ABSTRACT

Amino alcohols are versatile molecules due to the presence of amino and hydroxyl groups in the same molecule. Depending on the position of the hydroxyl and the amino group, the amino alcohols may be classified as 1, 2; 1, 3 and 1, 4 amino alcohols. Out of these 1, 2-amino alcohols are very important.

1,2-amino alcohols **I** are present in some naturally occurring and biologically important molecules such as Bestatin **(II)** , a syn-α-hydroxy-β-amino acid, which is an amino peptidase inhibitor and used in cancer chemotheraphy[1]. They are also present in lipids and lipid like molecules such as Sphingosine **(III)**, a 2-amino-1, 3-diol which has been found to be important in cell signaling and in Myrocin **(IV)**, which is a potent immunostimulatory agent[2]. Cyclic amino alcohols like Penaresidin-A **(V)** an azetidine aminoalcohol is a potent inhibitor in protein biosynthesis useful as an anticancer agent[3]. 1, 2-Amino alcohols are present in some sugar molecules such as Daunomycin **(VI)**, a member of a large class of glycosylated anthracycline natural products[4]. A host of synthetic molecules used as drugs or pharmacological agents also contain the amino alcohol moiety. Some of the examples are Saquinavir **(VII)**, a HIV protease inhibitor[5]. Other than these, amino alcohols are extensively used as chiral auxiliaries as part of a cyclic system and even acyclic amino alcohols have been used as auxiliaries in asymmetric synthesis. Some of the cyclic systems which have been used as auxiliaries are oxazolidines**VIII**, oxazolidinones **IX** and oxazolines **X**.

Since both the enantiomers of 2-Amino-1-butanol were readily available we have chosen it for our studies. We have focused on using both the enantiomers of 2-Amino-1-butanol **XI, XII** as chiral building blocks for the synthesis of some important heterocyclic compounds having potential biological activity.

Chapter I describes the documented literature, the general method of preparation, the importance of amino alcohols, their reactions specially their use as chiral auxiliaries.

In **chapter II** we have focused on the methods of synthesis of oxazolo[2,3-a]isoindol-5-ones. As reviewed recently by Meyers *et al*[6], the bicyclic N,O acetal product commonly known as bicyclic lactam, has proven to be an exceptional building block for the asymmetric construction of a wide variety of natural and synthetic carbocyclic and

heterocyclic compounds containing one or more stereogenic centres. However structurally related aromatic tricyclic lactams are little explored in literature. Oxazolo [2, 3-a] isoindol-5-one derivatives also exhibit anticonvulsant and anti-inflammatory activities[7]. An earlier attempt to synthesize oxazolo[2,3-a]isoindol-5(9bH) one using (*R*) or (*S*)-2-Amino-1-butanol via Meyers methodology of reduction of imide and cyclisation using trifluoroacetic acid resulted in the formation of a novel ten membered ring system[8]. This prompted us to carry out additions of a number of substituted Grignard reagents on the imide system and cyclisation of the dihydroxy system with trifluoroacetic acid. It yielded the desired phenyl and substituted phenyl 3-ethyl-2,3,5,9b-tetrahydo[1,3]oxazolo[2,3-a]isoindol-5-ones **XIII** in moderate yields[9]. The absolute configuration of the phenyl substituted oxazolo [2, 3-a] isoindol-5-one obtained from (*S*)-2-Amino-1-butanol was determined by single crystal x-ray diffraction as (3*S*, 9bR).The factors responsible for the stereoselectivity and plausible mechanism of the reaction is also discussed. A different methodology involving cyclocondensation of 2-Acyl benzoic acids and (*R*) and (*S*)-2-Amino-1-butanols was also carried out to obtain the corresponding substituted oxazolo [2, 3-a] isoindolinones. Refluxing 2-(1-bromobutyl) phthalimide in different alcohols in alkaline conditions resulted in the formation of alkoxy substituted oxazolo [2, 3-a] isoindolinones **XIV** in good yields.

. In order to study the reaction selectively at the amino function the hydroxyl group has been protected. Limited methods of protection of the hydroxyl group of 2-Amino-1-butanol have been reported in literature.

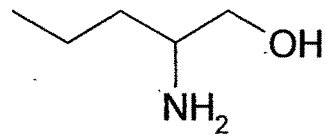
Chapter III describes two different methods for the protection of free hydroxyl group of the N-phthaloyl protected aminobutanols and Schiff bases of 2-Amino-1-butanols using conventional protecting groups like 3, 4-Dihydropyran and benzyl chloride.

Natural and synthetic azetidinone derivatives occupy a central place among medicinally important compounds due to their diverse and interesting antibiotic activities. Recent years have seen a resurgence of interest in development of stereo and enantioselective methodologies for the synthesis of azetidinones[10]. Section II of chapter III describes the synthesis of a few chiral azetidinones **XV** using the conventional Straudinger ketene imine cycloaddition reaction. The utility of azetidinones as synthons

for various biologically active compounds has given an impetus to these studies. Protection of the hydroxyl group is found to be essential for the desired formation of the four membered ring.

Chapter IV describes the synthesis of some chiral thiazolidinones **XVI** using (*R*) and (*S*)-2-Amino-1-butanols as chiral templates and calculation of the diastereomeric ratios of the products obtained during the course of the reaction from PMR spectral data.

In recent years there has been a growing interest in chiral non racemic aldehydes because of the development of new and efficient methods of controlling the stereochemistry of several basic organic reactions such as metaloorganic addition to the carbonyl group, aldol condensation and [4+2] cycloaddition with carbonyl dienophiles. Protected α-hydroxy and α-amino aldehydes are of special interest owing to their ready availability in both the enantiomeric forms from natural sources and to pronounced versatility due to the presence of both the formyl group and suitably protected hydroxyl or amino functionality in the molecule. There are limited reports of synthesis of N-phthaloyl protected aminobutanal in the literature. **Chapter V** deals with the synthesis of (*R*) & (*S*) - N-Phthaloyl aminobutanal **XVII** derivatives from (*R*) & (*S*)-N-Phthalimidobut anol and the synthesis of a few unsubstituted and substituted alkenes **XVIII** by Wittig reaction of the aminoaldehyde with some Wittig reagents.



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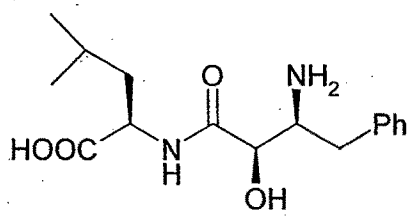

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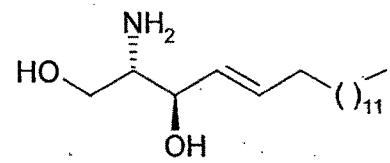

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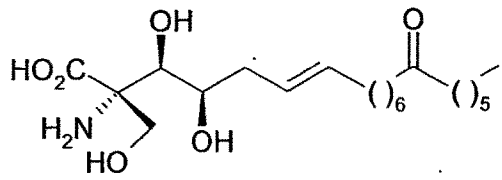

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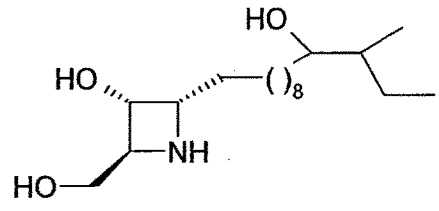

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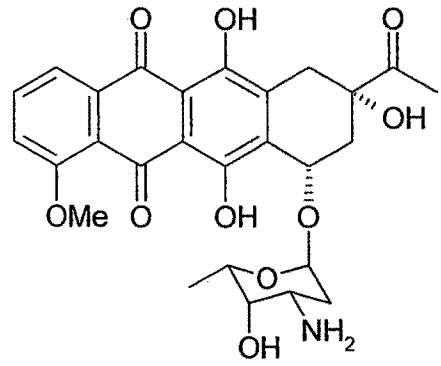

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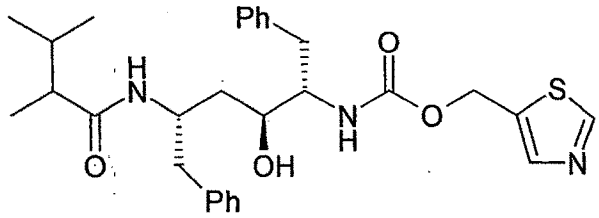

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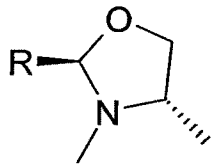
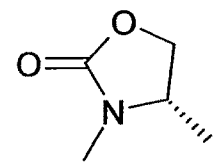


VIII



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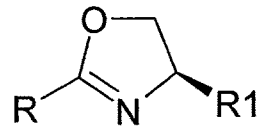

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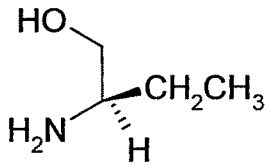

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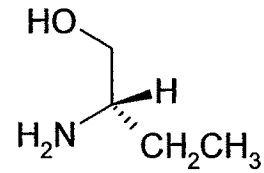

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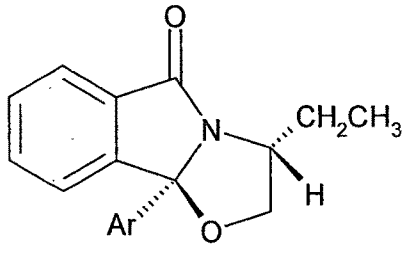
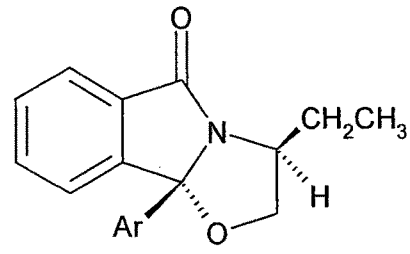
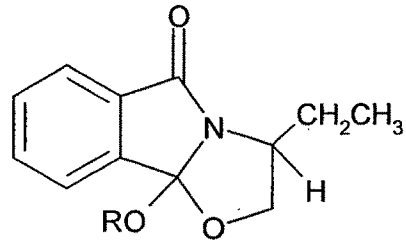




XIII

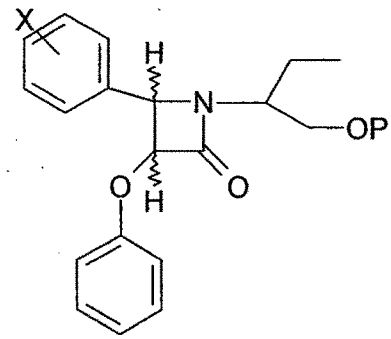
Ar = -C_6H_5, p- FC_6H_4, p-ClC_6H_4, p-$OCH_3C_6H_4$, p-$CH_3C_6H_4$.



XIV

R = -CH_3, -CH_2CH_3, -$CH_2CH_2CH_3$, CH $(CH_3)_2$, -CH_2 $(CH_2)_2CH_3$,

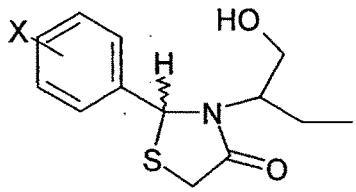
-CH_2 $(CH_2)_3CH_3$



XV

X= -H, -Cl, -OCH_3, -CH:CHC_6H_5

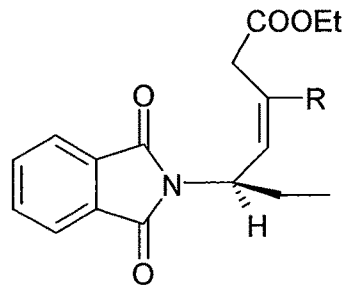
P = -THP, -Benzyl



XVI

X= -H, -NO_2, -Cl, -OCH_3, –OCH_3 -OCH_3.

XVII



XVIII

R = -H, Allyl.

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