



Ring size effects on the pinacol rearrangement
by Ramanujan Srinivasa

A thesis submitted in partial fulfillment of the requirements for the degree of DOCTOR OF PHILOSOPHY in Chemistry
Montana State University
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Abstract:

The pinacol rearrangement of 1.1'-bicycloalkyl diols, symmetrical and unsymmetrical, under acidic conditions is discussed. The present study has attempted to probe some very controversial aspects such as whether carbonium ion stability or product stability is the driving force for the ring size effects on the course of the rearrangement. The results of the present study point out the importance of the reaction conditions. When evaluating the ring size effects on the course of the pinacol rearrangement it is essential that the reaction conditions be well defined for otherwise interpretation of results may lead to erroneous conclusions. For instance, the rearrangement of cyclopentyl cyclohexane-1,1'-diol with concentrated sulfuric acid at 0° yields mainly Spiro [4,6] undecan-6-one as the primary rearrangement product reflecting carbonium ion stability as the chief factor in the course of the rearrangement. On the other hand, the rearrangement with dilute sulfuric acid at reflux produces mainly Spiro [5,5] undecan-7-one, the thermodynamically more stable product. This is consistent with the secondary skeletal rearrangement of the initially formed product.

Further, it was attempted to study the possibilities of the rearrangement occurring under non-acidic conditions. It was found that certain sulfur transfer reagents, such as N,N'-thiobisbenzimidazole, could affect the rearrangement of 1,2-glycols.

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To
My Parents

RING SIZE EFFECTS ON THE
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RAMANUJAN SRINIVASA

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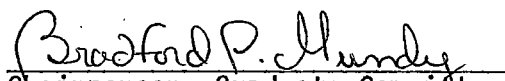
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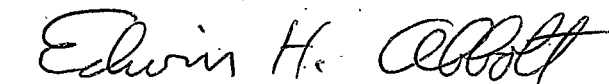
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Abstract

The pinacol rearrangement of 1,1'-bicycloalkyl diols, symmetrical and unsymmetrical, under acidic conditions is discussed. The present study has attempted to probe some very controversial aspects such as whether carbonium ion stability or product stability is the driving force for the ring size effects on the course of the rearrangement. The results of the present study point out the importance of the reaction conditions. When evaluating the ring size effects on the course of the pinacol rearrangement it is essential that the reaction conditions be well defined for otherwise interpretation of results may lead to erroneous conclusions. For instance, the rearrangement of cyclopentylcyclohexane-1,1'-diol with concentrated sulfuric acid at 0° yields mainly Spiro [4,6] undecan-6-one as the primary rearrangement product reflecting carbonium ion stability as the chief factor in the course of the rearrangement. On the other hand, the rearrangement with dilute sulfuric acid at reflux produces mainly Spiro [5,5] undecan-7-one, the thermodynamically more stable product. This is consistent with the secondary skeletal rearrangement of the initially formed product.

Further, it was attempted to study the possibilities of the rearrangement occurring under non-acidic conditions. It was found that certain sulfur transfer reagents, such as N,N'-thiobisbenzimidazole, could affect the rearrangement of 1,2-glycols.

Pleasure is frail like a dew drop,
while it laughs it dies.

Rabindranath Tagore.

INTRODUCTION

Perhaps the most familiar among the molecular rearrangements is the so-called "Pinacolic Rearrangement" of 1,2- glycols. Following the discovery by Fittig in 1859-1860³¹ that tetramethyl ethylene glycol (Pinacol) rearranged to form methyl t-butyl ketone (Pinacolone) in concentrated sulfuric acid (Chart 1), abundant literature concerning many aspects of the rearrangement has accumulated over the past decades and excellent discussions of this topic have appeared.^{32,33,34}

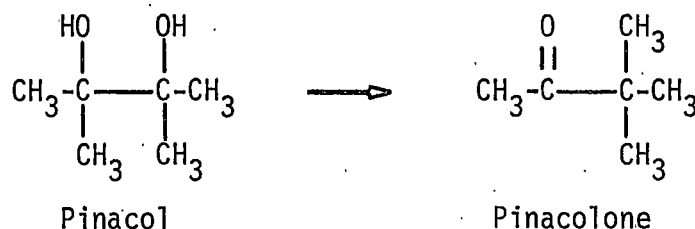
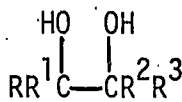


Chart 1. The Pinacol Rearrangement

In general, the pinacol may be represented by the structure (1).



1

(R, R¹, R², and R³ are hydrogen, alkyl, aryl or any combination of these.)

Besides sulfuric acid, many other agents such as phosphoric, ox-

alic, perchloric, and formic acids are known to catalyze the rearrangement. In certain instances,^{30, 35,36} certain Lewis acids such as Al_2O_3 , BF_3 , POCl_3 , etc., at high temperatures have been effective.

From a mechanistic view, the pinacol rearrangement can be regarded as a special case of a Wagner-Meerwein rearrangement involving 1,2- shifts.³³ The generally accepted mechanism in concurrence with the results of the kinetic, oxygen exchange, and tracer studies³⁷ for the pinacol rearrangement of tetramethyl ethylene glycol is outlined in Chart 2.

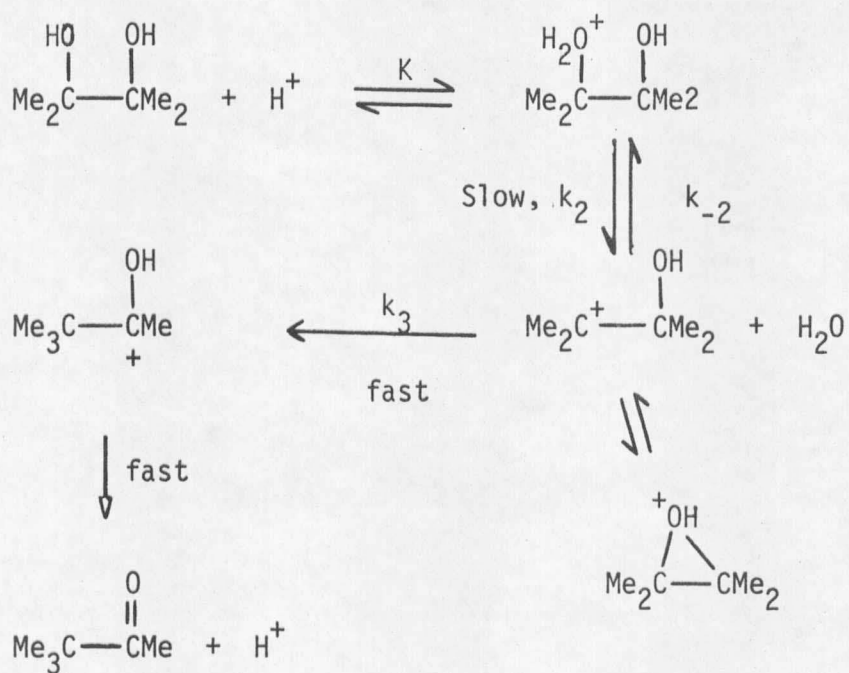


Chart 2. Mechanism of Pinacol Rearrangement.

The kinetic equation consistent with the A-1 mechanism as suggested by Duncan and Lynn³⁸ is,

$$\text{Rate} = \frac{Kk_2k_3h_0 [\text{Glyco}]}{(k_{-2} + k_3)}$$

From this it follows that,

$$k_{\text{exp}} = \frac{Kk_2k_3h_0}{(k_{-2} + k_3)}$$

where k_{exp} is the experimental rate constant, h_0 is the antilog of the Hammett acidity function, H_0 , and K is the thermodynamic equilibrium constant. Smith and co-workers,³⁹ based on their isotope kinetic data and those of Ley and Vernon,³⁶ showed that the term $k_3/(k_{-2} + k_3)$ is constant. On the other hand, plots of $\log k_{\text{exp}}$ versus H_0 and of $\log k_{\text{exp}}/(H^+)$ versus (H^+) have been found to be linear.³⁸

Supporting evidence for the carbonium ion intermediate stems from the works of many other investigators.^{40,41,44} Further, oxygen exchange studies³⁷ have shown that the rate of rearrangement in low acidities is 25-30% with 70-75% of the carbonium ion reverting to pinacol and the pinacol/pinacolone ratio decreases linearly with decrease in the activity of water (a_{H_2O}). The formation and subsequent hydrolysis of the epoxide to provide the carbonium ion intermediate could merely be an alternate path for the reaction. Although reports in sup-

port of the pinacol rearrangement involving the epoxide intermediate for open chain pinacols have appeared in the literature,^{42,43} such an intermediate does not seem to be possible for hindered glycols, especially the 1,1'-bicycloalkyl pinacols. No epoxide could be detected during the rearrangement of cis-1,2- and trans-1,2- diols (2) and (5).⁴⁴ Similar results have been reported for the rearrangement of cis- and trans-perhydroindan-8,9-diols.⁵⁶

The pinacolic rearrangement has been looked upon from several points of view. The "migratory aptitudes" of the substituents, the direction of the rearrangement, glycol stereochemistry, the stability of the products themselves under reaction conditions, the effect of reaction media, etc., are a few to mention. In cyclic systems, the direction of rearrangement and the "migratory aptitudes" are probably reflected by ring expansion/contraction trends.

A considerable attempt has been made to study the steric course of the rearrangement of cyclic glycols. Thus, Bartlett and Pockel⁴⁵ studied the rearrangement of the cis-1,2- and the trans-1,2- dimethyl-cyclohexane-1,2- diols with 20% sulfuric acid under reflux and reported the following results (Chart 3):

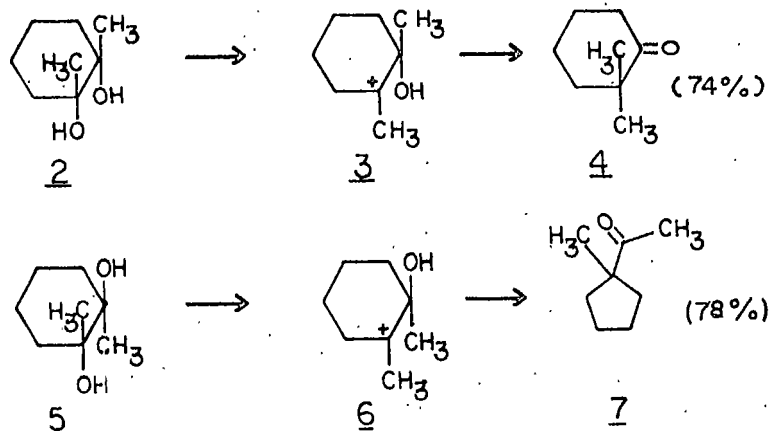


Chart 3. Pinacol Rearrangement of cis-1,2- and trans-1,2- dimethyl- cyclohexane-1,2-diols.

2,2-Dimethylcyclohexanone (4) and 1- acetyl-1-methyl cyclopentane (7) were characterized as semicarbazones in 74% and 78% yields, respectively. These reactions were carried out during the time when the very concept of the "free carbonium ion" was still in its infancy. The argument offered, however, to explain the rearrangement was on the basis of the "open sextet theory" as put forth by Whitmore⁴⁶ and it was always the group being trans to the carbon atom, from which the hydroxyl group was removed, that migrated. Thus different products were produced for the 1,2-diols.

Bunton and Carr⁴⁴ studied the kinetics of the rearrangement of

cis-1,2- and trans-1,2- dimethylcyclohexane-1,2-diols in aqueous perchloric acid solutions at various temperatures and found from the variation of the rate with acidity, the solvent deuterium isotope effect, and the Arrhenius parameters that both the diols produced the same ketone (7) in 91-98% yield via a common carbonium ion intermediate, in contrast to the above results.⁴⁵ This then suggested that the cis-diol would first isomerize to the trans-diol via the carbonium ion intermediate and thus contribute equally to the ring contraction product. Bunton and Carr also noted that the proportion of the 2,2-dimethylcyclohexanone (4) increased slightly with the increasing temperature and that a common intermediate such as (8) could account for the interconversion of the ketones (Chart 4). They further noted that the rate of formation of the carbonium ion from the trans-diol relative to that of the cis-diol was approximately 2, but the rates of the reverse reactions were almost the same. The interpretation was that in water the cis-form was thermodynamically more stable. Mundy and Otzenberger⁴⁸ have offered similar arguments on the rearrangement of the cis- and trans-diols to show that the work of Bartlett and Pockel⁴⁵ was incorrect.

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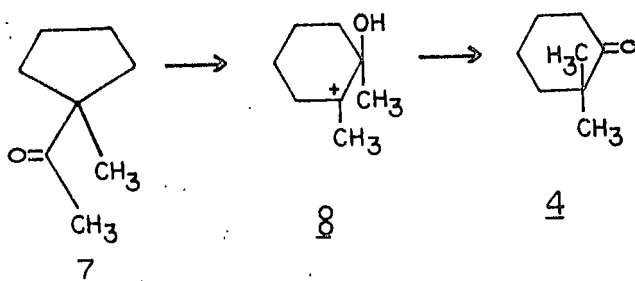


Chart 4. Interconversion of 2,2-dimethylcyclohexanone and 1-acetyl-1-methylcyclopentane.

Contrary to these results are those obtained from the rearrangement of *cis*-1,2- and *trans*-1,2-dimethylcyclopentane-1,2-diols in aqueous perchloric acid.⁴⁴ The major rearrangement product is 2,2-dimethylcyclopentanone (11) in both the cases (Chart 5), indicating isomerization of the *trans*- to the *cis*-diol. The oxygen exchange studies have shown that the rate of exchange for the *trans*-diol is five times faster than the rearrangement. That the *cis*-diol does not exchange, but rearranges to the *trans*-diol, suggests that two non-interconvertible intermediates are involved in these reactions.⁴⁴

