Chapter-6
SUMMARY OF THE THESIS

The thesis entitled ‘Analytical and synthetic investigations in olefinic compounds’ embodies the results of extensive investigations on simple and effective reagents for stereospecific and enantioselective dihydroxylation of olefinic compounds.

A general introduction of various reagents employed for the dihydroxylation of olefinic compounds is presented in chapter I with special emphasis on the stereospecificity of such reagents. Chapter II deals with a review of various osmium reagents currently available for the asymmetric synthesis of 1, 2-diols by the dihydroxylation of olefinic compounds.

Chapter III describes our endeavors to explore the possibility of asymmetric synthesis of 1, 2-diols from olefins without using osmium reagents. An exhaustive investigation conducted by Ashrof has revealed that olefins can be hydroxylated using silver succinate and iodine in dry benzene medium. Our aim was to find whether silver salts of some optically active derivatives of succinic acid can be used in place of silver succinate, along with iodine to achieve enantioselective dihydroxylation of olefinic compounds. The naturally occurring L-(+)-tartaric acid was esterified and the diethyl ester was then methylated using silver oxide and methyl iodide following the method of Purdie and Irvine. The diethyl dimethoxy succinate thus obtained was hydrolysed to get the crystalline L-(+)-dimethoxy succinic acid. The L-(+)-dimethoxy succinic acid was then converted to silver salt and the L-(+)-silver
dimethoxy succinate thus obtained was used along with iodine for the enantioselective dihydroxylation of olefinic compounds. Hydroxylation of oleic acid (octadec-cis-9-enoic acid) using L- (+)-silver dimethoxy succinate and iodine in benzene medium by employing the procedure analogous to that used in silver succinate-iodine method gave erythro-9, 10-dihydroxy stearic acid (52), melting at 131-132°C.

The product was identified by comparing its $^1$H NMR, $^{13}$C NMR and IR spectra with those reported for erythro-9, 10-dihydroxy stearic acid.

The optical activity of the product obtained was measured and compared with the activity of erythro-9, 10-dihydroxy stearic acid obtained by dihydroxylation of oleic acid using silver succinate and iodine. The dihydroxy acid obtained by hydroxylation of oleic acid using L- (+)-silver dimethoxy succinate and iodine gave a specific rotation of (+)-0.312° (C, 0.71, MeOH) whereas that produced using silver succinate and iodine was optically inactive. The reported value of $\alpha_D$ for d- erythro-9, 10-dihydroxy stearic acid is ±0.25°(MeOH).

Elaidic acid (octadec-trans-9-enoic acid) and petroselenic acid (octadec-cis-6-enoic acid) also were subjected to dihydroxylations using L- (+)-silver dimethoxy succinate and iodine. The dihydroxy acid, threo-9, 10-dihydroxy stearic acid (53), obtained by hydroxylation of elaidic acid showed a specific rotation of (+)-2.364° (C, 0.73, MeOH) while that formed on using
Chapter IV deals with the dihydroxylation of olefinic compounds of various types using lead acetate and iodine in aqueous acetic acid medium. Raman has described the hydroxylation of erucic acid (docos-13-enoic acid) to 13, 14- dihydroxy docosanoic acid using silver acetate and iodine in acetic acid medium by the Woodward method. A similar procedure was adopted in the present work for hydroxylating olefinic compounds using lead acetate and iodine. The compounds selected for hydroxylation included some 1, 2-disubstituted olefinic compounds such as naturally occurring unsaturated fatty acids as well as some trisubstituted and cyclic olefinic hydrocarbons. The 1, 2-diols obtained were characterized by mixed melting points, $^1$H NMR, $^{13}$C NMR and IR spectral techniques. In all cases studied, where stereochemistry is relevant, syn-hydroxylation occurred. Thus the reagent can hydroxylate cis-olefinic fatty acids to the corresponding erythro-dihydroxy acids and, trans-acids to the corresponding threo-dihydroxy acids.

Presence of water has been reported to influence the products of hydroxylation by Woodward’s procedure. Hence attempt was made to investigate the effect of moisture in the hydroxylation of olefins using lead silver succinate and iodine showed no optical activity. The reported value of $[\alpha]_D$ for d-threo-9,10-dihydroxy stearic acid is (+)-22.5° (C,2.81, MeOH). The dihydroxy acid, erythro-6,7-dihydroxy stearic acid (54), obtained from petroselenic acid using L-(+)-silver dimethoxy succinate and iodine gave a specific rotation of (+)-3.482° (C, 0.762, MeOH) whereas the one formed on hydroxylation using silver succinate and iodine showed no activity.

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acetate and iodine. The study revealed that, unlike in Woodward’s reaction, dihydroxylation using lead acetate and iodine can be accomplished only in presence of water.

Chapter V describes our endeavors on the study of the mechanistic aspects including the intermediate(s) involved in hydroxylation of olefinic compounds using lead acetate and iodine in ‘wet’ acetic acid medium. The product of reaction of lead acetate and iodine with ethyl oleate was investigated in detail in an attempt to characterize the intermediate of this hydroxylation procedure and to assign a mechanism for the syn-hydroxylation by the reagent. The intermediate was obtained by heating ethyl oleate with lead acetate, iodine and acetic acid containing water. It was purified and separated into fractions using column chromatography. Analysis by chemical and IR spectral techniques revealed that the intermediate involved is mainly the 9, 10-diacetoxy ethyl stearate along with small amounts of the iodoacetates. The presumed intermediate was synthesised by standard methods and its IR spectrum was found superimposable with that of the intermediate isolated. Thus the main product of reaction of an olefin with lead acetate and iodine appears to be an ester of the diol and acetic acid which may be represented by the general formula, 55.
Hydroxylation of ethyl oleate was also attempted by heating with lead acetate and iodine in complete absence of water. It was observed that unlike in dihydroxylations by Prevost, Woodward and silver succinate-iodine methods, there was no hydroxylation taking place in this case.

Accordingly, a mechanism has been proposed for the dihydroxylation of olefins using lead acetate and iodine. The dihydroxylation by lead acetate and iodine is found to operate by a mechanism different from that of Woodward, Prevost and silver succinate-iodine methods of hydroxyltion of olefinic compounds.

In conclusion, the present work reveals that asymmetric dihydroxylation of olefinic compounds can be achieved by the use of silver salts of optically active derivatives of succinic acid and iodine. L-(+)-silver dimethoxy succinate and iodine in benzene medium is shown to be an effective reagent for accomplishing asymmetric synthesis of 1,2-diols from olefinic compounds by dihydroxylation. The development of L-(+)-silver dimethoxy succinate and iodine as a syn-hydroxylating agent also amounts to yet another extension of the well known Prevost-Woodward methods of hydroxylation of olefinic compounds. Lead acetate and iodine in ‘wet’ acetic acid medium is also proved to be a simple and effective reagent for stereospecific dihydroxylation of olefinic compounds. The dihydroxylation by lead acetate and iodine is found to operate by a mechanism different from that of Woodward, Prevost and silver succinate-iodine methods.