on standing in air for several hours; hence, each kinetic run employed a freshly prepared solution of the catalyst. Vanadium(III) acetylacetonate (MacKenzie) and vanadium(III) octoate (K and K Laboratories), employed as catalysts in preliminary experiments, were used as received. The latter, a glue-like material, contained, by our analysis, no more than 58% vanadium octoate by weight, together with a considerable quantity of the parent carboxylic acid; attempts at purification of this material were unsuccessful.

Cyclohexene (Matheson Chromatoquality) was purified before each kinetic run by passage through neutral activated alumina (E. Merck AG, Activity I, Darmstadt, Germany). Triphenylphosphine (Matheson) was resublimed *in vacuo* at 100° and kept at −40°.[6] Acetone and benzene (Matheson Spectroquality) and cyclohexane (Matheson Chromatoquality) were used as received without further purification.

Analyses. Hydroperoxide was determined by adding the sample to a mixture of 10 ml of *n*-propyl alcohol and 5 ml of glacial acetic acid, refluxing gently for 20 min with potassium iodide, cooling, and, after addition of 1 ml of water, titrating the iodine released with standard aqueous $Na_2S_2O_3$.

Epoxide content in the oxidation mixtures was determined by adding a sample to a solution of triphenylphosphine in acetone (1.2 equiv of phosphine per equiv of hydroperoxide present) and then analyzing the mixture gas chromatographically. Analyses were carried out on a Hewlett-Packard instrument (F & M Model 700), equipped with an electronic digital integrator (Varian Model 475/476); the column was 10% carbowax on firebrick. In all analyses, known amounts of chlorobenzene were added as an internal standard.

Preliminary Observations. Decompositions of *t*-butyl hydroperoxide in refluxing cyclopentene (45–47°) or cyclohexene (84–86°) under nitrogen in the presence of 0.00014–0.0021 *M* vanadium(III) octoate gave 95–100% yields of the corresponding epoxides at conversions up to 90% of the hydroperoxide, in accord with previous observations with the vanadium acetylacetonates as catalysts;[5] reaction times were 6–24 hr for cyclopentene and 2–6 hr for cyclohexene. Decomposition of *sec*-butyl hydroperoxide in refluxing cyclopentene in the presence of 0.0003 *M* vanadium(III) octoate likewise gave a 98% yield of the epoxide at 85% hydroperoxide conversion in 6 hr.

Epoxide yields decrease as the olefin is diluted with inert solvent. At 30% (v/v) cyclohexene in cyclohexane at 86°, epoxide yields fall to about 92% at 0.0006 *M* catalyst, and, still further, to 60% at 0.002 *M* catalyst. At a given catalyst concentration, epoxide yields are very nearly independent of conversion. Since glpc traces of these nonquantitative oxidations showed no additional volatile products (particularly cyclohexenol or cyclohexenone), it may be inferred that epoxidation competes with decomposition of the hydroperoxide to *t*-butyl alcohol and oxygen. For most kinetic runs, carried out at 25–50° in the absence of inert diluent, decomposition to oxygen is negligible.

Boron(III) is much less effective than vanadium as an epoxidation catalyst. The rate of decomposition of *t*-butyl hydroperoxide in cyclohexene was less than one-tenth as great in the presence of 0.0016 *M* $B(OAc)_3$ as in the presence of 0.00025 *M* vanadium(III) octoate, and the yield of epoxide at 63% hydroperoxide conversion was found to be only 14%. Cobalt(II) octoate strongly catalyzes the decomposition of the hydroperoxide in refluxing cyclopentene, but the yield of epoxide was only 2.5% at 99% hydroperoxide conversion. The metal chelates $Cu(acac)_2$, $Co(acac)_2$, $Mn(acac)_3$, and $Fe(acac)_3$ catalyze the decomposition of hydroperoxide but not the epoxidation; di-*t*-butyl peroxalate catalyzes neither. The decomposition of hydroperoxide is retarded by addition of acetonitrile, being about one-third as rapid in 70:30 acetonitrile–cyclohexene as in 70:30 cyclohexane–cyclohexene at comparable concentrations of catalyst and peroxide. Yields of epoxide from the reactions in acetonitrile were about four-fifths as large as those in cyclohexane under similar conditions.

In both the octoate-catalyzed and the chelate-catalyzed epoxidations, colored transient species are observed almost immediately after mixing hydroperoxide with catalyst. These colors, orange for octoate catalysis and red for acetylacetonate catalysis, fade rapidly as the reaction proceeds, turning first to yellow, then to colorless; they are most persistent at low reaction temperatures and low hydroperoxide/catalyst ratios but, in all cases, have disappeared before 0.2% of the hydroperoxide has decomposed. The formation of these colors and the species responsible for them are currently being investigated.

Addition of acetic acid to the $V(acac)_3$-catalyzed epoxidation results in further acceleration. Typically, oxidation in a solution

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[3] For a brief summary of this area, see A. G. Davies, "Organic Peroxides," Butterworth and Co., Ltd., London, 1961, pp 174–182.

[4] (a) J. Kollar, Belgian Patent 641,452 (June 18, 1964). (b) For studies of reactions of this type in aqueous solution, see G. B. Payne and P. H. Williams, *J. Org. Chem.*, 24, 54 (1959); K. A. Saegebarth, *ibid.*, 24, 1212 (1959).

[5] N. Indictor and W. F. Brill, *ibid.*, 30, 2074 (1965).

[6] Nonsublimed triphenylphosphine, when used to reduce *t*-butyl hydroperoxide, gave erratic results. In some cases, peroxide reduction was incomplete, even after 15 min at 25°. Freshly sublimed material behaved more satisfactorily but deteriorated perceptibly after standing several weeks at room temperature.

0.014 M in $V(acac)_3$ and 0.70 M in acetic acid proceeds about 10 times as rapidly (as judged by half-life for hydroperoxide disappearance) as in the absence of added acid.[7]

The epoxidation reactions in this study are strongly self-inhibitory. During the early stages of reaction, inhibition may be attributed almost solely to the *t*-butyl alcohol formed along with the epoxide. Superimposed on this effect is a further mode of inhibition which appears to arise from oxidative degradation of the catalyst; it may be observed most readily by comparing the effectiveness of a "used" catalyst preparation (present in a solution in which a known quantity of hydroperoxide has decomposed) with that of a freshly prepared catalyst preparation to which the corresponding amount of *t*-BuOH has been added. In such cases, the rates with the fresh catalyst invariably exceed those with the aged catalyst, and the rate difference increases with the length of the preaging period.

Kinetic Experiments. Because of the uncertain character of the vanadium(III) octoate preparation available and the instability of $V(acac)_3$ solutions in air, kinetic runs were made with $VO(acac)_2$ as catalyst. The major difficulty was the autoinhibitory nature of the reaction, for it precluded obtaining meaningful kinetic points from a single reaction mixture at early, intermediate, and later stages in the same reaction. Instead, average rates were measured as early in the reaction as was practicable (during the first 1–4% reaction) in the presence of small measured quantities of added *t*-BuOH, then extrapolated to zero alcohol, taking into consideration also the alcohol formed during the course of the reaction.[8a] Concentrations of catalyst were between 5×10^{-5} and 1×10^{-3} M, and concentrations of hydroperoxide between 0.027 and 0.5 M.[8b] In most experiments, cyclohexene itself was used as the solvent, but a series of runs, to measure rate dependence on olefin, was carried out in cyclohexane with variation in the olefin concentration between 0.0875 and 1.8 M. Temperatures were constant to within better than 0.1° during a given series of runs.

Before each reaction, both the catalyst solution (containing a measured quantity of $VO(acac)_2$ and 250 μl of chlorobenzene diluted to 10.00 ml with benzene) and the hydroperoxide solution (containing 15–500 μl of hydroperoxide diluted to 5.00 ml with cyclohexene) were allowed 5 min for thermal preequilibration. The reaction was then initiated by adding 0.50 ml of catalyst solution to the hydroperoxide–olefin mixture. After a measured time interval (2.0–20 min), a 0.50-ml sample of the solution was withdrawn and the reaction quenched by adding to a solution of triphenylphosphine (1.2 mequiv for each mequiv of hydroperoxide in the sample) in 0.10 ml of acetone. The resulting mixtures were kept at Dry Ice temperature until glpc analysis for cyclohexene oxide; the sample size for analysis was 12–15 μl, but, since an internal standard (chlorobenzene) had been added, volume control was unnecessary. Where possible, samples were analyzed very soon after quenching, for the epoxide content was found to rise slowly as the solutions stood for several hours. Detector response was very nearly proportional to epoxide content for concentrations greater than 0.005 M; below this value, calibration of response with known concentrations of epoxide was necessary. Concentrations below 0.002 M could not be measured satisfactorily. Duplicate analyses of the same sample generally agreed to within better than 0.0002 M, provided that there was no delay between analyses. Thus, the relative error in epoxide content is less for higher conversions, but, at the same time, the error in rate due to uncertainties in extrapolation to zero *t*-BuOH is greater.

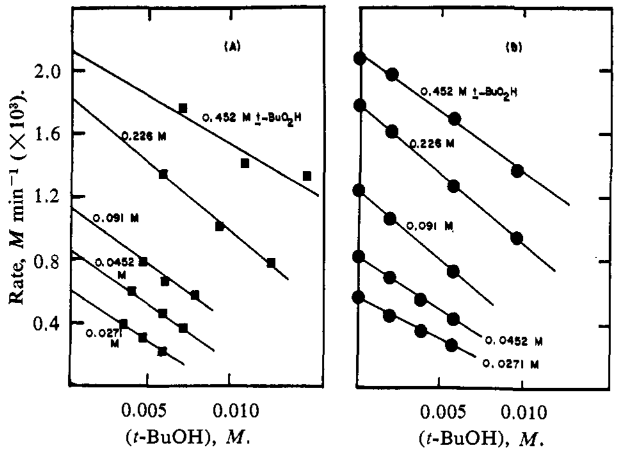

Figure 1. Extrapolation of rate data to zero *t*-butyl alcohol (epoxidation reactions in cyclohexene, 41.3°; $[VO(acac)_2]_{initial}$ $1.04 \times 10^{-4} M$): (A) observed rates, (B) rates calculated from eq 3; parameters taken from Table III and Figure 4. Note the close approach to linearity with the calculated rates.

For runs with extra *t*-BuOH, the concentration of added alcohol was between 0.003 and 0.030 M. With alcohol contents significantly higher than this, reaction times needed to obtain reliably measurable quantities of epoxide were sufficiently great so that oxidative deterioration of the catalyst became troublesome. Since alcohol, in addition to that added, was formed during the reaction, an average value of (*t*-BuOH), midway between the initial and final concentrations, was used in subsequent calculations.

Typical extrapolations to zero alcohol are shown in Figure 1A. Such extrapolation probably is the chief source of error in the present study, for the extrapolated sections comprise 25–40% of the total estimated rates. Thus, an error of 10% in evaluation of the slope would result in an error of 2.5% in the rate at high peroxide concentrations and about 4% at low concentrations. A further question is concerned with the use of a straight line function for this extrapolation; the principal justification for this (see Discussion section) is that plots of rate *vs.* alcohol content calculated using rate and equilibrium constants obtained in the resulting treatment are found to approach linearity closely in the concentration ranges employed and that this approximation to linearity persists even if substantial changes are made in these constants.

Results and Discussion

The failure of the very effective radical initiator, di-*t*-butyl peroxalate,[9] to catalyze the epoxidation, and the very low yields of epoxide obtained when cobalt, rather than vanadium, derivatives are used as catalysts, appear to rule out a radical chain path for this reaction. The deeply colored species formed upon mixing catalyst with hydroperoxide are intermediates in conversion of vanadium to its active form(s), but do not intervene in the catalytic sequence itself since very nearly all of the reaction occurs after these species have disappeared. A sequence involving recycling of vanadium between the +3 and +5 oxidation states is, in principle, possible but is highly unlikely, for there is virtually no evidence that vanadium(V) compounds will undergo two-electron reductions by organic substrates under conditions similar to those used here.[10] More probably, vanadium is converted to the +5 state at the beginning of the reaction and remains in that state throughout. If this be so, catalysis may be ascribed to vanadium(V)–

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[7] Since our vanadium(III) octoate preparation is undoubtedly contaminated with the parent carboxylic acid, it is likely that this material is a more effective catalyst than the pure salt.

[8] (a) If hydroperoxide content during a single run is followed as a function of time, the combination of peroxide loss and catalyst deactivation results in what appears to be a close approximation to a second-order hydroperoxide dependence with, however, some deviation very early and very late in the reaction; varying the initial hydroperoxide concentration clearly shows such an apparent relationship to be illusory. The necessity for measuring rates very early in the course of the reaction opens to serious question any attempted kinetic study which follows the reaction by measuring hydroperoxide loss instead of appearance of product, for such a procedure requires the very accurate estimate of small hydroperoxide differences in the presence of large amounts of hydroperoxide. (b) Measurement of rates at hydroperoxide concentrations much above 0.5 M was not satisfactory using the present procedure. The *t*-BuOH, formed in the reaction and by subsequent reduction of excess hydroperoxide with triphenylphosphine, precedes the epoxide off the glpc column but exhibits appreciable "tailing." At high concentrations of *t*-BuOH, this tailing seriously interferes with quantitative estimate of epoxide.

[9] P. D. Bartlett, E. P. Benzing, and R. E. Pincock, *J. Am. Chem. Soc.*, **82**, 1766 (1960).

[10] Vanadium(V) is an effective oxidizing agent for a number of alcohols and ketones (see, for example, J. S. Littler and W. A. Waters, *J. Chem. Soc.*, 4046 (1959)). These oxidations, however, require addition of strong acid and appear to involve one-electron, rather than two-electron, changes.

hydroperoxide interaction, in analogy to the mechanisms suggested[4b,11] for the tungsten(VI)-catalyzed reaction of H_2O_2 and olefins in hydroxylic solvents.

Typical kinetic data are presented in Tables I and II. The values at 42.1° in Table I clearly show the reaction to be first order in catalyst in the range 6×10^{-5} to 1.2×10^{-3} *M* $VO(acac)_2$, in contrast to the half-order dependency reported for the epoxidation of 1-octene.[5] The experiments summarized in Table II, which were carried out with cyclohexane the major solvent component, show the reaction to be first order also in cyclohexene within the range 0.0875 to 1.795 *M* olefin.

Table I. Typical Kinetic Data for the Vanadium-Catalyzed Epoxidation of Cyclohexene with *t*-Butyl Hydroperoxide. Solvent, Cyclohexene

Temp, °C	[Catalyst] $\times 10^4$ [a]	$[BuO_2H]$	Rate $\times$ 10^4 [b]
42.1	12.10	0.452	246
	6.00		117
	2.00		39.1
	0.61		12.5
34.1	2.22	0.452	15.9
		0.0452	6.43
	1.11	0.452	7.85
		0.0452	3.44
	1.05	0.226	6.11
		0.0452	3.39
31.0	1.10	0.452	11.4
		0.226	9.45
		0.135	8.54
		0.0904	6.98
		0.0452	4.51
		0.0271	3.34
36.0	1.11	0.452	16.5
		0.226	14.5
		0.135	12.3
		0.0904	10.4
		0.0452	7.05
		0.0271	4.72
41.3	1.03	0.452	23.0
		0.226	18.0
		0.135	16.2
		0.0904	13.5
		0.0452	9.10
		0.0271	6.05
50.6	1.04	0.452	34.1
		0.226	29.7
		0.135	23.7
		0.0904	21.3
		0.0452	14.2
		0.0271	9.86

[a] Total concentration of $VO(acac)_2$ added. [b] Rates in *M* min^{-1}, extrapolated to zero *t*-BuOH.

Table II. Kinetic Data for the Vanadium-Catalyzed Epoxidation of Cyclohexene with *t*-Butyl Hydroperoxide.[a] Solvent, Cyclohexane

[Olefin]	Rate $\times 10^3$ [b]	k_2[c]
1.795	2.69	3.19
0.897	1.37	3.28
0.449	0.630	2.98
0.180	0.253	2.99
0.0875	0.109	2.66
	k_2 (av) 3.02 ± 0.20	

[a] Reactions at 41.3°. Hydroperoxide, [P], = 0.181 *M*. Total concentration of $VO(acac)_2$, $[V_0]$, = 5.62×10^{-4} *M*. [b] Rates in *M* min^{-1}, extrapolated to zero *t*-BuOH. [c] Calculated second-order rate constant (in l. $mole^{-1}$ min^{-1}), $(1/V_0)\{1/K[P]) + 1\}$(rate/[olefin]), where *K* is taken as 11.6 M^{-1} (see Table III).

The variation of rate with hydroperoxide concentration (Table I) does not correspond to an integral reaction order. At low hydroperoxide concentrations, rate is nearly proportional to (t-BuO_2H), but, at higher concentrations, rates level off and appear to approach a limiting value (which, however, is proportional to concentration of catalyst). This type of behavior strongly indicates that reaction rate varies as the concentration of a partially dissociated complex involving hydroperoxide; at low (t-BuO_2H), the concentration of such a complex is proportional to hydroperoxide concentration, whereas, at high (t-BuO_2H), conversion to such a complex is nearly complete and its concentration is limited by the coreactant present in the lesser concentration, *i.e.*, the vanadium catalyst. This situation is analogous to the Michaelis–Menten picture of enzyme catalysis and corresponds to the rate law

$$\text{rate} = \frac{k[V_0]}{(1/[P]K_p) + 1} \qquad (2)$$

where *k* is the limiting specific rate (which would be observed at very high ratios of hydroperoxide to catalyst[8b]), $[V_0]$ is the total concentration of added vanadium, [P] is the concentration of hydroperoxide, and K_p is the association constant of the vanadium–hydroperoxide complex. In such cases, both the limiting rate and the association constant may be obtained conveniently by plotting (rate/[P]) *vs.* rate.[12] In the present system, plots so constructed are very nearly linear for data within the temperature range 24–51°; a typical plot (for 36.0°) is shown in Figure 2, together with the least-squares line.

Values of K_p (obtained as slopes of plots of this type) and *k* (obtained as intercepts) are given in Table III for measurements at five temperatures. Note that the mean deviations in K_p values are considerably greater than those associated with the *k* values, reflecting the circumstance that *k* is determined, in the main, by the rates at high hydroperoxide concentrations, whereas K_p depends markedly also on rates measured at low (t-BuO_2H), which are relatively more uncertain. An Arrhenius plot of log *k* *vs.* $1/T$ closely approaches a straight line (Figure 3) indicating that the extrapolation procedure used to obtain rates is free from large random errors (but not necessarily from systematic error): the

Table III. Limiting Specific Rates (*k*) and Association Constants (K_p) of Vanadium–Hydroperoxide Complex, VP[a]

Temp, °C	*k*, min^{-1}	K_p, M^{-1} [b]
24.1	7.30 ± 0.04	15.3 ± 2.0
31.0	12.1 ± 0.2	13.2 ± 1.0
36.0	17.2 ± 0.4	12.4 ± 0.9
41.3	24.7 ± 2.0	11.6 ± 0.8
50.6	39.3 ± 1.3	10.3 ± 0.7

[a] Evaluated from intercepts and slopes of Hofstee-type plots (Figure 2); solvent, cyclohexene. [b] K_p = [VP]/[V][P], where P is hydroperoxide, and V is hydroperoxide-free vanadium.

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(11) M. Mugdan and D. P. Young, *J. Chem. Soc.*, 2988 (1949). For tungsten(VI)-catalyzed peroxide reactions, the possibility that catalytic action involves recycling of tungsten between oxidation states is virtually ruled out by the low reduction potential of W(VI).

(12) B. H. J. Hofstee, *Nature*, **184**, 1296 (1959); see also M. Dixon and E. C. Webb, "Enzymes," 2nd ed, Academic Press Inc., New York, N. Y., 1964, p 69.

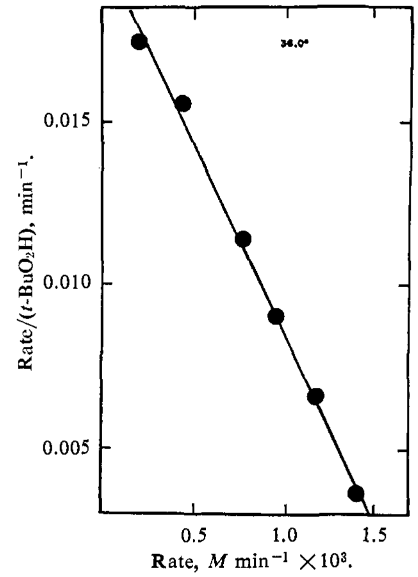


Figure 2. Hofstee-type plot, rate/[hydroperoxide] *vs.* rate (epoxidation in cyclohexene, 36.0°; $[VO(acac)_2]_{initial}$ 1.11 × 10^{-4} *M*). Rates adjusted to zero *t*-BuOH. The slope of the least-squares line shown indicates an association constant of 11.8 M^{-1} for the vanadium–hydroperoxide complex. The intersection of this line with the abscissa (at 0.001985 *M* $\min^{-1}$) corresponds to a specific rate of heterolysis, *k*, of 17.8 $\min^{-1}$.

resulting activation parameters associated with *k* are $\Delta H^{\ddagger} = 12.7 \pm 0.4$ kcal/mole and $\Delta S^{\ddagger} = -19.8 \pm 1.9$ eu. The uncertainties associated with the K_p values are too great to allow a reliable estimate of the enthalpy of association of the hydroperoxide-vanadium complex, but the trend toward lower K_p values at higher temperatures is unmistakable (and is expected for a reaction of this type).

Representative rate data for reactions in the presence of known quantities of *t*-butyl alcohol are given in Table IV, which shows inhibition by alcohol to be quite striking. Typically, the epoxidation rate with 0.226 *M* hydroperoxide is reduced to less than one-half of its extrapolated value (for zero alcohol) by addition of only $^1/_{20}$ mole of alcohol per mole of hydroperoxide. This emphasizes the necessity for examining this reaction at very low conversions to obtain reliable specific rates.

Table IV. Typical Kinetic Data for *t*-Butyl Alcohol Inhibition of the Vanadium-Catalyzed Epoxidation of Cyclohexene with *t*-Butyl Hydroperoxide at 41.3°

[P], M^a	[A], $M \times 10^{3\,b}$	$[V_0]$, $M \times 10^{4\,c}$	Rate (obsd) $\times 10^{3\,d}$	Rate (calcd) $\times 10^{3\,e}$
0.452	10.37	1.08	1.47	1.37
0.226	5.55	1.08	1.41	1.35
	8.85		1.10	1.04
	12.05		0.81	0.81
0.181	5.07	1.04	1.18	1.21
	8.65		0.85	0.89
	11.22		0.70	0.70
0.091	4.33	1.04	0.78	0.86
	7.45		0.58	0.62
0.045	3.76	1.10	0.63	0.58
	5.46		0.48	0.48
	6.72		0.38	0.40
0.027	3.16	1.10	0.47	0.42
	4.45		0.32	0.35
	5.57		0.27	0.24

[a] t-BuO_2H. [b] *t*-BuOH, average value. [c] Total concentration of $VO(acac)_2$ added. [d] Rates in *M* $\min^{-1}$. [e] Rates calculated using eq 3. Values of *k* and K_p taken from Table III. $K_i = 119\ M^{-1}$. $K_i' = 2.1 \times 10^4\ M^{-2}$.

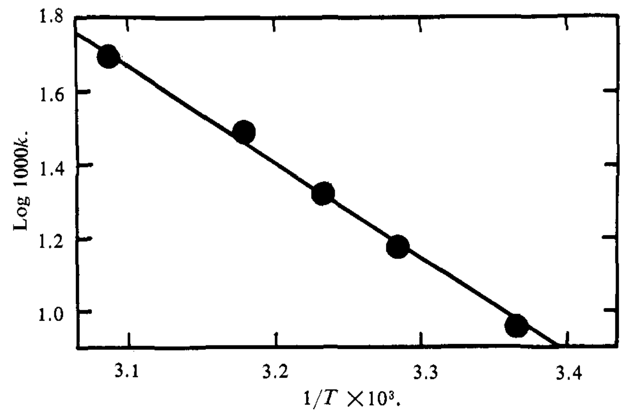


Figure 3. Arrhenius plot, log *k* *vs.* 1/*T*, for the rate-determining step in the epoxidation of cyclohexene with *t*-butyl hydroperoxide in the presence of added $VO(acac)_2$ (solvent cyclohexene). From the slope of this plot, a $\Delta H^{\ddagger}$ value of 12.7 ± 0.4 kcal/mole and a $\Delta S^{\ddagger}$ value of −19.9 ± 1.9 eu were obtained.

The inhibitory action of *t*-butyl alcohol doubtlessly arises from the formation of one or more alcohol–vanadium complexes which are less dissociated than the hydroperoxide–vanadium complex but are catalytically inactive. Reaction rate in a competitive inhibition of this sort depends upon the number and stoichiometry of the alcohol–vanadium complexes. In particular, if there are two such alcohol complexes, VA and VA_2, the rate law assumes the form[13]

$$\text{rate} = \frac{k[V_0]}{(1/[P]K_p)(K_i[A] + K_i'[A]^2 + 1) + 1} \tag{3}$$

where K_i and K_i' are the association constants of VA and VA_2, and [A] is the concentration of alcohol (the inhibitor); if only complex VA is kinetically significant, a simpler form, without $K_i'[A]^2$ in the denominator, describes the rate behavior. The sum of the terms involving [A] represents the total of alcohol-bound vanadium, here designated $\Sigma[VA_n]$, which is equal to $[V_0] - [VP] - [V]$ (where [VP] is the concentration of vanadium–hydroperoxide complex and [V] is the concentration of vanadium bound neither to hydroperoxide nor alcohol). Values of $\Sigma[VA_n]$ may be obtained from rate measurements at known concentrations of catalyst, hydroperoxide, and alcohol. If only the 1 : 1 alcohol–vanadium complex is important, the ratio $\Sigma[VA_n]/[V][A]$ will show no systematic variation with [A]; if, on the other hand, higher complexes play any part in the inhibition, this ratio will increase with [A]. A plot of $\Sigma[VA_n]/[V][A]$ *vs.* [A] is shown in Figure 4.[14] Although there is considerable scatter,

(13) See, for example, C. Walter and E. Frieden in "Advances in Enzymology," Vol. XXV, F. F. Nord, Ed., Interscience Publishers, New York, N. Y., 1963, p 175. Equation 3 is analogous to a simpler expression given by these authors which considers the formation only of a single inhibitor complex and therefore does not contain the $K_i'[A]^2$ term. Note also that in the usual formalism of enzyme kinetics $1/[P]K_p$ would be replaced by $K_m/[P]$, where K_m, the Michaelis constant, is a dissociation, rather than an association, constant.

(14) For convenience in computation, use was made of the relationship

$$\frac{\Sigma[VA_n]}{[V][A]} = \frac{[P]K_p[([V_0]k/\text{rate}) - 1] - 1}{[A]}$$

which may be obtained by combining the defining equations for *k* and K_p

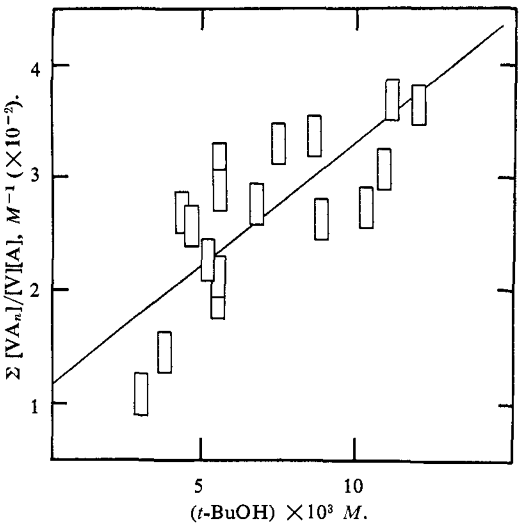


Figure 4. Variation of the ratio $\Sigma[VA_n]/[V][A]$ with concentration of t-BuOH. $\Sigma[VA_n]$, the total of alcohol-bound vanadium, is obtained by measuring the decrease in epoxidation rates as measured quantities of t-butyl alcohol are added (see ref 14). Epoxidation reactons in cyclohexene, 41.3°. The intercept of the least-squares line shown gives a value of 119 M^{-1} for the association constant of the 1:1 vanadium-alcohol complex, VA. The slope of this line gives the value 2.1×10^4 M^{-2} for the association constant of VA_2.

due mainly to the uncertainties in measured rates, the plot shows a definite upward slope, indicating inhibitory action both by VA and VA_2. A least-squares treatment of the plot, assuming it to be of the form

$$\frac{\Sigma[VA_n]}{[V][A]} = K_i + K_i'[A] \qquad (4)$$

leads to a K_i value (intercept) of 119 l. mole^{-1} and a K_i' value (slope) of 2.1×10^4 l.^{2} mole^{-2}. The quality of the data does not justify a more elaborate analysis.

Rates calculated from eq 3, using the K_i and K_i' values above and the K_p and k values from Table III, are compared to the observed values in Table IV. In Figure 1B, rates calculated in the same manner are plotted against alcohol concentration; it is seen that these plots are very nearly linear in the range of alcohol concentrations employed. This, then, is taken as justification for the linear extrapolation used to obtain epoxidation rates in the absence of alcohol. It is emphasized that even if sizable changes (up to about 30%) are made in the values of k or in the various association constants, the approach to linearity in such plots persists, although the slopes may change.[15]

Rate laws 2 and 3, although strongly indicating the formation of a vanadium–hydroperoxide complex, do not demand that such a complex be involved in the epoxidation reaction. Indeed, reflecting their fundamental limitation, kinetic studies alone cannot distinguish between a reaction proceeding through such a complex and one involving unbound catalyst and unbound hydroperoxide in mobile equilibrium with the complex, for the composition of the transition state would be the same in both cases. However, the experiments in cyclohexane, which show the epoxidation to be first order also in olefin, tend to implicate the hydroperoxide–vanadium complex as an intermediate. The transition state contains one molecule each of hydroperoxide, olefin, and vanadium catalyst; and, assuming a termolecular collision to be unlikely, two of these components must interact before the third intervenes. Since there is no evidence on hand which points to a catalyst–olefin or a hydroperoxide–olefin complex, a catalyst–peroxy complex appears to be the most likely intermediate. The following reaction sequence (eq 5–10), then, is consistent with the information in the present study. The experiments here shed little light either on the preliminary activation process (which almost certainly occurs in two or more steps) or the ligand environment of the active form of the complex (represented noncommittally above as pentapositive vanadium (i in eq 5)). It should be noted, however, that although these preliminary steps are fast compared to the reaction here studied, they are not immeasurably fast; further study of these steps is in progress.

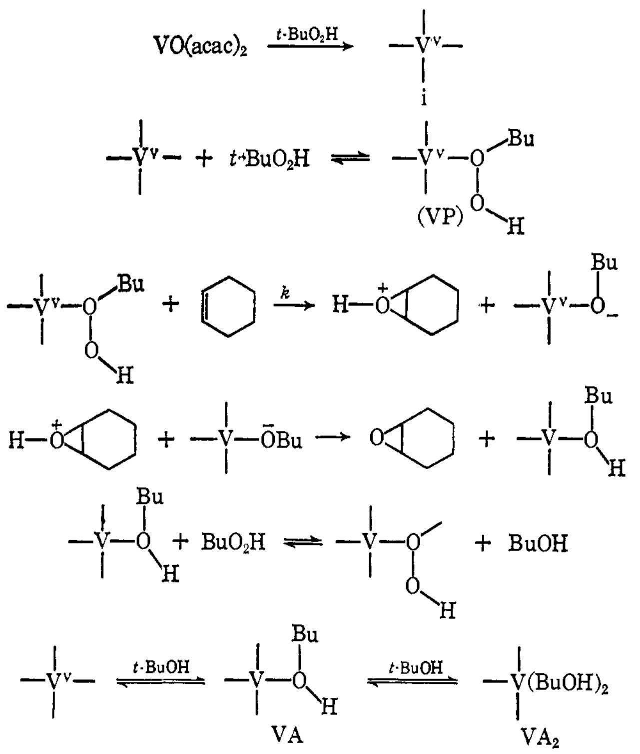
If, as we suspect, the reaction passes through the peroxy complex VP, the catalytic effectiveness of vanadium may be ascribed to its ability to polarize the O–O bond in the hydroperoxide and thus facilitate its heterolysis under the action of the weak nucleophile, cyclohexene. In that sense, the epoxidation involves electropositive oxygen, although the positive fragment in this case never achieves freedom. Other metal oxidation states which act in a similar manner (molybdenum(VI) and tungsten(VI)) are, like vanadium(V), small, highly charged ions having low-lying, although unoccupied, d orbitals. The rate-determining heterolysis as represented (eq 7) involves a partial charge separation,[16] but, in the nonpolar medium used, the resulting charged particles almost certainly remain closely associated until the subsequent proton transfer (eq 8) occurs.

The final two steps (eq 9 and 10) are ligand-exchange reactions at vanadium(V), and, like eq 6, are represented as being rapid and reversible. Catalysis of the type proposed implies that the complexes of the active metal be substitution labile; if this were not the case, the catalytic action at a vanadium center would end with one act of epoxidation.

with the equation of material balance applied to vanadium, then rearranging terms.

(15) In an alternative kinetic treatment of competitive inhibition, applicable to systems having only one catalyst-inhibitor complex (see, for example, M. Dixon, *Biochem. J.*, **55**, 170 (1953)), values of (rate)$^{-1}$ are plotted against inhibitor concentration, giving a series of straight lines, one line for each concentration of substrate (in this case, hydroperoxide); these lines ideally intersect at a common point from which both the limiting rate (in the absence of inhibitor) and the association constant of the inhibitor complex may be determined. Such a procedure is, in principle, preferable to the treatment used in the present study, for it replaces the arbitrary and approximate extrapolation of rate with a rigorous extrapolation of (rate)$^{-1}$. In practice, however, it is less satisfactory, for although rates in the presence of alcohol fall reasonably close to such a series of lines, the intersection is very close to the origin (a consequence of the high association constant for the inhibitor complex). As a result, a small absolute error in determining the position of intersection is reflected in a large relative error. More important, rates calculated using parameters determined in this way do not agree with observed rates as closely as do those calculated from eq 3.

(16) The lower expoxidation rate observed in the more polar solvent, acetonitrile, would not have been predicted from consideration of the proposed rate-determining step. It is not, however, incompatible with the suggested reaction sequence, for the presence of a large concentration of donor molecules would be expected to alter the ligand environment of vanadium(V) and, hence, to change the nature of the catalytic species. How such a change would affect the various proposed steps cannot be readily predicted.



catalyst activation; rapid, irreversible (5)

complex formation; rapid, reversible, K_p (6)

heterolysis; rate-determining (7)

proton transfer; rapid (8)

ligand exchange; rapid, reversible (9)

inhibition; reversible, K_i and K_i' (10)

To summarize, effective action of a metal ion in the role of an oxygen atom carrier in reactions of this type requires: (a) that the ion have a high charge, a small size, and low-lying d orbitals which are at least partly unoccupied; (b) that it not participate significantly in any one-electron redox reactions under strongly oxidizing conditions; and (c) that it form complexes which are substitution labile. Lower oxidation states (such as VO^{2+}) may act in this way also if, upon oxidation, they are converted to ions fulfilling these conditions. Although none of these requirements is in itself severe, taken together they rule out all but a few of the available metals in their accessible oxidation states.[17]

Acknowledgments. The authors are grateful to Drs. Frank Mayo and Theodore Mill for initiating interest in this problem. We are also indebted to Professor D. L. Fishel and Mr. David Hutchings for help in improvement of the chromatographic analyses, and to Professors Jay Taylor and Milton Manes for valuable discussions.

(17) It has been suggested that a number of oxygen-transfer reactions catalyzed by noble metal derivatives proceed through a ternary complex containing one molecule each of metal, oxidant, and reductant: J. P. Collman, M. Kubota, and J. W. Hosking, *J. Am. Chem. Soc.*, **89**, 4809 (1967). Such a path, applied principally to d^8 and d^{10} systems, is consistent also with our kinetic picture. However, the lack of independent evidence that either vanadium(IV) or vanadium(V) readily forms olefin complexes under our conditions leads us to favor the route proposed here. In a related study of the $Mo(CO)_6$-catalyzed epoxidations of 1- and 2-octene with *t*-butyl hydroperoxide, N. M. Sheng and J. G. Zajacek (International Oxidation Symposium, San Francisco, Calif., Aug 1967; Advances in Chemistry Series, No. 75, American Chemical Society, Washington, D. C., in press) observed simple first-order dependence on hydroperoxide with no apparent autoinhibition. The mechanism proposed by these workers is similar to ours; the different kinetic picture indicates that at the higher temperature used in the octene studies (85.5°), and with the molybdenum catalyst, only a small portion (proportional to the hydroperoxide concentration) of the catalyst is converted to the catalyst–peroxide complex.