Dedicated to my loving parents...

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It is certified that the work contained in the thesis titled **"Synthesis of Uronic Acid Building Blocks and Their Application in Oligosaccharide Synthesis"** by **Ms. Varsha Tiwari** has been carried out under my supervision and that this work has not been submitted elsewhere for a degree.

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DECLARATION BY THE CANDIDATE

I, ***Ms. Varsha Tiwari***, certify that the work embodied in this thesis is my own bonafide work and carried out by me under the supervision of "***Dr. Jeyakumar Kandasamy***" from "***July-2016***" to "***May-2022***," at the ***Department of Chemistry***, ***Indian Institute of Technology (BHU), Varanasi***. The matter embodied in this thesis has not been submitted for the award of any other degree/diploma. I declare that I have faithfully acknowledged and given credits to the research workers wherever their works have been cited in my work in this thesis. I further declare that I have not willfully copied any other's work, paragraphs, text, data, results, etc., reported in journals, books, magazines, reports dissertations, theses, etc., or available at websites and have not included them in this thesis and have not cited as my own work.

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It is certified that the above statement made by the student is correct to the best of ~~my~~/our knowledge.

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Date: 05/05/2022

05/05/2022

(Ms. Varsha Tiwari)

Research Scholar

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LIST OF NOTATION, SYMBOLS ANDABBREVIATIONS

Notations	Abbreviations
%	Percentage
<	Less than
>	More than
°	Degree
°C	Degree Celsius
©	Copyright
Å	Angstrom
Ac	Acetyl group
Ac_2O	Acetic anhydride
AIBN	Azobisisobutyronitrile
AcOH	Acetic acid
Aq.	Aqueous
atm.	Atmosphere
Bn	Benzyl
Bz	Benzoyl group
BAIB	Bis acetoxy iodobenzene
Calc.	Calculated
calcd	Calculated
$CHCl_3$	Chloroform
cm	Centimeter
$CDCl_3$	Deuterated Chloroform
CD_3OD	Methanol-d_4
c	Concentration
cc	Column chromatography
CSA	Camphorsulfonic acid
D_2O	Deuterated water
DCE	1,2-Dichloroethane
DMAP	4-Dimethylaminopyridine
DMF	Dimethylformamide
DMSO	Deuterated dimethyl sulfoxide- d_6
DCM	Dichloromethane
d	Doublet
dd	Doublet of doublet
ddd	Doublet of doublet of doublet
ddt	Doublet of doublet of triplet
dq	dq

dt	Doublet of triplet
DNA	Deoxyribonucleic acid
DABCO	1,4-Diazabicyclo[2.2.2]octane
EDG	Electron donating group
EWG	Electron withdrawing group
equiv.	Equivalent
EtOH	Ethanol
EtOAc	Ethyl acetate
Et_3N	Triethylamine
ESI	Electrospray ionization
g	Gram; Gravitational force
GC-MS	Gas Chromatography Mass Spectrometry
h	Hour
HRMS	High Resolution Mass Spectrometry
Hz	Hertz
i-Pr	*Iso*-propyl
IR	Infra Red
J	Coupling constant
KI	Potassium iodide
KOH	Potassium hydroxide
LG	Leaving group
lit.	Literature
m	Multiplet
m/z	Mass to charge ratio
MeOH	Methanol
mg	Milligram
MHz	Megahertz
min	Minute
mL	Milliliter
mm	Millimeter
mmol	Milli Mole
µm	Micrometer
µL	Microliter
m.p.	Melting Point
MS	Molecular sieve
MeOD	Dutereted methanol
nm	Nanometer
NaCl	Sodium chloride
NMR	Nuclear Magnetic Resonance
n-BuLi	*n*-Butyllithium

NMP	N-Methyl-2-pyrrolidone
nr	Not reported
nd	Not determined
NBS	N-Bromosuccinimide
NIS	N-Iodosuccinimide
NCS	N-Chlorosuccinimide
Nap	Naphthyl
Obser.	Observed
Piv	Pivaloyl group
PBB	Para bromo benzyl
PDC	Pyridinium dichromate
PG	Protectin group
pH	Potential of hydrogen
ppm	Parts per million
Py	Pyridine
PTSA	*p*-Toluenesulfonic acid
Pd-C	Palladiun on carbon
Quant.	Quantitative
RT	Room Temperature
RNA	Ribonucleic acid
R*f*	Retardation Factor
s	Singlet
t-Bu	Tertiary butyl
TBN	*tert*-Butyl nitrite
THF	Tetrahydrofuran
TLC	Thin-Layer Chromatography
TMS	Tetramethylsilane
TMEDA	Tetramethylethylenediamine
TBAI	Tetran-n-Butyl Ammonium Iodide
TBAF	Tetran-n-Butyl Ammonium Fluoride
TBAB	Tetran-n-Butyl Ammonium Bromide
TBS	*tert*-Butyldimethylsilyl
TBDMS	*tert*-Butyldimethylsilyl
TBDPS	*tert*-Butyldiphenylsilyl
TEMPO	(2,2,6,6-Tetramethylpiperidin-1-yl)oxyl
TFA	Trifluoroacetic acid
TfOH	Trifluoromethanesulfonic acid
t	Triplet
TMSOTf	Trimethylsilyl trifluoromethanesulfonate
TsCl	4-Toluenesulfonyl chloride

UV	Ultraviolet
XRD	X-ray diffraction
α	Alpha
β	Beta
δ	Chemical shift
δ	Delta
[ox]	Oxidation
[α]	Specific rotation
i.e.	that is
o	Ortho
m	Meta
p	Para

GENERAL EXPERIMENTAL CONSIDERATIONS

All the reactions were carried out in oven dried glass wares. Starting materials were prepared using modified literature procedures and modified procedures as described in the experimental sections. Solvents, chemicals were purchased from commercial sources (Aldrich, Alfa Aesar, SD fine and Avra) and used without further purifications, unless otherwise stated. **Melting points** of products were measured with Staurt SMP10 melting point apparatus using in open capillary tubes. **FT-IR** for the products were recorded on ALPHA BRUKER Eco-ATR fitted out on ZnSe ATR crystal in the range of 500-3000 cm^{-1}. **^{1}H NMR and ^{13}C NMR** spectra were recorded on Bruker Avance 500 MHz NMR spectrometer using deuterated solvents. Chemical shifts are given in ppm, using tetramethylsilane (TMS) as an internal standard. **Mass spectra (HRMS)** were measured on water's Quattro Micro V 4.1. **Optical rotation** was measured using JASCO-2000 polarimeter. **Thin layer chromatography (TLC)** was performed using pre-coated plates obtained from E. Merck (TLC silica gel 60 F254). The TLCs were visualized in UV Chamber with 254 nm wavelength lamp, then further analyzed by charring in stain solution (5% H_2SO_4 in MeOH) and also sometimes in iodine chamber. **Column chromatography** was performed on silica gel (60-120 or 100-200 mesh) using different eluents. Optical rotation for all compounds has been performed using Jasco P-2000 polarimeter. **IR spectra** of the new compounds have been recorded using PerkinElmer instrument. The details of other fine chemicals, reaction conditions, substrate preparation etc. are given in respective chapters.

PREFACE

Uronic acids are found in nature as complex polysaccharides which show various biological activities. These are main constituents of glycosaminoglycans (GAGs) such as heparin sulphate, dermatan sulphate, chondroitin sulphate and hyaluronan which are highly significant in medicinal chemistry. Recently, there has been tremendous interest towards the development and synthesis of sugar-based drugs, vaccines, cosmetics, etc. due to their structural diversity and compatibility with living systems.

In this context, the thesis entitled "**Synthesis of Uronic Acid Building Blocks and Their Application in Oligosaccharide Synthesis**" will introduce methods for synthesis of uronic acids and their utility in glycosylation and oligosaccharide synthesis. **Chapter 1** will give a general introduction to uronic acids and briefly discusses the structure and functions of some vital polysaccharides containing uronic acids. It will also accumulate few strategies for the synthesis of uronic acid containing oligosaccharides. **Chapter 2** will include the synthesis of various orthogonally protected uronic acids using TEMPO and iodine (III) reagent at room temperature. **Chapter 3** will describe the synthesis of uronic esters using H_2SO_4-SiO_2 at room temperature. **Chapter 4** will highlight the use of photolabile protecting group in the protection of uronic acids and their efficient and selective deprotection under UV light (355nm) with the assistance of continuous flow photoreactor. **Chapter 5** will present the synthesis of photolabile group protected anomeric acetals and their selective photo deprotection to obtain corresponding hemiacetals in high yields. Finally, **Chapter 6** will summarize and conclude the total thesis work.