



Theoretical and experimental nonaromatic heterocyclic chemistry
by Kenneth Barry Lipkowitz

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

New methodologies have been developed for the synthesis of the 6,8-dioxabicyclo[3.2.1]octane substructure; particularly the seven substituted derivatives. The unusual intramolecular ketalization induced by hydrogen over palladium of a substituted pyran has been rationalized in terms of effective hydronium ion character. An isomer enrichment scheme using a pseudo-surface of Titanium Tetrachloride in a Carbon Tetrachloride matrix reveals the unusual stability of these dioxabicyclic ketals.

Carbon 14 labeling indicates the migrating group plays a passive role during the pyrolysis of N-acyllactams over calcium oxide. A dual reaction pathway, dependent on reaction conditions, has also been elucidated. This methodology permits one to prepare 2-substituted cyclic imines and heretofore difficult to prepare pyrrolidenes have been synthesized in this manner.

An empirical and theoretical discussion of through-space participation in the cis-8-hetero[4.3.0]non-3-ene substructure is presented. Conformational and configurational analysis of various related heterocycles and the analysis of the stereospecificity of 2,3-disubstituted pyrrolidine quaternizations has been scrutinized. The observation that paramagnetic shift reagents induce proton shifts in sulfonium ions and the implication that these pseudocontact shifts are due to complexation of the counterion is presented. An attempt to analyze anchimeric participation with respect to binding constants of shift reagents has also been looked at.

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to

Professor Richard F. Smith

"He who has achieved oneness
Should move on to twoness..."

Ken Kesey

THEORETICAL AND EXPERIMENTAL NONAROMATIC
HETEROCYCLIC CHEMISTRY

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Approved:

Bradford P. Mundy
Chairman, Examining Committee

E. W. Anacker
Head, Major Department

Henry L. Parsons
Graduate Dean

MONTANA STATE UNIVERSITY
Bozeman, Montana

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ABSTRACT

New methodologies have been developed for the synthesis of the 6,8-dioxabicyclo[3.2.1]octane substructure; particularly the seven substituted derivatives. The unusual intramolecular ketalization induced by hydrogen over palladium of a substituted pyran has been rationalized in terms of effective hydronium ion character. An isomer enrichment scheme using a pseudo-surface of Titanium Tetrachloride in a Carbon Tetrachloride matrix reveals the unusual stability of these dioxabicyclic ketals.

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Chapter 1

SYNTHESES AND INATE CHARACTERISTICS OF THE
6,8-DIOXABICYCLO[3.2.1]OCTANE
SUBSTRUCTURE

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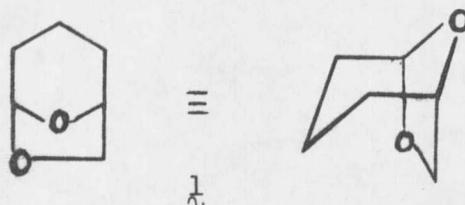
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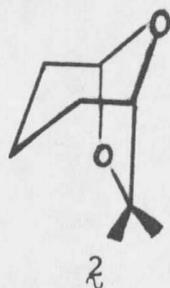
INTRODUCTION

6,8-dioxabicyclo[3.2.1]octanes in Natural Products¹

Apart from sugars, in which the 6,8-dioxabicyclo[3.2.1]octane structure $\underline{1}$ is found in abundance, it has been noted that these bicyclic ketals are present in a variety of natural products.

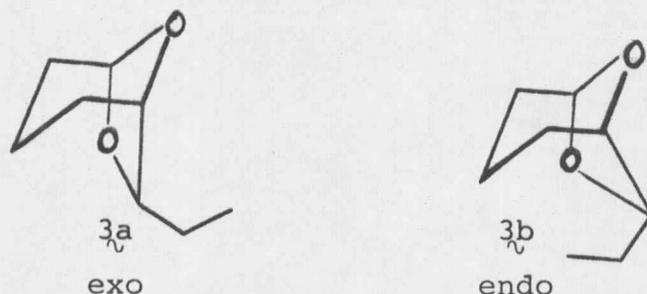


One of the earliest references to this dioxabicyclo[3.2.1]octane substructure was associated with a constituent of Japanese hop oil from *Humulus lupulus*.² Spectral analysis, coupled with a low-yield, but unambiguous synthesis, proved the constituent to have structure $\underline{2}$.

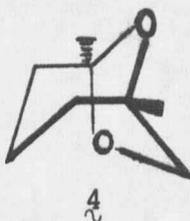


Real impetus towards a better understanding of this skeletal system came after the careful isolation and elegant structure assignment of the aggregating sex pheromone

of the female pine bark beetle, *Dendroctonus brevicomis*.³ This compound, assigned structure $\underset{\sim}{3}$, was given the trivial name, "brevicomins." The exo isomer, $\underset{\sim}{3a}$, is the active pheromone for *D. brevicomis*. The endo isomer has been implicated as an attractant for *D. frontalis*.



A second ketal was isolated from the male pine bark beetle and was demonstrated to be the same as the aggregating sex pheromone of *Dendroctonus frontalis*.⁴ This was given the trivial name, "frontalin," and was assigned structure $\underset{\sim}{4}$.



Several bicyclic ketals, including 4,9-dioxabicyclo[3.3.1]octanes and 6,8-dioxabicyclo[3.2.1]octanes have been isolated from tobacco.⁵ In the latter series, ketals of the general structure, $\underset{\sim}{5}$, have been found.

