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SYNTHETIC STUDIES IN REDUCTION

AND REARRANGEMENT

A THESIS

PRESENTED TO THE UNIVERSITY OF AUCKLAND

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by

GORDON W. REWCASTLE

DEPARTMENT OF CHEMISTRY

UNIVERSITY OF AUCKLAND

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# A B S T R A C T

## PART ONE

### SYNTHESIS AND ACID-CATALYSED REARRANGEMENT OF CYCLOPROPANE-1,2-DIOLS

A number of cyclopropane-1,2-diyl diacetates have been synthesized by the anhydrous Clemmensen reduction [Zn(Hg)-HCl-organic solvent] of  $\beta$ -diketones and  $\beta$ -keto-aldehydes, and this reaction was found to be a general one for those substrates that did not exist mainly in the enol form. Cyclopropanediol formation does occur with some highly enolized compounds under aqueous conditions but, with the anhydrous system, enol acetate formation or enolic reduction was found to compete with reduction of the diketo form.

Acid-catalysed rearrangement of the free diols generally gave  $\alpha$ -hydroxy-ketones, or their corresponding  $\alpha\beta$ -unsaturated enones, with  $\beta$ -hydroxy-ketone formation only being observed with one substrate. A strong preference for methyl ketone formation was observed in all cases and this phenomenon was rationalized by consideration of the apparent relative thermodynamic stabilities of the  $\alpha$ -ketol conjugate acids.

## PART TWO

### AROMATIZATION OF 2 $\alpha$ -HYDROXY [4-<sup>13</sup>C]CHOLEST-4-EN-3-ONE

The aromatization of 2 $\alpha$ -hydroxy[4-<sup>13</sup>C]cholest-4-en-3-one has been found to occur with migration of the labelled carbon to C-10, thereby lending support to previous mechanistic proposals. The aromatization of [4-<sup>13</sup>C]cholesta-1,4-dien-3-one similarly gave a product with the label at C-10, in agreement with earlier work involving carbon-14 labelling studies. The ease with which these rearrangements could be studied is in marked contrast to earlier work, and the combination of carbon-13 labelling and <sup>13</sup>C n.m.r. spectroscopy offers many advantages over the degradative techniques required with carbon-14 labelling.

## PART THREE

### CLEMMENSEN REDUCTION OF (5R)-5-HYDROXYHEXAN-2-ONE

Previous work in this department suggested that the Clemmensen reduction of  $\gamma$ -substituted ketones involved an intramolecular displacement of the  $\gamma$ -substituent by the carbonyl oxygen atom. However, the reduction of (5R)-5-hydroxyhexan-2-one had given a mixture of

hexan-2-ol and *cis*- and *trans*-hex-4-en-2-ol, with no inversion of stereochemistry occurring with the saturated isomer. The opposite signs of rotation for the two geometrically isomeric alkenols suggested the possibility of different chiralities, but this was disproved when the 2*R*-configuration was determined for each alcohol by analysis of the <sup>1</sup>H n.m.r. spectra of the esters with (-)-(*S*)- $\alpha$ -methoxy- $\alpha$ -trifluoromethyl-phenylacetic acid. This result thus invalidates the earlier hypothesis.