REGARDING THE TRANSITION STATE OF PINACOL CLEAVAGE BY Cr^{VI}; A BRIEF REVIEW

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RESUMEN

Un análisis sobre el estado de transición en la ruptura pinacólica causada por el Cr^{VI}.

Al revisar la bibliografía sobre las velocidades de reacción y las energías de ruptura de pinacoles con ácido crómico, se ha encontrado que no están de acuerdo con los puntos de vista que se aceptan actualmente para estos mecanismos de reacción. Se discute también el significado que tienen estos resultados sobre el mecanismo de la oxidación de alcoholes con ácido crómico, mecanismo que actualmente está en discusión en la literatura química. Se considera la posibilidad de que la formación de un éster crómico cíclico sea el paso determinante en la reacción de ruptura del pinacol y los datos obtenidos de estos análisis están de acuerdo con los hechos conocidos en la actualidad.

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The earliest reliable studies of the kinetics of chromic acid oxidation of pinacols were carried out only relatively recently by Chatterji and Mukherjee (1). Since then the very fine work of Chang and Westheimer (2) and Rocek and Westheimer (3) have contributed extensively to clarification of the mechanistic picture. Thus, it has been established that *cis* pinacols oxidize cleanly with cleavage to ketonic products at rates which are considerably faster than their *trans* diastereomers. It has also been found that the rate of oxidation in the case of pinacol itself is 2.7 times as fast in D_2O as in H_2O, a fact which was interpreted as evidence that breaking of an —OH bond (normally a non-activation controlled process) in the pinacol is not involved in the rate determining step. Furthermore, when the monomethyl ether of pinacol is oxidized under these conditions, reaction takes place much more slowly (2).

All these facts have been reconciled (1-2) with the occurrence of a cyclic chromate ester intermediate. A similar structure has been advanced (4) to explain the kinetic behavior of a variety of α-glicols where oxidation to the α-diketone is competing with cleavage. However, Rocek and Westheimer (3), mostly on the basis of an assumed analogy to the oxidation of secondary alcohols by chromic acid, have postulated that the transition state of the pinacol oxidation bears a strong structural resemblance to the products (5, 6). In other words, they have assumed that the carbonyl groups, which appear as the cleavage products, are almost fully formed in the transition state. This conclusion was supported by consideration of the energetics of fission of several substituted pinacols and α-glycols, as summarized in Table I.

However, the assumption that the transition state of the chromic acid oxidation of secondary alcohols looks like the products and that the carbonyl group is well developed in the activated complex may indeed be at fault. The objections to this picture, which is used by Rocek and Westheimer (3) as the basis for their proposal of an analogous transition state for pinacol oxidative cleavage, have been extensively disputed (6, 9). Briefly stated, it has been shown that this view is not in accord with the frequently made observation that the carbonyl product stabilities do not always correlate with relative rates of oxidation (10). Furthermore, some of the entries in

Table I, as presented by Rocek and Westheimer (3), particularly the relative rates of fission, are extremely approximate, and, since some of the compounds considered therein submit to oxidation with-

TABLE I
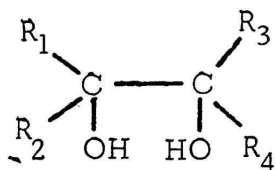
Approximate* Enthalpy Differences Between Fission Products and Reactants (Using Ethylene Glycol as Reference. Standard)

R_1	R_2	R_3	R_4	$\Delta(\Delta_H)$ $Kcal/mole$	Relative Rate of Fission by Cr^{VI}
H	H	H	H	—	10^{-5}
CH_3	H	H	H	3	10^{-3}
CH_3	H	CH_3	H	7	10^{-2}
CH_3	CH_3	CH_3	H	8	—
CH_3	CH_3	CH_3	CH_3	10	1

out undergoing fission, it is difficult to accept their postulate without qualifications.

A direct test of the R and W proposal was therefore sought through comparison of the rates of cleavage of two pinacols. In the cases chosen for study, the reaction enthalpy differences, $\Delta(\Delta H)$, could be anticipated to be of significant magnitude. In addition, experimental data on heats of combustion differences are available as a check on the calculated magnitudes of $\Delta(\Delta H)$. A final consideration that recommended the cases chosen for test is the fact that both the direction and magnitude of the relative oxidation rates could be unequivocally assigned on the basis of Rocek and Westheimer mechanism (3). Thus, the chromic acid cleavage of (bicyclohexyl)-1,1'-diol, (I), and (bicyclopentyl)-1,1'-diol, (II), gives two moles (each) respectively of cyclohexanone and cyclopentanone. Table II illustrates the results of calculations of respective enthalpies of fission of these pinacols (11).

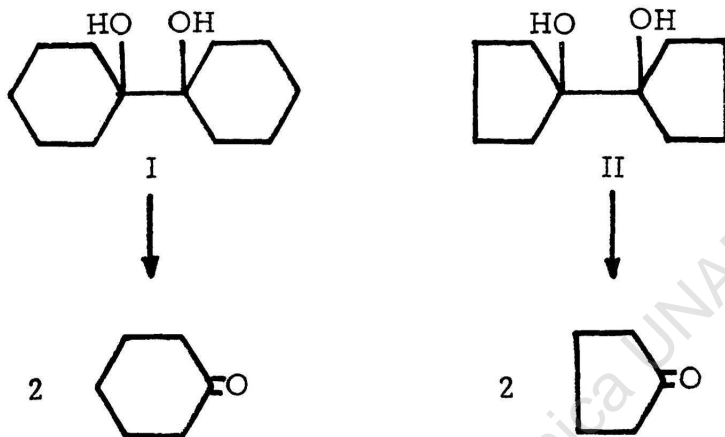* Average of results obtained using the methods of Franklin (7) and of Klages (8).

TABLE II

ΔH Fission by	Kcal/Mole	
	The Klages Method	The Franklin Method
of Cyclohexyl Pinacol I	−33.3	−35.0
of Cyclopentyl Pinacol II	−38.1	−41.8
Δ (ΔH)	4.8	6.8

Probable value $\Delta(\Delta H) \cong$ 5.8 Kcal/mole

The approximate (average) value of the calculated $\Delta(\Delta H)$, arrived at in Table III, may be regarded as quite plausible in view of the assumption of Rocek and Westheimer that the energetics of the fision of glycols is to be compared to secondary alcohol oxidation. Thus, utilizing the experimental data of Sellers and Sunner (12),

ΔH (Cyclohexanol-Cyclohexanone)
minus   ΔH (Ciclypentanol-Cyclopentanone)
_____

$\Delta(\Delta H)$ = 3.1 Kcal/mole

Since two moles of ketone are formed per mole of pinacol undergoing fission, $\Delta(\Delta H)_{\text{fission}} = 6.2$ Kcal/mole to be compared to the value of 5.8 in Table III. Consequently, if the mechanism of chromic acid cleavage of *cis* pinacols, as proposed by Rocek and Westheimer, is to be relied upon, it is to be expected that cyclopentyl pinacol (II) is oxidized to cleavage products about ten thousand times faster than cyclohexyl pinacol (I).

Experimentally, it has been found (11) that under reaction conditions (3) similar to those employed previously to estimate the cleavage rate differences of *cis* and *trans*-dimethylcyclopentanediol, the pinacol I oxidizes some 120 times faster than II. Apparently the experimental relative rates are exactly opposite in direction and more than *6* orders of magnitude different than could have been anticipated by the Rocek and Westheimer mechanism (3).

Clearly, then, the carbonyl-structured transition state of chromic acid cleavage must be rejected on the basis of this analysis and the observed rate data. By the same token the corresponding product-like transition state of secondary alcohol oxidation, which has so often been invoked (5, 6) to account for the substituent effects on oxidation rate to be noted for sterically hindered alcohols, must also be regarded with suspicion.

A Possible Mechanism of Pinacol Cleavage by Chromic Acid

It is interesting to recall here some of the facts concerning diol cleavage reactions which may be pertinent to the subject of this discussion. In choromic acid oxidation of diols which have hydrogen on at least one of the carbinol centers, there is a very apparent tendency to form some non-cleavage product; i. e., α-hydroxy aldehyde or α-hydroxy ketone. Bearing in mind that most tertiary and secondary alcohols form chromate esters very rapidly, (and, in our experience, to comparable extents at equilibrium) in polar media, this observation of competitive rates of direct alcohol oxidation and cleavage could hold great significance. The direct alcohol oxidation is known to occur *via* a concerted cyclic transition state of *H* abstraction from the carbinol carbon. It follows that the *cis*-pinacol cleavage, which has been identified to involve a cyclic chromate

ester (1, 3) could represent a competition of rate determining steps possessing similar geometric requirements, as viewed in III and IV (below).

III
Transition State
for Cleavage

IV
Transition State
for (Direct)
Alcohol Oxidation
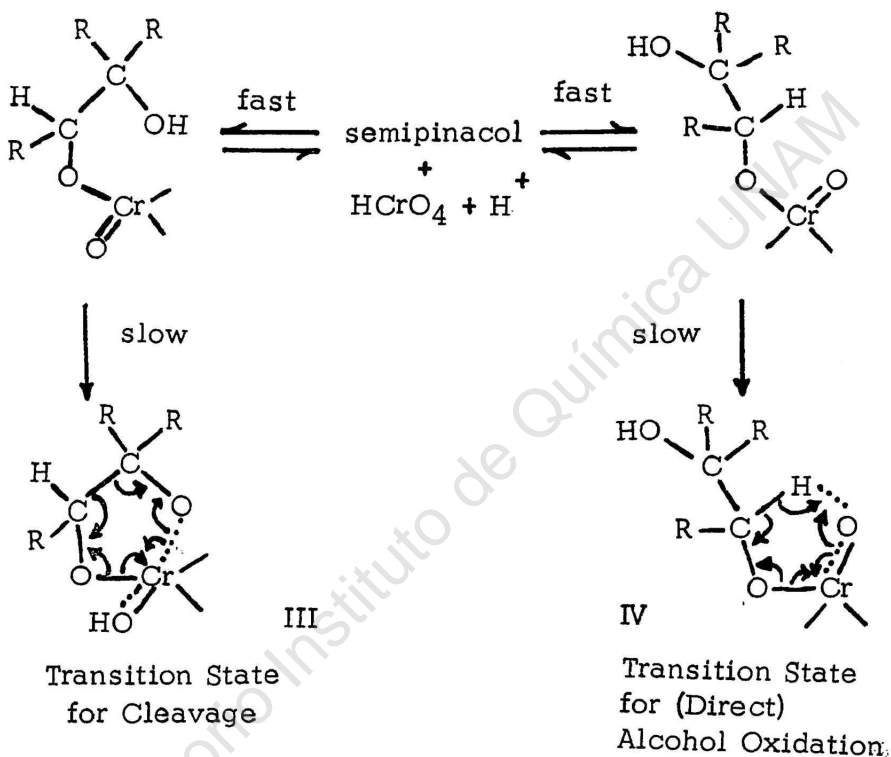
In the related glycol cleavage with periodic acid, increasing the number of alkyl groups substituted on the cleavage centers of the reactive substrate causes first an increase in the cleavage rate and then a decrease (13). This has been interpreted to signify that the formation of the cyclic periodate ester becomes rate controlling only when the glycol is completely substituted. On the other hand, increasing the number of alkyl groups causes a continuous increase in the rate of chromic acid cleavage of glycols (3). One possible way of viewing these facts is to assume that a cyclic chromate ester

is much more unstable than the corresponding periodate. Judging from the cyclic structural requirement of the transition state for chromic acid oxidation of alcohols, forming Cr^{VI} and two of its substituent oxygens into a nearly planar 5 membered ring produces repulsions between the non-bonded orbitals substituent on the chromium-oxygen covalencies that result in bond rupture. Such elements of instability in cyclic structures have been implicated in the cyclic decomposition of peracids, cyclic peroxides and molozonides (14). On this basis, the increased rates of chromic acid cleavage associated with a greater degree of alkyl substitution on the pinacol must be correlated with the greater degree of restriction to free rotation that enforces cyclization and is reminiscent of the so called Thorpe-Ingold effect (16). A similar interpretation has been conferred on the observed influence of alkyl substitution on the rate of oxidation of secondary alcohols (9, 10, 15).

On the basis of this analysis, then, it is possible to explain the greater rate of cleavage of cyclohexyl pinacol (I) *versus* cyclopentyl pinacol (II). In the latter case the rate determining formation of cyclic chromate ester tends to arrest the pseudo rotation of the cyclopentane rings through which non-bonded interactions of vicinal hydrogens are normally relieved. The evidence of cyclic hydrogen bonding in pinacols I and II may be cited in support of this thesis; $\Delta v_{II} = 36$ cm^{-1} *vs* $\Delta v_I = 46$ cm^{-1} is a clear indication of greater difficulties in fashioning a 5-membered cyclic relationship of O---H—O bonds with vicinal cyclopentyl substituents.

ABSTRACT

The data available on the rates and energetics of chromic acid cleavage of pinacols have been reviewed and found to be inconsistent with the currently accepted view of this reaction mechanism. The significance that these results hold for the mechanism of chromic acid oxidation of alcohols, a matter presently under dispute in the literature, is also discussed. The suggestion that the formation of a cyclic chromate ester may be the rate determining step of the pinacol cleavage reaction is briefly considered and found to be in accord with the facts as presently known.

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