THE SYNTHESIS OF CHIRAL COMPOUNDS OF BIOLOGICAL AND SYNTHETIC INTEREST USING ANHYDRIDE OF *L*-TARTARIC ACID

Islamabad

A dissertation submitted to the Department of Chemistry, Quaid-i-Azam University, Islamabad, in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

in

Organic Chemistry

by

SHER WALI KHAN

Department of Chemistry
Quaid-i-Azam University
Islamabad
2013

IN THE NAME OF ALLAH

THE COMPASSIONATE

THE MERCIFUL

Dedicated to

My Loving parents and family

CONTENTS

ACKNOWLEDGEMENTS

By the grace of Allah, the Almighty, the creator of universe, who granted Hidayah to the mankind and peace and blessings be upon his prophet, Hazrat Muhammad (Peace be upon Him), who exhorted his followers to seek knowledge from cradle to grave, I've been able to complete this academic enterprise.

It is my first and foremost obligation to express my sincere gratitude to Dr. Javid Hussain Zaidi my supervisor. His proper supervision, time devotion and keen interest enable me to accumulate this humble work. Some special words are due to my foreign supervisor, Dr. M. Carmen Galan, School of Chemistry, University of Bristol, UK for her great help and encouragement during my stay in UK.

I am thankful to Higher Education Commission Pakistan for financial support in the form of Indigenous scholarship and also support for my six months stay at University of Bristol UK, under scheme International Research Support Initiative Programme (IRSIP).

I am thankful to Prof. Dr. Amin Badshah Chairman Deptt. of Chemistry, Prof. Dr. Shahid Hameed (Head of the Organic Section) and all my teachers, whom I learned a lot during my stay here in the Deptt. of Chemistry QAU.

Thanks are due to Dr. Khalid Muhammad Khan (HEJ research institute of chemistry Karachi) for assistance in providing spectral as well as X-ray crystal data.

I am also thankfull to Prof. Dr. M. Masoom Yasinzai, Prof. Dr. Asghari Bano, Momin khan, akhter Nadhman and Sami Ullah for performing antimicrobial and anti-leshmanial bioassays.

I wish to acknowledge the support and encouragement provided by my lab. Fellows Dr. M. Arfan, Tahir Mehmood, Dr.Iftekhar, Hidayat Ullah, Azhar H. Shah. I ought to submit my thanks to my friends Rafaqat Ali, Amir Badshah, Saad Ullah Mir, M. Said, Hizb Ullah, M.Rafique, M. Iftekhar, M. Ayaz, Rashid Saeed, M. Siraj and Wajid Shah.

My special thanks goes to my friends Dr. M. Naveed Umar, Dr Gul Shah zadah Khan, Dr. Hafiz Zia Urrehman, Momin Khan, Muhammad Tariq, Mushtaq Ahmad, Mr. Ismat Ullah for their nice company and help.

I am also thankful to my colleagues in university of Bristol, Dr. David Benito, Mr Edward Balmond, Miss Rachel Jones, Mr. Hamid and Abdullatif for their support, encouragement and help to pursue this work and all others, whom I have missed here do deserve equal credit.

Thanks also goes to Mr. Ali Zaman (librarian), Mr. Shams Pervaiz, Mr. M. Mehmood, Mr. Sharif Chohan (A.S.O), Mr. Muhammad Ilyas (A.S.O), and all members of technical sections (NMR, IR, MS, CHNS etc) Deptt. of Chemistry QAU.

Finally I express my heartiest gratitude and respect to my mother, father, dearest brothers and sisters and my family who encouraged me throughout my studies and supported me what and whenever they could.

Sher Wali Khan 25-09-2013

Abstract

Chiral protected and deprotected amides were synthesized by using commercially available *L*-tartaric acid having two asymmetric centers and C_2 axis of symmetry. In the synthetic sequence, diacid functionality of *L*-tartaric acid was protected as dimethyl ester and diol as 1,3-dioxolane. The partial hydrolysis of 1,3-dioxolane dimethyl ester gave the corresponding monoester. Monoester upon treatment with different substituted anilines gave desired amides (**2a-2t**). Amides (**2a-2t**) afforded compounds (**3a-3t**) with the aid of acetyl chloride in methanol. All the compounds were characterized by using sophisticated spectroscopic techniques including IR, ^{1}H NMR, ^{13}C NMR, EI-MS and elemental analysis. The structures of compounds **2g**, **2r** and **3i** were also unambiguously confirmed by X-ray crystallography.

Protected (**2a-2l**) and deprotected amides (**3a-3l**) were tested for their antimicrobial activities at different concentrations against different fungal and bacterial strains and were found effective. Monoaryl esters of *L*-tartaric acid (**4a-4h**) were prepared and processed further in Fries rearrangement. The structure of compound **4e** in the series was also confirmed by X-ray crystallography.

N-Linked glycopyranosides (**10a-10e**) and *O*-Linked glycopyranosides (**11a-11e**) were synthesized from monoester of *L*-tartaric acid. The synthesized compounds were confirmed with the aid of spectroscopic techniques. The structure of compound **11c** in the series was supported by X-ray analysis. Antileishmanial activity of the glycopyranosyl amides (**10a-10e**) and glycopyranosides (**11a-11e**) was assayed which showed moderate to good activities. Synthesis of glycoconjugates (**13a-13e**) was carried out by using glycopyranosyl α-trichloroacetimidates and dimethyl-*L*-tartrate.

Chiral imides and amides were prepared from diacetyl-*L*-tartaric acid anhydride and aliphatic, substituted aromatic amines and amino acids. The imides (**14g-14m**) were subjected for their antifungal and antibacterial activities against different fungal and bacterial strains. All the compounds showed good antifungal and moderate to good antibacterial activities.

Abbreviations

Ar	Aromatic
Ac_2O	Acetic Anhydride
AcOH	Acetic Acid
AgOTf	Silver Trifluoromethanesulfonate
BF_3. Et_2O	Borontrifluoride-Diethyl Ether
CSA	Camphorsulfonic Acid
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCC	Dicyclohexyl Carbodiimide
DIC	Diisopropyl Carbodiimide
DCU	Dicyclohexylurea
DMF	*N*,*N*-Dimethylformamide
DMAP	4-(Dimethlyamino)pyridine
EDC	1-Ethyl-3-(3-dimethylamino)carbodiimide
Eq	Equivalent
DBTA	Dibenzoyl-Tartaric Acid
DTTA	Dibenzoyl-4-Toluoyl-Tartaric Acid
DEHPA	Di-(2-ethylhexyl) Phosphoric Acid
EtOH	Ethanol
ee	Enantiomeric Excess
ESI	Electro Spray Ionization
EI-MS	Electron Impact Mass Spectrometry
EtOAc	Ethyl Acetate
FBS	Foetal Bovine Serum
HRMS	High Resolution Mass Spectrometry
hr	Hour
HOBT	*N*-hydroxybenzotriazole
IC_{50}	Half Maximal Inhibitory Concentration
IR	Infrared Spectroscopy
KWH23	Kuwait Hospital patient # 23
m.p	Melting Point
MeOH	Methanol
NMR	Nuclear Magnetic Resonance

o-HAP	*ortho*-hydroxyacetophenone
p-HAP	*para*-hydroxyacetophenone
PAc	Phenyl Acetate
rpm	Revolutions Per Minute
rt	Room Temperature
SAR	Structure Activity Relationship
$Sn(OTf)_2$	Tin(II) Trifluoromethanesulfonate
SDA	Sabouraud Dextrose agar
TMSOTf	Trimethylsilyl Trifluoromethanesulfonate
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TEA	Triethylamine
UV	Ultraviolet Spectroscopy

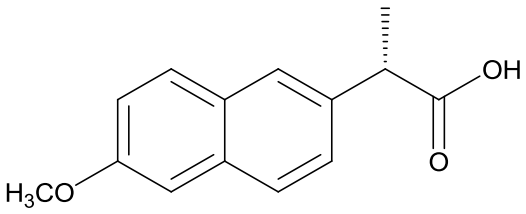
1.1 **Chirality**

Chirality (originated from the Greek word "*cheir*", meaning "hand") is an expression of nature, which is observed in its various forms. Traditionally, a lack of symmetry is considered to be the signature of chirality. In nature, diverse macroscopic objects such as hands, animal organs, biological organisms and macromolecules, as well as microscopic objects such as molecules are chiral. From a molecular point of view, molecules with equal atomic composition (same molecular formula) could be superimposable (homomeric; identical) or non-superimposable (isomeric; structural isomers). Chirality is a property that often determines the action and behavior of molecules in chiral environment e.g. living cell. A chiral compound is one that exists in two different forms called enantiomers. These isomers are mirror images of each other like a pair of hands. Almost all of their physical properties are identical including melting and boiling points and their results of spectroscopic analysis. Superficially, the only difference is the direction in which the plane polarized light is rotated. World (nature) around us is chiral and most of the important building blocks which make up the biological macromolecules of living systems do so in one enantiomer only (*L*-form). Chirality is a major concern in biological systems.[1a]

1.1.1 Biological significance of chirality

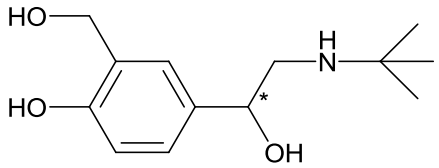
Enantiomeric forms of a drug can differ in potency, toxicity and behavior in biological systems. Most synthetic drugs developed in the past were not chiral, though some were. Drugs synthesized from natural products are largely chiral in nature.

In the late 1990s, a number of single enantiomer drugs were developed and launched. The body is highly chiral selective; it will interact with each racemic drug differently and metabolize each enantiomer by a separate pathway to produce different pharmacological activity.[1b] One isomer may thus produce the desired therapeutic activities, while the other may be inactive or produce some unwanted side effects. For example *S*-enantiomer of the non-steroidal anti-inflammatory drug Naproxen **(1)** is 28 times more effective than its *R*-enantiomer, which is extremely toxic to liver.



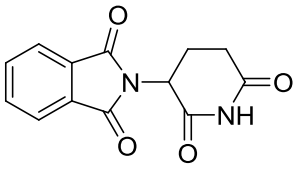
(1)

Most drugs fit into an active site on a cell or an enzyme. One enantiomer fits into this receptor site while other doesn't, rather like trying to put a left hand into a right glove. In many cases, the undesired enantiomer merely behaves as ballast and does nothing. For the treatment of asthma disease, we use drug Albuterol **(2)** in which its *R*-isomer cause therapeutic effect. Where as its *S*-isomer causes the side effects such as increase of pulse rate and decrease the sugar level etc.



(2)

Another good example is the drug Thalidomide **(3)** for which both enantiomers have the same sedative effect but only the (-) enantiomer causes foetal deformities. Who can forget the tragic consequences brought by this drug in early 1960s? A high incidence of foetal deaths and malformations occurred due to its use by pregnant women. Unfortunately even if the pure (+) enantiomer had been used problems would have arisen since the two are interconvertable under physiological conditions.[2]

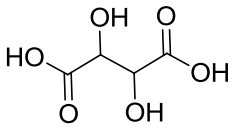


(3)

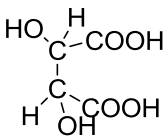
In 1848 Pasteur resolved (separated) an optically inactive substance (tartaric acid) into two optically active components.[3] Each of the optically active components had properties identical to tartaric acid (density, m.p, solubility etc) except that they rotated the plane polarized light in opposite direction. Pasteur made a proposal that still stands as the foundation of stereochemistry the twin molecules of tartaric acid were mirror images of each other.

1.2 Tartaric acid

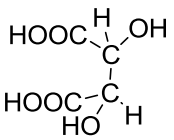
Tartaric acid is a white crystalline solid. Any of the stereo isomeric forms of 2,3-dihydroxy butanedioic acid *L*-, *D*- and meso are of great importance due to the two stereogenic centers. Tartaric acid was first isolated from potassium tartrate; by the Persian alchemist Jabir bin Hayyan, who was also responsible for numerous other basic chemical processes still in use today. The chirality of tartaric was discovered in 1832 by Jean Baptiste Biot, who observed its ability to rotate plane polarized light. Louis Pasteur continued this research in 1847 by investigating the shapes of tartaric acid crystals, which he found to be asymmetric. Pasteur was the first to produce a pure sample of levotartaric acid. *L*-tartaric acid occurs naturally in many plants, particularly grapes, bananas, and tamarinds. Important derivatives of tartaric acid include its salt, cream of tartar (potassium bitartrate), Rochelle salt (potassium sodium tartrate, a mild laxative) "tartaro emetic" (antimony potassium tartrate).[4]



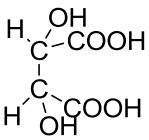
Tartaric acid



***L*-Tartaric acid**



***D*-Tartaric acid**



Meso-Tartaric acid

Both *L*- and *D*-tartaric acid and esters are inexpensive compounds and are used as chiral auxiliary reagents in the oxidation of alkenes. It is used as an acidulant in foods and also as chelating agent. Tartaric acid is a muscle toxin, which works by inhibiting the production of malic acid and in high doses causes paralysis and death. In spite of that, it is included in many foods, especially sour tasting sweets. As a food additive, tartaric acid is used as an antioxidant with E number E334; tartrates are other additives serving as antioxidants or emulsifiers.[5] When cream of tartar is added to water, a suspension is formed which serve to clean copper coins very well. This is due to the fact that the tartrate solution can dissolve the layer of copper (II) oxide present on the surface of coin. Copper (II) tartrate complex that is formed is easily soluble in water. Tartaric acid plays an important role chemically; lowering the pH of fermenting "must" to a level where many undesirable spoilage bacteria cannot live, and acting as a preservative after fermentation. Tartaric acid is used in the synthesis of many chiral and bioactive compounds.[6,7]

1.2.1 Chiral building blocks

The construction of chiral building blocks containing quaternary center is a continuing synthetic challenge in the organic chemistry.[8] Synthesis of these chiral compounds from the chiral pool precursors is of great advantage because of low cost and rich source of chirality associated with the chiral pool compounds. It would be even more rewarding to synthesize both antipodes of the chiral quaternary compounds from a single abundant chiral source, thus avoiding the use of unnatural sources. Consider the example which involves the synthesis of α-methoxyaryl acetic acid starting from *L*-tartaric acid[9] (Figure 1.1).

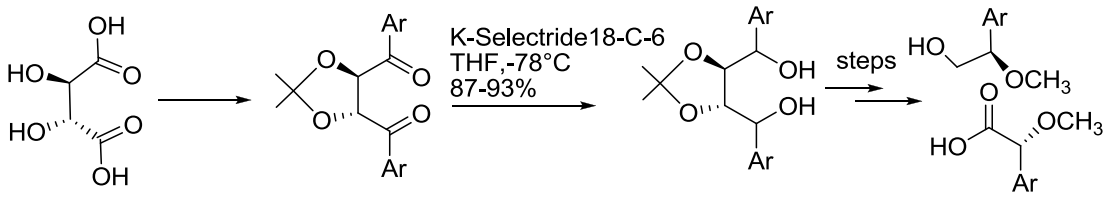
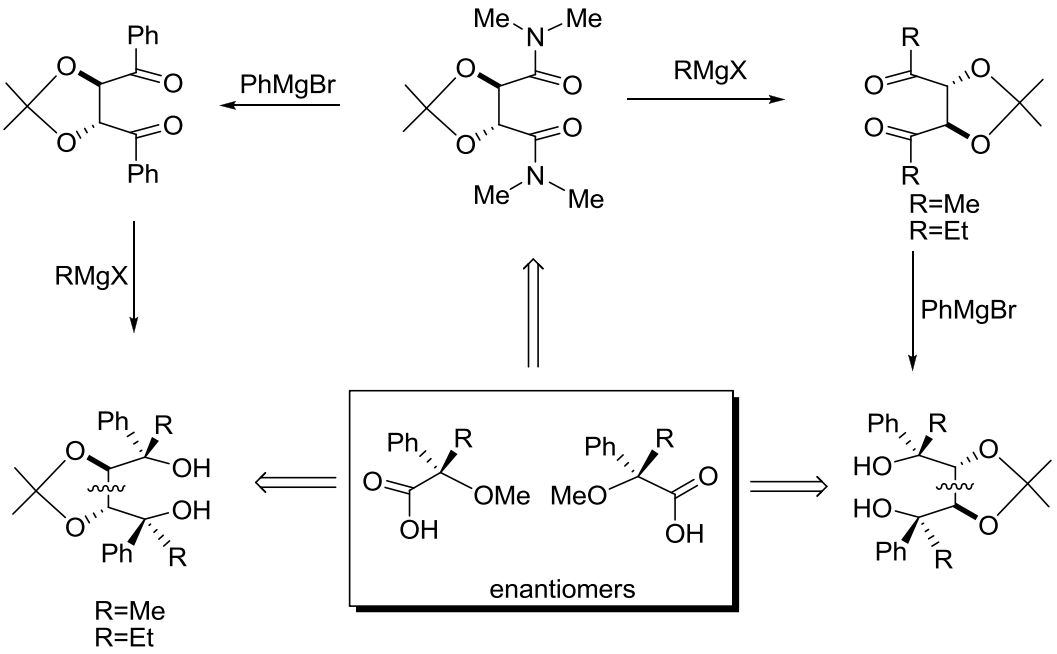


Figure 1.1: Asymmetric synthesis of α-methoxyaryl acetic acid derivatives.

The synthesis involves the stereoslective reduction of 1,4-diketone, and elaboration of the 1,4-diol to the α-methoxyaryl acetic acid derivative.

Tartaric acid is used as a chiral building block in the synthesis of many compounds,[10] e.g. α- alkyl- α-methoxy aryl acetic acid derivatives in both enantiomeric forms starting from single chiral precursor, that is, *L*-tartaric acid.

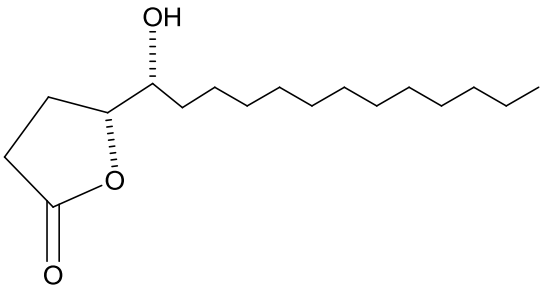


In addition, the utility of this methodology was applied in the synthesis of pine beetle pheromone (–)-frontalin.[11]

1.2.2 Bioactive precursors

Annonaceae acetogenins extracted from the "*Annonaceae*" plants have attracted considerable interest owing to their potential biological properties including cytotoxic, antitumoral and immune suppressive activities.[12] One of the common structural components of their increasingly significant natural products is the chiral 5-hydroxyalkylbutan-4-olide nucleus. Some of the compounds possessing this moiety have been shown to exhibit varied biological activities and also to be the precursor for the synthesis of complex natural products.[13] One of the simple molecules belonging to this group is muricaticin **(4)** isolated as a mixture of enantiomers from the seeds of *Anona muricata L*; commonly known as sour soup or guanabana which is known commercially as a fruit crop in tropical regions.[14] Muricaticin is a bioactive lactone comprising of a 5-hydroxyalkylbutan-4-olide which can be synthesized from *L*-tartaric acid. The enantiomers of muricaticin exhibit potent toxicity towards several

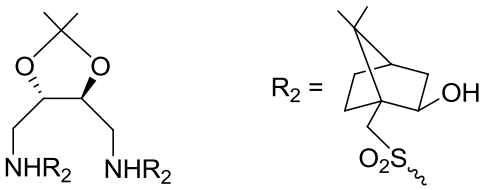
human tumor cell lines. Structure activity relationship (SAR) studies indicated that the activity is influenced by the nature of side chain.[15]



(4)

1.2.3 Chiral ligands

Chiral alcohols are ubiquitous in the structures of the natural products and drug compounds are also important precursors for many other functional organic molecules.[16] One of the most useful methods of asymmetric preparation of sec-alcohols and tert-alcohols is the enantioselective addition of dialkylzinc reagents to the carbonyl compounds with chiral ligands.[17] Although many existing chiral ligands can induce good to excellent selectivity, it is still desirable to develop new chiral ligands for high enantioselectivity. Due to two stereogenic centers, tartaric acid has attracted much attention recently. A variety of sulfonamide ligands have been reported to be effective in the enantioselective addition of dialkylzinc reagents to aldehyde[18] or ketones.[19] Chiral sulfonamide ligand **(5)** can be easily prepared from *L*-tartaric acid and camphor sulfonylchloride.



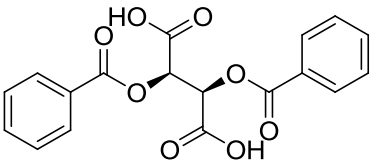
(5)

This ligand has been successfully used in the asymmetric addition of diethylzinc to aldehyde and ketone in the presence of titanium tetraisopropoxide under mild conditions affording the chiral alcohols in high yields with good ee value.[20] Diels-

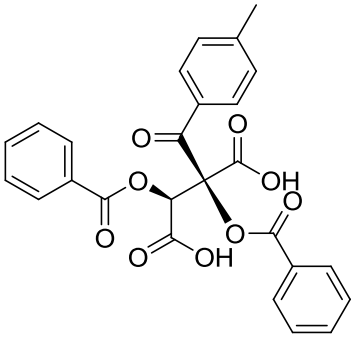
Alder reaction of *o*-quinodimethane with olefins is a useful method for constructing the corresponding tetrahydronaphthalene frameworks bearing up to four stereocenters, which are the key intermediates for the synthesis of polycyclic compounds in one step.[21] The Diels-Alder reaction of α-hydroxy *o*-quinodimethane is useful for affording oxygen functionalized tetrahydonaphthalene.[22] Although several diastereoselective Diels-Alder reactions of *o*-quinodimethane have been reported for the synthesis of optically active tetrahydronaphthalene.[23] A novel chiral system was designed using the tartaric acid ester to carry out 1,3-dipolar cycloaddition reactions of nitrile oxides and nitrones are useful asymmetric hetro Diels-Alder reaction of nitro compounds.[24]

1.2.4 Resolution of racemates

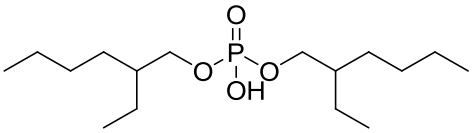
Amino acids are biologically active compounds. They play an important role in living systems. Most amino acids are chiral. The separation of amino acids is of great importance in many scientific fields, such as pharmaceuticals, food processing, amino acid biochemistry, proteins and related areas and also asymmetric synthesis in organic chemistry.[25] Although previously only *L*-amino acids were available, *D*-amino acids now becoming increasingly available as a result of being required as component materials of industrial interest.[26] Enantiomers can be separated after derivatization[27,28] (diastereomeric ester or a diastereomeric salt) or in one step by complex formation. *O*,*O*'-dibenzoyl-(2*R*,3*R*)-tartaric acid (DBTA) and *O*,*O*'-dibenzoyl-(2*S*,3*S*)-4-toluoyl-tartaric acid (DTTA) have been reported as a very good complex forming compounds for efficient resolution of racemates.[29] The carboxylic acid groups of DBTA and DTTA can donate protons for hydrogen bonding, while they can also behave as a proton acceptor due to eight oxygen atoms they contain. It has been recently reported that di-(2-ethylhexyl) phosphoric acid (DEHPA) and DBTA can form complexes which can be used as chiral selectors for the resolution of amino acid enantiomers and both showed good enantioselectivity and high distribution ratio.[30]



DBTA



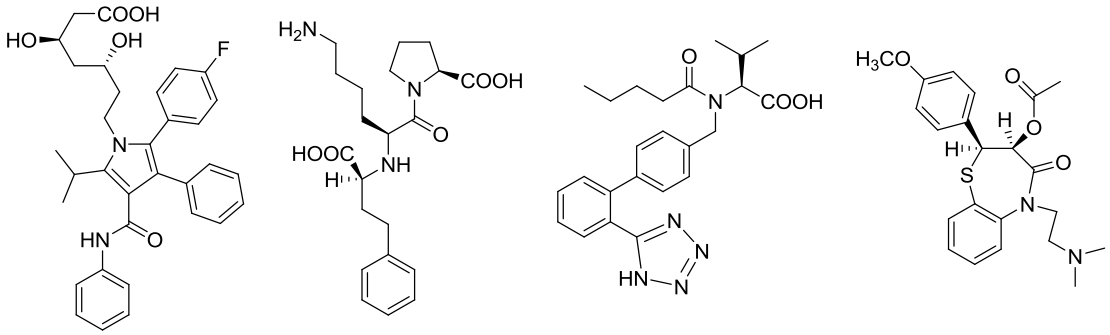
DTTA



DEHPA

1.3 Amides

Amide bonds play a major role in the elaboration and composition of biological systems, representing for example the main chemical bonds that link amino acid building blocks together to give proteins. Amide bonds are not limited to biological systems and are indeed present in a huge array of molecules, including major marketed drugs. For example, Atorvastatin (Figure 1.2), the top selling drug worldwide since 2003, blocks the production of cholesterol and contains an amide bond,[31] as do Lisinopril (inhibitor of angiotensin converting enzyme),[32] Valsartan (blockade of angiotensin-II receptors)[33] and Diltiazem (calcium channel blocker used in the treatment of angina and hypertension).[34]



Atorvastatin **Lisinopril** **Valsartan** **Diltiazem**

Figure 1.2: Examples of drugs containing an amide bond.

Synthetic development of new macrocyclic peptide antibiotics such as biphenomycin B[35] and vancomycine type glycopeptides antibiotics[36] has brought dramatic changes during the last few years. Cyclic peptides with open pores are useful as transport vehicles for biologically important ions and neutral molecules.[37,38] Synthetic biphenyl based cyclic amides have been reported for anion complexation.[39] Cyclic tetra-amide receptors having barbiturate binding domain have also been reported.[40] Supramolecular amides are also used as molecular receptors[41] and in molecular recognition[42]; some recently reported synthesis of permanent fluorescence sensing chiral fluorophoric macrocycles with antibacterial activity[43] and cyclophane amides with anti-inflammatory activity have been reported[44] but no carbazole based amide macrocycles have been reported. Synthesis of carbazolophane amides along with their antibacterial and antifungal activities has also been reported. An in-depth analysis of the comprehensive medicinal chemistry database revealed that the carboxamide group appears in more than 25% of known drugs.[45] This can be expected, since carboxamides are neutral, stable and have both hydrogen-bond accepting and donating properties.

1.3.1 Biologically active amides from tartaric acid

Many tartaric acid derivatives having amide bond show important biological activities like inhibitors of chitin synthase,[46,47] anti inflammatory,[48] antifungal,[49] β-secretase inhibitor,[50] antimicrobial[51] and as a thrombin inhibitor.[52]

1.3.2 Methods for amide bond formation

1.3.2.1 Amide bond formation using activating agents

Amide or ester bond formations between an acid and respectively, an amine or an alcohol are formally condensations. The usual esterifications are an equilibrium reaction, whereas, on mixing an amine with a carboxylic acid, an acid-base reaction occurs first to form a stable salt (Figure 1.3). In other words, the amide bond formation has to fight against adverse thermodynamics as the equilibrium lies on the side of hydrolysis rather than synthesis.[53] The direct condensation of the salt can be achieved at high temperature (160-180°C),[54] which is usually quite incompatible with the presence of other functional groups.

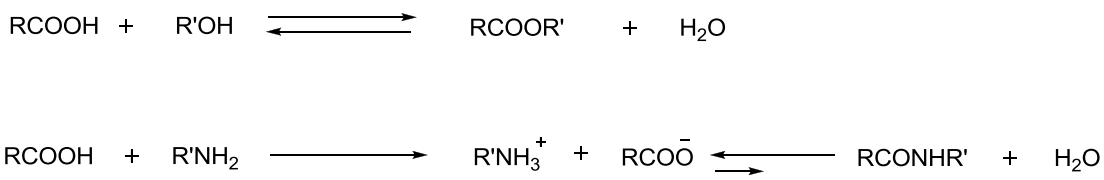


Figure 1.3: Ester bond versus amide bond formation.

Therefore, activation of the acid, attachment of a leaving group to the acyl carbon of the acid, to allow attack by the amino group is necessary as shown in Figure 1.4.

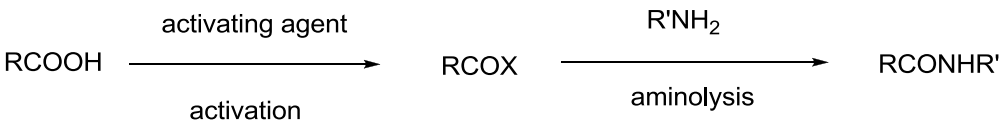


Figure 1.4: Acid activation and aminolysis.

Carboxy components can be activated as acyl halides, acyl azides, acylimidazoles, anhydrides, esters etc. There are different ways of coupling reactive carboxy derivatives with an amine. Dicyclohexyl carbodiimide (DCC), diisopropyl carbodiimide (DIC) and 1-ethyl-3-(3-dimethylamino)carbodiimide HCl salt (EDC) are frequently used for amide bond formation (this method can also be used to synthesize anhydrides and esters).[55]

Carbodiimides were the first coupling agents to be synthesized. DCC has been used for coupling since 1955[56] and the mechanism for coupling carboxylic acids to amines is given below (Figure 1.5). The first step involves the reaction of the carboxylic acid with DCC to form the *O*-acylurea. This intermediate can then yield a number of different products: The amide via direct coupling with the amine (the by-product formed dicyclohexylurea (DCU) is usually insoluble in the reaction solvent and can be removed via filtration).

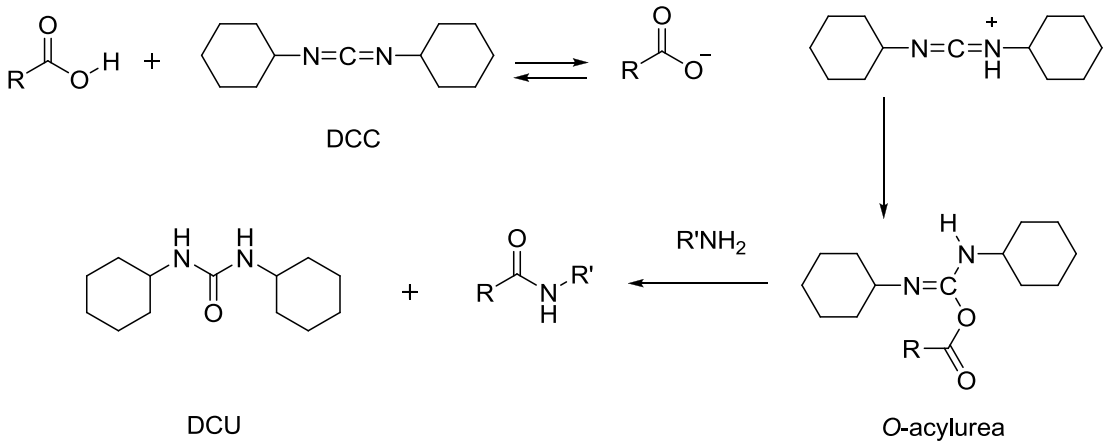


Figure 1.5: Amide bond formation using coupling agent.

The formation of mixed anhydrides is a classic method for amide bond formation. It is important to note that many mixed anhydrides can be generated using different coupling agents. The mixed anhydride method was first reported by Vaughan,[57] who tested many acid chloride derivatives and concluded that the success of the amide-bond formation was governed by steric and inductive effects.

The use of chloroformates for amide-bond formation was first reported by Vaughan[58] and was based on the mixed anhydride method. In the presence of a base, the reaction between a carboxylate and a chloroformate yields a mixed carbonic anhydride which reacts quickly with amines to form amides as shown in Figure 1.6.

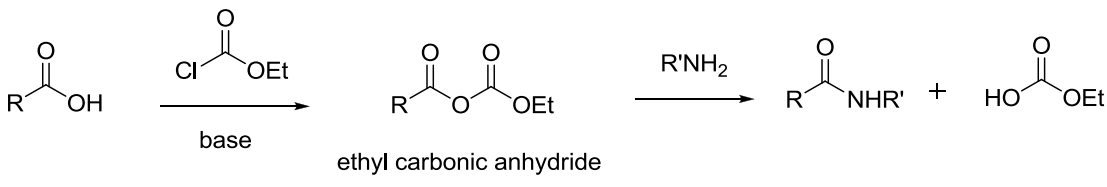


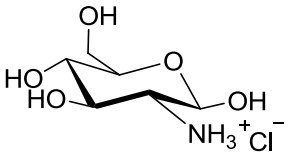
Figure 1.6: Amide bond formation via ethyl carbonic anhydride.

1.3.2.2 Microwave assisted amide bond formation (direct method)

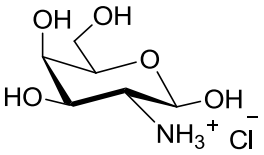
In several cases, microwave irradiation has been a successful alternative to conventional high temperatures to perform direct condensation of amines to carboxylic acids without prior activation. The use of direct microwave heating is reported to reduce the chemical reaction time, reduce side reactions, increase yields and improve reproducibility.[59] The microwave irradiation may be run with or without catalyst.[60] Different kinds of catalysts such as K-10 montmorillonite,[61] imidazole,[62] zeolite-HY,[63] polyphosphoric acid,[64] *p*-toluenesulfonic acid,[65] $TaCl_5$-silica gel,[66] KF-alumina and -silica gel[67] have been used.

1.4 Glycopyranosyl amines

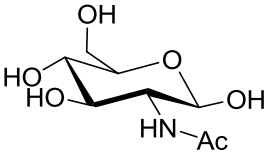
Cell surface glycolipid and glycoprotein oligosaccharides are known to play important roles in many biological events such as cellular recognition, adhesion and cell growth regulation. A major class of glycoprotein oligosaccharides consists of *N*-linked oligosaccharides which are linked to asparagines by an amide bond.[68] Glycopyranosyl amines are important compounds in the chemical synthesis of *N*-glycopeptides[69-71] and therefore valuable intermediates for the synthesis of glycoconjugates and neoglycoconjugates. The latter two are very useful tools for elucidating the biological roles of oligosaccharides.[72-74] glucosamine, 2-amino-2-*deoxy*-D-glucose, is an amino monosaccharide that is an essential component of mucopolysaccharides and chitin. Glycosaminoglycans (mucopolysaccharides) are large complexes of negatively-charged carbohydrate chains that are incorporated into mucous secretions, connective tissue, skin, tendons, ligaments and cartilage. Glucosamine and its acetylated derivative, *N*-acetylglucosamine are readily synthesized in the body from glucose. Because of its high concentration in joint tissues, the hypothesis that glucosamine supplements would provide symptomatic relief for osteoarthritis was developed more than 30 years ago (D_Ambrosio *et al*. 1981). Many clinical trials have tested this hypothesis (Institute of Medicine, 2004) and glucosamine supplements are widely used to relieve arthritic complaints.



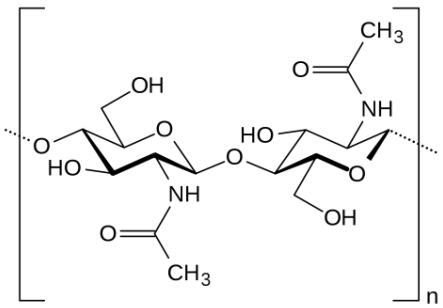
Glucosamine



Galactcosamine



***N*-Acetyl glucosamine**



Chitin

1.4.1 Synthesis of glycopyranosyl amines

The most reliable methods for the synthesis of glycopyranosyl amines are based on the reaction of a nonprotected carbohydrate with aqueous ammonium hydrogen carbonate[75-76] (Figure 1.7), the hydrogenolysis of the corresponding azide[77-79] catalyzed by Pd/C,[80-82] Lindlar catalyst,[83-84] PtO_2, Raney-Ni[85] or with 1,3-propanedithiol in the presence of triethylamine and methanol.[86-87] The conversion of azides into amines or amino derivatives by the Staudinger reaction[88] provides an alternative mild route for the synthesis of *N*-acylglycopyranosyl amines.[89-90]

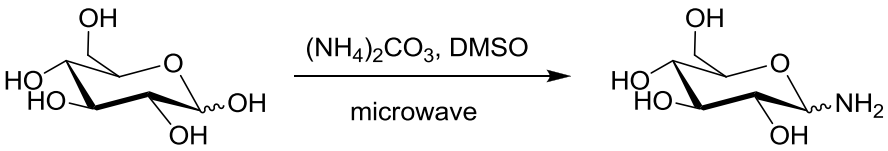


Figure 1.7: Microwave assisted synthesis of glycopyranosyl amines.

1.5 *O*-Glycoside bond formation

Glycoside synthesis is a very common reaction in nature providing a great variety of

oligosaccharides and glycoconjugates as glycolipids, glycoproteins and glycopeptides. As recognized only recently, the structural diversity of the oligosaccharide portion, which is inherent in the variability in the glycoside bond formation, makes them ideal as carrier of biological information and specificity. For this fact, the field of the synthetic carbohydrate chemistry grew up exponentially in the last twenty years in order to synthesize oligosaccharides for specific purposes which include their use in antibody production, screening of antibodies, lectin and selectin specificity, interaction studies with virus[91-92] and bacterial receptors,[93-95] substrates for glycosidases,[96-97] glycosyltransferases[98] and probes in molecular recognition studies including conformational analysis. To date, it is the challenge for the synthetic chemist to build up glycosidic linkages with high regio- and stereocontrol similar to the naturally occurring ones. Two different approaches are generally used for the *O*-glycoside bond formation.

- Enzymatic *O*-glycoside bond formation
- Chemical *O*-glycoside bond formation

1.5.1 Enzymatic *O*-glycoside bond formation

The enzymatic *O*-glycosylation is generally based on specific glycosyl-transferases which uses nucleoside diphosphate or, in some cases, nucleoside monophosphate sugars as glycosyl donors. The nucleoside di- or monophosphate residues are the leaving groups and sugars, or other aglycones are the glycosyl acceptors.[99]

1.5.2 Chemical *O*-glycoside bond formation

The chemical synthesis of oligosaccharides is based on the glycosylation reactions, coupling different building blocks with generating a glycosidic bond. As a general principle of most of the glycosylation methods a glycosyl donor is formed by combining a leaving group with the anomeric centre of one appropriately protected glycosyl building block (Figure 1.8). In the glycosylation reaction the activated glycosyl donor react with one hydroxy group of the completely or partially protected glycosyl acceptor.

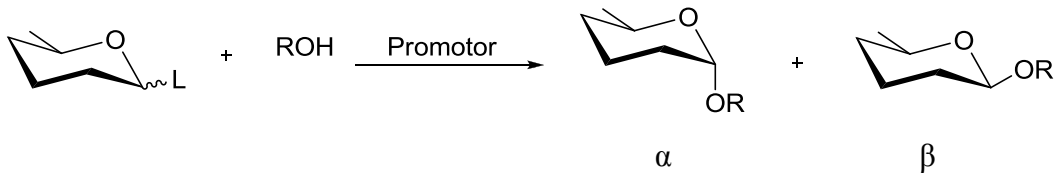


Figure 1.8: Glycosylation reactions.

1.5.2.1 The Koenigs-Knorr method

The oldest glycosylation method was published by Koenigs and Knorr in 1901,[100] it was variously modified and it is still in use.[101] The glycosyl donors are usually chlorides and bromides which are activated with various silver or mercury salts (Figure 1.9). Advanced modifications make use of glycosyl fluorides as donor compounds.[102-103]

Figure 1.9: Koenigs-Knorr glycosylation method.

In order to favour a stereocontrolled SN_2-type reaction, solvents of low polarity (dichloromethane, cyclohexane and petroleum ether) and low temperatures are commonly used. The application of this method led to excellent results, for example the synthesis of numerous oligosaccharides including the blood group A-, B-, and Lea-determinants.[104] However, the main disadvantages of the Koenigs-Knorr method are the need of at least stoichiometric amounts of the promoters and the thermal instability of many glycosyl halides.

1.5.2.2 Schmidt method

A universal glycosylation method which avoids the use of heavy metal salts as promoters were developed by R. R. Schmidt and J. Michel in 1980.[105] *O*-Glycosyl trichloroacetimidates were introduced as a new type of glycosyl donors as shown in Figure 1.10. It is easily prepared, sufficiently stable and it can be activated for the glycosylation reactions with catalytic amounts of Lewis acids such as TMSOTf, $BF_3.Et_2O$, $Sn(OTf)_2$, AgOTf and $ZnCl_2.Et_2O$.[106-107]

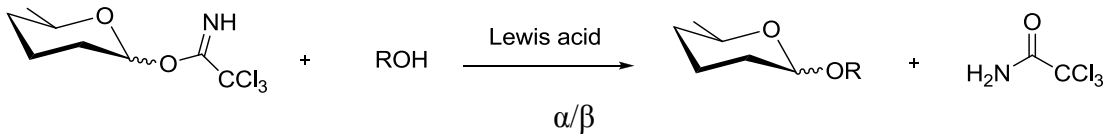


Figure 1.10: The trichloroacetimidate glycosylation method.

The anomeric configuration (α or β) of the trichloroacetimidate donors is crucial for the anomeric sterocontrol of the glycosidic bond formation. β-Trichloroacetimidates can be selectively prepared with K_2CO_3 as base[108] (kinetic control), whereas the use of NaH, $CsCO_3$ or KOH[109] with phase transfer catalyst[110] exclusively gives the α-trichloroacetimidates (thermodynamic control). Electron-deficient nitriles are known to undergo direct and reversible base-catalyzed addition of alcohols to the triple-bond system, thereby providing *O*-alkyl imidates.[111-112] The imidate synthesis has the advantage that the free imidates can be directly isolated as stable adducts, which are less sensitive to hydrolysis than the corresponding salts. Therefore, base-catalyzed transformation of the anomeric oxygen atom into a good leaving group should be possible, for instance, by addition to trichloroacetonitrile in the presence of base (Figure 1.11). Thus, with different bases (K_2CO_3, $CaCO_3$, NaH, 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU), or others) trichloroacetimidates can be isolated, often in pure form and in high yields.

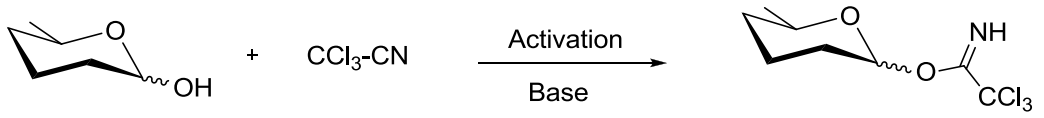


Figure 1.11: Trichloroacetimidate formation (activation step).

After base-catalyzed generation of *O*-glycosyl trichloroacetimidates (activation step), mild acid treatment in the presence of acceptors leads to the desired glycosides in an irreversible manner. Under the reaction conditions, the Lewis acid ($BF_3.OEt_2$) or the strong acidic catalysts (TMSOTf, TfOH) are requird for the activation of the basic *O*-glycosyl trichloroacetimidates.

Trichloroacetimidates have been used for the glycosylation of oligosaccharides,[113] glycosylation of inositol derivatives,[114] glycosylation of sphingosine derivatives,[115] glycosylation of amino acids,[116] polycyclic and macrocyclic glycosides. Glycosides of

polycycles or macrocycles (anthracyclines, chalicheamicin, macrolactones, *etc*.) are of great interest because of their antibiotic and antitumor activities.[117-118]

1.6 Imides

Imides are classically defined as cyclic secondary amides of dibasic acids. Imido group is an interesting functionality, due to its wide presence in the natural products pool and in the pharmacologically active compounds.[119] Imides can be prepared by different methods by using the different techniques**.**

1.6.1 Methods for the synthesis of imides

The most important methods for the synthesis of imides are;

- Solid phase synthesis of cyclic imides
- Microwave assisted synthesis of imides

1.6.1.1 Solid phase synthesis of cyclic imides

This strategy is used for the synthesis of cyclic imides,[120] a small array of succinimides and phthalimides was synthesized. The methodology was then applied to a drug discovery project. Synthesis of cyclic imide is quiet important,[121] because they often show interesting biological activity. In particular, succinimides and phthalimides have been reported to exhibit anticonvulsant, antiviral, anxiogenic, antipsychotic and anti-inflammatory activity.[122] This method involves coupling a cyclic acid anhydride **(6)** and hydroxymethyl polystyrene resin **(7)** using 4-(dimethlyamino)pyridine (DMAP) in *N*,*N*-dimethylformaamide (DMF). The resulting carboxylic acid **(8)** was then converted into an amide **(9)** using primary amine in the presence of DIC and *N*-hydroxybenzotriazole (HOBT). Finally, heating promoted cyclization and released cyclic imide **(10)** from the resin (Figure 1.12).

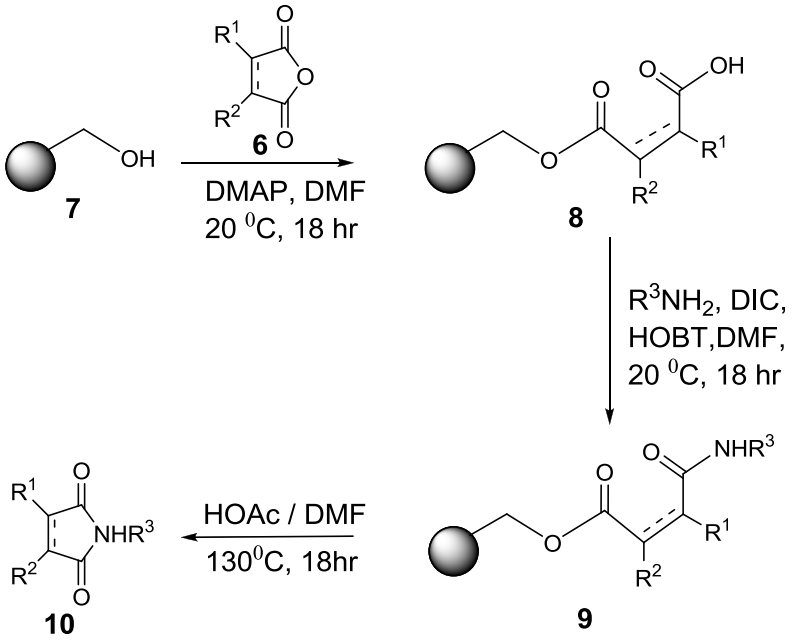
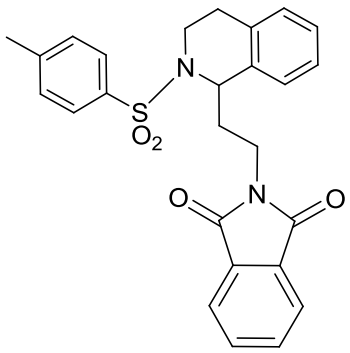


Figure 1.12: Solid phase synthesis of cyclic imides.

Solid phase strategy is used to synthesize the imides on large scale. This methodology is very useful in the synthesis of many compounds; it was used to synthesize a new class of δ–opioid receptor ligand **(11)**, which is used as an analgesic.

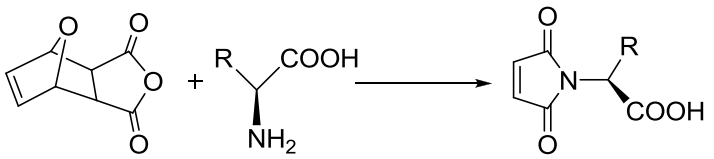


(11)

1.6.1.2 Microwave assisted synthesis of imides

The development of simple and versatile synthetic route that can be applied to a wide variety of commercially available materials continues to be one of the most exciting topics in organic synthesis.[123] Microwave assisted organic synthesis has been known since 1986.[124] This "non conventional" synthetic method has shown broad applications as a very efficient way to accelerate the course of many organic

reactions, giving better yields and higher selectivity, lower quantities of side products and consequently, easier work-up and purification of the products.[125] Microwave reactions can be done with or without solvent. We can also synthesize the imides by using water as a solvent.[126] For example a cheap and readily available exo-Diels-Alder adduct of furan and maleic anhydride **(12)** treated with amino acids **(13)** in the presence of water as a solvent and irradiated in domestic microwave (Figure 1.13). Water was evaporated by azeotropic distillation with toluene in vacuo and the residue was treated with acetone until it solidified. Filtration gave analytically pure compounds.



12 **13** **14**

R= -CH_2OH Time =5× 45 sec Yield = 92%

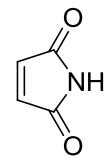
Figure 1.13: Microwave assisted synthesis of imides.

This route was used for the synthesis of chiral and achiral malieimides in good yields. This synthetic pathway is very short and simple.

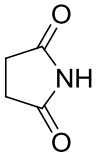
1.6.2 Biologically important imides

Bacterial resistance to antibiotics is an increasing problem that concerns clinicians, the pharmaceutical industry and chemist. The multidrug resistant bacteria are the major cause of failure in the treatment of infection diseases. Thus the need for novel antibiotics is more and more important. Important biological properties concerning bactericidal, fungicidal and anticancer were reported for *N*-substituted imides such as malieimides and related compounds.[127] Maleimides **(15)** are an important class of substrates for biological, pharmacological and chemical applications. In biological applications they are used as chemical probes of protein structures,[128] as immunoconjugates for cancer therapy and as solid supported enzymes for synthetic applications for the production of antibiotics.[129] In pharmacological applications they are used as analogues of the cyclic tetra peptide chlamydocin,[130] photoactivatable

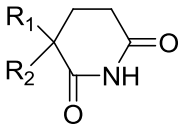
fluoresce derivatives[131] or as a new herbicides and pesticides.[132] Maleimides moiety can be used as a versatile platform in synthesis due to Michael accepting ability dienophile nature[133] as well as a dipolarophile in 1,3-dipolar cycloaddition.[134] Many other imides such as succinimide **(16)**, glutarimide **(17)**, and phthalimide **(18)** are stable and well known compounds. Succinimide itself has antiurolithic properties[135] and two of its derivative that still contains NH group is aldose reductase inhibitor[136] and cytotoxic agent.[137]



(15)

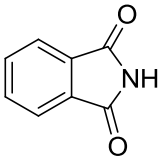


(16)



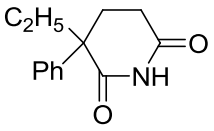
(17)

$R_1 = R_2 = H$
$R_1 = Et, R_2 = Ph$
$R_1 = Et, R_2 = p\text{-}NH_2\text{-}Ph$

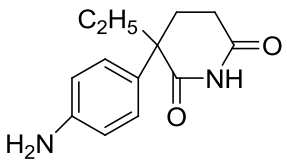


(18)

In addition its *N*-substituted derivatives bear a variety of biological activities such as antiepileptic,[138] anticonvulsive[139] and fungicidal.[140] Glutarimide is a parent molecule for an array of ambecidal, antitumor and fungicidal glutarimide antibiotics. The phenyl derivative glutethimide **(19)** is a hypnotic and sedative,[141] while the related compounds aminogletethimide **(20)** is successfully used in the treatment of breast cancer.[142]



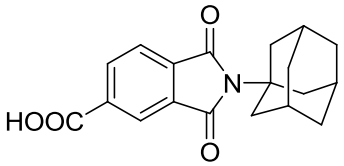
(19)



(20)

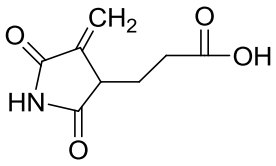
Other and not less important use of the imides lies in the production of polyimide, which are readily exploited materials for a variety of purposes, including their use in

the electronics and spacecraft industry. The adamantane derivative **(21)** of phthalimide has also shown antimicrobial activity.[143]

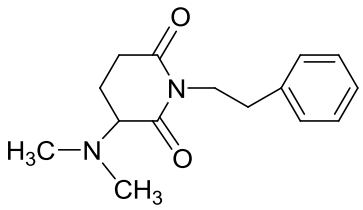


(21)

The antimicrobial activity of adamantly derivatives of phthalimide was first tested by the agar disc-diffusion method against Gram-positive bacteria. *Staphylococcus aureus*, *Micrococus flavus*, *Enterococeus faecium* and certain strains of *Bacillus*. Gram-negative bacteria: *Bordella bronchiseptica*, *Pseudomonas aeruginosa* and strains belong to the family *Enterobacteriaceae* as well as the fungus *Candida albicans* were resistant to all tested compounds. There are some other examples of biological active compounds containing imide moiety, Isohematinic acid **(22)** is a natural antibiotic which is found in *Actinoplanes philippinensis* plant and phyllanthimide **(23)** shows the activity which is antimicrobial.[144]



(**22**)



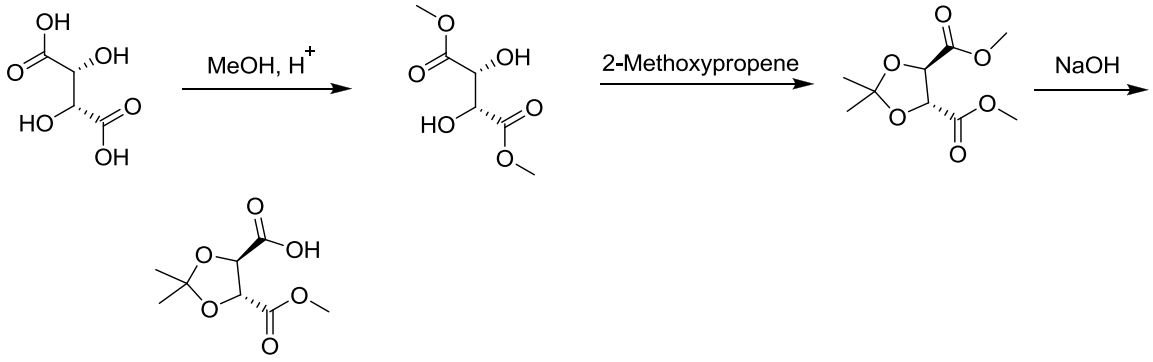
(**23**)

Plan of work

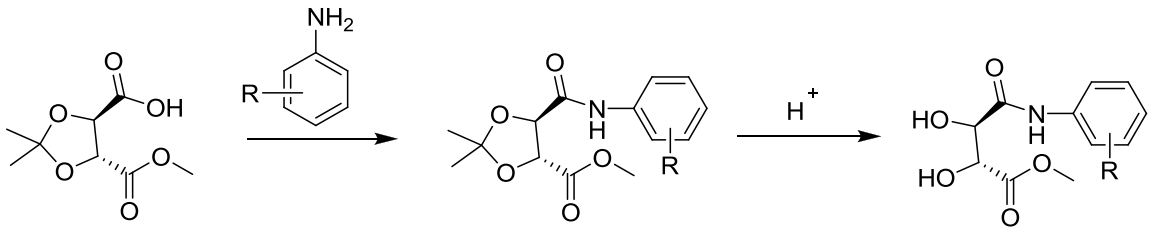
In view of the biological and synthetic importance of *L*-tartaric acid derivatives, we planned to synthesize some new derivatives mainly amides, esters, glycosides and imides from *L*-tartaric acid. To achieve the above objectives, the following synthetic routes will be derived.

Synthesis of monoester from *L*-tartaric acid. Synthesis of chiral amides from monoester of *L*-tartaric acid and different substituted anilines. Synthesis of monoaryl esters of *L*-tartaric acid using substituted phenols. Synthesis of glycopyranosyl amines from monosaccharides. Synthesis of *N*-Linked glycopyranosides from monoester of *L*-tartaric acid and glycopyranosyl amines. Synthesis of *O*-Linked glycopyranosides from monoester of *L*-tartaric acid and acetylated hemiacetals of monosaccharides. Synthesis of glycoconjugates from dimethyl-*L*-tartrate and glycopyranosyl trichloroacetimidates. Synthesis of chiral imides from diacetyl-*L*-tartaric acid anhydride and different aliphatic and aromatic amines and amino acids.

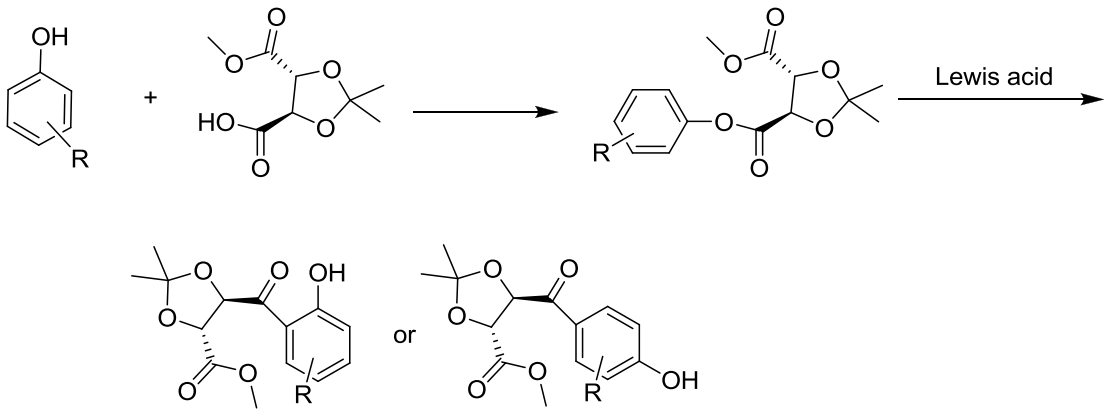
The synthesized compounds will be confirmed using different spectroanalytical techniques. Finally, biological evaluation of all these chiral derivatives will be carried out.



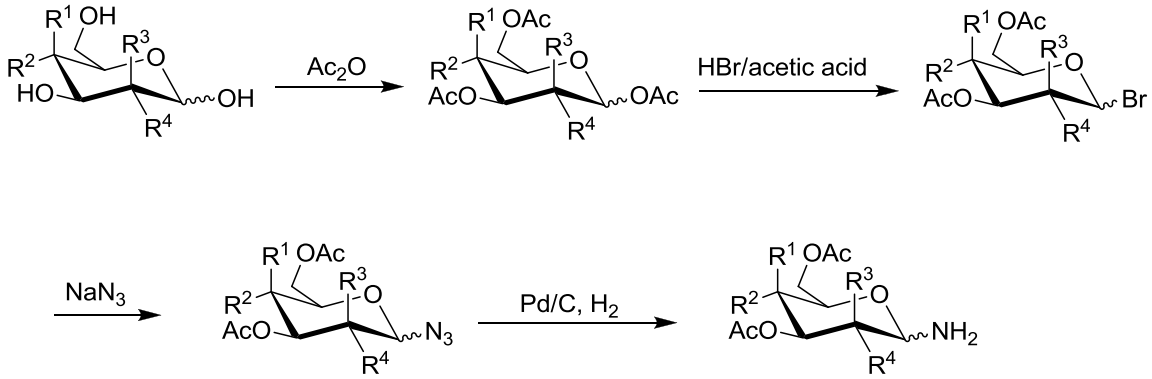
Scheme 1.1: Synthesis of monoester.



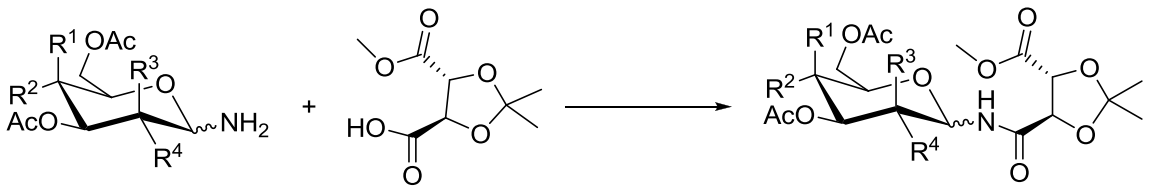
Scheme 1.2: Synthesis of chiral amides.



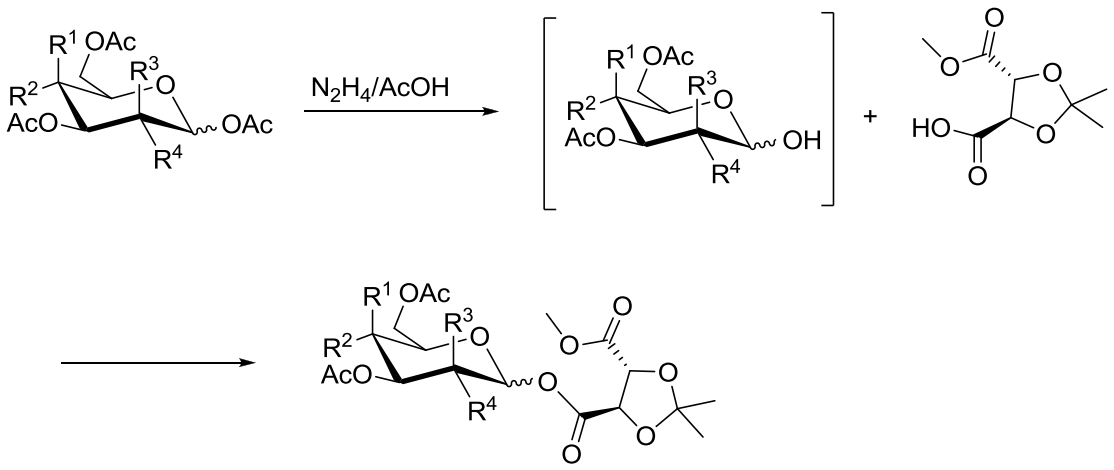
Scheme 1.3: Synthesis of monoaryl esters.



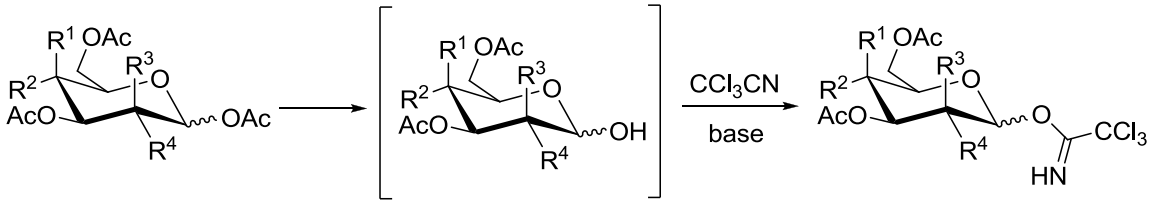
Scheme 1.4: Synthesis of glycopyranosyl amines.



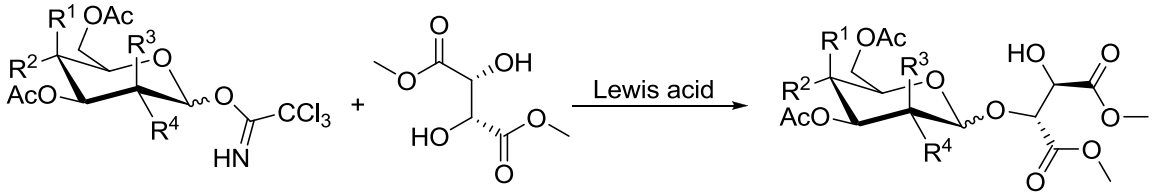
Scheme 1.5: Synthesis of glycopyranosyl amides.



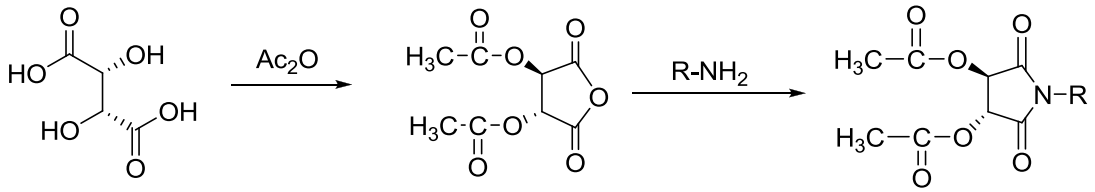
Scheme 1.6: Synthesis of glycopyranosides.



Scheme 1.7: Synthesis of glycopyranosyl trichloroacetimidates.



Scheme 1.8: Synthesis of Glycoconjugates.



Scheme 1.9: Synthesis of chiral imides.

2.1 Overview

Tartaric acid is an important optically active compound. It has been used to study the stereochemistry. The different derivatives of tartaric acid have wide applications in the synthesis of numerous chiral derivatives. In addition, it is also used as a precursor of chiral ligands, auxiliaries and resolving agents.[144] Keeping in view the importance of chiral substrates in organic syntheses, we planned to synthesize some new chiral derivatives of tartaric acid of potential synthetic and biological applications. In our research work, an inexpensive and commercially available *L*-tartaric acid **(1)** was selected. It can also exist as *D*-tartaric acid **(2)**. *L*-tartaric acid is a polar, polyfunctional and chiral molecule with two asymmetric carbon atoms with the absolute configuration (*2R,3R*) having C_2 axis of symmetry (Figure 2.1).

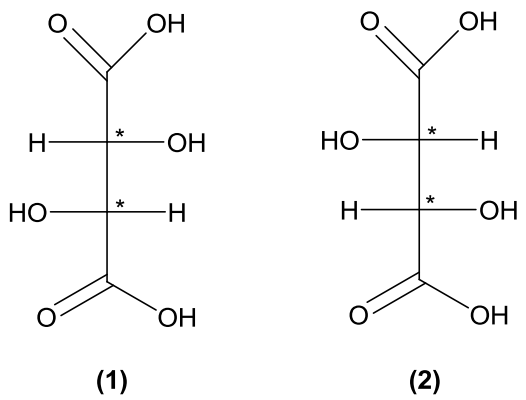


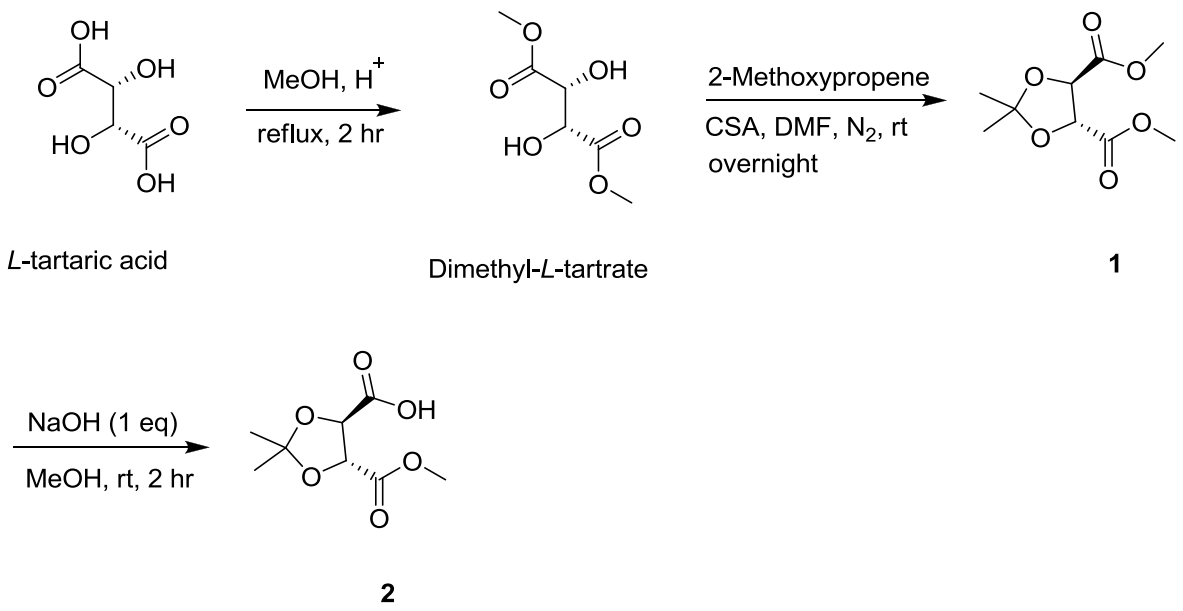
Figure 2.1: Structure of *L* and *D* tartaric acid.

2.2 Synthesis of 1,3-dioxolane dimethyl *L*-tartrate (1) and monoester (2)

To synthesize *L*-tartaric acid derivatives, the first step was to protect the diacid functionality as dimethyl ester and diol as 1,3-dioxolane. Different protecting groups can be used to avoid unwanted side reactions of hydroxyl groups. We chose 2-methoxypropene as a protecting group to furnish 1,3-dioxolane. 1,3-Dioxolanes are widely used in natural product syntheses as protecting groups for ketones, aldehydes and 1,2-diols. It is stable in basic condition. It is also an important intermediate and end-product in different pharmaceutical, fragrance and polymer industries.[145-147,51] Musich *et al.* have reported the synthesis of 1,3-dioxolane derivatives of *L*- and *D*-tartaric acid using 2,2-dimethoxy propane.[148]

First the dimethyl-*L*-tartate was prepared from *L*-tartaric acid and methanol[149] (Scheme 2.1). 1,3-Dioxolane dimethyl-*L*-tartrate (**1**) was prepared from dimethyl-*L*-tartate.[145-149,178] The initial yield was poor and once the reaction conditions were optimized, the yield was improved to 89 %. The product was purified through column chromatography.

Our next step was to partially hydrolyse compound (**1**) using sodium hydroxide (1 eq) in methanol.[148,179] Initial attempts to prepare the desired monoester resulted in low yield. When the reaction time was increased from one to two hour and dropwise addition of sodium hydroxide solution, the yield was further improved. The resultant salt was acidified with aquous $KHSO_4$ (1 M). To remove some of the unreacted starting material and diacid, the product was purified with column chromatograpy to get the monoester (**2**) as colourless oil, in 79 % yield.



Scheme 2.1: Synthesis of 1,3-dioxolane dimethyl-*L*-tartrate (**1**) and monoester (**2**).

The compounds (**1**) and (**2**) were characterized using IR, ^{1}H NMR, ^{13}C NMR and EI-MS.

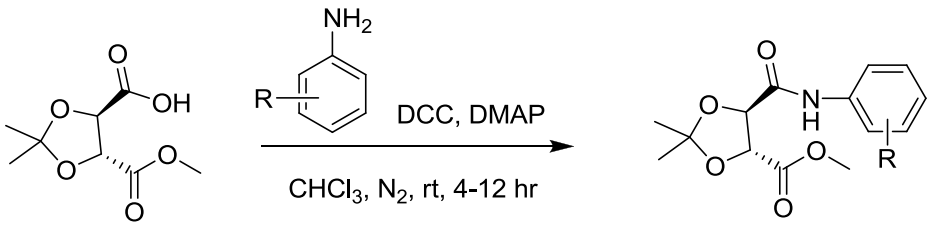
The IR absorption spectrum of the compound (**1**) showed characteristic bands at 2928 and 1738 cm^{-1}. These absorptions were attributed to C-H, and CO respectively. In ^{1}H NMR spectrum a singlet at 4.45 ppm with integration of 2 protons was attributed to CH, singlet at 3.82 ppm with integration of 6 protons was assigned to two methoxy groups, another singlet at 1.57 ppm with integration of 6 protons was assigned to two

methyl groups of 1,3-dioxolane. In ^{13}C NMR spectrum, peak at 170.3 ppm was assigned to CO of ester group. Another peak at 113.5 ppm was attributed to quaternary carbon. The chiral methine carbon appeared at 76.4 ppm. The two carbon of the methoxy groups appeared at 52.3 ppm. The methyl carbon of 1,3-dioxolane appeared at 25.7 ppm respectively.

The IR spectral data of compound (**2**) showed characteristic stretching bands at 3467, 2928, 1730 and 1708 cm^{-1}. These absorptions were assigned to OH, C-H, CO (ester) and CO (acid) respectively. In ^{1}H NMR a broad singlet at 9.32 ppm with integration of 1 proton was attributed to OH group. The two methine protons appeared as doublets in 4.87-4.72 ppm with coupling constant of 5.4 Hz in each. The two methyl groups of 1,3-dioxolane appeared as singlets at 1.49 and 1.48 ppm with integration of three protons for each singlet. In ^{13}C NMR spectrum, peak at 173.8 ppm was assigned to CO (acid) and 169.7 to CO (ester). Methine carbons appeared at 76.8 and 75.7 ppm respectively. EI-MS described in the experimental protocol also confirmed the synthesis of monoester, the molecular ion (m/z) appeared in the mass spectrum was in agreement with the molecular weight of the compound.

2.3a Method A: Synthesis of chiral amides (2a-2t)

After monoester (**2**) in hand, it was coupled with different substituted anilines to give amides (**2a-2t**) in 68-86 % yield (Scheme 2.2a).



2 **2a-2t**

R = 2-CF_3 (**2a**), 3-CF_3 (**2b**), 4-CF_3 (**2c**), 2-OCH_3 (**2d**), 3-OCH_3 (**2e**), 4-OCH_3 (**2f**), 2-CH_3 (**2g**)

R = 3-CH_3 (**2h**), 4-CH_3 (**2i**), 2-Cl, (**2j**), 3-Cl (**2k**), 4-Cl (**2l**), 2-F (**2m**), 4-OCF_3 (**2n**), 2-Br (**2o**)

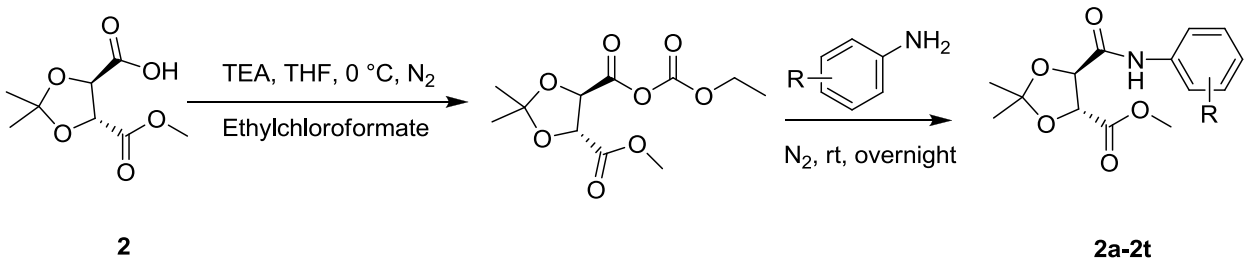
R = 4-Br (**2p**), 2,4-dimethyl (**2q**), 2,6-diethyl (**2r**), 4-Br-2-CH_3 (**2s**), 2-Cl-4-CH_3 (**2t**)

Scheme 2.2a: Synthesis of chiral amides (**2a-2t**).

The amide bond formation was carried out using DCC[150,56] as dehydrating agent with catalytic amount of DMAP as activator. The reaction of compound (**2**) with anilines having electron donating groups was almost complete (reaction time 4-6 hours) as followed through TLC. Anilines with electron withdrawing groups showed some unreacted amines and compound (**2**) (4-6 hours); when reaction time was increased from 4-12 hours the unreacted amines and compound (**2**) disappeared as indicated by TLC. The yield of the products was affected by the removal of solvent insoluble DCU due to multiple filtrations, extraction with water and column chromatography.

2.3b Method B: Synthesis of chiral amides (2a-2t)

In order to improve the yields of the synthesized amides (**2a-2t**), another reported method was adapted. This method was first reported by Vaughan[57-58] and was based on the mixed anhydride method (Scheme 2.2b).



2 **2a-2t**

R = 2-CF_3 **(2a)**, 3-CF_3 **(2b)**, 4-CF_3 **(2c)**, 2-OCH_3 **(2d)**, 3-OCH_3 **(2e)**, 4-OCH_3 **(2f)**, 2-CH_3 **(2g)**

R = 3-CH_3 **(2h)**, 4-CH_3 **(2i)**, 2-Cl, **(2j)**, 3-Cl **(2k)**, 4-Cl **(2l)**, 2-F **(2m)**, 4-OCF_3 **(2n)**, 2-Br **(2o)**

R = 4-Br **(2p)**, 2,4-dimethyl **(2q)**, 2,6-diethyl **(2r)**, 4-Br-2-CH_3 **(2s)**, 2-Cl-4-CH_3 **(2t)**

Scheme 2.2b: Synthesis of chiral amides (**2a-2t**).

The reaction of compound (**2**) with ethylchloroformate under basic condition resulted in a white mass formation. The intermediate mixed anhydride was found difficult to isolate in pure form due its instability and therefore substituted anilines were added immediately without further purification. Formation of *in situ* mixed anhydride and subsequent reaction with amines resulted in 79-93 % yields of the compounds.

All the synthesized compounds were characterized by spectroscopic techniques. The IR spectral data of amides **(2a-2t)** exhibited characteristic N-H stretching bands in the range of 3405-3230, CO (ester) in 1754-1740 while CO (amide) in 1706-1693 cm^{-1}. ^{1}H NMR spectral data shows the appearance of broad singlets for N-H protons in the range of 8.40-7.92 ppm with integration of one proton each. The aromatic protons showed doublets in *para* substituted anilines while *ortho* and *meta* substituted anilines showed multiplets and singlets respectively. In ^{13}C NMR, peaks in the range of 172.5-167.7 and 170.9-168.3 ppm were assigned to CO (amide) and CO (ester) respectively; the aromatic carbons appeared in 142.3-120.1 ppm. Elemental analysis of the synthesized compounds, described in the experimental protocol further supported the structures of all the compounds. Electron impact mass spectrometry (EI-MS) also confirmed the synthesized amides, the molecular ion peaks (m/z) for **2a**, **2d**, **2g** and **2j** appeared in 347.1, 309.0, 293.1 and 313.1 respectively which were the corresponding molecular weights of the compounds. Finally the amide bond formation was supported by two of the crystal structures for (4*R*,5*R*)-Methyl-2,2-dimethyl-5-(*O*-tolylcarbamoyl)-1,3-dioxolane-4-carboxylate (**2g**) and (4*R*,5*R*)-Methyl-5-((2,6-diethylphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (**2r**) by X-ray crystallography as shown in Figure 2.2 and Figure 2.3.

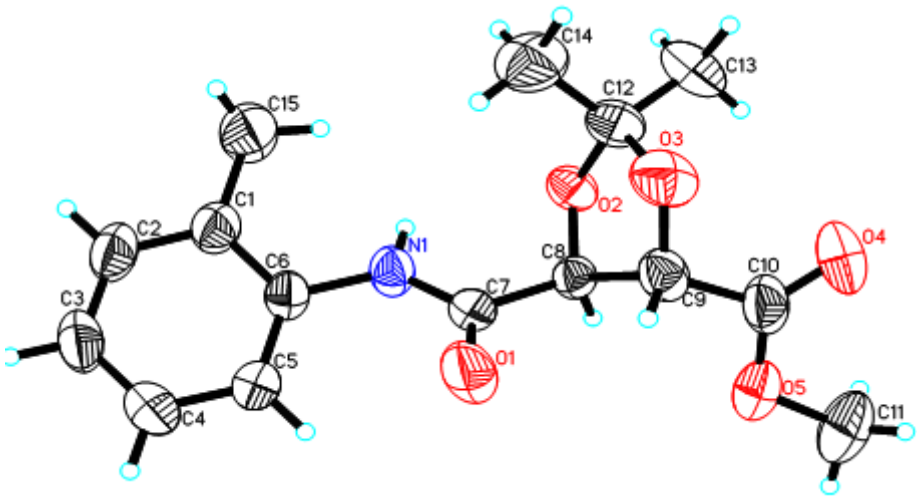


Figure 2.2: Crystal structure of (4*R*,5*R*)-Methyl 2,2-dimethyl-5-(*O*-tolylcarbamoyl)-1,3-dioxolane-4-carboxylate (**2g**).

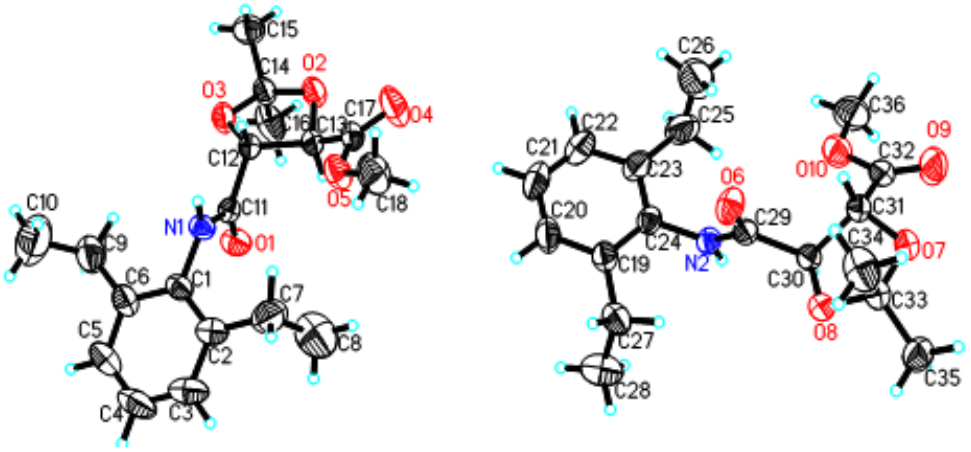
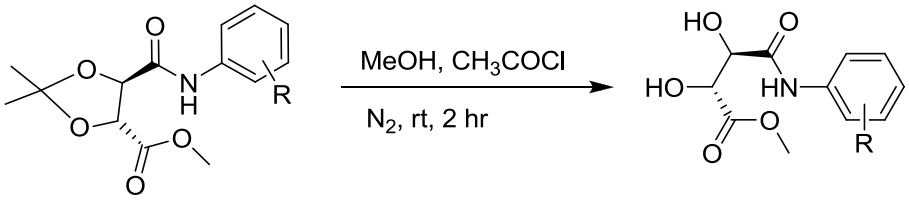


Figure 2.3: Crystal structure of (4*R*,5*R*)-Methyl-5-((2,6-diethylphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (**2r**).

2.4 Deprotection of 1,3-dioxolanes

For the deprotection of 1,3-dioxolanes in amides (**2a-2t**) methanol and acetyl chloride were used (Scheme 2.3).



2a-2t **3a-3t**

Scheme 2.3: deprotection of 1,3-dioxolanes.

First the amide was dissolved in methanol and freshly distilled acetyl chloride was added drop wise with gentle stirring and cooling. The controlled amount of HCl generated *in situ* is enough to deprotect the acid labile 1,3-dioxolanes. All the compounds were purified by column chromatography. The deprotection was confirmed by spectral analysis. IR spectral data of the compounds (**3a-3t**) exhibited characteristic OH stretchings in the range of 3479-3330 in addition to N-H stretching from 3361-3178 cm^{-1}. ^{1}H NMR spectral data shows the disappearance of signals for six methyl protons and appearance of either doublet of the doublets 5.99-5.48 ppm

(**3a, 3b**) or doublets in the range of 4.71-4.66 ppm (**3g, 3h**) for the CH protons. The OH protons appeared as doublets or broad singlets. In ^{13}C NMR, peaks due to quaternary and two methyl carbons of the 1,3-dioxolane also disappeared which confirm that deprotection was successful. Elemental analysis of the deprotected amides, described in the experimental protocol further supported the structures of amides. EI-MS also confirmed the deprotection, the molecular ion peaks (m/z) for **3a**, **3d**, **3g** and **3j** appeared in 307.1, 269.1, 253.1 and 273.1 respectively which were the exact molecular weights of the compounds. The deprotection was further supported by the crystal structure for **(**2*R*,3*R*)-Methyl-4-(*p*-toluidino)-2,3-dihydroxy-4-oxobutanoate (**3i**) by X-ray crystallography (Figure 2.4).

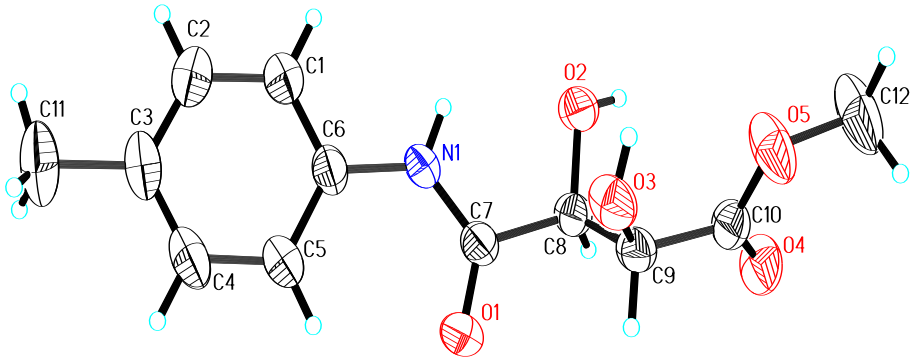
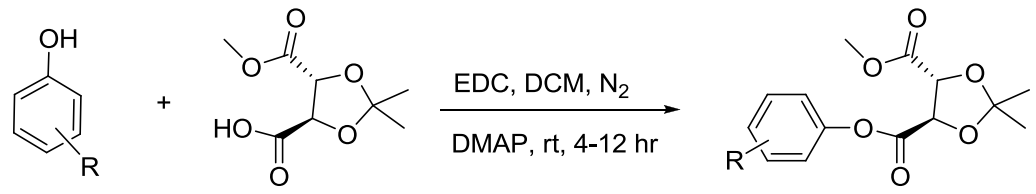


Figure 2.4: Crystal structure of (2*R*,3*R*)-Methyl-4-(*p*-toluidino)-2,3-dihydroxy-4-oxobutanoate (**3i**).

2.5 Synthesis of monoaryl esters (4a-4h)

In contrast to the availability of dialkyl tartrates, which are readily synthesized by Fischer esterification of tartaric acid or transesterification of a tartrate with the use of excess alcohols, di or monoaryl tartrates remained until now virtually unknown. We tried many synthesis procedures for acid activation toward the synthesis of aryl esters; however, they did not afford any aryl esters on reaction with tartaric acid. Cysewski *et. al* have reported the synthesis of diaryl tartrates from dimethyl-2,3-*O*-benzylidene-*L*-tartrate and addressed the difficulties for direct esterification of tartaric acid with aryl alcohols.[151]

Herein we report a facile synthesis of monoaryl ester derivatives of *L*-tartaric acid. The monoester **2** was coupled with different substituted phenols using EDC as dehydrating agent to afford compounds (**4a-4h**) in 55-79 % yields (Scheme 2.4).



2 **4a-4h**

R = H (**4a**), 4-Me (**4b**), 3-Br (**4c**), 3-Cl-4-Me (**4d**)

R = 3-Br-4-Me (**4e**), 3-Me (**4f**), 2-Br (**4g**), 2,4-di-Cl (**4h**)

Scheme 2.4: Synthesis of monoaryl esters (**4a-4h**).

All the compounds were purified and characterized by spectral analysis.

IR spectral data of the monoaryl esters (**4a-4h**) exhibited characteristic CO stretching bands in the range of 1756-1743 and C-O-C in 1324-1311 cm^{-1}. ^{1}H NMR spectral data shows doublets in *para* substituted phenol (**4b**) while *ortho* and *meta* substituted phenols (**4g, 4f**) showed multiplets and singlets respectively. In ^{13}C NMR, peaks in 170.7-169.3 and 168.2-167.7 ppm were assigned to CO (aryl) and CO (methyl) respectively; the aromatic carbons appeared in the range of 150.8-121.8 ppm. Elemental analysis of these compounds, described in the experimental protocol further supported the structures of all the compounds. Formation of monoaryl esters was also confirmed by high resolution mass analysis. Observed HRMS-ESI of the $[M+Na]^{+}$ and calculated values were in good agreement with each other. Finally the synthesis of monoaryl ester derivatives were supported by the crystal structure of (4*R*,5*R*)-4-(3-Bromo-4-methylphenyl)-5-methyl-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (**4e**) by X-ray crystallography (Figure 2.5).

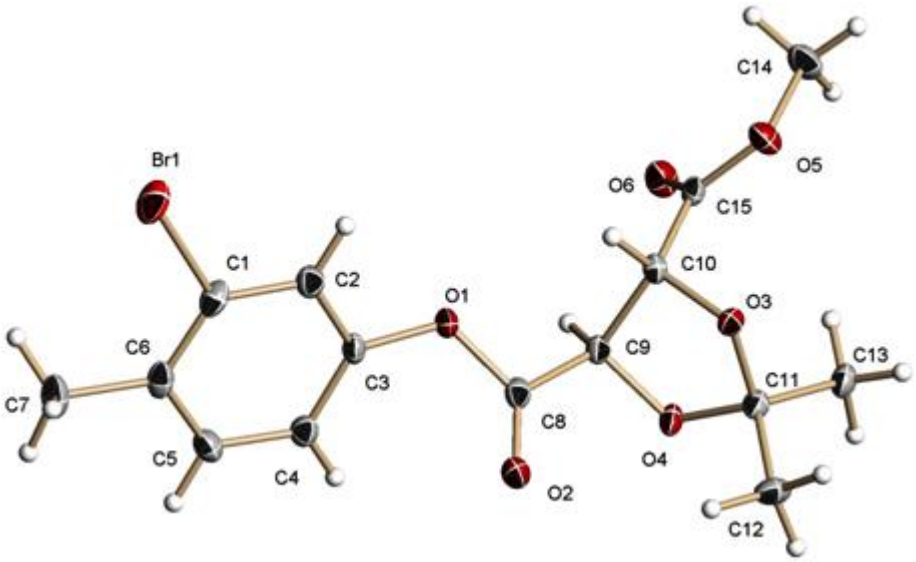


Figure 2.5: **Crystal structure of (4*R*,5*R*)-4-(3-Bromo-4-methylphenyl)-5-methyl-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (**4e**). Thermal ellipsoids are shown at the 50% probability level.**

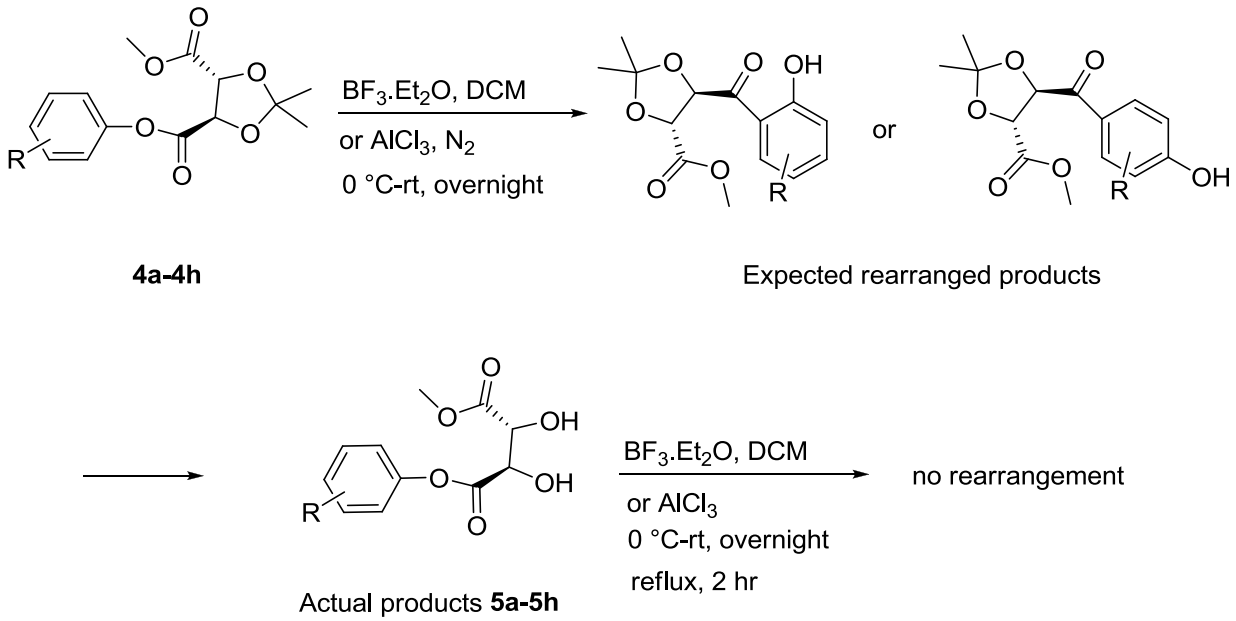
On the basis of IR, ^{1}H NMR, ^{13}C NMR, HRMS-ESI and single crystal X-ray analysis it was confirmed that the monoaryl ester derivatives were synthesized successfully.

2.6 Attempted Fries rearrangement of monoaryl esters (4a-4h)

The selective Fries rearrangement of esters of aromatic alcohols serves as a valuable synthesis step in the production of industrial pharmaceuticals, dyes and agrochemicals.[152] The reaction involves acylium ion intermediates that are generated from the ester by interaction with an acid catalyst. More specifically, the Fries rearrangement of phenyl acetate (PAc) yields *ortho*- and *para*-hydroxyacetophenones (*o*-HAP and *p*-HAP) which are very valuable precursors in the pharmaceutical industry, being this reaction the first step of the Hoechst Celanese manufacturing process of paracetamol.[153] Classical Fries rearrangement are generally catalyzed by acids like hydrofluoric acid (HF),[154] the most frequently used $AlCl_3$,[155] BF_3,[156] $TiCl_4$ or $SnCl_4$.[157]

In an effort to generate new C-C bond and chiral substrates, monoaryl esters (**4a-4h**) were processed following the above mentioned literature procedures for the Fries rearrangement.

The Fries rearrangement of compound (**4a**) was first tried using $BF_3.Et_2O$ in DCM (Scheme 2.5).



Scheme 2.5: Attempted Fries rearrangement of monoaryl esters (**4a-4h**).

After overnight stirring and purification of new product as indicated by TLC, unfortunately no rearrangement occurs instead we got the deprotected product which was confirmed by ^{1}H NMR.

The reaction was then tried with $AlCl_3$. After purification and characterization with ^{1}H NMR, we got compound **4a** with free diol. The reactions were then tried for rest of the compounds (**4b-4h**) using different Lewis acids but all the products obtained were only the deprotected analogues and no rearrangement as confirmed by spectral analysis. The deprotected compounds (**5a-5h**) obtained were also tried using the same reaction conditions and with additional reflux for 2 hours but no reactions occur.

All the deprotected compounds were purified and characterized by spectral analysis.

IR spectral data of the compounds (**5a-5h**) showed characteristic OH stretching bands in the range of 3548-3508, CO at 1749-1743 and C-O-C in 1323-1312 cm^{-1}. ^{1}H NMR spectral data shows the disappearance of signals for six methyl protons. The OH protons appeared as broad singlets in the range of 3.28-3.24 ppm respectively. In ^{13}C NMR, peaks due to quaternary and two methyl carbons of the 1,3-dioxolane also disappeared which confirm only the deprotection of 1,3-dioxolane and no

rearrangement. Elemental analysis of the deprotected compounds, described in the experimental protocol further supported the structures of all the compounds.

2.7 Synthesis of glycopyranosyl amines

Glycopyranosyl amines are very attractive precursors for glycan derivatization. They have a primary amine moiety at the reducing terminus, allowing for selective derivatization with a variety of acetylated reagents.[158] Typically, carbohydrates are reacted with an excess of ammonium carbonate in anhydrous solvent to produce glycosyl amines (Kochetkov amination).[75] However, long incubation time (e.g. up to 5 days) and laborious purification procedure limit the application of Kochetkov amination.

After successful synthesis of amides with available substituted anilines, we prepared different glycopyranosyl amines from monosaccharides. Our aim was also to prepare different glycopyranosyl amides using monoester of *L*-tartaric acid. In our research work, commercially available monosaccharides namely D-glucose, D-galactose, D-mannose, D-glucosamine hydrochloride and D-galactosamine hydrochloride were selected for the synthesis of glycopyranosyl amines.

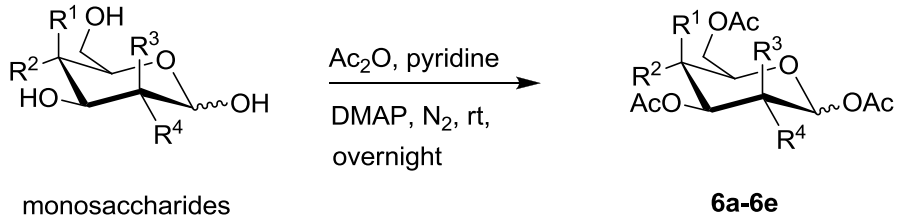
The synthesis was started from acetylation of hydroxyl groups in these monosaccharides followed by anomeric derivatization like bromination, azide formation and reduction of azides into the corresponding amines.

2.7.1 Synthesis of acetylated monosaccharides (6a-6e)

One of the most commonly used techniques for the protection of hydroxyl groups in the synthesis of oligosaccharides is acetylation. In carbohydrate chemistry, acetylated sugars are inexpensive and useful intermediates towards the synthesis of several natural products containing glycosides, oligosaccharides and other glycoconjugates.[159]

The most often used protocol for the acetylation of sugar alcohols employes a large excess of acetic anhydride and pyridine as solvent despite its toxicity and unpleasant odor.[160-161] In some cases, pyridine derivatives, such as, DMAP and 4-pyrrolidinopyridine have been added to the reaction as co-catalyst to speed up the acetylation reaction.[162-163]

The acetylation of monosaccharides was carried out by using acetic anhydride in pyridine and catalytic amount of DMAP to afford acetylated compounds (**6a-6e**) in 70-78 % yields
(Scheme 2.6).



monosaccharides

6a-6e

(a) D-Glucose

(b) D-Galactose

(c) D-Mannose

(d) D-Glucosamine hydrochloride

(e) D-Galactosamine hydrochloride

(a) R^1, R^3 = H; R^2, R^4 = OAc

(b) R^1, R^4 = OAc; R^2, R^3 = H

(c) R^1, R^4 = H; R^2, R^3 = OAc

(d) R^1, R^3 = H; R^2 = OAc; R^4 = NHAc

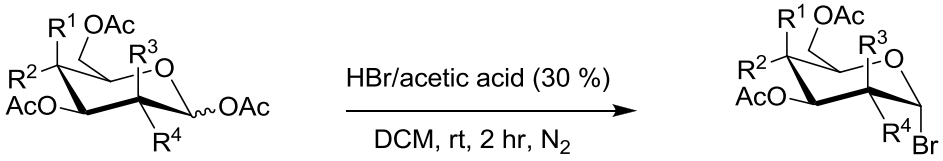
(e) R^1 = OAc; R^2, R^3 = H; R^4 = NHAc

Scheme 2.6: Synthesis of acetylated monosaccharides (**6a-6e**).

All the acetylated compounds were purified and characterized by spectral analysis.
IR spectral data of the compounds (**6a-6e**) showed characteristic CO stretching in 1738-1733 in addition to CH stretching in 2989-2966 cm^{-1}. ^1H NMR confirmed both the formation of α and β anomers in 3: 1. The anomeric protons appeared as doublets in the range of 6.35-6.31 ppm with coupling constant of 4.0-3.7 Hz for α anomers and 5.66-5.58 ppm with coupling constant of 8.4-8.0 Hz for β anomers respectively. 5 singlets observed in the range of 2.21, 2.19, 2.13, 2.11, 2.10-2.20, 2.16, 2.10, 1.91, 1.80 ppm with integration of 3 protons each for 5 acetyl CH_3 groups. In ^{13}C NMR, peaks at 170.2, 170.3, 169.7, 168.5, 168.2 ppm were assigned to CO (acetyl), the anomeric carbons appeared in the range of 89.8-89.2 ppm while the methyl carbons in 20.3, 19.7, 19.5, 18.9 ppm respectively.

2.7.2 Synthesis of glycopyranosyl bromides (7a-7e)

The bromination of anomeric mixture of acetylated monosaccharides (**6a-6e**) was carried out using HBr/Acetic acid (30 %)[164] in DCM (Scheme 2.7).



6a-6e **7a-7e**

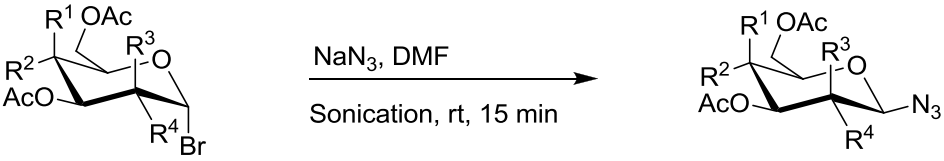
Scheme 2.7: Synthesis of glycopyranosyl bromides (**7a-7e**).

The thermodynamically more stable α-anomers, were synthesized in 69-88 % yields as confirmed by ^{1}H NMR.

IR spectral data of the compounds (**7a-7e**) exhibited the characteristic C-Br stretching bands in the range of 559-552 in addition to CO stretching in 1745-1732 cm^{-1}. ^{1}H NMR spectral data shows characteristic doublets for the anomeric protons in the range of 6.62-6.52 ppm with coupling constant of 4.0-3.7 Hz which confirm the formation of α anomers. 4 singlets in the range of 2.09, 2.02, 1.95, 1.91 ppm with integration of 3 protons for each singlets were assigned to 4 acetyl CH_3 groups which further supported the replacement of anomeric acetyl group with bromine. In ^{13}C NMR, peaks at 170.6, 169.4, 169.2, 169.1 ppm were assigned to CO and the anomeric carbons appeared in the range of 86.9-86.2 ppm.

2.7.3 Synthesis of glycopyranosyl azides (8a-8e)

The glycopyranosyl azides (**8a-8e**) were prepared from tetra acetylated glycopyranosyl bromides and NaN_3 in DMF under sonication[165] (Scheme 2.8).



7a-7e **8a-8e**

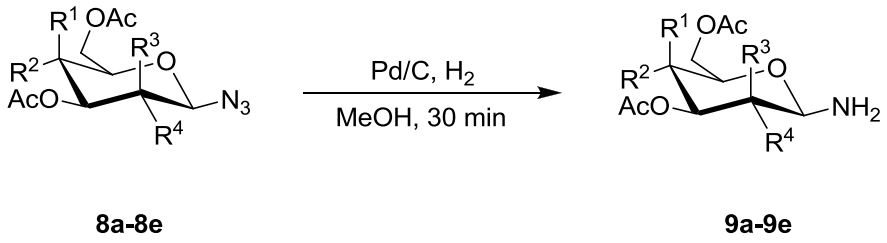
Scheme 2.8: Synthesis of glycopyranosyl azides (**8a-8e**).

IR spectral data of the compounds (**8a-8e**) showed (N_3) stretching bands in the range of 2146-2117 cm^{-1}. ^{1}H NMR spectral data showed doublets for the anomeric protons

in the range of 5.56-5.26 ppm with coupling constant of 9.8-9.5 Hz which also confirm the formation of β anomers. The replacement involves inversion of configuration at the anomeric site and thus the α-glycopyranosyl bromides (**7a-7e**) gave β-glycopyranosyl azides (**8a-8e**) in 77-90 % yields. In ^{13}C NMR the anomeric carbons appeared in the range of 87.5-87.3 ppm respectively. Elemental analysis of the synthesized compounds further supported the structures of all the compounds.

2.7.4 Synthesis of glycopyranosyl amines (9a-9e)

glycopyranosyl amines (**9a-9e**) were synthesized from glycopyranosyl azides using pd/C[165] (10 %) under hydrogen atmosphere in 61-79 % yields (Scheme 2.9).



8a-8e **9a-9e**

Scheme 2.9: Synthesis of glycopyranosyl amines (**9a-9e**).

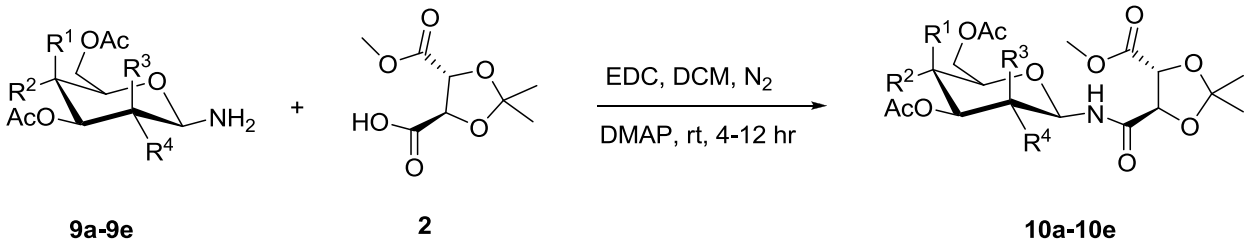
IR spectral data of the compounds (**9a-9e**) showed characteristic (NH_2) stretching bands ranging from 3418-3333 cm^{-1} and disappearance of (N_3) absorptions. ^1H NMR spectral data showed doublets for the anomeric protons in the range of 5.47-542 ppm with coupling constant in 8.9-8.4 Hz which confirm the formation of β anomers. The heterogeneous reduction of β-glycopyranosyl azides gave the β-glycopyranosyl amines with retention of configuration at the anomeric site. In ^{13}C NMR the anomeric carbons appeared in the range of 85.3-84.5 ppm. Elemental analysis further supported the structures of all the synthesized glycopyranosyl amines.

2.8 Synthesis of glycopyranosyl amides (10a-10e)

glycopyranosyl amides represent a long known class of carbohydrate derivatives readily available by acetylation of glycosylamines[166] or more advantageously from glycosyl azides and carboxylic acids or their activated derivatives via an *N*-glycosyl iminophosphorane intermediate (Staudinger reaction).[167] Gyorgydeak *et al.,* reported

the synthesis of several glycopyranosyl amides from glycopyranosyl azides using carboxylic acids and anhydrides via a PMe_3 mediated Staudinger protocol.[168]

After having glycopyranosyl amines in hand, the amino and hydroxyl termini from glycopyranosyl amines and monoester were coupled to get glycopyranosyl amides (**10a-10e**) in 65-72 % yields (Scheme 2.10).



Scheme 2.10: Synthesis of glycopyranosyl amides (**10a-10e**).

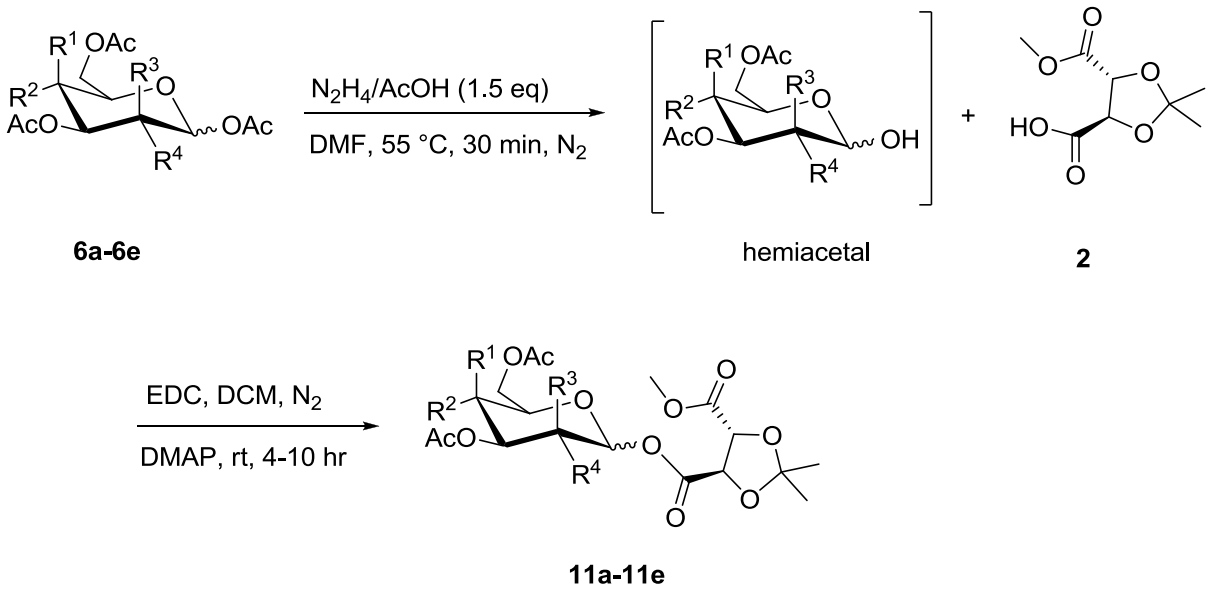
The synthesized compounds were purified and characterized by spectral analysis.

IR spectral data of the compounds (**10a-10e**) exhibited the appearance of characteristic (NH) stretching bands in the range of 3347-3331 cm^{-1} and dissappearence of NH_2 stretching. Two CO stretchings ranging from 1742-1736 and 1701-1692 cm^{-1} were assigned to CO (ester) and CO (amide) respectively. ^1H NMR spectral data shows characteristic doublets for the NH protons in the range of 7.69-7.18 ppm with coupling constant of 9.6-9.3 Hz. The anomeric protons appeared as pseudotriplets in the range of 5.42-5.36 ppm with coupling constant of 12.2-6.5 Hz which confirm the formation of β-anomer. In ^{13}C NMR, peaks ranging from 172.8-171.2 ppm were assigned to CO (amide) and 170.9-170.2 ppm to CO (ester) respectively. Elemental analysis of the glycopyranosyl amides (**10a-10e**), described in the experimental protocol also confirmed the structures of the compounds. The exact mass of the glycopyranosyl amides were confirmed by HRMS-ESI the observed and calculated $[M+Na]^+$ were in good agreement with each other.

On the basis of IR, ^1H NMR, ^{13}C NMR and HRMS-ESI it was confirmed that the glycopyranosyl amides were synthesized successfully.

2.9 Synthesis of glycopyranosides (11a-11e)

The glycopyranosides **(11a-11e)** were synthesized in 63-74 % yields, starting from (**6a-6e**) (Scheme 2.11).



Scheme 2.11: Synthesis of glycopyranosides (**11a-11e**).

The anomeric acetyl group was hydrolyzed by using hydrazinium acetate[169-170] in DMF; the resulting hemiacetal was washed by combine work up and used without further purification. To the crude hemiacetal, monoester (**2)** was added using EDC.

All the synthesized glycopyranosides were purified by column chromatography and characterized by spectroscopic techniques. IR spectral data of the compounds (**11a-11e**) showed characteristic (CO) stretching bands ranging from 1745-1739 cm^{-1} in addition to C-O-C stretchings in 1366-1356. The NH stretching bands (**11d-11e**), appeared in 3348-3342 cm^{-1}. ^{1}H-NMR spectral data showed doublets (**11d-11e**), for the NH protons in the range of 7.87-7.86 ppm with coupling constant of 9.7-9.5 Hz. Both α and β anomers were synthesized in 1: 3 except compound **11c** for which α and β ratio was 1,1 as confirmed by ^{1}H NMR. The anomeric protons appeared as doublets in the range of 5.67-5.43 ppm with coupling constant of 8.3-8.0 Hz for β-anomers and in 6.52-6.42 ppm with coupling constant of 4.0-3.7 Hz for the α-anomers respectively. The coupling constant of anomeric hydrogen for mannopyranoside (**11c**) was 4.0 Hz in both the anomer dut to axial equatorial and equatorial equatorial interaction. In ^{13}C NMR peaks at 173.3 and 172.6 ppm were assigned to CO (ester). Elemental analysis of the compounds also confirmed all the synthesized glycopyranosides. The exact mass of the compounds was confirmed by HRMS-ESI, the observed and calculated $[M+Na]^{+}$ described in the experimental protocol, were in agreement with each other.

finally the synthesis of glycopyranosides was supported by one of the crystal structure for α-anomer, (4*R*,5*R*)-4-Methyl-5-((2*R*,3*R*,5*R*,6*R*)-3,4,5-triacetoxy-6-(acetoxymethyl)tetrahydro-2H-pyran-2-yl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (**11c**) by X-ray crystallography (Figure 2.6).

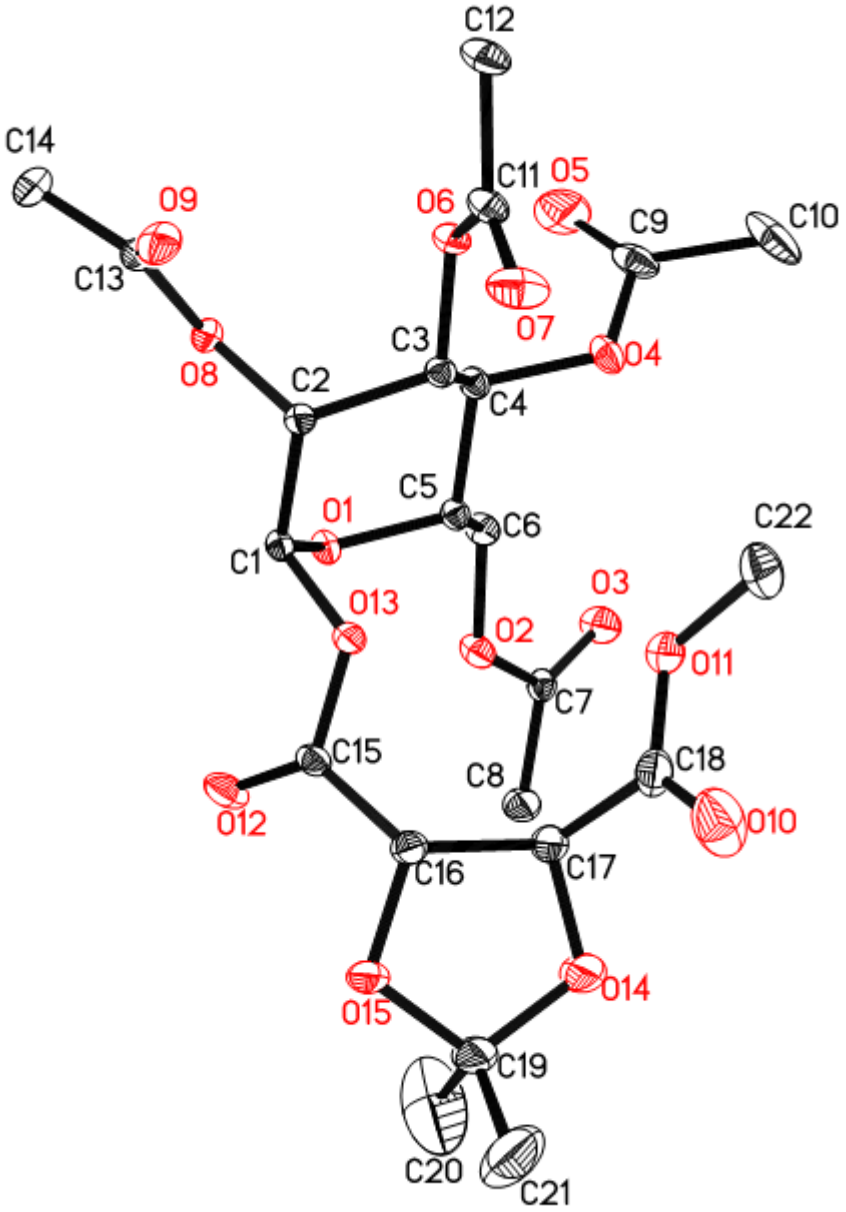


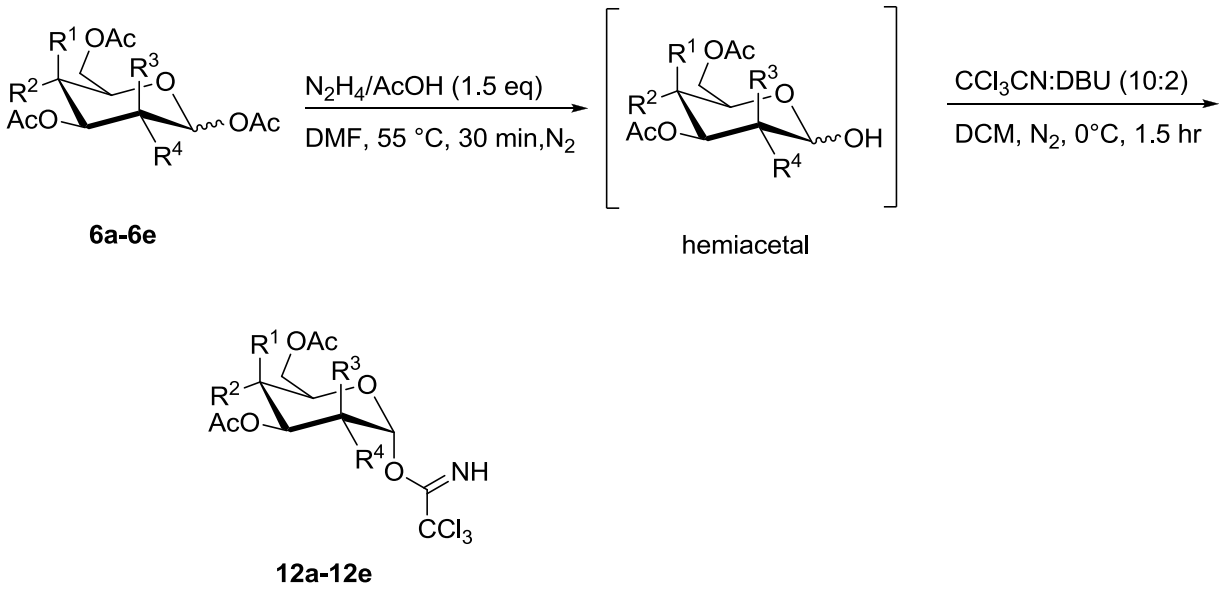
Figure 2.6: Crystal structure of α-anomer, (4*R*,5*R*)-4-Methyl-5-((2*R*,3*R*,5*R*,6*R*)-3,4,5-triacetoxy-6-(acetoxymethyl)-tetrahydro-2H-pyran-2-yl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (**11c**).

On the basis of IR, ^{1}H NMR, ^{13}C NMR, HRMS-ESI and X-ray crystallography it was confirmed that the glycopyranosides (**11a-11e**) were synthesized successfully.

2.10 Synthesis of glycopyranosyl α-trichloroacetimidates (12a-12e)

In glycosyl trichloroacetimidates the anomeric oxygen atom has been derivatized with a group that is easily removed i.e a good leaving group and this makes glycosyl trichloroacetimidates good glycosyl donors. They can be activated by Lewis acids such as borontrifluoride etherate complex $BF_3.Et_2O$ or TMSOTf for glycosylation reactions.

Different glycopyranosyl α-trichloroacetimidates **(12a-12e)** were prepared in 75-90 % yields, starting from (**6a-6e**) (Scheme 2.12).



Scheme 2.12: Synthesis of glycopyranosyl α-trichloroacetimidates (**12a-12e**).

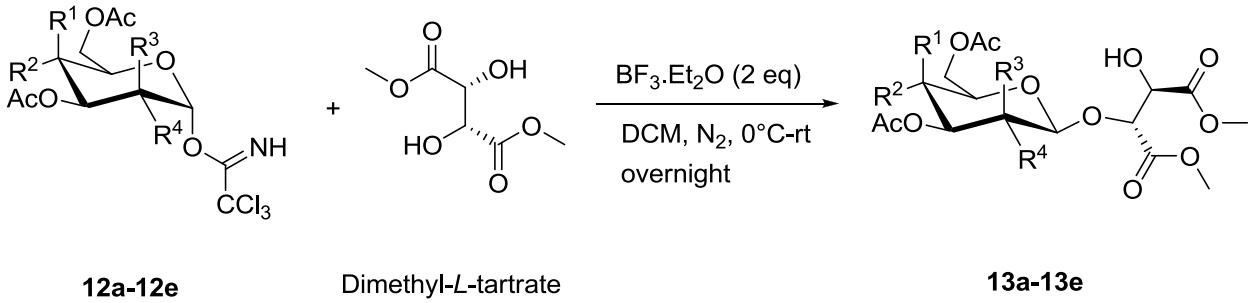
The synthesis of glycopyranosyl α-trichloroacetimidates were started with chemoselective removal of the acetyl groups in compounds (**6a-6e**) by hydrazinium acetate. The resultant hemiacetals were treated with large excess of trichloroacetonitrile using DBU[169-170] as catalyst. The thermodynamically more stable α-anomers were synthesized. The corresponding β-anomers were not detected by ^{1}H NMR.

^{1}H NMR spectral data showed broad singlets in the range of 8.63-8.59 ppm with integration of one proton for the NH groups. The anomeric hydrogens appeared as doublets ranging from 6.62-6.55 ppm with coupling constant of 4.0-3.7 Hz. These

coupling constants were in the range of axial equatorial and equatorial equatorial configuration of H-1 and H-2 and therefore an α-trichloroacetimidate is assigned. In ^{13}C NMR peaks ranging from 161.6-160.3 ppm were assigned to O-C-NH of acetimidates. The anomeric carbons appeared in the range of 93.5-91.4 ppm respectively.

2.11 Synthesis of glycoconjugates (13a-13e)

After synthesizing successfully the glycopyranosyl α-trichloroacetimidates,[169] they were used further as glycopyranosyl donors. The glycoconjugates (**13a-13e)** were prepared in 59-70 % yields using dimethyl-*L*-tartrate as acceptor (Scheme 2.13). Both the donors and acceptor were mixed in 1,1 ratio.



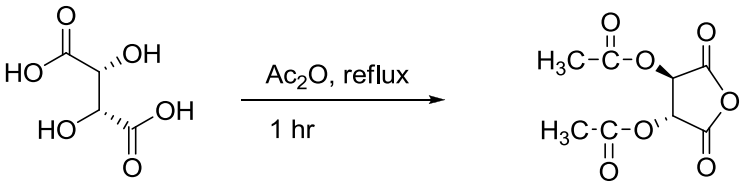
Scheme 2.13: Synthesis of glycoconjugates (**13a-13e**).

The synthesis of glycocongugates was supported by spectral analysis. IR data of the compounds **(13a-13e)** showed (OH) stretching bands ranging from 3423-3411 in addition to CO stretching in 1746-1732, C-O-C stretching in 1336-1313 cm^{-1} respectively. ^{1}H NMR spectral data shows characteristic doublets for the NH protons (**13d-13e**), in the range of 6.98-6.93 ppm with coupling constant of 9.5 Hz. The anomeric protons appeared as doublets ranging from 5.69-5.46 ppm with coupling constant of 8.3 Hz which confirm the formation β anomers. The α-anomers were not detected by ^{1}H NMR. The monoglycoconjugates formation were supported by the appearance of doublet of the doublets in the range of 4.77-4.72 ppm with coupling constant of 9.6, 2.4 Hz for the chiral methine protons of tartrate with one OH group. Another doublet appeared in the range of 4.66-4.61 ppm with coupling constant of 2.4 Hz for the second methine proton. In ^{13}C NMR peaks at 172.3-171.4 ppm were assigned to CO (ester). The anomeric carbons appeared in the range of 96.5-95.9 ppm

respectively. Elemental analysis of the synthesized compounds further supported the structures of all the compounds.

2.12 Synthesis of diacetyl-*L*-tartaric acid anhydride (14)

Diacetyl *L*-tartaric acid anhydride is not commercially available however it was synthesized from *L*-tartaric acid and acetic anhydride[171] under reflux in 85 % yield (Scheme 2.14).



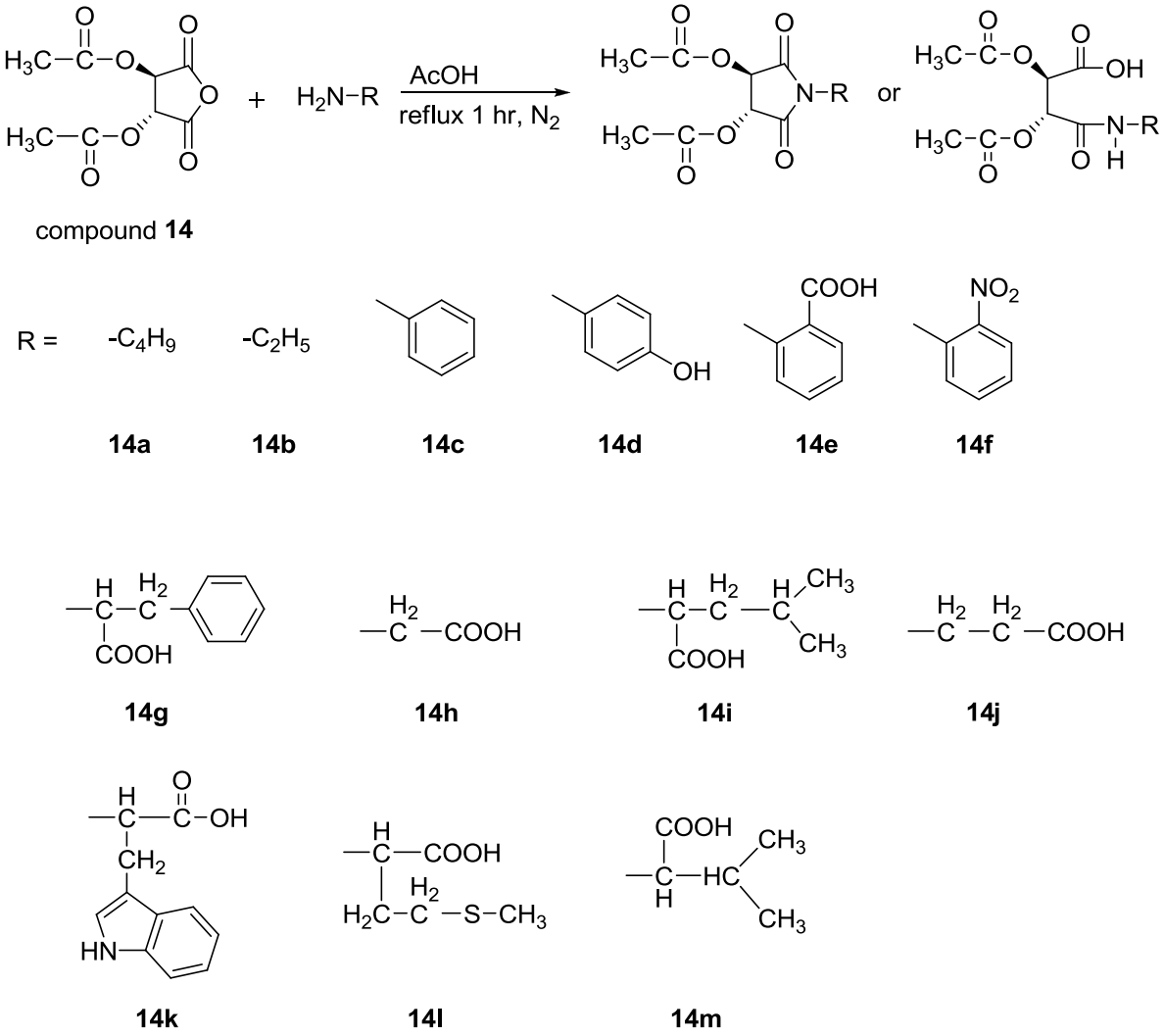
L-tartaric acid **14**

Scheme 2.14: Synthesis of diacetyl *L*-tartaric acid anhydride (**14**).

The compound was purified and characterized by spectral analysis.
The IR spectral data of compound (**14**) showed stretching bands at 2939, 1827 and 1761 cm^{-1}. These absorptions were assigned to C-H, CO (anhydride) and CO (ester) respectively. In ^{1}H NMR spectrum a singlet at 2.25 ppm with integration of six protons was assigned to two CH_3 groups, singlet at 5.69 ppm with integration of two protons was attributed to two methine hydrogen. In ^{13}C NMR, peak at 169.7 ppm was assigned to CO (ester) and 163.3 to CO (anhydride), two peaks at 72.1 and 20.2 ppm were assigned to methine and methyl carbons respectively.

2.13 Synthesis of chiral imides and amides (14a-14n)

In our continuation of studies towards the development of new routes for the synthesis of organic compounds,[172] we herein report a facile synthesis of chiral imides[173] and amides (**14a-14n**) by using compound (**14**), aliphatic, substituted primary aromatic amines and amino acids (Scheme 2.15).



Scheme 2.15: Synthesis of chiral imides and amides (**14a-14n**).

In our studies we found that the stereoelectronic factors determine the formation of amides or imides. *ortho*-substituted aromatic primary amines only give amides irrespective of the nature of substituent which suggests that once the amide is formed the steric hindrance offered by the *ortho*-substituent prevents the ring closure to yield the imide. On the other hand when the same substituent is at the *para*- position they exclusively gave imides as major product which supports our argument given above. The difference in the nucleophilicity of amino group may be rationalized on electronic and steric factors, respectively. It is assumed that the reaction follows the following pathway.

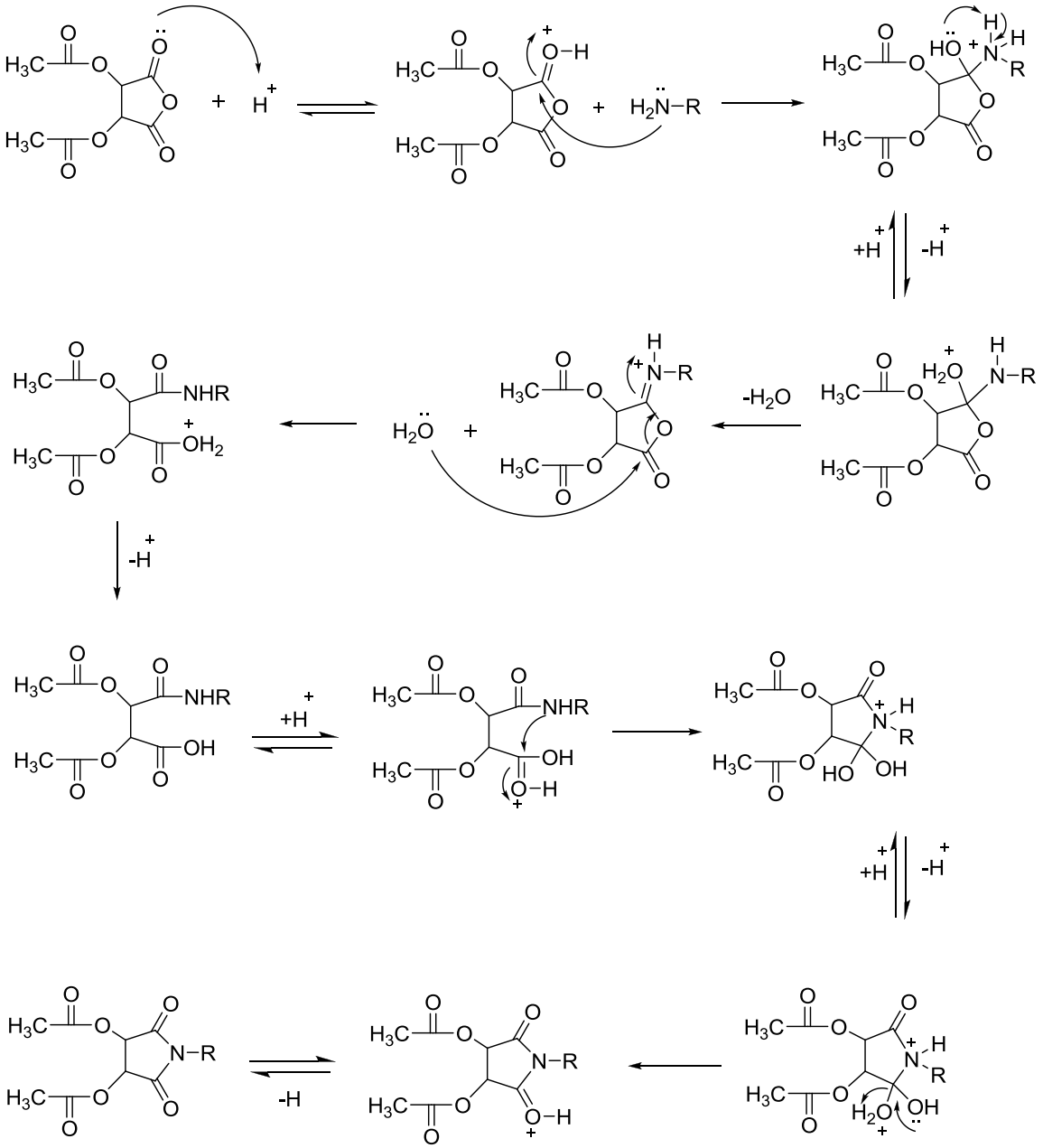


Figure 2.7: Mechanism of imide synthesis.

All the synthesized imides and amides were purified by column chromatography and characterized by spectral analysis. The IR spectral data of the imides **14a-14d** and **14g-14m** showed characteristic bands in the range of 1740-1735, 1780-1670 and sharp bands ranging from 2963-2874 cm^{-1}. These absorptions were assigned CO (ester), CO (imide), and C-H respectively.

In ^{1}H NMR spectrum, singlets ranging from 2.25-2.20 ppm with integration of six protons were assigned to two CH_3 of acetoxy groups, singlets in the range of 6.39-5.50 ppm with integration of two protons were assigned to two methine hydrogen. In ^{13}C NMR spectrum, peaks in the range of 178.9-169.9 ppm were assigned to CO of ester groups while peaks for CO of imides appeared in 170.1-168.5 ppm respectively. The methine carbons appeared in the range of 72.8-72.0 ppm. Elemental analysis further supported the structures of the imides.

The IR spectral data of the amides **14e-14f** and **14n** exhibited characteristic stretching bands in the range of 1753-1743, 1730-1725, 1690-1670, 3511-3410, and broad bands in 3250-2615 cm^{-1}. These absorptions were assigned to CO (ester), CO (acid), CO (amide), -NH and OH respectively. In ^{1}H NMR spectrum singlets were observed in the range of 2.30-2.05 ppm with integration of three protons for methyl groups. Two doublets in the range of 5.86-5.60 ppm having integration of one proton for each with coupling constants of 7.0 and 7.2 Hz were assigned to two methine hydrogen respectively. In ^{13}C NMR peaks in the range of 169.4-167.7 ppm were attributed to CO (ester). Similarly two peaks in the range of 72.4-72.0 and 71.2-70.9 ppm were attributed to two methine carbons respectively.

Conclusion

Monoester was synthesized in good yield (79 %) starting from *L*-tartaric acid. Chiral amides were prepared from monoester of *L*-tartaric acid and substituted anilines in good to excellent yields (79-93 %). Deprotection of 1,3-dioxolanes were carried out successfully under mild conditions. Monoaryl esters were prepared from monoester of *L*-tartaric acid and substituted phenols in good yields (55-79 %). Fries rearrangement of monoaryl esters was attempted using different reaction conditions.

Glycopyranosyl amines were synthesized from monosaccharides by the successive acetylation, bromination, azide formation and reduction of azides into amines. Glycopyranosyl amides were prepared from monoester of *L*-tartaric acid and glycopyranosyl amines in good yields (65-72 %). *O*-Linked glycopyranosides were synthesized by the reaction of acetylated hemiacetals and monoester of *L*-tartaric acid in good yields (63-74 %). Glycopyranosyl α-trichloroacetimidates were synthesized from the corresponding acetylated hemiacetals in good to excellent yields (75-90 %). Synthesis of glycoconjugates was carried out by using glycopyranosyl α-trichloroacetimidates and dimethyl-*L*-tartrate in appreciable yields (59-70 %).

Chiral imides and amides were synthesized in 65-80 % yields from diacetyl-*L*-tartaric acid anhydride and different aliphatic and aromatic amines and amino acids.

Different series of the synthesized compounds were evaluated for different biological activities.

3.1 General experimental

All chemicals were of highest purity available and used as supplied. *L*-tartaric acid was purchased from Sigma Aldrich, 2-methoxypropene, HBr/acetic acid and DBU were purchased from Merck and used without further purification. D-Glucose, D-Mannose, D-Galactose, D-Glucosamine and D-Galactosamine hydrochloride were purchased from Fluka and Sigma Aldrich. Liquid amines were dried by distilling over potassium hydroxide and stored under nitrogen atmosphere over potassium hydroxide pellets. Dry solvents like THF, methanol, DCM, choloroform and n-hexane were obtained by distillation using standard procedures or by passage through a column of anhydrous alumina using equipment from anhydrous engineering (University of Bristol, UK) based on the Grubbs' design. Reactions under anhydrous conditions were carried out under nitrogen gas using three way stopcock and rubber septa.

Glassware and needles were either flame dried immediately prior to use or placed in an oven (150 °C) for at least 2-3 hours and allowed to cool either in desiccators or under reduced pressure. Liquid reagents, solutions or solvents were added via syringe or cannula through rubber septa. Solid reagents were added via Schlenk type adapters. All Reactions were monitored by TLC on Kieselgel 60 F254 (Merck), ethyl acetate/n-Hexane and methanol/chloroform were used as eluent. Chromatograms were detected under UV light (λ_{max} 254 and 365 nm) and by charring with 10% sulfuric acid in ethanol, ninhydrine and vanilline respectively.

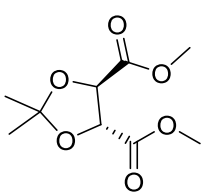
Column chromatography was performed using silica gel [Merck, 230−400 mesh (40−63 μm)]. Extracts were concentrated under reduced pressure using both a Buchi rotary evaporator (bath temperature up to 40 °C) at a pressure of either 15 mm Hg (diaphragm pump) or 0.1 mm Hg (oil pump), as appropriate and a high vacuum line at room temperature. Melting points were determined in degree Celsius (°C) using Gallenkamp digital melting point apparatus and are uncorrected. IR spectra were recorded on Bruker IFS 66 (FT IR), Nicolet 205 FT IR; Nicolet 360 smart orbit (ATR); thermo scientific Nicolet 6700 FT IR and Schimadzu Fourier Transform Infrared Spectrophotometer Model 270. Solid samples were taken in KBr pellets and oils were used in NaCl cell for recording their spectra. ^{1}H NMR spectra were recorded on NMR Bruker apparatus at 300 MHz and varian 400 MHz INOVA instrument. ^{13}C NMR spectra were recorded on NMR Bruker apparatus at 75 MHz and varian 100

MHz INOVA instrument. Chemical shifts are quoted in parts per million from $SiMe_4$ or residual solvent proton signals and coupling constants (*J*) given in Hertz. Multiplicities are abbreviated as: b (broad), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) or combinations thereof. Electron impact (EI) mass spectra were performed on VG: 70 SE mass spectrometer JEOL MSRoute instrument with direct probe as inlet system. Positive ion Matrix Assisted Laser Desorption Ionization Time-Of-Flight (MALDI-TOF) mass spectra were recorded using an HP-MALDI instrument using gentisic acid as matrix material. The optical rotations of the compounds were measured on ATAGO, AP-100 Automatic polarimeter. Single crystal X-ray diffraction data were collected on a Bruker Smart APEX II, CCD detector diffractometer.[174] Data reductions were performed by using SAINT program. The structures were solved by direct methods[175] and refined by full-matrix least squares on F2 by using the SHELXTL-PC package.[176] The figures were plotted with the aid of ORTEP program.[177]

3.2 Synthesis of 1,3-dioxolane dimethyl *L*-tartrate (1) and monoester (2)

3.2.1 General procedure for the synthesis of 1,3-dioxolane dimethyl-*L*-tartrate (**1**)[145-149,178]

In a round bottom flask (250 ml) dimethyl-*L*-tartrate (35.60 g, 200 mmol) and catalytic amount of camphor sulphonic acid were placed under nitrogen. DMF (100 ml) was added through a syringe and stirred with a magnetic stirrer. 2-Methoxypropene (22.90 ml, 240 mmol,) was added dropwise over I hour and left overnight. After completion of the reaction as monitored by TLC, water (300 ml) was added to the reaction mixture and extracted with ethyl acetate (100 ml × 3). The organic layer was washed with saturated $NaHCO_3$ (100 ml × 2), water and brine (100 × 3). The combined organic layer was dried over anhydrous magnesium sulphate; the crude was purified by column chromatography using ethyl acetate: n-hexane (2:8) as eluent.



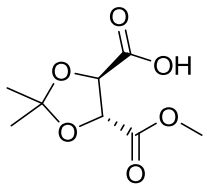
Chemical Formula: $C_9H_{14}O_6$
Exact Mass: 218.0790

Light yellow oil. Yield: 89 %. IR (neat) cm^{-1}: 2928 (CH), 1738 (CO). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm): 4.78 (s, 2H, CH), 3.80 (s, 6H, OCH_3) 1.47 (s, 6H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.0

(CO), 113.8 (qt C), 76.6 (CH), 52.7 (OCH_3), 26.2 (CH_3).

3.2.2 General procedure for the synthesis of monoester (2)[148,179]

In a round bottom flask (250 ml), solution of compound (**1**) (22.74 ml, 120 mmol) in methanol (30 ml) was added a solution of NaOH (4.80 g, 120 mmol) in methanol (30 ml) over 1 hour. The reaction mixture was stirred at room temperature an additional 1 hour and methanol was evaporated under reduced pressure to give a residue. Water (30 ml) was added and extracted with DCM (30 ml × 3) to recover some unreacted diester. The aqueous layer was acidified with $KHSO_4$ (1 M) and extracted with DCM (30 ml × 3). The solvent was evaporated and the crude was purified by column chromatography using methanol: dichloromethane (2:8) as eluent.



Chemical Formula: $C_8H_{12}O_6$
Exact Mass: 204.0634

Colourless oil. Yield: 79 %. IR (neat) cm^{-1}: 3467 (OH), 2928 (CH), 1730 ($COOCH_3$), 1708 (COOH). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm): 9.31 (bs, 1H, OH), 4.87 (d, *J* = 5.4 Hz, 1H, CH), 4.82 (d, *J* = 5.4 Hz, 1H, CH), 3.82 (s, 3H, OCH_3), 1.49 (s, 3H, CH_3), 1.47 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 173.8 (COOH), 169.7 ($COOCH_3$), 114.1 (qt C), 76.5 (CH), 76.3 (CH), 52.8 (OCH_3), 26.1 (CH_3), 25.5 (CH_3). HRMS-ESI for $C_8H_{12}O_6$: (M-H) calcd: 203.0634, found: 203.0570. EI-MS *m/z* (%): 204.0 M^+ (10.6), 189.1 (35.9), 59.0 (100).

3.3a Method A: General procedure for the synthesis of chiral amides (2a-2t)[150,56]

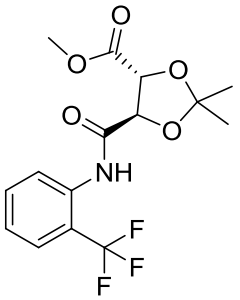
In a round bottom flask (100 ml) compound **(2)** (0.81 g, 4 mmol) in chloroform (30 ml), DCC (1.00 g, 4.8 mmol) and catalytic amount of DMAP were placed under nitrogen. After half hour substituted anilines (4 mmol) was added and stirred for 4-12 hours. The byproduct DCU was removed by multiple filterations and by extraction the reaction mixture with ethyl acetate or chloroform and water (50 ml × 3). The crude was purified by column chromatography using ethyl acetate: n-hexane (2:8) as eluent.

3.3b Method B: General Procedure for the synthesis of chiral amides (2a-2t)[57-58]

In a round bottom flask (100 ml), compound **(2)** (0.81 g, 4 mmol) in THF (20 ml), Triethylamine (0.72 ml, 5.2 mmol) were placed at $0^{\circ}C$ under nitrogen atmosphere. Ethylchloroformate (0.42 ml, 4.8 mmol) was added and stirred for 30 minutes; substituted aniline (4 mmol) in THF (10 ml) was added and allowed to warm to room temperature and left overnight. After the completion of reaction as indicated by TLC,

solvent was removed under reduced pressure and the crude was dissolved in ethyl acetate (30 ml), washed with saturated $NaHCO_3$, water and brine (30 ml × 3). The organic layer was dried over anhydrous magnesium sulphate; the crude was purified by column chromatography using ethyl acetate: n-hexane (2:8) as eluent.

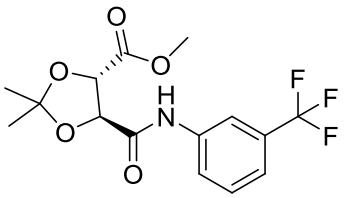
Synthesis of (4*R*,5*R*)-Methyl-2,2-dimethyl-5-((2-(trifluoromethyl)phenyl)carbamoyl)-1,3-dioxolane-4-carboxylate (2a)



Chemical Formula: $C_{15}H_{16}F_3NO_5$
Exact Mass: 347.0981

The compound (**2a**) was synthesized by the general procedures as described above (Method A and B). Yield: 68 % (Method A), 79 % (Method B). Yellow oil. $[\alpha]_D^{25}$ = 41.20° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3405 (NH), 2928 (CH), 1738 ($COOCH_3$), 1679 (CONH), 1537 (Ar), 1206 (C-F_3). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.40 (bs, 1H, NH), 7.64-7.57 (m, 4H, ArH), 4.92 (d, *J* = 5.4 Hz, 1H, CH), 4.81 (d, *J* = 5.4 Hz, 1H, CH), 3.82 (s, 3H, OCH_3), 1.57 (s, 3H, CH_3), 1.54 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm): 171.5 (CONH), 170.3 ($COOCH_3$), 133.3 (Ar-C-NH), 132.5, 126.4, 124.5, 120.3 (Ar-C), 124.1 (CF_3), 112.6 (qt C), 76.3 (CH), 75.2 (CH), 52.3 (OCH_3), 26.1 (CH_3), 25.6 (CH_3). Anal. Calc. For $C_{15}H_{16}F_3NO_5$ (347.0) C, 51.88; H, 4.64; F, 16.41; N, 4.03; O, 23.03 Found C, 51.45; H, 3.96; F, 16.50; N, 4.09; O, 22.83. EI-MS *m/z* (%): 347.1 M^+ (63.6), 332.1 (87.9), 288.1 (39.4), 59.1 (100).

(4*R*,5*R*)-Methyl-2,2-dimethyl-5-((3-(trifluoromethyl)phenyl)carbamoyl)-1,3-dioxolane-4-carboxylate (2b)

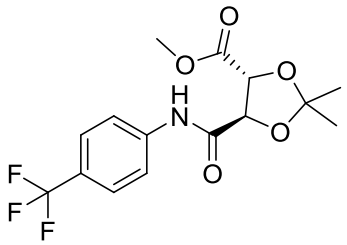


Chemical Formula: $C_{15}H_{16}F_3NO_5$
Exact Mass: 347.0981

Yield: 70 %, 89 %. White crystalline solid, m.p = 118-119 °C. $[\alpha]_D^{25}$ = 38.41° (c = 24 mg /2 ml CH_2Cl_2). (IR υ cm^{-1}): 3336 (NH), 2992 (CH), 1741 ($COOCH_3$), 1683 (CONH), 1540 (Ar), 1208 (C-F_3). ^{1}H NMR (300 MHz, $CDCl_3$): *δ* (ppm): 8.47 (bs, 1H, NH), 7.91 (s, 1H, Ar-H), 7.77-7.37 (m, 3H, Ar-H), 4.91 (d, *J* = 5.4 Hz, 1H, CH), 4.87 (d, *J* = 5.4 Hz, 1H, CH), 3.85 (s, 3H, OCH_3), 1.56 (s, 3H, CH_3), 1.55 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): *δ* (ppm): 170.3 (CONH) 167.8 ($COOCH_3$), 137.2 (Ar-C-NH), 131.3, 129.3, 125.2,

124.8, 120.5 (Ar-C), 123.7 (CF_3), 113.8 (qt C), 76.2 (CH), 75.6 (CH), 53.2 (OCH_3), 26.4 (CH_3), 25.3 (CH_3). Anal. Calc. For $C_{15}H_{16}F_3NO_5$ (347.0) C, 51.88; H, 4.64; F, 16.41; N, 4.03; O, 23.03 Found C, 51.45; H, 3.96; F, 16.50; N, 4.09; O, 22.83. EI-MS *m/z* (%): 347.1 M^+ (43.8), 332.1 (66.9), 288.1 (26.9), 159.2 (100), 59.1 (35.9).

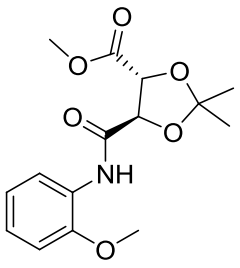
(4*R*,5*R*)-Methyl-2,2-dimethyl-5-((4-(trifluoromethyl)phenyl)carbamoyl)-1,3-dioxolane-4-carboxylate (2c)



Chemical Formula: $C_{15}H_{16}F_3NO_5$
Exact Mass: 347.0981

Yield: 76 %, 89 %. White crystalline solid, m.p. = 115-117 °C. $[\alpha]_D^{25}$ = 43.21° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3347 (NH), 3009 (CH), 1758 ($COOCH_3$), 1686 (CONH), 1527 (Ar) , 1223 (C-F_3). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.47 (bs, 1H, NH), 7.73 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.61 (d, *J* = 8.4 Hz, 2H, Ar-H), 4.92 (d, *J* = 5.4 Hz, 1H, CH), 4.88 (d, *J* = 5.4 Hz, 1H, CH), 3.86 (s, 3H, OCH_3), 1.57 (s, 3H, CH_3), 1.53 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.3 (CONH), 167.7 ($COOCH_3$), 139.7 (Ar-C-NH), 132.1 (2), 120.2 (2) (Ar-C), 125.4 (CF_3), 113.6 (qt C), 76.4 (CH), 75.7 (CH), 53.0 (OCH_3), 26.3 (CH_3), 25.1 (CH_3). Anal. Calc. For $C_{15}H_{16}F_3NO_5$ (347.0) C, 51.88; H, 4.64; F, 16.41; N, 4.03; O, 23.03 Found C, 51.45; H, 3.96; F, 16.50; N, 4.09; O, 22.83. EI-MS *m/z* (%): 347.1 M^+ (7.9), 332.1 (16.4), 288.1 (9.5), 59.1 (100).

(4*R*,5*R*)-Methyl-5-((2-methoxyphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4 carboxylate (2d)

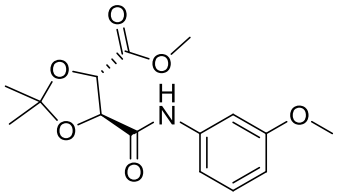


Chemical Formula: $C_{15}H_{19}NO_6$
Exact Mass: 309.1212

Yield: 69 %, 88 %. White crystalline solid, m.p. = 79-81 °C. $[\alpha]_D^{25}$ = 49.23° (c = 24 mg / 2 ml CH_2Cl_2). (IRυcm^{-1}): 3390 (NH), 2989 (CH), 1739 ($COOCH_3$), 1688 (CONH), 1600 (Ar). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.35 (bs, 1H, NH), 7.92-7.08 (m, 4H, ArH), 4.94 (d, *J* = 5.4 Hz, 1H ,CH), 4.86 (d, *J* = 5.4 Hz, 1H ,CH), 3.95 (s, 3H, Ar-OCH_3), 3.81 (s, 3H, OCH_3), 1.56 (s, 3H, CH_3), 1.54 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.5 (CONH), 167.5 ($COOCH_3$), 141.5 (Ar-C-NH), 148.2, 124.5, 124.4, 121.0, 119.6, (Ar-C), 113.6 (qt, C), 76.2 (CH), 75.1 (CH), 55.7 (Ar-OCH_3), 52.8

(O<u>C</u>H$_3$), 26.4 (<u>C</u>H$_3$), 25.3 (<u>C</u>H$_3$). Anal. Calc. For $C_{15}H_{19}NO_6$ (309.1) C, 58.25; H, 6.19; N, 4.53; O, 31.04 Found C, 57.95; H, 6.30; N, 4.50; O, 30.88. EI-MS *m/z* (%): 309.0 M^+ (97.4), 293.9 (27.4), 123.0 (100).

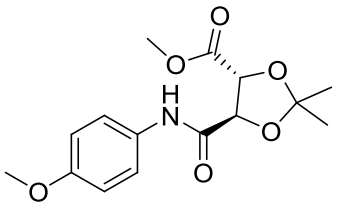
(4*R*,5*R*)-Methyl-5-((3-methoxyphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (2e)



Chemical Formula: $C_{15}H_{19}NO_6$
Exact Mass: 309.1212

Yield: 75 %, 87 %. White crystalline solid. m.p = 90-91 °C. $[\alpha]_D^{25}$ = 46.51° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm-1): 3336 (NH), 2937 (CH), 1748 (COOCH3), 1683 (CONH), 1597 (Ar). ^{1}H NMR (300 MHz, CDCl3): δ (ppm): 9.20 (bs, 1H, NH), 7.48 (s, 1H, Ar-H), 7.47-7.30 (m, 3H, Ar-H), 4.93 (d, *J* = 5.3 Hz, 1H, CH), 4.85 (d, *J* = 5.3 Hz, 1H, CH), 3.80 (s, 3H, Ar-OCH3), 3.78 (s, 3H, OCH3), 1.49 (s, 3H, CH3), 1.44 (s, 3H, CH3). ^{13}C NMR (75 MHz, $CDCl_3$): *δ* (ppm): 170.3 (<u>C</u>ONH), 167.4 (<u>C</u>OOCH$_3$), 137.7 (Ar-<u>C</u>-NH), 146.2, 124.5, 124.4, 121.0, 119.6 (Ar-<u>C</u>), 113.4 (qt <u>C</u>), 76.3 (<u>C</u>H), 75.2 (<u>C</u>H), 56.3 (Ar-O<u>C</u>H$_3$), 52.6 (O<u>C</u>H$_3$), 26.5 (<u>C</u>H$_3$), 25.3 (<u>C</u>H$_3$). Anal. Calc. For $C_{15}H_{19}NO_6$ (309.1), C, 58.25; H, 6.19; N, 4.53; O, 31.04 Found C, 57.95; H, 6.30; N, 4.50; O, 30.88. EI-MS *m/z* (%): 309.0 M^+ (92.4), 293.9 (37.5), 123.0 (100).

(4*R*,5*R*)-Methyl-5-((4-methoxyphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4 carboxylate (2f)



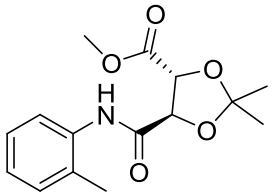
Chemical Formula: $C_{15}H_{19}NO_6$
Exact Mass: 309.1212

Yield: 80 %, 89 %. White crystalline solid. m.p. = 109-110 °C. $[\alpha]_D^{25}$ = 51.71° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3357 (NH), 2989 (CH), 1747 (COOCH$_3$), 1681 (CONH), 1509 (Ar).

^{1}H NMR (300 MHz, $CDCl_3$): *δ* (ppm): 8.21 (bs, 1H, NH), 7.50 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.89 (d, *J* = 8.4 Hz, 2H, Ar-H), 4.88 (d, *J* = 5.5 Hz, 1H, CH), 4.68 (d, *J* = 5.5 Hz, 1H, CH), 3.85 (s, 3H, Ar-OCH$_3$), 3.79 (s, 3H, OCH$_3$), 1.55 (s, 3H, CH$_3$), 1.49 (s, 3H, CH$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): *δ* (ppm): 170.9 (<u>C</u>ONH),167.7 (<u>C</u>OOCH$_3$), 130.3 (Ar-<u>C</u>-NH), 153.2, 124.5(2), 119.0 (2) (Ar-<u>C</u>), 114.2 (qt <u>C</u>), 76.3 (<u>C</u>H), 75.5 (<u>C</u>H) 55.3 (Ar-O<u>C</u>H$_3$), 52.3 (O<u>C</u>H$_3$), 26.3 (<u>C</u>H$_3$), 25.1 (<u>C</u>H$_3$). Anal. Calc. For $C_{15}H_{19}NO_6$ (309.1) C,

58.25; H, 6.19; N, 4.53; O, 31.04 Found C, 57.95; H, 6.30; N, 4.50; O, 30.88. EI-MS *m/z* (%): 309.0 M^+ (90.4), 293.9 (25.4), 123.0 (100).

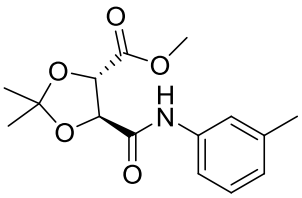
(4*R*,5*R*)-Methyl-2,2-dimethyl-5-(*o*-tolylcarbamoyl)-1,3-dioxolane-4-carboxylate (2g)



Chemical Formula: $C_{15}H_{19}NO_5$
Exact Mass: 293.1263

Yield: 68 %, 83 %. White crystalline solid, m.p = 92-94 °C. $[\alpha]_D^{25}$ = 70.41° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3393 (NH), 2998 (CH), 1754 ($COOCH_3$), 1693 (CONH), 1552 (Ar). (^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.30 (bs, 1H, NH), 8.06-7.45 (m, 4H, Ar-H), 4.93 (d, *J* = 5.4 Hz, 1H, CH), 4.88 (d, *J* = 5.4 Hz, 1H, CH), 3.87 (s, 3H, OCH_3), 2.29 (s, 3H, Ar-CH_3), 1.60 (s, 3H, CH_3), 1.56 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.4 (CONH), 167.9 ($COOCH_3$), 134.8 (Ar-C-NH), 130.4, 127.7, 127.0, 125.1, 121.5 (Ar-C), 113.3 (qt C), 76.5 (CH), 75.1 (CH) 52.8 (OCH_3), 26.3 (CH_3), 25.2 (CH_3), 17.7 (Ar-CH_3). Anal. Calc. For $C_{15}H_{19}NO_5$ (293.1) C, 61.42; H, 6.53; N, 4.78; O, 27.27 Found C, 60.90; H, 6.43; N, 4.94; O, 26.79. EI-MS *m/z* (%): 293.1 M^+ (100), 278.1 (17.4), 234.1 (21.6), 59.0 (22.1).

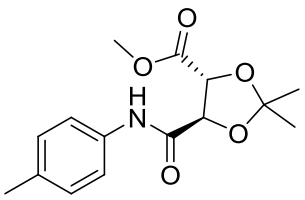
(4*R*,5*R*)-Methyl-2,2-dimethyl-5-(*m*-tolylcarbamoyl)-1,3-dioxolane-4-carboxylate (2h)



Chemical Formula: $C_{15}H_{19}NO_5$
Exact Mass: 293.1263

Yield: 86 %, 92 %. White crystalline solid, m.p. = 122-123 °C. $[\alpha]_D^{25}$ = 79.31° (c = 24 mg / 2 ml CH_2Cl_2). (IR υ cm^{-1}): 3325 (NH), 2990 (CH), 1743 ($COOCH_3$), 1681 (CONH), 1613 (Ar). (^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.23 (bs, 1H, NH), 7.44 (s, 1H, Ar-H), 7.38-6.99 (m, 3H, Ar-H), 4.91 (d, *J* = 5.4 Hz, 1H, CH), 4.68 (d, *J* = 5.4 Hz, 1H ,CH), 3.87 (s, 3H, OCH_3), 2.36 (s, 3H, Ar-CH_3), 1.58 (s,3H, CH_3), 1.55 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.4 (CONH), 167.9 ($COOCH_3$), 135.1 (Ar-C-NH), 136.4, 128.7, 125.0, 120.1, 119.5 (Ar-C), 112.4 (qt C), 76.1 (CH), 75.4 (CH), 52.8 (OCH_3), 26.2 (CH_3), 25.3 (CH_3), 21.1 (Ar-CH_3). Anal. Calc. For $C_{15}H_{19}NO_5$ (293.1) C, 61.42; H, 6.53; N, 4.78; O, 27.27 Found C, 60.90; H, 6.43; N, 4.94; O, 26.79. EI-MS *m/z* (%): 293.1 M^+ (100), 278.1 (17.4), 234.1 (21.6), 59.0 (22.1).

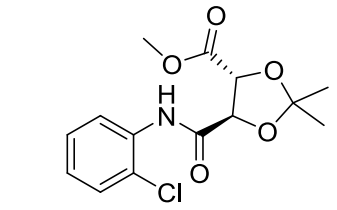
(4*R*,5*R*)-Methyl-2,2-dimethyl-5-(*p*-tolylcarbamoyl)-1,3-dioxolane-4-carboxylate (2i)



Chemical Formula: $C_{15}H_{19}NO_5$
Exact Mass: 293.1263

Yield: 79 %, 89 %. White crystalline solid, m.p. = 117-118 °C. $[\alpha]_D^{25}$ = 74.41° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3348 (NH), 2969 (CH), 1739 ($COOCH_3$), 1679 (CONH), 1596 (Ar). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.24 (bs, 1H, NH), 7.47 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.16 (d, *J* = 8.4 Hz, 2H, Ar-H), 4.89 (d, *J* = 5.4 Hz, 1H, CH), 4.79 (d, *J* = 5.4 Hz, 1H, CH), 3.86 (s, 3H, OCH_3), 2.31 (s, 3H, Ar-CH_3), 1.54 (s, 3H, CH_3), 1.51 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.1 (CONH), 168.9 ($COOCH_3$), 134.3 (Ar-C-NH), 130.4 (2), 127.7 (2), 122.4 (Ar-C), 113.8 (qt C), 76.2 (CH), 75.3 (CH), 52.5 (OCH_3), 25.8 (CH_3), 25.2 (CH_3), 19.8 (Ar-CH_3). Anal. Calc. For $C_{15}H_{19}NO_5$ (293.1) C, 61.42; H, 6.53; N, 4.78; O, 27.27 Found C, 60.90; H, 6.43; N, 4.94; O, 26.79. EI-MS *m/z* (%): 293.1 M^+ (100), 278.1 (17.4), 234.1 (21.6), 59.0 (22.1).

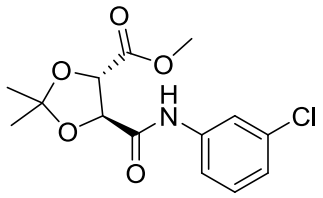
(4*R*,5*R*)-Methyl-5-((2-chlorophenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (2j)



Chemical Formula: $C_{14}H_{16}ClNO_5$
Exact Mass: 313.0717

Yield: 73 %, 81 %. White crystalline solid. m.p. = 73-74 °C. $[\alpha]_D^{25}$ = 56.31° (c = 24 mg /2 ml CH_2Cl_2). (IR υ cm^{-1}): 3378 (NH), 2928 (CH), 1754 ($COOCH_3$), 1680 (CONH), 1590 (Ar), 1110 (C-Cl). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.46 (bs, 1H, NH), 7.43-7.38 (m, 4H, Ar-H), 4.92 (d, *J* = 5.5 Hz, 1H, CH), 4.84 (d, *J* = 5.4 Hz, 1H, CH), 3.87 (s, 3H, OCH_3), 1.54 (s, 3H, CH_3), 1.53 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.2 (CONH), 167.3 ($COOCH_3$), 133.8 (Ar-C-NH), 129.3, 125.7, 123.0, 122.1, 120.5 (Ar-C) 113.3 (qt C), 77.9 (CH), 76.4 (CH), 52.7 (OCH_3), 26.6 (CH_3), 25.7 (CH_3). Anal. Calc. For $C_{14}H_{16}ClNO_5$ (313.0) C, 53.60; H, 5.14; Cl, 11.30; N, 4.46; O, 25.50 Found C, 54.12; H, 5.09; Cl, 10.95; N, 4.65; O, 24.90. EI-MS *m/z* (%): 313.1 M^+ (13.5), 298.1 (10.4), 254.0 (6.6), 59.0 (100).

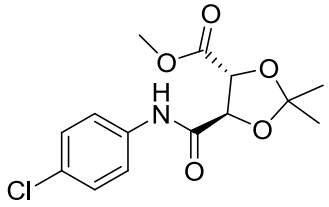
(4*R*,5*R*)-Methyl-5-((3-chlorophenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (2k)



Chemical Formula: $C_{14}H_{16}ClNO_5$
Exact Mass: 313.0717

Yield: 81 %, 91 %. White crystalline solid. m.p. = 80-81 °C. $[\alpha]_D^{25}$ = 59.31° (c = 24 mg /2 ml CH_2Cl_2). (IR υ cm^{-1}): 3392 (NH), 2951 (CH), 1752 ($COOCH_3$), 1682 (CONH), 1586 (Ar), 1100 (C-Cl). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.96 (bs, 1H, NH), 7.81 (s, 1H, Ar-H), 7.71-7.44 (m, 3H, Ar-H), 4.90 (d, *J* = 5.6 Hz, 1H, CH), 4.88 (d, *J* = 5.6 Hz, 1H, CH), 3.86 (s, 3H, OCH_3), 1.56 (s, 3H, CH_3), 1.52 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.4 (CONH), 169.4 ($COOCH_3$), 137.1 (Ar-C-NH), 134.5, 127.7, 126.0, 122.1, 119.5 (Ar-C), 113.6 (qt C), 76.4 (CH), 75.1 (CH), 53.5 (OCH_3), 26.8 (CH_3), 25.4 (CH_3). Anal. Calc. For $C_{14}H_{16}ClNO_5$ (313.0) C, 53.60; H, 5.14; Cl, 11.30; N, 4.46; O, 25.50 Found C, 54.12; H, 5.09; Cl, 10.95; N, 4.65; O, 24.90. EI-MS *m/z* (%): 313.1 M^+ (16.5), 298.1 (10.4), 254.0 (6.6), 59.0 (100).

(4*R*,5*R*)-Methyl-5-((4-chlorophenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (2l)

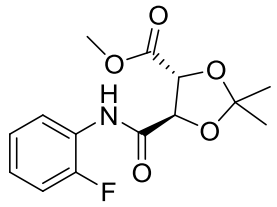


Chemical Formula: $C_{14}H_{16}ClNO_5$
Exact Mass: 313.0717

Yield: 77 %, 82 %. White crystalline solid. m.p. = 89-90 °C.

$[\alpha]_D^{25}$ = 52.42° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3348 (NH), 2984 (CH), 1755 ($COOCH_3$), 1680 (CONH), 1592 (Ar), 1033 (C-Cl). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.29 (bs, 1H, NH), 7.56 (d, *J* = 8.7 Hz, 2H, Ar-H), 7.34 (d, *J* = 8.6 Hz, 2H, Ar-H), 4.93 (d, *J* = 5.4 Hz, 1H, CH), 4.85 (d, *J* = 5.4 Hz, 1H, CH), 3.87 (s, 3H, OCH_3), 1.57 (s, 3H, CH_3), 1.55 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.1 (CONH), 167.9 ($COOCH_3$), 135.3 (Ar-C-NH), 129.3, 127.7 (2), 122.1 (2) (Ar-C), 113.1 (qt C), 76.3 (CH), 75.5 (CH) 53.3 (OCH_3), 26.3 (CH_3), 25.1 (CH_3). Anal. Calc. For $C_{14}H_{16}ClNO_5$ (313.0) C, 53.60; H, 5.14; Cl, 11.30; N, 4.46; O, 25.50 Found C, 54.12; H, 5.09; Cl, 10.95; N, 4.65; O, 24.90. EI-MS *m/z* (%): 313.1 M^+ (13.5), 298.1 (10.4), 254.0 (6.6), 59.0 (100).

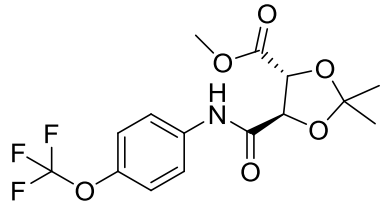
(4*R*,5*R*)-Methyl-5-((2-fluorophenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (2m)



Chemical Formula: $C_{14}H_{16}FNO_5$
Exact Mass: 297.1013

Yield: 72 %, 93 %. White crystalline solid. m.p = 85-86 °C. $[\alpha]_D^{25}$ = 44.79° (c = 24 mg/2 ml CH_2Cl_2). IR (neat) cm^{-1}: 3399 (NH), 2967 (CH), 1739 ($COOCH_3$), 1700 (CONH), 1529 (Ar), 1112 (C-F). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.63 (bs, 1H, NH), 7.98-7.59 (m, 4H, Ar-H), 4.93 (d, *J* = 5.5 Hz, 1H, CH), 4.86 (d, *J* = 5.5 Hz, 1H, CH), 3.88 (s, 3H, OCH_3), 1.55 (s, 3H, CH_3), 1.52 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.1 (CONH), 169.7 ($COOCH_3$), 148.6, 128.4, 125.7, 123.0, 122.1 (Ar-C), 143.4 (Ar-C-NH), 113.5 (qt C), 76.2 (CH), 75.6 (CH), 52.2 (OCH_3), 26.7 (CH_3), 25.9 (CH_3). Anal. Calc. For $C_{14}H_{16}FNO_5$ (297.1) C, 56.56; H, 5.42; F, 6.39; N, 4.71; O, 26.91 Found C, 56.12; H, 5.67; F, 6.70; N, 3.98; O, 26.45. EI-MS *m/z* (%): 297.0 M^+ (85.5), 282.1 (72.4), 238.0 (29.6), 203 (100), 59.0 (30.7).

(4*R*,5*R*)-Methyl-2,2-dimethyl-5-((4-(trifluoromethoxy)phenyl)carbamoyl)-1,3-dioxolane-4-carboxylate (2n)

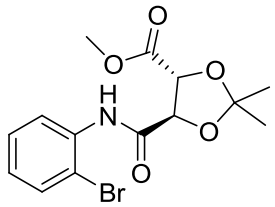


Chemical Formula: $C_{15}H_{16}F_3NO_6$
Exact Mass: 363.0930

Yield: 70 %, 89 %. White crystalline solid. m.p = 72-74 °C. $[\alpha]_D^{25}$ = 63.20° (c = 24 mg/2 ml CH_2Cl_2).

IR (neat) cm^{-1}: 3350 (NH), 2990 (CH), 1762 ($COOCH_3$), 1681 (CONH), 1605 (Ar), 1302 (C-F_3). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.32 (bs, 1H, NH), 7.64 (d, *J* = 8.5 Hz, 2H, Ar-H), 7.53 (d, *J* = 8.4 Hz, 2H, Ar-H), 4.92 (d, J = 5.4 Hz, 1H, CH), 4.87 (d, J = 5.4 Hz, 1H, CH), 3.87 (s, 3H, OCH_3), 1.57 (s, 3H, CH_3), 1.55 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.1 (CONH), 168.8 ($COOCH_3$), 142.1 (Ar-C-OCF_3), 137.3 (Ar-C-NH), 126.3 (OCF_3), 122.3 (2), 117.3 (2) (Ar-C) 113.6 (qt C), 76.3 (CH), 75.1 (CH), 53.5 (OCH_3), 26.8 (CH_3), 25.7 (CH_3). Anal. Calc. For $C_{15}H_{16}F_3NO_6$ (363.0) C, 49.59; H, 4.44; F, 15.69; N, 3.86; O, 26.42 Found C, 49.67; H, 3.97; F, 16.19; N, 3.38; O, 26.22. EI-MS *m/z* (%): 363.1 M^+ (15.5), 348.1 (42.4), 161.0 (49.6), 159 (61.6), 59.0 (100).

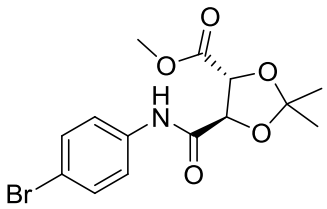
(4*R*,5*R*)-Methyl-5-((2-bromophenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (2o)



Chemical Formula: $C_{14}H_{16}BrNO_5$
Exact Mass: 357.0212

Yield: 76 %, 89 %. White crystalline solid. m.p = 98-99 °C. $[\alpha]_D^{25}$ = 61.41° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3277 (NH), 2927 (CH), 1737 ($COOCH_3$), 1680 (CONH), 1541 (Ar), 1050 (C-Br). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.28 (bs, 1H, NH), 7.34-7.32 (m, 4H, Ar-H), 4.90 (d, *J* = 5.3 Hz, 1H, CH), 4.80 (d, *J* = 5.3 Hz, 1H, CH), 3.78 (s, 3H, OCH_3), 1.55 (s, 3H, CH_3), 1.52 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.6 (CONH), 169.9 ($COOCH_3$), 137.4 (Ar-C-NH), 127.7, 126.0, 124.9, 122.1, 119.5 (Ar-C), 113.3 (qt C), 76.3 (CH), 75.6 (CH), 52.2 (OCH_3), 26.5 (CH_3), 25.8 (CH_3). Anal. Calc. For $C_{14}H_{16}BrNO_5$ (357.0) C, 46.95; H, 4.50; Br, 22.31; N, 3.91; O, 22.33 Found C, 46.90; H, 3.99; Br, 22.34; N, 4.14; O, 21.87. EI-MS *m/z* (%): 357.1 M^+ (2.5), 342.1 (8.4), 298.0 (2.6), 59.0 (100).

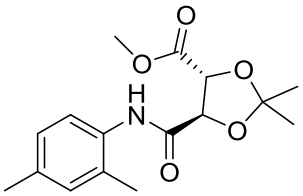
(4*R*,5*R*)-Methyl-5-((4-bromophenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (2p)



Chemical Formula: $C_{14}H_{16}BrNO_5$
Exact Mass: 357.0212

Yield: 69 %, 83 %. White crystalline solid. m.p = 112-113 °C. $[\alpha]_D^{25}$ = 64.31° (c = 24 mg/2 ml CH_2Cl_2) (IR υ cm^{-1}): 3345 (NH), 2983 (CH), 1755 ($COOCH_3$), 1681 (CONH), 1588 (Ar), 1020 (C-Br). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.30 (bs, 1H, NH), 7.51 (d, *J* = 8.6 Hz, 2H, Ar-H), 7.46 (d, *J* = 8.5 Hz, 2H, Ar-H), 4.93 (d, *J* = 5.6 Hz, 1H, CH), 4.89 (d, *J* = 5.5 Hz, 1H, CH), 3.86 (s, 3H, OCH_3), 1.56 (s, 3H, CH_3), 1.54 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.3 (CONH), 167.9 ($COOCH_3$), 135.7 (Ar-C-NH), 131.8 (2), 120.3 (2), 117.2 (Ar-C), 113.7 (qt C), 76.4 (CH), 75.2 (CH), 53.2 (OCH_3), 26.1 (CH_3), 25.6 (CH_3). Anal. Calc. For $C_{14}H_{16}BrNO_5$ (357.0) C, 46.95; H, 4.50; Br, 22.31; N, 3.91; O, 22.33 Found C, 46.90; H, 3.99; Br, 22.34; N, 4.14; O, 21.87. EI-MS *m/z* (%): 357.1 M^+ (2.5), 342.1 (8.4), 298.0 (2.6), 59.0 (100).

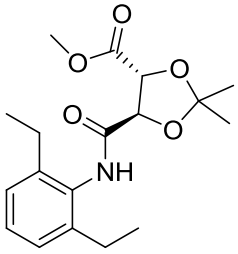
(4*R*,5*R*)-Methyl-5-((2,4-dimethylphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (2q)



Chemical Formula: $C_{16}H_{21}NO_5$
Exact Mass: 307.1420

Yield: 79 %, 87 %. White crystalline solid. m.p = 150-151 °C. $[\alpha]_D^{25}$ = 45.91° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3392 (NH), 2928 (CH), 1750 ($COOCH_3$), 1675 (CONH), 1596 (Ar). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.21 (bs, 1H, NH), 7.88 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.79 (d, *J* = 8.6 Hz, 1H, Ar-H), 7.05 (s, 1H, Ar-H), 4.95 (d, *J* = 5.4 Hz, 1H, CH), 4.87 (d, *J* = 5.4 Hz, 1H, CH), 3.87 (s, 3H, OCH_3), 1.60 (s, 3H, CH_3), 1.57 (s, 3H, CH_3), 2.30 (s, 3H, Ar-CH_3), 2.25 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.9 (CONH), 167.7 ($COOCH_3$), 134.9 (Ar-C-NH), 132.1, 131.1, 128.2, 126.2 (Ar-C), 113.1 (qt C), 76.4 (CH), 75.7 (CH), 53.2 (OCH_3), 26.2 (CH_3), 25.5 (CH_3), 20.1 (Ar-CH_3), 17.3 (Ar-CH_3). Anal. Calc. For $C_{16}H_{21}NO_5$ (307.1) C, 62.53; H, 6.89; N, 4.56; O, 26.03 Found C, 61.90; H, 6.45; N, 4.45; O, 26.29. EI-MS *m/z* (%): 307.1 M^+ (30.5), 248.1 (7.0), 121.0 (82.6), 59.0 (100).

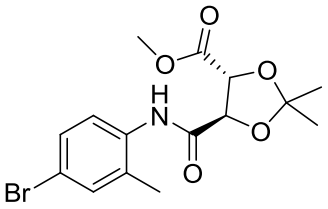
(4*R*,5*R*)-Methyl-5-((2,6-diethylphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (2r)



Chemical Formula: $C_{18}H_{25}NO_5$
Exact Mass: 335.1733

Yield: 74 %, 91 %. White crystalline solid. m.p = 160-161 °C $[\alpha]_D^{25}$ = 35.31° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3244 (NH), 2929 (CH), 1731 ($COOCH_3$), 1681 (CONH), 1592 (Ar). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.99 (bs, 1H, NH), 7.68-7.55 (m, 3H, Ar-H), 5.01 (d, *J* = 5.5 Hz, 1H ,CH), 4.96 (d, *J* = 5.5 Hz, 1H ,CH), 3.86 (s, 3H , OCH_3), 2.63 (q, *J* = 7.6 Hz, 4H, 2×CH_2), 1.54 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 1.23 (t, *J* = 7.6 Hz, 6H, 2×CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.2 (CONH), 168.8 ($COOCH_3$), 141.2 (Ar-C-NH), 131.3 (2) (Ar-C-C_2H_5), 124.2, 123.5 (2) (Ar-C), 113.2 (qt C), 75.8 (CH), 74.9 (CH), 53.1 (OCH_3), 26.3 (CH_3), 25.6 (CH_3), 23.4 (CH_2), 15.6 (CH_3). Anal. Calc. For $C_{18}H_{25}NO_5$ (335.1) C, 64.46; H, 7.51; N, 4.18; O, 23.85 Found C, 64.65; H, 7.78; N, 4.12; O, 24.07. EI-MS *m/z* (%): 335.1 M^+ (3.5), 276.1 (7.0), 218.0 (22.6), 59.0 (100).

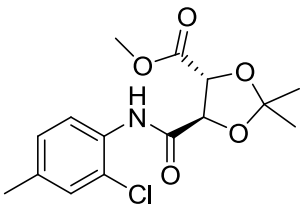
(4*R*,5*R*)-Methyl-5-((4-bromo-2-methylphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (2s)



Chemical Formula: $C_{15}H_{18}BrNO_5$
Exact Mass: 371.0368

Yield: 81 %, 78 %. White crystalline solid. m.p = 141-143 °C. $[\alpha]_D^{25}$ = 37.21° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3390, (NH), 2933, (CH), 1753 ($COOCH_3$), 1674 (CONH), 1602 (Ar), 1060 (C-Br). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.27 (bs, 1H, NH), 7.87 (s,1H, Ar-H), 7.35 (d, *J* = 8.4 Hz, 1H, Ar-H), 7.15 (d, *J* = 8.4 Hz, 1H, Ar-H), 4.93 (d, *J* = 5.4 Hz, 1H, CH), 4.84 (d, *J* = 5.4 Hz, 1H, CH), 3.86 (s, 3H, OCH_3), 2.26 (s, 3H, Ar-CH_3), 1.59 (s, 3H, CH_3), 1.56 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.2 (CONH), 167.9 ($COOCH_3$), 133.1 (Ar-C-NH), 130.6, 129.2, 122.7, 117.8 (Ar-C), 113.2 (qt C), 77.8 (CH), 75.9 (CH), 53.1 (OCH_3), 26.3 (CH_3), 25.5 (CH_3), 19.5 (Ar-CH_3). Anal. Calc. For $C_{15}H_{18}BrNO_5$ (371.0) C, 48.40; H, 4.87; Br, 21.47; N, 3.76; O, 21.49 Found C, 48.67; H, 5.03; Br, 21.78; N, 4.12; O, 21.42. EI-MS *m/z* (%): 371.1 M^+ (9.5), 356.1 (7.0), 312.0 (22.6), 59.0 (100).

(4*R*,5*R*)-Methyl-5-((2-chloro-4-methylphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (2t)



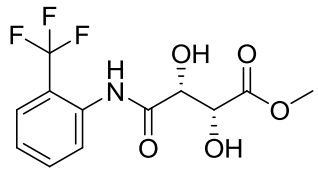
Chemical Formula: $C_{15}H_{18}ClNO_5$
Exact Mass: 327.0874

Yield: 79 %, 88 %. White crystalline solid. m.p = 113-115 °C. $[\alpha]_D^{25}$ = 59.49° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3373 (NH), 2994 (CH), 1749 ($COOCH_3$), 1695 (CONH), 1610 (Ar), 1090 (C-Cl). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.30 (bs, 1H, NH), 7.19 (s, 1H, Ar-H), 7.09 (d, *J* = 8.4 Hz, 1H, Ar-H), 6.89 (d, *J* = 8.4 Hz, 1H, Ar-H), 4.92 (d, *J* = 5.4 Hz, 1H, CH), 4.82 (d, *J* = 5.4 Hz, 1H, CH), 3.85 (s, 3H, OCH_3), 2.29 (s, 3H, Ar-CH_3), 1.59 (s, 3H, CH_3), 1.54 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.8 (CONH), 167.3 ($COOCH_3$), 135.9 (Ar-C-NH), 131.0, 129, 127, 120 (Ar-C), 113.1 (qt C), 77.7 (CH), 76.3 (CH), 53.2 (OCH_3), 26.5 (CH_3), 25.2 (CH_3), 20.2 (Ar-CH_3). Anal. Calc. For $C_{15}H_{18}ClNO_5$ (327.0) C, 54.97; H, 5.54; Cl, 10.82; N, 4.27; O, 24.41 Found C, 55.12; H, 5.43; Cl, 10.17; N, 4.47; O, 24.30. EI-MS *m/z* (%): 327.1 M^+ (12.5), 312.0 (22.6), 268.1 (7.0), 141.1 (94.8), 59.0 (100).

3.4 General procedure for the deprotection of 1,3-dioxolanes

To carry out deprotection of 1,3-dioxolanes in amides (**2a-2t**) methanol and acetyl choloride were used. In a round bottom flask (100 ml) with a magnetic stirrer, appropriate amount of protected amide (2 mmol) was dissolved in methanol under nitrogen. Freshly distilled acetyl chloride was added dropwise with gentle stirring and cooling and followed through TLC. After the completion of the reaction, the solvent was evaporated on rotavap. Ethyl acetate (30 ml) was added to the crude and washed with water and brine (30 ml × 3). The organic layer was dried over anhydrous magnesium sulphate and the crude was purified by column chromatography using methanol: chloroform (2:8) as eluent.

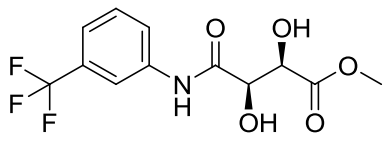
(2*R*,3*R*)-Methyl-2,3-dihydroxy-4-oxo-4-(2-(trifluoromethyl)phenylamino)butanoate (3a)



Chemical Formula: $C_{12}H_{12}F_3NO_5$
Exact Mass: 307.0668

Yield: 65 %, White crystalline solid, m.p. = 130-132 °C. $[\alpha]_D^{25}$ = 43.47° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3479 (OH), 3361 (NH), 2926 (CH), 1726 ($COOCH_3$), 1693 (CONH), 1591 (Ar), 1314 (C-F_3). ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 9.37 (bs, 1H, NH), 7.97-7.87 (m, 4H, ArH), 5.99 (d, *J* = 6.9 Hz, 1H, OH), 5.89 (d, *J* = 6.9 Hz, 1H, OH), 4.73 (dd, *J* = 6.9, 2.4 Hz, 1H ,CH), 4.64 (dd, *J* = 6.9, 2.4 Hz, 1H, CH), 3.77 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.8 (CONH) 170.6 ($COOCH_3$), 135.3 (Ar-C-NH), 133.5, 127.4, 125.5, 120.7 (Ar-C), 124.7 (CF_3), 75.4 (CH), 74.1 (CH), 51.1 (OCH_3). Anal. Calc. For $C_{12}H_{12}F_3NO_5$ (307.0) C, 46.91; H, 3.94; F, 18.55; N, 4.56; O, 26.04 Found C, 47.03; H, 3.55; F, 18.30; N, 4.59; O, 26.20. EI-MS *m/z* (%): 307.1 M^+ (13.5), 248.0 (13.9), 161.0 (100), 59.0 (30.6).

(2*R*,3*R*)-Methyl-2,3-dihydroxy-4-oxo-4-(3(trifluoromethyl)phenylamino)butanoate (3b)

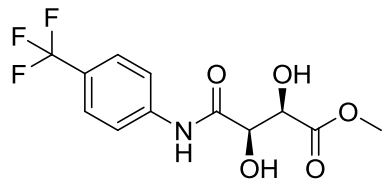


Chemical Formula: $C_{12}H_{12}F_3NO_5$
Exact Mass: 307.0668

Yield: 78 %, White crystalline solid, m.p = 186-187 °C. $[\alpha]_D^{25}$ = 36.21° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3308 (OH), 3110 (NH), 2955 (CH), 1735 ($COOCH_3$), 1675 (CONH), 1547 (Ar), 1233

(C-F_3). ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 10.05 (bs, 1H, NH), 8.26 (s, 1H, Ar-H), 7.99-7.87 (m, 3H, Ar-H), 6.12 (d, *J* = 6.9 Hz, 1H, OH), 5.58 (d, *J* = 6.9 Hz, 1H, OH), 4.55 (dd, *J* = 6.9, 2.4 Hz, 1H, CH), 4.45 (dd, *J* = 6.9, 2.4 Hz, 1H, CH), 3.95 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 170.9 (CONH), 170.2 ($COOCH_3$), 139.2 (Ar-C-NH), 132.3, 130.3, 126.2, 125.8, 121.5 (Ar-C), 122.7 (CF_3), 74.7 (CH), 72.0 (CH), 52.6 (OCH_3). Anal. Calc. For $C_{12}H_{12}F_3NO_5$ (307.0) C, 46.91; H, 3.94; F, 18.55; N, 4.56; O, 26.04 Found C, 47.03; H, 3.55; F, 18.30; N, 4.59; O, 26.20. EI-MS *m/z* (%): 307.1 M^+ (13.5), 248.0 (13.9), 161.0 (100), 59.0 (30.6).

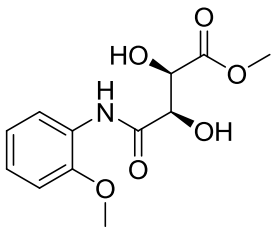
(2*R*,3*R*)-Methyl-2,3-dihydroxy-4-oxo-4-(4-(trifluoromethyl)phenylamino)butanoate (3c)



Chemical Formula: $C_{12}H_{12}F_3NO_5$
Exact Mass: 307.0668

Yield: 81 %, White crystalline solid, m.p = 223-225 °C. $[\alpha]_D^{25}$ = 45.27° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3413 (OH) , 3304 (NH), 2957 (CH), 1735 ($COOCH_3$), 1670 (CONH), 1597 (Ar) , 1330 (C-F_3). ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 10.04 (bs, 1H, NH), 7.98 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.69 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.11 (d, *J* = 6.9 Hz, 1H, OH), 5.59 (d, *J* = 6.9 Hz, 1H, OH), 4.54 (dd, *J* = 6.9, 2.5 Hz, 1H, CH), 4.44 (dd, *J* = 6.9, 2.5 Hz, 1H, CH), 3.89 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.1 (CONH), 169.2 ($COOCH_3$), 138.2 (Ar-C-NH), 133.1(2), 121.2(2) (Ar-C), 126.4 (CF_3), 74.3 (CH), 73.1 (CH), 52.7 (OCH_3). Anal. Calc. For $C_{12}H_{12}F_3NO_5$ (307.0) C, 46.91; H, 3.94; F, 18.55; N, 4.56; O, 26.04 Found C, 47.03; H, 3.55; F, 18.30; N, 4.59; O, 26.20. EI-MS *m/z* (%): 307.1 M^+ (13.5), 248.0 (13.9), 161.0 (100), 59.0 (30.6).

(2*R*,3*R*)-Methyl-2,3-dihydroxy-4-(2-methoxyphenylamino)-4-oxobutanoate (3d)

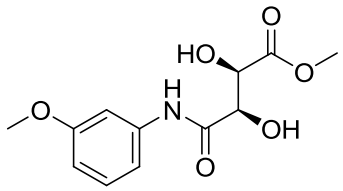


Chemical Formula: $C_{12}H_{15}NO_6$
Exact Mass: 269.0899

Yield: 78 %, White crystalline solid, m.p. = 98-100 °C. $[\alpha]_D^{25}$ = 47.49° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3400 (OH), 3371 (NH), 2929 (CH), 1726 ($COOCH_3$), 1662 (CONH), 1599 (Ar). ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 9.37 (bs, 1H, NH), 8.31-8.28 (m, 4H, ArH), 5.88 (d, *J* = 6.9 Hz, 1H, OH), 5.70 (d, *J* = 6.8 Hz, 1H, OH), 4.89 (dd, *J* = 6.8, 2.4 Hz, 1H , CH), 4.69 (dd, *J* =

6.9, 2.4 Hz, 1H , CH), 3.90 (s, 3H, Ar-OCH_3), 3.82 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 170.8 (CONH), 170.2 ($COOCH_3$), 148.5 (Ar-C-NH), 155.2, 126.5, 125.4, 122.0, 121.6 (Ar-C), 73.7 (CH), 72.3 (CH), 54.7 (Ar-OCH_3), 51.8 (OCH_3). Anal. Calc. For $C_{12}H_{15}NO_6$ (269.0) C, 53.53; H, 5.62; N, 5.20; O, 35.65 Found C, 53.77; H, 5.43; N, 4.91; O, 35.78. EI-MS *m/z* (%): 269.1 M^+ (20.0), 210.1 (4.6), 123.1 (100), 59.0 (19.7).

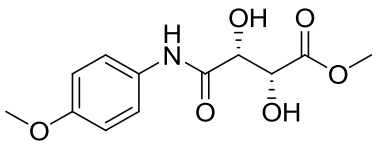
(2*R*,3*R*)-Methyl-2,3-dihydroxy-4-(3-methoxyphenylamino)-4-oxobutanoate (3e)



Chemical Formula: $C_{12}H_{15}NO_6$
Exact Mass: 269.0899

Yield: 80 %. White crystalline solid, m.p. = 98-99 °C. $[\alpha]_D^{25}$ = 48.37° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3440 (OH), 3314 (NH), 2998 (CH), 1739 ($COOCH_3$), 1667 (CONH), 1595 (Ar). ^1H NMR (300 MHz, DMSO-d_6): δ (ppm): 9.37 (bs, 1H, NH), 7.51 (s, 1H, Ar-H), 7.55-7.53 (m, 3H, Ar-H), 5.79 (d, *J* = 6.9 Hz, 1H, OH), 5.72 (d, *J* = 6.9 Hz, 1H, OH), 4.72 (dd, *J* = 6.9, 2.4 Hz, 1H ,CH), 4.62 (dd, *J* = 6.9, 2.4 Hz, 1H ,CH), 3.78 (s, 3H, Ar-OCH_3), 3.76 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.3 (CONH),169.4 ($COOCH_3$), 139.7 (Ar-C-NH), 160.2, 125.5, 124.7, 122.0, 120.6 (Ar-C), 74.3 (CH), 73.6 (CH), 55.3 (Ar-OCH_3), 51.6 (OCH_3). Anal. Calc. For $C_{12}H_{15}NO_6$ (269.0) C, 53.53; H, 5.62; N, 5.20; O, 35.65 Found C, 53.77; H, 5.43; N, 4.91; O, 35.78. EI-MS *m/z* (%): 269.1 M^+ (20.0), 210.1(4.6), 123.1(100), 59.0 (19.7).

(2*R*,3*R*)-Methyl-2,3-dihydroxy-4-(4-methoxyphenylamino)-4-oxobutanoate (3f)

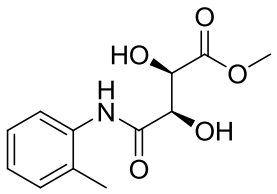


Chemical Formula: $C_{12}H_{15}NO_6$
Exact Mass: 269.0899

Yield: 83 %, White crystalline solid, m.p = 118-119 °C. $[\alpha]_D^{25}$ = 44.91° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3390 (OH), 3306 (NH), 2951 (CH), 1737 ($COOCH_3$), 1653 (CONH), 1599 (Ar). ^1H NMR (300 MHz, DMSO-d_6): δ (ppm): 9.10 (bs, 1H, NH), 7.69 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.91 (d, *J* = 8.4 Hz, 2H, Ar-H), 5.58 (d, *J* = 6.9 Hz, 1H, OH), 5.50 (d, *J* = 6.9 Hz, 1H, OH), 4.89 (dd, *J* = 6.9, 2.4 Hz, 1H , CH), 4.69 (dd, *J* = 6.9, 2.4 Hz, 1H, CH), 3.89 (s, 3H, Ar-OCH_3), 3.80 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.4 (CONH), 169.4 ($COOCH_3$), 131.3 (Ar-C-NH), 156.2, 126.5 (2), 122.0 (2) (Ar-C), 74.3 (CH), 72.4 (CH), 56.3 (Ar-OCH_3), 51.3 (OCH_3). Anal. Calc. For $C_{12}H_{15}NO_6$ (269.0) C, 53.53; H, 5.62; N, 5.20; O, 35.65

Found C, 53.77; H, 5.43; N, 4.91; O, 35.78. EI-MS *m/z* (%): 269.1 M^+ (20.0), 210.1 (4.6), 123.1 (100), 59.0 (19.7).

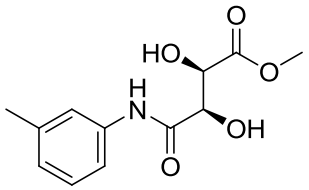
(2*R*,3*R*)-Methyl-4-(*o*-toluidino)-2,3-dihydroxy-4-oxobutanoate (3g)



Chemical Formula: $C_{12}H_{15}NO_5$
Exact Mass: 253.0950

Yield: 65 %. White crystalline solid, m.p = 131-133 °C. $[\alpha]_D^{25}$ = 69.30° (c = 24 mg/2 mL CH_2Cl_2). (IR υ cm^{-1}): 3390 (OH), 3378 (NH), 2956 (CH), 1748 ($COOCH_3$), 1663 (CONH), 1602 (Ar). ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 8.89 (bs, 1H, NH), 8.52-8.49 (m, 4H, Ar-H), 4.71 (d, *J* = 5.4 Hz, 1H, CH), 4.66 (d, *J* = 5.4 Hz, 1H, CH), 3.77 (s, 3H, OCH_3), 3.29 (bs, 2H, OH), 2.29 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.4 (CONH), 169.9 ($COOCH_3$), 134.1 (Ar-C-NH), 130.9, 127.8, 126.0, 124.1, 121.5 (Ar-C), 74.6 (CH), 73.7 (CH), 51.8 (OCH_3), 17.7 (Ar-CH_3). Anal. Calc. For $C_{12}H_{15}NO_5$ (253.0) C, 56.91; H, 5.97; N, 5.53; O, 31.59 Found C, 56.70; H, 6.23; N, 5.41; O, 31.33. EI-MS *m/z* (%): 253.1 M^+ (20.1), 194.1 (7.9), 107.1 (100), 59.0 (22.2).

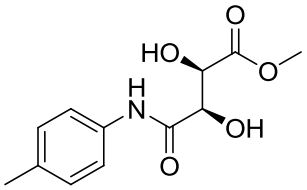
(2*R*,3*R*)-Methyl-4-(*m*-toluidino)-2,3-dihydroxy-4-oxobutanoate (3h)



Chemical Formula: $C_{12}H_{15}NO_5$
Exact Mass: 253.0950

Yield: 76 %. White crystalline solid. m.p. = 140-141 °C. $[\alpha]_D^{25}$ = 81.29° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3396 (OH), 3309 (NH), 2949 (CH), 1740 ($COOCH_3$), 1660 (CONH), 1551 (Ar). (^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 9.11 (bs, 1H, NH), 7.53 (s, 1H, Ar-H), 7.50-7.48 (m, 3H, Ar-H), 4.70 (d, *J* = 5.5 Hz, 1H, CH), 4.66 (d, *J* = 5.5 Hz, 1H ,CH), 3.76 (s, 3H, OCH_3), 3.22 (bs, 2H, OH), 2.31 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.6 (CONH), 168.8 ($COOCH_3$), 139.2 (Ar-C-NH), 136.9, 129.7, 125.0, 120.1, 119.5 (Ar-C), 74.4 (CH), 73.3 (CH), 51.8 (OCH_3), 21.1 (Ar-CH_3). Anal. Calc. For $C_{12}H_{15}NO_5$ (253.0) C, 56.91; H, 5.97; N, 5.53; O, 31.59 Found C, 56.70; H, 6.23; N, 5.41; O, 31.33. EI-MS *m/z* (%): 253.1 M^+ (20.1), 194.1 (7.9), 107.1 (100), 59.0 (22.2).

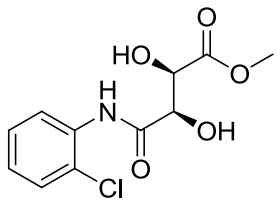
(2*R*,3*R*)-Methyl-4-(*p*-toluidino)-2,3-dihydroxy-4-oxobutanoate (3i)



Chemical Formula: $C_{12}H_{15}NO_5$
Exact Mass: 253.0950

Yield: 82 %, White crystalline solid. m.p. = 125-127 °C. $[\alpha]_D^{25}$ = 88.26° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3398 (OH), 3305 (NH), 2947 (CH), 1739 ($COOCH_3$), 1658 (CONH), 1594, (Ar). ^1H NMR (300 MHz, DMSO-d_6): δ (ppm): 8.89 (bs, 1H, NH), 7.51 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.16 (d, *J* = 8.4 Hz, 2H, Ar-H), 5.59 (d, *J* = 6.9 Hz, 1H, OH), 5.56 (d, *J* = 6.9 Hz, 1H, OH), 4.67 (dd, *J* = 6.9, 2.5 Hz, 1H ,CH), 4.57 (dd, *J* = 6.9, 2.5 Hz, 1H ,CH), 3.81 (s, 3H, OCH_3), 2.32 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.5 (CONH), 169.9 ($COOCH_3$), 139.3 (Ar-C-NH), 132.4 (2), 128.7 (2), 124.4 (Ar-C), 74.7 (CH), 73.4 (CH), 51.5 (OCH_3), 19.8 (Ar-CH_3). Anal. Calc. For $C_{12}H_{15}NO_5$ (253.0) C, 56.91; H, 5.97; N, 5.53; O, 31.59 Found C, 56.70; H, 6.23; N, 5.41; O, 31.33. EI-MS *m/z* (%): 253.1 M^+ (20.1), 194.1 (7.9), 107.1 (100), 59.0 (22.2).

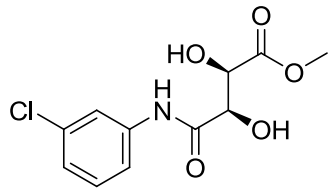
(2*R*,3*R*)-Methyl-4-(2-chlorophenylamino)-2,3-dihydroxy-4-oxobutanoate (3j)



Chemical Formula: $C_{11}H_{12}ClNO_5$
Exact Mass: 273.0404

Yield: 85 %, White crystalline solid. m.p. = 90-91 °C. $[\alpha]_D^{25}$ = 65.23° (c = 24 mg /2 ml CH_2Cl_2). (IR υ cm^{-1}): 3426 (OH), 3361 (NH), 2941 (CH), 1732 ($COOCH_3$), 1672 (CONH), 1591 (Ar), 1100 (C-Cl). ^1H NMR (300 MHz, DMSO-d_6): δ (ppm): 8.96 (bs, 1H, NH), 7.53-7.48 (m, 4H, Ar-H), 4.85 (d, *J* = 5.5 Hz, 1H, CH), 4.66 (d, *J* = 5.5 Hz, 1H, CH), 3.77 (s, 3H, OCH_3), 2.97 (bs, 2H, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.2 (CONH), 170.3 ($COOCH_3$), 134.8 (Ar-C-NH), 129.3, 125.2, 123.2, 122.1, 120.5 (Ar-C), 74.7 (CH), 73.9 (CH), 52.1 (OCH_3). Anal. Calc. For $C_{11}H_{12}ClNO_5$ (273.0) C, 48.28; H, 4.42; Cl,12.95; N, 5.12; O, 29.23 Found C, 48.60; H, 4.30; Cl, 13.08; N, 5.34; O, 29.67. EI-MS *m/z* (%): 273.1 M^+ (9.0), 214.1 (5.5), 127.0 (100), 59.0 (38.1).

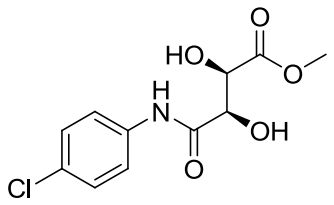
(2*R*,3*R*)-Methyl-4-(3-chlorophenylamino)-2,3-dihydroxy-4-oxobutanoate (3k)



Chemical Formula: $C_{11}H_{12}ClNO_5$
Exact Mass: 273.0404

Yield: 77 %, White crystalline solid, m.p. = 101-102 °C. $[\alpha]_D^{25}$ = 66.31° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3370 (OH), 3302 (NH), 2950 (CH), 1733 ($COOCH_3$), 1664 (CONH), 1588 (Ar), 1110 (C-Cl). ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 9.88 (bs, 1H, NH), 7.95 (s, 1H, Ar-H), 7.84-7.79 (m, 3H, Ar-H), 6.10 (d, *J* = 6.7 Hz, 1H, OH), 5.91 (d, *J* = 6.7 Hz, 1H, OH), 4.71 (dd, *J* = 6.7, 2.4 Hz, 1H ,CH), 4.61 (dd, *J* = 6.7, 2.4 Hz, 1H ,CH), 3.68 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.4 (CONH), 169.4 ($\underline{C}OOCH_3$), 139.1 (Ar-$\underline{C}$-NH), 135.5, 128.7, 127.0, 123.1, 121.5 (Ar-$\underline{C}$), 75.4 ($\underline{C}H$), 73.7 ($\underline{C}H$), 52.5 ($O\underline{C}H_3$). Anal. Calc. For $C_{11}H_{12}ClNO_5$ (273.0) C, 48.28; H, 4.42; Cl, 12.95; N, 5.12; O, 29.23 Found C, 48.60; H, 4.30; Cl, 13.08; N, 5.34; O, 29.67. EI-MS *m/z* (%): 273.1 M^+ (9.0), 214.1 (5.5), 127.0 (100), 59.0 (38.1).

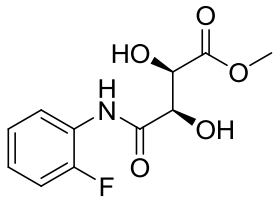
(2*R*,3*R*)-Methyl-4-(4-chlorophenylamino)-2,3-dihydroxy-4-oxobutanoate (3l)



Chemical Formula: $C_{11}H_{12}ClNO_5$
Exact Mass: 273.0404

Yield: 87 %, White crystalline solid, m.p. = 110-112 °C. $[\alpha]_D^{25}$ = 71.31° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3423 (OH), 3343 (NH), 2981 (CH), 1745 ($COOCH_3$), 1670 (CONH), 1532 (Ar), 1023 (C-Cl). ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 8.99 (bs, 1H, NH), 7.86 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.74 (d, *J* = 8.4 Hz, 2H, Ar-H), 4.71 (d, *J* = 5.4 Hz, 1H, CH), 4.65 (d, *J* = 5.4 Hz, 1H, CH), 3.77 (s, 3H, OCH_3), 2.96 (bs, 2H, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.1 (CONH), 169.4 ($\underline{C}OOCH_3$), 137.3 (Ar-$\underline{C}$-NH), 129.7, 128.9 (2), 121.5 (2) (Ar-$\underline{C}$), 74.3 ($\underline{C}H$), 72.8 ($\underline{C}H$), 52.3 ($O\underline{C}H_3$). Anal. Calc. For $C_{11}H_{12}ClNO_5$ (273.0) C, 48.28; H, 4.42; Cl, 12.95; N, 5.12; O, 29.23 Found C, 48.60; H, 4.30; Cl, 13.08; N, 5.34; O, 29.67. EI-MS *m/z* (%): 273.1 M^+ (9.0), 214.1 (5.5), 127.0 (100), 59.0 (38.1).

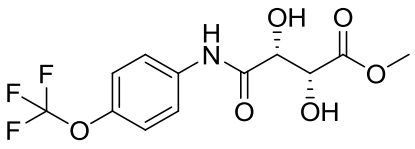
(2*R*,3*R*)-Methyl-4-(2-fluorophenylamino)-2,3-dihydroxy-4-oxobutanoate (3m)



Chemical Formula: $C_{11}H_{12}FNO_5$
Exact Mass: 257.0700

Yield: 79 %. White crystalline solid. m.p = 110-111 °C. $[\alpha]_D^{25}$ = 48.91° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3450 (OH), 3309 (NH), 2977 (CH), 1749 ($COOCH_3$), 1678 (CONH), 1527 (Ar), 1118 (C-F). ^1H NMR (300 MHz, DMSO-d_6): δ (ppm): 8.93 (bs, 1H, NH), 7.88-7.57 (m, 4H, Ar-H), 4.86 (d, *J* = 5.6 Hz, 1H, CH), 4.66 (d, *J* = 5.6 Hz, 1H, CH), 3.78 (s, 3H, OCH_3), 2.98 (bs, 2H, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 170.9 (CONH), 169.7 ($COOCH_3$), 152.6, 128.4, 125.7, 123.0, 122.1 (Ar-C), 146.4 (Ar-C-NH), 74.2 (CH), 73.3 (CH), 51.2 (OCH_3). Anal. Calc. For $C_{11}H_{12}FNO_5$ (257.0) C, 51.36; H, 4.70; F, 7.39; N, 5.45; O, 31.10 Found C, 51.12; H, 4.90; F, 7.67; N, 5.18; O, 31.33. EI-MS *m/z* (%): 257.1 M^+ (9.0), 198.0 (5.7), 111.0 (100), 59.0 (18.9).

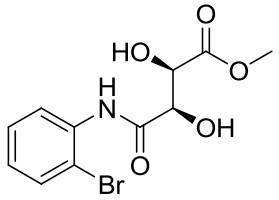
(2*R*,3*R*)-Methyl-2,3-dihydroxy-4-oxo-4-(4(trifluoromethoxy)Phenylamino)butanoate (3n)



Chemical Formula: $C_{12}H_{12}F_3NO_6$
Exact Mass: 323.0617

Yield: 72 %. White crystalline solid. m.p = 87-88 °C. $[\alpha]_D^{25}$ = 60.29° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3509 (OH), 3358 (NH), 2996 (CH), 1752 ($COOCH_3$), 1671 (CONH), 1615 (Ar), 1312 (C-F_3). ^1H NMR (300 MHz, DMSO-d_6): δ (ppm): 9.94 (bs, 1H, -NH), 7.84 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.73 (d, *J* = 8.4 Hz, 2H, Ar-H), 4.84 (d, *J* = 5.3 Hz, 1H, CH), 4.76 (d, *J* = 5.3 Hz, 1H, CH), 3.77 (s, 3H, OCH_3), 3.12 (bs, 2H, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.5 (CONH), 169.9 ($COOCH_3$), 144.1 (Ar-C-OCF_3), 139.9 (Ar-C-NH), 127.3 (OCF_3), 125.3 (2), 119.3 (2), (Ar-C), 75.1 (CH), 74.4 (CH), 52.5 (OCH_3). Anal. Calc. For $C_{12}H_{12}F_3NO_6$ (323.0) C, 44.59; H, 3.74; F, 17.63; N, 4.33; O, 29.70 Found C, 44.23; H, 3.45; F, 17.79; N, 4.88; O, 29.35. EI-MS *m/z* (%): 323.1 M^+ (13.7), 264.1 (6.7), 177.0 (100), 59.0 (38.0).

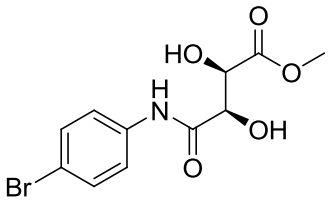
(2*R*,3*R*)-Methyl-4-(2-bromophenylamino)-2,3-dihydroxy-4-oxobutanoate (3o)



Chemical Formula: $C_{11}H_{12}BrNO_5$
Exact Mass: 316.9899

Yield: 80 %. White crystalline solid. m.p = 145-146 °C. $[\alpha]_D^{25}$ = 62.41° (c = 24 mg / 2 mL CH_2Cl_2). (IR υ cm^{-1}): 3500 (OH), 3272 (NH), 2937 (CH), 1747 ($COOCH_3$), 1670 (CONH), 1521 (Ar), 1030 (C-Br). ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 9.28 (bs, 1H, NH), 7.84-7.72 (m, 4H, Ar-H), 4.80 (d, *J* = 5.4 Hz, 1H, CH), 4.70 (d, *J* = 5.4 Hz, 1H, CH), 3.77 (s, 3H, OCH_3), 3.21 (bs, 2H, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.6 (CONH), 170.9 ($COOCH_3$), 138.4 (Ar-C-NH), 128.7, 127.0, 125.9, 123.1, 121.5 (Ar-C), 74.3 (CH), 72.8 (CH), 51.2 (OCH_3). Anal. Calc. For $C_{11}H_{12}BrNO_5$ (316.9) C, 41.53; H, 3.80; Br, 25.12; N, 4.40; O, 25.15 Found C, 41.67; H, 4.30; Br, 25.06; N, 4.75; O, 25.45. EI-MS *m/z* (%): 317.1 M^+ (2.9), 197.1 (5.9), 119.0 (11.2), 60.1 (100).

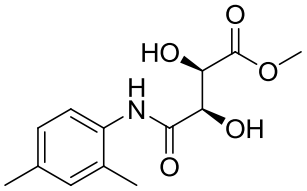
(2*R*,3*R*)-Methyl-4-(4-bromophenylamino)-2,3-dihydroxy-4-oxobutanoate (3p)



Chemical Formula: $C_{11}H_{12}BrNO_5$
Exact Mass: 316.9899

Yield: 84 %. White crystalline solid. m.p = 115-116 °C. $[\alpha]_D^{25}$ = 68.39° (c = 24 mg /2 ml CH_2Cl_2). (IR υ cm^{-1}): 3499 (OH), 3301 (NH), 2947 (CH), 1735 ($COOCH_3$), 1661 (CONH), 1591 (Ar), 1025 (C-Br). ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 9.90 (bs, 1H, NH), 7.53 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.46 (d, *J* = 8.4 Hz, 2H, Ar-H), 4.93 (d, *J* = 5.4 Hz, 1H, CH), 4.89 (d, *J* = 5.4 Hz, 1H, CH), 3.86 (s, 3H, OCH_3), 3.02 (bs, 2H, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.2 (CONH), 168.9 ($COOCH_3$), 136.1 (Ar-C-NH), 130.9 (2), 120.9 (2), 118.6 (Ar-C), 74.3 (CH), 73.1 (CH), 52.2 (OCH_3). Anal. Calc. For $C_{11}H_{12}BrNO_5$ (316.9) C, 41.53; H, 3.80; Br, 25.12; N, 4.40; O, 25.15 Found C, 41.67; H, 4.30; Br, 25.06; N, 4.75; O, 25.45. EI-MS *m/z* (%): 317.1 M^+ (2.9), 197.1 (5.9), 119.0 (11.2), 60.1 (100).

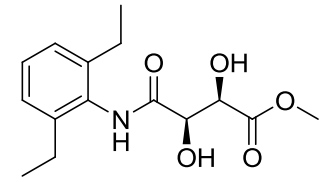
(2*R*,3*R*)-Methyl-4-(2,4-dimethylphenylamino)-2,3-dihydroxy-4-oxobutanoate (3q)



Chemical Formula: $C_{13}H_{17}NO_5$
Exact Mass: 267.1107

Yield: 78 %. White crystalline solid. m.p = 160-161 °C. $[\alpha]_D^{25}$ = 47.99° (c = 24 mg / 2 ml CH_2Cl_2). (IR υ cm^{-1}): 3456 (OH), 3376 (NH), 2954 (CH), 1749 ($COOCH_3$), 1662 (CONH), 1506 (Ar). ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 8.81 (bs, 1H, NH), 7.89 (d, *J* = 8.4 Hz, 1H, Ar-H) , 7.69 (d, *J* = 8.4 Hz, 1H, Ar-H) , 7.60 (s, 1H, Ar-H) , 4.85 (d, *J* = 5.5 Hz, 1H, CH), 4.67 (d, *J* = 5.5 Hz, 1H, CH), 3.79 (s, 3H, OCH_3), 3.11 (bs, 2H, OH), 2.31 (s, 3H, Ar-CH_3), 2.28 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 170.9 (CONH), 168.2 ($COOCH_3$), 135.9 (Ar-C-NH), 132.8, 131.8, 128.5, 126.8 (Ar-C), 74.9 (CH), 72.5 (CH), 52.2 (OCH_3), 20.5 (Ar-CH_3), 17.8 (Ar-CH_3). Anal. Calc. For $C_{13}H_{17}NO_5$ (267.1) C, 58.42; H, 6.41; N, 5.24; O, 29.93 Found C, 58.66; H, 6.12; N, 5.68; O, 30.05. EI-MS *m/z* (%): 267.2 M^+ (8.1), 208.1 (2.7), 147.2 (30.8), 121.2 (100), 59.0 (20.5).

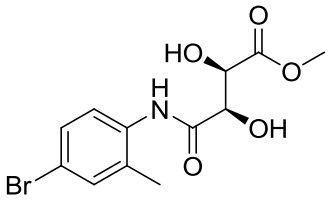
(2*R*,3*R*)-Methyl-4-(2,6-diethylphenylamino)-2,3-dihydroxy-4-oxobutanoate (3r)



Chemical Formula: $C_{15}H_{21}NO_5$
Exact Mass: 295.1420

Yield: 79 %. White crystalline solid. m.p = 123-124 °C. $[\alpha]_D^{25}$ = 42.91° (c = 24 mg /2 ml CH_2Cl_2). (IR υ cm^{-1}): 3422 (OH), 3269 (NH), 2965 (CH), 1735 ($COOCH_3$), 1665 (CONH), 1525 (Ar). ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 8.73 (bs, 1H, NH), 7.37-7.35 (m, 3H, Ar-H), 5.34 (bs, 2H, OH), 4.89 (d, *J* = 5.4 Hz, 1H ,CH), 4.76 (d, *J* = 5.4 Hz, 1H ,CH), 3.81 (s, 3H , OCH_3), 2.66 (q, *J* = 7.6 Hz, 4H, 2×CH_2), 1.26 (t, *J* = 7.6 Hz, 6H, 2× CH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 170.9 (CONH), 169.1 ($COOCH_3$), 142.2 (Ar-C-NH), 131.7 (2) (Ar-C-C_2H_5), 124.4 123.3 (2) (Ar-C), 73.1 (CH), 72.3 (CH), 52.1 (OCH_3), 23.7 (CH_2), 15.8 (CH_3). Anal. Calc. For $C_{15}H_{21}NO_5$ (295.1) C, 61.00; H, 7.17; N, 4.74; O, 27.09 Found C, 60.78; H, 7.46; N, 4.34; O, 27.29. EI-MS *m/z* (%): 295.2 M^+ (3.9), 236.2 (2.7), 176.1 (100), 119.1 (19.1), 59.1 (20.3).

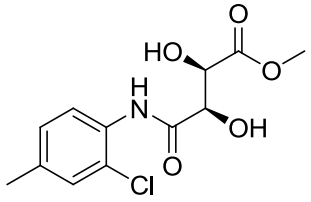
(2*R*,3*R*)-Methyl-4-(4-bromo-2-methylphenylamino)-2,3-dihydroxy-4-oxobutanoate (3s)



Chemical Formula: $C_{12}H_{14}BrNO_5$
Exact Mass: 331.0055

Yield: 85 %. White crystalline solid. m.p = 155-157 °C. $[\alpha]_D^{25}$ = 43.99° (c = 24 mg /2 ml CH_2Cl_2). (IR υ cm^{-1}): 3411 (OH), 3387 (NH), 2949 (CH), 1732 ($COOCH_3$), 1673 (CONH), 1579 (Ar), 1084 (C-Br). ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 8.73 (bs, 1H, NH), 7.42 (s, 1H, Ar-H), 7.35 (d, *J* = 8.4 Hz, 1H, Ar-H), 7.05 (d, *J* = 8.4 Hz, 1H, Ar-H), 4.73 (d, *J* = 5.4 Hz, 1H, CH), 4.64 (d, *J* = 5.4 Hz, 1H, CH), 3.88 (s, 3H, OCH_3), 3.24 (bs, 2H, OH), 2.27 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.2 (CONH), 168.9 ($COOCH_3$), 134.7 (Ar-C-NH), 131.6, 129.4, 124.7, 117.8 (Ar-C), 73.9 (CH), 72.3 (CH), 52.1 (OCH_3), 19.7 (Ar-CH_3). Anal. Calc. For $C_{12}H_{14}BrNO_5$ (331.0) C, 43.39; H, 4.25; Br, 24.06; N, 4.22; O, 24.08 Found C, 43.69; H, 4.65; Br, 24.16; N, 3.90; O, 24.50. EI-MS *m/z* (%): 331.1 M^+ (34.0), 271.1 (8.4), 185.1 (100), 59.1 (29.5).

(2*R*,3*R*)-Methyl-4-(2-chloro-4-methylphenylamino)-2,3-dihydroxy-4-oxobutanoate (3t)



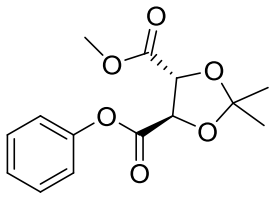
Chemical Formula: $C_{12}H_{14}ClNO_5$
Exact Mass: 287.0561

Yield: 81 %. White crystalline solid. m.p = 89-90 °C. $[\alpha]_D^{25}$ = 62.99° (c = 24 mg /2 ml CH_2Cl_2). (IR υ cm^{-1}): 3489 (OH), 3345 (NH), 2958 (CH), 1724 (CO OCH_3), 1670 (CONH), 1610 (Ar), 1092 (C-Cl). ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 8.90 (bs, 1H, NH), 7.79 (s,1H, Ar-H), 7.59 (d, *J* = 8.4 Hz, 1H, Ar-H), 6.99 (d, *J* = 8.4 Hz, 1H, Ar-H), 5.91 (bs, 2H, OH), 4.82 (d, *J* = 5.3 Hz, 1H, CH), 4.72 (d, *J* = 5.3 Hz, 1H , CH), 3.82 (s, 3H, OCH_3), 2.22 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.1 (CONH), 168.8 ($COOCH_3$), 136.9 (Ar-C-NH), 131.9 (Ar-C-CH_3), 129.6, 127.3, 120.6 (Ar-C), 74.3 (CH), 73.5 (CH), 53.9 (OCH_3), 21.2 (Ar-CH_3). Anal. Calc. For $C_{12}H_{14}ClNO_5$ (287.0) C, 50.10; H, 4.90; Cl, 12.32; N, 4.87; O, 27.81 Found C, 50.43; H, 5.13; Cl, 12.63; N, 4.33; O, 28.20. EI-MS *m/z* (%): 287.1 M^+ (13.1), 228.0 (5.6), 141.2 (100), 59.0 (24.5).

3.5 General procedure for the synthesis of monoaryl esters (4a-4h)

In a round bottom flask (100 ml), compound (**2**) (0.61 g, 3 mmol) in DCM (30 ml), EDC (0.68 g, 3.6 mmol) and catalytic amount of DMAP were placed under nitrogen. After half an hour substituted phenols (3 mmol) was added and stirred for 4-12 hours. After the completion of the reaction, byproduct urea was removed by extraction with ethyl acetate or chloroform and water (30 × 3). Crude was purified by column chromatography using ethyl acetate: n-hexane (3:7) as eluent.

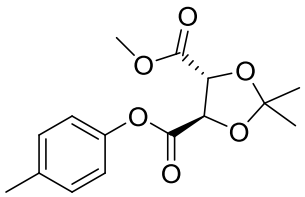
(4*R*,5*R*)-4-Methyl-5-phenyl-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (4a)



Chemical Formula: $C_{14}H_{16}O_6$
Exact Mass: 280.0947

Yield: 74 %. Colourless oil. $[\alpha]_D^{25}$ = 72.58° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 2992 (CH), 1756 (COOPh), 1732 ($COOCH_3$) 1592 (Ar), 1324 (C-O-C). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.44-7.14 (m, 5H, Ar-H), 5.06 (d, 1H, *J* = 5.3 Hz, CH), 4.99 (d, 1H, *J* = 5.3 Hz, CH), 3.87 (s, 3H, O-CH_3), 1.58 (s, 3H, CH_3), 1.51 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.7 (COOPh), 168.5 ($COOCH_3$), 150.8 (Ar-C-OR), 129.6, 126.5, 121.8 (Ar-C), 114.7 (qt, C) , 76.5 (CH), 75.2 (CH), 53.4 (OCH_3), 26.3 (CH_3), 25.1 (CH_3). HRMS-ESI for $C_{14}H_{16}O_6$ Na: $[M+Na]^+$ calcd: 303.0945, found: 303.0845. Anal. Calc. For $C_{14}H_{16}O_6$: C, 59.99; H, 5.75; O, 34.25. Found C, 59.96; H, 5.77; O, 34.27.

(4*R*,5*R*)-4-Methyl-5-*p*-tolyl-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (4b)

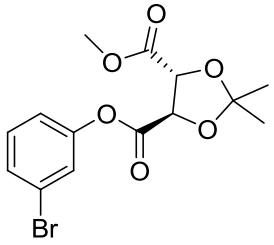


Chemical Formula: $C_{15}H_{18}O_6$
Exact Mass: 294.1103

Yield: 79 %. Yellow Oil. $[\alpha]_D^{25}$ = 70.51° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 2994 (CH), 1751 (COOPh), 1730 ($COOCH_3$), 1590 (Ar), 1321 (C-O-C). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.54 (d, *J* = 8.3 Hz, 2H, Ar-H), 6.99 (d, *J* = 8.4 Hz, 2H Ar-H), 5.03 (d, 1H, *J* = 5.3 Hz, CH), 4.96 (d, 1H, *J* = 5.3 Hz, CH), 3.85 (s, 3H, O-CH_3), 2.35 (s, 3H, Ar-CH_3), 1.56 (s, 3H, CH_3), 1.46 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.3 (COOPh), 169.4 ($COOCH_3$), 147.5 (Ar-C-OR), 136.4, 130.5, 120.9 (Ar-C), 113.7 (qt, C), 75.3 (CH), 74.3 (CH), 52.5 (O-CH_3), 26.6 (CH_3), 25.6 (CH_3), 20.4 (Ar-CH_3). HRMS-ESI for $C_{15}H_{18}O_6$ Na: $[M+Na]^+$ calcd: 317.1001,

found: 317.0984. Anal. Calc. For $C_{15}H_{18}O_6$: C, 61.22; H, 6.16; O, 32.62 Found C, 61.25; H, 6.13; O, 32.66.

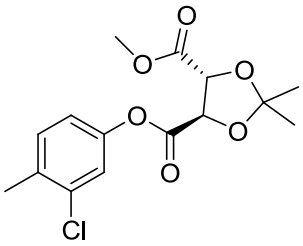
(4*R*,5*R*)-4-(3-Bromophenyl)-5-methyl-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (4c)



Chemical Formula: $C_{14}H_{15}BrO_6$
Exact Mass: 358.0052

Yield: 65 %. Yellow Oil. $[\alpha]_D^{25}$ = 54.17° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 2984 (CH), 1751 (COOPh), 1722 ($COOCH_3$), 1594 (Ar), 1311 (C-O-C), 563 (C-Br). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.39 (s, 1H, Ar-H), 7.36-7.30 (m, 3H, Ar-H) 5.00 (d, 1H, *J* = 5.5 Hz, CH), 4.92 (d, 1H, *J* = 5.5 Hz, CH) 3.83 (s, 3H, O-CH_3), 1.55 (s, 3H, CH_3), 1.51 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.5 (<u>C</u>OOPh), 169.8 (<u>C</u>OOCH$_3$), 150.5 (Ar-<u>C</u>-OR), 130.4, 129.6, 124.7, 122.5 (Ar-<u>C</u>), 114.1 (qt, <u>C</u>), 76.3 (<u>C</u>H), 75.6 (<u>C</u>H), 53.4 (O<u>C</u>H$_3$), 26.8 (<u>C</u>H$_3$), 25.4 (<u>C</u>H$_3$). HRMS-ESI for $C_{14}H_{15}BrO_6$ Na: $[M+Na]^+$ calcd: 380.9950, found: 380.9948. Anal. Calc. For $C_{14}H_{15}BrO_6$: C, 48.28; H, 4.59; Br, 21.41; O, 25.72 Found C, 48.30; H, 4.56; Br, 21.44; O, 25.70.

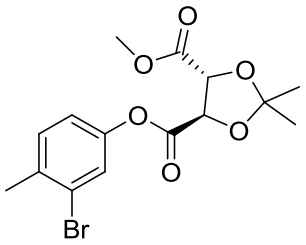
(4*R*,5*R*)-4-(3-Chloro-4-methylphenyl)-5-methyl-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (4d)



Chemical Formula: $C_{15}H_{17}ClO_6$
Exact Mass: 328.0714

Yield: 64 %. Yellow oil. $[\alpha]_D^{25}$ = 60.35° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 2983 (CH), 1747 (COOPh), 1723 ($COOCH_3$) 1581 (Ar), 1316 (C-O-C), 736 (C-Cl). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.63 (s, 1H, Ar-H), 6.95 (d, *J* = 8.4 Hz, 2H, Ar-H), 5.01 (d, 1H, *J* = 4.9 Hz, CH), 4.94 (d, 1H, *J* = 4.9 Hz, CH), 3.85 (s, 3H, OCH_3), 2.35 (s, 3H, Ar-CH_3), 1.56 (s, 3H, CH_3), 1.46 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 169.6 (<u>C</u>OOPh), 168.2 (<u>C</u>OOCH$_3$), 148.5 (Ar-<u>C</u>-OR), 134.4, 134.1, 131.3, 121.5, 119.7 (Ar-<u>C</u>), 114.6 (qt, <u>C</u>), 75.5 (<u>C</u>H), 74.3 (<u>C</u>H), 53.5 (O-<u>C</u>H$_3$), 26.8 (<u>C</u>H$_3$), 25.8 (<u>C</u>H$_3$), 19.7 (Ar-<u>C</u>H$_3$). HRMS-ESI for $C_{15}H_{17}ClO_6$ Na: $[M+Na]^+$ calcd: 351.0611, found: 351.0602. Anal. Calc. For $C_{15}H_{17}ClO_6$: C, 54.80; H, 5.21; Cl, 10.78; O, 29.20 Found C, 54.83; H, 5.24; Cl, 10.75; O, 29.17.

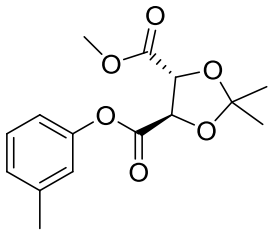
(4*R*,5*R*)-4-(3-Bromo-4-methylphenyl)-5-methyl-2,2-dimethyl-1,3-dioxolane-4,5dicarboxylate (4e)



Chemical Formula: $C_{15}H_{17}BrO_6$
Exact Mass: 372.0209

Yield: 69 %. White crystalline solid m.p 145-146 °C. $[\alpha]_D^{25}$ = 61.14° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 2980 (CH), 1748 (COOPh), 1736 ($COOCH_3$), 1580 (Ar), 1326 (C-O-C), 559 (C-Br). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.35 (s, 1H, Ar-H), 6.99 (d, *J* = 8.4 Hz, 2H Ar-H), 5.02 (d, 1H, *J* = 5.0 Hz, CH), 4.94 (d, 1H, *J* = 5.0 Hz, CH), 3.86 (s, 3H, OCH_3), 2.39 (s, 3H, Ar-CH_3), 1.55 (s, 3H, CH_3), 1.45 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 169.9 (COOPh), 168.3 ($COOCH_3$), 148.5 (Ar-C-OR), 136.7, 131.8, 125.5, 124.3, 120.3 (Ar-C), 114.8 (qt, C), 76.1 (CH), 75.3 (CH), 53.6 (OCH_3), 26.7 (CH_3), 25.5 (CH_3), 22.3 (Ar-CH_3). HRMS-ESI for $C_{15}H_{17}BrO_6$ Na: $[M+Na]^+$ calcd: 395.0106, found: 395.0209. Anal. Calc. For $C_{15}H_{17}BrO_6$: C, 48.28; H, 4.59; Br, 21.41; O, 25.72 Found C, 48.30; H, 4.57; Br, 21.44; O, 25.70.

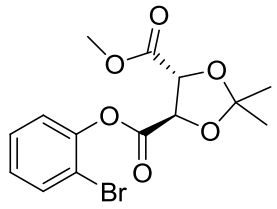
(4*R*,5*R*)-4-Methyl-5-*m*-tolyl-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (4f)



Chemical Formula: $C_{15}H_{18}O_6$
Exact Mass: 294.1103

Yield: 77 %. Brown Oil. $[\alpha]_D^{25}$ = 74.51° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 2983 (CH), 1753 (COOPh), 1733 ($COOCH_3$), 1581 (Ar), 1321 (C-O-C). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.38 (s, 1H, Ar-H), 7.05-6.99 (m, 3H Ar-H), 5.03 (d, 1H, *J* = 5.3 Hz, CH), 4.96 (d, 1H, *J* = 5.3 Hz, CH), 3.85 (s, 3H, OCH_3), 2.36 (s, 3H, Ar-CH_3), 1.56 (s, 3H, CH_3), 1.46 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 169.7 (COOPh), 168.6 ($COOCH_3$), 150.7 (Ar-C-OR), 139.7, 129.6, 127.6, 121.0,118.2 (Ar-C), 114.6 (qt, C), 76.3 (CH), 75.5 (CH), 53.5 (OCH_3), 26.7 (CH_3), 25.7 (CH_3), 21.8 (Ar-CH_3). HRMS-ESI for $C_{15}H_{18}O_6$ Na: $[M+Na]^+$ calcd: 317.1001, found: 317.0984. Anal. Calc. For $C_{15}H_{18}O_6$: C, 61.22; H, 6.16; O, 32.62 FoundC, 61.25; H, 6.18; O, 32.60.

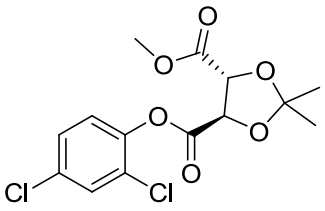
(4*R*,5*R*)-4-(2-Bromophenyl)-5-methyl-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (4g)



Chemical Formula: $C_{14}H_{15}BrO_6$
Exact Mass: 358.0052

Yield: 56 %. Brown Oil. $[\alpha]_D^{25}$ = 49.15° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 2973 (CH), 1749 (COOPh), 1727 ($COOCH_3$), 1591 (Ar), 1311 (C-O-C), 567 (C-Br). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.63-7.14 (m, 4H, Ar-H), 5.15 (d, 1H, *J* = 5.4 Hz, CH), 5.11 (d, 1H, *J* = 5.4 Hz, CH), 3.86 (s, 3H, O-CH_3), 1.55 (s, 3H, CH_3), 1.45 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 169.9 (COOPh), 167.8 ($COOCH_3$), 147.9 (Ar-C-OR), 133.8, 128.7, 127.5, 123.6 (Ar-C), 114.6 (qt, C) , 76.1 (CH), 75.3 (CH), 52.7 (OCH_3), 26.3 (CH_3), 25.7 (CH_3). HRMS-ESI for $C_{14}H_{15}BrO_6$ Na: $[M+Na]^+$ calcd: 380.9950, found: 380.9946. Anal. Calc. For $C_{14}H_{15}BrO_6$: C, 48.28; H, 4.59; Br, 21.41; O, 25.72 Found C, 48.31; H, 4.53; Br, 21.40; O, 25.70.

(4*R*,5*R*)-4-(2,4-Dichlorophenyl)-5-methyl-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (4h)



Chemical Formula: $C_{14}H_{14}Cl_2O_6$
Exact Mass: 348.0167

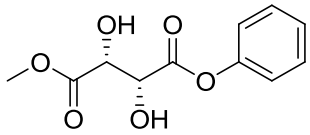
Yield: 55 %. Brown Oil. $[\alpha]_D^{25}$ = 61.15° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 2983 (CH), 1748 (COOPh), 1724 ($COOCH_3$), 1581 (Ar), 1321 (C-O-C), 765 (C-Cl). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.48 (s, 1H, Ar-H), 7.13 (d, *J* = 8.1 Hz, 1H, Ar-H), 6.93 (d, *J* = 8.1 Hz, 1H, Ar-H), 5.12 (d, 1H, *J* = 5.0 Hz, CH), 5.02 (d, 1H, J = 5.0 Hz, CH), 3.86 (s, 3H, O-CH_3), 1.56 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.6 (COOPh), 169.4 ($COOCH_3$), 145.7 (Ar-C-OR), 132.8, 130.5, 128.9, 127.4, 124.7 (Ar-C), 114.7 (qt, C), 75.8 (CH), 74.9 (CH), 53.8 (OCH_3), 26.3 (CH_3), 25.5 (CH_3). HRMS-ESI for $C_{14}H_{14}Cl_2O_6$ Na: $[M+Na]^+$ calcd: 371.0065, found: 371.0069. Anal. Calc. For $C_{14}H_{14}Cl_2O_6$: C, 48.16; H, 4.04; Cl, 20.31; O, 27.49 Found C, 48.13; H, 4.06; Cl, 20.35; O, 27.47.

3.6 General procedure for the synthesis of compounds (5a-5h)

In a round bottom flask (100 ml) solution of monoaryl esters (**4a-4h**) (1 eq) in DCM was stirred at 0 °C. $BF_3.Et_2O$ (2 eq) was added dropwise under nitrogen atmosphere.

The reaction mixture was then allowed to warm to room temperature and stirred overnight. After the completion as indicated by TLC, Solvent was evaporated under reduced pressure. The crude was dissolved in ethyl acetate (30 ml), washed with water and brine (30 ml × 3). The organic layer was dried over anhydrous magnesium sulphate. The crude was further purified by column chromatography using methanol: chloroform (2:8) as eluent.

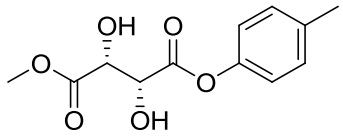
(2*R*,3*R*)-1-Methyl-4-phenyl-2,3-dihydroxysuccinate (5a)



Chemical Formula: $C_{11}H_{12}O_6$
Exact Mass: 240.0634

Yield: 86 %. White solid m.p 75-77 °C. $[\alpha]_D^{25}$ = 73.51° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3508 (OH), 2965 (CH), 1749 (COOPh), 1733 ($COOCH_3$), 1589 (Ar), 1314 (C-O-C). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.45-7.15 (m, 5H, Ar-H), 4.84 (d, 1H, *J* = 5.5 Hz, CH), 4.80 (d, 1H, *J* = 5.5 Hz, CH), 3.91 (s, 3H, OCH_3), 3.25 (bs, 2H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 171.3 (<u>C</u>OOPh), 170.5 (<u>C</u>$OOCH_3$), 150.7 (Ar-<u>C</u>-OR), 129.9, 126.3, 121.7 (Ar-<u>C</u>), 74.5 (<u>C</u>H), 73.5 (<u>C</u>H), 53.9 ($O\underline{C}H_3$). Anal. Calc. For $C_{11}H_{12}O_6$: C, 55.00; H, 5.04; O, 39.96 Found C, 55.03; H, 5.07; O, 39.94.

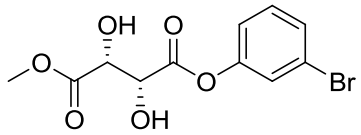
(2*R*,3*R*)-1-Methyl-4-*p*-tolyl-2,3-dihydroxysuccinate (5b)



Chemical Formula: $C_{12}H_{14}O_6$
Exact Mass: 254.0790

Yield: 78 %. White solid m.p 112-114 °C. $[\alpha]_D^{25}$ = 70.41° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3528 (OH), 2975 (CH), 1743 (COOPh), 1731 ($COOCH_3$), 1579 (Ar), 1311 (C-O-C). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.43 (d, *J* = 8.9 Hz, 2H, Ar-H), 7.06 (d, *J* = 8.8 Hz, 2H, Ar-H), 4.82 (d, 1H, *J* = 5.4 Hz, CH), 4.79 (d, 1H, *J* = 5.4 Hz, CH), 3.92 (s, 3H, OCH_3), 3.28 (bs, 2H, OH), 2.37 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 171.6 (<u>C</u>OOPh), 170.1 (<u>C</u>$OOCH_3$), 148.7 (Ar-<u>C</u>-OR), 136.8, 130.5, 120.3 (Ar-<u>C</u>), 75.1 (<u>C</u>H), 74.1 (<u>C</u>H), 53.7 ($O\underline{C}H_3$), 20.7 (Ar-$\underline{C}H_3$). Anal. Calc. For $C_{12}H_{14}O_6$: C, 56.69; H, 5.55; O, 37.76 FoundC, 56.64; H, 5.51; O, 37.73.

(2*R*,3*R*)-1-(3-Bromophenyl)-4-methyl-2,3-dihydroxysuccinate (5c)

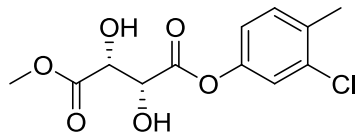


Chemical Formula: $C_{11}H_{11}BrO_6$
Exact Mass: 317.9739

Yield: 81 %. Colourless Oil. $[\alpha]_D^{25}$ = 51.25° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3538 (OH), 2985 (CH), 1748 (COOPh), 1724 ($COOCH_3$), 1569 (Ar), 1321 (C-O-C), 550 (C-Br).

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.41 (s, 1H, Ar-H), 7.37-7.31 (m, 3H, Ar-H) 5.06 (d, 1H, *J* = 4.9 Hz, CH), 4.96 (d, 1H, *J* = 4.9 Hz, CH), 3.86 (s, 3H, OCH_3), 3.27 (bs, 2H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 171.5 (COOPh), 170.3 ($COOCH_3$), 148.8 (Ar-C-OR), 132.7, 130.4, 127.6, 126.2 (Ar-C), 75.4 (CH), 73.9 (CH), 52.6 (O-CH_3). Anal. Calc. For $C_{11}H_{11}BrO_6$: C, 41.40; H, 3.47; Br, 25.04; O, 30.08 Found C, 41.42; H, 3.49; Br, 25.01; O, 30.10.

(2*R*,3*R*)-1-(3-Chloro-4-methylphenyl)-4-methyl-2,3-dihydroxysuccinate (5d)

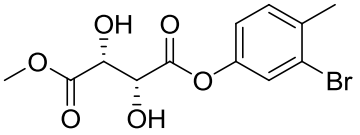


Chemical Formula: $C_{12}H_{13}ClO_6$
Exact Mass: 288.0401

Yield: 77 %. Yellow Oil. $[\alpha]_D^{25}$ = 67.25° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3548 (OH), 2982 (CH), 1745 (COOPh), 1733 ($COOCH_3$), 1567 (Ar), 1323 (C-O-C), 766 (C-Cl).

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.33 (s, 1H, Ar-H), 7.12 (d, *J* = 8.4 Hz, 2H Ar-H), 5.11 (d, 1H, *J* = 5.5 Hz, CH), 4.92 (d, 1H, *J* = 5.5 Hz, CH), 3.87 (s, 3H, OCH_3), 3.30 (bs, 2H, OH), 2.35 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.5 (COOPh), 169.8 ($COOCH_3$), 147.4 (Ar-C-OR), 134.9, 134.5, 131.4, 120.7, 117.3 (Ar-C), 74.7 (CH), 73.7 (CH), 53.6 (O-CH_3), 19.8 (Ar-CH_3). Anal. Calc. For $C_{12}H_{13}ClO_6$: C, 49.93; H, 4.54; Cl, 12.28; O, 33.25 Found C, 49.91; H, 4.51; Cl, 12.25; O, 33.27.

(2*R*,3*R*)-1-(3-Bromo-4-methylphenyl)-4-methyl-2,3-dihydroxysuccinate (5e)

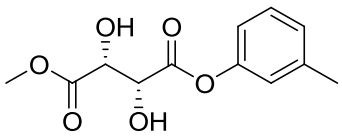


Chemical Formula: $C_{12}H_{13}BrO_6$
Exact Mass: 331.9896

Yield: 72 %. White solid. m.p = 176-177 °C. $[\alpha]_D^{25}$ = 68.15° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3541 (OH), 2980 (CH), 1747 (COOPh), 1731 ($COOCH_3$), 1568 (Ar), 1320 (C-O-C), 566 (C-Br). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.57 (s, 1H, Ar-H), 7.13 (d, *J* = 8.4 Hz, 2H Ar-H), 5.13 (d, 1H, *J* = 5.4 Hz, CH),4.99 (d, 1H, *J* = 5.4 Hz, CH), 3.86 (s, 3H, OCH_3), 3.29 (bs, 2H, OH), 2.39 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.3 (COOPh),

169.9 (COOCH$_3$), 149.7 (Ar-C-OR), 137.5, 133.1, 128.0, 124.9, 120.9 (Ar-C), 75.0 (CH), 74.6 (CH), 52.3 (OCH$_3$), 22.6 (Ar-CH$_3$). Anal. Calc. For $C_{12}H_{13}BrO_6$: C, 43.26; H, 3.93; Br, 23.99; O, 28.82 Found C, 43.25; H, 3.95; Br, 23.97; O, 28.84.

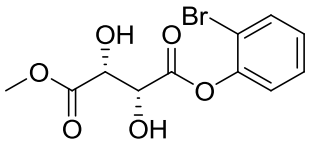
(2*R*,3*R*)-1-Methyl-4-*m*-tolyl-2,3-dihydroxysuccinate (5f)



Chemical Formula: $C_{12}H_{14}O_6$
Exact Mass: 254.0790

Yield: 79 %. Colourless oil. $[\alpha]_D^{25}$ = 74.51° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3531 (OH), 2960 (CH), 1750 (COOPh), 1732 (COOCH$_3$), 1569 (Ar), 1310 (C-O-C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.32 (s, 1H, Ar-H), 7.12-6.99 (m, 3H Ar-H), 4.83 (dd, *J* = 6.9, 2.4 Hz, 1H, CH), 4.80 (dd, *J* = 6.9, 2.4 Hz, 1H, CH), 3.91 (s, 3H, OCH$_3$), 3.40 (d, *J* = 6.9 Hz, 1H, OH), 3.35 (d, *J* = 7.2 Hz, 1H, OH), 2.38 (s, 3H, Ar-CH$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 171.3 (COOPh), 170.2 (COOCH$_3$), 150.9 (Ar-C-OR), 139.5, 129.1, 127.8, 121.2, 118.5 (Ar-C), 74.6 (CH), 73.3 (CH), 53.8 (O-CH$_3$), 21.7 (Ar-CH$_3$). Anal. Calc. For $C_{12}H_{14}O_6$: C, 56.69; H, 5.55; O, 37.76 Found C, 56.66; H, 5.57; O, 37.73.

(2*R*,3*R*)-1-(2-Bromophenyl)-4-methyl-2,3-dihydroxysuccinate (5g)

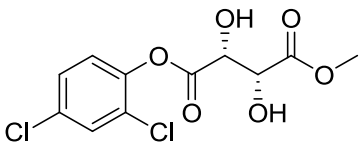


Chemical Formula: $C_{11}H_{11}BrO_6$
Exact Mass: 317.9739

Yield: 76 %. Yellow oil. $[\alpha]_D^{25}$ = 57.15° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3521 (OH), 2980 (CH), 1748 (COOPh), 1725 (COOCH$_3$), 1579 (Ar), 1313 (C-O-C), 559 (C-Br).

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.65-7.19 (m, Ar-H), 5.16 (d, *J* = 5.4 Hz, 1H, CH),5.13 (d, *J* = 5.4 Hz, 1H, CH), 3.87 (s, 3H, OCH$_3$), 3.25 (bs, 2H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.5 (COOPh), 168.9 (COOCH$_3$), 145.8 (Ar-C-OR), 136.9, 134.1, 129.0, 127.7 (Ar-C), 76.3 (CH), 75.2 (CH), 52.5 (O-CH$_3$). Anal. Calc. For $C_{11}H_{11}BrO_6$: C, 41.40; H, 3.47; Br, 25.04; O, 30.08 Found C, 41.43; H, 3.49; Br, 25.01; O, 30.10.

(2*R*,3*R*)-1-(2,4-Dichlorophenyl)-4-methyl-2,3-dihydroxysuccinate (5h)



Chemical Formula: $C_{11}H_{10}Cl_2O_6$
Exact Mass: 307.9854

Yield: 70 %. White crystalline solid. m.p = 103-105 °C. $[\alpha]_D^{25}$ = 66.15° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3531 (OH), 2970 (CH), 1744

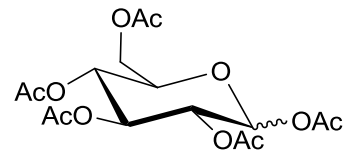
(COOPh), 1725 ($COOCH_3$), 1569 (Ar), 1311 (C-O-C), 768 (C-Cl). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.51 (s, 1H, Ar-H), 7.19 (d, *J* = 7.7 Hz, 1H, Ar-H), 6.89 (d, *J* = 7.7 Hz, 1H Ar-H), 5.14 (d, *J* = 5.5 Hz, 1H, CH), 5.08 (d, *J* = 5.5 Hz, 1H, CH), 3.88 (s, 3H, OCH_3), 3.29 (bs, 2H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 171.4 (CO-O-Ph), 170.7 (CO-O-CH_3), 146.9 (Ar-C-OR), 134.6, 133.4, 129.3, 128.2, 126.8 (Ar-C), 73.2 (CH), 53.6 (O-CH_3). Anal. Calc. For $C_{11}H_{10}Cl_2O_6$: C, 42.74; H, 3.26; Cl, 22.94; O, 31.06 Found C, 42.76; H, 3.28; Cl, 22.99; O, 31.08.

3.7 Synthesis of glycopyranosyl amines

3.7.1 General procedure for the Synthesis of acetylated monosaccharides (6a-6e)[169]

In a round bottom flask (500 ml) with a magnetic stirrer, D-Glucose (21.60 g, 120 mmol), was dissolved in pyridine (200 ml) with catalytic amount of DMAP. Acetic anhydride (113.32 ml, 1200 mmol) was added dropwise with gentle stirring under nitrogen atmosphere and left overnight. After the completion, reaction mixture was diluted with DCM and water (200 ml). The phases were separated and the aqueous phase was extracted with DCM (100ml × 2). The organic layer was washed carefully with 4 N HCl, $NaHCO_3$ and brine (200ml × 2). The combined organic layer was dried over anhydrous magnesium sulphate and filtered; the crude was concentrated on rotavap and purified by column chromatography using ethyl acetate: n.hexane (1:1) as eluent.

1,2,3,4,6-Penta-*O*-acetyl-α/β-D-glucopyranoside (6a)

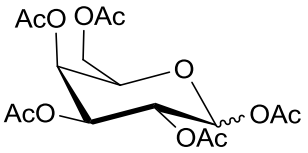


Chemical Formula: $C_{16}H_{22}O_{11}$
Exact Mass: 390.1162

Yield: 75 %. White solid. m.p = 109-112 °C. (IR υ cm^{-1}): 2966 (CH), 1738 (CO). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 6.32 (d, *J* = 4.0 Hz, 1H, H-1^{α}), 5.66 (d, *J* = 8.0 Hz, 1H, H-1^{β}), 5.43, 5.33, 5.13, (3 pseudo t, *J* ~ 10.3 Hz in each, 3H, H-3, H-4, H-2), 4.28 (dd, *J* = 12.4, 4.2 Hz, 1H, H-6^a), 4.21 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.02 (dd, *J* = 12.5, 4.1 Hz, 1H, H-6^b), 2.17, 2.09, 2.04, 2.02, 2.01 (5s, 15 H, 5 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.2, 170.3, 169.7, 168.5, 168.2, (5 × CO, acetyl), 89.3 (C-1), 72.7, 70.1 (C-3, C-5), 69.4 (C-2), 69.2 (C-4), 60.7 (C-6), 20.1 (2),

19.8, 19.4, 19.2, (5 × $\underline{C}H_3$, acetyl). Anal. Calc. For $C_{16}H_{22}O_{11}$: C, 49.23; H, 5.68; O, 45.09 Found C, 49.20; H, 5.66; O, 45.11.

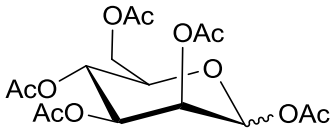
1,2,3,4,6-Penta-*O*-acetyl-α/β-D-galactopyranoside (6b)



Chemical Formula: $C_{16}H_{22}O_{11}$
Exact Mass: 390.1162

Yield: 70 %. Yellow foam. m.p = 113-114 °C. (IR υ cm^{-1}): 2961 (CH), 1735 (CO). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 6.35 (d, *J* = 3.7 Hz, 1H, H-1^{α}), 5.62 (d, *J* = 7.8 Hz, 1H, H-1^{β}), 5.42, 5.36, 5.10, (3 pseudo t, *J* ~ 6.7 Hz in each, 3H, H-3, H-4, H-2), 4.28 (dd, *J* = 12.4, 3.5 Hz, 1H, H-6^a), 5.12 (ddd, *J* = 12.4, 3.6, 2.1 Hz, 1H, H-5), 4.01 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 2.20, 2.18, 2.17,2.15, 2.10 (5s, 15 H, 5 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.4, 170.7, 169.8, 168.5, 168.1, (5 × $\underline{C}O$, acetyl), 89.4, ($\underline{C}$-1), 71.3, 70.3 (C-3, C-5), 69.2 (C-2), 69.0 (C-4), 60.6 ($\underline{C}$-6), 20.3 (2), 19.5, 19.3, 19.2, (5 × $\underline{C}H_3$, acetyl). Anal. Calc. For $C_{16}H_{22}O_{11}$: C, 49.23; H, 5.68; O, 45.09 Found C, 49.24; H, 5.68; O, 45.14.

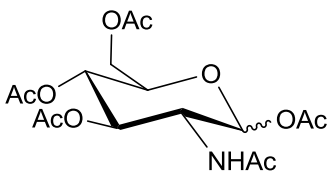
1,2,3,4,6-Penta-*O*-acetyl-α/β-D-mannopyranoside (6c)



Chemical Formula: $C_{16}H_{22}O_{11}$
Exact Mass: 390.1162

Yield: 77 %. Yellow oil. (IR υ cm^{-1}): 2960 (CH), 1733 (CO). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 6.33 (d, J = 3.9 Hz, 1H, H-1^{α}), 5.61 (d, *J* = 7.9 Hz, 1H, H-1^{β}), 5.41, 5.12, (2 pseudo t, *J* = 4.0, 4.3 Hz in each, 2H, H-3, H-2), 5.34, (t, *J* = 12.0 Hz, 1H, H-4), 4.27 (dd, *J* = 12.4, 3.5 Hz, 1H, H-6^a), 5.11 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.02 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 2.21, 2.19, 2.16,2.12, 2.10 (5s, 15 H, 5 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.1, 169.7, 169.3, 168.5, 168.1 (5 × $\underline{C}O$, acetyl), 89.2, ($\underline{C}$-1), 70.3, 69.5 (C-3, C-5), 69.1 (C-2), 68.0 (C-4), 60.8 ($\underline{C}$-6), 20.2 (2), 19.3, 19.2, 19.1 (5 × $\underline{C}H_3$, acetyl). Anal. Calc. For $C_{16}H_{22}O_{11}$: C, 49.23; H, 5.68; O, 45.09 Found C, 49.19; H, 5.65; O, 45.07.

1,3,4,6-Tetra-*O*-acetyl-2-acetamido-α/β-D-glucopyranoside (6d)

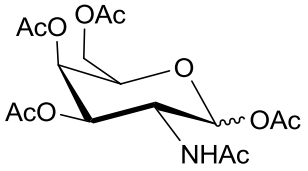


Chemical Formula: $C_{16}H_{23}NO_{10}$
Exact Mass: 389.1322

Yield: 78 %. Dark yellow oil. (IR υ cm^{-1}): 2961 (CH), 1735 (CO). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.63 (d, J = 8.3 Hz, NH), 6.31 (d, *J* = 3.7

Hz, 1H, H-1$^{\alpha}$), 5.59 (d, *J* = 7.8 Hz, 1H, H-1$^{\beta}$), 5.40, 5.33, (2H, 2 pseudo t, *J* ~ 9.5 Hz in each, 1H, H-3, H-4), 5.31, (m, 1H, H-2), 4.24 (dd, *J* = 12.4, 3.5 Hz, 1H, H-6^{a}), 5.11 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.02 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^{b}), 2.22, 2.19, 2.16, 2.15, 2.11 (5s, 15 H, 5 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.6, 170.5, 169.8, 168.2, 168.1 (5 × CO, acetyl), 89.7, (C-1), 70.4, 69.3 (C-3, C-5), 69.2 (C-2), 68.6 (C-4), 60.9 (C-6), 20.4 (2), 19.1, 19.0, 18.9 (5 × CH_3, acetyl). Anal. Calc. For $C_{16}H_{23}NO_{10}$: C, 49.36; H, 5.95; N, 3.60; O, 41.09 Found C, 49.34; H, 5.91; N, 3.62; O, 41.06.

1,3,4,6-Tetra-*O*-acetyl-2-acetamido-α/β-D-galactopyranoside (6e)



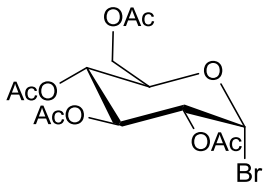
Chemical Formula: $C_{16}H_{23}NO_{10}$
Exact Mass: 389.1322

Yield: 71 %. White solid. m.p = 230-232 °C (decompose). (IR υ cm^{-1}): 2965 (CH), 1737 (CO). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.68 (d, *J* = 8.7 Hz, 1H, NH), 6.34 (d, *J* = 3.8 Hz, 1H, H-1$^{\alpha}$), 5.58 (d, *J* = 7.9 Hz, 1H, H-1$^{\beta}$), 5.41, 5.34 (2 pseudo t, *J* ~ 7.9 Hz in each, 2H, H-3, H-4), 5.31 (m, 1H, H-2), 4.26 (dd, *J* = 12.4, 3.5 Hz, 1H, H-6^{a}), 5.13 (ddd, *J* = 12.4, 3.6, 2.1 Hz, 1H, H-5), 4.03 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^{b}), 2.23, 2.19, 2.16, 2.14, 2.11 (5s, 15 H, 5 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.2, 170.1, 169.8, 168.5, 168.3, (5 × CO, acetyl), 89.8, (C-1), 70.2, 69.6 (C-3, C-5), 69.3 (C-2), 68.8 (C-4), 60.8 (C-6), 20.3 (2), 19.7, 19.5, 18.9, (5 × CH_3, acetyl). Anal. Calc. For $C_{16}H_{23}NO_{10}$: C, 49.36; H, 5.95; N, 3.60; O, 41.09 Found C, 49.33; H, 5.93; N, 3.64; O, 41.07.

3.7.2 General procedure for the Synthesis of glycopyranosyl bromides (7a-7e)[164]

In a round bottom flask (250 ml) with magnetic stirrer, dissolved anomeric mixture of (**6a-6e**) (11.70 g, 30 mmol) in DCM (60 ml). HBr/AcOH (30 %) (29.87 ml, 150 mmol) was carefully added dropwise under nitrogen atmosphere and stirred for two hours. After the completion as indicated by TLC, DCM (50 ml) was added and poured onto iced water (100 ml). The phases were separated and the aqueous phase was extracted with DCM (50 × 2). The combined organic layer was carefully neutralized with $NaHCO_3$, washed with cool water and brine (100 ml × 2). The organic layer was dried over anhydrous magnesium sulphate. After filteration and evaporation of solvents, the crude product was purified by column chromatography using ethyl acetate: n.hexane (3:7) as eluent.

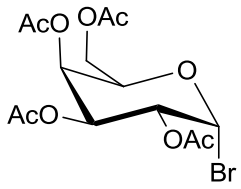
2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (7a)



Chemical Formula: $C_{14}H_{19}BrO_9$
Exact Mass: 410.0212

Yield: 76 %. White solid. m.p = 87-89 °C (lit.;[164] 86-88 °C). (IR υ cm^{-1}): 2964 (CH), 1739 (CO), 552 (C-Br). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 6.52 (d, *J* = 4.0 Hz, 1H, H-1), 5.43, 5.40, 5.25 (3 pseudo t, *J* ~ 10.5 Hz in each, 3H, H-3, H-4, H-2), 4.76 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.24 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.03 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 1.99, 1.98, 1.94,1.92 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.6, 169.4, 169.2, 169.1 (4 × CO, acetyl), 86.9 (C-1), 72.7 (C-5), 71.2 (C-2), 70.7 (C-3), 67.5 (C-4), 60.8 (C-6), 20.2, 20.1, 19.6, 19.5, (4 × CH_3, acetyl). Anal. Calc. For $C_{14}H_{19}BrO_9$: C, 40.89; H, 4.66; Br, 19.43; O, 35.02 Found C, 40.91; H, 4.64; Br, 19.41; O, 35.04.

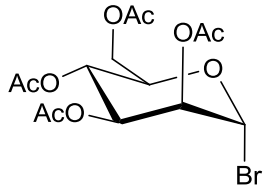
2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl bromide (7b)



Chemical Formula: $C_{14}H_{19}BrO_9$
Exact Mass: 410.0212

Yield: 69 %. Yellow solid. m.p = 81-83 °C (lit.;[164] 82-83 °C). (IR υ cm^{-1}): 2963 (CH), 1737 (CO), 559 (C-Br). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 6.60 (d, *J* = 4.0 Hz, 1H, H-1), 5.41, 5.40, 5.35 (3 pseudo t, *J* ~ 3.8 Hz in each, 3H, H-3, H-4 , H-2), 4.78 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.25 (ddd, *J* = 4.0, 3.6, 2.1 Hz, 1H, H-5), 4.01 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 1.98, 1.97, 1.95,1.93 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.7, 169.6, 169.3, 169.2 (4 × CO, acetyl), 86.8, (C-1), 72.6 (C-5), 71.3 (C-2), 70.8 (C-3), 67.4 (C-4), 60.4 (C-6), 20.1, 20.0, 19.6, 19.2 (4 × CH_3, acetyl). Anal. Calc. For $C_{14}H_{19}BrO_9$: C, 40.89; H, 4.66; Br, 19.43; O, 35.02 Found C, 40.87; H, 4.63; Br, 19.40; O, 35.04.

2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl bromide (7c)

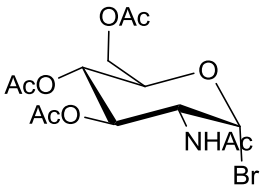


Chemical Formula: $C_{14}H_{19}BrO_9$
Exact Mass: 410.0212

Yield: 88 %. Yellow oil. (IR υ cm^{-1}): 2967 (CH), 1735 (CO), 558 (C-Br). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 6.61 (d, *J* = 3.8 Hz, 1H, H-1), 5.42, 5.41 (2 pseudo t, *J* = 4.0 Hz in each, 2H, H-3, H-2), 5.37 (t, *J* = 10.9 Hz, 1H, H-4), 4.79 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.35 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.11 (dd, *J* = 12.5, 2.1 1H, Hz, H-6^b), 2.08, 1.97, 1.95,1.92 (4s, 12

H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.9, 169.8, 169.6, 169.4 (4 × CO, acetyl), 86.7, (C-1), 72.8 (C-5), 71.7 (C-2), 70.7 (C-3), 67.3 (C-4), 60.2 (C-6), 20.3, 20.2, 19.7, 19.4 (4 × CH_3, acetyl). Anal. Calc. For $C_{14}H_{19}BrO_9$: C, 40.89; H, 4.66; Br, 19.43; O, 35.02 Found C, 40.90; H, 4.64; Br, 19.46; O, 35.04.

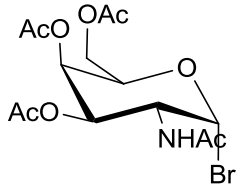
3,4,6-Tri-*O*-acetyl-2-acetamido-α-D-glucopyranosyl bromide (7d)



Chemical Formula: $C_{14}H_{20}BrNO_8$
Exact Mass: 409.0372

Yield: 78 %. Yellow oil. (IR υ cm^{-1}): 2964 (CH), 1733 (CO), 555 (C-Br). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.58 (d, *J* = 9.6 Hz, 1H, NH), 6.62 (d, *J* = 3.8 Hz, 1H, H-1), 5.45, 5.42 (2 pseudo t, *J* ~ 10.3 Hz in each, 2H, H-3, H-4), 5.34 (m, 1H, H-2), 4.78 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.33 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.12 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 2.07, 1.99, 1.94, 1.93, (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.6, 169.7, 169.4, 169.2 (4 × CO, acetyl), 86.4 (C-1), 72.5 (C-5), 71.5 (C-2), 70.3 (C-3), 67.4 (C-4), 60.3 (C-6), 20.5, 20.2, 19.8, 19.5, (4 × CH_3, acetyl). Anal. Calc. For $C_{14}H_{20}BrNO_8$: C, 40.99; H, 4.91; Br, 19.48; N, 3.41; O, 31.20Found C, 40.95; H, 4.94; Br, 19.45; N, 3.42; O, 31.23.

3,4,6-Tri-*O*-acetyl-2-acetamido-α-D-galactopyranosyl bromide (7e)



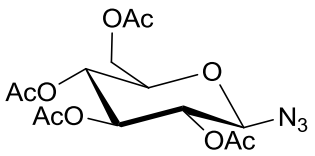
Chemical Formula: $C_{14}H_{20}BrNO_8$
Exact Mass: 409.0372

Yield: 76 %. Yellow oil. (IR υ cm^{-1}): 2966 (CH), 1731 (CO), 557 (C-Br). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.66 (d, *J* = 9.5 Hz, 1H, NH), 6.60 (d, *J* = 3.8 Hz, 1H, H-1), 5.44, 5.39 (2 pseudo t, *J* ~ 5.6 Hz in each, 2H, H-3, H-4), 5.43 (m, 1H, H-2), 4.74 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.32 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.11 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 2.08, 1.97, 1.95, 1.93 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.4, 169.6, 169.4, 169.3 (4 × CO, acetyl), 86.7 (C-1), 72.4 (C-5), 71.2 (C-2), 70.1 (C-3), 67.8 (C-4), 61.3 (C-6), 20.4, 20.3, 19.8, 19.3 (4 × CH_3, acetyl). Anal. Calc. For $C_{14}H_{20}BrNO_8$: C, 40.99; H, 4.91; Br, 19.48; N, 3.41; O, 31.20 Found C, 40.95; H, 4.94; Br, 19.45; N, 3.42; O, 31.23.

3.7.3 General procedure for the synthesis of glycopyranosyl azides (8a-8e)[165]

In a round bottom flask (100 ml) with a magnetic stirrer, solution of glycopyranosyl bromide (8.22 g, 20 mmol) and sodium azide (2.60 g, 40 mmol) in DMF (30 ml) was kept in sonication for 15 minutes and followed through TLC. After the completion, reaction mixture was diluted with water (90 ml) and extracted with ethyl acetate (40 ml × 3). The organic layer was further washed with water and brine (30 ml × 2). The combined organic layer dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude was further purified by column chromatography usin ethyl acetate: n.hexane (3:7) as eluent.

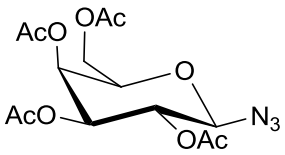
2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl azide (8a)



Chemical Formula: $C_{14}H_{19}N_3O_9$
Exact Mass: 373.1121

Yield: 86 %. White solid. m.p = 125-128 °C (lit.;[164] 127 °C). (IR υ cm^{-1}): 2969 (CH), 2117 (N_3), 1745 (CO). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 5.25 (d, *J* = 9.6 Hz, 1H, H-1), 5.14, 5.12, 5.11 (3 pseudo t, *J* ~ 12.0 Hz in each, 3H, H-3, H-4, H-2), 4.29 (dd, J = 12.5, 3.6 Hz, 1H, H-6[a]), 4.96 (ddd, *J* = 10.4, 3.5, 2.3 Hz, 1H, H-5), 4.18 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6[b]), 2.10, 2.07, 2.02, 2.00 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.3, 169.5, 169.3, 169.0 (4 × CO, acetyl), 87.4 (C-1), 74.4 (C-5), 73.1 (C-3), 71.0 (C-2), 68.1 (C-4), 61.6 (C-6), 20.2, 20.1,19.7,19.3 (4 × CH_3, acetyl). Anal. Calc. For $C_{14}H_{19}N_3O_9$: C, 45.04; H, 5.13; N, 11.26; O, 38.57 Found C, 45.01; H, 5.11; N, 11.29; O, 38.52.

2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl azide (8b)

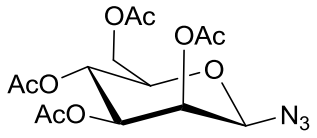


Chemical Formula: $C_{14}H_{19}N_3O_9$
Exact Mass: 373.1121

Yield: 77 %. White solid. m.p = 92-94 °C (lit.;[164] 94-95., lit.;[180] 91-92 °C). (IR υ cm^{-1}): 2966 (CH), 2146 (N_3), 1735 (CO). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 5.26 (d, *J* = 9.6 Hz, 1H, H-1), 5.13, 5.10 (2 pseudo t, *J* ~ 6.4 Hz in each, 2H, H-3, H-4), 5.13 (t, *J* = 12.0 Hz, 1H, H-2) 4.27 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6[a]), 4.94 (ddd, *J* = 3.4, 3.5, 2.3 Hz, 1H, H-5), 4.17 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6[b]), 2.11, 2.08, 2.06, 2.02 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.4, 169.2, 169.1, 169.0 (4 × CO, acetyl), 87.2 (C-1), 74.5 (C-5), 73.3 (C-3), 71.1 (C-2), 68.2 (C-4), 61.5

(C-6), 20.1, 20.0,19.6,19.4 (4 × $\underline{C}H_3$, acetyl). Anal. Calc. For $C_{14}H_{19}N_3O_9$: C, 45.04; H, 5.13; N, 11.26; O, 38.57 Found C, 45.06; H, 5.10; N, 11.25; O, 38.50.

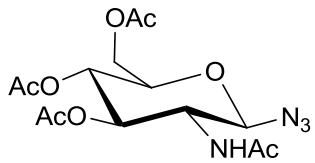
2,3,4,6-Tetra-*O*-acetyl-β-D-mannopyranosyl azide (8c)



Chemical Formula: $C_{14}H_{19}N_3O_9$
Exact Mass: 373.1121

Yield: 90 %. White solid. m.p = 116-118 °C (lit.;[181] 104.1-104.9 °C). (IR υ cm^{-1}): 2962 (CH), 2142 (N_3), 1733 (CO). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 5.56 (d, *J* = 3.9 Hz, 1H, H-1), 5.23, 5.13 (2 pseudo t, *J* ~ 5.3 Hz in each, 2H, H-3, H-2), 5.12 (t, *J* = 12.2 Hz, 1H, H-4), 4.26 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.95 (ddd, *J* = 10.4, 3.5, 2.3 Hz, 1H, H-5), 4.16 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 2.13, 2.11, 2.08, 2.06 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.3, 169.1, 169.0, 168.5 (4 × $\underline{C}O$, acetyl), 87.4 ($\underline{C}$-1), 74.3 (C-5), 73.2 (C-3), 71.1 (C-2), 68.5 (C-4), 61.3 ($\underline{C}$-6), 20.3, 20.1, 19.6, 19.3 (4 × $\underline{C}H_3$, acetyl). Anal. Calc. For $C_{14}H_{19}N_3O_9$: C, 45.04; H, 5.13; N, 11.26; O, 38.57 Found C, 45.06; H, 5.10; N, 11.23; O, 38.55.

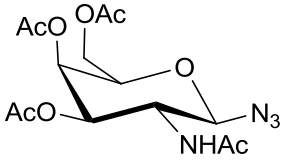
3,4,6-Tri-*O*-acetyl-2-acetamido-β-D-glucopyranosyl azide (8d)



Chemical Formula: $C_{14}H_{20}N_4O_8$
Exact Mass: 372.1281

Yield: 87 %. White solid. m.p = 160-161 °C (lit.;[182] 158-161 °C). (IR υ cm^{-1}): 2976 (CH), 2140 (N_3), 1733 (CO). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 6.98 (d, J= 8.6 Hz, 1H, NH), 5.56 (d, *J* = 9.8 Hz, 1H, H-1), 5.14, 5.13 (2pseudo t, *J* ~ 6.3 Hz in each, 2H, H-3, H-4), 5.12 (m, 1H, H-2), 4.29 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.95 (ddd, *J* = 10.4, 3.5, 2.3 Hz, 1H, H-5), 4.18 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 2.13, 2.09, 2.07, 2.03 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.6, 169.7, 169.4, 169.2 (4 × $\underline{C}O$, acetyl), 87.5 ($\underline{C}$-1), 74.2 (C-5), 73.3 (C-3), 71.4 (C-2), 68.2 (C-4), 61.8 ($\underline{C}$-6), 20.3, 20.2, 19.7, 19.3 (4 × $\underline{C}H_3$, acetyl). Anal. Calc. For $C_{14}H_{20}N_4O_8$: C, 45.16; H, 5.41; N, 15.05; O, 34.38 Found C, 45.12; H, 5.43; N, 15.00; O, 34.34.

3,4,6-Tri-*O*-acetyl-2-acetamido-β-D-galactopyranosyl azide (8e)



Chemical Formula: $C_{14}H_{20}N_4O_8$
Exact Mass: 372.1281

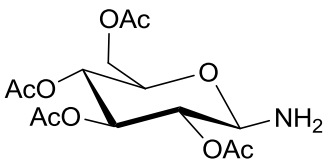
Yield: 77 %. Colourless gel. (IR υ cm^{-1}): 2977 (CH), 2145 (N_3), 1735 (CO). ^{1}H NMR (400 MHz,

$CDCl_3$): δ (ppm): 7.45 (d, *J* = 8.9 Hz, 1H, NH), 5.54 (d, *J* = 9.5 Hz, 1H, H-1), 5.24, 5.22 (2 pseudo t, *J* ~ 6.4 Hz in each, 2H, H-3, H-4), 5.13 (m, 1H, H-2), 4.27 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6[a]), 4.92 (ddd, *J* = 10.4, 3.5, 2.3 Hz, 1H, H-5), 4.16 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6[b]), 2.12, 2.10, 2.08, 2.05 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.7, 169.4, 169.2, 169.1 (4 × CO, acetyl), 87.3 (C-1), 74.1 (C-5), 73.4 (C-3), 71.1 (C-2), 68.3 (C-4), 61.6 (C-6), 20.4, 20.2, 19.8, 19.3(4 × CH_3, acetyl). Anal. Calc. For $C_{14}H_{20}N_4O_8$: C, 45.16; H, 5.41; N, 15.05; O, 34.38 Found C, 45.10; H, 5.45; N, 15.08; O, 34.34.

3.7.4 General procedure for the synthesis of glycopyranosyl amines (9a-9e)[165]

Solution of glycopyranosyl azide (10 mmol) in methanol was stirred with Pd/C (10 % wt. 10 mmol) under the atmosphere of hydrogen at room temperature for 30 minutes. After the completion of reaction as indicated by TLC, reaction m ixture was filtered through celite bed and washed with methanol. The filtrate was concentrated under reduced pressure and the crude product was further purified by column chromatography usin ethyl acetate: n.hexane (3:7) as eluent.

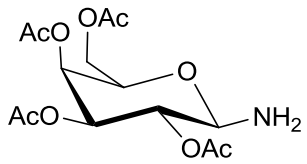
2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl amine (9a)



Chemical Formula: $C_{14}H_{21}NO_9$
Exact Mass: 347.1216

Yield: 61 %. Yellow solid. m.p = 112-115 °C (lit.;[164] 113-116 °C**)**. (IR υ cm^{-1}): 3411-3335 (NH_2), 2964 (CH), 1749 (CO). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 5.46 (d, *J* = 8.6 Hz, 1H, H-1), 5.05, 5.03, 4.80 (3 pseudo t, *J* ~ 10.9 Hz in each, 3H, H-3, H-4 , H-2), 4.26 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6[a]), 3.70 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.15 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6[b]), 2.19, 2.16, 2.12, 2.10 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.7, 170.3, 170.0, 169.5 (4 × CO, acetyl), 85.5 (C-1), 73.8 (C-3), 73.0 (C-5), 72.3 (C-2), 69.3 (C-4), 62.5 (C-6), 20.2, 20.1, 19.5, 19.2 (4 × CH_3, acetyl). Anal. Calc. For $C_{14}H_{21}NO_9$: C, 48.41; H, 6.09; N, 4.03; O, 41.46 Found C, 48.43; H, 6.05; N, 4.09; O, 41.50.

2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl amine (9b)

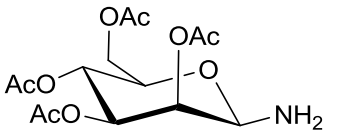


Chemical Formula: $C_{14}H_{21}NO_9$
Exact Mass: 347.1216

Yield: 79 %. Yellow crystalline solid. m.p = 120-121 °C (lit.;[180] 120-122 °C). (IR υ cm^{-1}): 3414-3333

(NH_2), 2966 (CH), 1739 (CO). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 5.42 (d, *J* = 8.9 Hz, 1H, H-1), 5.12, 5.09 (2 pseudo t, *J* ~ 6.2 Hz in each, 2H, H-3, H-4), 4.90 (t, *J* = 12.3 Hz, 1H, H-2), 4.26 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 3.72 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.13 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 2.17, 2.14, 2.12, 2.11 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.8, 170.4, 170.3, 169.2 (4 × CO, acetyl), 84.6 (C-1), 73.8 (C-3), 73.0 (C-5), 72.3 (C-2), 69.3 (C-4), 62.5 (C-6), 20.3, 20.2, 19.7, 19.5 (4 × CH_3, acetyl). Anal. Calc. For $C_{14}H_{21}NO_9$: C, 48.41; H, 6.09; N, 4.03; O, 41.46 Found C, 48.44; H, 6.06; N, 4.08; O, 41.51.

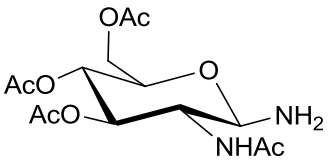
2,3,4,6-Tetra-*O*-acetyl-β-D-mannopyranosyl amine (9c)



Chemical Formula: $C_{14}H_{21}NO_9$
Exact Mass: 347.1216

Yield: 61 %. Yellow oil. (IR υ cm^{-1}): 3415-3337 (NH_2), 2963 (CH), 1735 (CO). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 5.43 (d, *J* = 3.8 Hz, 1H, H-1), 5.13, 4.80 (2 pseudo t, *J* ~ 5.8 Hz in each, 2H, H-3, H-2), 5.12 (t, *J* = 11.7 Hz, 1H, H-4) , 4.27 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 3.77 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.15 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 2.18, 2.17, 2.11, 2.10 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 171.8, 170.6, 170.5, 169.7 (4 × CO, acetyl), 84.5 (C-1), 73.5 (C-3), 73.1 (C-5), 72.2 (C-2), 69.1 (C-4), 62.7 (C-6), 20.4, 20.3, 19.6, 19.2 (4 × CH_3, acetyl). Anal. Calc. For $C_{14}H_{21}NO_9$: C, 48.41; H, 6.09; N, 4.03; O, 41.46 Found C, 48.45; H, 6.07; N, 4.06; O, 41.48.

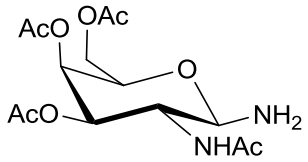
3,4,6-Tri-*O*-acetyl-2-acetamido-β-D-glucopyranosyl amine (9d)



Chemical Formula: $C_{14}H_{22}N_2O_8$
Exact Mass: 346.1376

Yield: 69 %. Yellow oil. (IR υ cm^{-1}): 3414-3333 (NH_2), 2966 (CH), 1739 (CO). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.31 (d, *J* = 7.8 Hz, 1H, NH), 5.44 (d, *J* = 8.4 Hz, 1H, H-1), 5.13, 5.12 (2 pseudo t, *J* ~ 6.8 Hz in each, 2H, H-3, H-4), 4.91 (m, 1H, H-2), 4.28 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 3.76 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.14 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 2.16, 2.14, 2.13, 2.11 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.3,170.1, 169.8, 169.5 (4 × CO, acetyl), 84.6 (C-1), 73.6 (C-3), 73.2 (C-5), 72.1 (C-2), 69.4 (C-4), 62.6 (C-6), 20.3, 20.2, 19.7, 19.5 (4 × CH_3, acetyl). Anal. Calc. For $C_{14}H_{22}N_2O_8$: C, 48.55; H, 6.40; N, 8.09; O, 36.96Found C, 48.52; H, 6.42; N, 8.05; O, 36.93.

3,4,6-Tri-*O*-acetyl-2-acetamido-β-D-galactopyranosyl amine (9e)



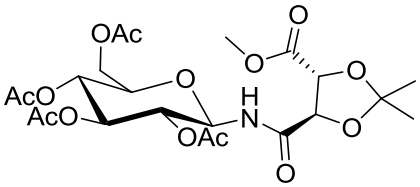
Chemical Formula: $C_{14}H_{22}N_2O_8$
Exact Mass: 346.1376

Yield: 65 %. Yellow oil. (IR υ cm^{-1}): 3418-3339 (NH_2), 2960 (CH), 1736 (CO). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.41 (d, *J* = 8.8 Hz, 1H, NH),5.47 (d, *J* = 8.9 Hz, 1H, H-1), 5.37, 5.21 (2 pseudo t, *J* ~ 5.9 Hz in each, 2H, H-3, H-4), 4.94 (m, 1H, H-2), 4.38 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 3.78 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.16 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 2.14, 2.12, 2.11, 2.10 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.5, 170.3, 169.8, 169.2 (4 × CO, acetyl), 85.3 (C-1), 73.9 (C-3), 73.2 (C-5), 72.0 (C-2), 69.2 (C-4), 62.4 (C-6), 20.4, 20.1, 19.6, 19.3 (4 × CH_3, acetyl). Anal. Calc. For $C_{14}H_{22}N_2O_8$: C, 48.55; H, 6.40; N, 8.09; O, 36.96 Found C, 48.51; H, 6.43; N, 8.12; O, 37.00.

3.8 General procedure for the synthesis of glycopyranosyl amides (10a-10e)

In a round bottom flask (100 ml) compound **(2)** (0.61 g, 3 mmol), EDC (0.68 g, 3 mmol) and catalytic amount of DMAP were placed under nitrogen. DCM (30 ml) was added as a solvent. After half an hour glycopyranosyl amine (3 mmol) was added and stirred for 4-12 hours. The byproduct urea was removed by extraction the reaction mixture with ethyl acetate or chloroform and water (30 ml × 2). The crude was further purified by column chromatography using ethyl acetate: n.hexane (3:7) as eluent.

(2*R*,3*R*,5*R*,6*R*)-2-(Acetoxymethyl)-6-((4*R*,5*R*)-5-(methoxycarbonyl)-2,2-dimethyl-1,3-dioxolane-4-carboxamido)tetrahydro-2H-pyran-3,4,5-triyl triacetate (10a)

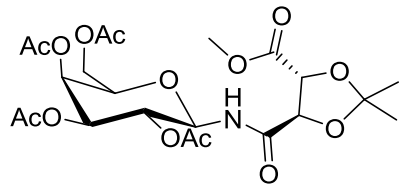


Chemical Formula: $C_{22}H_{31}NO_{14}$
Exact Mass: 533.1745

Yield: 72 %. Colourless oil. $[\alpha]_D^{25}$ = 12.50° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3347 (NH), 2955 (CH), 1742 ($COOCH_3$), 1701 (CONH), 1299 (C-O-C). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.18 (d, *J* = 9.3 Hz, 1H, NH), 5.23, 5.18, 5.05, 4.96 (4 pseudo t, *J* ~ 12.2 Hz in each, 4H, H-1, H-2, H-3, H-4), 4.65 (d, *J* = 5.4 Hz, 1H, CH), 4.59 (d, *J* = 5.4 Hz, 1H, CH), 4.30 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.21 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 3.95 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 3.75 (s, 3H ,OCH_3), 1.94, 1.92, 1.91,1.89 (4s, 12 H, 4 × CH_3), 1.56 (s,3H, CH_3), 1.50 (s, 3H,

CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 171.2 (CONH), 170.7 ($COOCH_3$), 170.0, 169.9, 169.5, 169.2 (4 × CO, acetyl), 113.3 (qt C), 81.8 (C-1), 76.3 (CH), 75.2 (CH), 73.3, 72.5, 70.0, 67.8 (C-2-C-5), 61.2 (C-6), 52.4 (OCH_3), 25.9, (CH_3), 25.2 (CH_3), 20.2, 20.1 (3), (4 × CH_3, acetyl). HRMS-ESI for $C_{22}H_{31}NO_{14}$ Na: $[M+Na]^+$ calcd: 556.1745, found: 556.1621. Anal. Calc. For $C_{22}H_{31}NO_{14}$: C, 49.53; H, 5.86; N, 2.63; O, 41.99 Found C, 49.43; H, 5.56; N, 2.78; O, 42.10.

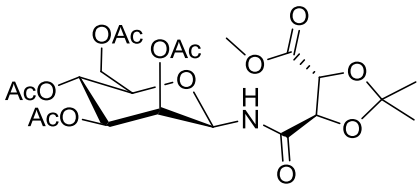
(2*R*,3*R*,5*R*,6*R*)-2-(Acetoxymethyl)-6-((4*R*,5*R*)-5-(methoxycarbonyl)-2,2-dimethyl-1,3-dioxolane-4-carboxamido)tetrahydro-2H-pyran-3,4,5-triyl triacetate (10b)



Chemical Formula: $C_{22}H_{31}NO_{14}$
Exact Mass: 533.1745

Yield: 69 %. Colourless oil. $[\alpha]_D^{25}$ = 13.33° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3337 (NH), 2925 (CH), 1732 ($COOCH_3$), 1703 (CONH), 1292 (C-O-C). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.47 (d, *J* = 9.3 Hz, 1H, NH), 5.34, 5.31, 5.24 (3 pseudo t, *J* = 12.0, Hz in each, 3H, H-1, H-2, H-3), 4.95 (t, *J* = 3.9 Hz, 1H, H-4), 4.93 (d, *J* = 5.5 Hz, 1H, CH), 4.80 (d, *J* = 5.5 Hz, 1H, CH), 4.28 (dd, *J* = 12.4, 3.5 Hz, 1H, H-6^a), 4.10 (ddd, *J* = 10.3, 3.6, 2.1 Hz, 1H, H-5), 3.95 (dd, *J* = 12.4, 3.5 Hz, 1H, H-6^b), 3.77 (s, 3H, OCH_3), 2.34, 2.23, 2.13, 1.99 (4s, 12 H, 4 × CH_3), 1.52 (s, 3H, CH_3), 1.46 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 172.2 (CONH), 170.9 ($COOCH_3$), 170.1, 169.6,169.3, 169.1 (4 × CO, acetyl), 114.3 (qt C), 81.4 (C-1), 76.5 (CH), 75.1 (CH), 73.1, 72.3, 70.1, 67.9 (C-2-C-5), 61.8 (C-6), 52.9 (OCH_3), 25.5 (CH_3), 25.1 (CH_3), 20.1, 20.0 (3) (CH_3, acetyl). HRMS-ESI for $C_{22}H_{31}NO_{14}$ Na: $[M+Na]^+$ calcd: 556.1745, found: 556.1627. Anal. Calc. For $C_{22}H_{31}NO_{14}$: C, 49.53; H, 5.86; N, 2.63; O, 41.99 Found C, 49.43; H, 5.56; N, 2.78; O, 42.10.

(2*R*,3*R*,5*R*,6*R*)-2-(Acetoxymethyl)-6-((4*R*,5*R*)-5-(methoxycarbonyl)-2,2-dimethyl-1,3-dioxolane-4-carboxamido)tetrahydro-2H-pyran-3,4,5-triyl triacetate (10c)

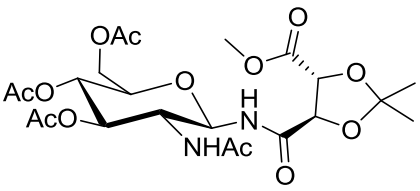


Chemical Formula: $C_{22}H_{31}NO_{14}$
Exact Mass: 533.1745

Yield: 65 %. Colourless oil. $[\alpha]_D^{25}$ = 27.12° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3339 (NH), 2928 (CH), 1736 ($COOCH_3$), 1700 (CONH), 1290 (C-O-C). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.37 (d, *J* = 9.3 Hz, 1H, NH), 5.42, 5.40, 5.36 (3 pseudo t, *J* ~ 6.5 Hz in each, 3H, H-1, H-2, H-3), 4.98 (t, *J* = 11.9 Hz, 1H, H-

4), 4.97 (d, *J* = 5.6 Hz, 1H, CH), 4.90 (d, *J* = 5.6 Hz, 1H, CH), 4.48 (dd, *J* = 12.7, 3.4 Hz, 1H, H-6^{a}), 4.12 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 3.92 (dd, *J* = 12.4, 3.5 Hz, 1H, H-6^{b}), 3.84 (s, 3H OCH_3), 2.11, 2.10, 2.09, 1.99 (4s, 12 H, 4 × CH_3), 1.54 (s, 3H, CH_3), 1.48 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 171.8 (CONH), 170.2 ($COOCH_3$), 170.3, 169.5,169.4, 169.2 (4 × CO, acetyl), 114.2 (qt C), 81.5 (C-1), 76.1 (CH), 75.2 (CH), 73.3, 72.2, 70.1, 67.5 (C-2-C-5), 61.9 (C-6), 52.5 (OCH_3), 26.5 (CH_3), 25.7 (CH_3), 20.4, 19.5 (3) (CH_3, acetyl). HRMS-ESI for $C_{22}H_{31}NO_{14}$ Na: $[M+Na]^+$ calcd: 556.1745, found: 556.1643. Anal. Calc. For $C_{22}H_{31}NO_{14}$: C, 49.53; H, 5.86; N, 2.63; O, 41.99 Found C, 49.43; H, 5.56; N, 2.78; O, 42.10.

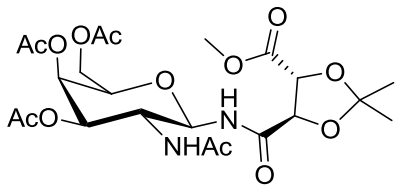
(2*R*,3*S*,5*R*,6*R*)-5-Acetamido-2-(acetoxymethyl)-6-((4*R*,5*R*)-5-(methoxycarbonyl)-2,2-dimethyl-1,3-dioxolane-4-carboxamido)tetrahydro-2H-pyran-3,4-diyl diacetate (10d)



Chemical Formula: $C_{22}H_{32}N_2O_{13}$
Exact Mass: 532.1904

Yield: 67 %. Colourless gel. $[\alpha]_D^{25}$ = 43.33° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3343 (NH), 2948 (CH), 1746 ($COOCH_3$), 1710 (CONH), 1293 (C-O-C). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.69 (d, *J* = 9.5 Hz, 1H, NH), 7.57 (d, *J* = 9.3 Hz, 1H, NH), 5.43 (t, *J* =10.0 Hz, 1H, H-1), 5.41 (m , 1H, H-2), 5.37, 4.99 (2 pseudo t, *J* ~ 10.0 Hz in each, 2H, H-3, H-4), 4.96 (d, *J* = 5.5 Hz, 1H, CH), 4.94 (d, *J* = 5.5 Hz, 1H, CH), 4.44 (dd, *J* = 12.7, 3.4 Hz, 1H, H-6^{a}), 4.22 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 3.91 (dd, *J* = 12.4, 3.5 Hz, 1H, H-6^{b}), 3.86 (s, 3H, OCH_3), 2.21, 2.20, 2.19, 2.13 (4s, 12 H, 4 × CH_3), 1.57 (s, 3H, CH_3), 1.49 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 172.8 (CONH), 171.2 ($COOCH_3$), 170.2, 169.8, 169.5, 169.1 (4 × CO, acetyl), 114.1 (qt C), 81.8 (C-1), 76.1 (CH), 75.3 (CH), 73.2, 72.1, 70.0, 67.8 (C-2-C-5), 61.4 (C-6), 52.2 (OCH_3), 26.2 (CH_3), 25.8 (CH_3), 20.3, 19.3 (3) (CH_3, acetyl). HRMS-ESI for $C_{22}H_{32}N_2O_{13}$ Na: $[M+Na]^+$ calcd: 555.1904, found: 555.1619. Anal. Calc. For $C_{22}H_{32}N_2O_{13}$: C, 49.62; H, 6.06; N, 5.26; O, 39.06 Found C, 49.32; H, 6.16; N, 5.21; O, 39.16.

(2*R*,3*S*,5*R*,6*R*)-5-Acetamido-2-(acetoxymethyl)-6-((4*R*,5*R*)-5-(methoxycarbonyl)-2,2-dimethyl-1,3-dioxolane-4-carboxamido)tetrahydro-2H-pyran-3,4-diyl diacetate (10e)



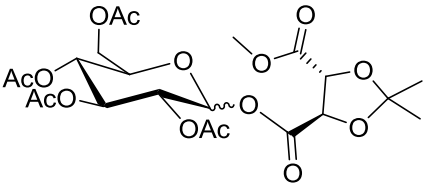
Chemical Formula: $C_{22}H_{32}N_2O_{13}$
Exact Mass: 532.1904

Yield: 68 %. Colourless gel. $[\alpha]_D^{25}$ = 47.10° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3341 (NH), 2942 (CH), 1745 ($COOCH_3$), 1711 (CONH), 1290 (C-O-C). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.67 (d, *J* = 9.6 Hz, 1H, NH), 7.55 (d, *J* = 9.3 Hz, 1H, NH), 5.41 (t, *J* = 10.8 Hz, 1H, H-1), 5.40 (m , 1H, H-2), 5.38, 4.97 (2 pseudo t, *J* ~ 6.9 Hz in each, 2H, H-3, H-4), 4.93 (d, *J* = 5.6 Hz, 1H, CH), 4.91 (d, *J* = 5.5 Hz, 1H, CH), 4.41 (dd, *J* = 12.7, 3.4 Hz, 1H, H-6^a), 4.21 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 3.90 (dd, *J* = 12.4, 3.5 Hz, 1H, H-6^b), 3.83 (s, 3H OCH_3), 2.23, 2.22, 2.20, 2.16 (4s, 12 H, 4 × CH_3), 1.56 (s, 3H, CH_3), 1.46 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 172.2 (CONH), 171.3 ($COOCH_3$), 170.5, 169.5, 169.2, 169.1 (4 × CO, acetyl), 113.4 (qt C), 81.6 (C-1), 76.4 (CH), 75.2 (CH), 73.4, 72.3, 70.1, 67.3, (C-2-C-5), 62.4 (C-6), 53.2 (OCH_3), 26.2 (CH_3), 25.7 (CH_3), 20.7, 19.5 (3) (CH_3, acetyl). HRMS-ESI for $C_{22}H_{31}NO_{14}$ Na: $[M+Na]^+$ calcd: 555.1904, found: 555.1719. Anal. Calc. For $C_{22}H_{32}N_2O_{13}$: C, 49.62; H, 6.06; N, 5.26; O, 39.06 Found C, 49.32; H, 6.16; N, 5.21; O, 39.16.

3.9 General procedure for the synthesis of glycopyranosides (11a-11e)[169-170]

To a stirred solution of anomeric mixture of (**6a-6e**) (3.12 g, 8 mmol) in DMF (40 ml) was added hydrazinium acetate (1.10 g, 12 mmol). The reaction mixture was heated at 55 °C for 30 minutes under nitrogen. After the completion, reaction mixture was diluted with water (100 ml) and extracted with ethyl acetate (40 ml × 3). The combined organic layer was further washed with brine (40 × 2), dried over anhydrous magnesium sulphate. The solvent was removed under reduced pressure and the crude was used without further purification. To the resulting hemiacetal (1.04 g, 3 mmol), compound (**2**) (0.61 g 3 mmol), EDC (0.68 g, 3mmol) and catalytic amount of DMAP were added under nitrogen with DCM (30 ml) as solvent. The reaction mixture was stirred for 4-10 hours; the byproduct urea was removed by extraction the reaction mixture with ethyl acetate or chloroform and water (30 ml × 3). The crude product was purified by column chromatography using ethyl acetate: n-hexane (3:7) as eluent.

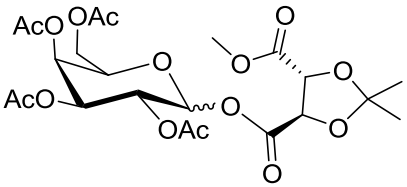
(4*R*,5*R*)-4-Methyl-5-((2*S*,3*R*,5*R*,6*R*)-3,4,5-triacetoxy-6-(acetoxymethyl)tetrahydro-2H-pyran-2-yl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (11a)



Chemical Formula: $C_{22}H_{30}O_{15}$
Exact Mass: 534.1585

Yield: 72 %. Colourless oil. $[\alpha]_D^{25}$ = 26.50° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 2991 (CH), 1742 (CO), 1366 (C-O-C). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 6.45 (d, *J* = 4.0 Hz, 1H, H-1$^{\alpha}$), 5.56 (d, *J* = 8.0 Hz, 1H, H-1$^{\beta}$) 5.48, 5.45, 4.93 (3 pseudo t, *J* ~ 9.8 Hz in each, 3H, H-2, H-3, H-4), 4.91 (d, *J* = 6.3 Hz, 1H, CH), 4.88 (d, *J* = 6.3 Hz, 1H, CH), 4.32 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^{a}), 4.12 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 3.93 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^{b}), 3.86 (s, 3H, OCH_3), 2.19, 2.17, 2.12, 2.04 (4s, 12 H, 4 × CH_3), 1.55 (s, 3H, CH_3), 1.46 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 172.6 $\underline{C}OOCH_3$), 171.2, 169.5, 169.3, 169.0 (4 × $\underline{C}O$, acetyl), 113.4 (qt $\underline{C}$), 92.3 ($\underline{C}$-1), 76.3 ($\underline{C}H$), 75.4 ($\underline{C}H$), 74.2, 73.3, 72.1, 70.3 ($\underline{C}$-2-$\underline{C}$-5), 56.6 ($\underline{C}$-6), 53.4 ($O\underline{C}H_3$), 26.6 ($\underline{C}H_3$), 25.9 ($\underline{C}H_3$), 20.3 (2), 19.8, 19.3, ($\underline{C}H_3$, acetyl). HRMS-ESI for $C_{22}H_{30}O_{15}$ Na: $[M+Na]^+$ calcd: 557.1585, found: 557.1452. Anal. Calc. For $C_{22}H_{30}O_{15}$: C, 49.44; H, 5.66; O, 44.90 Found C, 49.39; H, 5.70; O, 44.81.

(4*R*,5*R*)-4-Methyl-5-((2*S*,3*R*,5*R*,6*R*)-3,4,5-triacetoxy-6-(acetoxymethyl)tetrahydro-2Hpyran-2-yl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (11b)



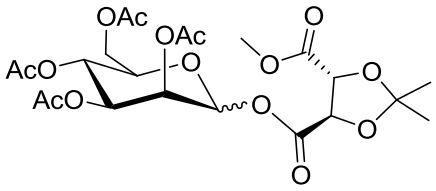
Chemical Formula: $C_{22}H_{30}O_{15}$
Exact Mass: 534.1585

Yield: 74 %. Colourless gel. $[\alpha]_D^{25}$ = 21.66° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 2993 (CH), 1744 (CO), 1361 (C-O-C).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 6.47 (d, *J* = 3.9 Hz, 1H, H-1$^{\alpha}$), 5.53 (d, *J* = 8.3 Hz, 1H, H-1$^{\beta}$), 5.47, 4.93 (2 pseudo t, *J* ~ 6.9 Hz in each, 2H, H-3, H-4), 5.50 (t, *J* = 8.9 Hz, 1H, H-2), 4.94 (d, *J* = 6.3 Hz, 1H, CH), 4.88 (d, *J* = 6.3 Hz, 1H, CH), 4.27 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^{a}), 4.14 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 3.96 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^{b}), 3.86 (s, 3H OCH_3), 2.19, 2.17, 2.12, 2.04 (4s, 12 H, 4 × CH_3), 1.55 (s, 3H, CH_3), 1.45 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 172.3 ($\underline{C}OOCH_3$), 171.7, 169.4, 169.3, 169.1 (4 × CO, acetyl), 113.3 (qt $\underline{C}$), 92.7 ($\underline{C}$-1), 76.2 ($\underline{C}H$), 75.6

(CH), 74.4, 73.5, 72.2, 70.2, (C-2-C-5), 56.5 (C-6), 53.2 (OCH_3), 25.6 (CH_3), 24.9 (CH_3), 20.6 (2), 19.7, 19.5, (CH_3, acetyl). HRMS-ESI for $C_{22}H_{30}O_{15}$ Na: $[M+Na]^+$ calcd: 557.1585, found: 557.1466. Anal. Calc. For $C_{22}H_{30}O_{15}$: C, 49.44; H, 5.66; O, 44.90 Found C, 49.39; H, 5.70; O, 44.81.

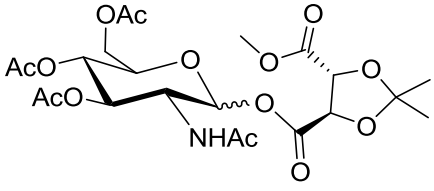
(4*R*,5*R*)-4-Methyl-5-((2*R*,3*R*,5*R*,6*R*)-3,4,5-triacetoxy-6-(acetoxymethyl)tetrahydro-2H-pyran-2-yl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (11c)



Chemical Formula: $C_{22}H_{30}O_{15}$
Exact Mass: 534.1585

Yield: 70 %. White foam. m.p = 151-153 °C. $[\alpha]_D^{25}$ = 17.33° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 2995 (CH), 1745 (CO), 1336 (C-O-C). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm): 6.42 (d, *J* = 3.7 Hz, 1H, H-1^{α}), 5.51 (d, *J* = 4.0 Hz, 1H, H-1^{β}), 5.46, 5.43 (2 pseudo t, *J* ~ 5.6 Hz in each, 2H, H-2, H-3), 4.96 (t, *J* = 9.8 Hz, 1H, H-4), 4.93 (d, *J* = 5.3 Hz, 1H, CH), 4.89 (d, *J* = 5.3 Hz, 1H, CH), 4.26 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.13 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 3.93 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 3.76 (s, 3H OCH_3), 2.15, 2.14, 2.12, 2.11 (4s, 12 H, 4 × CH_3), 1.56 (s, 3H, CH_3), 1.46 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 171.3 ($COOCH_3$, 170.7, 169.6, 169.3, 169.1 (4 × CO, acetyl), 113.4 (qt C), 92.4 (C-1), 76.1 (CH), 75.6 (CH), 74.2, 73.2, 72.1, 70.5 (C-2-C-5), 56.7 (C-6), 53.3 (OCH_3), 26.6 (CH_3), 25.8 (CH_3), 20.2 (2), 19.8, 19.4 (CH_3, acetyl). HRMS-ESI for $C_{22}H_{30}O_{15}$ Na: $[M+Na]^+$ calcd: 557.1585, found: 557.1475. Anal. Calc. For $C_{22}H_{30}O_{15}$: C, 49.44; H, 5.66; O, 44.90 Found C, 49.39; H, 5.70; O, 44.88.

(4*R*,5*R*)-4-((2*S*,3*R*,5*S*,6*R*)-3-Acetamido-4,5-diacetoxy-6-(acetoxymethyl)tetrahydro-2H-pyran-2-yl)-5-methyl-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (11d)

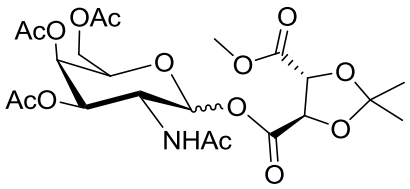


Chemical Formula: $C_{22}H_{31}NO_{14}$
Exact Mass: 533.1745

Yield: 67 %. Colourless oil. $[\alpha]_D^{25}$ = 45.00° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3342 (NH), 2981 (CH), 1739 (CO), 1360 (C-O-C). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.87 (d, *J* = 9.5 Hz, 1H, NH), 6.49 (d, *J* = 3.7 Hz, 1H, H-1^{α}), 5.57 (d, *J* = 8.3 Hz, 1H, H-1^{β}), 5.46 (m, 1H, H-2) 5.43, 4.96 (2 pseudo t, *J* ~ 7.4 Hz in each, 2H, H-3, H-4), 4.94 (d, *J* = 6.3 Hz, 1H, CH), 4.83 (d, *J* = 6.3 Hz, 1H, CH), 4.37 (dd, *J*

= 12.5, 3.6 Hz, 1H, H-6^{a}), 4.23 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 3.93 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^{b}), 3.87 (s, 3H OCH_3), 2.13, 2.11, 2.10, 2.04 (4s, 12 H, 4 × CH_3), 1.57 (s, 3H, CH_3), 1.49 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 171.6 ($\underline{C}OOCH_3$), 170.3, 169.3, 169.2, 169.0 (4 × $\underline{C}O$, acetyl), 113.6 (qt $\underline{C}$), 92.6 ($\underline{C}$-1), 76.2 ($\underline{C}H$), 75.1 ($\underline{C}H$), 74.5, 73.3, 72.6, 70.1 ($\underline{C}$-2-$\underline{C}$-5), 57.9 ($\underline{C}$-6), 53.5 ($O\underline{C}H_3$), 26.4 ($\underline{C}H_3$), 25.6 ($\underline{C}H_3$), 20.1 (2), 19.5, 19.2, ($\underline{C}H_3$, acetyl). HRMS-ESI for $C_{22}H_{31}NO_{14}$ Na: $[M+Na]^+$ calcd: 556.1745, found: 556.1614. Anal. Calc. For $C_{22}H_{31}NO_{14}$: C, 49.53; H, 5.86; N, 2.63; O, 41.99 Found C, 49.55; H, 5.76; N, 2.60; O, 41.90.

(4*R*,5*R*)-4-((2*S*,3*R*,5*S*,6*R*)-3-Acetamido-4,5-diacetoxy-6-(acetoxymethyl)tetrahydro-2H-pyran-2-yl)-5-methyl-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate(11e)



Chemical Formula: $C_{22}H_{31}NO_{14}$
Exact Mass: 533.1745

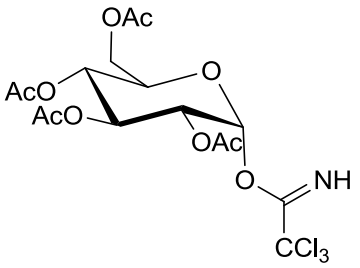
Yield: 63 %. Colourless oil. $[\alpha]_D^{25}$ = 33.36° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3348 (NH), 2990 (CH), 1741 (CO), 1356 (C-O-C). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.86 (d, *J* = 9.7 Hz, 1H, NH), 6.52 (d, *J* = 3.9 Hz, 1H, H-1$^{\alpha}$), 5.67 (d, *J* = 8.7 Hz, 1H, H-1$^{\beta}$), 5.46 (m, 1H, H-2), 5.43, 4.96 (2 pseudo t, *J* ~ 6.0 Hz in each, 2H, H-3, H-4), 4.93 (d, *J* = 5.4 Hz, 1H, CH), 4.82 (d, *J* = 5.3 Hz, 1H, CH), 4.38 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^{a}), 4.33 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 3.93 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^{b}), 3.85 (s, 3H OCH_3), 2.14, 2.12, 2.10, 2.06 (4s, 12 H, 4 × CH_3), 1.56 (s, 3H, CH_3), 1.46 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 171.4 ($\underline{C}OOCH_3$), 170.3, 169.5, 169.4, 169.2 (4 × $\underline{C}O$, acetyl), 114.4 (qt $\underline{C}$), 93.4 ($\underline{C}$-1), 76.3 ($\underline{C}H$), 75.2 ($\underline{C}H$), 74.5, 73.4, 72.6, 70.1 ($\underline{C}$-2-$\underline{C}$-5), 58.7 ($\underline{C}$-6), 53.5 ($O\underline{C}H_3$), 26.6 ($\underline{C}H_3$), 25.6 ($\underline{C}H_3$), 20.1 (2), 19.4, 19.1 ($\underline{C}H_3$, acetyl). HRMS-ESI for $C_{22}H_{31}NO_{14}$ Na: $[M+Na]^+$ calcd: 556.1745, found: 556.1616. Anal. Calc. For $C_{22}H_{31}NO_{14}$: C, 49.53; H, 5.86; N, 2.63; O, 41.99 Found C, 49.55; H, 5.81; N, 2.60; O, 41.91.

3.10 General procedure for the synthesis of glycopyranosyl α-trichloroacetimidates (12a-12e)[169-170,183]

To the crude hemiacetals (3.48 g, 10 mmol) in DCM (50 ml) was added trichloroacetonitrile (10 ml, 100 mmol) and DBU (2.81ml, 20 mmol) under nitrogen

atmosphere and stirred at 0 °C for 1.5 hour. After the completion as indicated by TLC, the solvent was evaporated under reduced pressure and the crude was purified by column chromatography using ethyl acetate: n.hexane (3:7) as eluent.

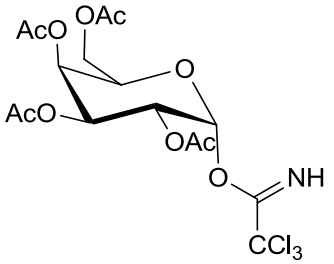
2,3,4,6-Tetra-*O*-acetyl-α-glucopyranosyl trichloroacetimidate (12a)



Chemical Formula: $C_{16}H_{20}Cl_3NO_{10}$
Exact Mass: 491.0153

Yield: 83 %. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.60 (bs, 1H, NH), 6.60 (d, *J* = 3.7 Hz, 1H, H-1), 5.41, 5.35, 5.34 (3 pseudo t, *J* ~ 8.2 Hz in each, 3H, H-2, H-3, H-4), 5.51 (dd, *J* = 11.9, 3.3 Hz, 1H, H-6^a), 4.43 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.85 (dd, *J* = 12.2, 2.1 Hz, 1H, H-6^b), 2.16, 2.04, 2.03, 2.00 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 171.6, 169.7, 169.5, 169.2 (4 × CO, acetyl), 160.5 (O-CNH), 91.5 (C-1), 72.6, 71.7, 69.5,68.9 (C-2-C-5), 61.7 (C-6), 20.2, 20.1, 19.4, 19.3 (4 × CH_3, acetyl). Anal. Calc. For $C_{16}H_{20}Cl_3NO_{10}$: C, 39.00; H, 4.09; Cl, 21.59; N, 2.84; O, 32.47 Found C, 39.03; H, 4.11; Cl, 21.57; N, 2.87; O, 32.50.

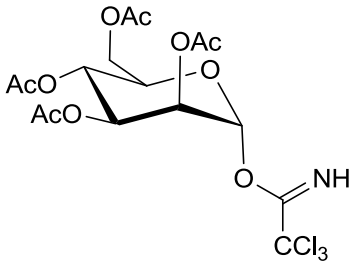
2,3,4,6-Tetra-*O*-acetyl-α-galactopyranosyl trichloroacetimidate (12b)



Chemical Formula: $C_{16}H_{20}Cl_3NO_{10}$
Exact Mass: 491.0153

Yield: 90 %. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.61 (bs, 1H, NH), 6.62 (d, *J* = 3.9 Hz, 1H, H-1), 5.42, 5.39, 5.37 (3 pseudo t, *J* ~ 7.0. Hz in each, 3H, H-2, H-3, H-4), 5.42 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.43 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.83 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 2.15, 2.08, 2.06, 2.05 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 171.8, 169.9, 169.6, 169.4, (4 × CO, acetyl), 160.3 (O-C-NH), 91.3 (C-1), 72.3, 71.6, 69.2, 68.1 , (C-2-C-5), 61.6 (C-6), 20.3, 20.2, 19.5, 19.2, (4 × CH_3, acetyl). Anal. Calc. For $C_{16}H_{20}Cl_3NO_{10}$: C, 39.00; H, 4.09; Cl, 21.59; N, 2.84; O, 32.47 Found C, 39.04; H, 4.05; Cl, 21.57; N, 2.86; O, 32.50.

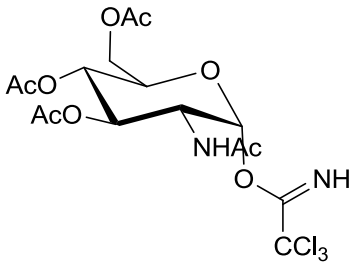
2,3,4,6-Tetra-*O*-acetyl-α-mannopyranosyl trichloroacetimidate (12c)



Chemical Formula: $C_{16}H_{20}Cl_3NO_{10}$
Exact Mass: 491.0153

Yield: 88 %. Brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.63 (bs, 1H, NH), 6.61 (d, *J* = 3.7 Hz, 1H, H-1), 5.41, 5.37 (2 pseudo t, *J* ~ 5.9 Hz in each, 2H, H-2, H-3), 5.36 (t, *J* = 8.9 Hz, 1H, H-4) 5.40 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.42 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.82 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 2.14, 2.09, 2.04,2.02 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 171.3, 170.5, 169.6, 169.3 (4 × C̲O, acetyl), 160.6 (O-C̲-NH), 91.4 (C̲-1), 72.5, 71.2, 69.7, 68.5 (C̲-2-C̲-5), 61.5 (C̲-6), 20.2, 20.0, 19.7, 19.4 (4 × C̲H$_3$, acetyl). Anal. Calc. For $C_{16}H_{20}Cl_3NO_{10}$: C, 39.00; H, 4.09; Cl, 21.59; N, 2.84; O, 32.47 Found C, 38.98; H, 4.10; Cl, 21.57; N, 2.88; O, 32.50.

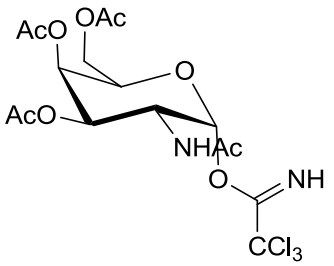
3,4,6-Tri-*O*-acetyl-2-acetamido-α-glucopyranosyl trichloroacetimidate (12d)



Chemical Formula: $C_{16}H_{21}Cl_3N_2O_9$
Exact Mass: 490.0313

Yield: 79 %. Brown yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.61 (bs, 1H, NH), 6.60 (d, *J* = 3.8 Hz, 1H, H-1), 5.40, 5.38 (2 pseudo t, *J* ~ 8.5 Hz in each, 2H, H-3, H-4), 5.44 (m, 1H, H-2), 5.33 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.44 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.83 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6^b), 2.13, 2.10, 2.06, 2.03 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.8, 169.8, 169.4, 169.3 (4 × C̲O, acetyl), 161.3 (O-C̲-NH), 91.3 (C̲-1), 72.4, 71.2, 69.6, 68.7 (C̲-2-C̲-5), 62.5 (C̲-6), 20.4, 20.3, 19.5, 19.1 (4 × C̲H$_3$, acetyl). Anal. Calc. For $C_{16}H_{21}Cl_3N_2O_9$: C, 39.08; H, 4.30; Cl, 21.63; N, 5.70; O, 29.28 Found 39.05; H, 4.33; Cl, 21.60; N, 5.67; O, 29.26.

3,4,6-Tri-*O*-acetyl-2-acetamido-α-galactopyranosyl trichloroacetimidate (12e)



Chemical Formula: $C_{16}H_{21}Cl_3N_2O_9$
Exact Mass: 490.0313

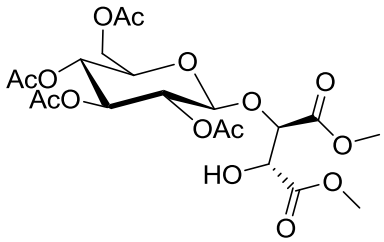
Yield: 75 %. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.59 (bs, 1H, NH), 6.55 (d, *J* = 3.8 Hz, 1H, H-1), 5.40, 5.37 (3 pseudo t, *J* ~ 6.0.0 Hz in each, 3H, H-3, H-4), 5.43 (m, 1H,

H-2), 5.32 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6[a]), 4.45 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 4.82 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6[b]), 2.16, 2.13, 2.09,2.07 (4s, 12 H, 4 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 170.4, 169.9, 169.5, 169.3 (4 × CO, acetyl), 161.6 (O-C-NH), 91.7 (C-1), 73.3, 71.8, 69.8, 68.2 (C-2-C-5), 62.6 (C-6), 20.5, 20.4, 19.5, 19.2 (4 × CH_3, acetyl). Anal. Calc. For $C_{16}H_{21}Cl_3N_2O_9$: C, 39.08; H, 4.30; Cl, 21.63; N, 5.70; O, 29.28 Found 39.05; H, 4.33; Cl, 21.60; N, 5.67; O, 29.26.

3.11 General procedure for the synthesis of glycoconjugates (13a-13e)[169]

In a round bottom flask (100 ml) to a solution of dimethyl-*L*-tartrate (0.89 g, 5 mmol) in DCM (30 ml), was added $BF_3.Et_2O$ (1.25 ml, 10 mmol) under nitrogen atmosphere and stirred for half an hour. Glycopyranosyl α-trichloroacetimidate (2.45 g, 5 mmol) was added at 0 °C and after 30 minutes the reaction mixture was allowed to warm to room temperature and left overnight. After the completion of reaction as indicated by TLC, solvent was evaporated under reduced pressure. The crude was dissolved in ethyl acetate (50 ml) and washed with water and brine (20 ml × 3). The organic layer was dried over anhydrous magnesium sulphate. The crude was purified by column chromatography using ethyl acetate: n.hexane (3:7) as eluent.

(2*R*,3*R*)-Dimethyl-2-hydroxy-3-((2*S*,3*R*,4*R*,5*R*,6*R*)-3,4,5-triacetoxy-6-(acetoxymethyl)tetrahydro-2H-pyran-2-yloxy)succinate (13a)

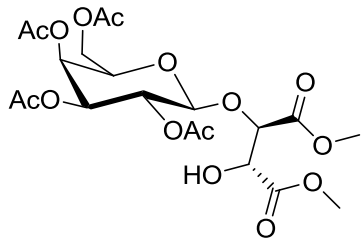


Chemical Formula: $C_{20}H_{28}O_{15}$
Exact Mass: 508.1428

Yield: 70 %. Colourless oil. $[\alpha]_D^{25}$ = 49.53° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3412 (OH), 2981 (CH), 1745 (CO) 1336 (C-O-C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 5.46 (d, *J* = 8.3 Hz, 1H, H-1), 5.44, 5.43, 4.93 (3 pseudo t, *J* ~ 10.2 Hz in each, 3H, H-2, H-3, H-4), 4.76 (dd, *J* = 9.6, 2.4 Hz, 1H, CH), 4.66 (d, *J* = 2.4 Hz, 1H, CH), 4.58 (d, *J* = 7.2 Hz, 1H, OH), 4.32 (dd, *J* = 12.5, 2.5 Hz, 1H, H-6[a]), 4.12 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 3.93 (dd, *J* = 12.5, 2.6 Hz, 1H, H-6[b]), 3.87 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 2.19, 2.17, 2.12, 2.04 (4s, 12 H, 4 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 172.3 ($COOCH_3$), 170.6, 169.7, 169.6, 168.1 (4 × CO, acetyl), 96.5 (C-1), 76.6 (CH), 75.3 (CH), 72.0, 69.6, 68.9, 68.6 (C-2-C-5), 65.7 (C-6), 53.1 (OCH_3), 52.9 (OCH_3), 20.8, 20.7, 20.6 (2) (4 × CH_3,

acetyl). Anal. Calc. For $C_{20}H_{28}O_{15}$: C, 47.25; H, 5.55; O, 47.20 Found C, 47.21; H, 5.57; O, 47.24.

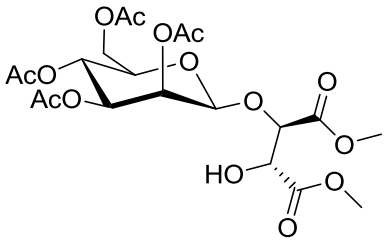
(2*R*,3*R*)-Dimethyl-2-hydroxy-3-((2*S*,3*R*,4*R*,5*R*,6*R*)-3,4,5-triacetoxy-6-(acetoxymethyl)tetrahydro-2H-pyran-2-yloxy)succinate (13b)



Chemical Formula: $C_{20}H_{28}O_{15}$
Exact Mass: 508.1428

Yield: 61 %. Colourless oil. $[\alpha]_D^{25}$ = 24.59° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3411 (OH), 2984 (CH), 1746 (CO) 1330 (C-O-C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 5.49 (d, *J* = 8.3 Hz, 1H, H-1), 5.40, 4.91 (2 pseudo t, *J* ~ 5.3 Hz in each, 2H, H-3, H-4), 5.41 (t, *J* = 11.6 Hz, 1H, H-2), 4.75 (dd, *J* = 9.5, 2.5 Hz, 1H, CH), 4.65 (d, *J* = 2.4 Hz, 1H, CH), 4.57 (d, *J* = 7.1 Hz, 1H, OH), 4.33 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.11 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 3.91 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^b), 3.88 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 2.18, 2.13, 2.12, 2.05 (4s, 12 H, 4 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 171.6 ($\underline{C}OOCH_3$), 170.1, 169.3, 169.2, 168.1 (4 × $\underline{C}O$, acetyl), 96.2 ($\underline{C}$-1), 76.3 ($\underline{C}H$), 75.1 ($\underline{C}H$), 72.1, 69.2, 68.7, 68.5 ($\underline{C}$-2-$\underline{C}$-5), 65.6 ($\underline{C}$-6), 53.2 ($O\underline{C}H_3$), 52.7 ($O\underline{C}H_3$), 20.3, 20.1, 20.0 (2) ($\underline{C}H_3$, acetyl). Anal. Calc. For $C_{20}H_{28}O_{15}$: C, 47.25; H, 5.55; O, 47.20 Found C, 47.23; H, 5.57; O, 47.23.

(2*R*,3*R*)-Dimethyl-2-hydroxy-3-((2*S*,3*R*,4*R*,5*R*,6*R*)-3,4,5-triacetoxy-6-(acetoxymethyl)tetrahydro-2H-pyran-2-yloxy)succinate (13c)

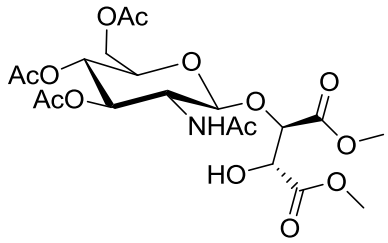


Chemical Formula: $C_{20}H_{28}O_{15}$
Exact Mass: 508.1428

Yield: 67 %. Colourless oil. $[\alpha]_D^{25}$ = 31.51° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3473 (OH), 2956 (CH), 1736 (CO), 1320 (C-O-C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 5.59 (d, *J* = 3.7 Hz, 1H, H-1), 5.43, 5.41 (2 pseudo t, *J* ~ 5.2 Hz in each, 2H, H-2, H-3), 4.98 (t, *J* = 12.0 Hz, 1H, H-4), 4.77 (dd, *J* = 9.2, 2.5 Hz, 1H, CH), 4.65 (d, *J* = 2.5 Hz, 1H, CH), 4.59 (d, *J* = 7.2 Hz, 1H, OH), 4.31 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.10 (ddd, *J* = 10.3, 3.5, 2.3 Hz, 1H, H-5), 3.92 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^b), 3.86 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 2.22, 2.20, 2.17, 2.15 (4s, 12 H, 4 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 171.7 ($\underline{C}OOCH_3$), 170.3, 169.4, 169.2, 168.5 (4 × $\underline{C}O$, acetyl), 95.9 ($\underline{C}$-1), 76.2 ($\underline{C}H$), 75.1 ($\underline{C}H$), 72.3,

69.1, 68.6, 68.3 (C-2-C-5), 65.1 (C-6), 53.5 (OCH_3), 52.7 (OCH_3), 20.2, 20.0, 19.4 (2) (4 × CH_3, acetyl). Anal. Calc. For $C_{20}H_{28}O_{15}$: C, 47.25; H, 5.55; O, 47.20 Found C, 47.22; H, 5.51; O, 47.16.

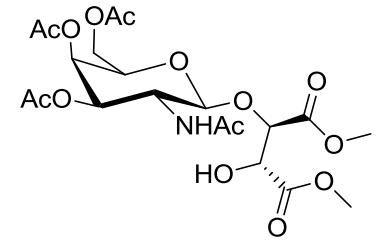
(2*R*,3*R*)-Dimethyl-2-((2*S*,3*R*,4*S*,5*S*,6*R*)-3-acetamido-4,5-diacetoxy-6-(acetoxymethyl)tetrahydro-2H-pyran-2-yloxy)-3-hydroxysuccinate (13d)



Chemical Formula: $C_{20}H_{29}NO_{14}$
Exact Mass: 507.1588

Yield: 68 %. Colourless gel. $[\alpha]_D^{25}$ = 29.41° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3421 (OH), 2974 (CH), 1732 (CO), 1310 (C-O-C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 6.98 (d, *J* = 9.5 Hz, 1H, NH), 5.69 (d, *J* = 8.3 Hz, 1H, H-1), 5.41, 4.95 (2 pseudo t, *J* ~ 8.5 Hz in each, 2H, H-3, H-4), 5.45 (m, 1H, H-2), 4.72 (dd, *J* = 9.3, 2.4 Hz, 1H, CH), 4.63 (d, *J* = 2.4 Hz, 1H, CH), 4.55 (d, *J* = 7.2 Hz, 1H, OH), 4.31 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.12 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 3.92 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^b), 3.87 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 2.17, 2.12, 2.11, 2.07 (4s, 12 H, 4 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 172.0 ($COOCH_3$), 170.5, 169.3, 169.3, 168.4 (4 × CO, acetyl), 96.1 (C-1), 76.2 (CH), 75.3 (CH), 72.2, 69.1, 68.6, 68.2 (C-2-C-5), 64.6 (C-6), 53.4 (OCH_3), 52.3 (OCH_3), 20.4, 20.2, 20.1 (2) (4 × CH_3, acetyl). Anal. Calc. For $C_{20}H_{29}NO_{14}$: C, 47.34; H, 5.76; N, 2.76; O, 44.14 Found C, 47.30; H, 5.73; N, 2.74; O, 44.11.

(2*R*,3*R*)-Dimethyl-2-((2*S*,3*R*,4*S*,5*S*,6*R*)-3-acetamido-4,5-diacetoxy-6-(acetoxymethyl)tetrahydro-2H-pyran-2-yloxy)-3-hydroxysuccinate(13e)



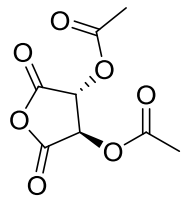
Chemical Formula: $C_{20}H_{29}NO_{14}$
Exact Mass: 507.1588

Yield: 59 %. Yellow gel. $[\alpha]_D^{25}$ = 22.51° (c = 24 mg/2 ml CH_2Cl_2). (IR υ cm^{-1}): 3423 (OH), 2984 (CH), 1735 (CO), 1313 (C-O-C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 6.93 (d, *J* = 9.2 Hz, 1H, NH), 5.66 (d, *J* = 8.3 Hz, 1H, H-1), 5.41, 4.93 (2 pseudo t, *J* ~ 4.8 Hz in each, 2H, H-3, H-4), 5.40 (m, 1H, H-2), 4.74 (dd, *J* = 9.3, 2.5 Hz, 1H, CH), 4.61 (d, *J* = 2.5 Hz, 1H, CH), 4.53 (d, *J* = 7.3 Hz, 1H, OH), 4.32 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^a), 4.14 (ddd, *J* = 10.4, 3.6, 2.1 Hz, 1H, H-5), 3.91 (dd, *J* = 12.5, 3.6 Hz, 1H, H-6^b), 3.86 (s, 3H, OCH_3), 3.82

(s, 3H, OCH_3), 2.16, 2.14, 2.11, 2.05 (4s, 12 H, 4 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 171.5 ($\underline{C}OOCH_3$), 170.3, 169.1, 169.0, 168.5 (4 × $\underline{C}O$, acetyl), 96.4 ($\underline{C}$-1), 76.2 ($\underline{C}H$), 75.5 ($\underline{C}H$), 72.1, 69.2, 68.2, 68.1 ($\underline{C}$-2-$\underline{C}$-5), 64.7 ($\underline{C}$-6), 53.5 ($O\underline{C}H_3$), 52.7 ($O\underline{C}H_3$), 20.5, 20.3, 20.1 (2) (4 × $\underline{C}H_3$, acetyl).Anal. Calc. For $C_{20}H_{29}NO_{14}$: C, 47.34; H, 5.76; N, 2.76; O, 44.14 Found C, 47.36; H, 5.70; N, 2.72; O, 44.17.

3.12 General procedure for the synthesis of diacetyl-*L*-tartaric acid anhydride (14)[171]

In a round bottom flask (250 ml) with a reflux condenser protected by calcium chloride drying tube, placed *L*-tartaric acid (15.0 g, 100 mmol) and freshly distilled acetic anhydride (9.44 ml, 100 mmol). The reaction mixture was refluxed on oil bath with occasional shaking until a clear solution was obtained (Ca. 1 hour) and then for a further ten minutes to ensure the completion of the reaction. Reaction mixture was then allowed to cool to room temperature and diluted with ether (150 ml) and was left for cooling overnight under nitrogen atmosphere in freezer. Crystals of diacetyl-*L*-tartaric acid anhydride separated out which were filtered and washed with ether and dried under vacuum.



Chemical Formula: $C_8H_8O_7$
Exact Mass: 216.0270

Yield: 85%. White crystalline solid. m.p = 126-128 °C $[\alpha]_D^{25}$ = 2.75° (c = 15 mg/20 ml Ethyl acetate). IR (KBr) cm^{-1}: 2939 (CH), 1827 (CO, anhydride) and 1761 (CO, ester). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm). 5.69 (s, 2H, CH), 2.25 (s, 6H CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 169.7 ($\underline{C}O$, ester), 163.3 ($\underline{C}O$, anhydride), 72.1 ($\underline{C}H$), 20.2 ($\underline{C}H_3$). Anal. Calc. for $C_8H_8O_7$: C, 44.44; H, 3.70. Found: C, 43.95; H, 3.46.

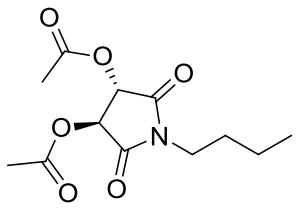
3.13 General procedure for the synthesis of chiral imides and amides (14a-14n)[172]

To carry out synthesis of chiral imides and amides aliphatic amines like ethyl amine butyl amine, substituted aromatic amines and amino acids were made to react with compound **(14)**.

In a round bottom flask (100 ml) compound **14** (1.08 g, 5 mmol) and amine (5 mmol) were placed with a reflux condenser. Glacial acetic (20 ml) was added as a solvent.

The reaction mixture was refluxed under nitrogen along with stirring for one hour, so that imide or amide was synthesized. Glacial acetic acid was removed by extraction the reaction mixture with ethyl acetate or chloroform and water (10 ml × 3). Crude product was purified by column chromatography using ethyl acetate: n.hexane (1:9) or methanol: chloroform (2:8) as eluent.

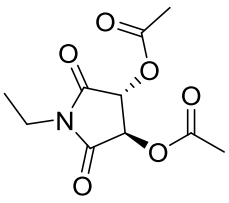
(3*S*,4*S*)-1-Butyl-2,5-dioxopyrrolidine-3,4-diyl diacetate (14a)



Chemical Formula: $C_{12}H_{17}NO_6$
Exact Mass: 271.1056

The compound 1-butyl-3,4-diacetoxy pyrrolidin-2, 5-dione **(14a)** was synthesized by the general procedure as described above. Yield: 74 %. Colourless Gel. $[\alpha]_D^{25}$ = 2.73° (c = 15 mg/20 ml Ethyl acetate). IR (NaCl) cm^{-1}: 2963 (CH_3), 2925 (CH_2), 2874 (CH), 1780 (CO, imide), 1740 (CO, ester). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 5.50 (s, 2H,CH), 3.58 (t, *J* = 7.0 Hz, 2H, N-CH_2), 2.20 (s, 6H, CH_3), 1.61 (q, *J* = 8.0 Hz, 2H, -CH_2-), 1.32 (m, 2H, CH_2-CH_3), 0.93 (t, 3H, 7.5, CH_3-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 169.9 (COOR), 169.4 (CON), 72.7 (CH), 39.3 (N-CH_2), 31.2 (-CH_2-), 20.4 (CH_3CO), 19.8 (CH_3-CH_2), 13.5 (CH_3-CH_2).

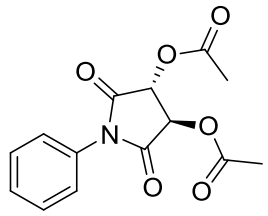
(3*R*,4*R*)-1-Ethyl-2,5-dioxopyrrolidine-3,4-diyl diacetate (14b)



Chemical Formula: $C_{10}H_{13}NO_6$
Exact Mass: 243.0743

Yield: 70 %. Orange solid. m.p = 80-82 ^{o}C. $[\alpha]_D^{25}$ = 0.40° (c = 15 mg/20 ml Ethyl acetate). IR (KBr) cm^{-1}: 2990 (CH_3), 2936 (CH_2), 2900 (CH), 1750 (CO, imide), 1735 (CO, ester). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 5.51 (s, 2H, CH), 3.65 (q, *J* = 7.2 Hz, 2H, CH_2-CH_3), 2.20 (s, 6H, CH_3), 1.23 (t, *J* = 7.0 Hz, 3H, CH_3-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 169.8 (COOR), 169.2 (CON), 72.7(CH), 34.5 (CH_2), 20.3 (CH_3-CO), 14.0 (CH_3-CH_2). Anal. Calc. for $C_{10}H_{13}O_6N$: C, 49.38; H, 5.38; N, 5.75. Found: C, 49.28; H, 5.33; N, 5.82. EI-MS *m/z* (%): 243 M^+ (17.2), 184 (23.5), 144 (4.9), 141 (58.8), 102 (100).

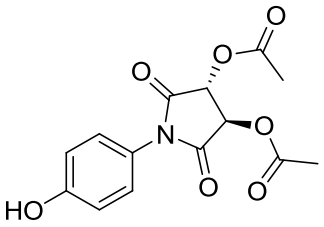
(3*R*,4*R*)-2,5-Dioxo-1-phenylpyrrolidine-3,4-diyl diacetate (14c)



Chemical Formula: $C_{14}H_{13}NO_6$
Exact Mass: 291.0743

Yield: 80 %. White crystalline solid. m.p = 83-85 ^{o}C. $[\alpha]_D^{25}$ = 3.35° (c = 15 mg/20 ml Ethyl acetate). IR (KBr) cm^{-1}: 2943 (CH), 1737 (CO, imide), 1735 (CO, ester). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.46-7.28 (m, 5H, Ar-H), 5.68 (s, 2H, CH), 2.25 (s, 6H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.0 (COOR), 168.5 (CON), 130.0-126.2 (Ar-C), 72.8 (CH), 20.4 (CH_3-CO). Anal. Calc. for $C_{14}H_{13}O_6N$: C, 57.73; H, 4.50; N, 4.81. Found: C, 57.25; H, 4.37; N, 4.94.

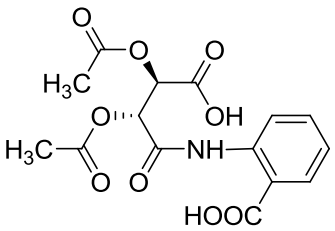
(3*R*,4*R*)-1-(4-Hydroxyphenyl)-2,5-dioxopyrrolidine-3,4-diyl diacetate (14d)



Chemical Formula: $C_{14}H_{13}NO_7$
Exact Mass: 307.0692

Yield: 75 %. White solid. m.p = 73-75 ^{o}C. $[\alpha]_D^{25}$ = 1.48° (c = 15 mg/20 ml Ethyl acetate). IR (KBr) cm^{-1}: 3250-2615 (OH), 2961 (CH), 1745 (CO, imide), 1735 (CO, ester). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.68-7.38 (m, 4H, Ar-H), 6.39 (s, 2H, CH), 2.63 (s, 6H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 178.9 (COOR), 170.1 (CON), 156.3-116.6 (Ar-C), 72.8 (CH), 20.4 (CH_3-CO). Anal. Calc. for $C_{14}H_{13}O_7N$: C, 54.32; H, 4.26; N, 4.55. Found: C, 53.95; H, 4.51; N, 4.46.

2-((2*R*,3*R*)-2,3-Diacetoxy-3-carboxypropanamido)benzoic acid (14e)

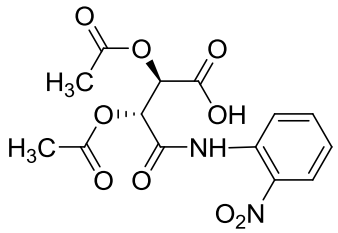


Chemical Formula: $C_{15}H_{15}NO_9$
Exact Mass: 353.0747

Yield: 75 %. Light brown solid. m.p = 104-105 ^{o}C. $[\alpha]_D^{25}$ = 1.07° (c = 15 mg/20 ml Ethyl acetate). IR (KBr) cm^{-1}: 3511 (NH), 3250-2615 (OH), 2903 (CH), 1750 (CO, ester), 1730 (CO, acid), 1670 (CO, amide). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.66-8.63 (dd *J* = 7.0, 2.5 Hz, 1H, Ar-H), 8.15-8.12 (dd, *J* = 6.8, 3.0 Hz, 1H, Ar-H), 7.64-7.58 (dd, *J* = 7.0, 2.0 Hz, 1H, Ar-H), 7.24-7.19 (dd *J* = 7.2, 3.1 Hz, 1H, Ar-H), 5.86 (d, *J* = 7.2 Hz, 1H,-CH-CON), 5.60 (d, *J* = 7.0 Hz, 1H, -CH-COOH), 2.30 (s, 3H, CH_3), 2.05 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.0 (CHCOOH), 169.4 (COOR-COOH), 168.4 (COOR-CON), 169.8 (CON), 165.4 (Ar-COOH), 140.0-116.1 (C_6H_4), 72.4 (CH-COOH), 71.2 (CH-CON),

19.1 (<u>C</u>H_3), 18.8 (<u>C</u>H_3). Anal. Calc. for $C_{15}H_{15}O_9N$: C, 50.99; H, 4.27; N, 3.96. Found: C, 49.67; H, 4.57; N, 3.88.

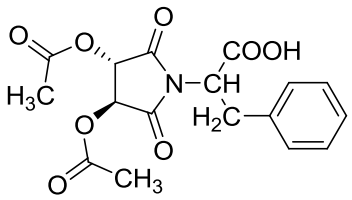
(2*R*,3*R*)-2,3-diacetoxy-4-(2-nitrophenylamino)-4-oxobutanoic acid (14f)



Chemical Formula: $C_{14}H_{14}N_2O_9$
Exact Mass: 354.0699

Yield: 71 %. Yellow solid. m.p = 110-111 ^{o}C. $[\alpha]_D^{25}$ = 3.23° (c = 15 mg/20 ml Ethyl acetate). IR (KBr) cm^{-1}: 3503 (NH), 3250-2615 (OH), 2941 (CH), 1753 (CO, ester), 1725 (CO, acid), 1690 (CO, amide), 1587&1346 (NO). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.59-8.56 (dd, *J* = 6.8,3.0 Hz, 1H, Ar-H), 8.28-8.25 (dd, *J* = 6.5, 3.0 Hz, 1H, Ar-H), 7.85-7.79 (dd, *J* = 7.1, 3.2 Hz, 1H, Ar-H), 7.44-7.39 (dd, *J* = 7.0, 2.0 Hz, 1H, Ar-H), 5.93 (d, *J* = 7.4 Hz, 1H, CH-CON), 5.69 (d, *J* = 7.5 Hz, 1H, CH-COOH), 2.25 (s, 3H, CH_3), 2.08 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 169.2 (CH<u>C</u>OOH), 167.7 (<u>C</u>OOR-COOH), 167.4 (<u>C</u>OOR-CON), 168.7 (<u>C</u>ON), 138.1-122.4 (C_6H_4), 72.4 (<u>C</u>H-COOH), 71.0 (<u>C</u>H-CON), 19.6 (<u>C</u>H_3), 19.4 (-<u>C</u>H_3). Anal. Calc. for $C_{14}H_{14}O_9N_2$: C, 47.46; H, 3.98; N, 7.90. Found: C, 46.65; H, 4.13; N, 7.77. EI-MS *m/z* (%): 354.0 M^+ (4.5), 217.1 (8.7), 189.2 (3.9), 137.1 (100), 91.1 (26.8), 65.3 (25.7).

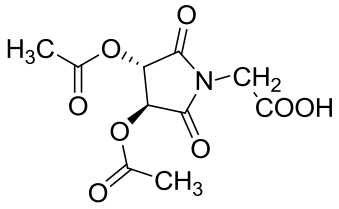
2-((3*S*,4*S*)-3,4-diacetoxy-2,5-dioxopyrrolidin-1-yl)-3-phenylpropanoic acid (14g)



Chemical Formula: $C_{17}H_{17}NO_8$
Exact Mass: 363.0954

Yield: 69 %. White solid. m.p = 98-99 ^{o}C. $[\alpha]_D^{25}$ = 3.80° (c = 15 mg/20 ml Ethyl acetate). IR (KBr) cm^{-1}: 3250-2615 (OH), 2943 (CH), 1742 (CO, imide), 1740 (CO, ester), 1671 (CO, acid). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.49-7.34 (m, 5H, Ar-H), 5.91 (s, 2H, CH), 4.92 (t, *J* = 7.0 Hz, 1H, CH), 3.33-3.31 (m, 2H), 2.20 (s, 6H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 172.6 (CH <u>C</u>OOH), 170.2 (<u>C</u>OOR), 169.2 (<u>C</u>ON), 131.3-126.3 (Ar), 72.7 (<u>C</u>H), 48.4 (-<u>C</u>H-CH_2), 34.1(CH-<u>C</u>H_2), 18.8 (<u>C</u>H_3-CO). Anal. Calc. for $C_{17}H_{17}O_8N$: C, 56.79; H, 4.71; N, 3.85. Found: C, 55.81; H, 5.04; N, 3.53. EI-MS *m/z* (%): 363.1 M^+ (3.2), 319.1 (4.5), 273.2 (23.9), 259.2 (27.4), 191.1 (5.3), 149.2 (100), 91.3 (68.5).

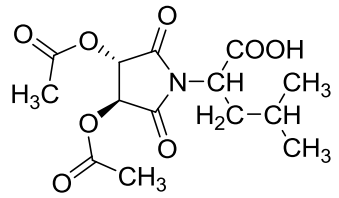
2-((3*S*,4*S*)-3,4-diacetoxy-2,5-dioxopyrrolidin-1-yl)acetic acid (14h)



Chemical Formula: $C_{10}H_{11}NO_8$
Exact Mass: 273.0485

Yield: 72 %. Colourless Gel. $[\alpha]_D^{25}$ = 4.08° (c = 15 mg/20 ml Ethyl acetate). IR (NaCl) cm^{-1}: 3250-2615 (OH), 2935 (CH), 1750 (CO, imide), 1748 (CO, ester), 1720 (CO, acid). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 5.67 (s, 2H, CH), 4.39 (s, 2H, CH_2), 2.22 (s, 6H, 2 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.2 (COOH), 170.0 (COOR), 168.6 (CON), 72.5 (CH), 39.5 (-CH_2), 20.3(CH_3).

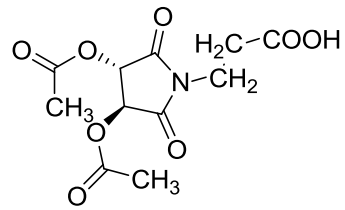
2-((3*S*,4*S*)-3,4-diacetoxy-2,5-dioxopyrrolidin-1-yl)-4-methylpentanoic acid (14i)



Chemical Formula: $C_{14}H_{19}NO_8$
Exact Mass: 329.1111

Yield: 65 %. Colourless Gel. $[\alpha]_D^{25}$ = 4.16° (c = 15 mg/20 ml Ethyl acetate). IR (NaCl) cm^{-1}: 3250-2615 (OH), 2962 (CH), 1740 (CO, imide), 1735 (CO, ester), 1727 (CO, acid). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 5.61 (s, 2H, CH), 4.88 (t, J = 8.0 Hz, 1H), 2.22 (s, 6H, CH_3), 1.47 (t, J = 7.5, 2H), 1.94-1.85 (m, 1H), 0.95 (d, J = 7.1 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 173.5(COOH), 169.9 (COOR), 168.5 (CON), 72.4 (CH), 51.4 (CH-CH_2), 35.7 (CH-CH_2), 29.7 (CH_3-CH-CH_3), 24.7 (CH_3-CH-CH_3), 20.3 (CH_3CO).

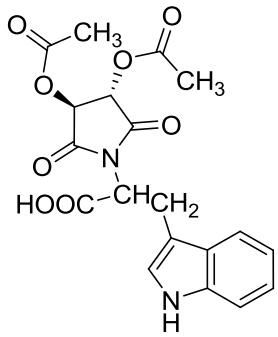
3-((3*S*,4*S*)-3,4-diacetoxy-2,5-dioxopyrrolidin-1-yl)propanoic acid (14J)



Chemical Formula: $C_{11}H_{13}NO_8$
Exact Mass: 287.0641

Yield: 73 %. Yellow Gel. $[\alpha]_D^{25}$ = 4.06° (c = 15 mg/20 ml Ethyl acetate). IR (NaCl) cm^{-1}: 3250-2615 (OH), 2936 (CH), 1785 (CO, imide), 1737 (CO, ester), 1725 (CO, acid). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 5.50 (s, 2H, CH), 3.79 (t, J = 6.5 Hz, 2H), 2.74 (t, J = 6.0 Hz 2H), 2.20 (s, 6H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 175.8 (COOH), 170.0 (COOR), 169.4 (CON), 72.7 (CH), 34.7 (N-CH_2), 31.0 (CH_2-COOH), 20.4 (CH_3).

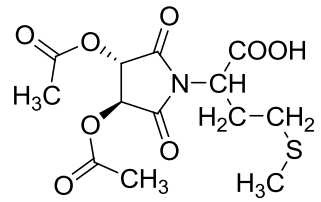
2-((3*S*,4*S*)-3,4-diacetoxy-2,5-dioxopyrrolidin-1-yl)-3-(1H-indol-3-yl)propanoic acid (14k)



Chemical Formula: $C_{19}H_{18}N_2O_8$
Exact Mass: 402.1063

Yield: 80 %. Light yellow solid. m.p = 87-88 °C. $[\alpha]_D^{25}$ = 4.38° (c = 15 mg/20 ml Ethyl acetate). IR (KBr) cm^{-1}: 3250-2615 (OH), 2932 (CH), 1760 (CO, imide), 1755 (CO, ester), 1720 (CO, acid). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.38-7.30 (m, 4H, Ar-H), 6.07(s, 1H, -CH-NH), 5.46 (s, 2H, CH-OCO), 5.20 (t, J = 9.0 Hz, 1H, -CH-CH_2), 3.75-3.67 (m, 2H, -CH-CH_2), 2.12 (s, 6H, CH3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 172.0 (COOH), 170.1 (COOR), 168.5 (CON), 136.1-109.7 (Ar), 72.0 (CH), 53.6 (-CH-CH_2), 23.2 (CH-CH_2), 20.3 (CH_3-CO). Anal. Calc. for $C_{19}H_{18}O_8N_2$: C, 56.71; H, 4.50; N, 6.96. Found: C, 55.40; H, 4.69; N, 6.72. EI-MS m/z (%): 402.1 M^+ (3.9), 272.2 (27.7), 130.1 (100), 104.0 (6.3), 77.1 (6.9).

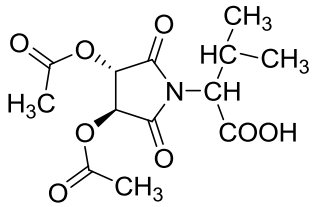
2-((3*S*,4*S*)-3,4-diacetoxy-2,5-dioxopyrrolidin-1-yl)-4-(methylthio)butanoic acid (14l)



Chemical Formula: $C_{13}H_{17}NO_8S$
Exact Mass: 347.0675

Yield: 75 %. Yellow gel. $[\alpha]_D^{25}$ = 4.78° (c = 15mg/20ml Ethyl acetate). IR (NaCl) cm^{-1}: 3250-2615 (OH), 2923 (CH), 1790 (CO, imide), 1730 (CO, ester), 1725 (CO, acid). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm): 5.60 (s, 2H, CH), 5.10, 5.07 (dd, J = 6.0, 6.1 Hz, 1H, -CH-CH_2), 2.64-2.52 (m, 2H, -CH-CH_2), 2.39 (t, J = 7.5 Hz, 2H,-CH_2-S), 2.22 (s, 6H, CH_3), 2.10 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 171.9 (COOH), 170.0 (COOR), 168.6 (CON), 72.5 (CH), 51.6 (-CH.COOH), 30.3 (-CH_2-S), 29.6 (-CH-CH_2), 20.3 (CH_3-COOR), 15.2 (-S-CH_3).

2-((3*S*,4*S*)-3,4-diacetoxy-2,5-dioxopyrrolidin-1-yl)-3-methylbutanoic acid (14m)

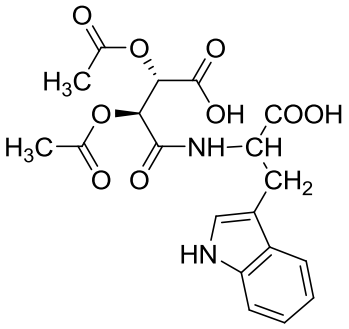


Chemical Formula: $C_{13}H_{17}NO_8$
Exact Mass: 315.0954

Yield: 69 %. Colourless Gel. $[\alpha]_D^{25}$ = 0.48° (c = 15 mg/20 ml Ethyl acetate). IR (NaCl) cm^{-1}: 3250-2615 (OH), 2968 (CH), 1780 (CO, imide), 1737 (CO, ester), 1728 (CO, acid). ^1H NMR (300 MHz,

$CDCl_3$): δ (ppm): 5.62 (s, 2H, CH), 4.49 (d, *J* = 7.0 Hz, 1H, -CH-COOH), 2.73-2.61 (m, 1H, CH_3-CH-CH_3), 2.24 (s, 6H, CH_3), 0.93 (d, 6H, CH_3-CH-CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 177.5 (COOH), 172.5 (COOR), 169.9 (CON), 72.4 (CH), 58.4 (-CH.COOH), 27.7 (-CH_3-CH-CH_3), 20.3 (-CH_3-COOR), 19.2 (CH_3-CH-CH_3).

(2*S*,3*S*)-2,3-diacetoxy-4-(1-carboxy-2-(1H-indol-3-yl)ethylamino)-4-oxobutanoic acid (14n)



Chemical Formula: $C_{19}H_{20}N_2O_9$
Exact Mass: 420.1169

Yield: 78 %. Light yellow solid. m.p = 92-94 ^{o}C. $[\alpha]_D^{25}$ = 0.43° (c = 15 mg/20 ml Ethyl acetate). IR (KBr) cm^{-1}: 3410 (NH), 3250-2615 (OH), 2939 (CH), 1743 (CO, ester), 1725 (CO, acid), 1672 (CO, amide). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.36-7.02 (m, 4H, Ar-H), 6.07 (s, 1H, -CH-NH), 5.62 (d, *J* = 7.2Hz, 1H, CH-CON), 5.49 (d, *J* = 7.0 Hz, 1H, -CH-COOH), 4.74, 4.71 (dd, *J* = 6.0, 6.2 Hz, 1H, -CH-CH_2), 3.39-3.32 (m, 2H, CH-CH_2), 1.98 (s, 3H, CH_3), 1.97 (s, 3H, CH_3) ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 172.9 (CH.CH_2COOH), 170.0 (-CH.COOH), 169.2 (CON), 167.1 (COOR) 136.6-109.0 (Ar), 72.0 (-CHCOOH), 70.9 (-CH-CONH), 53.0 (CH-CH_2), 26.4 (CH_3-CO), 23.2 (CH-CH_2), 18.8 (CH_3-CO) .Anal. Calc. for $C_{19}H_{20}O_9N_2$: C, 54.28; H, 4.79; N, 6.66. Found: C, 53.98; H, 5.11; N, 6.66.

4.1 Biological screening

4.1.1 Antimicrobial activity

About 24 chiral amides, 12 protected (**2a-2l**) and 12 deprotected (**3a-3l**) were tested to study their inhibitional potential against 3 selected fungal and 3 bacterial strains. Similarly chiral imides (**14g-14m**) were also evaluated for their antimicrobial activities using the same selected fungal and bacterial strains. Following methods were used to check these activities. In the present experiment three concentrations (12 mg/ml, 6 mg/ml, and 3 mg/ml) of the selected compounds were used to study the inhibition potential against 3 fungal and 3 bacterial strains. The agar tube dilution method was used for determination of antifungal activity of compounds. (*Washington and Sutter*, 1980).[184] The following fungal strains were used in this study.
Fussarium solani, Helmentosporium sativum and *Aspergillus niger*.

Each fungal strain was maintained on Sabouraud dextrose agar (SDA) medium at 4°C.

The samples for antifungal assay were prepared from initial stock of 12 mg of each compound per ml of DMSO. Media for fungus was prepared by dissolving 6.5 g of SDA per 100 ml in distilled water pH was adjusted at 5.6. Test tubes were marked to 10 cm mark. The Sabouraud dextrose agar (MERCK) dispensed as 4 ml volume into screw capped tubes or cotton plugged test tubes and was autoclaved at 121 °C for 21 minutes. Tubes were allowed to cool to 50 °C and non-solidified SDA was loaded with 67 µl of compound pipette from the stock solution. This would give the final concentration of 200 µg/ml of the pure compound in media. Tubes were then allowed to solidify in slanting position at room temperature. Three slants of the samples were prepared for each fungus species. The tubes containing solidified media and test compound were inoculated with 4 mm diameter piece of inoculum, taken from a seven days old culture of fungus. One sample of each compound was prepared, which were used for positive control. Slants without samples were used for negative control.

The test tubes were incubated at 28 °C for 7 days. Cultures were examined twice weekly during the incubation. Reading was taken by measuring the linear length of fungus in slant by measuring growth (mm) and growth inhibition was calculated with

reference to negative control. Percentage inhibition of fungal growth for each concentration of compound was determined by the following formula.

$$\text{Percentage inhibition of fungal growth} = 100 - \frac{\text{Linear growth in test (mm)}}{\text{Linear growth in control (mm)}} \times 100$$

Three strains of bacteria were used in the study *Enterobacter sp. Vibro cholra and Klebsila*.

Nutrient broth medium was prepared by dissolving 0.4 g of nutrient broth per 50 ml of distilled water for the growth of bacterial inocula; pH was adjusted at 7.0 and was autoclaved. Nutrient agar medium was prepared by dissolving 2.3 g agar in 100 ml of distilled water; pH was adjusted at 7.0 and was autoclaved at 121 °C.

The standard was prepared by adding 0.5 ml 0.048 M Barium chlorides to 99.5 ml 0.36 N sulphuric acid. Barium sulphate turbidity standard (4-6 ml) and was taken in screw capped test tube and poured to inoculums till the inoculum give the same colour as that of turbidity standard.[185] The organisms were maintained on nutrient agar medium at 4 °C.

Centrifuged pallets of bacteria from 24 hours old culture in nutrient broth (SIGMA) of selected bacterial strains were mixed with physiological normal saline solution until a Mcfarland turbidity standard [10^6 colony forming unit (CFU) ml^{-1}] was obtained. Then this inoculum was used for seeding the nutrient agar.

Nutrient agar medium was prepared by adding nutrient agar (MERCK) 2.3 g in 100 ml of distilled water; pH was adjusted at 7.0 and was autoclaved. It was allowed to cool up to 45° C. Petri plates were prepared by pouring 75 ml of seeded nutrient agar and allowed to solidify. Four wells per plate were made with sterile cork borer (5 mm).

Using micropipette, 100 µl of test solutions was poured in respective wells. These plates were incubated at 37 °C. After 24 hours of incubation the diameter of the clear zones of inhibitions was measured by a ruler. Antibacterial activity of two dilutions of each sample was determined against three bacterial strains.

4.1.1.1 Results

In the present experiment three concentrations (12 mg/ml, 6 mg/ml, and 3 mg/ml) of the selected compounds (protected amides (**2a-2l)**, deprotected amides (**3a-3l)** and imides (**14g-14m)** were used to study the inhibition potential against 3 fungal and 3 bacterial strains.

All twenty four, protected amides (**2a-2l**) and deprotected (**3a-3l**) were screened for their *in vitro* antifungal and antibacterial potential against different strains of fungi (*Fausarium solani*, *Helminthosporium sativum*, and *Aspergillus niger*) and bacteria (*Enterobacter sp*, *Vibrio cholerae*, *Klebsiella sp*). The results are listed in Table 4.1 and Table 4.2.

All the compounds showed good activity against *Fusarium solani, Helminthosporium sativum* and *Aspergillus niger* at 12 mg/ml concentration. Compounds **2c** (88 %, 89 %, 78 %), **2f** (81 %, 79 %, 68 %), **2i** (84 %, 70 %, 63 %), and **2l** (73 %, 70 %, 53 %) with substituents at *para* position showed significant activity against three fungal strains at 12 mg/ml concentration. However, as the concentration decrease to 6 mg/ml and 3 mg/ml these compounds showed a clear decline in activity. Compounds **2a** and **2j** with the *ortho* substitutions of halogens showed (67 %, 65 %, 70 %) and (67 %, 62 %, 67 %) inhibition at 12 mg/ml concentration in all the three strains of fungi, respectively, although compounds **2d** and **2g** with *ortho* methoxy and methyl substitutions showed only (3 mg/ml, 64 %, 53 %) and (47 %, 46 %, 57 %) inhibition against all three strains at 12 mg/ml concentration, respectively. The activity of compounds **2b** (73 %), **2e** (50 %), **2h** (66 %), and **2k** (83 %) with *meta* substitution at 12 mg/ml concentrations reveals that compounds **2b** and **2k** with *meta* flouro and chloro substitutions showed significant activity. When the concentration decrease to 6 mg/ml and 3 mg/ml there is a decrease in activity is observed in all the compounds. The results reveal that the same way of inhibition is observed in the activity of compounds of (**3a**-**3l**). Compound **3c** with *para* flouro substitution was found to be the most active compound showed inhibition 91 %, 91 %, 89 %, at 12 mg/ml concentration in all three strains. Compound **3f** with *para* methoxy showed 89 %, 88 %, 68 % activity at 12 mg/ml concentration. Compound **3i** and **3l** with *para* methyl and *para* chloro showed inhibition at 12 mg/ml concentration (88 %, 76 %, 66 %), (78 %, 77 %, 56 %), respectively. Compounds **3b**, **3e**, **3h**, **3k** with *meta* substituents

showed 88 %, 68 %, 72 % and 90 % inhibition for *Fausarium solani* and 70 %, 57 %, 58 %, and 78 % inhibition for *Helminthosporium sativum* and 71 %, 40 %, 38 % and 79 % inhibition for *Aspergillus niger* at 12 mg/ml concentration, respectively. Compounds **3a**, **3d**, **3g**, **3j**, with *ortho* substitution displayed 88 %, 68 %, 72 % and 90 % inhibition for *Fausarium solani* 65 % 64 % 46 %, and 62 % inhibition *Helminthosporium sativum* and 70 %, 53 %, 57 % and 67 % inhibition for *Aspergillus niger* at 12 mg/ml concentration, respectively. A declined in activity was observed in all the compounds when decreasing the concentration from 12 mg/ml to 6 mg/ml and 3 mg/ml. On the basis of the above results, we can say that the compounds with halogens substitution at *ortho*, *meta*, and *para* positions particularly when substituted at *para* and *meta* positions showed an excellent inhibitory potential against all the tested fungal strains and can be serve as a lead molecules for the further drug and medicinal research and studies.

Table 4.1: Antifungal activity of the protected amides (**2a-2l**) at three different concentrations against three fungal strains.

S. No.	Compounds	*Fausarium solani*			*Helminthosporium sativum*			*Aspergillus niger*		
		12 mg/ml	6 mg/ml	3 mg/ml	12 mg/ml	6 mg/ml	3 mg/ml	12 mg/ml	6 mg/ml	3 mg/ml
1	**2a**	67	41	33	65	28	29	70	38	17
2	**2b**	71	33	22	70	34	22	71	28	10
3	**2c**	88	70	15	89	16	20	78	23	22
4	**2d**	60	46	31	64	33	29	53	33	21
5	**2e**	50	48	45	57	22	17	40	33	23
6	**2f**	81	30	29	79	08	06	68	41	22
7	**2g**	47	45	13	46	56	40	57	45	33
8	**2h**	66	52	30	58	27	25	38	34	25
9	**2i**	84	58	30	70	38	35	63	41	25
10	**2j**	67	43	39	62	48	38	67	33	33
11	**2k**	83	51	38	78	25	19	79	71	47
12	**2l**	73	65	71	70	50	34	53	30	31

	+Ve control	-	-	-	-	-	-	-	-	-
	Terbinafine	94	94	94	98	98	98	98	98	98

Table 4.2: Antifungal activity of the deprotected amides (**3a-3l**) at three different concentrations against three fungal strains.

S. No.	Compounds	*Fausarium solani*			*Helminthosporium sativum*			*Aspergillus niger*		
		12 mg/ml	6 mg/ml	3 mg/ml	12 mg/ml	6 mg/ml	3 mg/ml	12 mg/ml	6 mg/ml	3 mg/ml
1	**3a**	70	43	40	78	32	33	72	44	23
2	**3b**	88	44	55	77	33	32	77	34	22
3	**3c**	91	72	21	91	22	22	89	44	43
4	**3d**	67	56	28	68	21	32	54	34	32
5	**3e**	68	50	54	60	22	22	43	45	45
6	**3f**	89	33	41	88	22	15	70	55	34
7	**3g**	57	56	22	43	67	45	63	60	55
8	**3h**	72	56	34	67	37	33	43	40	50
9	**3i**	88	65	44	76	40	45	66	44	34
10	**3j**	70	55	51	66	66	48	69	53	48
11	**3k**	90	66	50	88	44	27	81	76	54
12	**3l**	78	59	77	77	55	55	56	47	41
	+Ve control	-	-	-	-	-	-	-	-	-
	Terbinafine	94	94	94	98	98	98	98	98	98

The chiral imides (**14g-14m)** showed varying degree of growth inhibition against all three tested fungal strains *i.e. Faussarium solani, Helmentosporium, sativum and Aspergillus niger*. The results showed that all the compounds were active against all three fungal strains used for the analysis as listed in Table 4.3. The compounds displayed good activity at 12 mg/ml concentration while at 6 mg/ml and 3 mg/ml concentration their activity decreases except compounds **14h** which showed moderate activity against *Faussarium solani*, at all three concentrations as compare to the activity of other compounds. Compounds **14l** exhibited excellent activity against all

the three fungus (93 %) *Faussarium solani*, (90 %) *Helmentosporium sativum*, and (89 %) *Aspergillus niger* and at 12 mg/ml concentration it showed the activity as equivalent to standard drug terbinafine. Compounds **14m** demonstrated good activity against two strains of fungi *Faussarium solani*, at 12 mg/ml (81 %) and 6 mg/ml (76 %) concentration and *Helmentosporium sativum*, at 12 mg/ml (92 %) and 6 mg/ml (86 %) concentration, it was found to be more active than compound **14l**. Compounds **14i**, **14j**, and **14k** displayed comparatively good activity against all the tested fungi. Compounds **14i** and **14j** demonstrated (76 %) and compound **14k** exhibited (70 %) inhibition against *Faussarium solani* at 12 mg/ml concentration. Compounds **14j** and **14k** showed (91 %) inhibition against *Aspergillus Niger* at 12 mg/ml concentration. Compound **14k** displayed (87 %) inhibition against *Helmentosporium sativum*, at 12 mg/ml concentration, and compound **14i** showed (89 %) inhibition against *Helmentosporium sativum*, and (88 %) inhibition against *Aspergillus niger* at 12 mg/ml concentration.

Table 4.3: Antifungal activity of the compounds (**14g-14m**) at three different concentrations against three fungal strains.

S. No.	Compounds	*Fausarium solani*			*Helminthosporium sativum*			*Aspergillus niger*		
		12 mg/ml	6 mg/ml	3 mg/ml	12 mg/ml	6 mg/ml	3 mg/ml	12 mg/ml	6 mg/ml	3 mg/ml
1	**14g**	73	67	24	90	78	66	68	56	30
2	**14h**	45	39	23	78	70	65	92	67	55
3	**14i**	76	67	48	89	60	55	88	78	67
4	**14j**	76	65	55	44	34	28	91	77	65
5	**14k**	70	60	45	87	75	52	91	76	57
6	**14l**	93	89	78	90	76	65	89	73	54
7	**14m**	81	76	69	92	86	76	67	42	35
	+Ve control	-	-	-	-	-	-	-	-	-
	Terbinafine	94	94	94	98	98	98	98	98	98

All the twenty four, protected (**2a**-**2l)** and deprotected amides (**3a**-**3l)** were also evaluated for their antibacterial activity and the results are collected in Table 4.4 and Table 4.5.

All the compounds demonstrated good activity against all the three (*Enterobacter sp, Vibrio cholerae, Klebsiella sp*) at 12 mg/ml concentration, the antibacterial activity of the compounds also decreases at 6 mg/ml and 3 mg/ml concentration, respectively. Compound **2c**, **2f**, **2i** and **2l** with substituents at *para* position show significant activity (27, 26, 29, 21, for *Enterobacter sp*, 29, 18, 25, 17 for *Vibrio cholerae,* and 22, 28, 22, 23 mm zone of inhibition, for *Klebsiella sp,* respectively) against three bacterial strains at 12 mg/ml concentration, while the deprotected compounds **3c**, **3f**, **3i**, **3l**, (30, 30, 30, 29, for *Enterobacter sp*, 31, 21, 27, 22 for *Vibrio cholerae,* and 28, 30, 25, 23 mm zone of inhibition for *Klebsiella sp,* respectively) were found to be more active as compared to the protected amides. When the substitution amended with *ortho* substitutions displayed less activity against all the bacterial strains as it shown in protected amides **2a**, **2d**, **2g**, **2j**, (16, 17, 15, 19, for *Enterobacter sp*, 27, 22, 22, 26 for *Vibrio cholerae,* and 19, 19, 18, 22 mm zone of inhibition for *Klebsiella sp,* respectively) at 12 mg/ml concentration.

It is worth mentioning that deprotected amides showed much better activity as compared to the protected amides **3a**, **3d**, **3g**, **3j**, (22, 27, 19, 22, for *Enterobacter sp,* 30, 23, 25, 29 for *Vibrio cholerae*, and 23, 21, 22, 29 mm zone of inhibition for *Klebsiella sp,* respectively). When compare the *meta* substitution in protected amides it was found that **2b**, **2e**, **2h**, **2l**, (14, 23, 22, 21 for *Enterobacter. sp*, 22, 25, 23, 17, for *Vibrio cholerae,* and 23, 16, 27, 23 mm zone of inhibition for *Klebsiella sp,* respectively) less active than *ortho* and *para* protected and *meta* deprotected amides **3b**, **3e**, **3h**, **3l**, (21, 24, 23, 29 for *Enterobacter sp*, 26, 31, 24, 22 for *Vibrio cholerae,* and 25, 18, 29 and 23 mm zone of inhibition for *Klebsiella sp,* respectively) at 12 mg/ml concentrations. Hence in the light of all the above finding it is confirmed that the deprotected amides are more active as compared to the protected amides and on the basis of substitution the *para* substituents is more active as compared to their *ortho* and *meta* counter parts while in the substituted groups halogen substituted amides are found more potential inhibitors. The inhibition potential is going to be decrease as concentrations moving down from 12 mg/ml to 6 mg/ml and 3 mg/ml, respectively.

Table 4.4: Antibacterial activity[a] of the protected amides (**2a-2l**) at three different concentrations against three bacterial strains.

S. No.	Compounds	*Enterobacter sp*			*Vibrio cholerae*			*Klebsiella sp*		
		12 mg/ml	6 mg/ml	3 mg/ml	12 mg/ml	6 mg/ml	3 mg/l	12 mg/ml	6 mg/ml	3 mg/ml
1	**2a**	16	10	08	27	20	15	19	13	12
2	**2b**	14	05	11	22	13	21	23	10	09
3	**2c**	27	17	12	29	23	11	22	08	11
4	**2d**	17	13	11	22	18	14	19	12	10
5	**2e**	23	12	16	25	13	16	16	11	12
6	**2f**	26	12	17	18	10	12	28	23	22
7	**2g**	15	11	17	22	18	14	18	12	09
8	**2h**	22	15	06	23	15	12	27	18	14
9	**2i**	29	22	18	25	13	11	22	16	11
10	**2j**	19	12	10	26	23	18	22	13	14
11	**2k**	26	16	19	29	22	17	12	11	10
12	**2l**	21	19	19	17	13	11	23	17	16
	A	32	25	34	32	25	34	32	25	34

A = Chloramphenicol. [a]Zone diameter (Activity): Below 9 mm (no activity), 9-12 mm (non significant), 13-15 mm (low activity), 16-18 mm (good activity), above 18 mm (significant activity).

Table 4.5: Antibacterial activity of the deprotected amides (**3a-3l**) at three different concentrations against three bacterial strains.

S. No.	Compounds	*Enterobacter sp*			*Vibrio cholerae*			*Klebsiella sp*		
		12 mg/ml	6 mg/ml	3 mg/ml	12 mg/ml	6 mg/ml	3 mg/ml	12 mg/ml	6 mg/ml	3 mg/ml
1	**3a**	22	12	12	30	23	23	23	17	19
2	**3b**	21	22	22	26	14	22	25	13	13
3	**3c**	30	25	23	31	26	14	28	12	22
4	**3d**	27	22	21	23	21	23	21	22	21
5	**3e**	24	16	18	31	17	21	18	21	16
6	**3f**	30	18	19	21	14	17	30	28	18
7	**3g**	19	21	22	25	20	14	22	22	12
8	**3h**	23	22	10	24	21	22	29	21	21
9	**3i**	30	28	21	27	24	21	25	18	19
10	**3j**	22	24	23	29	29	22	29	22	17
11	**3k**	28	21	21	31	28	24	21	14	21
12	3l	29	23	23	22	21	20	23	22	18
	A	32	25	34	32	25	34	32	25	34

Compounds (**14g-14m)** showed varying degree of zone inhibition against all three selected bacterial strains *i.e Enterobacter sp., Vibrio cholerae, Klebsila. Sp* and results are summarized in Table 4.6. All the compounds showed good activity against all bacterial strains used at 12 mg/ml concentration, the activity of the compounds declined at 6 mg/ml and 3 mg/ml concentrations, respectively. Compound **14m** displayed excellent growth inhibition potential against *Enterobacter sp.* (29 mm), *Vibrio cholera* (30 mm), *Klebsiella sp.* (23 mm), respectively, at 12 mg/ml concentration as compared to standard drug chloramphenicol. Compound **14l** exhibited good zone of inhibition (23 mm) against *Enterobacter sp.*, (27 mm) against *Vibrio cholerae,* and (22 mm) against *Klebsiella sp.* at 12 mg/ml concentration. Compound **14h** also exhibited good zone of inhibition against *Enterobacter sp.* (24 mm), *Vibrio cholerae* (25 mm), *Klebsiella sp.* (22 mm) at 12 mg/ml concentration. Compound **14i** exhibited good zone of inhibition against *Enterobacter sp.* (18 mm),

Vibrio cholerae (22 mm), *Klebsiella sp.* (18 mm) at 12 mg/ml concentration. Compounds **14j-14l** found to be inactive against *Enterobacter sp.* at 3 mg/ml concentration. Compound **14j** also found to be inactive at 6 mg/ml and 3 mg/ml concentration against *Vibrio cholerae* and *Klebsiella sp.* at 3 mg/ml concentration. Compound **14k** and **14l** were also found to be inactive against *Enterobacter sp.* at 3 mg/ml concentration. Compound **14l** also found to be inactive against *Enterobacter sp.* at 3 mg/ml concentration.

Table 4.6: Antibacterial activity of the imides (**14g-14m**) at three different concentrations against three bacterial strains.

S. No.	Compounds	*Enterobacter sp*			*Vibrio cholerae*			*Klebsiella sp*		
		12 mg/ml	6 mg/ml	3 mg/ml	12 mg/ml	6 mg/ml	3 mg/ml	12 mg/ml	6 mg/ml	3 mg/ml
1	**14g**	20	17	16	26	18	13	23	19	10
2	**14h**	24	20	14	25	12	09	22	12	10
3	**14i**	18	12	11	22	17	15	18	13	11
4	**14j**	12	08	inactive	12	inactive	inactive	22	10	inactive
5	**14k**	16	13	inactive	19	11	inactive	18	13	12
6	**14l**	23	12	inactive	27	12	10	22	15	12
7	**14m**	29	23	17	30	24	16	23	18	16
	A	32	25	34	32	25	34	32	25	34

4.1.2 Antileishmanial activity

Antileishmanial activity of the glycopyranosyl amides (**10a-10e**) and glycopyranosides (**11a-11e**) was assayed by Zhai's method (1999)[186] using a pre-established culture of *Leishmania.* Triple-N media slants overlayed with 199 media were used for leishmanial growth.

NNN medium was prepared by mixing 4g of agar in 100 ml of distilled water. The mixture was then dissolved and sterilizied by autoclaving at 121 ºC and then allowed to cool to 55 ºC. 15-20 ml of defibrinated sheep blood was aseptically added to the mixture with gentle rolling with glass beads, 1 ampoule of gentamicin was mixed in

blood and mixed with agar mixture. Slopes of culture medium were prepared by dispensing 2-3 ml of the blood agar mixture into sterile tubes that were then set in a slant position until the agar completely solidified

To prepare 199 medium different constituents were mixed in 1000 ml of distilled water. pH was adjusted at 7.4 and medium was filtered, sterilized and kept in 37 ºC for 24 hours to check sterility. Pre-established culture of *Leishmania tropica* KWH23 were inoculated in 199 medium in Triple-N medium slants, incubated at 24 ºC for 6-7 days.

In vitro cultivation of parasite plays an important role in the study and treatment of disease. Traditionally, medium available do not meet the requirement for the bulk cultivation of *Leishmania* parasites, so it requires foetal bovine serum (FBS).

Parasites from the log phase were centrifuged at 3000 rpm for 3 minutes. Supernatant was discarded and pellet was washed with 3 × phosphate buffer and centrifuged. Parasites were diluted in fresh medium. To count number of parasite/ml, 200 µl of trypan blue and 20 µl of formaldehyde was added to 200 µl of parasite solution and mixed well. About 20 µl was taken from this mixture and parasites were counted under neubar counting chamber. After counting, the total number of parasites in 4 big squares, the total number was put in the following formula.

$C=T\times tb \times ¼\times 10^4$

Where

C =Observed count

T = Total number of parasites in 4 big square

Tb = Trypan blue

To attain the final concentration of parasite 2×10^6 cells per ml, dilution factor was calculated by following formula:

d=required count/observed count

Required concentration of parasite was obtained by diluting parasite with fresh medium.

To prepare stock solution of compounds for antilesihmanial assay, 1 mg of each compound was dissolved in 1 ml of DMSO to get the concentration of 1000 µg/ml. This stock solution was further diluted serially. Approximately, 180 µl of 199 medium was added in different wells of 96 well microtiter plates. For each test compound, 20 µl was added in the first well and then serially diluted. To keep the final volume 180 µl, 20 µl was discarded from the last well. About 100 µl of parasite was added in each well and 2 rows were left for positive and negative control. DMSO was taken as negative control and serially diluted in the 199 medium. Amphotericin B was taken as positive control and was also serially diluted in 199 medium. Microtiter plates were incubated in a shaker incubator at 24 ^{o}C for 72 hours. Assay was run in triplicate. After the incubation period, 20 µl was taken from each dilution and put on improved neubar counting chamber and live parasites were counted under microscope. IC_{50} values of compounds possessing antileishmanial activity, was calculated by Prism software.

Criteria for IC_{50} are:

Significant level	=	Inhibition
Non-significant activity	=	0.99
Low activity	=	0.80-0.95
Moderate activity	=	0.70-0.79
Good activity	=	0.60-0.69
Significant activity	=	below 0.56-0.59

4.1.2.1 Results

All the synthesized glycopyranosyl amides (**10a-10e**) and glycopyranosides (**11a-11e**) were tested for their antileishmanial activity using *Leishmania tropica* KWH23 promastigotes for *in vitro* screening. The results are shown in Table 4.7 and Table 4.8. Among the synthesized glycopyranosyl amides, Compounds (**10a**), (**10b**) and **(10d**) showed good activity while the compounds (**10c**) and (**10e**) exhibited low activity.

Table 4.7: % Inhibition of glycopyranosyl amides (**10a-10e**) against *L. tropica* leishmania.

Compound	*L. tropica*
10a	0.65 ± 0.01
10b	0.68 ± 0.09
10c	0.81 ± 0.16
10d	0.68 ± 0.27
10e	0.89 ± 0.11
Standard Drug IC_{50}	(μg/mL± S.D)
Amphotericin B	0.56 ± 0.20

Among the synthesized glycopyranosides (**11a-11e**) compounds (**11c**) and (**11e**) showed good activity, (**11b**) and (**11d**) showed moderate activity. The compound **11a** showed non significant activity.

Table 4.8 % Inhibition of glycopyranosides (**11a-11e**) against *L. tropica* leishmania.

Compound	*L. tropica*
11a	1.35 ± 0.04
11b	0.73 ± 0.12
11c	0.63 ± 0.18
11d	0.77 ± 0.08
11e	0.66 ± 0.18
Standard Drug IC_{50}	(μg/mL± S.D)
Amphotericin B	0.56 ± 0.20

Conclusion

The compounds with halogens substitution at *ortho*, *meta*, and *para* positions particularly when substituted at *para* and *meta* positions showed an excellent inhibitory potential against all the tested fungal and bacterial strains. The deprotected amides (**3a-3l)** were found more active against fungal and bacterial strains as compared to protected amides (**2a-2l)**. The emerging resistance in bacteria, to

currently available antibiotics is a serious threat to patients suffering from various bacterial diseases. There is need for new therapeutics to be evaluated as antibacterial agents. The protected and deprotected amides may serve as lead compounds for further research in drug designing and medicinal chemistry. These compounds may prove to be best candidates against different pathogenic strains of bacteria and fungi.

Compounds **14l** found more active against *Fausarium solani* (93 %), *Helminthosporium sativum* (90 %), and *Aspergillus niger* (89 %) and may be served as lead compounds for further research as useful antifungal agents. Compounds **14g-14i** and **14l** showed (20-18 mm) and 23 mm zone of inhibition against *Enterobecter sp.*, (26-22 mm) and 27 mm zone of inhibition against *Vibrio cholerae,* and (23-18) and 22 mm against *Klebsiella sp.* Compounds **14j, 14k** showed inhibitions only at 12 mg/ml concentrations. Compound **14j** showed 12, 12, 22 mm zone of inhibition against *Enterobecter sp.*, *Vibrio cholerae, Klebsiella sp.,* respectively. Compound **14m** also demonstrated excellent growth inhibition potential 29, 30, 23 mm zone against *Enterobecter.sp, Vibrio cholerae, Klebsiella sp.,* respectively, and serve lead compounds for further research on these compounds in search of better antibacterial agents.

Most of the synthesized glycopyranosyl amides (**10a-10e)** and glycopyranosides (**11a-11e)** showed moderate to good activities against *Leishmania tropica* KWH23 promastigotes. Compounds **10a**, **10b** and **10d** were found more active. Among the glycopyranosides (**11a-11e)**, **11c** and **11e** were found more active as compared to **11a**, **11b** and **11d**. Drug resistance has been reported in various species of *Leishmania* against various antileishmanial drugs like antimonials, amphotericin B, pentamidine and miltifosine etc. In this scenario these synthetic compounds may be further explored for research in medicinal chemistry and drug designing against leishmaniasis. These compounds may prove to be good candidates against leshmaniasis.

4.2 Data for X-ray crystal structures

Data for compound 2g chapter 2

Compound	2g
Identification code	2g
Empirical formula	$C_{30}\ H_{38}\ N_2\ O_{10}$
Formula weight	586.62
Temperature	298(2) K
Wavelength	0.71073 A
Crystal system,	*Orthorhombic*
space group	P212121
Unit cell dimensions	
a	*7.3162(8) A alpha = 90 deg.*
b	8.6520(10) A beta = 90 deg.
c	24.217(3) A gamma = 90 deg.
Volume	1532.9(3) A^3
Z, Calculated density	2, 1.271 Mg/m^3
Absorption coefficient	0.096 mm^{-1}
F(000)	624
Crystal size	0.56 x 0.46 x 0.09 mm
Theta range for data collection	2.50 to 28.30 deg.
Limiting indices	-9<=h<=9, -11<=k<=11, -32<=l<=24
Reflections collected / unique	11098 / 2210 [R(int) = 0.0242]
Completeness to theta	28.30 100.0 %
Max. and min.transmission	0.9914 and 0.9484
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2210 / 0 / 190
Goodness-of-fit on F^2	1.070
Final R indices [I^2sigma(I)]	R1 = 0.0483, wR2 = 0.1245
R indices (all data)	R1 = 0.0609, wR2 = 0.1336
Absolute structure parameter	0(10)
Largest diff. peak and hole	0.187 and -0.136 $e.A^{-3}$

Data for compound 2r chapter 2

Compound	2r
Identification code	2r
Empirical formula	$C_{18}\ H_{25}\ N\ O_5$
Formula weight	335.39
Temperature	298(2) K
Wavelength	0.71073 A
Crystal system,	*Monoclinic*
space group	C2
Unit cell dimensions	
a	*19.8936(9) A alpha = 90 deg.*
b	9.2888(3) A beta = 115.932(2) deg.
c	22.4221(8) A gamma = 90 deg.
Volume	3726.1(2) A^3

Z, Calculated density	8, 1.196 Mg/m^3
Absorption coefficient	0.087 mm^{-1}
F(000)	1440
Crystal size	0.56 x 0.29 x 0.24 mm
Theta range for data collection	1.01 to 25.50 deg.
Limiting indices	-24<=h<=24, -11<=k<=11, -27<=l<=27
Reflections collected / unique	21161 / 3707 [R(int) = 0.1098]
Completeness to theta	25.50 100.0 %
Max. and min.transmission	0.9794 and 0.9530
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3707 / 1 / 434
Goodness-of-fit on F^2	1.050
Final R indices [I^2sigma(I)]	R1 = 0.0548, wR2 = 0.1596
R indices (all data)	R1 = 0.0609, wR2 = 0.1683
Absolute structure parameter	0(10)
Extinction coefficient	0.0025(7)
Largest diff. peak and hole	0.482 and -0.197 $e.A^{-3}$

Data for compound 3i chapter 2

Compound	3i
Identification code	3i
Empirical formula	$C_8 H_{10} N_{0.67} O_{3.33}$
Formula weight	168.83
Temperature	298(2) K
Wavelength	0.71073 A
Crystal system,	*Monoclinic*
space group	P21
Unit cell dimensions	
a	*4.8714(4) A alpha = 90 deg.*
b	9.1134(8) A beta = 97.539(2) deg.
c	14.0967(12) A gamma = 90 deg.
Volume	620.41(9) A^3
Z, Calculated density	3, 1.356 Mg/m^3
Absorption coefficient	0.106 mm^{-1}
F(000)	268
Crystal size	0.56 x 0.26 x 0.23 mm
Theta range for data collection	2.67 to 28.36 deg.
Limiting indices	-6<=h<=6, -12<=k<=12, -18<=l<=18
Reflections collected / unique	8533 / 3098 [R(int) = 0.0230]
Completeness to theta	28.36 99.8 %
Max. and min.transmission	0.9760 and 0.9429
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3098 / 1 / 163
Goodness-of-fit on F^2	1.042
Final R indices [I^2sigma(I)]	R1 = 0.0408, wR2 = 0.1146
R indices (all data)	R1 = 0.0427, wR2 = 0.1174

Absolute structure parameter	1.0(9)
Largest diff. peak and hole	0.206 and -0.229 e.A^{-3}

Data for compound 4e chapter 2

Compound	aa3Br4MePhO4_0m
Colour, habit	colourless lath
Size/mm	0.52×0.13×0.04
Empirical Formula	$C_{15}H_{17}BrO_6$
M	373.20
Crystal system	monoclinic
Space group	$P2_1$
a/Å	5.4765(3)
b/Å	9.1510(5)
c/Å	15.3685(8)
□/°	90.00
□/°	93.221(2)
□/°	90.00
V/$Å^3$	768.98(7)
Z	2
□/mm^{-1}	2.699
T/K	100
$□_{min,max}$	2.59,27.50
Completeness	0.999 to □ = 27.50°
Reflections: total/independent	18512/3512
R_{int}	0.0188
Final *R*1 and *wR*2	0.0204, 0.0503
Largest peak, hole/e$Å^{-3}$	0.589, -0.303
$□_{calc}$/g cm^{-3}	1.612
Flack parameter	-0.007(5)

Data for compound 11c chapter 2

Compound	11c
Identification code	11c
Empirical formula	C_{22} H_{30} O_{15}
Formula weight	534.46
Temperature	273(2) K
Wavelength	0.71073 A
Crystal system,	*Monoclinic*
space group	P21
Unit cell dimensions	
a	*11.2486(7) A alpha = 90 deg.*
b	9.1624(6) A beta = 98.2960(10) deg.
c	13.3010(9) A gamma = 90 deg.
Volume	1356.51(15) A^3
Z, Calculated density	2, 1.308 Mg/m^3
Absorption coefficient	0.112 mm^{-1}
F(000)	564

Crystal size	0.55 x 0.55 x 0.21 mm
Theta range for data collection	2.22 to 28.30 deg.
Limiting indices	-14<=h<=15, -12<=k<=12, -13<=l<=17
Reflections collected / unique	9944 / 3474 [R(int) = 0.0149]
Completeness to theta	28.30 96.8 %
Max. and min.transmission	0.9769 and 0.9410
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3474 / 1 / 334
Goodness-of-fit on F^2	1.038
Final R indices [I^2sigma(I)]	R1 = 0.0471, wR2 = 0.1329
R indices (all data)	R1 = 0.0509, wR2 = 0.1379
Absolute structure parameter	0(10)
Largest diff. peak and hole	0.212 and -0.187 e.A^{-3}

References

1. (a) Jennings, K.; Diamond, D. Enantioselective molecular sensing of aromatic amines using tetra-(*S*)-di-2-naphthylprolinol calix[4]arene, *Analyst*, **2001**, *126*, 1063-1067. (b) Vermeulen, N. P. E.; Koppele, J. M. te. Stereoselective biotransformation: toxicological consequences and implications. In Drug Stereochemistry: Analytical Methods and Pharmacology, 2nd Ed.; Wainer, W. I., Ed.; Marcel Dekker, Inc.: New York, **1993**, 245-280.
2. Friedmann, J. M.; Kimmel, C.A. Birth defects research part A: Clinical and molecular tetratology. *Teratology*, 1**992**, *59*, 120.
3. Wikipedia free encyclopedia (web).
4. Moure, A.; Cruz, J.; Franco, D. Natural antioxidants from residual sources. *Food Chemistry*, **2001**, *72*, 145.
5. Wikipedia free encyclopedia (web).
6. Prasad, K. R.; Anbarasan, P. Stereoselective synthesis of (-)-muricatacin from *L*-(+)-tartaric acid. *Tetrahedron Asym.* **2006**, *71*, 2465.
7. Li, S.; Purdy, W. C. Liquid chromatographic separation of the enantiomers of dinitrophenyl amino acids using a *β*-cyclodextrin-bonded stationary phase. *J. Chromatog*. **1991**, *543*, 105-112.
8. Prasad, K. R.; Chandrakumar, A. Asymmetric synthesis of *α*-methoxyarylacetic acid derivatives. *Tetrahedron Asym*. **2005**, *16*, 1897.
9. Prasad, K. R.; Anbarasan, P. Stereoselective synthesis of (+)-boronolide and (-)-5-epi-boronolide. *Tetrahedron Asym*. **2006**, *17*, 1146.
10. Prasad, K. R.; Anbarasan, P. Chandrakumar, A. Asymmetric synthesis of both enantiomers of a-methyl-a-methoxyphenylacetic acid from *L*-(+)-tartaric acid: formal enantioselective synthesis of insect pheromone (-)-frontalin. *Tetrahedron Asym*. **2006**, *17*, 1979.
11. Berthod, A.; Liu, Y.; Bagwill, C.; Armstrong, D. W. Facile liquid chromatographic enantioresolution of native amino acids and peptides using a teicoplanin chiral stationary phase. *J. Chromatograph*. **1996**, *731*, 123-137.
12. Crosby, J. Synthesis of optically active compounds: A large scale perspective. *Tetrahedron*, **1991**, *47*, 4789.
13. Aboul-Enein, H.; Hefnawy, M. M.; Ehmer, P. B.; Hartmann, R. W. Enantiomeric resolution of some human *aldosterone synthase* CYP 11 B2

inhibitors on derivatized polysaccharide chiral stationary phases. *J. Sep. Sci*. **2003**, *26*, 1455.

14. Bortolini, O.; Fantin, G.; Fogagnolo, Marco. Bile acid derivatives as enantiodifferentiating host molecules in inclusion processes. *Chirality*, **2005**, *17*, 121.
15. Hui, A.; Zhang, J.; Fan, J.; Wong, Z. A new chiral sulfonamide ligand based on tartaric acid: synthesis and application in the enantioselective addition of diethylzinc to aldehydes and ketones. *Tetrahedron Asym*. **2006**, *17*, 2101.
16. Choy, W.; Yang, H. Diels-Alder reactions of .*alpha*.-oxy-*o*-xylylenes. *J. Org. Chem*. **1988**, *53*, 5796.
17. Kundig, E. P.; Leresche, J.; Saudan, L.; Bernardinelli, G. Chiral tricarbonyl(η^6-cyclobutabenzene)chromium complexes. Diastereoselective synthesis and use in asymmetric cycloaddition reactions. *Tetrahedron*, **1996**, *52*, 7363.
18. Xia, D.; Ukaji, Y.; Fujinami, S.; Inomata, K. The first enantioselective Hetero Diel-Alder reaction of nitroso compound utilizing tartaric acid ester as chiral auxiliary. *Chem. Lett*. **2003**, *32*, 582.
19. Buchanan, J.G.; Sable, H. Z. Selective Organic Transformations, Wiley Interscience, New York. **1972**, *2*, 1.
20. Yamada, S.; Mashiko T.; Therashima, S. (Acetylacetonato)[(-)-*N*-alkylephedrinato]dioxomolybdenum, a new class of chiral chelate complexes which catalyze asymmetric epoxidation of allylic alcohol. *J. Am. Chem. Soc*. **1977**, *99*, 1988.
21. Jorgensen, K. A. Transition-metal-catalyzed epoxidations. *Chem. Rev*. **1989**, *89*, 431.
22. McCoy, M.; Reisch, M. S. Northern Lights: Mix of entrepeneurs and government support nurtures Canada's fine chemicals industry. *Chem. Eng. News*. **2001**, *79*, 42.
23. Sharpless, K.B.; Verhoeves, T. R. Metal-Catalyzed, highly selective oxygenations of olefins and acetylenes with tert-butyl hydroperoxide. *Aldrichimica Acta*, **1979**, *12*, 63.
24. Daniel, C.; Foulon, C.; Park, C.; Yous, S.; Bonte, J. P.; Vaccher, C. Enantioseparation of chiral *N*-imidazole derivatives by electrokinetic

chromatography using highly sulfated cyclodextrins: Mechanism of enantioselective recognition. *J. Sep. Sci*. **2005**, *28*, 428.

25. Chen, Z.; Uchiyama, K.; Hobo, T. Interaction between 18-crown-6-tetracarboxylic acid and positional substituents ofenantiomers and simultaneous separation ofpositional enantiomers ofmethyl-*DL*-tryptophans by capillary electrophoresis. *Electrophoresis*, **2001**, *22*, 2136.
26. Demirel, N.; Bulut, Y.; Hosg, H. Enantioselective transport and liquid–liquid extraction of amino acids as their potassium and sodium salts by optically active diaza-18-crown-6 ethers. *Chirality*, **2004**, *16*, 347.
27. Kahle, C.; Holzgrabe, U. Determination of binding constants of cyclodextrin inclusion complexes with amino acids and dipeptides by potentiometric titration. *Chirality*, **2004**, *16*, 509.
28. Ramon, D. J.; Yus, M. First enantioselective addition of dialkylzinc to ketones promoted by titanium (IV) derivatives. *Tetrahedron. Lett*. **1998**, *39*, 1239.
29. Mehta, G.; Kotha, S. Recent chemistry of benzocyclobutenes. *Tetrahedron*, **2001**, *57*, 625.
30. Naumov, P.; Jovanovski, G. An update to the combined vibrational-diffraction experimental and theoretical studies of small biologically important cyclic imides: Reference to saccharin. *Curr. Org. Chem.* **2001**, *5*, 1059.
31. Graul, A.; Castaner, J. "Atorvastatin Calcium" Drugs of the Future, Barcelona, ES *Drugs Future*, **1997**, *22*, 956-968.
32. Patchett, A. A. Excursions in drug discovery. *J. Med. Chem*. **1993**, *36*, 2051-2058.
33. Gasparo, M.; Whitebread, S. *Effect* of *aging* on *regulation* of *brain stem circulation during hypotension. Regul. Pept*. **1995**, *59*, 303-311.
34. Ananthanarayanan, V.S.; Tetreault S.; Saint-Jean, A. Interaction of calcium channel antagonists with calcium: spectroscopic and modeling studies on diltiazem and its Ca^{2+} complex. *J. Med. Chem*. **1993**, *36*, 1324-1332.
35. Yavuz, M.; Yagci, M.; Hans, G. B. Synthesis of poly(tartar amides) as bio-inspired antifreeze additives. *Macromole. Rapid Commun.* **2006**, *27*, 1660.
36. (a) Cupido, T.; Puche, J.; Spengler, J.; Albericio, F. The synthesis of naturally occurring peptides and their analogs. *Curr. Opinion Drug Discov. Develop.* **2007**, *10*, 768. (b) Bode, J. *Curr. Opinion Drug Discov. Develop.* **2006**, *9*, 765.

37. Nicolaou, K.; Boddy, N.; BraaSe S.; Winssinger, N. Chemistry, biology, and medicine of the glycopeptide antibiotics. *Angew. Chem.* Int Ed.; **1999**, *38*, 2096.

38. Kataoka, H.; Katagi, T. Syntheses of macrocycles from *L*-amino acid and their selective transport of amino ester salts through an organic liquid membrane. *Tetrahedron*, **1987**, *43*, 4519.

39. Costero, A. M.; Banuls, M. J.; Aurell, M. J.; Ward, M. D.; Argent, S. Biphenyl macrolactams in anion complexation. Selective naked-eye fluoride recognition. *Tetrahedron*, **2004**, *60*, 9471.

40. Brian, R.; Unai, E.; Troels, S. Synthesis and binding properties of chiral macrocyclic barbiturate receptors: application to nitrile oxide cyclizations. *J. Chem. Soc. Perkin Trans*. **2002**, *1*, 1723.

41. Christopher, A. H.; Duncan, H. P. A binary quinone receptor. *Angew. Chem.* Int Ed.; **1992**, *31*, 792.

42. Kyu, C. S.; Donna, V. E.; Erkang, F.; Andrew, D. H. Hydrogen bonding and molecular recognition: synthetic, complexation, and structural studies on barbiturate binding to an artificial receptor. *J. Am. Chem. Soc*. **1991**, *113*, 7640.

43. Rajakumar, P.; Selvam, S. V.; Shanmugaiah, Mathivanan, M. Synthesis and antibacterial activity of some novel chiral fluorophoric biscyclic macrocycles. *Bioorg. Med. Chem. Lett*. **2007**, *17*, 5270.

44. Rajakumar, P.; Abdul Rasheed, A. M.; Rabia, A. I.; Chamundeeswar, I. D. Synthesis and study of anti-inflammatory activity of some novel cyclophane amides. *Bioorg. Med. Chem. Lett*. **2006**, *16*, 60.

45. Ghose, A. K.; Viswanadhan, V. N.; Wendoloski, J. J. A knowledge-based approach in designing combinatorial or medicinal chemistry libraries for drug discovery. 1. A Qualitative and quantitative characterization of known drug databases. *J. Comb. Chem*. **1999**, *1*, 55-68.

46. Behr, J.; Gourlain, T.; Helimi, A.; Guillerm, G. Design, synthesis and biological evaluation of hetaryl-nucleoside derivatives as inhibitors of chitin synthase. *Bioorg. Med. Chem. Lett*. **2003**, *13*, 1713-1716.

47. Xiea, J.; Thellend, A.; Becker, H.; Vidal-Crosb, A. Synthesis and evaluation of a C-glycosyl nucleoside as an inhibitor of chitin synthase. *Carbohyd. Res*. **2001**, *334* 177-182.

48. Dai, C.; Li, D.; Popovici-Muller, J.; Zhao L.; Girijavallabhan, V. Rosner, K.; Lavey, B.; Rizvi, R.; Shankar, B. B.; Wong, M.; Guo, Z.; Orth, P.; Strickland, C. O.; Jing Sun, J.; Niu, X.; Chen, S.; Kozlowski, J. A.; Lundell, D. J.; Piwinski, J. J.; Shih, N.; Siddiqui, M. A. 2-(2-Aminothiazol-4-yl)pyrrolidine-based tartrate diamides as potent, selective and orally bioavailable TACE inhibitors. *Bioorg. Med. Chem. Lett*. **2011**, *21*, 3172-3176.

49. Behr, J. B.; Gourlain, T.; Helimi, A.; Guillerm, G. Design, synthesis and biological evaluation of hetaryl-nucleoside derivatives as inhibitors of chitin synthase. *Bioorg. Med. Chem. Lett*. **2003**, *13*, 1713-1716.

50. Li, S.; Liao, G.; Xiao, J.; Nie, A.; Wang, L.; Zhong, W.; Zheng, Z. Derivatives of substituted tartaric acid and usage for preparing *beta* secretase inhibitors. *US Patent*, **2012**, no 8, 268, 884 B_2.

51. Kucuk, H.B.; Yusufoglu, A.; Mataraci, E.; Dosler, S. Synthesis and biological activity of new 1,3-dioxolanes as potential antibacterial and antifungal compounds. *Molecules*, **2011**, *16*, 6806-6815.

52. Dahlgren, A.; Branalt, J.; Kvarnstrom, I.; Nilsson, I.; Musilc, D.; Samuelssond, B. Synthesis of potential thrombin inhibitors. Incorporation of tartaric acid templates as P2 proline mimetics. *Bioorg. Med. Chem*. **2002**, *10*, 1567-1580.

53. Ulijn, R. V.; Moore, B. D.; Janssen, A. E. M.; Halling, P. J. A single aqueous reference equilibrium constant for amide synthesis–hydrolysis. *J. Chem. Soc. Perkin Trans*. **2002**, *2*, 1024-1028.

54. (a) Jursic, B. S.; Zdravkovski, Z. A simple preparation of amides from acids and amines by heating of their mixture. *Synth. Commun*. **1993**, *23*, 2761-2770. (b) Beckwith, A. L. J. In The Chemistry of Amides; Zabicky, J., Ed.; Synthesis of Amides; Interscience: London, **1970**, 105-109.

55. Sheehan, J.C.; Cruickshank, P. A. Notes- a convenient synthesis of water-soluble carbodiimides. *J. Org. Chem*. **1961**, *26*, 2525-2528.

56. Sheehan, J. C.; Hess, G. P. A new method of forming peptide bonds. *J. Am. Chem. Soc*. **1955**, *77*, 1067-1068.

57. Vaughan, J. R.; Osato, R. L. The preparation of peptides using mixed carbonic-carboxylic acid anhydrides. *J. Am. Chem. Soc*. **1951**, 5553-5555.

58. Vaughan, J. R. Acylalkylcarbonates as acylating agents for the synthesis of peptides. *J. Am. Chem. Soc*. **1951**, 3547.

59. Kappe, C. O. Controlled microwave heating in modern organic synthesis. *Angew*. *Chem*. Int. Ed. **2004**, *43*, 6250-6284.

60. (a) Perreux, L.; Loupy, A.; Volatron, F. Solvent-free preparation of amides from acids and primary amines under microwave irradiation. *Tetrahedron*, **2002**, *58*, 2155-2162. (b) Vazquez-Tato, M. P. Microwave-mediated synthesis of amides. *Synlett*, **1993**, 506. (c) Marrero-Terrero, A. L.; Loupy, A. synthesis of 2-oxazolines from carboxylic acids and α,α,α-Tris(hydroxymethyl)methylamine under microwaves in solvent-free conditions. *Synlett*, **1996**, 245-246. (d) Seijas, J. A.; Vazquez-Tato, M. P.; Martinez, M. M.; Nunez-Corredoira, G. Direct synthesis of imides from dicarboxylic acids using microwaves. *J. Chem. Res. Synop*. **1999**, *7*, 420-421.

61. Ruault, P.; Pilard, J.-F.; Touaux, B.; Texier-Boullet, F.; Hamelin, J. Rapid generation of amines by microwave irradiation of ureas dispersed on clay. *Synlett*, **1994**, 935-936.

62. (a) Baldwin, B. W.; Hirose, T.; Wang, Z.-H. Improved microwave oven synthesis of amides and imides promoted by imidazole; convenient transport agent preparation. *Chem. Commun*. (Cambridge) **1996**, 23, 2669-2670. (b) Hirose, T.; Baldwin, B. W.; Wang, Z. H. Jpn. Kokai Tokkyo Koho **1998**, 4.

63. Gadhwal, S.; Dutta, M. P.; Boruah, A.; Prajapati, D.; Sandhu, J. S. *Indi*. *J. Chem*. *Sect*. *B*-Organic chemistry including medicinal chemistry. **1998**, *37*, 725-727.

64. Eltsov, A. V.; Martynova, V. P.; Sokolova, N. B.; Dmitrieva, N. M.; Brykov, A. S. Microwave activation of heterocyclization in reactions of carboxylic acid. *Zh. Obshch. Khim*. **1995**, *65*, 511-513.

65. Hajipour, A. R.; Ghasemi, M. A rapid and convenient synthesis of amides from aromatic acids and aliphatic amines in dry media under microwave irradiation. *Indi J. Chem. Sect*. *B*-Organic chemistry including medicinal chemistry. **2001**, *40*, 504-507.

66. Chandrasekhar, S.; Takhi, M.; Uma, G. Solvent free *N*-alkyl and *N*-arylimides preparation from anhydrides catalyzed by $TaCl_5$-silica gel. *Tetrahed. Lett*. **1997**, *38*, 8089-8092.

67. Marquez, H.; Plutin, A.; Rodriguez, Y.; Perez, E.; Loupy, A. Efficient synthesis of 1-(4′-Methylbenzoyl)-3,3-diethylthiourea under microwave irradiation using potassium fluoride on alumina. *Synth. Commun*. **2000**, *30*, 1067-1073.

68. Lis, H.; Sharon, N. Protein glycosylation. Structural and functional aspects. *Eur. J. Biochem*. **1993**, *218*, 1-27, Varki, A. *Glycobiology* **1993**, *3*, 97-130.

69. Garg, H.; Jeanloz, R. W. Synthetic *N*-and *O*-glycosyl derivatives of *L*-asparagine, *L*-serine and *L*-threonine. *Adv. Carbohydr. Chem. Biochem*. **1985,** *43*, 135-201.

70. Paulsen, H.; Peters, S.; Bielfeldt, T. in Glycoproteins (Eds.: J. Montreuil, J. F. G. Vliegenthart, H. Schachter), Elsevier, Amsterdam, **1995**, 87-122.

71. Arsequell, G.; Valencia, G. Recent advances in the synthesis of complex *N*-glycopeptides. *Tetrahedron. Asym*. **1999**, *10*, 3045-3094.

72. Childs, R. A.; Drickamer, K.; Kawasaki, T.; Thiel, S.; Mizouchi, T.; Feizi, T. Neoglycolipids as probes of oligosaccharide recognition by recombinant and natural mannose-binding proteins of the rat and man. *Biochem. J.* **1989,** *262*, 131-138.

73. Y. C. Lee, Biochemistry of carbohydrate-protein interaction. *Faseeb J*. **1992**, *6*, 3193-3200.

74. Wong, S. Y. C.; Guile, R.; Dwek, R. A.; Arsequell, G. Synthetic glycosylation of proteins using *N*-(beta-saccharide) iodoacetamides: Applications in site-specific glycosylation and solid-phase enzymic oligosaccharide synthesis. *Biochem. J.* **1994**, *300*, 843-850.

75. Likhosherstov, L. M.; Novikova, O. S.; Dervitskaja, V. A.; Kochetkov, N. K. A new simple synthesis of amino sugars *β*-D-glycosylamines. *Carbohydr. Res.* **1986,** *46*, C1-C5.

76. Lubineau, A.; Auge, J.; Drouillat, B. Improved synthesis of glycosylamines and a straightforward preparation of *N*-acylglycosylamines as carbohydrate-based detergents**.** *Carbohydr. Res*. **1995**, *266*, 211-219.

77. Meldal, M. in Neoglycoconjugates: Preparation and Applications. (Eds.: Y.C. Lee, R.T. Lee), Glycopeptide synthesis, academic press, inc., San Diego. **1994**, 145-198.

78**.** Nakabayashi, S.; Warren, C. D.; Jeanloz, R. W. The preparation of a partially protected heptasaccharide-asparagine intermediate for glycopeptide synthesis *Carbohydr. Res*. **1988**, *174*, 279-289.

79. McDonald, F. E.; Danishefsky, S. J. A stereoselective route from glycals to asparagine-linked *N*-protected glycopeptides. *J. Org. Chem*. **1992**, *57*, 7001-7002.

80. Marks, G. S.; Neuberger, A. Synthetic studies relating to the carbohydrate-protein linkage in egg albumin. *J. Chem. Soc*. **1961**, 4872-4879.

81. Teshima, T.; Nakajima, K.; Takahashi, M.; Shiba, T. Total synthesis of nephritogenic glycopeptide, nephritogenoside. *Tetrahedron Lett*. **1992**, *33*, 363-366.

82. Thiem, J.; Wiemann, T. Combined chemoenzymatic synthesis of *N*-glycoprotein building blocks. *Angew. Chem*. Int. Ed. Engl. **1990**, *29*, 80-82.

83. Nakabayashi, S.; Warren, C. D.; Jeanloz, R. W. The preparation of a partially protected heptasaccharide-asparagine intermediate for glycopeptide synthesis. *Carbohydr. Res*. **1988**, *174*, 279-289.

84. Mehta, S.; Meldal, M.; Duus, J. O.; Bock, K. *N,N,N,N-(2-Aminoethyl)-1,4,8,11-tetraazacyclotetradecane (TAEC) as a polyammonium receptor for anions.* J. Chem. Soc. Perkin Trans. 1999, 1, 1445-1451.

85. McDonald, F. E.; Danishefsky, S. J. A stereoselective route from glycals to asparagine-linked *N*-protected glycopeptides *J. Org. Chem*. **1992**, *57*, 7001-7002.

86. Bayley, H.; Standering, D. N.; Knowles, J. R. Propane-1,3-dithiol: A selective reagent for the efficient reduction of alkyl and aryl azides to amines. *Tetrahedron Lett*. **1978**, 3633-3634.

87. Garcıa-Lopez, J. J.; Santoyo-Gonzalez, F.; Vargas-Berenguel, A.; Gimenez-Martinez, J. Synthesis of cluster *N*-Glycosides based on a *β*-cyclodextrin core. *J. Chem. Eur. J.* **1999**, *5*, 1775-1784.

88. (a) Scriven, E. F.; Turnbull, K. Azides: their preparation and synthetic uses. *Chem. Rev*. **1988**, *88*, 297-368. (b) Gololobov, Y. G.; Kasukhin, L. F. Recent advances in Staudinger reaction. *Tetrahedron*, **1992**, *48*, 1353-1406.

89. Mizuno, M.; Haneda, K.; Iguchi, R.; Muramoto, I.; Kawakami, T.; Aimoto, S.; Yamamoto, K.; Inazu, T. Synthesis of a glycopeptide containing oligosaccharides: Chemoenzymatic synthesis of Eel calcitonin analogues having natural *N*-Linked Oligosaccharides. *J. Am. Chem. Soc*. **1999**, *121*, 284-290.

90. Inazu, T.; Kobayashi, K. A New Simple Method for the Synthesis of N^{α}-Fmoc- N^{β}-glycosylated-*L*-asparagine derivatives. *Synlett*, **1993**, 869-870.

91. Pritchett, T. J.; Brossmer, R.; Rose, U.; Paulson, J. C. Recognition of monovalent sialosides by influenza virus H3 hemagglutinin. *Virology* **1987**, *100*, 502-506.

92. Gruters, R. A.; Neefjes, J. J.; Tersmette, M.; Tulp, A.; Huisman, G. Interference with HIV-induced syncytium formation and viral infectivity by inhibitors of trimming glucosidase. *Nature*, **1987**, *330*, 74-77.

93. Bock, K.; Breimer, M. E.; Brignole, A. ; Hasson, G. C.; Karlsson, K-A.; Larson, G. Specificity of binding of a strain of uropathogenic *Escherichia coli* to Gal alpha 1----4Gal-containing glycosphingolipids. *J. Biol. Chem*. **1985**, *260*, 8545-8555.

94. Krivan, H. C.; Roberts, D. D.; Ginsburg, V. Many pulmonary pathogenic bacteria bind specifically to the carbohydrate sequence GalNAc *beta* 1-4Gal found in some glycolipids. *Proc. Natl. Acad. Sci*. **1988**, *85*, 6157-6164.

95. Karlsson, K.-A. Differentiation between transmembrane helices and peripheral helices by the deconvolution of circular dichroism spectra of membrane proteins. *Ann. Rev. Biochem.* **1989**, *59*, 309-328.

96. Thieme, J.; Sauerbrei, B. Chemoenzymatische synthesen via sialyloligosacchariden mit immobilisierter sialidase. *Angew. Chem*. 1991, *103*, 1521-1523; *Angew. Chem*. Int. Ed. Engl. **1991**, *30*, 1503-1505.

97. Nilsson, K. G. In Modern Methods in Carbohydrate Synthesis, Khan, S. H.; O'Neil, R. A. Eds, Harwood academic publisher. **1996**.

98. Beyer, T. A.; Sadler, J. E.; Rearick, J. I.; Paulson, J. C. Glycosyltransferases and their use in assessing oligosaccharide structure and structure-function relationships. *Adv. Enzymol*. **1981**, *52*, 23-175.

99. Wong, C.-H. In Modern Methods in Carbohydrate Synthesis, Khan, S. H.; O'Neil, R. A. Eds, Harwood academic Publ GmbH. **1996**, 467.

100. Koenigs, W.; Knorr, E. Koenig-Knorr glycosidation. *Chem. Ber*. **1901**, *34*, 957-981.

101. Wulff, G.; Rohle, G. Results and problem of *O*-glycosides. *Angew. Chem*. **1974**, *86*, 173-187; *Angew. Chem*. Int. Ed. Engl. **1974**, *13*, 157-174.

102. Mukayama, T.; Murai, Y.; Shoda, S. An efficient method for glucosylation of hydroxy compounds using glucopyranosyl fluoride. *Chem. Lett*. **1981**, 431-432.

103. Randall, J. L.; Nicolau, K. C. In Fluorinate carbohydrates: chemical and biological aspects, N. F. Taylor Eds., *A. Chem. Soc* Washington, **1988**.

104. Paulsen, H. *Angew. Chem*. **1982**, *94*, 184-201; *Angew. Chem*. Int. Ed. Engl. **1982**, *21*, 155-182.

105. Schmidt, R. R.; Michel, J. *Angew. Chem*. **1980**, *92*, 763-764; *Angew. Chem*. Int. Ed. Engl. **1980**, *19*, 731-732.

106. Stauch, T. Novel trichloroacetimidates and their reactions. Ph. D. thesis, University of Konstanz, **1995**.

107. Douglas, S. P.; Whitfield, D. M.; Krepinsky, J. Silver trifluoromethanesulfonate(triflate) activation of trichloroacetimidates in glycosylation reactions. *J. Carbohydr. Chem*. **1993**, *12*, 131-136.

108. Schmidt, R. R.; Michel, J. Glycosylimidate, 12 direct synthesis of *O*-*α*-and *O*-*β*-glycosyl imidates. *Liebigs Ann. Chem*. **1984**, 1343-1357.

109. Urban, F. J.; Moore, B. S.; Breitenbach, R. Synthesis of tigogenyl *β*-*O*-cellobioside heptaacetate and glycoside tetraacetate via Schmidt's

trichloroacetimidate method; some new observatons. *Tetrahedron Lett*. **1990**, *31*, 4421-4424.

110. Patil, V. J. A simple access to trichloroacetimidates. *Tetrahedron Lett*. **1996**, *37*, 1481-1484.

111. Schmidt, R. R.; Jung, K.-H. In Trichloroacetimidates in carbohydrates in chemistry and biology, part I: Chemistry of saccharides, Vol 1 (B. Ernst, G. W. Hart, P. Sinay, Eds.) Wiley-VCH, Weinheim, **2000**, 5-59.

112. Nef, J. U. About the zweiwerthige carbon atom. The chemistry of cyanogen and isocyans. *Liebigs Ann. Chem*. **1895**, *287*, 265-359.

113. Lubineau, A.; Carpentier, K. B.; Auge, C. Porcine liver (2 → 3)-α-sialyltransferase: substrate specificity studies and application of the immobilized enzyme to the synthesis of various sialylated oligosaccharide sequences.*Carbohydr. Res*. **1997**, *300*, 161-167.

114. Mayer, T. G.; Schmidt, R. R. Glycosyl imidates, 78.An efficient synthesis of galactinol and isogalacatinol. *Liebigs Ann. /Recl*. **1997**, 859-863.

115. Ishida, H.; Ando, H.; Ito, H.; Ishida, H.; Kiso, M.; Hasegawa, A. Synthetic studies on sialoglycoconjugates 91: Total synthesis of gangliosides GD1C and GT1A. *J. Carbohydr. Chem*. **1997**, *16*, 413-328.

116**.** Kinzy, W.; Schmidt, R. R. Application of the trichloroacetimidate method to the synthesis of glycopeptides of the mucin type containing a *β*-D-Galp-(1→3)-D-GalpNAc unit. *Carbohydr. Res*. **1987**, *164*, 265-276.

117. Depew, K. M.; Zeman, S. M.; Boyer, S. H.; Denhart, D. J.; Ikemoto, N.; Danishefsky, S. J.; Crothers, D. M. *Angew. Chem*. Int. Ed. Engl. **1997**, *35*, 2797-2800.

118. Olson, S. H.; Danishefsky, S. Reductive desilanolation as a route to benzonitriles. An application to a concise synthesis of the aromatic sector of calicheamicin. *Tetrahedron Lett*. **1994**, *35*, 7901-7904.

119. David, R. B.; Morphy, J. R. Solid-phase synthesis of cyclic imides. *J. Comb. Chem*. **1999**, *1*, 151.

120. Yang, C. C.; Merrifield, R. B. .beta.-Phenacyl ester as a temporary protecting group to minimize cyclic imide formation during subsequent treatment of aspartyl peptides with hydrofluoric acid. *J. Org. Chem*. **1976**, *41*, 1032.

121. Ramage, R.; Stewart, A. S. J. Use of tributylphosphine in deprotecting a thiol-protected compound as a disulfide. *J. Chem. Soc. Perkin Trans*. **1993**, *1*, 1947.

122. Diego, G. L.; Natalya, V. L.; Herbert, H.; Javier, G. Efficient microwave-assisted synthesis of bisimides. *Arkivoc*, **2006**, *10*, 7

123. Giguere, R. J.; Bray, T. L.; Duncan, S. M.; Majetich, G. Application of commercial microwave ovens to organic synthesis. *Tetrahedron Lett*. **1986**, *27*, 4945.

124. Mingos, D. M. P.; Whittaker, A. G. Chemistry under Extreme on Non-Classical Conditions;van Eldrik, R.; Hubbard, C. D., Eds.; Wiley: New York, **1997**, 479.

125. Vladimir, O.; Lubor F.; Vladimir, B. On the use of water as a solvent - simple and short one- step synthesis of maleimides. *Arkivok*, **2001**, *5*, 60.

126. Filho, V. C.; Pinheiro, T.; Nunes, R. J. Antibacterial activity of *N*-phenylmaleimides, *N*-phenylsuccinimides and related compounds. Structure-activity relationships. *Farmaco*, **1994**, *49*, 675.

127. Corrie, J. E. T. Thiol-reactive fluorescent probes for protein labelling. *J. Chem. Soc. Perkin Trans*. **1994**, *1*, 2975.

128. Janda, K. D.; Ashley, J. A.; Jones, T. M.; McLeod, D. A.; Schloeder, D. M.; Weinhouse, M. I. Immobilized catalytic antibodies in aqueous and organic solvents. *J. Am. Chem. Soc*. **1990**, *112*, 8886.

129. Rich, D. H.; Jasensky, R. D.; Mueller, G. C.; Anderson, K. E. Analogs of the cytostatic cyclic tetrapeptide chlamydocin. Synthesis of *N*.beta.-(*N*-maleoylglycyl) and *N*.beta.-(*tert-butyloxycarbonyl*) derivatives of *cyclo(Gly-L-Phe-D-Pro-L-Dap). J. Med. Chem*. **1981**, *24*, 567.

130. Corrie, J. E. T.; Trentham, D. R. *J. Chem. Soc. Perkin Trans*. **1995**, *1*,1993.

131. Matocsy, G.; Nadasi, M.; Adriska, V. In Pesticide Chemistry, Akademiai Kiado: Budapest, **1988**.

132. Baldwin, S. P.; Greenspan, P.; Alaimo, C.; McPhail, A. T. Diastereoselective diels-alder reactions between substituted 1,3-butadienes and n-*α*-methylbenzylmaleimide. *Tetrahedron Lett*. **1991**, *32*, 5877.

133. Philp, D.; Booth, C. A. Efficient recognition-induced acceleration of a [3+2] dipolar cycloaddition reaction. *Tetrahedron Lett*. **1998**, *39*, 6987.

134. The Merck index, An Encyclopedia of Chemicals, Drugs and Biologicals; S. Budavari, Ed.; Ed. MERCK & CO., Inc. Rahway: New Jersey, **1989**, 1399.

135. Malamas, M.S.; Hohman, T.C.; Millen, J. Novel spirosuccinimide *Aldose Reductase* inhibitors derived from isoquinoline-1,3-diones: 2-[(4-Bromo-2-fluorophenyl)methyl]-6-fluorospiro[isoquinoline-4(*11H*),3'-pyrrolidine]-1,2',3,5'(*2H*)-tetrone and congeners. *J. Med. Chem*. **1994**, *37*, 2043.

136. Toupet, L.; Biard, J.-F.; Verbist, J.-F. Dichlorolissoclimide from lissoclinum voeltzkowi Michaelson (Urochordata): Crystal structure and absolute stereochemistry. *J. Nat. Prod.* **1996**, *59*, 1203.

137. Argay, Gy; Seres, J. Structural crystallography and crystal chemistry. *Acta Crystallogr*. **1973**, *B29*, 1146.

138. (a) Kwiatkowski, W.; Karolak-Wojciehowska, J.; Obniska, J.; Zejc, A. *Acta Crystallogr*. **1990**, *C46*, 108. (b) Kwiatkowski, W.; Karolak-Wojciehowska, J. *Acta Crystallogr*. **1992**, *C48*, 206.

139. Taira, Z.; Takayama, C.; Terada, H. Molecular and crystal structures of *N*-phenylsuccinimides, and their fungicidal activities. *J. Chem. Soc. Perkin Trans*. **1988**, 1439.

140. Harris, A. L. Gender effects in pharmacokinetics and pharmacodynamics. *Drugs of Today*, **1984**, *20*, 167.

141. Dowsett, M.; Lee, K.; Macaulay, V.M.; Detre, S.; Rowlands, M.; Grimshaw, R. The control and biological importance of intratumoural aromatase in breast cancer. *J. Steroid Biochem. Mol. Biol*. **1996**, *56*, 145.

142. Orzeszho, A.; Gralewska, R.; Sharoseiak, B. J.; Kazimierczuk, Z. Synthesis and antimicrobial activity of new adamantane derivatives. *Acta Biochemica Polonica*. **2000**, *47*, 87.

143. Frederic, Z.; Alain, V.; Guillou, R. L.; Roger, L.; Mathot , A.G.; Danielle, S. Synthesis and antimicrobial activities of *N*-substituted imides. *Farmaco,* **2002**, *57*,421.

144. (a) Gawronski, J.; Gawronska, K. Tartaric and Malic Acids in Synthesis-A Source Book of Building Blocks, Ligands, Auxiliaries, and Resolving Agents; J. Wiley and Sons: New York, **1999**. (b) Coppola, G. M.; Schuster, H. F. R-

Hydroxy Acids in Enantioselective Synthesis; Wiley-VCH: Weinheim, **1997**. (c) Ghosh, A. K.; Koltun, E. S.; Bilcer, G. Tartaric acid and tartrates in the synthesis of bioactive molecules. *Synthesis*, **2001**, 1281.

145. (a) Greene, T. W.; Wuts, P. G. M. Protective Groups in Organic Synthesis, 2nd ed.; John Wiley & Sons: New York, NY, USA, **1991**, 129-133.
146. Kociensky, P. J. Protecting Groups; Georg Thieme Verlag: New York, NY, USA, **1994**.
147. Gemal, A. L.; Luche, J.-L. Lanthanoids in Organic Synthesis. 4. Selective ketalization and Reduction of Carbonyl Groups. *J. Org. Chem*. **1979**, *44*, 4187-4189.
148. Musich, J. A.; Rapoport, H. Synthesis of anthopleurine, the alarm pheromone from Anthopleura elegantissima. *J. Am. Chem. Soc*. **1978**, *100*, 4865-4872.
149. Kozikowski, A. P.; Ognyanov, V. I.; Fauq, A. H.; Nahorski, S. R.; Wilcox, R. A. Synthesis of l*D*-3-deoxy-, 1*D*-2,3-dideoxy-and 1d-2,3,6-Trideoxy-myo-inositol, l,4 ,5-trisphosphate from quebrachitol, their binding affinities, and calcium release activity. *J. Am. Chem. Soc*. **1993**, *115*, 4429-4434.
150. Valeur, E.; Bradley, M. Amide bond formation: beyond the myth of coupling reagents. *Chem. Soc. Rev*. **2009**, *38*, 606-631.
151. Cysewski, R.; Kwit, M.; Warzajtis, B.; Rychlewska, U.; Gawronski, J. Synthesis, conformation and chiroptical properties of diaryl esters of tartaric acid. *J. Org. Chem.* **2009**, *74*, 4573-4583.
152. Kintner, R. R. In: S. Patai (Ed.), the Chemistry of the Carbonyl Group, Interscience, New York, **1996**, 749.
153. Davenport, K. G. EP 251 552 **1988**, to Celanese Corp. USA.
154. Hocking, M. B.; 2-Hydroxyacetophenone via fries rearrangement and related reactions: A comparative applied study. *J. Chem. Technol. Biotechnol*. **1980**, *30*, 626.
155. Ramesh, B. B. IN 171 970, **1993**, Shasun Chemicals (m) Ltd. India.
156. Boyer, J. L. Synthetic utility and mechanistic implications of the Fries rearrangement of hydroquinone diesters in boron trifluoride complexes. *J. Org. Chem*. **2000**, *65*, 4712.
157. Martin, R. Fries rearrangement. *Org. Prep. Proc. Int*. **1992**, *24*, 369.
158. (a) Kamoda, S.; Nakano, M.; Ishikawa, R.; Suzuki S.; Kakehi, K. Rapid and sensitive screening of *N*-glycans as 9-fluorenylmethyl derivatives by high-

performance liquid chromatography: A method which can recover free oligosaccharides after analysis. *J. Proteome Res*. **2005**, *4*, 146-152. (b) Manger, I. D.; Rademacher T. W.; Dwek, R. A. 1-*N*-Glycyl .*beta*.-oligosaccharide derivatives as stable intermediates for the formation of glycoconjugate probes. *Biochemistry*, **1992**, *31*, 10724-10732.

159. Garegg, P. Saccharides of biological importance: challenges and opportunities for organic synthesis. *J. Acc. Chem. Res*. **1992**, *25*, 575-580.
160. Hofle, G.; Steglich, W.; Vorbruggen, H. *Angew. Chem*. Int. Ed. Engl. **1978**, *17*, 569-583.
161. Scriven, E. F. V. 4-Dialkylaminopyridines: super acylation and alkylation catalysts. *Chem. Soc. Rev*. **1983**, *12*, 129-161.
162. Hudson, C. S.; Dale, J. K. A comparison of the optical rotatory powers of the *alpha* and *beta* forms of certain acetylated derivatives of glucose. *J. Am. Chem. Soc*. **1915**, *37*, 1264-1270.
163. Yu, B.; Xie, J.; Deng, S.; Hui, Y. First synthesis of a bidesmosidic triterpene saponin by a highly efficient procedure. *J. Am. Chem. Soc*. **1999**, *121*, 12196-12197.
164. Berthold, H. J.; Franke, S.; Thiem, J.; Schotten, T. Ex post glycoconjugation of phthalocyanines. *J. Org. Chem*. **2010**, *75*, 3859-3862.
165. Sureshbabu, V. V.; Venkataramanarao, Rao.; Hemantha, H. P. A facile synthesis of c-terminal neoglycopeptides: incorporation of urea moiety between sugars and peptides employing curtius rearrangement. *Int. J. Pept. Res. Therap*. **2008**, *14*, 34-40.
166. Paulsen, H.; Pflughaupt, K. W. Glycosylamines. In The Carbohydrates Chemistry and Biochemistry; Pigman, W.; Horton, D. Eds.; Academic: New York, **1980**, 881-927.
167. Kovacs, L.; Osz, E.; Domokos, V.; Holzer, W.; Gyorgydeak, Z. An easy access to anomeric glycosyl amides and imines (Schiff bases) via transformation of glycopyranosyl trimethylphosphinimides. *Tetrahedron*, **2001**, *57*, 4609-4621.
168. Gyorgydeak, Z.; Hadady, Z.; Felfoldi, N.; Krakomperger, A.; Nagy, V.; Toth, M.; Brunyanszki, A.; Docsa, T.; Gergelyb, P.; Somsaka, L. Synthesis of *N*-(*β*-D-glucopyranosyl) and *N*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl) amides

as inhibitors of glycogen phosphorylase. *Bioorg. Med. Chem*. **2004**, *12*, 4861-4870.

169. Ren, T.; Liue, D. Synthesis of targetable cationic amphiphiles. *Tetrahedron lett*. **1999**, *40*, 7621-7625.

170. (a) Schmidt, R. R. *Angew Chem*. Int. Ed. Engl. **1986**, *25*, 212, (b) Excoffier, G.; Gagnaire, D.; Utille, J. P. *Carbohydr. Res*. **1975**, *39*, 368.

171. Shriner, R. L.; Furrow, C. L. Org. Synth. Coll. **1955**, *4*, 49. (b) Shriner, R. L.; Furrow, C. L. Org. Synth. Coll. **1963**, *4*, 242.

172. Naz, S.; Zaidi, J. H.; Mehmood, T.; Wali, S.; Ali, M.; Taha, M.; Khan, K. M. Synthesis of imides and amides from diacetyl-*L*-tartaric acid anhydride. *lett. Org. Chem*. **2010**, *7*, 319-322.

173. Vogel's Textbook of Practical Organic Chemistry, 4th Ed., ELBS Edition, William Clowes Limited, Beccles and London, **1996**, 1131.

174. Siemens. SMART and SAINT. Siemens Analytical X-Ray Instruments Inc., Madison, Wisconsin, USA, **1996**.

175. Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A. *J. Appl. Crystallogr*. **1993**, *26*, 343

176. Sheldrick GM: SHELXTL-PC (Version 5.1), Siemens Analytical Instruments, Inc., Madison, WI, **1997**.

177. Jhnson CK: 'ORTEPII', Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA. **1976**.

178. Ilmarinen, K.; Kriis, K.; Paju, A.; Pehk, T.; Margus Lopp, M. Synthesis of new *N*-tetrasubstituted derivatives of *R,R*-tartaric acid and their use as chiral ligands in oxidation catalysts. *Proc. Estonian Acad. Sci. Chem*. **2001**, *50*, 147-155.

179. Dahlgren, A.; Branalt, J.; Kvarnstrom, I.; Nilsson, I.; Musil, D.; Samuelsson B. Synthesis of potential thrombin inhibitors. Incorporation of tartaric acid templates as P2 proline mimetics. *Bioorg. Med. Chem.* **2002**, *10*, 1567-1580.

180. Jarrahpour, A. A.; Shekarriz, M.; Taslimi, A. Synthesis and antimicrobial activity of some new sugar-based monocyclic *β*-lactams. *Molecules*, **2004**, *9*, 29-38.

181. Slamova, K.; Marhol, P.; Bezouska, K.; Kren, V.; Lindkvist, L.; Hansen, S. G.; Jensen, H. H. Synthesis and biological activity of glycosyl-1*H*-1,2,3-triazoles. *Bioorg. Med. Chem. Lett*. **2010**, *20*, 4263.

182. Macmillan, D.; Daines, A. M.; Bayrhuber, M.; Flitsch, S. L. Solid-phase synthesis of thioether-linked glycopeptide mimics for application to glycoprotein semisynthesis. *Org. Lett*. **2002**, *4*, 1467.

183. Cheng, H.; Cao, X.; Xian, M.; Fang, L.; Cai, T. B.; Ji, J. J.; Tunac, J. B.; Sun, D.; Wang, P. G. Synthesis and enzyme-specific activation of carbohydrate-geldanamycin conjugates with potent anticancer activity. *J. Med. Chem*. **2005**, *48*, 645-652.

184. Washington, J. A. H.; Sutter, V. L. **1980**, 453-458; In E. H. Lennette.; Balows, A.; Hausler, W. J.; Truant, J. P. (ed.), Manual of clinical microbiology, 3rd ed. American Society for Microbiology, Washington, D. C.

185. Koneman, E. Diagnostic microbiology. Vogel's Textbook of Practical Organic Chemistry, 4th Ed., ELBS Edition, William Clowes Limited, Beccles and London, **1996**, 1131.

186. Zhai, L.; Chen, M.; Blom, J.; Theander, T. G.; Christensen, S. B.; Kharazmi, A. The antileishmanial activity of novel oxygenated chalcones and their mechanism of action. *J. Antimicro. Chemother*. **1999**, *43*, 793-803.