Chromic Acid Oxidation of Cyclopropanols[1]

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Abstract: The chromic acid oxidation of secondary cyclopropanols is 10^3 to 10^6 times faster than that of other secondary alcohols. Tertiary cyclopropanols are even more reactive with 1,2,2,3,3-pentamethylcyclopropanol being the most reactive organic compound known toward this oxidant. The free hydroxyl group is a necessary prerequisite for the high reactivity; cyclopropyl alkyl ethers and cyclopropyl esters are relatively unreactive. Only ring cleavage products are obtained; secondary cyclopropanols form β-hydroxypropionaldehydes, and tertiary alcohols yield β-hydroxy ketones. The formation of free radical intermediates has been demonstrated by the initiation of polymerization of acrylonitrile and acrylamide and by trapping with oxygen. Oxidation of cyclopropanol in the presence of oxygen leads to the formation of a substantial amount of malonaldehyde; 1-alkylcyclopropanols yield the corresponding 3-ketoaldehydes. The proposed mechanism consists of a rate-limiting two-electron carbon–carbon bond ring cleavage of a chromate ester. The release of ring strain in the transition state of the oxidative decomposition is believed to be responsible for the high rates and for the preference toward carbon–carbon cleavage instead of the usual carbon–hydrogen bond oxidation. A free radical is formed by subsequent reaction between cyclopropanol and chromium(IV).

Ring strain can have a profound effect on the rate and mechanism of oxidation reactions. In several recent studies,[3-6] we have shown that one-electron oxidants react with cyclobutanols up to 10^5 times faster than with strain-free alcohols and that the oxidation invariably results in ring cleavage. The relief of ring strain in the transition state is obviously responsible both for the increase in rate and for the change in mechanism from carbon–hydrogen to carbon–carbon bond cleavage.

The tendency of chromium(VI) to react with the α-carbon–hydrogen bond and thus to oxidize secondary alcohols to the corresponding ketones[7] is strong enough to make this the preferred route even in the oxidation of cyclobutanols,[3] benzocyclobutenol,[8] and of other strained systems like 7-norbornanol.[9] Other two-electron oxidants like chromium(V)[3,10] and permanganate[1a] share, with chromium(VI), the preference for attacking the carbon–hydrogen bond of cyclobutanol rather than reacting by ring cleavage.

The purpose of this study was to expand our investigation of the oxidation of small ring alcohols to the even more strained cyclopropanols.[11] We were particularly interested in learning whether chromium(VI) would retain its preference for carbon–hydrogen bond oxidation even in this highly strained system in spite of the well-known instability of the corresponding ketone, cyclopropanone,[12] or whether a change in mechanism toward ring cleavage would take place.

Tertiary cyclopropanols were also included in our study. Because of the absence of the α-hydrogen atom, tertiary alcohols are rather unreactive toward chromium(VI) and, in general, can be oxidized only after previous dehydration to olefins.[13-15] However, in the one-electron oxidative cleavages of cyclobutanols, the tertiary alcohols have been found to be even more reactive than the corresponding secondary alcohols,[5] reflecting the higher stability of the keto group relative to the aldehydic carbonyl. The comparison of the reactivity of closely related secondary and tertiary alcohols therefore provides important information about the nature of the oxidation process.

Experimental Section

Melting points were determined in a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 257 spectrophotometer using 0.1-mm KBr cells. The mass spectra were obtained on a Perkin-Elmer Model 270 mass spectrometer at 70 eV. Nuclear magnetic resonance spectra were recorded on Varian A-60 or T-60 spectrometers, using tetramethylsilane as internal standard. A Hewlett-Packard Model 5750 research gas chromatograph was used to determine the purity of liquid alcohols. Preparative GLC was carried out on a Nester-Faust 850 Prepkromatic chromatograph using a 0.75 × 72 in. two-wall stainless steel column of 20% Carbowax 20M. Electronic spectra were recorded on Cary spectrophotometers Model 14 or 15. Some optical density measurements were obtained on a Carl Zeiss PMQ II spectrophotometer. Both this instrument and the Cary Model 15 were equipped with Lauda K-2/R constant temperature baths and were used for the kinetic measurements.

Materials. Chromic acid solutions were made from chromium trioxide (Mallinckrodt, Analytical or Fisher Certified Reagent) by weighing, and the concentrations were checked by determining their optical density at 350 nm. Perchloric acid (B & A or Baker Analyzed Reagent) was diluted with distilled water and standardized against standard sodium hydroxide to phenolphthalein indicator end point.

Alcohols. Commercially available isopropyl alcohol, cyclohexanol, and cyclopropylcarbinol were distilled before use. Cyclobutanol was prepared from cyclopropylcarbinol[18] and purified by preparative GLC.

Synthesis. Unless otherwise indicated, liquid cyclopropanols were purified by preparative GLC.

Cyclopropanol was prepared by the modified Cottle procedure:[19] bp 100–102° (lit.[19] bp 100–103°); ir (CCl_4) 3629, 3310 (OH), 3100, 3013, 1020 (cyclopropyl) cm^{-1}; NMR (CCl_4) δ 3.35 (m, 1), 4.35 (s, 1), 0.45 (m, 4); mass spectrum *m/e* 58, 57, 29.

1-Substituted cyclopropanols were prepared, unless indicated otherwise, from 1,3-dichloroacetone and the corresponding alkyl- or arylmagnesium bromide by the procedure of DePuy and coworkers.[19,20]

1-Methylcyclopropanol was obtained in 13% yield: pb 101–103° (lit.[21] bp 103°); ir (CCl_4) 3610, 3330 (OH), 3090, 3013, 1020 (cyclopropyl) cm^{-1}; NMR (CCl_4) δ 3.60 (s, 1), 1.36 (s, 3), cyclopropyl protons at 0.70 (m, 2) and 0.33 (m, 2); mass spectrum *m/e* 72, 71, 57, 43.

1-Ethylcyclopropanol was obtained in 12% yield: bp 38–40° (0.05 mm); ir (CCl_4) 3600, 3340 (OH), 3080, 3002, 1018 (cyclopropyl) cm^{-1}; NMR (CCl_4) δ 3.59 (s, 1), 1.51 (m, 2), 1.0 (t, 3), cyclopropyl protons at 0.63 (m, 2) and 0.38 (m, 2); mass spectrum *m/e* 86, 57, 29. After standing for several days at room temperature, the ir spectrum of a solution of this alcohol in CCl_4 showed neither hydroxyl nor cyclopropyl absorptions but developed a carbonyl bond at 1715 cm^{-1}. The NMR spectrum of this solution consists of δ 2.40 (q, 2), and 1.00 (t, 3). This spectrum is identical with that of 3-pentanone, which is the expected acyclic rearrangement product.

1-Isopropylcyclopropanol was obtained in less than 10% yield, bp 36–48° (0.01 mm). Purification by preparative GLC at 82° yielded the alcohol which solidifies into white crystals in the receiv-

ing trap (at ice-water temperature), but liquifies at room temperature: ir (CCl_4) 3607, 3350, (OH), 3088, 2960, 1020 (cyclopropyl) cm^{-1}; NMR (CCl_4) δ 2.40 (s, 1), an AB_6 pattern at 1.0 (d, J = 5 Hz, superimposed on multiplet, 7), cyclopropyl protons at 0.60 (m, 2) and 0.38 (m, 2); mass spectrum *m/e* 100, 71, 57, 43. After several days the cyclopropyl and hydroxyl bonds in the ir spectra disappeared, and a carbonyl bond at 1710 cm^{-1} developed. Changes in the NMR spectrum were also consistent with a rearrangement of the compound to ethyl isopropyl ketone.

1-Phenylcyclopropanol was obtained in 22% yield, bp 46-48° (0.02 mm). The alcohol was purified by column chromatography on silica gel using petroleum ether as eluent. Samples used for kinetic measurements were further purified by recrystallization from *n*-pentane at −30°: ir (CCl_4) 3600, 3370 (OH), 3090, 1015 (cyclopropyl) cm^{-1}; NMR (CCl_4) δ 7.27 (s, 5), 3.20 (s, 1), cyclopropyl protons at 1.15 (m, 2) and 0.95 (m, 2); mass spectrum *m/e* 134, 105, 77. The NMR data are in good agreement with a previously reported spectrum for this alcohol.[22]

1-*p*-Tolylcyclopropanol was obtained in 30% yield: mp 38.5-40° (lit.[19] mp 39-40°) after two recrystallizations from *n*-pentane at −10 to −20°: ir (CCl_4) 3602, 3370 (OH), 3092, 2928, 1025 (cyclopropyl) cm^{-1}; NMR (CCl_4) δ 7.08 (s, 4), 3.17 (s, 1), 2.29 (s, 3), cyclopropyl protons at 1.05 (m, 2) and 0.86 (m, 2). Samples of this alcohol used for kinetic measurements were further purified by sublimation.

1-*p*-Chlorophenylcyclopropanol, obtained using *p*-chlorophenylmagnesium iodide, formed a pale amber liquid, bp 94-99° (0.1 mm). Three recrystallizations from *n*-pentane afforded the alcohol as white crystals: mp 68-69.5° (lit.[23] mp 68-69°); ir (CCl_4) 3600, 3330 (OH), 3092, 1025 (cyclopropyl) cm^{-1}; NMR (CCl_4) δ 7.20 (s, 4), 2.52 (s, 1), cyclopropyl protons at 1.10 (m, 2) and 0.90 (m, 2). The alcohol was sublimed prior to using it for kinetic measurements.

1-*p*-Anisylcyclopropanol was obtained as a white solid from pentane: mp 60.5-62° (lit.[22] mp 62-63°); ir (CCl_4) 3600, 3460 (OH), 1038, 1011 (cyclopropyl) cm^{-1}; NMR (CCl_4) aromatic protons at δ 7.20 (m, 2) and 6.74 (m, 2), 3.73 (s, 3), 2.10 (s, 1), cyclopropyl protons at δ 1.05 (m, 2) and 0.86 (m, 2). Samples used for kinetic runs were further purified by sublimation, mp 61-62.5°.

Pentamethylcyclopropanol was prepared by treating tetramethylcyclopropane methyl hemiketal[24a] with methyllithium according to DePuy et al.[24b] Two recrystallizations from diethyl ether at −30° afforded the alcohol as a white solid: mp 93-95° (lit.[25] 93-94°); ir ($CDCl_3$) 3595 (OH) cm^{-1}; NMR ($CDCl_3$) δ 1.54 (s, 1), 1.31 (s, 3, C_1 methyl), 1.04 (s, 6), 0.94 (s, 6). Samples used for kinetic runs were further purified by sublimation.

2,2,3,3-Tetramethylcyclopropanol was prepared according to the procedure of Turro et al.,[26] and obtained as a white solid from *n*-pentane at −55°: mp 38-42°; ir (CCl_4) 3605, 937 cm^{-1}; NMR (CCl_4) δ 2.70 (s, 1), 1.73 (s, -OH), 0.98 (s, 12). Samples for kinetic measurements were sublimed before use.

1,2,2-Trimethylcyclopropyl acetate was prepared by thermal decomposition of 3-acetoxy-3,5,5-trimethyl-1-pyrazoline:[27] bp 127-130° (lit.[27] 126-128°); ir (CCl_4) 3050 (cyclopropyl), 1725 cm^{-1} (C=O); NMR (CCl_4) δ 1.95 (s, 3, $-COCH_3$), 1.47 (s, 3, C-1 methyl), 1.13 (s, 3, C-2 methyl), 1.06 (s, 3, C-2 methyl), 0.59 (d, 1, J = 6 Hz, ring C-H), 0.32 (d, 1, J = 6 Hz, ring C-H); mass spectrum *m/e* 142 (s), 99, 85, 43.

1,2,2-Trimethylcyclopropanol was obtained from 1,2,2-trimethylcyclopropyl acetate and methyllithium:[27] bp 39-42° (18 mm) (lit.[27] bp 54-57° (35 mm)); ir (CCl_4) 3600, 3410 (OH), 3065 (cyclopropyl) cm^{-1}; NMR (CCl_4) δ 2.37 (s, 1), singlets of equal area at 1.37, 1.15, and 1.03 (3 each), cyclopropyl protons at 0.40 (d, 2) and 0.13 (d, 2); mass spectrum *m/e* 100 (s), 85. Samples for kinetic runs were purified by column chromatography on silica gel using petroleum ether as eluent.

Cyclopropyl methyl ether was prepared by the method of Krantz and Drake:[28] ir (CCl_4) 3090, 3010 (cyclopropyl), 1098 (C-O) cm^{-1}; NMR (CCl_4) δ 3.27 (s, superimposed on multiplet, 4), 0.45 (m, 4); mass spectrum *m/e* 72, 71, 57, 41. Samples for kinetic runs were purified according to Olson et al.[29] by treating the ether with concentrated aqueous sodium bisulfite and distilling it from sodium hydroxide pellets. Although hydroxyl and carbonyl containing impurities were removed, a small amount of impurity was still detected in the NMR spectrum.

β-Hydroxypropionaldehyde was prepared according to the method of Hall and Stern[30] and isolated as its 2,4-dinitrophenylhydrazone. Acrolein (289.5 mg) distilled under nitrogen was mixed with 25 ml of water and 4.2 ml of 11.6 *M* perchloric acid. The mixture was diluted to 50 ml with water, shaken, and stored in the dark. After 2 days, a 10-ml aliquot was added to a filtered solution of 2,4-dinitrophenylhydrazine in 2 *N* HCl at ice-bath temperature. A yellow precipitate formed immediately and was collected within 10 min (124 mg). Column chromatography on silica gel using benzene as eluent afforded acrolein-2,4-dinitrophenylhydrazone (15 mg), mp 163-165° (lit.[24] mp 161-162°); elution with benzene-ethyl acetate (95:5, v/v) gave 6 mg of 3-formyl-Δ^3-dihydropyran-2,4-dinitrophenylhydrazone, mp 226-229° (crude), and elution with benzene-ethyl acetate (85:15), v/v) afforded β-hydroxypropionaldehyde-2,4-dinitrophenylhydrazone (93 mg), mp 133-133.5° (lit.[24] 132.5-133°). The β-hydroxypropionaldehyde derivative was found to be unstable in the acidic 2,4-dinitrophenylhydrazine solution, undergoing dehydration to form acrolein-2,4-dinitrophenylhydrazone. When the 2,4-dinitrophenylhydrazone derivatives of a hydrated acrolein solution remained in the hydrazine solution for several hours, no β-hydroxypropionaldehyde derivative was isolated, while the yield of the acrolein derivative was essentially quantitative (95%).

Malonaldehyde (aqueous solution) was prepared by hydrolysis from 1,1,3,3-tetraethoxypropane (J. T. Baker Chemical Co.) in dilute hydrochloric acid,[31-33] followed by distillation at 15 mm: uv (H_2O) 244 nm (lit.[31] 245 nm (ϵ 1.34 × 10^4)).

Acetoacetaldehyde. A mixture of 0.12 *N* hydrochloric acid (50 ml) and 4,4-dimethyoxy-2-butanone (Eastman Organic Chemicals; 5.3 g) was stirred for 26 hr at room temperature. A solid precipitate was removed by filtration and identified as 1,3,5-triacetylbenzene: mp 158-161°, (mmp 158-161°); NMR ($CDCl_3$) δ 2.70 (s, 9), 8.73 (s, 3). The clear, pale yellow filtrate was distilled at 15 mm giving a light yellow aqueous solution of acetoacetaldehyde, uv (H_2O) 251-252 nm; in basic medium, the maximum shifts to 281-282 nm (lit.[34,35] λ_{max} 280-282 nm, (ϵ 1.77 × 10^4)).

4-Methyl-3-oxopentanal was prepared in the form of its sodium salt from 3-methyl-2-butanone and methyl formate:[36] mass spectrum *m/e* 114, 71, 43; uv (H_2O) 283 nm (ϵ 1.04 × 10^4).

Reaction Products. Cyclopropanol. A solution of cyclopropanol (4.78 mmol) and chromic acid (3.20 mmol)[37] in 20 ml of 0.5 *M* $HClO_4$ was allowed to react in an ice bath. After 20 min, when the reaction was essentially complete, a portion (7.3 ml) of the reaction mixture was added to 350 ml of an ice-cold saturated solution of 2,4-dinitrophenylhydrazine in 2 *N* HCl. After 5 min, the resulting precipitate was collected, washed with water until neutral to litmus paper, and dried. Column chromatography of 45.0 mg of the product yielded 11.9 mg (26%) of the acrolein derivative, mp 163-164° (lit.[30] mp 161-162°), 29.8 mg (66%) of the β-hydroxypropionaldehyde derivative, mp 131-132° (lit.[30] mp 132.5-133°), and 2.2 mg (5%) of unreacted 2,4-dinitrophenyl hydrazine. If the oxidation mixture was added to the 2,4-dinitrophenylhydrazine solution and allowed to stand for several hours, only the acrolein derivative was isolated, accounting for up to 95% of the reaction product.

1-*p*-Tolylcyclopropanol (1.23 g, 8.36 mmol) was dissolved in 30 ml of 50% aqueous dioxane,[38] and the resulting solution was cooled to ca. 5°; 4.9 ml of 4.1 *M* perchloric acid and 5.56 ml of 1 *M* chromium(VI) solution (5.56 mmol) were added dropwise over a period of 1.5 hr, and the reaction mixture was allowed to stand at room temperature for 15 min and extracted with seven 20-ml portions of diethyl ether. The extracts were dried ($MgSO_4$), the solvent removed, and the crude product (887 mg) purified by column chromatography on silica gel. The major component (72% of crude product, 46% overall yield) was eluted with 1:1 benzene-hexane (v/v) and was identified as β-hydroxyethyl tolyl ketone: ir (CCl_4) 3480 (broad) (OH), 1675 (C=O) cm^{-1}; NMR (CCl_4) δ aromatic protons at 7.74 (d, 2) and 7.16 (d, 2), 3.87 (t, J = 5 Hz, 2), 3.50 (s, 1), 3.02 (t, J = 5 Hz, 2), 2.33 (s, 3); mass spectrum *m/e* 146, 119, 91. A small amount of another carbonyl compound, eluded with hexane, was not fully characterized. The oxidation of **1-phenylcyclopropanol** under similar conditions afforded β-hydroxyethyl phenyl ketone in 43% yield: ir (CCl_4) 3480 (broad) (OH), 1680 (C=O) cm^{-1}; NMR (CCl_4) δ aromatic protons at 7.90 (m, 2) ad 7.44 (m, 3), 3.90 (t, J = 5 Hz, 2), 3.10 (t, J = 5 Hz, 2), 2.54 (s, 1); mass spectrum *m/e* 132, 105, 77.

Kinetic Measurements. The oxidations of cyclopropanols were

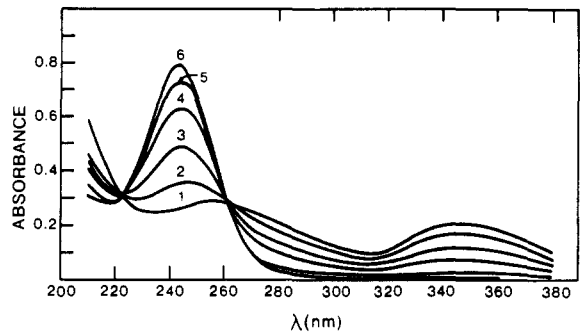


Figure 1. Spectrum of the chromic acid oxidation of cyclopropanol as reaction progresses. [Cr(VI)] = 1.36×10^{-4} M; [ROH] = 1.28×10^{-3} M; [$HClO_4$] = 6.6×10^{-2} M; 20.0°. Time (min): (1) 0; (2) 8.4; (3) 25.4; (4) 55.4; (5) 100; (6) 183.

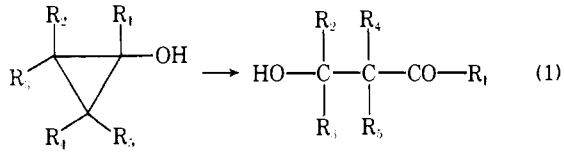
carried out under pseudo-first-order conditions, with at least a tenfold excess of substrate over oxidant concentrations. The rates of oxidation were determined spectrophotometrically by following the disappearance of the chromium(VI) species at either 350 or 450 nm at 25.0 ± 0.1°. Pseudo-first-order rate constants were determined from the slope of plots of ln ($A_t - A_\infty$) vs. time; second-order rate constants were obtained by dividing the value of the first-order rate constant by the substrate concentration. Each alcohol oxidation was carried out at least twice; the reproducibility was usually within ±5% but somewhat lower (ca. ±10%) for runs carried out in dioxane–water.

Dissociation constants were determined spectrophotometrically[39] by measuring the absorbance as a function of the pH in buffer solutions.

Results and Discussion

Reaction Products. A. β-Hydroxy Carbonyl Compounds. When cyclopropanol was oxidized by chromic acid and the oxidation products isolated as 2,4-dinitrophenylhydrazones in the usual way, the dinitrophenylhydrazone of acrolein was isolated in yields up to 95%. However, when the reaction mixture was monitored at 210 nm, the absorption maximum of acrolein, it became obvious that no acrolein is formed directly during the oxidation; the unsaturated aldehyde thus must have been formed from another product during the work-up procedure. This conclusion was confirmed when rapid work-up of the reaction products yielded a mixture of dinitrophenylhydrazones of β-hydroxypropionaldehyde and acrolein with up to 71% of the hydroxyaldehyde. A solution of β-hydroxypropionaldehyde (85% hydroxypropionaldehyde, 15% acrolein) prepared by acid catalyzed hydration of acrolein showed a completely analogous behavior, yielding a mixture of the two dinitrophenylhydrazones upon rapid work-up and only the dinitrophenylhydrazone of acrolein upon longer standing.

Because of their lower solubility in water, oxidation products from 1-arylcyclopropanols could be isolated directly without conversion to dinitrophenylhydrazones. The corresponding β-hydroxyethyl aryl ketones were isolated as the principal oxidation products in a satisfactory yield (43 and 46%, respectively) from the oxidation of 1-phenylcyclopropanol and 1-*p*-tolylcyclopropanol. Thus, the principal reaction taking place in the chromic acid oxidation of cyclopropanols can be expressed by eq 1.[40]



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B. 1,3-Dicarbonyl Compounds. When the oxidation of cyclopropanol is carried out with low (ca. 10^{-4} M) concentrations of chromic acid typically used in kinetic experiments, the formation of an additional product in fairly high yields can be detected (Figure 1). The new product absorbs strongly in the uv region of the spectrum and exhibits an absorption maximum at 244 nm; the position of the maximum shifts (reversibly) to 266 nm upon the addition of base. The absorbancy at λ_{max} in basic solutions is 2.3 times higher than in acid. The compound was identified as malonaldehyde by the 2-thiobarbituric acid test,[42,43] by determination of the pK_a value, and by comparison of spectra in both acid and basic solutions with those of an authentic sample of malonaldehyde (Figure 2). Table I gives the spectral properties and the pK_a values for malonaldehyde and for 3-ketoaldehydes formed under similar conditions during the oxidation of 1-alkylcyclopropanols.

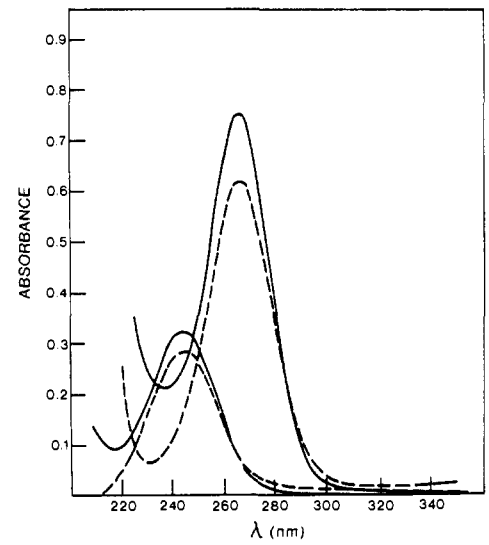


Figure 2. Ultraviolet absorption spectra of product from chromic acid oxidation of cyclopropanol (—) and known malonaldehyde (- - -) in acidic (λ_{max} 244 nm) and basic (λ_{max} 266 nm) media.

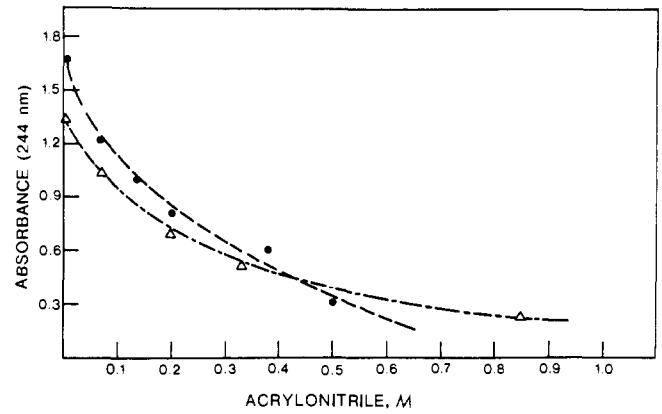


Figure 3. Effect of arcylonitrile on the formation of malonaldehyde in the oxidation of cyclopropanol. (●) Cr(VI) = 2.08×10^{-4} M, ROH = 3.20×10^{-3} M, $HClO_4$ = 0.25 M. (△) Cr(VI) = 1.45×10^{-4} M, ROH = 2.79 M, $HClO_4$ = 0.41 M.

The yield of malonaldehyde is sharply reduced by the presence of acrylonitrile (Figure 3). Also, degassing of the solutions before mixing results in a reduction of the yield of malonaldehyde to 15–33% of the yield normally observed.

At very low concentration of chromic acid, the yield of malonaldehyde is approximately proportional to the initial concentration of chromic acid; with increasing concentration of chromic acid, the yield of malonaldehyde reaches an approximate constant value; however, when oxygen is bub-

Table I. Absorption Maxima in Acidic and Basic Solutions, Relative Absorbancies, and pK_a Values of Authentic 1,3-Dicarbonyl Compounds and of Chromic Acid Oxidation Products of Cyclopropanols

	H—C(=O)CH$_2$C(=O)—R			Oxidation product of			
R:	-H	-CH_3	-$CH(CH_3)_2$	-H	-CH_3	-CH_2CH_3	-$CH(CH_3)_2$
Acidic							
λ_{max} (nm)	244	251	260	244	252	254	260
Basic							
λ_{max} (nm)	266	280	285	266	280	282	285
A_{max} (basic) / A_{max} (acidic)	2.3	13.0	18.3	2.3	13.1	18.4	18.2
pK_a	4.57[a]	6.33[a]	6.68[a]	4.60[a]	6.31[a]	6.71[b]	6.64[b]

[a] Acetic acid–acetate buffer, 25°C. [b] Citric acid–phosphate buffer, 25°C.

Table II. Malonaldehyde (MA) Formation in Excess of Chromium(VI)[a]

$[Cr(VI)]_0 \times 10^4, M$	$[Cr(VI)]_\infty \times 10^4, M$	$[\Delta Cr(VI)] \times 10^4$, mmol	Exp A_{244}	[MA] × 10^4, mmol	[ROH]/[Cr(VI)]	[MA]/[ROH]	[MA]/[Cr(VI)]
1.70	0.76	4.71	0.588	2.04	1.63	0.27	0.43
2.55	1.59	4.81	0.568	2.12	1.60	0.28	0.44
3.40	2.37	5.15	0.587	2.16	1.50	0.28	0.42
4.25	3.32	4.64	0.573	2.14	1.66	0.28	0.46
5.10	4.15	4.74	0.577	2.15	1.62	0.28	0.45

[a] [ROH] = 1.54 × 10^{-4} M (7.70 × 10^{-4} mmol); [H^+] = 0.4 M; total volume = 5.0 ml.

Table III. Chromic Acid Oxidation of Cyclopropanol and 1-Methylcyclopropanol. Rate Dependence on the Concentration of the Alcohol ([Cr(VI)] = 1.3 × 10^{-4} M; 20°)

$[HClO_4] \times 10^2, M$	[Alcohol] × $10^3, M$	k, M^{-1} sec^{-1}	$k/[H^+]^2$
	Cyclopropanol		
6.6	0.111	0.20	43
6.6	0.121	0.22	50
6.6	0.254	0.21	49
6.5	0.618	0.21	50
6.6	1.25	0.22	51
6.6	1.28	0.26	60
6.3	5.62	0.20	51
6.1	9.93	0.22	60
6.7	15.5	0.25	55
	1-Methylcyclopropanol		
6.7	0.092	1.7	370
6.7	0.150	1.8	400
6.6	0.529	1.8	410
6.6	1.32	1.8	410
6.5	3.21	1.8	410
6.3	6.40	1.5	380

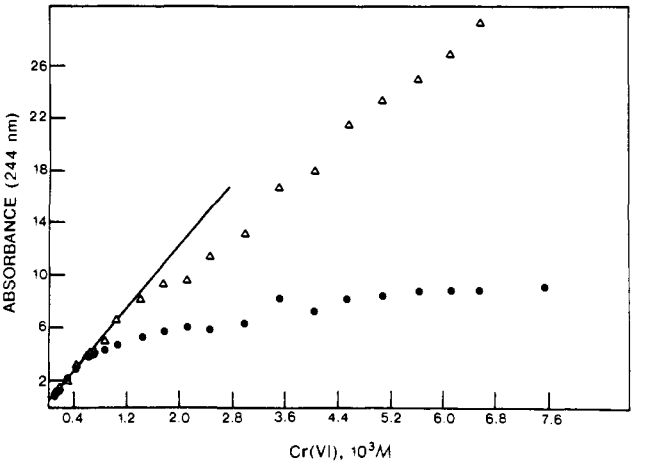


Figure 4. Effect of oxygen on the formation of malonaldehyde: yield of malonaldehyde as a function of the initial concentration of chromic acid under normal conditions (●) and when oxygen was bubbled through the solution during the reaction (△).

bled through the solution during the course of the reaction, the yield of malonaldehyde continues to increase (Figure 4).

It thus becomes apparent that the formation of malonaldehyde is due to the reaction of a free radical intermediate, presumably ·CH_2CH_2CHO, with oxygen normally present in the solution. As the solubility of oxygen in water at normal air pressure is approximately 9 parts per million[44] or ca. 2.8 × 10^{-4} M and the limiting concentration of malonaldehyde formed is about 6.7 × 10^{-4} M, one can conclude that two molecules of malonaldehyde are formed from each molecule of oxygen available. The value of the initial slope of the curve showing the yield of malonaldehyde as a function of the starting concentration of chromic acid suggests that 0.5 mol of malonaldehyde is formed for every mole of chromic acid reduced. The latter value is in fair agreement with the results of a series of experiments in which cyclopropanol was oxidized with an excess of chromic acid (Table II); the data in the table show that slightly more than 1.5 mol of cyclopropanol is oxidized and almost 0.5 mol of malonaldehyde formed per 1 mol of chromic acid reduced. Other series of experiments, in which cyclopropanol was used in excess, led to somewhat higher values (0.6 to 0.8) for the amount of malonaldehyde which could be formed per one molecule of chromic acid.

The formation of malonaldehyde and related 1,3-dicarbonyl compounds in the oxidation of cyclopropanols parallels a similar formation of succinaldehyde in the cerium(IV) oxidation of cyclobutanol in the presence of oxygen.[4]

Kinetics. In all kinetic runs, at least a tenfold excess of alcohol over chromic acid was used; under these conditions, excellent straight line plots of ln ($A_{350} - A_\infty$) were consistently obtained, indicating that the oxidation was first order in chromic acid. The results given in Table III for cyclopropanol and for 1-methylcyclopropanol demonstrate that the reaction is also first order in the alcohol.

Table IV shows the dependence of the rate constant for the oxidation of cyclopropanol on the pH of the solution over more than four pH units. In spite of some fluctuations, due to experimental difficulties, it is clear that the reaction

Table IV. Dependence of the Oxidation Rate of Cyclopropanol on Acidity ([Cr(VI)] = 5.1 × 10^{-4} M, [cyclopropanol] = 0.01 M; 20°)

pH	$10^3 k$, M^{-1} sec^{-1}	$k/[H^+]$
4.68[a]	0.039	1.9
3.40[a]	0.80	2.5
3.36[b]	0.99	1.8
3.05[b]	1.5	1.7
3.02[a]	1.8	1.9
2.85[a]	2.6	1.9
2.68[b]	3.9	1.7
2.52[b]	5.1	1.7
2.30[c]	11.5	2.2
2.24[b]	9.8	1.7
2.00[b]	17	1.7
2.00[c]	16	1.6
1.60[c]	70	2.8
1.30[c]	150	3.1
1.00[c]	500	4.9
0.60[c]	2600	10.3
0.30[c]	7800	16

[a] Acetic acid–sodium acetate buffer. [b] Chloroacetic acid–sodium chloroacetate buffer. [c] Perchloric acid.

Table V. Dependence of the Oxidation Rate of 1-Methylcyclopropanol on Acidity ([Cr(VI)] = 5.1 × 10^{-4} M, [1-methylcyclopropanol] = 0.01 M; 20°)

$[HClO_4]$ × $10^2 M$	$10^2 k$, M^{-1} sec^{-1}	$k/[H^+]$	$10^{-2}k/[H^+]^2$
0.1	0.77	7.7	77
0.51	4.4	8.6	17
1.02	9.7	9.5	9.3
1.99	22	11.3	5.7
2.53	30	11.9	4.7
2.97	38	12.9	4.3
5.00	80	16.1	3.2

is first order in the concentration of hydrogen ions at lower acidities up to about pH 2; at higher acidities, a term which is second order in hydrogen ions becomes important. Table V gives similar data for 1-methylcyclopropanol for a smaller range of acidities. The data can be fitted to eq 2

$$k = k'[H^+] + k''[H^+]^2 \quad (2)$$

with $k' = 1.8$ M^{-2} sec^{-1} and $k'' = 30$ M^{-3} sec^{-1} for cyclopropanol, and $k' = 7.9$ and $k'' = 160$ for 1-methylcyclopropanol. The oxidation of cyclopropanols thus exhibits the same dependence on the concentration of hydrogen ions which is found generally for other alcohols,[7] e.g., isopropyl alcohol,[45] and indicates that, at lower acidities, the oxidation rate is proportional to the concentration of the undissociated chromic acid, H_2CrO_4 (or to its ester $ROCrO_3H$), whereas, at higher acidities, the reaction depends on the positively charged species $H_3CrO_4^+$ (or $ROCrO_3H_2^+$). One reason for extending the measurements to very low acidities was to examine whether a term corresponding to oxidation by the anion $HCrO_4^-$ could be found. The results, however, show no evidence of an acid independent term. It is thus safe to conclude that $HCrO_4^-$ is too weak an oxidant to react even with a substrate as unusually reactive as cyclopropanol.[46]

It is well known that the oxidation of isopropyl alcohol[50] and of a number of other compounds[7] is proportional to the concentration of $HCrO_4^-$ rather than to the total concentration of chromium(VI); for reasons which are not well understood, $Cr_2O_7^{2-}$, which is formed from $HCrO_4^-$ at higher chromic acid concentrations, appears to be unreactive. The results summarized in Table VI show that the oxidation of cyclopropanol does not follow this pattern and that the oxidation rates appear approximately proportional to the total

Table VI. Dependence of the Oxidation Rate on the Concentration of Chromic Acid ([Cyclopropanol] = 0.05 M, $[HClO_4]$ = 0.01 M, 20°)

[Chromic acid] × 10^5, M	$[H^+]$ × 10^2, M	$HCrO_4^-$, %[a]	$10^2 k$, M^{-1} sec^{-1}	$k/[H^+]$
4.6	1.00	99.1	1.28	1.28
8.7	1.01	98.3	1.23	1.22
21.5	1.02	96.1	1.32	1.29
42.9	1.04	92.8	1.33	1.28
88.8	1.08	86.9	1.34	1.24
179	1.17	78.7	1.38	1.18
246	1.23	73.8	1.48	1.20
347	1.32	68.3	1.67	1.26
437	1.41	64.4	2.04	1.44

[a] Calculated from $K = [Cr_2O_7^{2-}]/[HCrO_4^-]^2 = 98$ (J. Y. Tong and E. L. King, *J. Am. Chem. Soc.*, 75, 6180 (1953)).

chromium(VI) concentration. This would suggest that $Cr_2O_7^{2-}$ is about twice as reactive as $HCrO_4^-$.

The overall rate law for the chromic acid oxidation of cyclopropanol thus can be expressed by eq 3.

$$\text{rate} = -\frac{d[Cr(VI)]}{dt} = [Cr(VI)][\text{cyclopropanol}](k'[H^+] + k''[H^+]^2) \quad (3)$$

Effect of Structure on Reactivity. Tables VII and VIII summarize the oxidation rates of a number of cyclopropanols and of some related compounds under three sets of conditions: at pH 1.2, where cyclopropanol could be compared directly with less reactive substrates; at pH 3.1, where convenient reaction rates for cyclopropanol and for the even more reactive β-substituted cyclopropanols could be obtained; and in aqueous dioxane which permitted the study of some of the 1-arylcyclopropanols which were only sparingly soluble in water. The results showed the following.

(1) Cyclopropanols are extremely reactive toward chromic acid oxidation relative to aliphatic alcohols or to higher cyclanols. This high reactivity is restricted to the cyclopropanol system and is not a more general property of the cyclopropane ring system, as cyclopropylcarbinol shows no enhanced reactivity.

(2) Tertiary cyclopropanols are more reactive than the corresponding secondary alcohols. The cyclopropanols are the only known class of alcohols where this is the case with respect to chromic acid oxidation. Within the series of 1-alkylcyclopropanols, the reactivity decreases along the series Me > Et > *i*-Pr.[51,52]

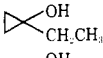
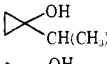
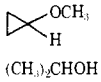
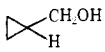
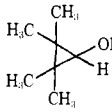
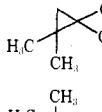
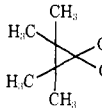
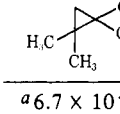
(3) Alkyl substitution in the β-position greatly increases the reactivity. 1,2,2-Trimethylcyclopropanol is oxidized 490 times faster than 1-methylcyclopropanol and 2,2,3,3-tetramethylcyclopropanol reacts 570 times faster than cyclopropanol.[53]

(4) Once one of the β-positions is substituted, similar substitution on the second β-position has little effect on the rate: 1,2,2,3,3-pentamethylcyclopropanol reacts only 1.4 times faster than 1,2,2-trimethylcyclopropanol; this is less than the statistical factor of 2 which could be expected simply by virtue of doubling the number of activated carbon–carbon bonds.

(5) A free hydroxyl group is a prerequisite for facile oxidation; methyl cyclopropyl ether is about 3 × 10^4 times less reactive than cyclopropanol, and 1,2,2-trimethylcyclopropyl acetate was completely stable toward oxidation under the same conditions under which the corresponding alcohol reacted very rapidly.

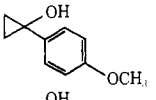
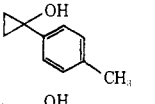
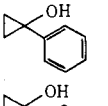
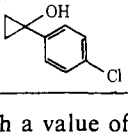
(6) Para substitution in 1-arylcyclopropanols has a marked effect on reactivity; the reaction is accelerated by electron-donating substituents which can better stabilize the keto group formed in the oxidation. A good Hammett

Table VII. Chromic Acid Oxidation Rates of Cyclopropanols and Related Compounds at 25°

Substrate	k, M^{-1} sec^{-1}	k_{rel}
pH 1.2 (6.2 × 10^{-2} M $HClO_4$)		
	0.36 0.25[a]	1.0
	2.28	6.4
	1.29	3.6
	0.95	2.6
	0.44	1.2
	⩽10^{-5}	⩽3 × 10^{5}
$(CH_3)_2CHOH$	0.69 × 10^{-4}	1.19 × 10^{-4}
$CH_2{=}CHCH_2OH$	4.2 × 10^{-4}[a]	1.7 × 10^{-3}[a]
	1.93 × 10^{-4}	5.4 × 10^{-4}
	1.41 × 10^{-4}	3.9 × 10^{-4}
	1.83 × 10^{-4}	5.1 × 10^{-4}
pH 3.1 (CH_3CO_2H–CH_3CO_2Na Buffer)		
	1.42 × 10^{-2}	1.0
	2.20 × 10^{-2}	1.6
	8.2	570
	11.2	780
	15.9	1120
	Unreactive	0

[a] 6.7 × 10^{-2} M $HClO_4$; 20°.

Table VIII. Chromic Acid Oxidation of 1-Arylcyclopropanols in 1:1 Dioxane–Water (v/v) at 25°, [$HClO_4$] = 6.2 × 10^{-2} M

Substrate	k, M^{-1} sec^{-1}	k_{rel}
	1.38	1.87
	1.02	1.38
	0.74	1.0
	0.46	0.63

plot with a value of $\rho = -1.01 \pm 0.11$ is obtained (Figure 5). This value is similar in magnitude to that obtained earlier by Kwart and Francis in the oxidation of α-arylethanols in 30% aqueous acetic acid.[54]

Mechanism. The reaction products show that the oxidation of cyclopropanols proceeds with ring cleavage. The high reactivity of 1-alkyl- and 1-arylcyclopropanols and the rate accelerating effect of β-substitution make it obvious that the ring cleavage must take place during the rate-limiting step. The negative ρ value obtained for a series of 1-arylcyclopropanols suggests that, in the transition state, the transformation of the original hydroxyl group to a carbonyl must have progressed to a significant extent. A similar conclusion can be drawn from the observation that the series of 1-alkylcyclopropanols follows the hyperconjugative (Baker-Nathan) series.

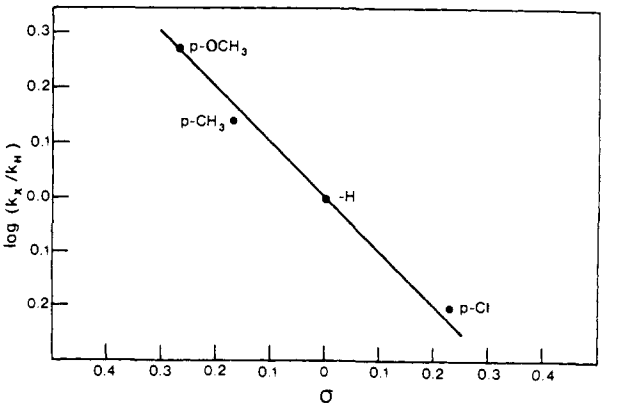


Figure 5. Effect of substituents on the rate of the chromic acid oxidation of parasubstituted 1-arylcyclopropanols.

The observation that cyclopropanol reacts about 3 × 10^4 faster than methyl cyclopropyl ether as well as the unreactivity of 1,2,2-trimethylcyclopropyl acetate demonstrates that the free hydroxyl group plays a vital role in the oxidation process. The situation is similar to that found in the oxidation of isopropyl alcohol, where the corresponding ether is also unreactive relative to the alcohol.[55] We therefore conclude that the oxidative cleavage of cyclopropanols proceeds through a similar chromate ester intermediate[7,56,57] as the carbon–hydrogen bond oxidation of less strained alcohols.

There is general agreement that the rate-limiting step in the typical chromic acid oxidation of an alcohol is a two-electron process in which chromium(VI) is reduced to chromium(IV).[7,58-60] However, the oxidative cleavage of cyclopropanols is a sufficiently different reaction so that the two-electron nature of the rate-limiting step cannot be taken for granted. Chromium(VI) could obviously act as a one-electron oxidant; it does so in numerous reactions with inorganic one-electron reducing agents.[61] Moreover, the reaction resembles in many respects the one-electron oxidative cleavages of cyclobutanols by chromium(IV),[3] cerium(IV),[4] manganese(III),[5] and vanadium(V)[5,6] as well as the one-electron oxidation of cyclopropanols by iron(III).[62]

There is ample evidence that free radicals are formed during the reaction. The oxidation of cyclopropanol, 1-alkylcyclopropanols (alkyl = Me, Et, and i-Pr), and 1-arylcyclopropanols (aryl = phenyl and p-tolyl) as well as of 1,2,2,3,3-pentamethylcyclopropanol in the presence of acrylonitrile led to the formation of polymeric precipitates. In the presence of oxygen, the 1,3-dicarbonyl compounds were formed clearly via free radical intermediates. There are, however, two points which are less clear and which need to be discussed: (1) are free radicals formed in the rate-limiting step, and (2) does the entire oxidation proceed via free radical intermediates?

In order for *all* of the cyclopropanol to be oxidized via a free radical intermediate, only one-electron oxidations would take place and the reaction would become autocatalytic, because of the necessity of chain branching in a mechanism of this type; e.g., see Scheme I.[63] If all of the above

Scheme I

$$S + Cr(VI) \longrightarrow \cdot R + Cr(V)$$
$$S + Cr(V) \longrightarrow \cdot R + Cr(IV)$$
$$S + Cr(IV) \longrightarrow \cdot R + Cr(III)$$
$$\cdot R + Cr(VI) \longrightarrow P + Cr(V)$$
$$\cdot R + Cr(V) \longrightarrow P + Cr(IV)$$

reactions were considered fast relative to the first one, the reaction rate would increase as more unstable intermediates were formed; however, no evidence of autocatalysis was observed. Furthermore, the presence of free radical scavengers would be expected to have a profound rate retarding effect on a reaction of this type; in reality, the addition of acrylonitrile or acrylamide had practically no effect on the rate of the oxidation of cyclopropanol.

When cyclopropanol was oxidized with an excess of chromic acid in the presence of oxygen slightly less than one-third of the alcohol was converted to the product obviously formed via the free radical intermediate, malonaldehyde (Table II). Furthermore, the yield of malonaldehyde did not increase even in the presence of a very large excess of oxygen provided by bubbling oxygen through the solution during the reaction. We therefore conclude that a mechanism in which all cyclopropanol is oxidized via a free radical intermediate is very unlikely.

The question whether the chromium(VI) oxidation step represents a one- or two-electron oxidation is more difficult to answer. One can write only one[56] such mechanism which would not involve chain branching (Scheme II).

Scheme II

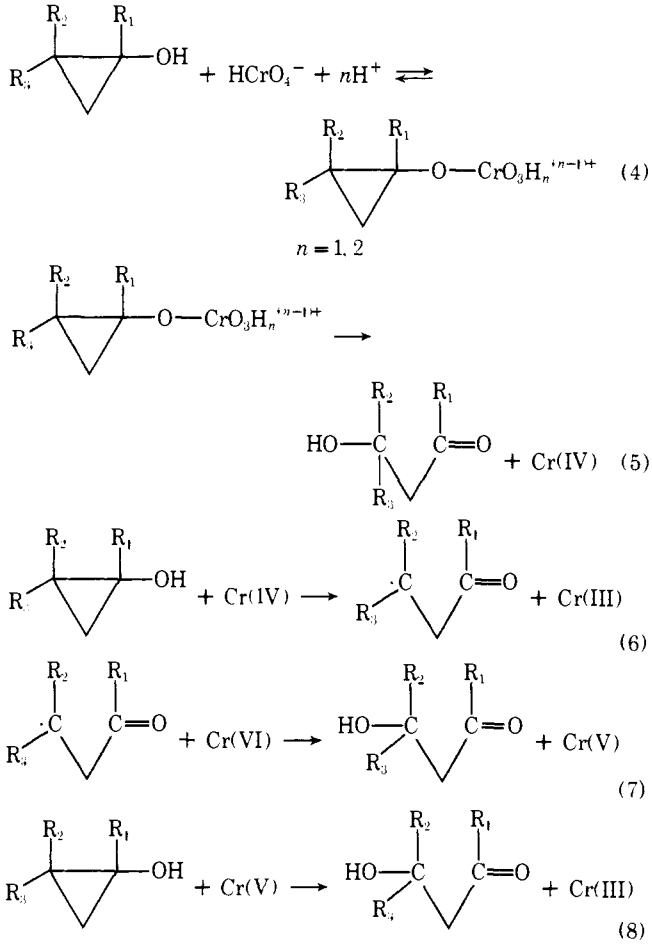
$$S + Cr(VI) \longrightarrow \cdot R + Cr(V)$$
$$\cdot R + Cr(VI) \longrightarrow P + Cr(V)$$
$$S + Cr(V) \longrightarrow P + Cr(III)$$

According to this mechanism, chromium(VI) would react as a one-electron oxidant, whereas chromium(V) would still remain a two-electron oxidant. This would make some sense, because the one-electron reduction product of chromium(VI) is the relatively stable chromium(V),[64] whereas the one-electron reduction of chromium(V) would yield the extremely reactive chromium(IV).[3,59,60,65-67] Although this mechanism would be in conflict with the general experience that chromium(VI) and chromium(V) react very similarly,[10,64,68-70] Scheme II represents an intriguing possibility to account for the results; it is radically different from the usual chromic acid oxidation of alcohols by involving chromium(VI) in a one-electron oxidation and by avoiding the formation of chromium(IV). If the two-electron oxidation of cyclopropanol by chromium(V) were slower than the one-electron oxidation by chromium(VI), which in this case would not appear unlikely, then chromium(V) should accumulate during the course of the reaction; however, no evidence of chromium(V) accumulation has been found.

Although mechanism II should not be ruled out, we believe that it is more likely that the chromic acid oxidation of cyclopropanol follows the usual reaction mechanism of alcohols with the important change that the rate-limiting step represents a two-electron carbon–carbon cleavage leading to a carbonium ion intermediate instead of the usual carbon–hydrogen cleavage (Scheme III). If this conclusion is correct, then the chromic acid oxidation of cyclopropanols represents the first case of facile carbon–carbon bond cleavage by chromium(VI) in the oxidation of a monohydric alcohol.[71]

In the presence of oxygen, the free radical intermediate

Scheme III



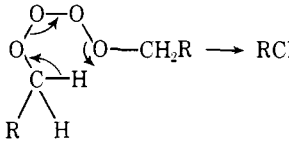
formed in the chromium(IV) oxidation (reaction 9) is oxidized to the 1,3-dicarbonyl compound.

$$OCHCH_2CH_2\cdot + O_2 \longrightarrow OCHCH_2CH_2OO\cdot \quad (9)$$

The reaction with oxygen probably goes through a peroxy radical which can dimerize to a tetroxide.

$$2RCH_2O_2\cdot \longrightarrow RCH_2O_4CH_2R \quad (R = OCHCH_2\text{-}) \quad (10)$$

Tetroxides are known to decompose either by disproportionation into an alcohol and a carbonyl compound[74] or by fragmentation into oxygen and alkoxy radicals.[75,76]



$$RCH_2O_4CH_2R \longrightarrow 2RCH_2O\cdot + O_2 \quad (12)$$

The alkoxy radical formed in reaction 12 would be expected to react with chromium(VI) to yield malonaldehyde

$$OCHCH_2CH_2O\cdot + Cr(VI) \longrightarrow OCHCH_2CHO + Cr(V) \quad (13)$$

while chromium(V) would oxidize another molecule of cyclopropanol to β-hydroxypropionaldehyde (reaction 8).

While either of the sequences would account for the formation of malonaldehyde, they differ with respect to the predicted stoichiometry and reaction rates. The disproportionation mechanism gives the following stoichiometry

$$4C_3H_5OH + 2Cr(VI) + O_2 \longrightarrow 3HOCH_2CH_2CHO + OCHCH_2CHO + 2Cr(III)$$

and predicts that the rate of chromium(VI) reduction in the presence of oxygen is reduced to one-half of its normal value, because reaction 7 of Scheme III is eliminated. The

Table IX. Nature of Bond Cleavage in One- and Two-Electron Oxidations of Cyclanols

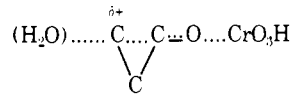
Oxidant	Cyclopropanols	Cyclobutanols	Higher cyclanols
One electron	C–C	C–C	C–H
Two electron	C–C	C–H	C–H

fragmentation process (reactions 12, 13, and 8) gives a different stoichiometry

$$3C_3H_5OH + 2Cr(VI) + \tfrac{1}{2}O_2 \longrightarrow 2HOCHCH_2CHO + OCHCH_2CHO + 2Cr(III)$$

and predicts no effect of oxygen on the reaction rate because the rapid reduction of chromium(VI) in reaction 7 is replaced by a similar process (reaction 13). Our experimental observations, both with respect to stoichiometry and to the effect of oxygen on reaction rates, are in much better agreement with the second mechanism.

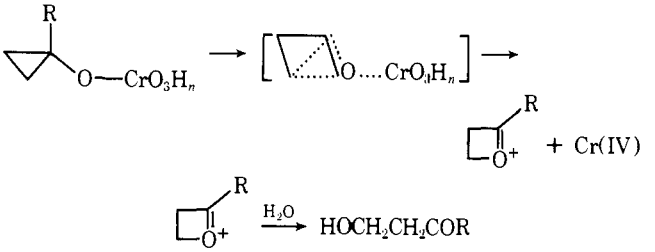
The transition state of the rate-limiting step can be best represented as



with a partially developed positive charge on the β-carbon atom and a partially developed carbonyl group. The relatively moderate effect of β-substitution (rate increase of 5×10^2 in going from a primary to a tertiary carbonium ion as contrasted with a factor of 10^6 in typical solvolytic reactions)[77] suggests that the carbonium ion has developed only to a limited extent either because only little carbon-carbon bond breaking had occurred in the transition state or because of strong association of the incipient carbonium ion with a solvent molecule. However, the solvent participation cannot be strong enough to regard the reaction as a nucleophilic displacement on the β-carbon atom; in the latter case, one would expect a decrease, rather than an increase, of reactivity with β-substitution.[77]

A ring expansion mechanism (Scheme IV) is conceivable, but does not appear to offer an effective way of relieving the

Scheme IV



strain of the cyclopropane ring; the bicyclic transition and even the four-membered intermediate state could well be more strained than the starting cyclopropanol in the light of the fact that the strain even in the saturated trimethylene oxide (oxetane) (strain energy 25.51 kcal/mol)[78] is only slightly lower than that of cyclopropane (strain energy 27.43 kcal/mol).[78] An attempt to summarize the results obtained in this and previous studies and to formulate a generalization concerning the mechanisms of one- and two-electron oxidations of cyclanols is given in Table IX.

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References and Notes

(1) (a) Presented at the 165th National Meeting of the American Chemical Society, Dallas, Texas, April 1973; (b) Preliminary communication: *J. Am. Chem. Soc.*, **95**, 5425 (1973). (c) The support of this work by the donors of the Petroleum Research Fund, administered by the American Chemical Society, by the National Science Foundation, and by the U.S. Army Research Office, Durham, N.C., is gratefully acknowledged.
(2) Work done at the Catholic University of America, Washington, D.C.
(3) J. Rocek and A. E. Radkowsky, *J. Am. Chem. Soc.*, **90**, 2986 (1968); **95**, 7123 (1973).
(4) K. Meyer and J. Rocek, *J. Am. Chem. Soc.*, **95**, 1209 (1972).
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Specific Acid Catalysis in the Oxidation of 6,7-Diphenyl-8-methyllumazine by Permanganate

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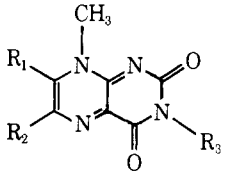
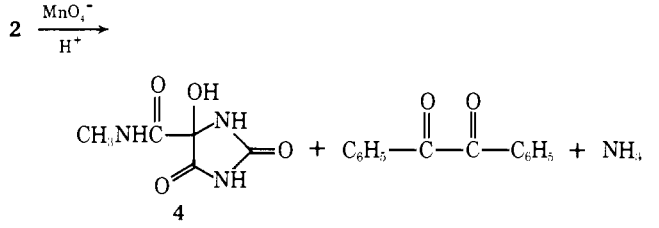
Abstract: The oxidation of 6,7-diphenyl-8-methyllumazine [6,7-diphenyl-8-methylpteridine-2(1*H*),4(3*H*)-dione] (**2**) by aqueous potassium permanganate is subject to specific acid catalysis and gives the methylamide of alloxanic acid, benzil, and ammonia. There are two pathways to the products; one is kinetically dependent on the permanganate concentration and the other is not. The latter reaction proceeds by rate-controlling hydration of **5**, the conjugate acid of **2**, followed by rapid reaction of permanganate with the hydrate. The former reaction proceeds either by reaction between permanganate ion and **5** or by reaction of **2** with an activated form of manganese(VII) formed by the action of acid on permanganate ion.

The kinetics of the acid-catalyzed permanganate oxidation of the riboflavine model compound 6,7,8-trimethyllumazine (**1**) are consistent with the existence of three paths, two of which are kinetically independent of the permanganate concentration and are believed to proceed via general acid catalyzed enolization and specific acid catalyzed hydration, respectively; the third is a permanganate-dependent path which is subject to specific acid catalysis.[1] In order to simplify the kinetics, we have studied the oxidation of 6,7-diphenyl-8-methyllumazine (**2**). This compound does not have enolizable protons and hence one of the three suspected paths is eliminated. Moreover, kinetic data for the hydration of 3,8-dimethyl-6,7-diphenyllumazine (**3**), a close structural analog of **2**, are available,[2] whereas corresponding information for **1** is not.



1, $R_1 = R_2 = CH_3$; $R_3 = H$
2, $R_1 = R_2 = C_6H_5$; $R_3 = H$
3, $R_1 = R_2 = C_6H_5$; $R_3 = CH_3$

The region of acidity covered in the present study is from pH 1.75 (aqueous phosphate buffer) to $H_0 = -0.42$ (10.8% sulfuric acid). The products of the reaction are the hydantoin **4** (the methylamide of alloxanic acid), benzil, and ammonia.



4

Results and Discussion

Using a large excess of permanganate, excellent first-order plots of the disappearance of **2** were observed in all cases, showing the oxidation to be first order in **2**. The order with respect to permanganate was then obtained by maintaining the acidity constant and varying the permanganate concentration. Plots of the pseudo-first-order rate constants against permanganate concentration give straight lines; extrapolations of these to zero permanganate concentration intercept the ordinate somewhat above the origin of the graph. This is observed over the whole acidity range studied and shows that permanganate-dependent and permanganate-independent paths exist. Typical plots of k_{obsd} against permanganate concentration are shown in Figure 1; such plots can be represented by the equation $k_{obsd} = k_1 + k_2[MnO_4^-]$.

In order to determine the acid dependency of these two paths, the intercepts k_1 and slopes k_2 of the plots of $\log_{obsd}$ against permanganate concentration were calculated by the method of least-squares and are shown in Table I. When