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One-Electron vs. Two-Electron Oxidations. Vanadium(V) Oxidation of Cyclobutanols[1]

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Abstract: Vanadium(V) in aqueous perchloric acid oxidized 2-ethylcyclobutanols and 2,2-dimethylcyclobutanol to 4-hydroxyhexanal and 4-hydroxy-4-methylpentanal, respectively. In $H_2{}^{18}O$ cyclobutanol gives 4-hydroxybutanol with ^{18}O incorporated in the hydroxyl group. The oxidation of the cyclobutanols follows the rate law $v = k[V(V)][ROH]h_0$, with the relative reactivities for cyclobutanol, 2-ethylcyclobutanol, and 2,2-dimethylcyclobutanol being 1.0, 6.6, and 147; *cis*- and *trans*-2-ethylcyclobutanol are equally reactive. Methyl cyclobutyl ether is 10^4 times less reactive than cyclobutanol. The results are consistent with a mechanism in which the rate limiting step is the carbon–carbon bond cleavage in a cyclobutyl ester intermediate, $C_4H_7OVO^{2+}(aq)$, leading to an acyclic free radical, $\cdot CR_2CH_2CH_2CHO$, which is subsequently oxidized to the hydroxy aldehyde. Methyl cyclohexyl ether is also found to be unreactive toward vanadium(V) oxidation; this suggests that the ester mechanism is generally applicable to vanadium(V) oxidations of alcohols.

Cyclobutanol exhibits the unique property of reacting in basically different ways with one-electron and two-electron oxidants. Chromium(VI) and chromium(V), which are known to react preferably as two-electron oxidants, oxidize cyclobutanol to cyclobutanone with the carbon–hydrogen cleavage occurring in the rate-limiting step.[2,3] A large isotope effect (k_H/k_D = 9.3), observed in a preliminary exploration of the permanganate oxidation of cyclobutanol,[4] indicates a similar course for the manganese(VII) oxidation.

With one-electron oxidants cyclobutanol reacts preferentially with carbon–carbon bond cleavage resulting in the opening of the cyclobutane ring. Chromium(IV) oxidation in aqueous solutions leads to the formation of γ-hydroxybutyraldehyde.[2,3] The same product is formed in the chromic acid oxidation in the presence of large amounts of manganese(II) under conditions where manganese(III) appears to be the actual oxidant.[5] Similarly, cerium(IV) oxidation gives only ring cleavage products formed through the free radical $\cdot CH_2CH_2CH_2CHO$.[6] Predominantly ring cleavage products were also obtained in the oxidation of cyclobutanol by lead tetraacetate[7] and of 1-methylcyclobutanol with iron(III) chloride.[8,9]

Despite its common occurrence in one-electron oxidations, the mechanism of the oxidation of cyclobutanols to γ-hydroxyaldehydes was not well understood; more detailed investigation of the reaction was hampered by the fact that in none of the above examples did the reaction occur alone. A further study of the reaction has now become possible due to the finding that vanadium(V)[12] reacts with cyclobutanol to give γ-hydroxybutyraldehyde in almost quantitative yields.[5]

The main questions to which we were seeking answers were the following. (1) Does the oxidation of cyclobutanol proceed through a free radical intermediate? (2) What is the effect of β-substitution on the direction of cleavage and on the rate of the reaction? (3) How important is the contribution of nonbonded interactions in determining the reactivity of cyclobutanols and their preference for ring cleavage? (4) Could the formation of the cleavage product be explained by a mechanism involving ring expansion to an oxygen containing a five-membered ring intermediate? (5) Is there evidence for the formation of an oxidant-substrate intermediate?

Experimental Section

All melting and boiling points are uncorrected. Infrared spectra were recorded on a Beckman IR-10 spectrophotometer, NMR spectra on a Varian Associates A-60A or T-60 spectrophotometer. GLPC analyses were carried out on an F and M Scientific Research Chromatograph, model 5750, equipped with flame ionization detectors, on ⅛ in. × 10 ft Carbowax 20M columns, unless otherwise specified. A Nester and Faust Prepomatic instrument with a ¾ in. × 6 ft Apiezon J Column was used for preparative scale gas chromatography.

Materials. Cyclobutanone (Aldrich Chemical Co.) was tested for purity by GLPC and used without further purification.

Cyclobutanol of better than 99% purity (by GLPC) was prepared by lithium aluminum hydride reduction of cyclobutanone[2b,13] followed by distillation through a Nester and Faust Model A-419 Teflon annular spinning band column; bp 126-127° (lit.[2a] 124.6°). Cyclobutanol prepared by the acid catalyzed isomerization of cyclopropylcarbinol[14] contained a small amount (2-3% by GLPC) of an impurity which we were unable to remove by either physical separation (distillation or preparative GLPC) or by chemical means (reaction with bromine, manganese dioxide, or trityl chloride). Therefore, only the product prepared from cyclobutanone was used in this study.

4-Hydroxybutanol. A dilute (0.043 *M*) solution of 4-hydroxybutyraldehyde was prepared by acid catalyzed hydrolysis of 2,3-dihydrofuran.[15] The aldehyde was characterized as the 2,4-dinitrophenylhydrazone, mp (ethanol) 121-123° (lit.[15] 120°).

Methyl Cyclobutyl Ether. Cyclobutanol (8.4 g, 0.12 mol) was added dropwise to a stirred suspension of sodium hydride (4.2 g, 0.175 mol) in ethyl ether (80 ml) which had been distilled from sodium hydride. Methyl sulfate (40.5 g, 0.36 mol) was added to the stirred suspension under reflux and the reaction mixture heated overnight and decomposed by the addition of water. The ether layer was washed with 0.25 *M* H_2SO_4, with 1 *M* NH_3 until all methyl sulfate was removed (by GLPC), and with water. About 2 g (0.023 mol, 17% yield) of methyl cyclobutyl ether was isolated by distillation on a spinning band column: bp 70-71°; NMR (CCl_4) δ 1.95 (m, 6, ring CH_2), 3.18 (s, 3, CH_3), 3.75 (m, 1, >CHOR); *m/e* 86.

Methyl cyclohexyl ether was prepared similarly in 18% yield from cyclohexanol (17.5 g, 0.175 mol), sodium hydride (6.3 g, 0.262 mol) and dimethyl sulfate (66 g, 0.524 mol): bp 137° (lit.[16] 133.5°); NMR (CCl_4) δ 1.05 to 2.15 (broad m, 10, CH_2), 3.25 (s, CH_3), 3.15 (m, CH) (combined area 4 H); *m/e* 114.

2,2-Dimethylcyclobutanone was prepared from 2,2,4,4-tetramethyl-1,3-cyclobutanedione and ethylene at 270-280° at about 2000 psi. It is assumed that the reaction proceeds via dimethyl ketene formed from the diketone.[17] Tetramethyl-1,3-cyclobutanedione (28 g, 0.2 mol) and tetralin (35 ml) were placed in a 472-ml stainless steel bomb (Paar Instrument Co.) equipped with a magnetic stirring bar. The bomb was filled with ethylene to 750 psi (approximately 0.9 mol) and heated for 52 hr to 270-280° with stirring. Distillation yielded several fractions containing up to 79% of the desired ketone, overall yield (by GLPC) 20%. The product could be purified by preparative GLPC to yield pure 2,2-dimethylcyclobutanone: ir (CCl_4) 1785 cm^{-1} (C=O) (lit.[18] (film) 1776 cm^{-1} (C=O)); NMR (CCl_4) δ 2.98 (m, 2, α-CH_2), 1.78 (m, 2, β-CH_2), 1.14 (s, 6, CH_3), (lit.[25] 2.97 (m, 2), 1.77 (m, 2), 1.13 (s, 6)); 2,4-dinitrophenylhydrazone, mp 137-138° (ethanol) (lit.[19] 140-141°).

2,2-Dimethylcyclobutanol was prepared by lithium aluminum hydride reduction of 2,2-dimethylcyclobutanone and purified by preparative GLPC on a 0.75 in. × 6 ft Carbowax 20M column at 115° (NMR (CCl_4) δ 1.0 (s, 6, CH_3), 1.0-2.2 (m, 4, CH_2), 3.9 (broad t, 2, $J = 8$ Hz, CHOH)); when the CCl_4 solution of the alcohol was shaken with D_2O, the broad triplet at δ 3.9 became a sharp triplet, with a relative area of one. The NMR spectrum agrees with that reported by Coyle.[20] In order to test the stability of 2,2-dimethylcyclobutanol toward acid catalyzed rearrangement under the conditions used in its oxidation, it was dissolved in 1 *M* $HClO_4$ and allowed to react for the length of time used in oxidation experiments. The solution was divided into two portions and each extracted with a different solvent (ethyl ether and butyl ether), and the extracts were analyzed by GLPC. No peaks other than those of the starting material and of the solvents were observed.

2-Ethylcyclobutanone was prepared by solvolysis of 3-hexynyl-nosylate in trifluoroacetic acid[21] in the presence of urea, 2,4-dinitrophenylhydrazone mp 114-117° (lit.[22] 116.5-117°).

2-Ethylcyclobutanols (mixture of trans and cis isomers) were obtained in a 68% yield by lithium aluminum hydride reduction of 2-ethylcyclobutanone: NMR (CCl_4) δ 0.9 (t, $J = 6$ Hz, CH_3), 1.1-2.3 (m) (combined area of triplet and multiplet = 10 H), 3.6, 4.2 (quartets, combined area 1 H, $J = 7$ Hz, *trans*- and *cis*-C*H*OH), 5.4 (broad s, 1, OH). The spectrum is in excellent agreement with published data.[21] Analysis of the product by GLPC on a 12 ft × ⅛ in. SE-30 column revealed two closely spaced peaks with relative areas of 1.00:0.39 (in the order of elution). The two peaks were assigned to the trans and cis isomer, respectively. This assignment is supported by several previous reports in the literature: 2-methylcyclobutanone reacts with lithium aluminum hydride to yield a mixture of *trans*- and *cis*-2-methylcyclobutanol in the ratio of 1.00: 0.32,[22] 2-*tert*-butylcyclobutanone gives *trans*- and *cis*-2-*tert*-butylcyclobutanols in a 1.00:0.43 ratio.[23] The ratio of the two products was reversed when the ketones were reduced with diisopinocampheylborane; a product containing more cis isomer (relative peak areas 0.15:1.00) was obtained; the result parallels that reported by Brown and Varma for 2-methylcyclobutanone.[22] The assignment of the two isomers is further supported by the NMR data. The ratio of signals at 3.6 and 4.2 is 1.00:0.36, which is very close to the trans to cis ratio determined by GLPC. The C*H*OH proton in the trans compound is shielded by the neighboring ethyl group as in 2,2-dimethylcyclobutanol (δ 3.76), whereas the proton in the cis compound is in a similar environment as in cyclobutanol (δ 4.1).[24] Similar values of chemical shifts were reported[23] for *trans*-2-*tert*-butylcyclobutanol (δ 3.88) and *cis*-2-*tert*-butylcyclobutanol (δ 4.47).

***trans*-2-Ethylcyclobutanol.** While the two isomers of 2-ethylcyclobutanol could be isolated sufficiently by GLPC for analysis, their isolation on a preparative scale could not be achieved. However, a mixture of the acetates prepared from the above mixture of 2-ethylcyclobutanols (3 g, 0.03 mol) and acetic anhydride (6 g, 0.06 mol) in pyridine (3 ml) was separated by preparative GLPC and gave an almost pure 2-ethylcyclobutyl acetate which, upon saponification and distillation yielded the trans-2-ethylcyclobutanol containing only 3-4% of the cis isomer (by GLPC).

***cis*-2-Ethylcyclobutanol.** The reduction of 2-ethylcyclobutanone with diisopinocamphenylborate[22,25,26] yielded a mixture of the two isomeric 2-ethylcyclobutanols in which the cis isomer predominated. An unidentified by-product with a somewhat longer retention time than the cis isomer, which contaminated the product despite the use of carefully purified reagents (diglyme,[27] boron trifluoride etherate,[28] and pinene) was removed by preparative GLPC on a 0.75 in. × 6 ft UC-W98 silicone rubber column. The resulting 2-ethylcyclobutanol contained 86% of the cis and 14% of the trans isomer.

Analysis of Oxidation Products. In a typical experiment, 2-ethylcyclobutanol (108 mg, 1.08 mmol) was dissolved in 10 ml of 1 *M* $HClO_4$ and mixed with a solution of NH_4VO_3 (32.6 mg, 0.278 mmol) in 3 ml of 1 *M* $HClO_4$ (a lower concentration of perchloric acid (0.15 *M*) was used for the oxidation of 2,2-dimethylcyclobutanol as this was found to increase the yield of isolable products by about 10%). After eight half-lives a solution of 2,4-dinitrophenylhydrazine (36 mg, 0.18 mmol) in 2 *M* $HClO_4$ was added and the precipitate collected. The filtrate and the water used to wash the precipitate were extracted with methylene chloride, the extract evaporated, the unreacted 2,4-dinitrophenylhydrazine removed by preparative TLC (pyridine-ethyl acetate, 1:3) and the remainder combined with the precipitate. The combined products were separated by preparative TLC on silica gel (ethyl acetate-benzene, 1:5) into five bands with the major one accounting for 75% of the crude product and corresponding to a 74% yield based on the vanadium(V) consumed. This material, which could not be resolved further by TLC using a variety of solvents was recrystallized (CH_2Cl_2) and identified as 4-hydroxyhexanal-2,4-dinitrophenylhydrazone, mp 119.5-124°. Anal. Calcd for $C_{12}H_{16}N_4O_5$: C, 48.64; H, 5.44; N, 18.91. Found: C, 48.85; H, 5.50; N, 18.89. NMR (pyridine) δ 1.1 (t, J = 6 Hz, CH_3), 1.3–2.3 (m, $CH_3CH_2CHOHCH_2$–) combined area of 1.1 and 1.3–2.3 = 7 H), 2.76 (m, 2, –$CH_2CH{=}N$–), 3.8 (quintuplet, 1, J = 6 Hz, $CHOH$), 9.0 (d, J = 2 Hz, aromatic –H, C3), 11.4 (s, 1, NH); NMR (CH_2Cl_2) in addition to the above signals: δ 7.6 (t, J = 5 Hz, $CH{=}N$), 7.9 (d, J = 9 Hz, aromatic –H, C6), 8.3 (2d, $J_{3,5}$ = 2 Hz, $J_{5,6}$ = 9 Hz, aromatic –H, C5); because of low solubility, the signals in CH_2Cl_2 were too weak to permit integration. None of the other products could be identified. The second largest band, corresponding to 11% of the crude product was a polymeric material. Comparison with an authentic sample showed that 2-ethylcyclobutanone was not present among the oxidation products.

The principal product from the oxidation of 2,2-dimethylcyclobutanol corresponding to a 73% yield based on vanadium(V), was identified as 4-hydroxy-4-methylpentanal-2,4-dinitrophenylhydrazone, mp 120–122°. Anal. Calcd for $C_{12}H_{16}N_4O_5$: C, 48.64; H, 5.44; N, 18.91. Found: C, 48.46; H, 5.33; N, 18.86. NMR (pyridine-d_6) δ 1.4 (s, 6, CH_3), 1.8 (t, 2, J = 8 Hz, CH_2COH), 2.6 (m, 2, $CH_2CH{=}N$), 5.4 (s, 1, OH), 9.0 (d, 1, J = 2 Hz, aromatic –H, C3), 11.4 (s, 1, NH); NMR (CH_2Cl_2) in addition to the above: δ 7.7 (t, J = 5 Hz, $CH{=}N$), 8.0 (d, J = 9 Hz, aromatic –H, C6), 8.3 (2d, $J_{3,5}$ = 2 Hz, $J_{5,6}$ = 9 Hz, aromatic –H, C5). Because of low solubility, spectra in CH_2Cl_2 were too weak to integrate. None of the other products could be identified; the second major component (9%) was polymeric. Comparison with an authentic sample showed the absence of 2,2-dimethylcyclobutanone among the oxidation products.

Oxidation of 2,2-dimethylcyclobutanol in the presence of acrylonitrile. When 2,2-dimethylcyclobutanol was oxidized with vanadium(V) in the presence of acrylonitrile, a dense white precipitate began forming immediately; a solution of 2,4-dinitrophenylhydrazine was added; the dried precipitate was extracted with methylene chloride, about 48% dissolved. TLC analysis of the extract showed the absence of any of the normal oxidation products of the alcohol. It was determined that even 1% of the usual oxidation products could have been easily detected. Acrylonitrile itself gave no reaction with vanadium(V).

3-(β-Hydroxyethyl)-1*H*-benz[*g*]indole formed instead of the expected α-naphthylhydrazone of 4-hydroxybutanal and was found to be the most suitable derivative for ^{18}O analysis of the hydroxyaldehyde. It was prepared in 65% yield by heating for 30 min on a steam bath a solution of 1-naphthylhydrazine (314 mg, 2.0 mmol) in tetrachloroethylene with a solution of 4-hydroxybutanal. 4-Hydroxybutanal was prepared by adding 2,3-dihydrofuran (30 mg, 0.43 mmol) to 10 ml of 1 *M* $HClO_4$. The crude, dark red indole was purified by sublimation and recrystallization from benzene–hexane: mp 154–157°; *m/e* 211. Anal. Calcd for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.83; H, 6.25; N, 6.63; NMR (DMSO-d_6) δ 2.8 (t, 2, J = 7 Hz, $ArCH_2$–), 3.6 (m, –CH_2OH), 4.6 (t, 1, J = 5 Hz, OH), 7–8.4 (m, 7, aromatic-H), 11.7 (broad, s, 1, NH). The area of the 3.6 peak could not be determined because of an impurity in the solvent.

3-(β-Acetoxyethyl)-1*H*-benz[*g*]indole acetate was prepared from the above indole by acetylation with acetic anhydride in pyridine, mp (benzene) 120–121°. Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.86; H, 5.96; N, 5.53. Found: C, 75.80; H, 6.02; N, 5.69; uv_{max} (MeOH) 215 nm (log ϵ 4.5), 266 (log ϵ 4.7), shoulders 300, 335, 355 nm. The spectrum resembles closely that of 7,8-benz-1,2,3,4-tetrahydrocarbazole.

7,8-Benz-1,2,3,4-tetrahydrocarbazole was prepared from 1-naphthylhydrazine hydrochloride and cyclohexanone:[29] mp 138–140° (lit.[29] 139–140°); NMR (CS_2) δ 1.85 (m, 4, CH_2 on C2 and C3), 2.7 (m, 4, CH_2 on C1 and C4), 7–8.2 (m, 7, aromatic-H and NH); uv_{max} (MeOH) 220 nm (log ϵ 4.5), 270 (log ϵ 4.7), shoulders 285, 325, 345 nm.

Analysis for ^{18}O. Cyclobutanol was oxidized with vanadium(V) under conditions similar to those described above in the section dealing with the analysis of oxidation products from ethylcyclobutanol except that the reaction was carried out in water enriched in ^{18}O (1.5 atom %). The solution was then treated with 1-naphthylhydrazine and the resulting indole derivative purified and analyzed by oxidation to CO_2 with $Hg(CN)_2$ and $HgCl_2$[30,31] and the amount of $CO^{18}O$ determined by mass spectrometry. The ^{18}O content in the sample was found to be identical with that of the ^{18}O enriched water used in the reaction.

Kinetic measurements were carried out in 10-cm or 1-cm cells using either a Cary Model 15 double beam or a Carl Zeiss PMQ II single beam spectrophotometer, each equipped with a water jacketed cell holder connected to a circulating constant temperature bath (Lauda K-2/R). Pseudo-first-order rate constants were determined graphically from ln A_{350} vs. time plots; excellent straight lines were generally obtained.

Results and Discussion

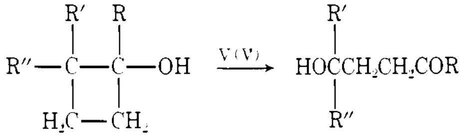
The vanadium(V) oxidation of cyclobutanols is first order in vanadium(V) as indicated by excellent straight line plots of ln A_{350} vs. time obtained under all conditions used in this study; A_{350} is the optical density at the absorption maximum of vanadium(V) at 350 nm; at this wavelength vanadium(V) is the only absorbing species. Table I shows that the reaction is also first order in the alcohol. Table II and Figure 1 show that the reaction exhibits a first-order dependence on the concentration of hydrogen ions and, at higher acidities on the acidity function h_0. The rate law of the reaction is given by eq 1

$$-\frac{d[V(V)]}{dt} = k[V(V)][ROH]h_0 \qquad (1)$$

The rate law differs from that found for strain-free monohydric alcohols[12,32] insofar as the reaction rates are clearly proportional to the acidity function h_0 (or, more precisely to $h_0^{1.1}$) rather than to the concentration of hydrogen ions. This acidity dependence is consistent with a mechanism in which there is no participation of a water molecule in the rate-limiting step of the reaction.[33,34]

The acidity dependence of the reaction suggests that $VO_2^+(aq)$, the species predominantly present in strong acid solutions,[35] is not a strong enough oxidant and that the oxidation actually proceeds through a protonated species $HVO_2^{2+}(aq)$.[38] The good first-order dependence on vanadium(V) observed in this work and generally in vanadium(V) oxidations of organic compounds[12] demonstrates that under the rather acidic conditions employed in these oxidations, vanadium(V) must be present and react predominantly in its monomeric form, in spite of its marked tendency toward the formation of polymeric ions.[39]

Vanadium(V) oxidizes cyclobutanols with ring cleavage toward the more substituted carbon atom:



R = R′ = R″ = H 93.7%[5]
R = CH_3; R′ = R″ = H 76%[5]
R = R′ = H; R″ = Et 74%
R = H; R′ = R″ = Me 73%

A small amount (1.5%) of the corresponding cyclobutanone formed by oxidation on the C–H bond rather than on the C–C bond was found in the oxidation of the parent cyclobutanol; however, in spite of special efforts, no cyclobutanones could be identified among the oxidation products of the higher cyclobutanols investigated in this study. No products resulting from cleavage toward the less branched carbon atom of the cyclobutane ring were found.

When the oxidation of 2,2-dimethylcyclobutanol was carried out in the presence of acrylonitrile only polymer formation was observed; none of the usual oxidation products could be identified. This result confirms the assumption that the reaction is a one-electron oxidation.

The second-order rate constants for the vanadium(V) oxidation of cyclobutanol, *cis*- and *trans*-2-ethylcyclobutanols

Table I. Vanadium(V) Oxidation of Cyclobutanol in 1 M HClO$_4$ at 25°

10^2[Cyclobutanol], M	10^3[V(V)], M	10^4k, sec^{-1}	10^3k/[cyclobutanol], M^{-1} sec^{-1}
5.06	4.20	1.06	2.10
46.6	6.36	10.8	2.32
74.5	6.36	17.0	2.28
108	6.36	25.3	2.34

Table II. Vanadium(V) Oxidation of Cyclobutanol and 2,2-Dimethylcyclobutanol at 25°, Acidity Dependence

[HClO$_4$], M	H_0[a]	$10^3 \times$ [Alcohol], M	$10^3 \times$ [V(V)], M	10^4k, M^{-1} sec^{-1}
		Cyclobutanol		
0.010	2.0	164	6.51	0.0480
0.10	1.0	609	6.54	0.840
0.25	0.60	394	6.50	2.78
0.50	0.02	569	6.52	7.05
1.0	−0.22	50.6	4.20	21.0
3.6	−1.60	28.7	3.11	614
5.0	−2.23	5.47	0.74	3780
		2,2-Dimethylcyclobutanol		
0.010	2.0	36.8	0.712	14.7
0.10	1.0	14.4	0.324	136
1.0	−0.22	3.30	0.649	3070

[a] K. Yates and H. Wai, *J. Am. Chem. Soc.*, 86, 5408 (1964).

Table III. Vanadium(V) Oxidations of Cyclobutanols in 1 M HClO$_4$ at 25°

Substrate ($10^3 M$)	$10^3 \times$ [V(V)], M	10^3k, M^{-1} sec^{-1}	k_{rel}
Cyclobutanol (5.06)	4.20	2.10	1.00
trans-2-Ethylcyclobutanol (3.78) (96% pure)	3.14	14.0	6.6
cis-2-Ethylcyclobutanol (0.605) (86% + 14% *trans*-)	0.77	14.0	6.6
2,2-Dimethylcyclobutanol (0.33)	0.65	306	147
Methyl cyclobutyl ether (4.04)	4.2	0.00022	0.000104

and 2,2-dimethylcyclobutanol are given in Table III. The increase in reactivity with substitution in the 2-position of cyclobutanol is consistent with the preferential cleavage toward the more substituted carbon atom and demonstrates that ring cleavage is taking place during the rate limiting step of the reaction. The observation that the two samples of 2-ethylcyclobutanol, one containing at least 96% trans and the other 86% cis isomer are oxidized at the same rate, demonstrates that the increase in reactivity with substitution in the 2-position is not due to nonbonded interactions between either the hydroxyl group or the α-hydrogen[41] atom and vicinal atoms or groups.

Methyl cyclobutyl ether is 10^4 times less reactive than cyclobutanol. This striking difference in reactivity indicates that the O-H bond plays a vital part in the oxidation process and is broken either prior or during the rate limiting step. A similar difference between the reactivity of alcohols and the corresponding ethers exists in the chromic acid oxidation of alcohols.[42] This large difference in reactivity was one of the principal arguments used to support the now well-established ester mechanism by which a chromic acid ester of the alcohol is formed as an intermediate in a rapid preoxidation step.[43,44] It seems only logical to assume that a similar intermediate, an ester of vanadic acid, is formed in vanadium(V) oxidations.

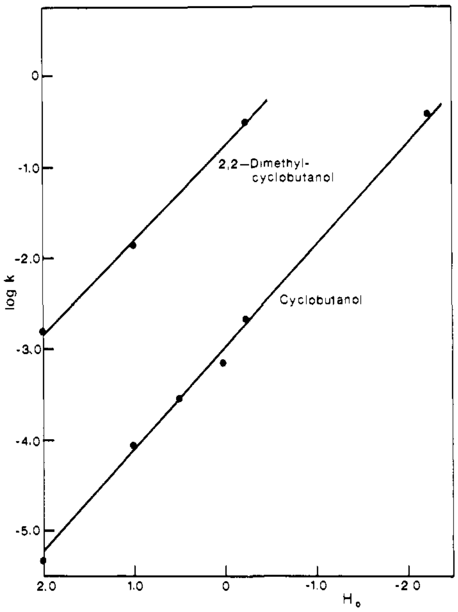
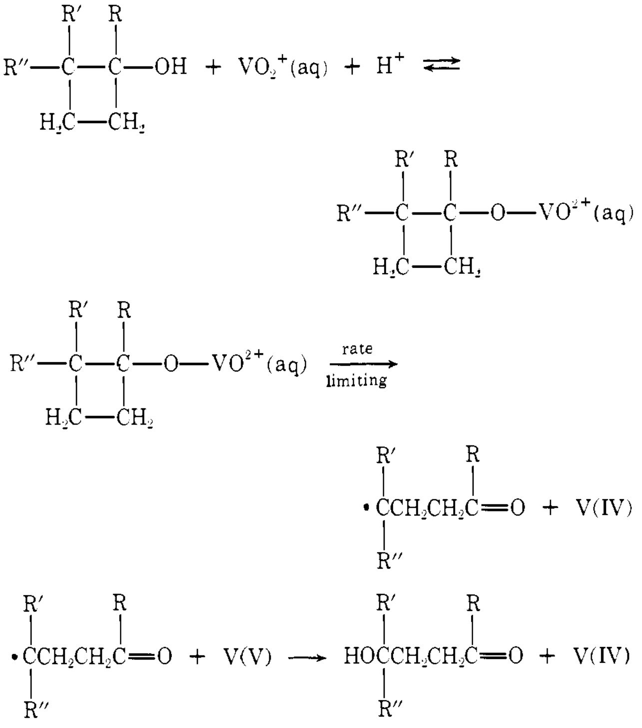


Figure 1. Acidity dependence of the vanadium(V) oxidation of cyclobutanol and 2,2-dimethylcyclobutanol in aqueous perchloric acid at 25°. Data from Table II.

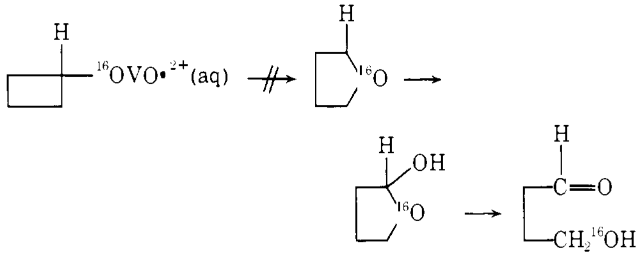
In order to determine whether the low reactivity of ethers relative to the corresponding alcohols represents a general feature or occurs only in oxidations leading to carbon-carbon bond cleavage, we attempted to determine the oxidation rate of methyl cyclohexyl ether (0.044 M) in 1 M perchloric acid at 25°. No significant oxidation over a period of 7 days could be detected. We therefore conclude that vanadium(V) oxidations of alcohols in general take place via a vanadate ester intermediate. The structure of the vanadate ester intermediate can be represented as RO-VO^{2+}(aq) or, more precisely, as ROV(OH)$_2$(OH$_2$)$_n$$^{2+}$ where n = 1, 2, or 3, with the pentacoordinated species (n = 2) appearing most attractive in analogy to the postulated structure of VO$_2$$^+$(aq).[36,37]

The overall mechanism of the reaction thus may be summarized by Scheme I.

Scheme I



The oxidation of cyclobutanol in ^{18}O enriched water shows that the hydroxyl oxygen in the product comes from the solvent; consequently, the oxygen atom originally present in the cyclobutanol molecule must be oxidized to the carbonyl group. This finding rules out any possibility of a ring expansion mechanism leading to a cyclic intermediate, e.g.,



Acknowledgment. One of us (J.R.) wishes to express his gratitude to the Department of Chemistry, Harvard University, for the hospitality and assistance offered during the preparation of the manuscript.

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(1) Support of this investigation by grants from the donors of the Petroleum Research Fund, administered by the American Chemical Society, and from the National Science Foundation is gratefully acknowledged.

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(9) The rule that one-electron oxidants react with cyclobutanols with ring cleavage apparently does not apply to the decomposition of metal alkoxides. Whitesides[10] has recently shown that the thermal decomposition of copper(I) cyclobutoxide yields a mixture of cyclobutanone and cyclobutanol and no ring cleavage products. Although this reaction may well be regarded as a two-electron oxidation in which copper(I) is reduced to a CuH intermediate, other alkoxides seem to be capable of decomposing to alkoxide radicals and Cu(0) corresponding to a one-electron oxidation of the alkoxide. Why then copper(I) cyclobutoxide does not react by the one-electron route is not clear. A similar observation of an oxidation of cyclobutanol to cyclobutanone via an alkoxide was also recently made in our laboratory: chromium(IV) tetra-*tert*-butoxide reacts with cyclobutanol to yield cyclobutanone (among other products) obviously via a chromium(IV) cyclobutoxide intermediate.[11]

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(34) Waters and Littler[12] suggested that H_0 dependence of vanadium(V) oxidations of glycols and hydroxy acids may suggest the formation of an intermediate bidentate complex of the bifunctional substrate with vanadium(V). Our finding that the oxidation of cyclobutanols depends on H_0 rather than on $[H_3O^+]$ does not fit this generalization and suggests therefore that caution must be exercised in drawing conclusions concerning the structure of intermediates from acidity dependence studies.

(35) The number of water molecules present in the $VO_2{}^+(aq)$ ion is not known with certainty. However, recent work[36,37] suggests that the ion is quinque-coordinated and may have a structure of $V(OH)_4(H_2O)^+$ or $OV(OH)_2(H_2O)_2{}^+$.

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