The oxidation of secondary alcohols with Cr(VI): A kinetic investigation of steric strain

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1 AUTHOR:

Timothy James Mason
Coventry University
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The Oxidation of Secondary Alcohols with Cr (VI)

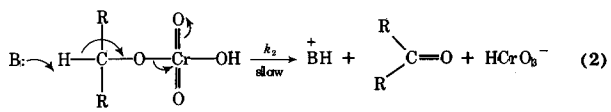
A Kinetic Investigation of Steric Strain

Timothy J. Mason
Department of Applied Chemistry, Coventry (Lanchester) Polytechnic, Coventry, CV1 5FB, England

In this paper a titrimetric method is described for the determination of the rate of acid dichromate oxidation of a series of secondary alcohols. Using an excess of the alcohol substrate, pseudo first-order rate constants may be calculated from which estimates of the relative steric strain within these molecules may be obtained. Although the results quoted apply to a series of cyclic alcohols, the technique can be applied to other secondary alcohols. The time involved in these kinetic experiments is such that all four oxidations can be completed in a 4-hr laboratory period.

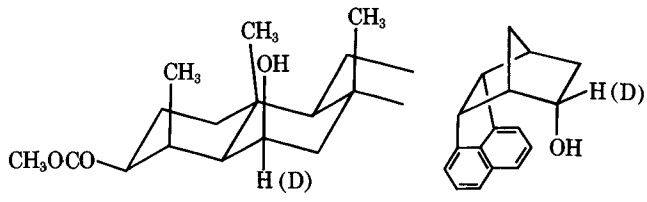
The mechanism of acid dichromate oxidation of secondary alcohols to ketones has been investigated extensively (*1*, *2*). In 1951 Westheimer (*3*) proposed a mechanism for the oxidation of propan-2-ol which was consistent with earlier findings that (a) in dilute aqueous acid the rate was first order in acid chromate ion, alcohol, and hydrogen ion, (b) using $CH_3CD(OH)CH_3$, a kinetic deuterium isotope effect (kH/kD) of 6.5 was found for the oxidation, and (c) it was possible to obtain solutions of intermediate chromate esters in benzene and toluene although these esters were unstable to water. The Westheimer mechanism involved the rapid initial formation of a chromate ester (eqn. 1) followed by the slower, rate determining, decomposition of the ester by removal of the α proton by base (B) (eqn. 2). In aqueous systems the base was considered to be water.

$$HCrO_4^- + R_2CHOH + H^+ \overset{K_E}{\rightleftharpoons} R_2CHOCrO_3H + H_2O \qquad (1)$$



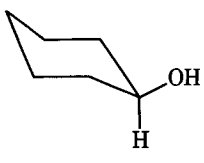
(2)

Strong support for this mechanism was obtained from studies of the oxidation of secondary alcohols in which the OH group was sterically crowded. The acid chromate oxidation of 3β-2,8-diacetoxy-6β-hydroxy-18β-12-oleanane (the partial structure for which is shown (I)) in solvents of high acetic acid



I

II



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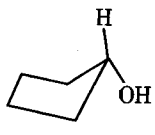

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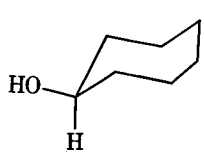

V

content, in the presence of mineral acid showed a kinetic isotope effect (kH/kD) of 1.0 for the oxidation of (I) with a deuterium label α to the hydroxyl group (*4*). This result was attributed to hindrance to chromate ester formation provided by the three methyl groups in close proximity to the hydroxyl group. The steric crowding is so severe in this case that the chromate ester formation step (eqn. 1) has become rate determining. Alcohol (II) has an hydroxyl group heavily shielded on one side by the naphthalene moiety. In this case we might again expect the formation of the chromate ester to be hindered. A deuterium isotope effect of 3.7 has been reported for the acid chromate oxidation of this substrate in aqueous acetic acid (*5*). This result is explained in terms of the rate of oxidation being governed by both ester formation and elimination steps (eqns. 1 and 2).

Although the oxidation of alcohols I and II, with highly hindered hydroxyl groups, provide evidence for the two-stage Westheimer mechanism, it must be emphasized that acid chromate oxidations of the majority of secondary alcohols proceed with rate controlling α-proton elimination (eqn 2). Schreiber and Eschenmoser suggested that the rate of oxidation of secondary alcohols was higher the greater the relief of steric strain on passage to the corresponding ketone (*6*), and several attempts have been made to place this suggestion on a more quantitative basis (*7–10*). The transition state for the oxidation is thought to resemble the starting alcohol rather than the product ketone. Thus, the relief of non-bonded interactions between the hydroxyl group and other groups in the molecule is considered to be a major factor in influencing the rate of formation of ketone.

In the following experiments the acid chromate oxidation rates of four alcohols—pentan-2-ol, cyclopentanol, cyclohexanol, and cycloheptanol—are determined and related to the differences in strain relief involved in the conversion of the alcohols to their respective ketone products.

Experimental

Solutions Required

Oxidant	• Potassium dichromate 0.04 M
Titrant	• Sodium thiosulfate 0.012 M
Stock Solvent	• Acetic acid (1000 cm^3) water (412 cm^3) + perchloric acid (70%) (18.8 cm^3)
Quench Solution	• (to be made fresh on the day of the experiment) Sodium bicarbonate (50 g) + potassium iodide (27 g) in water (500 cm^3)
Sulfuric Acid	• 5 M

Solutions Check

This is an important preliminary to the kinetic runs in that it serves not only to check that the maximum titer is about 10 cm^3 but also allows the student to familiarize himself with the operations required during the titrations.

The oxidant (2.5 cm^3) is made up to 25 cm^3 with stock solvent. An aliquot (5 cm^3) of this solution is run into quench solution (20 cm^3), cooled in ice water, mixed, and then acidified with 5 *M* sulfuric acid (5 cm^3). After the liberated iodine has been allowed to develop for 3 min, it is titrated with thiosulfate using soluble starch as indicator. This procedure is repeated until reproducible results are obtained.

The redox reactions involved in the titration are

$$Cr_2O_7^{2-} + 6I^- + 14H^+ \rightarrow 2Cr^{3+} + 3I_2 + 7H_2O$$

$$I_2 + 2S_2O_3^{2-} \rightarrow 2I^- + S_4O_6^{2-}$$

Thus, 1 mole $Cr_2O_7^{2-}$ = 6 moles $S_2O_3^{2-}$ and with the concentrations used (dichromate 0.004 *M*, thiosulfate 0.012 *M*) titration value of 10 cm^3 should be obtained.

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Kinetic Runs

For each run a sample of the alcohol is weighed to provide a 0.12 *M* solution when made up to 50 cm^3 with solvent.

The preweighed alcohol is dissolved in stock solvent (45 cm^3) in a volumetric flask and equilibrated at 25°C. Oxidant (5 cm^3, also at 25°C) is rapidly added, with mixing, to this solution. Aliquots (5 cm^3) are removed at intervals, quenched, and titrated as described in "solutions check." The first aliquot (Time = 0) should be removed as soon as possible after mixing.

As a guide to the timing of the points taken in a kinetic run, all nine aliquots should be removed within the following time periods: pentan-2-ol (20 min), cyclohexanol (20 min), cyclopentanol (12 min), and cycloheptanol (9 min).

The redox reaction involved in the oxidation of the alcohol is

$$Cr_2O_7^{2-} + 3R_2CHOH + 8H^+ \rightarrow 2Cr^{3+} + 3R_2CO + 7H_2O$$

Thus, 1 mole dichromate = 3 moles secondary alcohol. The concentrations employed in each kinetic run (alcohol 0.12 *M*, dichromate 0.004 *M*) provide a tenfold excess of alcohol and allow the kinetics to be treated as pseudo first order in dichromate. If the thiosulfate titration figure at time t is A_t then, since this titer is directly related to dichromate concentration, a plot of log A_t versus t for each kinetic run yields a straight line whose slope is the pseudo first-order rate constant. Reasonable straight line plots were obtained for the oxidation of each of the four alcohols.

Discussion

The ratio of reaction rates for the four alcohols determined by this method is 1.0:1.0:1.4:2.8 for pentan-2-ol:cyclohexanol:cyclopentanol:cycloheptanol and compares favorably with results obtained for the second order rates of oxidation of these alcohols in 60% acetic acid at 45°C of 1.0:1.0:1.4:2.1 (*11*).

The results may be interpreted in terms of the differing amounts of strain relief involved in the conversion of the alcohols to ketones. The oxidations of pentan-2-ol and cyclohexanol proceed at the same rate which is not unexpected since very little strain is associated with a chair form cyclohexane ring with hydroxyl group equatorial (III).

It has been shown that both cyclopentane and cycloheptane are strained relative to cyclohexane from heats of combustion measurements per methylene group of these cycloalkanes (*12*). For 5- and 7-membered rings this strain, generally termed I (internal) strain is mostly due to partial eclipsing interactions of neighboring protons which are unavoidable in cyclopentane or any of the possible conformations of cycloheptane but are absent from the chair conformation of cyclohexane.

The first step in the oxidation of (3), (4), and (5) involves rapid and reversible conversion to their chromate esters which are subject to similar non-bonded interactions to the parent alcohols. In the rate-determining step of the oxidation, proton removal changes the hybridization at the α-carbon from sp^3 to sp^2 which reduces the eclipsing interactions in both (IV) and (V) and results in the enhanced rates of oxidation for these alcohols compared with cyclohexanol. Confirmation that strain relief is associated with the change from sp^3 to sp^2 hybridization in 5- and 7-membered rings comes from a study of the acetolysis of the *p*-toluenesulfonate derivatives of (III), (IV), and (V). These S_N1 reactions also involve sp^3 to sp^2 hybridization change in the rate-determining step and show precisely the same reactivity order as the oxidation kinetics that is a 7 membered ring >5-membered ring >6-membered ring (*12*).

Literature Cited

(1) Wiberg, K. B., "Oxidation in Organic Chemistry," Academic Press, New York, **1965**, pp. 69–184.
(2) Stewart, R., "Oxidation Mechanisms," W. A. Benjamin, Menlo Park, California, **1964**, Ch. 4.
(3) Holloway, F., Cohen, M., and Westheimer, F. H., *J. Amer. Chem. Soc.*, **73**, 65 (1951).
(4) Rocek, J., Westheimer, F. H., Eschenmoser, A., Moldovanyi, L., and Schreiber, J., *Helv Chim Acta*, **45**, 2554 (1962).
(5) Baker, R. and Mason, T. J., *J. Chem. Soc.* (C), 596 (1970).
(6) Schreiber, J. and Eschenmoser, A., *Helv Chim Acta*, **38**, 1529 (1955).
(7) Winsein, S. and Holness, N. J., *J. Amer. Chem. Soc.*, **77**, 5562 (1955).
(8) Kwart, H. and Francis, P. S., *J. Amer. Chem. Soc.*, **81**, 2116 (1959).
(9) Wilcox, C. F., Sexton, M., and Wilcox, M. F., *J. Org. Chem.*, **28**, 1079, (1963).
(10) Eliel, E. L., Schroeter, S. H., Brett, T. J., Biros, F. J., and Richer, J. C., *J. Amer. Chem. Soc.*, **88**, 3327 (1966)
(11) Srinivasan, G. and Venkatasubramanian, N., *Proc. Indian Acad. Sci. A*, **65**, 30 (1967).
(12) McQuillin, F. J., "Alicyclic Chemistry," Cambridge University Press, England, **1972**, pp. 44–47.