Rate and product studies on the oxidative cleavage of some bicyclic alcohols with ceric ammonium nitrate

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RATE AND PRODUCT STUDIES ON THE OXIDATIVE CLEAVAGE
OF SOME BICYCLIC ALCOHOLS WITH
CERIC AMMONIUM NITRATE

by

Patrick John Flash

A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of
The Requirements for the Degree of
DOCTOR OF PHILOSOPHY

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Approved:

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1970
## TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>QUOTATION</td>
<td>vii</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>HISTORICAL</td>
<td>3a</td>
</tr>
<tr>
<td>Some Aspects of Alcohol Oxidations</td>
<td>3a</td>
</tr>
<tr>
<td>RESULTS AND DISCUSSION</td>
<td>23</td>
</tr>
<tr>
<td>Product Studies</td>
<td>23</td>
</tr>
<tr>
<td>Kinetics</td>
<td>46</td>
</tr>
<tr>
<td>Equilibrium Constants</td>
<td>58</td>
</tr>
<tr>
<td>Mechanism</td>
<td>71</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>79</td>
</tr>
<tr>
<td>EXPERIMENTAL</td>
<td>82</td>
</tr>
<tr>
<td>Equipment</td>
<td>82</td>
</tr>
<tr>
<td>Chemicals</td>
<td>83</td>
</tr>
<tr>
<td>General Procedures</td>
<td>85</td>
</tr>
<tr>
<td>Synthetic Procedures</td>
<td>99</td>
</tr>
<tr>
<td>Product Analysis of Cerium(IV)-Alcohol Oxidations</td>
<td>110</td>
</tr>
<tr>
<td>SUMMARY</td>
<td>116</td>
</tr>
<tr>
<td>BIBLIOGRAPHY</td>
<td>118</td>
</tr>
<tr>
<td>ACKNOWLEDGMENTS</td>
<td>125</td>
</tr>
<tr>
<td>APPENDIX</td>
<td>126</td>
</tr>
</tbody>
</table>
LIST OF CHARTS

Chart 1. Structure proofs of the nitrate products from the CAN oxidation of bicyclo[2.2.2]octan-2-ol

Page 27
LIST OF TABLES

Table 1. Slopes and slope ratios for some bicyclic alcohols

Table 2. A summary of the products from ceric ammonium nitrate oxidation of various bicyclic alcohols in 50% aqueous acetonitrile

Table 3. Relative rates of the CAN oxidation of some bicyclic alcohols at 10°C in 70% aqueous acetonitrile-0.49M nitric acid

Table 4. Pseudo first order rate constants for CAN oxidation of alcohols in 70% and 90% acetonitrile at various temperatures

Table 5. Activation parameters for the pseudo first order CAN oxidation of some alcohols in 70% acetonitrile at 1°C with nitric acid 0.49 M

Table 6. Formation constants for cerium(IV)-alcohol complexes in 70% aqueous acetonitrile containing 0.02 M CAN and 0.5 M nitric acid at 21.0°C

Table 7. Equilibrium constants for 1:1 cerium-alcohol complexes in 70% aqueous acetonitrile

Table 8. Equilibrium constants for 1:1 cerium-alcohol complexes in 90% aqueous acetonitrile

Table 9. Thermodynamic parameters for the complex formation of CAN with exo- or endo-norbornanol in 79% or 90% acetonitrile at 20°C

Table 10. Rates and equilibrium constants for some representative bicyclic alcohols in 90% aqueous acetonitrile at 20°C

Table 11. Chemicals purchased
Table 12. Pseudo first order rate constants for the CAN oxidation of some bicyclic alcohols in 70% acetonitrile-30% water at 10°C with nitric acid 0.49 M

Table 13. Pseudo first order rate constants for the oxidation of the 2-norbornanols and 2-methyl-2-norbornanols as functions of temperature and solvent

Table 14. Spectrophotometric equilibrium constant data for alcohols and ceric ammonium nitrate in 70% acetonitrile-30% water with nitric acid 0.49 M

Table 15. Spectrophotometric equilibrium constant data for alcohols and ceric ammonium nitrate in 90% acetonitrile-10% water with nitric acid 0.15 M

Table 16. Pseudo first order rate constants for the kinetic determination of equilibrium constants
## LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMR of 4-cyclohexeneacetaldehyde</td>
<td>26</td>
</tr>
<tr>
<td>2</td>
<td>NMR spectra of 4-hydroxycyclohexylethanols</td>
<td>29</td>
</tr>
<tr>
<td>3</td>
<td>Infrared spectra of 4-hydroxycyclohexylethanols</td>
<td>32</td>
</tr>
<tr>
<td>4</td>
<td>NMR spectra of the crude oxidation mixtures from CAN with 2-methyl and 2-phenyl-endoc-2-norbornanol</td>
<td>37</td>
</tr>
<tr>
<td>5</td>
<td>NMR spectra from the CAN oxidation of norbornenol</td>
<td>43</td>
</tr>
<tr>
<td>6</td>
<td>A typical plot of spectrophotometric data for a 1:1 cerium-exo-2-norbornanol complex</td>
<td>61</td>
</tr>
<tr>
<td>7</td>
<td>A typical plot of kinetic data for determination of the equilibrium constant for a 1:1 ceric ammonium nitrate-alcohol complex</td>
<td>68</td>
</tr>
<tr>
<td>8</td>
<td>Hammett plot for p-substituted 1-phenyl-exo-2-norbornanols in 50% aqueous acetonitrile at 10°C</td>
<td>74</td>
</tr>
<tr>
<td>9</td>
<td>Free-energy diagram for the oxidation of the 2-norbornanols by ceric ammonium nitrate in 70% aqueous acetonitrile at 10°C</td>
<td>77</td>
</tr>
<tr>
<td>10</td>
<td>Mechanism for the ceric ammonium nitrate oxidation of bicyclic alcohols</td>
<td>81</td>
</tr>
</tbody>
</table>
It is not enough that you should understand about applied science in order that your work may increase man's blessings. Concern for man himself and his fate must always form the chief interest of all technical endeavours...in order that the creations of our mind shall be a blessing and not a curse to mankind. Never forget this in the midst of your diagrams and equations.

ALBERT EINSTEIN

Address to the student body

California Institute of Technology
INTRODUCTION

For many years cerium(IV) salts have been known to be powerful one electron oxidants. The oxidative properties of ceric salts with organic substrates have been studied extensively and a recent review has appeared (1). In our labs there has been considerable interest in the ceric salt ceric ammonium nitrate (CAN) and it has been studied from both a synthetic (2-5) and a mechanistic (6-11) viewpoint. This author's M.S. thesis dealt with the cleavage reaction of ceric ammonium nitrate on either exo or endo-2-norboranol. Both alcohols cleaved to give a mixture of 3- and 4-cyclopenteneacetaldehydes and 3-nitratocyclopenteneacetaldehyde in fairly good yields.

Spurred on by the unusual cleavage reaction of the norbornanols and intrigued by a system seemingly pregnant with rich information, we initiated a study to examine other bicyclic alcohols, mainly in the [2.2.1]heptane system, and to complete the study of the [2.2.2]octane system begun in the M.S. thesis. Initially we set out to do product studies of the oxidation reaction. However, the emphasis of the project has changed since conception. A search of the literature revealed that there had been no systematic study of the effect of alcohol structure on the rate of oxidation by ceric salts. Nor had any correlation been made with both rate and equilibrium studies on the same series
of alcohols. Since the [2.2.1]heptyl system offered a rather rigid, controlled steric environment, we decided to examine the rate and equilibrium reactions of some representative bicyclic alcohols with ceric ammonium nitrate. Some mechanistic aspects of the cleavage reaction have also been examined. The results of the above studies are reported in the following pages.
HISTORICAL
Some Aspects of Alcohol Oxidations

Since this thesis examines three aspects of the alcohol-cerium(IV) interaction, the historical will be divided into three sections: the cleavage aspect of metal ion oxidations, the pertinent rate and equilibrium studies, and the effect of steric environment on alcohol oxidation. A brief examination of previous product analysis from the oxidation of bicyclic alcohols by other oxidants may be found in the author's M.S. thesis.

Oxidative cleavage by transition metal ions

While the oxidative cleavage of diols by transition metal ions has received much attention (1, 7, 12), in most cases the similar cleavage of monohydric alcohols has received scant attention. Bawn and White (13) and Hoare and Waters (14, 15) have reported the cleavage reaction of cobalt(III) with secondary and tertiary alcohols to give carbonyl and carbon radical products. They proposed alkoxy radical formation and subsequent fragmentation to give carbon radicals and carbonyl products. With secondary alcohols they proposed competitive paths as shown below.

\[ \text{RCHOH} \cdot \cdot \cdot \text{Co(III)} \rightarrow \text{complex} \]
Vanadium(V) has been shown to cleave phenyl-t-butylcarbinol and the monomethyl ether of pinacol to give respectively benzaldehyde and acetone as products (16, 17). Iron(III) chloride and nitrate have been used by de Boer and co-workers to cleave 1-methoxycyclopropanol and 1-methylcyclopentanol (18, 19). The same group also reported the facile cleavage of 1-methoxycyclopropanol by copper(II) sulfate (19).

As early as 1944, Mosher and Whitmore briefly reported that chromic anhydride cleaved methyl-t-amylcarbinol and
isopropyl-\textit{t}-amylcarbinol to give \textit{t}-amylcarbinol (20). A full paper followed (21). Mosher and Langerak later reported similar cleavages (22, 23) and they also found that chromic acid oxidation of isoborneol (1) led to 2\% of a cleavage product, campholenic acid (2). However, they failed to specify the actual chromium species involved in the cleavage step of the oxidation. Phenyl-\textit{t}-butylcarbinol is also cleaved by chromium to give large amounts of benzaldehyde (24, 25). Mosher and Cohen have reported that isobornyl-p-tolylcarbinol was cleaved by chromium to give isobornyl acetate. In the same paper they also examined 3-methyl-3-phenyl-2-pentanol and found that it cleaved to 2-phenyl-2-butanol (26). More recently Nave has conducted a comparison of the cleavage reactions of chromium and cerium(IV) on 2-aryl-1-phenylethanols (27, 28). With chromium he found competitive cleavage and ketone formation. The $c$ value for the cleavage was -1.0 using $\sigma^+$ values. From the $\phi$ value and trapping experiments using oxygen, Nave concluded that chromium cleaved the alcohols to give benzyl radicals by a one electron process. He further conclusively showed that chromium(IV) was the species effecting the cleavage. In this respect he concurred with Rocek who also had
suggested recently that chromium(IV) was the cleaving species in the oxidation of cyclobutanol (29).

Cerium (IV) has been used extensively as a glycol cleaving agent (1, 12, 30) but has received little attention as a cleaving agent for monohydric alcohols. Mosher and co-workers reported an almost quantitative cleavage of phenyl-\textit{t}-butylcarbinol and \textit{p}-anisyl-\textit{t}-butylcarbinol to give the benzaldehydes (31).

De Boer has oxidized one substituted cyclopropanols with cerium and found products from both an abstraction and dimerization process. He pictured the reaction as going \textit{via} an alkoxy radical, a process not consistent with evidence found in this thesis. The process is shown below. Attempts to repeat the reaction with one substituted cyclopentanols failed.

\begin{center}
\includegraphics[width=0.8\textwidth]{reaction_diagram.png}
\end{center}

Trahanovsky, Flash, and Smith have examined the ceric ammonium nitrate cleavage of a few bicyclic alcohols, the 2-norbornanols, borneol (3), and isoborneol (9, 32). While the norbornanols cleaved to give clean product mixtures of 3- and 4-cyclopenteneacetaldehydes and 3-nitratocyclopentane-
acetaldehyde in good yields, the trimethyl substituted cases gave product mixtures reminiscent of radical reactions with a multitude of products in small yields. The main product with either isomer was campholenic aldehyde (4).

\[
\text{\begin{tikzpicture}
  \node (a) at (0,0) {OH};
  \node (b) at (1,0) {CHO};
  \node (c) at (2,0) {CHO};
  \node (d) at (3,0) {CHO};
  \node (e) at (4,0) {OH};
  \node (f) at (5,0) {CHCNC_2};

  \draw (a) -- (b);
  \draw (b) -- (c);
  \draw (c) -- (d);
  \draw (d) -- (e);
  \draw (e) -- (f);
\end{tikzpicture}}
\]

Recently Nave has completed a study of the cleavage reaction of some 1,2-diphenylethanols with coric ammonium nitrate (27, 28). A Hammett treatment of the data using $\sigma^+$ values led to a $\rho$ for the reaction of -2.0. The $\rho$ value combined with oxygen trapping experiments led him to propose a benzyl radical as an intermediate in the reaction as shown below.

\[
\text{\begin{tikzpicture}
  \node (a) at (0,0) {CHCH_2-\text{Z-CH}_2-\text{OH}};
  \node (b) at (1,0) {CHO-\text{CH}_2-\text{Z-\text{OH}}};

  \draw (a) -- (b);
\end{tikzpicture}}
\]

From the examples given above, it should be apparent that oxidative cleavage of monohydric alcohols appears to be a one electron process. Most of the metals studied are known
one electron oxidants and chromium(IV) has been implicated as the cleaving species in chromium oxidations. It might also be noted that cleavage reactions tend to occur when a good radical, such as benzyl or t-butyl, can be ejected from the molecule. Another requirement for many of the cleavage reactions seems to be a rather bulky substrate. Both the above observations make the cerium(IV) cleavage of the bicyclic alcohols seem even more remarkable as the substrates are not particularly crowded nor do they produce stabilized radicals. Yet, they cleave facily with ceric ammonium nitrate and other ceric salts.

Cerium(IV)-alcohol complexes

Shortly after the Gay Nineties, and probably reminiscent of the era, Meyers and Jacoby made the initial observation that ceric salts reacted with ethanol to give red colors (33). The discovery lay dormant for a considerable time. In 1940 Duke and Smith proposed that the red color was due to a complex formation between the alcohol and cerium(IV) (34). They examined a number of alcohols and even looked at the sugars sucrose and glucose. However, they failed to examine that ubiquitous sugar ambidextrose. Following the work of Duke and Forist (35) in 1949 on the reaction of ceric

1King, R., Iowa State University, Ames, Iowa. Private communication to the author, Iowa State University, Ames, Iowa. 1968.
ammonium nitrate with 1,4-butanediol, many studies have been made on complex formation between various ceric salts and alcohols. This section of the historical will cover that work.

The first really thorough study on the cerium-alcohol complex was done by Ardon in 1957 (36). He examined the reaction of ceric perchlorate with ethanol and found an equilibrium constant for the reaction of 4.3 for a one to one complex at 20°.

Littler and Waters (37) have reported an equilibrium constant of 13 for cyclohexanol at 50° in 0.24N sulfuric acid. Again, they found a 1:1 complex. However, recent work in the area casts doubt on their value. Santappa and Sethuram report an equilibrium constant for cyclohexanol of 0.32 in 1 M nitric acid (38). Hintz and Johnson report an equilibrium constant of 3.9 by a spectrophotometric method and 2.9 by a kinetic method both in 1 M perchloric acid (39). Since sulfate is known to depress complexation, the value of 13 which Littler and Waters gave seems to be much too high compared to the other values. Even the differences in temperature among the studies doesn't seem great enough to account for the large equilibrium constant in sulfuric acid.

Muhammad and Rao looked at the reaction of methanol with ceric perchlorate in perchloric acid (40). They found an
equilibrium constant of 1.36 for 1:1 complex in 1 M acid and 2.97 in 3 M acid at 20°. In sulfuric acid they found no complexation and the overall oxidation was found to be second order. The oxidation in perchloric acid was retarded by addition of potassium acid sulfate.

Offner and Skoog looked at the complexation constants for the three butanols in both perchloric and nitric acids (41). The equilibrium constants were lower in nitric as expected. The values found were \textit{t}-butyl alcohol, 0.6; \textit{sec}-butanol, 1; and \textit{n}-butanol, 1 in 2 M nitric acid and 13, 11, and 16 in 1.69 M perchloric acid.

Rangaswamy and Santappa (42) examined \textit{n}-butanol in perchloric acid and also found rate determining 1:1 complex formation with ceric perchlorate. In another article they examined benzyl alcohol and found no complexation with cerium in perchloric acid (43). The results with benzyl alcohol conflict with those found in our labs in nitric acid where benzyl alcohol does form a complex with ceric ammonium nitrate (8). Without citing any evidence, Rangaswamy and Santappa postulated a mechanism of ceric ion oxidation via an alkoxy radical.

Sethuram and Muhammed looked at the ceric nitrate oxidation of isopropanol and \textit{sec}-butanol in nitric acid (44). In both cases they found a 1:1 complex between alcohol and cerium. The equilibrium constants were 2.07 for isopropanol
and 2.21 for sec-butanol at 22°. A negative salt effect in which the rate was inversely proportional to the square of the nitrate concentration was found. The rate was accelerated by hydrogen ion. They proposed an alkoxy radical as a mechanistic pathway for the reaction. In a subsequent article the same authors looked at the ceric sulfate and perchlorate oxidations of isopropanol (45). The perchlorate oxidation was found to be the same as in nitric acid but the ceric sulfate was found not to complex with the alcohol. Rather, the order was first order with respect to isopropanol.

Allyl alcohol has been oxidized by Sethuram (46). He found a 1:1 complex with ceric nitrate and an equilibrium constant of 3.08 at 20°.

Santappa and Sethuram have examined the ceric nitrate oxidation of n-propyl, allyl, cyclohexyl, and benzyl alcohols (38). The first three were found to follow the usual Michaelis-Menten type kinetics and equilibrium constants of 2.31, 2.78, and 0.32 respectively were determined for them. Again, benzyl alcohol was anomalous and gave a first order plot. Thermodynamic parameters for the reactions were determined and may be found in the article.

Venkatasubramanian and Balasubramanian examined the ceric perchlorate oxidation of isopropanol, α-methylbenzyl alcohol, and benzhydrol (47). They assumed ketonic products apparently and gave no product analysis. No cleavage was reported for
the alcohols. In acetic acid-water solvent they reported that increasing the acetic acid concentration raised the rate and therefore postulated an ion-dipole type reaction, that is, one in which the alcohol (dipole) and cerium(IV) (ion) react more easily in the solvent of lower dielectric constant since the solvent separates the reactants less effectively.

In one of the more general surveys to date, Rangaswamy and Santappa examined the ceric perchlorate oxidation of a series of primary, secondary, and tertiary alcohols (48). Included were methanol, ethanol, \( n \)-propanol, \( n \)-butanol, \( iso \)-butanol, \( iso \)-amyl alcohol, \( iso \)-propanol, \( sec \)-butanol, \( sec \)-amyl alcohol, cyclohexanol, \( t \)-butyl alcohol, and \( t \)-amyl alcohol. They obtained equilibrium constants and thermodynamic parameters for the alcohols. Unfortunately, the different classes of alcohols were run at different temperatures and so no real comparison can be made among them or their equilibrium constants. At constant ionic strength the rates were found to increase with added hydrogen ion and a positive salt effect was found. No product studies were conducted. It was assumed that primary alcohols gave acids and secondary and tertiary alcohols ketones.

Gorbachev and co-workers have oxidized seven alcohols with ceric sulfate and were able to correlate the activation energies for the oxidations with the dipole moment of the
alcohols (49). The reactions were overall second order and apparently no complexes were formed.

Probably the most useful study to date on the complex reaction of cerium(IV) with alcohols was done by Young and Trahanovsky (8). They examined a comprehensive series of alcohols to determine structural and electronic effects on the reaction equilibrium. Using acetonitrile-water as solvent, ceric ammonium nitrate as ceric species, and nitric acid they found some surprising results. Various para substituted benzyl alcohols showed that there was no large electronic effect on the equilibrium constants. Most values were in the range 0.45-0.85. For aliphatic alcohols what amounts to an inverse steric effect was observed. Within certain limits, the more sterically crowded alcohols in a series of similar alcohols had the larger complexation constants. For example, in 70% aqueous acetonitrile some trends found were: trans-4-t-butylcyclohexanol, 3.6; cis, 36; t-butyl > isopropyl > ethanol; neopentyl > isorrop-anol; 1-methylcyclohexanol > t-butyl. To explain this novel trend the authors advanced the postulate that for their system the steric requirements for complexation were less than the steric requirements for solvation of the uncomplexed components. Thus a more crowded alcohol would have a greater tendency to complex rather than to be solvated.
Kinetic studies

Kinetic studies on the cerium(IV) oxidation of alcohols have been many and varied. However, they have been disorganized and present no body of useful information. Nitric, perchloric and sulfuric acid solvent systems have been used with the three respective salts. The references cited in the equilibrium constant section may be consulted for specific values. Young seems to have made the only systematic study on cerium(IV) kinetics with alcohol substrates (50). For a series of substituted benzyl alcohols he found the rate of oxidation by CAN in aqueous acetonitrile to be accelerated by electron doners on the ring and retarded by electron withdrawers. There appears to be no study of steric effects in cerium oxidations of monohydric alcohols. However, some work has been done on steric effects on glycol cleavage.

Hintz and Johnson examined the ceric perchlorate cleavage of cis and trans-cyclohexane-1,2-diol (39). They found the cis faster than the trans by a factor of 2.4. In a mixture of perchloric and sulfuric acids they found similar results for the six membered diol but opposite results for the five membered ring (trans>cis). They attributed the rate differences to chelate formation.
Cerium species in solution

Studies have been made on the cerium(IV) nitrate species present in various solvents. As far back as 1900, Meyers and Jacoby reported isolation of a Ce(OH)(NO$_3$)$_3$H$_2$O species from nitric acid (51). They also reported that the ceric species existed as an anion (52). More recently Wylie (53) has extracted H$_2$[Ce(NO$_3$)$_6$] from 5N nitric acid. He postulated a six coordinate cerium. Blaustein and Gryder, however, reported that the cerium species present in nitric acid was dependent on acid concentration with ion migration to the anode in 6F nitric acid and no migration in 2F nitric acid (54). To further confuse matters, Henshall concluded from recovery, ion migration, and freezing point depression studies that in glacial acetic acid the main species from ceric ammonium nitrate was the neutral ceric nitrate (55). In 1964 Larsen and Brown performed a solution X-ray analysis on 54% ceric ammonium nitrate in water (2.25 M CAN) (56). They found twelve cerium-oxygen interactions with a bond length of 2.85Å. Evidence for nitrogen-oxygen interactions at 1.35Å and oxygen-oxygen interactions at 2.15Å was also obtained. They found no evidence for dimeric cerium interactions. Attenuated total reflectance infrared studies of ceric nitrate species in solution indicated nitrate-cerium species. A Raman band at 1528 cm$^{-1}$ suggested bidentate nitrates (57). Finally in 1968 Beineke and Delgaudio completed
an X-ray analysis of ceric ammonium nitrate. They found ammonium cations and hexanitratocerate anions (58). The anion had close to $T_h$ symmetry and the nitrates were bidentate with cerium-oxygen bond lengths of 2.508 Å. The work of Young (50) and Sethuram and Muhammed (44, 48) with rate and complex formation using cerium in nitric acid demonstrated competition between nitrate and alcohol for ligand sites on ceric ion. It may be concluded, then, that the ceric species in nitric acid solutions are probably highly nitrated by bidentate nitrates. The number and arrangement of the nitrate ligands remains obscure, though. Also, nothing is known of the effects of acetonitrile on the complex equilibria which must be occurring in acetonitrile-nitric acid solutions.

**Steric effects in metal ion oxidations**

The main body of work in this area had been done using chromium oxidations. Vavon and Zaremba observed that axial alcohols were more readily oxidized than the equatorial epimers (59). Pursuing this line of research further, Schreiber and Eschenmoser examined a series of steroidal alcohols for steric effects on the oxidation rates (60). They found that cholestan-3α-ol (axial hydroxy) (5A) was oxidized only three times as fast as its 3β isomer (5B). However, the 2β-ol (5C), which is crowded by the $C_{10}$ methyl, was oxidized at twenty times the rate of the 3β-ol and
5α-pregnane-3,20-dione-11β-ol (5D), where the hydroxy has two 1,3-diaxial methyl interactions, is oxidized 60 times faster than the 3β-ol. Thus, the more crowded a particular hydroxy group, (other factors held constant) the faster is its rate of oxidation by chromium. This finding was rationalized by arguing that the severe crowding in the ground state was relieved in progression to the transition state. Since both epimers give the same transition state for ketonic products, the one having the most strain release would oxidize faster.

Winstein and Holness examined the chromium oxidation of cis- and trans-4-t-butyl cyclohexanol in 75% acetic acid (61). They found the cis isomer (axial hydroxy) faster by a factor of 2.97 further confirming Eschenmoser's work. In addition they found cyclohexanol to have essentially the same rate as the trans-t-butyl case.

Chromic acid oxidation of some other steroidal alcohols has been examined by Burstein and Ringold (62). The 6α and β isomers conformed to the previous results. In addition, they
studied the 7-ene-6α and β isomers (6) and found dramatic rate increases. These they attributed to α,β unsaturated ketone resonances in the transition state.

A considerable amount of work has been done on steric and polar rate effects in the chromium oxidation of various bicyclic alcohols. Kwart and co-workers (63, 64) looked at chromic acid oxidations in 30% acetic acid solutions. They found the following rates, relative to cyclohexanol: exo-norboranol, 3.85; endo-norbornanol, 9.67; borneol, 25; and isoborneol, 49.1. The reactions were pictured as going through a rate determining step of chromate ester decomposition. The rate differences were again attributed to steric and geometric (entropy) effects with the more crowded alcohol being faster due to more strain release in the transition state.

Wilcox, Sexton, and Wilcox examined the epimeric equilibrium between exo- and endo-norbornanol, borneol, and isoborneol (65). The data, combined with similar calculations from Eschenmoser's work, enabled them to correlate relative rates of oxidation of the epimers with the calculated or measured stability differences.
Other bicyclic alcohols have been examined by Rothberg and Russo (66). They again found the more crowded hydroxy to be oxidized faster. In fact, endo-5,6-trimethylene-endo-2-norbornanol was an amazing 311 times faster than the exo parent.

Baker and Hudec examined bicyclic alcohols of the type shown below and found no inductive effect due to the phenyl group (67).

\[
\text{\includegraphics[width=0.5\textwidth]{figure.png}}
\]

Rothberg and co-workers have recently looked at the chromic acid oxidation of the exo and endo-tetracyclo [5.2.1.0.2,6,04,8] decan-9-ols (7) (68). In 40% aqueous acetic acid the endo alcohol was oxidized faster by a factor of 73, a number not unreasonable when considering the severe steric crowding of the endo face of the bicyclo[2.2.1]heptane skeleton.

Lastly, Awasthy, Rocek, and Moriarty examined some bicyclic alcohols looking for a polar effect on chromium
oxidations (69). Comparing alcohols 8 and 9 with 10 and 11, they postulated rate retardation in 10 and 11 due to a polar dipole effect (12).

$$\begin{align*}
\text{Relative rates:} & \\
0.842 & 4.58 & 0.0214 & 0.1605
\end{align*}$$

From the examples cited above, it seems that at least with chromium the rate of oxidation of an alcohol is dependent to a large degree on the steric environment about the hydroxy group. If this is true, studies elucidating that steric environment should be helpful in rationalizing the relative rates of alcohol oxidation. Some studies in that area are reported in the following section.

**NMR studies of hydroxyl environment**

Some recent articles have appeared in the literature which relate the steric environment of the hydroxy proton in alcohols to NMR chemical shifts. Ouellette, in a series of two papers, studied highly dilute carbon tetrachloride solu-
two papers, studied highly dilute carbon tetrachloride solutions of various t-butylcyclohexanol epimeric pairs (70, 71). The chemical shift at infinite dilution was related to the steric environment about the hydroxy proton. Chapman and King looked at the hydroxy resonance in DMSO solution and found the chemical shift to be characteristic only of the magnetic environment (72). They proposed that the difference in chemical shifts for epimeric hydroxys might help detect conformational differences and examined cis- and trans-4-t-butylcyclohexanol. The equatorial hydroxy was downfield from the axial. Unfortunately, the above studies had a limited range and were not directly useful to the present study.

In 1965 Ouellette and co-workers developed a method for measuring the steric environment about the hydroxy proton in various bicyclic alcohols (73). In dilute carbon tetrachloride (0.002-0.015 molal in alcohol) the hydroxy proton resonance linearly approaches a finite value. A plot of peak position in cps versus the mole fraction of alcohol gave a straight line whose slope was related to steric crowding about the hydroxy proton. The relation held true, reasoned Ouellette, due to the fact that at the extremely dilute concentrations studied the alcohols were in a monomer-dimer equilibrium which would be expected to reflect crowding about the hydroxy proton. Thus, the more crowding, the
less dimer formation by hydrogen bonding. Ouellette measured the limiting slopes of a series of methyl substituted norbornanols. He defined a slope ratio: the slope of the less hindered alcohol divided by the slope of the more hindered. The slopes and slope ratios are found in Table 1.

Table 1. Slopes and slope ratios for some bicyclic alcohols (73)

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Slope</th>
<th>Slope Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>endo-alcohols</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-norboranol</td>
<td>1860</td>
<td>1.0</td>
</tr>
<tr>
<td>borneol</td>
<td>1480</td>
<td>1.26</td>
</tr>
<tr>
<td>1-methyl-2-norbornanol</td>
<td>1460</td>
<td>1.27</td>
</tr>
<tr>
<td>7,7-dimethyl-2-norbornanol</td>
<td>1850</td>
<td>1.00</td>
</tr>
<tr>
<td>camphenilol</td>
<td>840</td>
<td>2.21</td>
</tr>
<tr>
<td><strong>exo-3-methyl-2-norbornanol</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>endo-3-methyl-2-norbornanol</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>exo-alcohols</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-norbornanol</td>
<td>2320</td>
<td>1.0</td>
</tr>
<tr>
<td>isoborneol</td>
<td>700</td>
<td>3.31</td>
</tr>
<tr>
<td>7,7-dimethyl-2-norbornanol</td>
<td>1050</td>
<td>1.49</td>
</tr>
<tr>
<td>l-methyl-2-norbornanol</td>
<td>1560</td>
<td>1.49</td>
</tr>
<tr>
<td>anti-1,7-dimethyl-2-norbornanol</td>
<td>1540</td>
<td>1.50</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Slope</td>
<td>Slope Ratio</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>-------</td>
<td>-------------</td>
</tr>
<tr>
<td>syn-1,7-dimethyl-2-norbornanol</td>
<td>720</td>
<td>3.22</td>
</tr>
<tr>
<td>1,4,7,7-tetramethyl-2-norbornanol</td>
<td>720</td>
<td>3.22</td>
</tr>
<tr>
<td>cyclopentanol</td>
<td>2650</td>
<td>-</td>
</tr>
</tbody>
</table>
RESULTS AND DISCUSSION

Product Studies

The most complete product studies were done on the parent norbornanols and the results may be found elsewhere (9, 32). With many of the current alcohols studied, the product mixtures were complex and a complete product analysis was unreasonable. In these cases, the main product was isolated and its structure determined by spectral means and by analogy to the parent system. The alcohols examined fell into three classes: normal secondary alcohols, tertiary alcohols, and abnormal secondary alcohols. An explanation of the spectral abbreviations used in the following discussion may be found in the Experimental section of the thesis. Table 2 lists the alcohols examined and also summarizes the products obtained from their oxidation by ceric ammonium nitrate. It may be found following the product studies. It is hoped that the table will aid in identifying alcohols unfamiliar to the reader.

Normal secondary alcohols

Because the structure of the product nitrates was important in later mechanistic discussions, a thorough product analysis was done on bicyclo[2.2.2]octan-2-ol. The alcohol was cleanly cleaved by two equivalents of ceric ammonium nitrate. The crude infrared spectrum of the product
mixture showed aldehyde absorption at 1725 cm\(^{-1}\) and nitrate at 1625(s), 1274(s), and 850 cm\(^{-1}\). The products were determined to be 4-cyclohexeneacetaldehyde and cis- and trans-4-nitratocyclohexaneacetaldehydes (13, 14). The yields were determined by a double extraction NMR technique and are shown below.

\[\text{OH} \quad \xrightarrow{2 \text{ CAN}} \quad \text{CHO} \quad \text{CHO} \quad \text{CHO} \]

\[\text{13} \quad 46\% \quad 14 \quad 20\% \quad \text{ONO}_2 \quad 29\% \]

The 4-cyclohexeneacetaldehyde was collected by glpc. It gave an NMR spectrum with resonances at \(\delta 9.7\) (t, 1H, J 2Hz); 5.5 (s, 2H); and 2.5-0.7 (m, 9H) as shown in Figure 1.

The structure of the nitrate products from the oxidation was proven via the scheme in Chart 1. The nitrates were converted to the diols with lithium aluminum hydride (LAH). They gave an NMR spectrum (CDCl\(_3\)) with peaks at \(\delta 4.2-3.4\), 2.13, and 2.1-0.8 (Figure 2). An authentic sample of the diols produced via \(p\)-hydroxyphenylacetic acid gave essentially the same spectrum (Figure 2). The identity of the cis-diol was proven by synthesis of an authentic sample via reduction of the lactone 2-oxabicyclo[3.2.2]nonan-3-one as shown in Chart 1. The cis diol thus prepared (Figure 2) was
Figure 1. NMR of 4-cyclohexeneacetaldehyde
Chart 1. Structure proofs of the nitrate products from the CAN oxidation of bicyclo[2.2.2]octan-2-ol
Figure 2. NMR spectra of 4-hydroxycyclohexylethanols

top: via the CAN oxidation
middle: via the phenyl acetate
bottom: via the bicyclic lactone
superimposable on the glpc peak of the 29% product from the ceric ammonium nitrate oxidation. The NMR spectrum of the pure cis-diol was the same as that of the mixtures. Infrared spectra for the three diol samples above were all identical for practical purposes (Figure 3).

A sample of \textit{exo-5,6-trimethylene-exo-2-norbornanol} (15) cleaved as cleanly as the parent to give products 16 and 17. The total aldehyde yield was 80% (NMR), and the olefin/nitrate ratio was similar to the parent (about 0.3). The olefin had an NMR spectrum with resonances at $\delta 9.7$ (t, 1H, $J = 2$Hz); 5.52 (s, 2H); and 3.4–0.8 (m, 11H). No evidence was seen for the other isomeric olefin possible. Product 17 gave an NMR spectrum with peaks at $\delta 9.7$ (t, 1H, $J = 2$Hz); 4.9 (m, 1H); and 3.3–0.8 (m, 13H) and an infrared spectrum with absorbances at 2940(s), 1725(s), 1630(s), 1275(s), and 855(s) cm$^{-1}$.

1-methyl-exo-2-norbornanol cleaved readily to give at least ten products by glpc analysis on FFAP at 125°. Only two product peaks were of considerable size. A NMR yield determination showed 48 ± 5% total aldehyde and 24% olefin.
Figure 3. Infrared spectra of 4-hydroxycyclohexylethanols

top: via the CAN oxidation
middle: via the phenyl acetate
bottom: via the bicyclic lactone
The largest peak in the glpc trace was collected and gave an NMR spectrum consistent with a mixture of \( l\)-methyl-4-cyclopenteneacetaldehyde (18) and \( l\)-methyl-3-cyclopenteneacetaldehyde (19). Absorbances appeared at \( \delta 9.65 \) (t, 1H, \( J = 2 \Pi z \)); 5.22 (s,b, 1H); 3.4-0.8 (m, 7); and 1.7 (s, 3H).

\[
\begin{align*}
\text{OH} & \quad \rightarrow \quad \begin{array}{c}
\text{CHO} \\
\text{18} \\
\text{CHO} \\
\text{19}
\end{array}
\end{align*}
\]

By difference (NMR), 24\% of the products were unassigned. There were trace nitrate absorptions in the infrared. However, work done in this lab (74) indicates that tertiary nitrates are unstable to the work up conditions and so the other 24\% aldehyde products are probably not largely nitrate. The alcohol would be a likely suspect but no positive evidence has been found to support this. A third product of significance was indicated by glpc (about 70\% of the olefin area) but isolation and identification could not be accomplished.

A sample of \( l\)-phenyl-exo-2-norbornanol cleaved to give a total aldehyde yield of 68\% by NMR analysis. The olefin product analysis was dubious having a value of 45 ± 10\%. Most probably the higher value is more believable as a glpc analysis showed only one major product. Its NMR spectrum
had resonances at $\delta 9.55$ (t, 1H, $\mathbf{J} = 2$Hz); 7.5-7.0 (m, 5H); 6.04 (m, 1H); and 3.5-1.0 (m, 7H). An infrared spectrum showed a carbonyl peak at 1720 cm$^{-1}$. The spectra identified the product as a mixture of l-phenyl-4-cyclopenteneacetaldehyde (20) and l-phenyl-3-cyclopenteneacetaldehyde (21). While the crude product mixture showed nitrate bands in the infrared, they were weak. As in the case of the 1-methyl derivative,

the amount of nitrate present was probably quite small, most of it having been lost in work up by hydrolysis.

By glpc analysis on Carbowax 20M, at least ten products were obtained from the ceric ammonium nitrate oxidation of $\alpha$-nopinol. A QF 1 column showed only seven peaks, four of which were separable. The peak areas in order of increasing retention time were 45.6%, 3.6%, 33%, and 17.7%. Compound one had a NMR spectrum with resonances at $\delta 3.55$ (d) and 2.5-0.8 (m) and an infrared spectrum that was rather featureless with a weak carbonyl absorption at 1720 cm$^{-1}$. Compound three gave a NMR spectrum (100 MHz) with a complex pattern from $\delta 2.5-0.8$. The infrared showed strong carbonyl and weak nitrate absorptions. Only infrared spectra could be obtained for compounds two and four. Compound two showed strong
carbonyl absorption; compound four strong carbonyl (doublet about 1720 cm\(^{-1}\)) and strong nitrate absorption where usually expected. Presently no sound ideas can be advanced as to the identity of any of the products from nopinol oxidation. It appears that extensive cleavage has taken place but the usually expected products of simple 1,2 bond cleavage or 2,3 cleavage do not appear. Considerable work remains to be done in the system and the current work should only be considered exploratory.

**Tertiary alcohols**

Both of the tertiary alcohols examined behave somewhat differently than their secondary counterparts as cleavage of the 2,3 bond of the norbornane skeleton also occurred along with the 1,2 bond cleavage. The alcohol 2-methyl-endo-2-norbornanol cleaved as expected to give a mixture of 3- and 4-cyclopentaneacetones (22) and 3-nitratocyclopentaneacetone (23). The NMR spectrum of the products (Figure 4) was similar to that for the parent alcohol with olefin absorption at 5.67(d) and the proton α to the nitrate at δ5.7-5.2. The olefin was isolated by reduction of the product mixture with LAH and collection by glpc of the resulting alcohol. It had a NMR spectrum with peaks at δ5.75 (m, 2H); 4.0-3.5 (q of d, 1H); 3.03(s, 1H); 3.0-1.0(m); and 1.13(d, 3H). The secondary nitrate was not isolated but its presence was
Figure 4. NMR spectra of the crude oxidation mixtures from CAN with 2-methyl and 2-phenyl-endo-2-norbornanol

top: the 2-methyl derivative

bottom: the 2-phenyl derivative
confirmed by the crude NMR and an infrared spectrum with peaks at 1640, 1275, and 860 cm$^{-1}$.

Surprisingly, the 2-methyl-2-norbornanol also cleaved with cerium(IV) to give a primary nitrate $24$. Although this product has not been isolated, its presence was demonstrated by spectral means. The NMR of the crude reaction mixture had a doublet centered at $\delta 4.4$ ($J = 7$Hz). This initially suggested the primary nitrate formed via cleavage of the 2,3 bond of the alcohol. To test whether a doublet was to be really expected, a sample of the hypochlorite (75) of 2-methyl-$\text{-endo}$-2-norbornanol was irradiated with ultra violet light. The two chloride products ($25$ and $26$) had peaks as expected for protons, both methine and methylene, $\alpha$ to a chloride at $\delta 4.5-4.1$ (b) and $3.45$ (d, $J = 6$Hz). The doublet,
shifted upfield, for methylene hydrogens α to chloride confirmed the expected pattern resulting from 2,3 bond cleavage by cerium(IV).

The yield of products from 2-methyl-endo-2-norbornanol oxidation by two equivalents of ceric ammonium nitrate were determined as usual by NMR analysis. The olefins were present in 40%, the secondary nitrate in 39%, and the primary nitrate in 7% yields. Multiple runs showed a constant ratio of secondary to primary nitrate.

Analogous to the 2-methyl case, 2-phenyl-endo-2-norbornanol also cleaved with two equivalents of ceric ammonium nitrate to break both the 1,2 and 2,3 bonds of the bicyclic system. By NMR, 27% olefin (27), 37% secondary nitrate (28), and 6% primary nitrate (29) were obtained. The crude spectrum of the oxidation mixture (Figure 4) had resonances at δ 8.1-7.6; 7.5-7.0; 5.7(d, J = 7Hz); 5.6-5.0(b); and 4.34(d, J = 6Hz). The infrared spectrum showed typical carbonyl and nitrate absorption. A glpc analysis showed only two peaks in an 80/20 ratio. The major peak proved to be the olefin mixture 27. It had an NMR spectrum with resonances at δ 8.0-7.1(m, 5H); 5.65(d, 2H, J = 6Hz); and 3.1-0.8(m, 7H). An infrared spectrum showed carbonyl absorption at 1740 cm⁻¹ but no nitrate bands. The minor peak showed no nitrate absorption in the infrared and had a NMR spectrum
(100 MHz) with peaks at 68.0-7.1; 4.3(b); and 3.3-0.9(m).
Since an integration could not be obtained, the identity of the product remains unknown. However, it is at least grossly a phenyl ketone as shown by the NMR spectrum phenyl region.

**Abnormal alcohols**

The oxidation of benzonorbornen-2-exo-ol (30) by two equivalents of ceric ammonium nitrate led to unusual results. The crude product mixture had no nitrate bands in the infrared spectrum (CHCl₃). The most obvious band was at 3448 cm⁻¹, a strong hydroxy absorption. A typical carbonyl absorption also appeared at 1710 cm⁻¹. The NMR spectrum of the crude reaction mixture (CDCl₃) had resonances at 69.93 (overlapping triplets, J = 2Hz); 7.2(m); and 5.3-4.8(m) plus the usual upfield signals expected. The glpc trace on SE 30 showed one major product and five or six quite minor ones. The main peak was collected. The product gave a NMR spectrum of a substituted indene with resonances at 69.66(t, 1H, J = 2Hz); 7.15(m, 4H); 6.75(m, 1H); 6.44(m, 1H); 3.84(m, 1H); and 3.1-2.5(m, 2H). The infrared spectrum confirmed
the presence of carbonyl. Based on the above evidence, the main product from the benzonorbornanol oxidation must be structure 31. The heat of the glpc detector or interaction with the column must cause facile loss of water to give the substituted indene 32.

The most anomolysis results obtained so far with the ceric ammonium nitrate oxidation of bicyclic alcohols have been with 2-norbornenol. Two equivalents of CAN led to a product mixture that showed no aldehyde triplet in the NMR (Figure 5) and no carbonyl and little nitrate absorption in the infrared. Instead, the NMR spectrum of the product mixture showed peaks at δ5.7(s and shoulder); 5.65-4.85 (looks like a doublet and a triplet); and 3.3-0.1(m). Attempts to separate the products by thick layer chromatography on silica gel were only partially successful. Three bands were obtained. Infrared and NMR spectra were useless in identification. However, the top two bands both gave mass spectra with parent peaks at m/e 108. IAH
Figure 5. NMR spectra from the CAN oxidation of nor-bornenol

top: crude mixture from 50% acetonitrile

bottom: 3-methoxy-2-oxabicyclo[3.2.1]octane
reduction of a crude product mixture gave another mixture whose NMR spectrum was remarkably like the original oxidation products. The solvent was then changed from the normal 50% aqueous acetonitrile to aqueous acetic acid. Preliminary indications (NMR) were that acetate(s) had been obtained but in low yield. Consequently a solvent of 10% methanol-90% acetonitrile was employed to trap the unstable intermediates. At last, an isolable product mixture was obtained. A glpc analysis showed at least four and possibly five products. The two long retention time products both gave infrared spectra with carbonyl absorption (1725 cm\(^{-1}\)). No further characterization was attempted. The two medium retention time products (main products) were collected and gave a NMR spectrum (100MHz) as shown in Figure 5. Resonances at \(\delta 5.7\) (s, 2H); 5.17-4.66 (m, 2H); 3.22 and 3.12 (s, 3H total); and 3.12-0.85 (m, 5H) show that structure \(33\) is the likely product. Additional support was found in the mass spectrum which gave a parent ion at m/e 140 and a large peak at m/e 108 corresponding to loss of methanol. The easy loss of methanol in the spectrum adds further support to the structure. Most probably product 33 is formed by carbonyl participation.
with the cationic center as shown below. Precedence for the process is found in the work of Pasto and Serve or Ward and Sherman (76, 77) who found carbonyl participation in solvolysis of halides and sulfonyl esters. Ward and Sherman were even able to isolate salts such as 34. Analogous to the results in methanol, the main product from the ceric ammonium nitrate oxidation of 2-norbornenol in aqueous acetonitrile probably has the structure 35. Whether Z is all nitrate or only partially has not been established. The weakness of the nitrate bands in the original oxidation mixtures suggests other Z groups. Hydroxy is possible, analogous to the benzo derivative, but no good evidence exists
to support the idea now.

A NMR yield determination of olefin product from the 2-norbornenol oxidation gave 60% olefin. The low yield suggested other products but no evidence for other major products was seen in the glpc traces. The diolefin 36 had been suggested as a possibility but the NMR spectrum of the crude reaction mixture ruled it out as no extra olefin peaks were observed.

While the product analyses have by no means been exhaustive, they have demonstrated the generality of the bicyclic alcohol cleavage by ceric ammonium nitrate. The glpc traces of product mixtures showed that ketones were not major products. The usual products were those from 1,2 or 1,3 bond cleavage of the bicyclic skeleton. The unusual products arose from steps after the initial cleavage reaction. Table 2 summarizes the product study results.

Kinetics

The main body of kinetic data has been accumulated in 70% aqueous acetonitrile at 10°C in 0.49 M nitric acid. The ceric ammonium nitrate concentration was 0.005 M and alcohols
Table 2. A summary of the products from ceric ammonium nitrate oxidation of various bicyclic alcohols in 50% aqueous acetonitrile

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Major Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>exo- or endo-2-norbornanol</td>
<td></td>
</tr>
<tr>
<td>bicyclo[2.2.2]octan-2-ol</td>
<td></td>
</tr>
<tr>
<td>2-methyl-endo-2-norbornanol</td>
<td></td>
</tr>
<tr>
<td>2-phenyl-endo-2-norbornanol</td>
<td></td>
</tr>
<tr>
<td>exo-5,6-trimethylene-exo-2-norbornanol</td>
<td></td>
</tr>
</tbody>
</table>

![Chemical structures and percentages]
<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Major Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>benzonorbornan-2-exo-ol</td>
<td>93%</td>
</tr>
<tr>
<td>norbornenols</td>
<td>60%</td>
</tr>
<tr>
<td>endo-fenchol</td>
<td>no product analysis</td>
</tr>
<tr>
<td>endo-camphenilol</td>
<td>no product analysis</td>
</tr>
<tr>
<td>α-nopinol</td>
<td>no product analysis</td>
</tr>
</tbody>
</table>
were in a 10 fold excess to ensure pseudo first order kinetics. The data is listed in Table 3.

The results in Table 3 can be used to explain the relative rates of alcohol oxidation by ceric ammonium nitrate. At least three factors are concurrently active in determining the relative rates: ring size or ring strain, stabilization of the transition state, and steric crowding. Undoubtedly the factors overlap.

The effect of ring strain is readily seen by comparison of the rates of the monocyclic model compound, cyclopentanol, and all the bicyclics. Even α-nopinol (37), which has its hydroxy group in a three membered bridge, is oxidized at four times the rate of cyclopentanol. The [2.2.2]octyl system is seven times faster and exo-2-norbornanol is an amazing 62 times faster. Camphenilol (38) is almost 7000 times faster. Within the bicyclic alcohols themselves, a hydroxy in a two carbon bridge is oxidized faster than in the three carbon bridge (α-nopinol) and lessening of the strain by going from the [2.2.1]heptyl to the [2.2.2]octyl system
Table 3. Relative rates of the CAN oxidation of some bicyclic alcohols at 10°C in 70% aqueous acetonitrile-0.49M nitric acid

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>$k'_\text{rel}$</th>
<th>$k' \times 10^2$ sec$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclopentanol</td>
<td>1.00</td>
<td>0.00378</td>
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<tr>
<td>$\alpha$-nopinol</td>
<td>4.28</td>
<td>0.0162</td>
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<tr>
<td>bicyclo[2.2.2]octan-2-ol</td>
<td>7.36</td>
<td>0.0278</td>
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<tr>
<td>2-methyl-exo-2-norbornanol</td>
<td>32.1</td>
<td>0.1210</td>
</tr>
<tr>
<td>1-p-nitrophenyl-exo-2-norbornanol</td>
<td>47.2</td>
<td>0.1780</td>
</tr>
<tr>
<td>2-methyl-endo-2-norbornanol</td>
<td>52.5</td>
<td>0.1984</td>
</tr>
<tr>
<td>exo-2-norbornanol</td>
<td>62.0</td>
<td>0.2345</td>
</tr>
<tr>
<td>exo-5,6-trimethylene-exo-2-norbornanol</td>
<td>63.0</td>
<td>0.2380</td>
</tr>
<tr>
<td>2-phenyl-endo-2-norbornanol</td>
<td>69.6</td>
<td>0.2632</td>
</tr>
<tr>
<td>endo-2-norbornanol</td>
<td>151</td>
<td>0.5700</td>
</tr>
<tr>
<td>1-p-chlorophenyl-exo-2-norbornanol</td>
<td>233</td>
<td>0.8820</td>
</tr>
<tr>
<td>1-phenyl-exo-2-norbornanol</td>
<td>295</td>
<td>1.115</td>
</tr>
<tr>
<td>1-p-methylphenyl-exo-2-norbornanol</td>
<td>550</td>
<td>2.080</td>
</tr>
<tr>
<td>1-methyl-exo-2-norbornanol</td>
<td>766</td>
<td>2.890</td>
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<tr>
<td>1-methyl-endo-2-norbornanol</td>
<td>1095</td>
<td>4.150</td>
</tr>
</tbody>
</table>
Table 3 (Continued)

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>$k'_\text{rel}$</th>
<th>$k' \times 10^2 \text{ sec}^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>isoborneol</td>
<td>1385</td>
<td>5.240</td>
</tr>
<tr>
<td>borneol</td>
<td>1420</td>
<td>5.370</td>
</tr>
<tr>
<td>benzonorbornen-2-exo-ol</td>
<td>4380</td>
<td>16.55</td>
</tr>
<tr>
<td>endo-camphenilol</td>
<td>6780</td>
<td>25.60</td>
</tr>
</tbody>
</table>

also lowers the rate. Addition of the **exo-5,6** trimethylene bridge to **exo-norbornanol** should not increase the strain much and it is found that the rates are experimentally the same. While benzonorbornen-2-exo-ol should be oxidized faster on other grounds also, the added strain of the olefin in the 5,6 position undoubtedly contributes to the large rate increase observed (4400X).

Since cleavage of the 1,2 bond of the bicyclic system occurs during the reaction to give a radical species at the former 1-carbon (see later discussion), substitution which would stabilize the radical and its preceding transition state should accelerate the cleavage. Thus 1-phenyl-exo-2-norbornanol, 1-methyl-exo-2-norbornanol, and isoborneol are all oxidized faster than the parent **exo** isomer, the former because cleavage results in a benzyl radical and the
others because tertiary radicals are formed rather than secondary. Benzonorbornan-2-exo-ol was also cleaved to give a benzylic radical and it too had a considerably accelerated rate, in fact it was almost 15 times as fast as the 1-phenyl derivative which was cleaved to a tertiary benzylic radical. Undoubtedly the added rate increase with the benzo derivative was a result of strain introduced by the unsaturation in the 5,6 position. The rate increase might also be attributed in part to the fact that the benzo derivative could have its phenyl π orbitals more easily aligned with the developing radical on the former 1-carbon. The endo alcohols examined also showed acceleration by substitution at the 1-carbon. Both 1-methyl-endo-2-norbornanol and borneol were faster than the parent endo alcohol.

A third factor which helps to explain the relative oxidation rates of the alcohols is steric crowding of the hydroxy group. As with chromium oxidations (20-29), ceric ammonium nitrate appears to oxidize a more crowded alcohol faster. This is readily seen in comparing epimeric pairs. The endo parent is oxidized 2.46 times faster than the exo. With the 1-methyl and 2-methylnorbornanols the endo isomer is the faster by factors of 1.43 and 1.64 respectively. In comparing borneol and isoborneol the factor is not as large, only 1.02, but the exo isomer is abnormally accelerated by the syn-7-methyl group. Further evidence for rate
acceleration due to crowding of the hydroxy group comes from the work of Ouellette and co-workers (73). He found slope ratios of 1, 1.49, and 3.31 for exo-2-norbornanol, the 1-methyl derivative, and isoborneol respectively. The steric crowding increased with larger slope ratios. The same trend was found with the oxidation of the alcohols by CAN, the relative rates being 1, 12.35, and 22.4. A similar trend between crowding of the hydroxy and oxidation rate was found in the series of four endo-2-norbornanols examined. The slope ratios were 1.0, 1.26, 1.27, and 1.77 for the parent, the 1-methyl, borneol, and comphenicol respectively while the relative oxidation rates were 1.0, 7.5, 9.3, and 48. An attempt to correlate Ouellette's slopes with relative oxidation rates was not successful. Using the parent norbornanols, the 1-methyl derivatives, borneol (3), isoborneol (1), and endo-fenchol a relative rate of oxidation would have been predicted as shown below:

\[
\begin{align*}
\text{Slope} & \quad \text{OH} \\
2620 & \quad 1860 \\
1560 & \quad 1480 \\
1460 & \quad 1050 \\
700 &
\end{align*}
\]
While borneol and the 1-methyl-endo compound are reversed, the difficulty is not serious as the rates are quite close and experimental error could easily account for the small error. The glaring irregularity in the trend is isoborneol which is actually three alcohols out of line. Why it should behave so abnormally is puzzling. A possible explanation is that the syn-7-methyl has a profound effect on the rate. This could be investigated using the four syn- and anti-7-methyl-2-norboranols and the 7,7-dimethyl-2-norbornanols. The possibility that the hydroxy group was so crowded that complexation couldn't occur was discounted on the basis of the fleeting red color. Later, equilibrium measurements also showed a higher, not lower, equilibrium constant with cerium(IV) than expected.

At this point a small amount of speculation might be in order. Ouellette was able to demonstrate the additivity of methyl crowding on his slope ratios. This additivity might hold for the ceric ammonium nitrate oxidation of the alcohols also. From a comparison of 1-methyl-exo-2-norbornanol and isoborneol with the parent it is seen that the 1-methyl group causes a rate increase of 12.35. Therefore, the syn-7-methyl group contributes a rate increase of 22.35/12.35 or 1.81. Examination of 7,7-dimethyl-exo-2-norbornanol should confirm the predicted rate increase. Another good system to test for the additivity would be 1-methyl-endo-
2-norbornanol, *endo*-camphenilol (3,3-dimethyl-*endo*-2-norbornanol), *endo*-fenchol (1,3,3-trimethyl-*endo*-2-norbornanol). Qualitatively, *endo*-fenchol was oxidized faster than *endo*-camphenilol. However, the rate was too fast to measure. A different solvent system might make the rates measurable and thus confirm (or deny) additivity of methyl crowding.

In addition to 70% aqueous acetonitrile at 10°, some of the bicyclic alcohols were examined in other solvents and at other temperatures. This data is found in Table 4. From the data at 10° and 20° in 70% acetonitrile, activation parameters were calculated for the parent epimers and their 2-methyl derivatives at 1°C. They are found in Table 5. Calculations were done using the program ACTPAR from the computer library in the I.S.U. organic department.

The values in Table 5 are not particularly unusual. It seems that entropy factors may play an important role in the rate of oxidation of the alcohols by ceric ammonium nitrate as they are the only activation parameters differing much among the alcohols in the table.
Table 4. Pseudo first order rate constants for CAN oxidation of alcohols in 70% and 90% acetonitrile at various temperatures^a

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Temp.-%MeCN</th>
<th>$k' \times 10^{-2}$ sec$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>exo-norbornanol</td>
<td>20 - 70</td>
<td>0.8155</td>
</tr>
<tr>
<td></td>
<td>20 - 90</td>
<td>0.0879</td>
</tr>
<tr>
<td></td>
<td>1 - 70</td>
<td>0.0571</td>
</tr>
<tr>
<td></td>
<td>1 - 90</td>
<td>0.00553</td>
</tr>
<tr>
<td>endo-norbornanol</td>
<td>20 - 70</td>
<td>1.63</td>
</tr>
<tr>
<td></td>
<td>20 - 90</td>
<td>0.202</td>
</tr>
<tr>
<td></td>
<td>1 - 70</td>
<td>0.1578</td>
</tr>
<tr>
<td></td>
<td>1 - 90</td>
<td>0.0111</td>
</tr>
<tr>
<td>2-methyl-exo-2-norbornanol</td>
<td>20 - 70</td>
<td>0.4300</td>
</tr>
<tr>
<td>2-methyl-endo-2-norbornanol</td>
<td>20 - 70</td>
<td>0.760</td>
</tr>
</tbody>
</table>

^aConsult Table 13 in experimental for cerium and alcohol concentrations.
Table 5. Activation parameters for the pseudo first order CAN oxidation of some alcohols in 70% acetonitrile at 1°C with nitric acid 0.49 M

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>$E_a$</th>
<th>$\Delta H^a$</th>
<th>$\Delta S^a$</th>
<th>$\Delta S^{e.u.}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>exo-norbornanol</td>
<td>20.59</td>
<td>20.05</td>
<td>19.96</td>
<td>+0.34</td>
</tr>
<tr>
<td>endo-norbornanol</td>
<td>17.19</td>
<td>16.64</td>
<td>19.36</td>
<td>-9.91</td>
</tr>
<tr>
<td>2-methyl-exo-2-norbornanol</td>
<td>20.90</td>
<td>20.35</td>
<td>20.33</td>
<td>+0.09</td>
</tr>
<tr>
<td>2-methyl-endo-2-norbornanol</td>
<td>22.18</td>
<td>21.63</td>
<td>20.10</td>
<td>+5.59</td>
</tr>
</tbody>
</table>

Values are in kcal/mole.

The measured endo/exo ratio for the parent epimers at 1°C in 70% aqueous acetonitrile was 2.76. The calculated rates were: exo $0.0704 \times 10^{-2}$ sec$^{-1}$ and endo $0.2109 \times 10^{-2}$ sec$^{-1}$. The calculated endo/exo ratio was 2.95, within 7% of the measured value.

An attempt was made to obtain rates for exo- and endo-norbornanol in 40% acetonitrile-60% water at 20°C. The alcohols were oxidized too rapidly for rate constants to be measured. Oxidation in 90% acetonitrile, however, slowed the rates considerably. Whether the rate decrease was due solely to the solvent change or in part due to the change
in nitric acid concentration (0.49 to 0.15 M) was not
determined as the rate decrease itself was the factor desired.
In 90% acetonitrile at 20°C the endo/exo rate ratio for the
parent norbornanols was 2.30. Lowering the temperature to
1°C lowered the ratio to 2.01, the opposite trend as that
found in 70% acetonitrile. The solvent change from 70%
to 90% acetonitrile had a drastic effect on the rates of
oxidation. Usually about a 10 fold change in rate was
observed. However, the solvent change did not affect rela-
tive rates to a large degree. Thus at 20°C, the difference
was only 15% and at 1°C it was 38%.

Equilibrium Constants

A previous work in the area by Young (50) had proposed
an inverse steric effect to explain larger complexation con-
stants for more crowded alcohols of a similar series. It was
decided to test the theory using the rigid bicyclic alcohols
whose steric environments could be controlled more accurately
than acyclic alcohols. Two methods were used to obtain
complexation constants. Initially the method used by Young
was tried, a plot of 1/ΔA versus 1/ROH. A sample plot is
shown in Figure 6. At 20°C in 70% aqueous acetonitrile with
nitric acid 0.49 M, the results in Table 7 were obtained.
The series n-hexanol, 3-heptanol; 1-methyl-cyclohexanol
gave equilibrium constants with ceric ammonium nitrate of
Table 6. Formation constants for cerium(IV)-alcohol complexes in 70% aqueous acetonitrile containing 0.02 M CAN and 0.5 M nitric acid at 21.0°C

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Equilibrium Constants $K$, 1/mole</th>
</tr>
</thead>
<tbody>
<tr>
<td>n-hexanol</td>
<td>1.59±0.03</td>
</tr>
<tr>
<td>n-heptanol</td>
<td>1.71-1.81</td>
</tr>
<tr>
<td>3-heptanol</td>
<td>4.06±0.01</td>
</tr>
<tr>
<td>1-methylcyclohexanol</td>
<td>10.21±0.01</td>
</tr>
</tbody>
</table>

\(^a\)Table taken from reference 50.

\(^b\)Estimated from the data for the primary alcohols.

2.71, 5.90, and 14.54 respectively. The results do not duplicate Young's actual values (see Table 6), but the trend $1^{\circ}<2^{\circ}<3^{\circ}$ still holds. It should be noted that the present results are a factor of 1.53 ± 0.12 larger than Young's values. This regular increase in each alcohol can probably be attributed to the different conditions of the two studies, Young's having 0.02 M ceric ammonium nitrate and this one 0.01 M ceric ammonium nitrate. Thus, this segment of the current work supports the "inverse steric effect."

Since the bicyclic alcohols were oxidized too rapidly in 70% acetonitrile at 20° to get complexation constants via the
Figure 6. A typical plot of spectrophotometric data for a 1:1 cerium-exo-2-norbornanol complex
Table 7. Equilibrium constants for 1:1 cerium - alcohol complexes in 70% aqueous acetonitrile

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Temperature</th>
<th>$K_{eq} \pm \text{av. dev.}$</th>
<th>Method$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>n-hexanol</td>
<td>20</td>
<td>2.71 $\pm$ 0.20</td>
<td>s</td>
</tr>
<tr>
<td>3-heptanol</td>
<td>20</td>
<td>5.90 $\pm$ 0.09</td>
<td>s</td>
</tr>
<tr>
<td>1-methylcyclohexanol</td>
<td>20</td>
<td>14.54 $\pm$ 1.89</td>
<td>s</td>
</tr>
<tr>
<td>cyclopentanol</td>
<td>1</td>
<td>1.57 $\pm$ 0.19</td>
<td>s</td>
</tr>
<tr>
<td>$\alpha$-nopol</td>
<td>1</td>
<td>9.67 $\pm$ 0.04</td>
<td>s</td>
</tr>
<tr>
<td>exo-2-norbornanol</td>
<td>1</td>
<td>5.49 $\pm$ 1.09sd.$^b$</td>
<td>k</td>
</tr>
<tr>
<td>endo-2-norbornanol</td>
<td>1</td>
<td>5.89 $\pm$ 0.98sd.$^b$</td>
<td>k</td>
</tr>
<tr>
<td>exo-2-norbornanol</td>
<td>20</td>
<td>14.70 $\pm$ 0.50sd.$^b$</td>
<td>k</td>
</tr>
<tr>
<td>endo-2-norbornanol</td>
<td>20</td>
<td>4.94 $\pm$ 0.05sd.$^b$</td>
<td>k</td>
</tr>
<tr>
<td>2-methyl-exo-2-norbornanol</td>
<td>20</td>
<td>14.65 $\pm$ 2.48sd.$^b$</td>
<td>k</td>
</tr>
<tr>
<td>2-methyl-endo-2-norbornanol</td>
<td>20</td>
<td>7.00 $\pm$ 0.60sd.$^b$</td>
<td>k</td>
</tr>
</tbody>
</table>

$^a$s indicates the spectrophotometric method and k indicates the kinetic method.

$^b$A standard deviation.
Table 8. Equilibrium constants for 1:1 cerium-alcohol complexes in 90% aqueous acetonitrile

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Temperature</th>
<th>$K_{eq} \pm$ av. dev.</th>
<th>Method$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol</td>
<td>1</td>
<td>2.31 $\pm$ 0.67</td>
<td>s</td>
</tr>
<tr>
<td>Isopropanol</td>
<td>1</td>
<td>2.80 $\pm$ 0.46</td>
<td>s</td>
</tr>
<tr>
<td>t-Butanol</td>
<td>1</td>
<td>3.21 $\pm$ 0.07</td>
<td>s</td>
</tr>
<tr>
<td>exo-2-norbornanol</td>
<td>1</td>
<td>3.65 $\pm$ 0.84sd.$^b$</td>
<td>s</td>
</tr>
<tr>
<td>exo-2-norbornanol</td>
<td>20</td>
<td>8.38 $\pm$ 0.38sd.$^b$</td>
<td>k</td>
</tr>
<tr>
<td>exo-2-norbornanol</td>
<td>20</td>
<td>7.79 $\pm$ 1.25sd.$^b$</td>
<td>s</td>
</tr>
<tr>
<td>endo-2-norbornanol</td>
<td>1</td>
<td>3.28 $\pm$ 0.41sd.$^b$</td>
<td>s</td>
</tr>
<tr>
<td>endo-2-norbornanol</td>
<td>20</td>
<td>5.90 $\pm$ 0.90sd.$^b$</td>
<td>k</td>
</tr>
<tr>
<td>endo-2-norbornanol</td>
<td>20</td>
<td>5.88 $\pm$ 0.22sd.$^b$</td>
<td>s</td>
</tr>
<tr>
<td>Isoborneol</td>
<td>20</td>
<td>10.86 $\pm$ 0.56sd.$^b$</td>
<td>k</td>
</tr>
<tr>
<td>1-Methyl-exo-2-norbornanol</td>
<td>20</td>
<td>4.54 $\pm$ 0.66</td>
<td>k</td>
</tr>
</tbody>
</table>

$^a$s indicates the spectrophotometric method and k indicates the kinetic method.

$^b$A standard deviation.
spectrophotometric method, the solvent was changed to 90% acetonitrile and the temperature to 1°C. Using the data in Table 8, the trend t-butyl alcohol > isopropanol > ethanol was observed, an inverse steric effect. However, a leveling effect was observed in the 90% solvent such that the primary alcohol had its equilibrium constant raised more than the secondary and the secondary more than the tertiary. The overall spread of equilibrium constants was much smaller than in Young's case.

Moving on to exo and endo-norbornanol in 90% acetonitrile, it was found that the exo alcohol had an equilibrium constant of 3.65 and the endo an equilibrium constant of 3.28 at 1°C. Since it is generally conceded (78) that the endo face of the [2.2.1] system is more crowded than the exo, the result was quite surprising. The "inverse steric effect" had disappeared. However, the experimental error in the numbers was large and so it was decided to examine the equilibrium constants at 20°C. The exo alcohol had an equilibrium constant of 7.79 ± 1.25 and the endo an equilibrium constant of 5.88 ± 0.22. Again, the exo equilibrium constant was larger than the endo equilibrium constant and the results seemed outside experimental error. Using the data in 90% acetonitrile, thermodynamic parameters were calculated for the complexation reaction of cerium(IV) with exo- and endo-norbornanol at 20°C. They are found in Table 9.
Table 9. Thermodynamic parameters for the complex formation of CAN with exo- or endo-norbornanol in 79% or 90% acetonitrile at 20°C

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Solvent</th>
<th>ΔH° kcal/mole</th>
<th>ΔG° kcal/mole</th>
<th>ΔS° e.u.</th>
</tr>
</thead>
<tbody>
<tr>
<td>exo</td>
<td>90</td>
<td>6.36 ± 3.2</td>
<td>-1.20 ± 0.1</td>
<td>25 ± 10</td>
</tr>
<tr>
<td>endo</td>
<td>90</td>
<td>4.90 ± 1.3</td>
<td>-1.03 ± 0.02</td>
<td>20 ± 5</td>
</tr>
<tr>
<td>exo</td>
<td>70</td>
<td>8.29 ± 0.45</td>
<td>-1.57 ± 0.01</td>
<td>34 ± 2</td>
</tr>
<tr>
<td>endo</td>
<td>70</td>
<td>-1.48 ± 1.39</td>
<td>-0.93 ± 0.01</td>
<td>-1.8 ± 4</td>
</tr>
</tbody>
</table>

The values conflict drastically with those of Santappa and Sethuram (38) both as to sign of ΔH° and ΔS° and magnitude of ΔG°. Since their ΔG°'s are obviously in error, doubt is also cast on their ΔH° and ΔS° values. Other articles by Sethuram (45, 46) also report puzzling results. While the current parameters are not highly accurate (errors are estimates based on maximum deviations of equilibrium constants not standard deviations), they seem more believable than some of the reported results.

Examination of Table 9 shows the ΔH° and ΔG° values to be similar for the two isomers in either solvent. The noteworthy point is the large difference in ΔS° in 70% acetonitrile compared to the small difference in 90%. Since the equilibrium constants differ greatly in 70% and hardly at
all in 90% solvent, this suggests that the equilibrium constants are highly solvent dependent. Entropy effects in solvation, then, probably account for much of the differences in equilibrium constants. Consequently, further work in the area would probably best be done in 70% acetonitrile.

At this point a second method of determining the complexation constant for an alcohol with cerium(IV) was tried, a kinetic approach involving a plot of $1/k'$ versus $1/\text{ROH}$. The results of this approach are found in Tables 7 and 8 and a sample plot is shown in Figure 7 for exo-2-norbornanol.

Since 70% acetonitrile seemed to spread the equilibrium constants more than 90%, it was chosen for the initial kinetic runs with the parent norbornanols. At 1°C the endo equilibrium constant was actually larger than the exo, 5.89 compared to 5.49. However, the experimental errors were large and could easily have inverted the values. Also the compression of equilibrium constants at low temperatures made the close values less than definitive. At 20°C a dramatic reversal occurred. The exo equilibrium constant was 14.7 while the endo was only 4.94. The large difference in the equilibrium constants immediately led to the suspicion that the kinetic method was giving erroneous results. To check the possibility, the equilibrium constants for exo- and endo-norbornanol in 90% acetonitrile at 20°C were determined by the kinetic method (see Table 8) and compared with the
Figure 7. A typical plot of kinetic data for determination of the equilibrium constant for a 1:1 ceric ammonium nitrate-alcohol complex
previously obtained spectrophotometric values. The \textit{exo} equilibrium constant was 8.38 (7.79 spectrophotometric) and the \textit{endo} equilibrium constant was 5.90 (5.88 spectrophotometric). Thus, the kinetic method was giving correct equilibrium constants. With that point settled, other alcohols were run to determine equilibrium constants by kinetics. In 70\% acetonitrile at 20°C, 2-methyl-\textit{exo}-2-norbornanol had an equilibrium constant of 14.68 while the \textit{endo}-hydroxy epimer had an equilibrium constant of only 7.00. In 90\% acetonitrile at 20°C, isoborneol was found to have an equilibrium constant of 10.80 and 1-methyl-\textit{exo}-2-norbornanol an equilibrium constant of 4.54. The thermodynamic parameters have also been calculated for \textit{exo}- and \textit{endo}-norbornanol in 70\% acetonitrile and the results are found in Table 9.

Comparing the above results for the various bicyclic alcohols, it is apparent that Young's "inverse steric effect" does not hold for the bicyclic alcohols examined. The \textit{exo} isomers have larger equilibrium constants than the \textit{endo} epimers and 1-methyl-\textit{exo}-2-norbornanol, while more crowded than its parent, has a lower equilibrium constant.

Table 10 presents a summary of the pertinent rate and equilibrium data in 90\% acetonitrile and points out the non-correlation of rates and equilibrium.
Table 10. Rates and equilibrium constants for some representative bicyclic alcohols in 90% aqueous acetonitrile at 20°C

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>$k' \times 10^{-2}$ sec$^{-1}$</th>
<th>$k^a \times 10^{-2}$ sec$^{-1}$</th>
<th>$K^b$ M$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>exo-2-norbornanol</td>
<td>0.0879</td>
<td>0.242</td>
<td>8.38</td>
</tr>
<tr>
<td>endo-2-norbornanol</td>
<td>0.202</td>
<td>0.649</td>
<td>5.90</td>
</tr>
<tr>
<td>1-methyl-exo-2-norbornanol</td>
<td>-</td>
<td>1.945</td>
<td>4.54</td>
</tr>
<tr>
<td>isoborneol</td>
<td>-</td>
<td>4.420</td>
<td>10.86</td>
</tr>
</tbody>
</table>

$^a$Rate constant for decomposition of cerium(IV)-alcohol complex determined by the kinetic method.

$^b$Determined by the kinetic method.

L. B. Young and Trahanovsky (8) had also postulated that the oxidation rates of alcohols might be directly related to the equilibrium constants, the higher the equilibrium constants, the faster the rate. The present work has shown that to be an incorrect idea. There is no correlation of rate and equilibrium. In fact, with exo- and endo-norbornanol and the 2-methyl epimers, the epimer with the lower equilibrium constant (the endo hydroxy) was oxidized faster.
Mechanism

From previous work in the area (1) the overall aspects of the oxidation of alcohols by nitrato ceric salts have been described. The ceric salts complex with the alcohols in an equilibrium process. The complex then decomposes in a rate determining step to give cerium(III) and a radical fragment. The present work reconfirms that mechanism. Even in the unusual solvent mixtures of 70% and 90% acetonitrile complex formation took place as evidenced by the dramatic color change on admixture of cerium(IV) and alcohol solutions. Both the spectrophotometric and kinetic methods confirmed complexation. The mechanism for the oxidation process is shown below.

\[
K \quad k
\]

\[
\text{Ce(IV)} + \text{ROH} \rightleftharpoons \text{Ce(IV)-ROH} \rightarrow \text{X} \quad \text{Ce(IV)} \quad \text{prdt.}
\]

Part of the aim of this study was to learn more about the nature of the species X and to determine its fate on the path to products.

In the glycol cleavage reaction, Trahanovsky, L. H. Young, and Bierman reported quantitative trapping of a radical fragment from the ceric ammonium nitrate oxidation bicyclohexyl-1,1'-diol (7). Similarly Nave (6) and Mino and co-workers (30, 79) also reported trapping a radical fragment in other systems. In the present investigation a sample of exo-2-norbornanol was oxidized with two equivalents
of ceric ammonium nitrate using acrylamide as a radical trap. As expected, no normal products were obtained from the reaction. Polymer was isolated in high yield. The finding adds additional evidence to the one electron nature of the bicyclic alcohol cleavage by cerium(IV) and supports an intermediate such as 39.

\[
\begin{align*}
\text{CHO} \\
\sim 39
\end{align*}
\]

Nave has recently reported a \( \rho \) of \(-2.0\) (using \( \sigma^+ \) values) for the ceric ammonium nitrate cleavage of some 1,2-diarylethanols (6). The relatively large negative value suggested a fair amount of positive charge on the \( \beta \) carbon atom in the transition state. To find out whether the transition state leading to 39 also had such high positive character, a Hammett plot was constructed for a series of four 1-\( \rho \)-phenyl substituted norbornanols, the \( \rho \)-chloro, the \( \rho \)-hydrogen, the \( \rho \)-nitro, and the \( \rho \)-methyl derivatives (see Figure 8). Unlike Nave's results, the \( \rho \) value fell in the normal range for radical reactions \(-0.69\) to \(-1.46\) (80-82). Using \( \sigma \) values a \( \rho \) of \(-1.09 \pm 0.09\) was obtained while \( \sigma^+ \) values gave a \( \rho \) of \(-0.998 \pm 0.045\). As Nave found, the \( \sigma^+ \) values gave the better correlation. These findings add more evidence to the postulated occurrence of 39 during the cleavage reaction of bicyclics by ceric ammonium nitrate.
Figure 8. Hammett plot for \( p \)-substituted \( 1 \)-phenyl-\textit{exo}-
2-norbornanols in 50\% aqueous acetonitrile at 10°C
Log $k_X/k_H^*$ vs. $\sigma^+$

- $p$-CH$_3$
- $p$-H
- $p$-Cl
- $p$-NO$_2$
Since a definite radical center is developed at the one carbon of the bicyclic system during cleavage by cerium(IV), the transition state might be pictured by species 40. The free energy difference between exo- and endo-norbornanol in the transition state should be less as a result of stretching in the 1,2 bond of the bicyclic system.

\[ \text{exo} \quad \text{endo} \]

The kinetics in 70% acetonitrile at 10° and 20°C confirm the idea. A free-energy diagram (83) (Figure 9) shows the two transition states to be nearly equal in energy. The exo epimer is still slightly more stable, probably due to residual crowding of the cerium on the endo face of the bicyclic system.

Two questions remain concerning structure 39. What is the stereochemistry of the radical and how does it go on to products? Previous work on the norbornanols had not solved the stereochemistry of the nitrate products (32). At that time the possibility of a concerted 1,2 bond breaking and nitrate transfer from a cerium species coordinated to the developing carbonyl was suggested. This process would lead exclusively to cis nitrate product. To test the hypothesis, a thorough product analysis was done on the
Figure 9. Free-energy diagram for the oxidation of the 2-norbornanols by ceric ammonium nitrate in 70% aqueous acetonitrile at 10°C
$\Delta G = 0.4 \text{ Kcal/mole}$

$\Delta G = 19.95 \text{ Kcal/mole}$

$\Delta G = 19.36 \text{ Kcal/mole}$

$\Delta G^\circ = 1.12 \text{ Kcal/mole}$
bicyclo[2.2.2]octanol oxidation. Both cis- and trans-nitrate products were obtained, eliminating the possibility of synchronous bond cleavage and coordinated nitrate transfer. Thus the radical species is a "free" radical and has no constrained stereochemistry.

The most likely path to products from the radical would follow the work of Kochi (84). He suggests that olefin products arise from electron transfer to give a cation which eliminates a hydrogen ion. The nitrate product in the CAN oxidation would then arise via a ligand transfer of nitrate from a cerium species. The transfer of the nitrate from the cerium species would not be unexpected as the Historical section has shown that ceric species in solution are probably highly nitrated.

Further evidence for the oxidation of the radical to the cation is found in the product study of the norbornenol oxidation. The cyclized product 33 would arise easily from carbonyl participation with the cationic center (76, 77)

![Diagram](image)

but no evidence exists at present to suggest a similar radical process.

Based on the above evidence and historical precedent,
the mechanism for the ceric ammonium nitrate oxidation of bicyclic alcohols may be pictured as in Figure 10. The cerium species is shown with only one nitrate ligand for simplicity.

Miscellaneous

Exploratory work has shown that ceric perchlorate is also an effective cleaving agent for bicyclic alcohols. Olefins are the only products from the norbornanols, thus eliminating the bothersome nitrate products. However, ceric sulfate appears to be a poor cleaving agent and ceric acetylacetone seems to be inert.

The one tricyclic alcohol examined, 1-adamantanol, appeared to form a very stable complex with ceric ammonium nitrate. However, the solution did decolorize, indicating that oxidation has taken place.
Figure 10. Mechanism for the ceric ammonium nitrate oxidation of bicyclic alcohols
All absorbance measurements were taken on a Beckman Model DU spectrophotometer fitted with a water cooled cell compartment. One cm cells were used for all measurements. A Haake Model F constant temperature circulator was used to maintain the temperature in the DU and also in an aluminum storage block. This block consisted of a 5" by 2" by 12" slab through which copper coils carried the cooling liquid. Six cavities were drilled in the block to accept a series of U-tubes containing the reaction solutions. The block was thoroughly insulated by encasing it in vermiculite and transite. Nuclear magnetic resonance (NMR) spectra were obtained on Varian A60 or HA 100 instruments or on a Hitachi-Perkin Elmer R201-B. The usual solvent was carbon tetrachloride with deuterochloroform used where noted. Tetramethylsilane was used as an internal standard and peak positions are reported in parts per million down field from TMS (δ values). The abbreviations used are: s, singlet; d, doublet; etc.; m, multiplet; and b, broad peak. Infrared spectra were obtained on a Perkin Elmer Model 21 and the solvent was carbon tetrachloride except where noted. Absorptions are reported in cm⁻¹ and abbreviations used are s, strong; m, medium; and w, weak. Mass spectra were obtained
on an Atlas CH-4. Melting points were obtained in capillaries and are uncorrected. GLPC work was done on a Varian Model 200. Computer calculations were done at the Iowa State University Computation Center using programs RAWDAT, PLOT, and ACTPAR.

RAWDAT is a linear least squares program which draws the line; calculates the slope, intercept, equilibrium constant; and calculates standard deviations for the above values. The program is iterative and uses the initial equilibrium constant to correct for complexed alcohol. The program then recalculates the equilibrium constant until a successive difference of 0.01 units is reached. The program is reproduced in the appendix. Plot is also a least squares program. It handled Hammett-type data and first and second order spectrophotometric data. ACTPAR calculates activation parameters at a specified temperature when fed a pair of rate constants and the respective temperatures. The program is also included in the appendix.

Chemicals

Chemicals bought commercially are listed in Table 11. Most were used as received, although some of the liquids were distilled before use. Those distilled are followed by a "dist" in the table.
Table 11. Chemicals purchased

<table>
<thead>
<tr>
<th>Compound</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceric Ammonium Nitrate</td>
<td>G. Frederick Smith</td>
</tr>
<tr>
<td>Bicyclo[2.2.2]octene</td>
<td>Columbia</td>
</tr>
<tr>
<td>Norcamphor</td>
<td>Aldrich</td>
</tr>
<tr>
<td>Borneol</td>
<td>Aldrich</td>
</tr>
<tr>
<td>Isoborneol</td>
<td>Aldrich</td>
</tr>
<tr>
<td>Ethanol dist</td>
<td>Aldrich</td>
</tr>
<tr>
<td>Isopropanol dist</td>
<td>Mallinckrodt</td>
</tr>
<tr>
<td>t-butanol</td>
<td>Mallinckrodt</td>
</tr>
<tr>
<td>1-methylcyclohexanol dist</td>
<td>Aldrich</td>
</tr>
<tr>
<td>3-heptanol</td>
<td>Matheson, Coleman, and Bell</td>
</tr>
<tr>
<td>n-hexanol dist</td>
<td>Matheson, Coleman, and Bell</td>
</tr>
<tr>
<td>Cyclopentanol</td>
<td>Aldrich</td>
</tr>
<tr>
<td>Fenchone                               dist</td>
<td>Eastman</td>
</tr>
<tr>
<td>Camphenilone</td>
<td>Columbia</td>
</tr>
<tr>
<td>Norbornenol</td>
<td>Aldrich</td>
</tr>
<tr>
<td>Dicyclopentadiene</td>
<td>K and K</td>
</tr>
<tr>
<td>Fenchol</td>
<td>K and K</td>
</tr>
<tr>
<td>ß-pinene</td>
<td>Aldrich</td>
</tr>
<tr>
<td>Camphor</td>
<td>George T. Walker</td>
</tr>
<tr>
<td>Cyclohexanol</td>
<td>MC and B</td>
</tr>
<tr>
<td>p-hydroxyphenylacetic acid</td>
<td>Aldrich</td>
</tr>
<tr>
<td>fen chol</td>
<td>Pfaltz and Bauer</td>
</tr>
</tbody>
</table>
General Procedures

Kinetics-70% acetonitrile

Sufficient alcohol was weighed out to make about a 0.0714 M solution when dissolved to five ml in acetonitrile. A 2.1 ml aliquot of this solution was syringed into a UV cuvette and the cuvette capped. It was cooled in the cell compartment for at least 30 minutes prior to reaction. The ceric solution was prepared by weighing sufficient ceric ammonium nitrate to make a 0.0166 M solution when diluted to five ml with 1.654 M nitric acid. This was also cooled for one half hour in the cell compartment. A syringe cooled to the reaction temperature in the storage block was used to transfer 0.9 ml of the cerium(IV) solution to the alcohol cuvette. At this point the reaction solution was 0.05 M in alcohol, 0.005 M in cerium, and 0.49 M in nitric acid. The solvent composition was 70% acetonitrile-30% water. The change in absorbance with time was followed at 458 nm, frequently using a tape recorder to obtain the data. The reactions were usually followed to at least 80% completion and an infinity reading was taken after at least 10 half lives. A plot of relative absorbance \( (A_t - A_\infty) / (A_0 - A_\infty) \) versus time was used to calculate rate constants by a graphical method. The final rate constants are the average of duplicate runs. The data is found in Tables 12 and 13.
Kinetics-90% acetonitrile

A five ml sample of ceric ammonium nitrate solution was made up in 1.516 M nitric acid such that when 0.3 ml was diluted to 3 ml, the ceric concentration was 0.01 M and the acid concentration 0.15 M. Five ml of alcohol solution was made up in acetonitrile such that a 2.7 ml aliquot diluted to three ml gave the required alcohol concentration. The cerium and alcohol solutions were cooled for one-half hour before mixing. The data is found in Table 13.

Spectrophotometric equilibrium constants

The following general method was used with minor modifications in solution concentrations to accommodate various percent acetonitrile solutions. A 70% aqueous acetonitrile solution will be used as an example.

A 0.5 M solution of the alcohol was made up in acetonitrile. Aliquots of the solution were transferred to one arm of a U tube as follows: 0 ml, 0.35 ml, 0.6 ml, 0.9 ml, 1.2 ml, and 1.5 ml. Acetonitrile was then added to each tube to make a total volume of 2.1 ml. The second arm of the U tube was filled with 0.9 ml of a 0.0333 M ceric ammonium nitrate in 1.654 M nitric acid solution. The U tubes were then cooled in the aluminum block for at least 30 minutes. The tubes were removed just before use, shaken thoroughly and the contents poured into cooled DU cells. The initial
Table 12. Pseudo first order rate constants for the CAN oxidation of some bicyclic alcohols in 70% acetonitrile-30% water at 10°C with nitric acid 0.49 M

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>$k' \times 10^2$ sec$^{-1}$</th>
<th>[CAN] M/l</th>
<th>[ROH] M/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclopentanol</td>
<td>0.00378, 0.00379</td>
<td>0.0051, 0.0051</td>
<td>0.049, 0.049</td>
</tr>
<tr>
<td>$\alpha$-nopinol</td>
<td>0.0158, 0.0166</td>
<td>0.0049, 0.0050</td>
<td>0.050, 0.050</td>
</tr>
<tr>
<td>bicyclo[2.2.2] octan-2-ol</td>
<td>0.0278, 0.0278</td>
<td>0.0049, 0.0051</td>
<td>0.049, 0.049</td>
</tr>
<tr>
<td>2-methyl-exo-2-norbornanol</td>
<td>0.1235, 0.1185</td>
<td>0.0050, 0.0050</td>
<td>0.050, 0.050</td>
</tr>
<tr>
<td>1-p-nitrophenyl-exo-2-norbornanol</td>
<td>0.173, 0.183</td>
<td>0.0051, 0.0051</td>
<td>0.050, 0.050</td>
</tr>
<tr>
<td>2-methyl-endo-2-norbornanol</td>
<td>0.1905, 0.2060</td>
<td>0.0050, 0.0049</td>
<td>0.051, 0.051</td>
</tr>
<tr>
<td>exo-2-norbornanol</td>
<td>0.251, 0.218</td>
<td>0.0049, 0.0049</td>
<td>0.051, 0.051</td>
</tr>
<tr>
<td>exo-5,6-trimethylene-exo-2-norbornanol</td>
<td>0.204, 0.272</td>
<td>0.0050, 0.0050</td>
<td>0.050, 0.050</td>
</tr>
<tr>
<td>2-phenyl-endo-2-norbornanol</td>
<td>0.2545, 0.2720</td>
<td>0.0050, 0.0050</td>
<td>0.050, 0.050</td>
</tr>
<tr>
<td>endo-2-norbornanol</td>
<td>0.586, 0.564</td>
<td>0.0049, 0.0049</td>
<td>0.0524, 0.0524</td>
</tr>
<tr>
<td>1-p-chlorophenyl-exo-2-norbornanol</td>
<td>0.919, 0.846</td>
<td>0.0051, 0.0051</td>
<td>0.051, 0.051</td>
</tr>
<tr>
<td>1-phenyl-exo-2-norbornanol</td>
<td>1.05, 1.18</td>
<td>0.0049, 0.0050</td>
<td>0.049, 0.049</td>
</tr>
<tr>
<td>1-p-methylphenyl-exo-2-norbornanol</td>
<td>1.96, 2.20</td>
<td>0.0050, 0.0050</td>
<td>0.050, 0.050</td>
</tr>
<tr>
<td>Alcohol</td>
<td>k' x 10^2 sec^{-1}</td>
<td>[CAN] M/\text{\textsc{l}}</td>
<td>[ROH] M/\text{\textsc{l}}</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------------------</td>
<td>---------------------------</td>
<td>---------------------------</td>
</tr>
<tr>
<td>1-methyl-exo-2-norbornanol</td>
<td>2.97</td>
<td>0.0049</td>
<td>0.051</td>
</tr>
<tr>
<td></td>
<td>2.82</td>
<td>0.0050</td>
<td>0.051</td>
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<tr>
<td>1-methyl-endo-2-norbornanol</td>
<td>4.12</td>
<td>0.0051</td>
<td>0.051</td>
</tr>
<tr>
<td></td>
<td>4.47</td>
<td>0.0051</td>
<td>0.051</td>
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<tr>
<td>isoborneol</td>
<td>5.74</td>
<td>0.0049</td>
<td>0.051</td>
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<tr>
<td></td>
<td>4.74</td>
<td>0.0050</td>
<td>0.051</td>
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<td>borneol</td>
<td>5.19</td>
<td>0.0049</td>
<td>0.051</td>
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<td></td>
<td>5.55</td>
<td>0.0050</td>
<td>0.051</td>
</tr>
<tr>
<td>benzonorbornen-2-exo-ol</td>
<td>17.8</td>
<td>0.0051</td>
<td>0.051</td>
</tr>
<tr>
<td>2-exo-ol</td>
<td>15.3</td>
<td>0.0051</td>
<td>0.051</td>
</tr>
<tr>
<td>endo-camphenilol</td>
<td>24.6^a</td>
<td>0.0050</td>
<td>0.050</td>
</tr>
<tr>
<td></td>
<td>26.6</td>
<td>0.0050</td>
<td>0.050</td>
</tr>
</tbody>
</table>

^aEstimated, based on the time for absorbance to fall to zero as 10 half lives.
Table 13. Pseudo first order rate constants for the oxidation of the 2-norbornanols and 2-methyl-2-norbornanols as functions of temperature and solvent^a

<table>
<thead>
<tr>
<th>Alcohol^b</th>
<th>Temperature %MeCN</th>
<th>k x 10^2 sec^{-1}</th>
<th>[CAN]</th>
<th>[ROH]</th>
</tr>
</thead>
<tbody>
<tr>
<td>exo-2-OH</td>
<td>20-70</td>
<td>0.7630</td>
<td>0.0050</td>
<td>0.0525</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.8680</td>
<td>0.0050</td>
<td>0.0525</td>
</tr>
<tr>
<td>endo-2-OH</td>
<td>20-70</td>
<td>1.59</td>
<td>0.0050</td>
<td>0.0514</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.67</td>
<td>0.0050</td>
<td>0.0514</td>
</tr>
<tr>
<td>exo-2-OH</td>
<td>1-70</td>
<td>0.0578</td>
<td>0.0099</td>
<td>0.0508</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0565</td>
<td>0.0099</td>
<td>0.0508</td>
</tr>
<tr>
<td>endo-2-OH</td>
<td>1-70</td>
<td>0.1609</td>
<td>0.0099</td>
<td>0.0506</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.1548</td>
<td>0.0099</td>
<td>0.0506</td>
</tr>
<tr>
<td>2-methyl-exo-2-OH</td>
<td>20-70</td>
<td>0.4140</td>
<td>0.0050</td>
<td>0.0505</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.4460</td>
<td>0.0050</td>
<td>0.0505</td>
</tr>
<tr>
<td>2-methyl-endo-2-OH</td>
<td>20-70</td>
<td>0.789</td>
<td>0.0051</td>
<td>0.0501</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.730</td>
<td>0.0051</td>
<td>0.0501</td>
</tr>
<tr>
<td>exo-2-OH</td>
<td>1-90</td>
<td>0.00562</td>
<td>0.0100</td>
<td>0.1001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0544</td>
<td>0.0100</td>
<td>0.1001</td>
</tr>
<tr>
<td>endo-2-OH</td>
<td>1-90</td>
<td>0.0114</td>
<td>0.0100</td>
<td>0.1065</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0108</td>
<td>0.0100</td>
<td>0.1065</td>
</tr>
<tr>
<td>exo-2-OH</td>
<td>20-90</td>
<td>0.0869</td>
<td>0.0100</td>
<td>0.1004</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0889</td>
<td>0.0100</td>
<td>0.1004</td>
</tr>
<tr>
<td>endo-2-OH</td>
<td>20-90</td>
<td>0.199</td>
<td>0.0100</td>
<td>0.1018</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.205</td>
<td>0.0100</td>
<td>0.1018</td>
</tr>
</tbody>
</table>

^aIn 70% acetonitrile the nitric acid was 0.49 M; in 90%, 0.15 M.

^bexo- of endo-2-OH refers to the hydroxy group stereochemistry.
absorption was noted at a wavelength of 540 nm. If the absorbance fell with time, an extrapolation to time zero was made by plotting log absorbance versus time for about 10-15% reaction. The data is found in Tables 14 and 15.

**Kinetic equilibrium constants**

The procedure was similar to that for the previous kinetic procedure with the exception that the cerium was 0.01 M at the start of the reaction in order to duplicate the spectrophotometric conditions. The data is recorded in Table 16.

**Typical NMR yield determination**

Approximately 2.5 mmols of the alcohol was dissolved in 3 ml of 50% aqueous acetonitrile. An amount of 5 mmoles of ceric ammonium nitrate was dissolved in 7 ml of solvent and poured into the alcohol. When the red color had faded, a standard was added to the reaction mixture. The reaction was then poured into 10 ml of water, extracted with 10 ml of ether, and the ether washed with 10 ml of saturated sodium bicarbonate solution. The ether was dried over magnesium sulfate, filtered, and distilled to about one to two ml. A NMR spectrum and integration of the products in ethereal solution was obtained. The ethereal solution was then transferred to an artificially prepared (ethanol and CAN) cerium(III) solution like that at the end of a reaction.
Table 14. Spectrophotometric equilibrium constant data for alcohols and ceric ammonium nitrate in 70% acetonitrile-30% water with nitric acid 0.49 M

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Temperature °C</th>
<th>slope+s.d.</th>
<th>intercept+s.d.</th>
</tr>
</thead>
<tbody>
<tr>
<td>n-hexanol</td>
<td>20</td>
<td>0.5732±0.0109</td>
<td>1.438±0.109</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5406±0.0114</td>
<td>1.571±0.114</td>
</tr>
<tr>
<td>3-heptanol</td>
<td>20</td>
<td>0.2518±0.0037</td>
<td>1.462±0.037</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.2366±0.0019</td>
<td>1.417±0.019</td>
</tr>
<tr>
<td>1-methylcyclo-hexanol</td>
<td>20</td>
<td>0.0987±0.0018</td>
<td>1.250±0.019</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0857±0.0035</td>
<td>1.408±0.036</td>
</tr>
<tr>
<td>cyclooctanol</td>
<td>1</td>
<td>0.5360±0.0101</td>
<td>0.945±0.118</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.4038±0.0145</td>
<td>0.558±0.172</td>
</tr>
<tr>
<td>α-nopinol</td>
<td>1</td>
<td>0.0831±0.0017</td>
<td>0.8014±0.0237</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0817±0.0099</td>
<td>0.7921±0.1304</td>
</tr>
<tr>
<td>exo-2-norbornanol</td>
<td>1</td>
<td>0.1418±0.0053</td>
<td>0.883±0.069</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.1603±0.0028</td>
<td>0.865±0.036</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.1645±0.0054</td>
<td>0.733±0.069</td>
</tr>
<tr>
<td>endo-2-norbornanol</td>
<td>1</td>
<td>0.1232±0.0019</td>
<td>0.771±0.028</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.1307±0.0026</td>
<td>0.584±0.034</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.1233±0.0022</td>
<td>0.744±0.029</td>
</tr>
</tbody>
</table>

The cerium concentration was 0.01 M.
Table 15. Spectrophotometric equilibrium constant data for alcohols and ceric ammonium nitrate in 90% acetonitrile-10% water with nitric acid 0.15 M

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Temperature °C</th>
<th>slope+s.d.</th>
<th>intercept+s.d.</th>
</tr>
</thead>
<tbody>
<tr>
<td>exo-2-norbornanol</td>
<td>1</td>
<td>0.2535±0.0118</td>
<td>1.237±0.153</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.2753±0.0120</td>
<td>0.851±0.120</td>
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<td></td>
<td></td>
<td>0.2806±0.0091</td>
<td>0.914±0.116</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.2918±0.0169</td>
<td>0.989±0.217</td>
</tr>
<tr>
<td>endo-2-norbornanol</td>
<td>1</td>
<td>0.2285±0.0067</td>
<td>0.818±0.086</td>
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<tr>
<td></td>
<td></td>
<td>0.2911±0.0115</td>
<td>1.028±0.148</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.2430±0.0055</td>
<td>0.663±0.075</td>
</tr>
<tr>
<td>ethanol</td>
<td>1</td>
<td>3.037±0.1642</td>
<td>4.98±2.06</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.099±0.251</td>
<td>9.24±2.86</td>
</tr>
<tr>
<td>isopropanol</td>
<td>1</td>
<td>1.740±0.112</td>
<td>5.678±1.09</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.168±0.116</td>
<td>5.081±1.42</td>
</tr>
<tr>
<td>t-butanol</td>
<td>1</td>
<td>1.167±0.0499</td>
<td>3.828±0.623</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.144±0.0191</td>
<td>3.587±0.191</td>
</tr>
<tr>
<td>endo-2-norbornanol</td>
<td>20</td>
<td>0.1287±0.0051</td>
<td>0.7299±0.0655</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.1261±0.0054</td>
<td>0.7691±0.0676</td>
</tr>
<tr>
<td>exo-2-norbornanol</td>
<td>20</td>
<td>0.1491±0.0023</td>
<td>0.9679±0.0264</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.1316±0.0064</td>
<td>1.1820±0.0785</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.1324±0.0022</td>
<td>1.0570±0.0276</td>
</tr>
<tr>
<td>cyclopentanol</td>
<td>20</td>
<td>0.2714±0.0106</td>
<td>1.168±0.1255</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.2681±0.0052</td>
<td>1.301±0.0619</td>
</tr>
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</table>

^aThe cerium concentration was 0.01 M.
Table 16. Pseudo first order rate constants for the kinetic determination of equilibrium constants\textsuperscript{a}

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>[Alcohol] moles/l</th>
<th>$k' \times 10^2$ sec\textsuperscript{-1}</th>
<th>Solvent\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>exo-2-norbornanol</td>
<td>0.1019</td>
<td>1.195</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>0.1523</td>
<td>1.370</td>
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<tr>
<td></td>
<td>0.2004</td>
<td>1.490</td>
<td></td>
</tr>
<tr>
<td>endo-2-norbornanol</td>
<td>0.0791</td>
<td>2.140</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>0.1015</td>
<td>2.540</td>
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<tr>
<td></td>
<td>0.1927</td>
<td>3.710</td>
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<tr>
<td>2-methyl-exo-2-norbornanol</td>
<td>0.1493</td>
<td>0.673</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>0.2219</td>
<td>0.724</td>
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<tr>
<td></td>
<td>0.2510</td>
<td>0.790</td>
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</tr>
<tr>
<td></td>
<td>0.3496</td>
<td>0.812</td>
<td></td>
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<tr>
<td>2-methyl-endo-2-norbornanol</td>
<td>0.1464</td>
<td>0.1086</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>0.2013</td>
<td>1.247</td>
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<tr>
<td></td>
<td>0.2510</td>
<td>1.315</td>
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<tr>
<td></td>
<td>0.3001</td>
<td>1.448</td>
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<tr>
<td></td>
<td>0.4049</td>
<td>1.607</td>
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<tr>
<td>exo-2-norbornanol</td>
<td>0.0687</td>
<td>0.0802</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>0.1010</td>
<td>0.1120</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.1256</td>
<td>0.1235</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.1510</td>
<td>0.1370</td>
<td></td>
</tr>
<tr>
<td>endo-2-norbornanol</td>
<td>0.0591</td>
<td>0.1250</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>0.0758</td>
<td>0.2070</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.0989</td>
<td>0.2400</td>
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<td>0.1517</td>
<td>0.3010</td>
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<tr>
<td>isoborneol</td>
<td>0.1009</td>
<td>2.330</td>
<td>B</td>
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<tr>
<td></td>
<td>0.1523</td>
<td>2.715</td>
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<tr>
<td></td>
<td>0.2508</td>
<td>3.270</td>
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<tr>
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<td>0.3006</td>
<td>3.390</td>
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<tr>
<td>1-methyl-exo-2-norbornanol</td>
<td>0.1540</td>
<td>0.808</td>
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<td></td>
<td>0.1954</td>
<td>0.891</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.2506</td>
<td>1.060</td>
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<tr>
<td></td>
<td>0.3002</td>
<td>1.115</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a}At 20°C with 0.01 M CAN.

\textsuperscript{b}A is in 70% acetonitrile with nitric acid 0.49 M and B is in 90% acetonitrile with nitric acid 0.15 M.
Ten ml of water and enough ether to make 10 ml total was added and the initial work up procedure repeated. A second NMR spectrum and integration was obtained. The yield of a particular product was then calculated knowing that the strength of a NMR signal is proportional to the number of moles present in the sample. We may write:

\[ \text{Moles standard} \times \frac{A_p}{A_s} \times W = M \]  

\[ \text{Moles standard} \times \frac{A'_p}{A'_s} \times W^2 = M \]  

Where

\( A_p \) = area of product signal divided by the number of protons in the signal from the first NMR spectrum

\( A_s \) = area of the standard signal divided by the number of protons in the signal from the first NMR spectrum

\( A'_p \) = the corrected areas from the second NMR spectrum

\( W \) = an extraction factor relating product and standard

\( M \) = moles of product present in the crude reaction mixture

Setting the left hand portion of Equations 1 and 2 equal to one another and solving for \( W \), we get Equation 3.

\[ W = \frac{A_p \times A'_s}{A_s \times A'_p} \]  

Substituting Equation 3 back into Equation 1 we get
\[ M = (\text{moles standard added}) \times \left( \frac{A_p}{A_s} \right)^2 \times \frac{A'_p}{A'_s} \] (4)

**Typical CAN oxidation**

Large scale runs used the same procedures as described in the yield determinations. The base wash was found to enhance product stability.

**Trapping experiments**

Attempts to trap the radical products from the ceric ammonium nitrate oxidation of exo-2-norbornanol by addition of 1 g of acrylamide to 2.5 mmoles of alcohol in a 10 ml reaction volume led to partial trapping. To enable the acrylamide to more effectively compete with the cerium(IV), a more dilute run was tried. Norbornanol (2 mmoles) and CAN (4 mmoles) were reacted in a total volume of 100 ml of 50% aqueous acetonitrile containing 10 g of acrylamide.\(^1\) The precipitated polymer was filtered, and the aqueous layer extracted twice with 50 ml of 50% pentane-dichloromethane. The organic layers were washed with 50 ml of saturated sodium chloride solution, dried over magnesium sulfate, and rotary evaporated. A NMR spectrum showed \(o\)-dichlorobenzene (standard) but no aldehyde protons. As a control run, a sample of pinacol was oxidized in the presence of dichlorobenzene or tetrachloroethane was added.
of acrylamide. The standard and a 1 mmole sample of the nitrate from norbornanol oxidation were added and the solution worked up as above. The one-extraction recovery of nitrate was 62%, in good agreement with similar studies in other cases.

**Treatment of spectrophotometric equilibrium data**

Equilibrium or complexation constants were calculated from absorption data using a linear least squares program, RAWDAT. The following derivation is that of Ardon (36), symbols used follow the derivation.

For the reaction

$$K$$

$$M + ns \rightleftharpoons MS_n$$

(5)

$$A = C_m \epsilon_{\text{complex}} X + C_m \epsilon_m [1-X]$$

(6)

where $X$ is the fraction of $M$ complexed.

$$K = \frac{X}{[1-X][S]}$$

(7)

or

$$X = \frac{K[S]^n}{1 + K[S]^n}$$

(8)

Substituting Equation (8) into Equation (6) gives

$$A = \frac{C_m \epsilon_{\text{complex}} K[S]^n}{1 + K[S]^n} + C_m \epsilon_m - \frac{C_m \epsilon_m K[S]^n}{1 + K[S]^n}$$

(9)
and since $C_m \varepsilon_m = A_0$

$$A - A_0 = \frac{\Delta \varepsilon C_m K[S]^n}{1 + K[S]^n}$$  \hspace{1cm} (10)

$$\frac{1}{\Delta A} = \frac{1 + K[S]^n}{\Delta \varepsilon C_m K[S]^n}$$  \hspace{1cm} (11)

$$= \frac{1}{[S]^n} \times \frac{1}{\Delta \varepsilon C_m K} + \frac{1}{\Delta \varepsilon C_m}$$  \hspace{1cm} (12)

For a 1:1 cerium(IV)-alcohol complex, Equation (12) may be rewritten as:

$$\frac{1}{\Delta A} = \frac{1}{[ROH]} \times \frac{1}{\Delta \varepsilon [Ce(IV)]^n_T K} + \frac{1}{\Delta \varepsilon [Ce(IV)]^n_T}$$  \hspace{1cm} (13)

If $1/\Delta A$ is plotted versus $1/[ROH]$, the slope of the line is $1/\Delta \varepsilon [Ce(IV)]^n_T K$ and the intercept is $1/\Delta \varepsilon [Ce(IV)]^n_T$. Therefore, the intercept divided by the slope is equal to the equilibrium constant.

In the above derivation $M$ is the metal ion, $S$ is the substrate (alcohol), $C$ is concentration, $\varepsilon$ is the molar extinction coefficient, and $K$ is the equilibrium or complexation constant for the reaction of metal ion with substrate. $A$ is the absorbance.
Treatment of kinetic equilibrium data

For the reaction in Equation (1), the following expression can be derived:

\[ \text{Ce(IV)} + \text{ROH} \overset{+}{\underset{\text{complex}}{\rightleftharpoons}} \text{k} \text{ products} \] (14)

\[ \frac{1}{k'} = \frac{1}{k_d} + \frac{1}{k_d K \text{[ROH]}} \] (15)

Where \( k_d \) is the rate constant for complex decomposition, \( k' \) the pseudo first order rate constant for alcohol oxidation, and \( K \) is the equilibrium or complexation constant for a 1:1 cerium(IV)-alcohol complex.

In the presence of excess alcohol

\[ -\frac{d[\text{Ce(IV)}]}{dt}_T = k'[\text{Ce(IV)}]_T \] (16)

where \([\text{Ce(IV)}]_T\) is total ceric ion

\[ -\frac{d[\text{Ce(IV)}]}{dt}_T = k_d [\text{complex}] \] (17)

\[ K = \frac{[\text{complex}]}{([\text{Ce(IV)}]_T - [\text{complex}])\text{[ROH]}} \] (18)

Solving (18) for complex and substituting into Equation (17)

\[ -\frac{d[\text{Ce(IV)}]}{dt}_T = \frac{k_d K \text{[ROH]}}{1 + K \text{[ROH]}} \frac{k_d}{[\text{Ce(IV)}]_T} \] (19)
Setting Equations (16) and (19) equal to one another it is easily shown that:

\[ k' = \frac{k}{1 + K \frac{[ROH]}{[R]}} \]

which may be rearranged to Equation (15) from which it is seen that a plot of $1/k'$ versus $1/[ROH]$ gives a straight line with slope equal to $1/k_d K$ and an intercept of $1/k_d$.

**Synthetic Procedures**

Before beginning the following syntheses it is suggested the reader prepare the following. The mixture is well known for its medicinal and analgesic properties and will aid in effecting smooth synthetic technique.

**Pat's special (85)**

Into a clean graduated cylinder measure 100 ml each of dry gin, sherry, and quinquina. Add one ml each of crème de cassis and apricot brandy. Shake well with crushed ice and filter into glasses. Add a cherry and a slice of orange. Serve cold.

**bicyclo[2.2.2]octan-2-ol**

The alcohol was prepared from bicyclooctene by Brown's oxymercuration procedure (86). Glpc analysis showed only one peak. The material was sublimed at 0.05 mm and 90° to
give a 60% yield of a white powder: mp 207-10° (lit. mp 208-10° (87)); NMR (CCl₄) δ 4.1-3.6 (m, 1H) and 2.2-1.0 (m, 13H).

**bicyclooctanone**

To a mixture of 0.83 g (2.8 mmoles) of potassium dichromate, 0.375 ml concentrated sulfuric acid, and five ml of water (88) was added in portions 0.4972 g (3.9 mmoles) of bicyclo[2.2.2]octan-2-ol. The mixture was stirred at room temperature for one-half hour then warmed to 50° for three hours. The reaction was then extracted three times with 15 ml of ether. The combined ether extracts were washed with three portions of 3 M sodium hydroxide and dried (MgSO₄). Distillation of the ether left a waxy substance: ir (CCl₄) 1720 cm⁻¹ (C=O) and 3400 cm⁻¹ (OH) weak. A glpc analysis of the material showed only one large peak and one small peak.

**2-oxabicyclo[3.2.2]nonan-3-one**

The lactone was prepared from the crude ketone by the procedure of Meinwald and Frauenglass (89): NMR (CCl₄) δ 4.4 (m), 2.75 (d, J = 4Hz), and 2.4-1.0 (m). A glpc trace on Carbowax 20 M or SE 30 showed two peaks in a 90:10 ratio.
**cis-2(4-hydroxycyclohexyl)ethanol**

An excess of lithium aluminum hydride was used to reduce the lactone prepared above. Continuous ether extraction of the product mixture and evaporation of the ether left an oil. A sample of the oil was collected by GLPC on a SE 30 column: NMR (100 MHz) (CDCl$_3$) $\delta$ 4.1-3.8 (s, 1H), 3.8-3.5 (t, 2H, $J = 6$Hz), and 2.1-0.8 (m, 13H); ir (CHCl$_3$) 3333 (OH) and 2900 cm$^{-1}$ (CH).

**Methyl (4-hydroxycyclohexyl)acetate**

An amount of about 2 g of the methyl ester of p-hydroxyphenylacetic acid was hydrogenated in absolute ethanol using a 5% rhodium on alumina catalyst. The temperature was maintained at 100° and the pressure varied from 500 to 1500 psi over two days. The reaction mixture was filtered through Celite and the ethanol distilled at atmospheric pressure. Vacuum distillation of the residue at 0.5 mm gave a single fraction: bp 95-103°; NMR (CCl$_4$) $\delta$ 4.2-2.8 (m); 3.6 (s, 3H); and 2.5-0.7 (m). Integration indicates some impurities were present. The crude product weighed 1.3 g for a 58% yield.

**cis,trans-2(4-hydroxycyclohexyl)ethanol (90)**

An amount of 0.5 g of the ester prepared above was added to an excess of lithium aluminum hydride in tetrahydrofuran. After refluxing for five days, the reaction was worked up as usual. The crude product was continuously extracted for two
days with ether. Distillation of the ether left an oily residue: NMR (CDCl$_3$) $\delta$4.2-3.4(s, t, 3H, $J = 6$Hz); 2.13(s, 2H); and 2.1-0.8 (broad s, 11H); ir was essentially the same as that for the pure cis isomer. Glpc analysis on SE 30 showed only one peak but on FFAP two peaks were observed with a ratio of 76:24. Peak enhancement showed the 76% product to be cis-diol.

**exo-2-norbornanol**

The parent was prepared by the oxymercuration-demercuration of norbornene using the procedure of Brown and co-workers (86). No acetate was detected in the sublimed product via glpc analysis: NMR (CCl$_4$) $\delta$3.65 (d, 1H, $J = 6$Hz), 3.1(m, 1H), and 2.4-0.7(m, 10H).

**endo-2-norbornanol**

The alcohol was prepared via lithium trimethoxyalumino-hydride reduction of norcamphor according to the procedure of Brown and Deck (91). The sublimed product showed no ketone via glpc analysis: NMR (CCl$_4$) $\delta$4.4-3.9(m, 1H), 2.7(s, 1H), and 2.3-0.7(m, 10H).

**dicyclopentenyl formate**

Prepared according to the procedure of Bergman and Japhe (92). Distilled at 20 mm and the third fraction collected: bp 130-133° (lit. bp 136 at 25 mm (92));
NMR (CCl₄) δ7.88 (s, 1H, H-COO), 5.29-5.2 (m, 2H), 4.9-4.5 (b, s, 1H), and 3.0-0.7 (m).

octahydro-exo-4,7-methanoindene-exo-5-yl formate or dihydro-dicyclopentenyl formate

The ene-formate prepared above was hydrogenated in ethyl acetate using Adam's catalyst with 52 psi of hydrogen for two hours. The reaction mixture was filtered through Celite and the solvent stripped.

octahydro-exo-4,7-exo-methanoindene-exo-5-ol or exo-5,6-trimethylene-exo-2-norbornanol

The dihydro formate was hydrolyzed following the procedure of Cristol, Siefert, and Soloway (93). The oil obtained was distilled at 0.8 mm: bp 98-101° (lit. bp 72-75° at 0.5 mm (93)). Recrystallization from nitromethane resulted in a waxy solid: mp 50-51° (lit. mp 53° (93)); NMR (CCl₄) δ3.7-3.5 (m, 1H), 2.95 (s, 1H), and 2.5-0.7 (m, 14H).

2-methyl-endo-2-norbornanol

The alcohol was prepared from norcamphor according to the procedure of Toivonen and Malkonen (94). Recrystallization from pentane gave needles: mp 32.5-33° (lit. mp 34° (94)); NMR (CCl₄) δ2.3-0.8 (m), and 1.48 (s, 3H, -CH₃); ir 3300 (OH), 2857, 1480, and 1000 cm⁻¹. A glpc trace on Carbowax 20M showed only one peak.
2-methyl-exo-2-norbornanol

This epimer was prepared using half the scale of Bartlett and Sargent (95). Thorough shaking was found to lead to a better conversion than stirring: mp 83-84° (lit. mp 84-85° (95)); NMR (CCl₄) was the same as for the endo hydroxy epimer; ir showed minor differences as reported by Bartlett and Sargent.

1-methyl-exo-2-norbornanol

A sample of the 1-methyl-exo-2-norbornyl acetate prepared according to Beckman and co-workers (96) was reduced with lithium aluminum hydride using standard procedures. The ethereal extract was dried (MgSO₄), concentrated, and distilled at 0.2 mm into an ice cooled flask. A solid was collected and sublimed to give crystals: mp 65-66°. Recrystallization from pentane led to needles: mp 74-75° (lit. mp 76° (96)); NMR (CCl₄) δ 3.5-3.25 (b, s, 1H), 2.3 (s, 1H), 2.3-0.89 (m, 9H), and 1.1 (s, 3H).

1-methyl-2-norbornanone

A 2.5-3 g sample of 1-methyl-exo-2-norbornanol was oxidized with potassium dichromate by the procedure of Beckman and Mezgar (97). The oil produced was homogeneous on Carbowax 20M and didecylphthalate glpc columns: ir 1740 (C=0) and 3300 cm⁻¹ (OH)(trace).
1-methyl-endo-2-norbornanol

The ketone prepared above was reduced with lithium trimethoxyaluminoaluminumhydride according to the procedure developed by Brown and Deck (91). Recrystallization from pentane gave crystals: mp 94-95° (lit. mp 90, 99, 103° (97, 98, 99)); NMR (CCl₄) δ 3.8-3.5 (m, b, 1H), 2.7 (s, 1H), 2.3-0.8 (m), and 1.08 (s, 3H, -CH₃).

2-phenyl-endo-2-norbornanol

Prepared by the method of Kleinfelter and Scheyer (100). The ethereal extract was concentrated and dried (MgSO₄). Vacuum distillation at 0.2 mm led to two fractions: fraction one, bp 30° (bromobenzene) and fraction two, bp 130°. Recrystallization from Skelly B gave a white solid: mp 44-45° (lit. mp 44.2-44.6° (100)); NMR (CCl₄) δ 7.5-7.0 (m, 5H) and 2.6-0.9 (m, 11H).

1-phenyl-exo-2-norbornanol

Prepared by the method of Kleinfelter and Schleyer (100). It was distilled under vacuum at 0.4 mm and the fraction boiling from 70-113° was collected. The NMR spectrum was consistent with the desired acetate. It was then reduced with lithium aluminum hydride using standard procedures. The resulting oil was crystallized from hexane giving plates: mp (67-68° (lit. mp 69.5-70° (100)). A glpc analysis on Carbowax 20M and Se 30 showed only one peak.
Sublimation under vacuum gave crystals: NMR (CCl₄) δ7.17 (s, 5H), 3.8-3.5 (b, 1H), and 2.4-0.9 (m, 10H).

1-p-methylphenyl-exo-2-norbornanol

A sample of 2-p-methylphenyl-endo-2-norbornanol was prepared via the p-bromotoluene Grignard and norcamphor as described for the methyl derivative (94). The alcohol was rearranged as described by Beckman and co-workers (96) to the acetate. A potassium hydroxide in ethanol hydrolysis according to Beckman and co-workers (96) resulted in an oil. Distillation at 0.5 mm led to one fraction: bp 95-110°. A glpc trace from Carbowax 20M showed three peaks. Multiple recrystallizations from pentane gave crystals: mp 58-59° (lit. mp 60.1-60.7° (100)); NMR (CCl₄) δ7.03 (s, 4H), 3.7-3.4 (1H), 2.5-0.9 (m, 13H), and 2.29 (s, 3H, -CH₃) A second glpc analysis on Carbowax 20M and tris(2-cyanoethoxy)propane showed only one peak.

1-p-chlorophenyl-exo-2-norbornanol

The procedure to 2-p-chlorophenyl-endo-2-norbornanol was analogous to the p-methylphenyl derivative. The p-chloro derivative was recrystallized from pentane: mp 84-86° (lit. mp 85.9-86.3° (100)). The alcohol was rearranged to the 1-p-chlorophenyl acetate as described previously (96) and the acetate distilled: bp 125-133° at 0.15 mm (lit. bp 158-170° at 0.7 mm (100)); NMR (CCl₄) δ7.15 (s, 4H), 4.9
(b, 1H), 2.5-1.0 (m), and 1.65 (s, 3H, CH₃C=0). The acetate was hydrolyzed in alcoholic potassium hydroxide as described by Kleinfelter and Schleyer (100). The alcohol was decolorized using activated carbon and recrystallized from pentane: mp 66-67° (lit. mp 68.4-69.2° (100)); NMR (CCl₄) δ 7.16 (s, 4H), 3.8-3.4 (b, s, 1H), and 2.5-1.0 (m, 10H).

**1-p-nitrophenyl-exo-2-norbornyl acetate**

Following the procedure of Kleinfelter and Schleyer (100), 1-phenyl-exo-2-norbornyl acetate was nitrated. The resulting crystals were recrystallized from ethanol-water: mp 92-98° (lit. mp 102.5-103.1° (100)).

**1-p-nitrophenyl-exo-2-norbornanol**

The acetate precursor was hydrolyzed as described by Kleinfelter and Schleyer (100). Instead of ligroin, hexane with a trace of dichloromethane was used as recrystallization solvent. Pale yellow needles resulted: mp 145-146° (lit. mp 147.4-148° (100)); NMR (CCl₄) δ 8.14 (d, 2H, J = 8Hz), 7.45 (d, 2H, J = 8Hz), 4.1-3.8 (b, 1H), 2.5-1.1 (m, 10H). A glpc trace on Carbowax 20M showed only one peak.

The diene was prepared according to Fieser and Haddadin (101). The crude material was distilled at 15mm of the six fractions, the one with bp 96-105° was the desired diene: NMR (CCl₄) δ 7.25-6.45 (m, 6H), 3.9-3.5 (m, 2H), and 2.4-2.0 (m, 2H).
benzonorbornan-2-exo-ol

The procedure of Brown and Sharp was used to hydroborate benzonorbornadiene (102). Cooling to -20° and use of a seed crystal resulted in crystals from pentane: mp 73-74° (lit mp 74.1-75.4° (103)); NMR the same as reported by Wells (104).

α-nopinol or 6,6-dimethylbicyclo[3.1.1]heptan-2-ol

An amount of 1.1 g of β-pinene in 100 ml of absolute ethanol was ozonized at dry ice-acetone temperatures for three hours using a Wellsbach ozonizer (settings at 90 volts, 0.02 ml ozone/min, and 6 mm of oxygen pressure). The ozonide was decomposed by cautious addition of 0.54 g sodium borohydride, (VIOLENT REACTION) The ethanol was distilled at atmospheric pressure and the residue taken up in pentane. The pentane was replaced by ether and the mixture further reduced with lithium aluminum hydride. The usual ether work-up and crystallization from pentane led to white needles. Sublimation under vacuum led to crystals: mp 99-100° (lit. mp 102° (105)); NMR (CCl₄) 4.4-4.0 (b, s, 1H), 3.0 (s, 1H), 2.5-0.7 (m), and 1.06 and 1.2 (s, 3H each). A glpc trace on Carbowax 20M of the sublimed material showed one peak. The sublimed crystals were used in the kinetic work.
endo-camphenilol

To a solution of 0.127 g (3.34 mmoles) of lithium aluminum hydride in 20 ml of ether was added 0.392 g (2.83 mmoles) of camphenilone. The solution was stirred for six hours, water and dilute hydrochloric acid added, and worked up by ether extraction. Recrystallization of the crude product from pentane-benzene gave crystals: mp 70-71° (lit. mp 72° (96)); NMR (CCl₄) δ 3.55 (d, J = 4Hz), 2.4-0.7 (m, 9H), and 0.95 and 0.81 (s, 3H each). A glpc analysis on Carbowax 20M showed one peak.

Preparation and irradiation of hypochlorites

Following the general procedure of Greene (106), a solution of 0.3089 g (2.4 mmoles) of 2-methyl-endo-2-norbornanol in 3 ml of carbon tetrachloride and 0.5 g of acetic acid was added slowly to 8 ml of Chlorox at 0°. The mixture was stirred vigorously for two hours at zero degrees. The carbon tetrachloride was separated and the acid layer extracted with two 2 ml portions of carbon tetrachloride. The combined halogen layers were washed with two 5 ml portions of 3% sodium bicarbonate solution and dried over magnesium sulfate. The hypochlorite solution was then degassed with nitrogen for 15 minutes and finally irradiated with a Black Ray ultraviolet lamp for 15 minutes. The yellow solution turned colorless. A glpc analysis on SE 30 showed three major
products: starting alcohol (10%), secondary chloride (53%), and primary chloride (30%). Two minor products were also detected but were not identified. Repetition of the above experiment led to the same products but in a different ratio. Attempted glpc collection of the pure chlorides failed due to decomposition on the column. A NMR spectrum of the crude product mixture showed a methine hydrogen $\alpha$ to a chlorine and methylenes $\alpha$ to chlorine at $\delta4.5-4.1$ and $3.45 \ (d, J = 6\text{Hz})$ respectively.

Product Analysis of Cerium(IV)-Alcohol Oxidations

General

The spectra data used as structure proofs have been included in the Results and Discussion section. NMR yield determinations are the results of two or more runs. Bicyclooctanol yields are reported with standard deviations. All other yields are $\pm5\%$ except where noted. Product analysis oxidations were run using scaled-up NMR yield procedures.

**bicyclo[2.2.2]octan-2-ol**

The diols produced by the lithium aluminum hydride reduction of the crude product mixture were separated by a 6' by 1/4" FFAP column at 170° and with a helium flow of about 110 ml/min. The cis diol had a retention time of 55
minutes and the trans diol of 61 minutes.

**exo-5,6-trimethylene-exo-2-bornornanol**

The residue after ether evaporation was vacuum distilled at 0.4 mm. Fractions between 78 and 135° were collected. The high boiling fraction contained nitrate and the low boiling fraction olefin. The center fractions were mixtures.

**1-methyl-exo-2-norbornanol**

A glpc analysis on a 6' by 1/4" FFAP column at 125° showed at least 13 products plus starting alcohol. Only two products were of any size. The peak at six minutes was collected. Unfortunately the other major product had a very long retention time and so it was not collected. Its area was about two-thirds that of the major peak.

**1-phenyl-exo-2-norbornanol**

A glpc analysis on SE 30 at 160° showed four products and the starting alcohol. The only major product had a retention time of 17 minutes. Two minor products at five to seven minutes seemed to change intensity with time. In fact, one peak eventually disappeared while the collecting was taking place. The peak collected integrated to about 85% of the products present.

**2-methyl-endo-2-norbornanol**

Only four products were detected by glpc on Carbowax 20M: 4' by 1/4", 180°, helium at 40 ml/min. Two of the
products were quite minor. The product mixture was reduced with LAH and analyzed on an SE 30 column at 150°. A major peak appeared at about one minute, an intermediate peak plus shoulder at 3.5 minutes, and a minor peak at eight minutes. The major peak was collected and spectra obtained.

2-phenyl-endo-2-bornornanol

The crude product mixture showed nitrate absorption in the infrared. However, glpc on SE 30 at 195° showed only two peaks in a ratio of 80:20 with retention times of 6.5 and 17 minutes respectively. Neither peak on collection showed nitrate absorption in the infrared, however.

g-nopinol

At least 10 products were detected on a Carbowax 20M column at 150°. A QF 1 column at 110° showed seven peaks, four of which were major and had retention times of 6, 12.5, 16.5, and 21.5 minutes respectively. The peaks had relative areas of 45.6:3.6:33.1: and 17.7. All four peaks were collected.

benzonorbornan-2-exo-ol

A NMR spectrum of the product mixture from aqueous acetonitrile solvent showed two aldehyde triplets at δ9.75, phenyl protons at 7.5-6.9, and a broad peak from 5.3-4.8. An infrared spectrum (CHCl₃) showed carbonyl absorption
at 1710 cm\(^{-1}\) and alcohol peak about 3390 cm\(^{-1}\). There were no nitrate absorptions. Glpc on SE 30 at 150° showed only two major peaks and four minor ones. The peak at six minutes accounted for 80\% of the total area. The only other peak of any size was about 10\%. The major peak at six minutes was collected.

2-norbornenol (exo and endo)

From 50\% aqueous acetonitrile solvent the product mixture gave a NMR spectrum with only a trace of aldehyde absorption. The major absorptions were at \(\delta 6.0-5.5\) (s); \(5.5-4.8\) (b, unresolved); and \(3.3-1.1\). An infrared spectrum of the mix showed weak alcohol at 3330 and weak carbonyl at 1730 cm\(^{-1}\). Strong nitrate bands appeared at 1640, 1275, and 860 cm\(^{-1}\). Various glpc columns were tried in order to separate the products but none seemed to be effective. Thick layer chromatography on silica gel led to three bands. The top two bands were collected and spectra obtained. The infrared spectra were rather featureless and showed no nitrate or carbonyl absorptions. Mass spectra of both bands was inconclusive as the fragmentation patterns were not interpretable. However, both bands gave parent ions at m/e 108. The NMR spectra were not well resolved and the integrations were inconsistent with any of the proposed structures.

In a solvent of 90\% acetonitrile-10\% methanol, CAN
oxidized the norbornenols to a workable product mixture.

Five products were seen on a 6' by 1/4" FFAP column at 140°.

The retention times in minutes and the relative percents were: 5, 22%; 9.5 and 10.5, 56%; 29, 16.8%; and 35, 5.2%.

All attempts to trap much of the first product failed. However, a weak infrared spectrum showed that it was not either of the solvents as was suspected. The last two products had infrared spectra with absorbances at 1730 (s), 1370 (m), and 1095 cm\(^{-1}\) and 2850 (w), 1730 (w), 1210 (m), and 1085 (w) cm\(^{-1}\), respectively.

**exo-2-norbornanol with ceric perchlorate**

A 2.5 mmoles sample of the alcohol was dissolved in five ml of acetonitrile and a 0.5 M ceric perchloric in 6 M perchloric acid solution was added until no red color was observed (about 10 ml). The mixture was extracted with ether, the ether washed with saturated sodium bicarbonate solution, dried (MgSO\(_4\)), and concentrated. A NMR spectrum showed typical olefin absorption about \(\delta\) 5.7. No further analysis was attempted.

**exo-2-norbornanol with ceric sulfate**

Using 2.5 mmoles of alcohol and 5 mmoles of cerium, no color change was noted. Following normal work-up, a NMR spectrum of the resulting solution showed only trace aldehyde.
exo-2-norbornanol with ceric acetylacetonate

The red color of the cerium(IV) failed to disappear over a period of one week in 50% aqueous acetonitrile.
SUMMARY

The cleavage reaction of ceric ammonium nitrate with various methyl substituted bicyclic alcohols has been examined. Many of the products from the reactions have been determined and factors affecting the rate of oxidation and complexation of the alcohols with cerium(IV) have been investigated. Some mechanistic aspects of the reaction have also been examined.

With all of the alcohols, cleavage of the 1,2 bond of the bicyclic system occurs. In addition, with the tertiary alcohols cleavage of the 2,3 bond also occurs to a small extent. The products were generally olefin-aldehyde and/or olefin-nitrate mixtures. The two cases with unsaturation in the 5,6 position of the bicyclo[2.2.1]heptyl system led to abnormal products. Benzonorbornen-2-exo-ol led to an alcohol-aldehyde from cleavage of the 1,2 bond and norbornenol led to recyclized products, most probably 3-substituted 2-oxabicyclo[3.2.1]octanes.

Kinetic studies have shown that a combination of ring strain, steric crowding of the hydroxy group, and stabilization of the transition state contribute to rate acceleration. A qualitative relation exists between crowding of the hydroxy group and rate such that increased crowding generally results in an increased rate. Using p-substituted
1-phenyl-exo-2-norbornanols, a Hammett treatment of the relative rates demonstrates the formation of a radical species at the one position of the bicyclic system. A $\rho$ value of $-0.998$ was determined using $\sigma^+$ values.

Mechanistically the reaction had been shown to proceed by a fast equilibrium between the alcohol and cerium(IV) to form a 1:1 complex. The complex then decomposes in a rate determining step to give the organic radical and cerium(III). A few of the equilibrium constants for the cerium(IV)-alcohol complex have been determined. There seems to be no general trend with the alcohols examined. However, limited data with exo- and endo-2-norbornanols and their 2-methyl derivatives suggests that the exo isomer is generally complexed to a greater degree than the endo.


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My thanks also to my wife, Sally, who has helped so much in the preparation of this thesis.

Finally, I would like to thank William Shakespeare (Hamlet, Act II, Scene III) for a fitting description of the evolution of this work: "Though this be madness, yet there is method in't."
APPENDIX
C CARD 1 - COLUMNS 1-28, DATA LABEL
C CARD 2 A(0), A(1), ..., A(N) 10 COLUMNS EACH
C CARD 3 XNUMML(C, 3, ........XNUMML(N), 10 COLUMNS EACH
C CARD 4 WTRDH, MWRQH 10 COLUMNS EACH
C CARD 5 WTCAN, COLUMNS 1-10

DIMENSION A(N), XNUMML(10), DATLAB(7)
DOUBLE PRECISION X(10), Y(10), OSQT, XK

42 READ (15) DATLAB, NPTS
IF (NPTS) 41, 41, 40
40 READ (1,1) AZERO, (A(I), I=1, NPTS)
READ (1,4) (XNUMML(I), I=1, NPTS)
READ (1,5) WTRDH, MWRQH
C (1,1) WTCAN
XK=0.0
CE41=WTCA*N3.0/(E43.26*G,16)
D113=1=1, NPTS
10 Y(I)=1.0/(A(I)-AZERO)
CONC=WTRDH/(XNUMML(I)-0.016)
30 IF (NPTS) 31, 31, 13
13 DO 14 I=1, NPTS
R/DH=(XNUMML(I)*CONC)/3.0
AA=XK
38=(XK*RQH+XK*CE41+1.0)
CC=XK*CE41*ROH
COM=-38-SORT(RQH-2-4.0*AA*CC1)/(2.0*AA)
14 X(I)=1.0/(RQH-COM)
GO TO 15
15 IF (I) 11, 11, 15
11 X(I)=3.0/(XNUMML(I)*CONC)
WRITE (3,101)
WRITE (3,10) DATLAB, NPTS
WRITE (3,14) WTRDH, MWRQH
WRITE (3,10) CONC
WRITE (3,103)
WRITE (3,107) (XNUMML(I), A(I), X(I), Y(I), I=1, NPTS)
WRITE (3,108) AZERO
WRITE (3,109) WTCAN
WRITE (3,110) CE4I
WRITE (2,103)
WRITE (2,102) (X(I),Y(I),I=1,NPTS)
WRITE (2,111) CE4I
CHECK=XK
CALL LEASQ (X,Y,NPTS,CE4I,AZERO,XK)
NAB=NAB+1
IF (XK-CHECK-0.01) 42,39,39

1 FORMAT (8F10.5)
3 FORMAT (2F10.5)
4 FORMAT (8F10.5)
5 FORMAT (7A4,I2)
6 FORMAT (' ',7A4,I2)
101 FORMAT (IH1)
102 FORMAT (8F10.4)
103 FORMAT (''.............'')
104 FORMAT ('ONEIGHT OF ALCOHOL',F10.5,5X,'MOLECULAR WEIGHT OF ALCOHOL
1',F10.5)
105 FORMAT ('INITIAL CONCENTRATION OF ALCOHOL=',F10.5)
106 FORMAT ('0',7X,'ML',4X,'ABSORB','7X','X',9X,'Y')
107 FORMAT (' ',4F10.5)
108 FORMAT ('0','INITIAL ABSORBANCE =',5X,F10.5)
109 FORMAT ('0','WT OF CAN =',5X,F10.5)
110 FORMAT ('0','CONC OF CAN =',5X,F10.5)
111 FORMAT (F10.7)
41 STOP
END

SUBROUTINE LEASQ (X,Y,N,CE4I,AZERO,EQUILK)
DOUBLE PRECISION SUMX,SUMY,SUMXX,SY,SM,0,S,B,EQUILK,SK,DSQRT
1 FORMAT(T20,'EQUIL CONST EQUALS',DI4.4)
2 FORMAT(1HO)
3 FORMAT(T20,'STANDARD DEV OF EQUIL CONSTANT',DI4.4)
5 FORMAT (T20,'EXTINCTION COEFFICIENT OF COMPLEX',F10.4)
104 FORMAT(T10,'SLOPE',T22,'INTERCEPT',T36,'STAND.DEV.(Y)',T54,
1'ST.DEV.SLOPE',T74,'ST.DEV.INTERCEPT')
PROGRAM FOR CALCULATION OF ACTIVATION PARAMETERS AND EXTRAPOLATION

JOBN0=JOB NUMBER (999 FOR EXIT)

TK2 AND TK1 = RATE CONSTANTS AT T2 AND T1

T2 AND T1 = TEMPERATURES

T3=TEMPERATURE AT WHICH ACTIVATION PARAMETERS ARE CALCULATED

TK3 IS CALCULATED FROM TK1 AND IS RATE CONSTANT AT T3

CARD 1: JOB NUMBER (999 FOR EXIT), K2, K1, T2, T1, T3. FORMAT (I10,

2E10.7, 3F10.5).

CARD 2: TITLE. FORMAT (20A4).

DIMENSION TITLE(20)

READ (1, 3) JOBNO, TK2, TK1, T2, T1, T3

IF (JOBNO=999) STOP

READ (1, 2) (TITLE(I), I=1, 20)

T2 = 273.16 + T2

T1 = 273.16 + T1

T3 = 273.16 + T3

EACT = (1.9872*TK2/T2 + TK2*ALOG(TK2/TK1))/(T2-T1)

ENTHA = EACT - (1.9872*TK1)

TK3 = EXP(ALOG(TK1) + EACT*(T3-T1))/(1.9872*TK3/TK1)

KSTAR = TK3*6.62377/(T3*1.33026*EXP(11.97/0.434/3))

FREEN = -1.9872*TK2*ALOG(KSTAR)

ENTRO = (ENTHA-FREEN)/T3

WRITE (3, 10) JOBNO, (TITLE(I), I=1, 15)

WRITE (3, 12) TK2, TK1, T2, T1, T3

WRITE (3, 11) EACT, ENTHA, TK3, KSTAR, FREEN, ENTR0

GO TO 1

FORMAT (I10, 2E10.7, 3F10.5)

FORMAT (20A4)

FORMAT (16H1, 4, 5X, 20A4)

FORMAT (5H0, K2 = E11.4 / 5H0, K1 = E11.4 / 5H0, T2 = F6.2 / 5H0, T1 = F6.2

X / 5H0, T3 = F6.2

FORMAT (23H0, ENERGY OF ACTIVATION = F9.3 / 11H0, ENTHALPY = F9.3 / 5H0

RATE = E11.4 / 8H0, KSTAR = E11.4 / 14H0, FREE ENERGY = F9.3 / 10H0, ENT

2ROPY = F8.3)

STOP

END