Improved Synthesis of 2, 3-Diacetamidouronates Which are Present in Bacterial Envelope

DISSERTATION

zur

Erlangung des akademischen Grades

doctor rerum naturalium (Dr. rer. nat.)

der Mathematisch-Naturwissenschaftlichen Fakultät

der Universität Rostock

vorgelegt von

Jaya Shanmuga Prakash Jegannathan

geb. am 02.09.1982 in Tamil Nadu, India

Rostock, Juni 2013

urn:nbn:de:gbv:28-diss2014-0005-4

Dekan: Prof. Dr. Martin Köckerling

Gutachter der Dissertation:

1. Prof. Dr. Christian Vogel (Universität-Rostock)
2. Prof. Dr. Till Opatz (Universität-Mainz)

Termin des wissenschaftlichen Kolloqiums mit Prüfungscharakter: 29.10.2013

Dedicated to my professor, Prof. Christian Vogel.

Preface

The presented work in this dissertation was carried out from Feb 2009 till Sep 2012 at the Institute of Chemistry at the University of Rostock.

I would like to thank my supervisor Prof. Dr. *Christian Vogel*, for everything that he has given me. The thesis work was possible only because of his help and support during all the problems, both scientific and personal. I feel extremely fortunate to have come across a person of his stature in my life.

I thank my dearest lab mates, who have been great to be with everyday. First of all, I would like to thank Alice for her unconditional support and care for all the people in the lab. I am fortunate to get her personal help during the initial period of my work in the lab. I thank my other colleagues and best of friends, Sabine, Hamik, Dilver, Eugenio, Andreas, Inga, Melanie, Kathaleen and Jule. My special thanks to Inga, for the effort she took in submitting my thesis. I also thank other peoples who have worked in the lab for a short term, but have left a lasting friendship.

I thank Prof. Dr. M. Köckerling for his friendly support and help in submission of the thesis. I thank Prof. Dr. P.Langer for referring me to Prof.Dr. Christian Vogel for the Ph.D position.

I thank all the colleagues in the analytical department for their excellent analysis and cooperation. With great respect and gratitude, I thank Dr. Dirk Michalik for NMR measurements and Dr. Alexander Villinger for X-ray studies. I thank Dr. C.Fischer for MS analysis. I thank all the technical staffs of the department, particularly, Ms. I.Schicht, Ms.B.Goronzi and Ms. Pries.

I would like to thank all the office staff of the department of chemistry, Ms. Jacob, Ms. Mohn, Ms. Kahmann and all the others who were extremely helpful and caring. I would like to thank all the other workers in the department, in the glassware section, waste treatment section, mechanical engineering section, etc., who were always willing to help. I would like to thank all the other staffs of the university of Rostock, who have helped me in the time of need.

I would like to thank my Indian friends, for the love and affection they showed on me during my complete stay in Rostock. With out them, it would not be possible for me to stay outside my country for such a long time. I am sure a page would not be enough to write about them.

I thank god, for making me to meet all the wonderful people who come across during the last few years in Rostock, Germany.

Last but not least, I thank all my family members and friends back home in India.

Table of Contents

Abbreviations

AA	acetic acid
abs.	absolute
Ac	acetyl
ACN	acetonitrile
Ac_2O	acetic anhydride
All	allyl
aq	aqueous
BAIB	bis(acetoxy)iodobenzene
Bz	benzoyl
Bn	benzyl
BnOH	benzyl alcohol
br.	broad
calcd	calculated
COSY	correlated spectroscopy
dd	doublet of doublets
ddd	doublet of doublet of doublets
dddd	doublet of doublet of doublet of doublets
DBAD	di-t-butyl azodicarboxylate
DCM	dichloromethane
DEAD	diethyl azodicarboxylate
DIAD	diisopropyl azodicarboxylate
dec.	decomposition
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
dq	doublet of quartets
dt	doublet of triplets
Et	ethyl
EtOH	ethanol
EtOAc	ethyl acetate
Fig.	figure
HRMS	high-resolution mass spectroscopy
HSQC	heteronuclear single quantum coherence
Hz	hertz

lit.	literature
m	multiplet
Me	methyl
MeOH	methanol
MHz	megahertz
mp	melting point
MS	mass spectroscopy
m/z	mass to charge ratio
NMR	nuclear magnetic resonance
NOESY	nuclear overhauser effect spectroscopy
PE	petroleum ether
pH	*pondus hydrogenii*
Ph	phenyl
q	quartet
ref.	referenced
R_f	retention factor
r.t.	room temperature
s	singlet
Sec	section
soln	solution
t	triplet
TBAHS	tetrabutylammonium hydrogen sulfate
TCC	trichlorocyanuric acid
TEMPO	2,2,6,6-tetramethylpiperidine-1-oxyl
TFA	trifluoroacetic acid
Tf_2O	trifluoromethanesulfonic anhydride
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
TLC	thin layer chromatography
Tol	toluene,
Trt	trityl
XRD	X-ray diffraction
[α]	optical rotation
δ	chemical shift

1. Introduction

The antibiotic resistance evoked by harmful bacterial strains, have seen a firm upsurge over a period of time even since the introduction of penicillin by Alexander Fleming in 1940.[1-5] The immunity of the microorganism towards host antigens and external antibiotics is facilitated by the strength of the bacterial envelope.[6-9] (Fig.1). The bacterial envelope of gram negative bacteria consists of Lipopolysaccharides which gives stability and antibiotic resistance to the bacterium. [10-12]. To circumvent the increased drug resistance of the bacteria the structural components of lipopolysaccharides are used in drugs (glycoconjucate vaccines). So the isolation, structural elucidation and synthesis of these potential drug candidates are the area of prime focus in the chemistry and biochemistry of carbohydrates.[14-20]

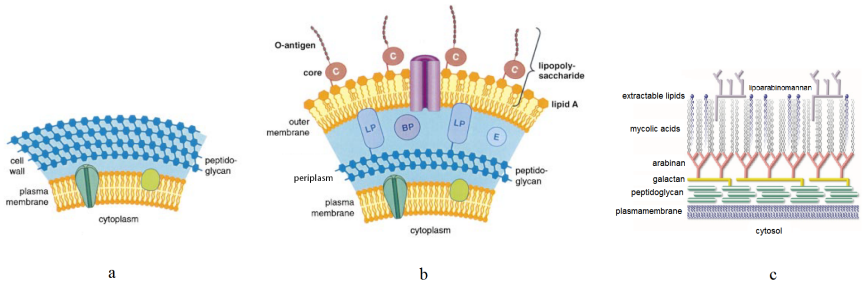


Figure 1. Bacterial envelope (**a**) Gram positive (**b**) Gram negative[21] (**c**) Mycobacteria

Lipopolysaccharides are present exclusively in the cell wall of Gram negative bacteria. (Fig. 1 shows the bacterial envelope of three major types of bacteria) It consists of Lipid A and layers of polysaccharides. Lipid A is composed of β-linked glucosamine disaccharides that are substituted with long chain fatty acids and phosphate groups.[22] The polysaccharides consists of core regions (inner and outer core containing various sugar residues) and O-chain or O-polysaccharide (See Fig 2). The outer most part of Lipopolysaccharides is the O-chain or O-polysaccharide which is also called as O-antigen due to its vulnerability to attack from host antibodies and external antibiotics.[23] Due to its proximity to hostile surroundings, the O-antigens evolve with limitless diversity in structure, composition and linkage of the constituent glycosyl residues. There are over 160 different strains of O-antigen structures produced by E.coli.[24] The surface of some bacterial envelope is associated with an S-layer (Surface layer) compromising of glycoprotein. The S-layers are associated to the lipopolysaccharides via ionic, carbohydrate–carbohydrate, protein–carbohydrate interactions and/or protein–protein interactions. These functional characteristics make the lipopolysaccharides as a lethal component of gram negative bacteria.

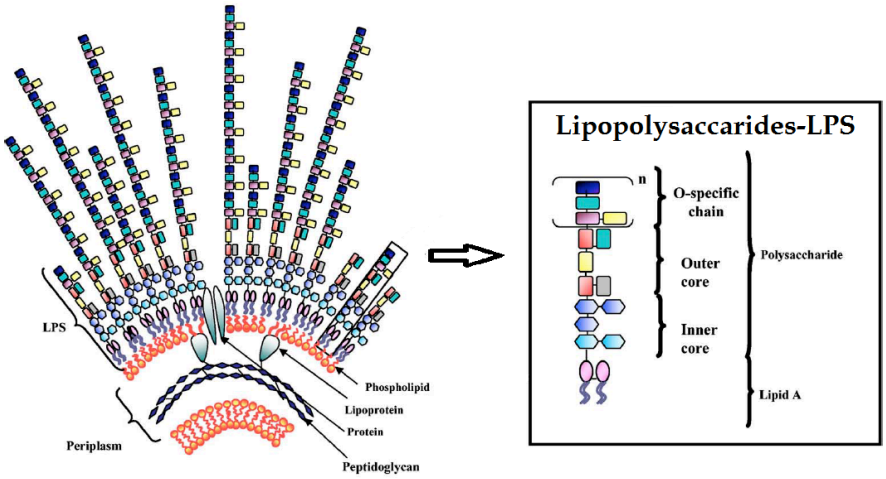


Figure 2. Lipopolysaccharides in bacterial cell wall[25]

Characterisation of highly complex molecules such as Lipopolysaccharides was possible due to various advancements in analytical techniques such as nuclear magnetic resonance (NMR) and mass spectroscopy (MS) methods.[26] The complete structure of LPS in B. pertussis strain 1414 (Fig. 3)[17,28,29] was determined by matrix-assisted laser desorption ionization mass spectrometry (MALDI) while the absolute configuration of the vaccine component in Band A trisaccharide was characterised by NMR NOE experiments. Characterisation of various strains of bacterial lipopolysaccharides has been reported and still many more are done.[30-34] Characterisation of absolute configuration of units present in bacteria such as Pseudomonas aeruginosa,[35,36] Bordetella parapertussis[37] and Bordetella pertussis has shown a presence of general class of 2,3-acetamido uronic acids which has motivated us to attempt a synthetic process for the same.

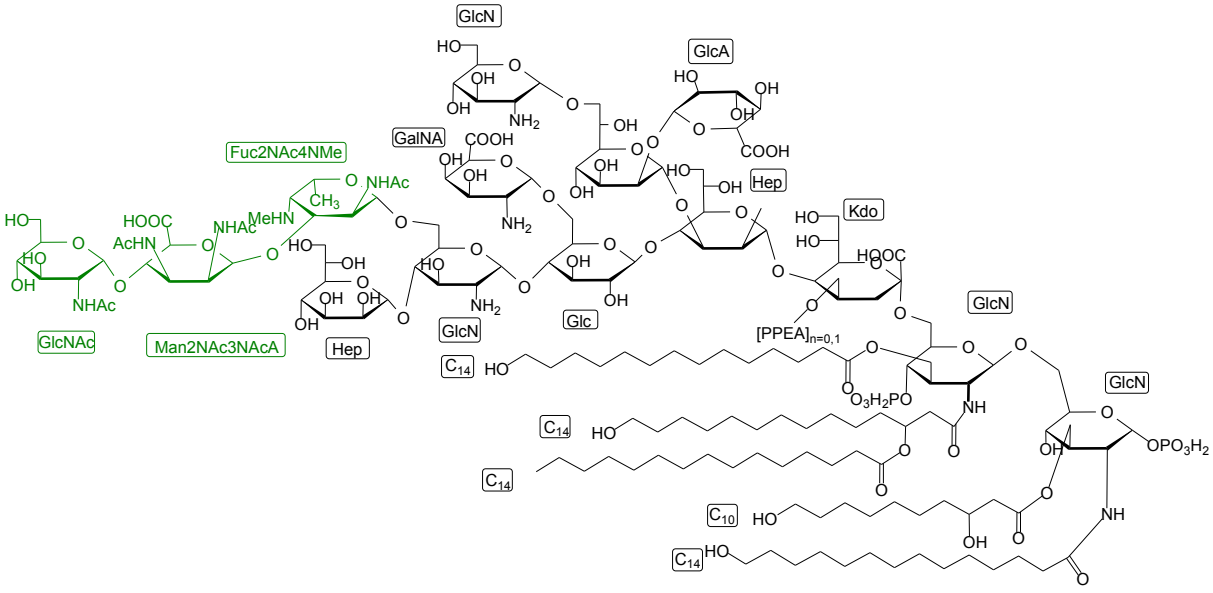


Figure 3. Complete structure LPS of B.pertussis (Band A trisaccharide coloured in green)

Synthesis of these LPS fragments forms an important part of the pharmacology of the antibiotics.[38,19,20] Synthesized LPS fragments could be used as a component of vaccine, to understand the mechanism of enzymatic synthesis and structural elucidation of natural products.[39,40] Challenges faced in such multi step synthesis are huge which can be simplified by identifying an array of sugars and synthesising it with a common strategy. So the identification of several sugars with the presence of 2,3-diacetamido uronate patterns has motivated us to devise a common strategy for its synthesis. So, current efforts are directed towards the synthesis of these uronic acid derivatives (Fig. 4), which can be used as glycosyl donors and acceptors in glycosylation reaction to produce oligosaccharides.

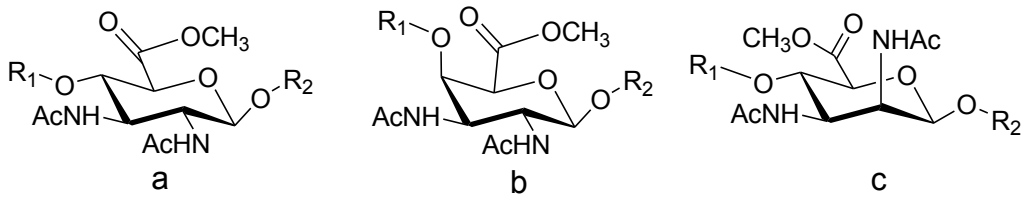


Figure 4. (**a**) *gluco*- (**b**) *galacto*- (**c**) *manno*-configurated 2,3-diacetamido uronates

These oligosaccharides can play an important role in the pharmacology of antibiotics against drug resistant gram-negative bacterial strains. Therefore, the following objectives were defined for my practical work of my thesis:

Objectives

- Improved synthesis of methyl 2,3-diacetamido-2,3-dideoxy-D-glucuronate starting from D-glucosamine
- Improved synthesis of methyl 2,3-diacetamido-2,3-dideoxy-D-galacturonate starting from D-glucosamine
- Improved synthesis of methyl 2,3-diacetamido-2,3-dideoxy-D-mannuronate via epoxide intermediates

2. Results and Discussion

2.1 Improved Synthesis of Methyl 2,3-diacetamido-2,3-dideoxy-D-glucuronate (28)

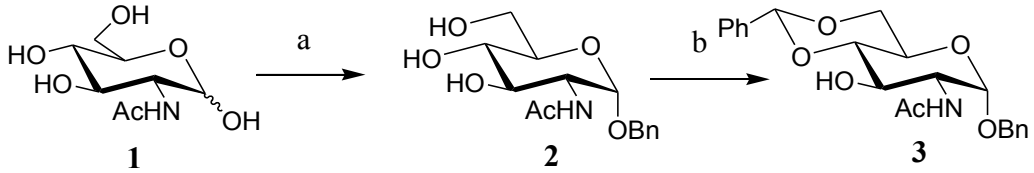
2.1.1 Synthesis of 2,3-diacetamido-2,3-dideoxy-D-glucopyranoside (11)

Procedures described in the literature

The simplest methodology described in the literature to get methyl 2,3-diaceamido-2,3-dideoxy-D-glucuronate used benzyl 2,3-diacetamido-2,3-dideoxy-α-D-glucopyranoside as an intermediate which was then oxidised to obtain the desired uronates. The preparation of 2,3-diacetamido glucopyranoside **11** was reported by Wolfgang Meyer zu Reckendorf.[41,42]

The key step is the double inversion at C-3 position including introduction of an azido group in equatorial position. After reduction the resulting amino function was acetylated to provide the desired benzyl 2,3-diacetamido-2,3-dideoxy-α-D-glucopyranoside. Similar strategies were employed by R.A.Field et al[40] and A. A. Nazarov, B. K. Keppler, et al[43] for the preparation of the pyranoside **11**.

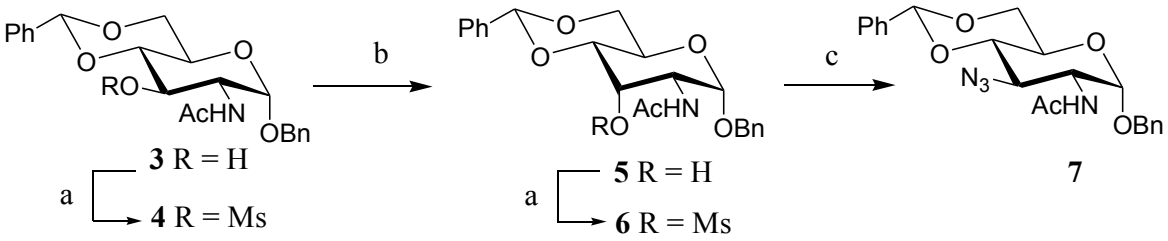
Proven method and their optimization



1 **2** **3**

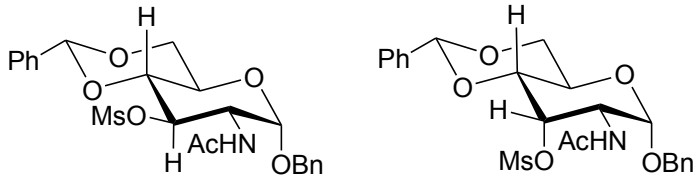
Scheme 1. Protection groups: (**a**) BnOH, HCl, 55 °C (**b**) $PhCH(OCH_3)_2$, 35 °C, 55%.

Classical Fischer glycosylation of *N*-acetylglucosamine (**1**) using anhydrous HCl as catalyst (obtained by adding AcCl to dry BnOH) in BnOH at 55 °C provided the benzyl glycoside **2** which was used without isolation in the next step. Introduction of benzylidene group at the 4,6-O-position was carried out by addition of benzaldehyde dimethyl acetal to the reaction mixture. After stirring overnight at 35 °C, derivative **3** was isolated in 55% yield. Purification was done by repeated crystallization from pyridine/water and EtOH. Importantly, the *N*-acetyl glucosamine should be well powdered and dried (80 °C for 4 h) before use.



Scheme 2. Double inversion at C-3 position: (**a**) MsCl, pyridine, 0 °C, 82% (**b**) H_2O, CH_3COONa, ethylene glycol monomethyl ether, reflux, 78% (**c**) NaN_3, TBAHS, DMF, 120°C, 65% (2 steps).

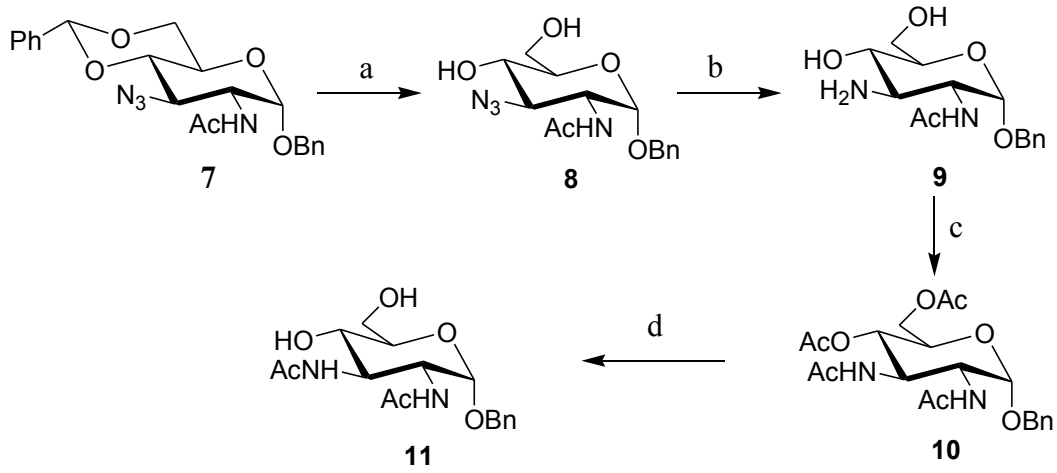
Transformation of the equatorial hydroxyl group at C-3 position of compound **3** in to an azido group at the same position and with the same configuration (compound **7**) was carried out by double inversion. First, mesylation with methanesulfonyl chloride in pyridine at 0 ºC provided compound **4** in 82% yield.[43] Second, nucleophilic substitution of the mesyl group by aq sodium acetate in ethylene glycolmonomethyl ether under reflux resulted in an inversion of configuration at the C-3 position to provide the *allo*-configurated sugar **5** in 78% yield. After renewed mesylation of the hydroxyl group at C-3 position, the substitution of the mesyl group by NaN_3 in the presence of tertrabutylammonium hydrogen sulfate (TBAHS) in DMF at 120 ºC resulted in inversion of configuration at C-3 position providing *gluco*-configurated compound **7** in 65% yield (2 steps).[43] When the reaction was carried out in the absence of TBAHS, incomplete conversion of the starting material was observed even at reflux temperatures.



$_3J^{3,4}$= 9.2 Hz $_3J^{3,4}$ = 2.8 Hz

Figure 5. ^{1}H NMR: Comparison of coupling constants at positions 3 and 4 of compounds **4** and **6**.

The change of configuration in the case of sugars **4** and **6** (Fig 5.) were evident by ^{1}H NMR coupling constants. The proton at C-3 position of compound **4** showed a *trans-axial* coupling constant of $^3J_{3,4}$= 9.2 Hz while the allose isomer **6** coupled at a lower frequency of $^3J_{3,4}$ = 2.8 Hz due to less intense *cis*-coupling.



Scheme 3. Preparation of benzyl 2,3-diacetamido-2,3-dideoxy-α-D-glucopyranoside: (a**)** H_2O, CH_3COOH, 80 °C, 79% (b) Pd/C, H_2, CH_3OH (c) Ac_2O, pyridine (d) CH_3ONa (0.5 M), CH_3OH, 55% (4 steps).

Cleavage of the benzylidene group of **7** was carried out by using 80% aqueous acetic acid at 90 °C to get the deprotected sugar **8** with free hydroxyl groups at 4 and 6 positions.[43] Furthermore, the azido group of compound **8** was converted into an acetamido group in three steps. First, the reduction of the azido group of compound **8** to an amino group (compound **9**) was done by catalytic hydrogenation using Pd (10% on activated charcoal) in methanol under an atmosphere of H_2.[43] Second, crude product **9** was directly used for consecutive acetylation with Ac_2O and pyridine providing complete acetylated product **10.** Finally, selective de-acetylation of the O-acetyl groups using 0.5 M CH_3ONa in methanol gave the diacetamido glucose derivative **11** in overall yield of 55% yield (over 4 steps, from compound **7**).

2.1.2 Synthesis of methyl 2,3-diacetamido-2,3-dideoxy-4-benzoyl-D-glucuronate

Methyl 2,3-diacetamido-2,3-dideoxy-D-glucuronate was prepared by oxidation of benzyl 2,3-diacetamido-2,3-dideoxy-α-D-glucopyranoside.

Procedures described in the literature

Oxidation of nucleic acid derivative of 2,3-diacetamido-2,3-dideoxy-glucopyranoside (see Fig. 6) by PtO_2 (prepared from high surface platinum and molecular O_2) was reported by Martin Rejzek et al.[40] Oxidation using TEMPO and several secondary oxidants was reported too.[44-52] An excellent composition of recent advances in TEMPO oxidation was compiled by Félix Calderón.[53]

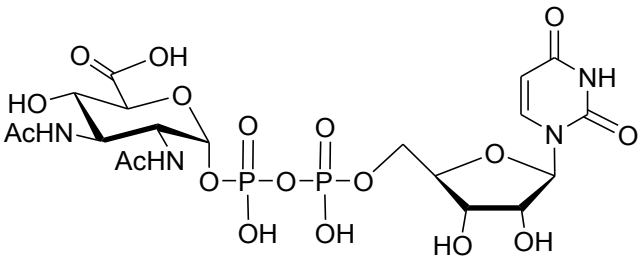
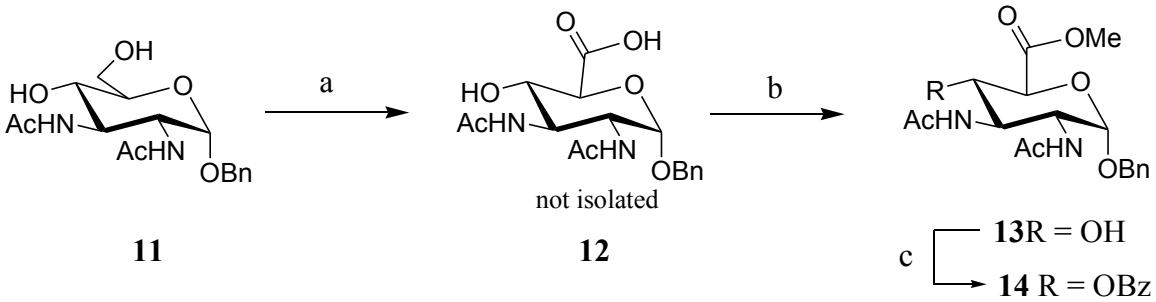


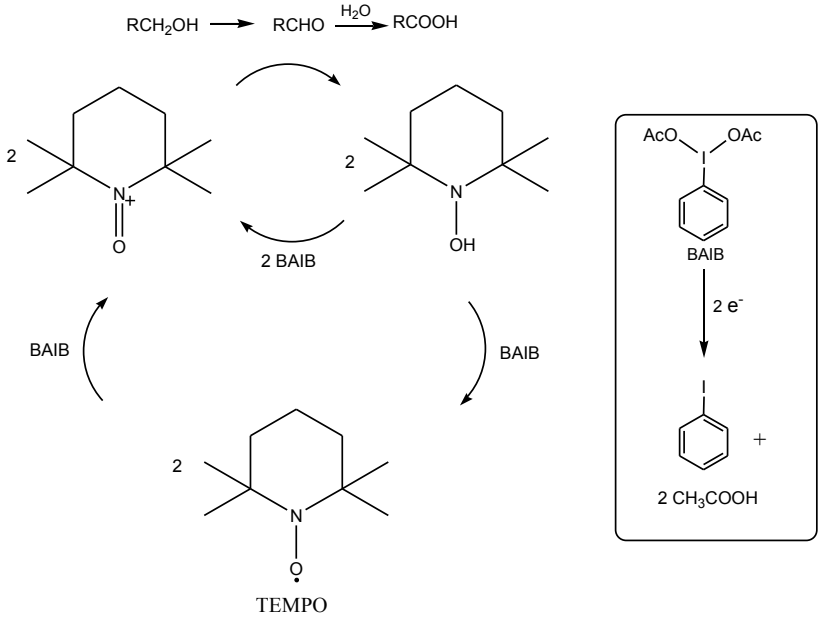
Figure 6. Martin Rejzek et al: Preparation of diacetamidoglucuronic acid.

Proven methods and their optimization



Scheme 4. Oxidation of benzyl 2,3-diacetamido-2,3-dideoxy-α-D-glucopyranoside: (a) TEMPO, BAIB, H_2O, DCM (b) CH_2N_2, CH_3OH, 68% (2steps) (c) BzCl, Pyridine, DCM, - 5 °C, 67%.

Selective oxidation of the primary hydroxyl group of pyranoside **11** in the presence of a secondary hydroxyl group was carried out by using catalytic amount of TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) radical (primary oxidant) and stochiometric amount of BAIB (bis(acetoxy)iodobenzene; secondary oxidant). Importantly, TLC strictly controlled the duration of the reaction because the reaction gives lower yields if prolonged for longer than the time of complete conversion of the starting material. Also, the duration of the reaction has to be optimized depending on the scale of the reaction. Treatment of crude carboxylic acid product **12** with diazomethane in methanol resulted in methyl ester **13** in 68% yield. Subsequent benzoylation was carried out with BzCl in pyridine at -10 °C to produce **14** in 67% yield.

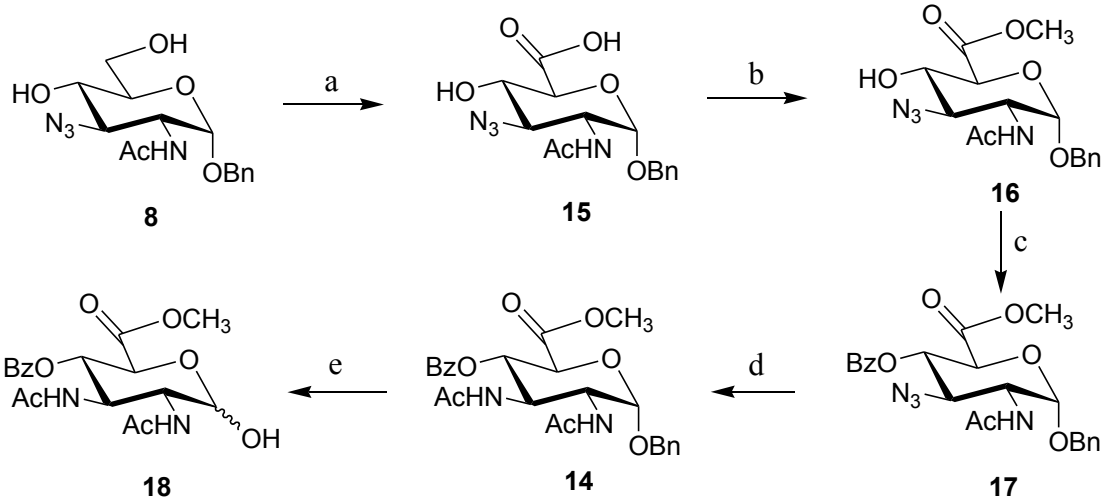


Scheme 5. Mechanism of TEMPO/BAIB oxidation

Various secondary oxidants for the TEMPO oxidation were tried. The NaOCl-KBr oxidant gave no conversion of the starting material controlled by TLC, while complete conversion is attained in case of the $CaOCl_2$ variant, but the yield of the reaction was only 25%.

2.1.3 Improvements in oxidation reactions

Even though oxidation of 2,3-diacetamido-D-glucopyranoside **11** was successful, the reaction gave lower yields when it was upscaled to 500 mg scale. So, as a modification to the present scheme, instead of using the diacetamido compound **11** as a starting material, compound **8** carrying an azido group instead of the acetamido group in the C-3 position was used.



Scheme 6. (**a**) TEMPO, BAIB, DCM, H_2O (**b**) CH_2N_2, CH_3OH 79% (2 steps) (**c**) BzCl, Pyridine, DCM, –5 °C, 89% (**d**) Pd/C, H_2, Ac_2O, MeOH (**e**) Pd/C, H_2, AcCl, MeOH, 90%. (2 steps).

Surprisingly, TEMPO/BAIB oxidation of compound **8** proceeded with excellent improvement in yield and scalability of the reaction. Compound **15**, which was obtained as a crude product after the oxidation reaction underwent esterification with diazomethane in methanol resulting in compound **16** at 79% yield. The remarkable improvement in the yield from 68% to 79% was achieved when the reaction was done in scale of 1g. Similar to the oxidation of 2,3-diacetamidoglucopyranoside (**11**, Sec 2.1.2), the duration of the reaction was strictly controlled by TLC to avoid the formation of side products after complete conversion of the starting material. Furthermore, the step of benzoylation showed an additional improvement of yield from 67% to 89% to get compound **17**. The benzoylation reaction which was definitely influenced by the presence of an azido group instead of an acetamido group at C-3 position was carried out using BzCl in pyridine/DCM mixture at –5 ºC. Next, the conversion of the azido group in to acetamido group at C-3 position and the reductive cleavage of the benzyl group at the anomeric position of compound **17** were carried out as a one pot reaction. First, the conversion of the azido group in to acetamido group was carried out by using Pd (on activated charcoal) in a mixture of Ac_2O and abs. methanol under an atmosphere of H_2. After completion of the reaction, small amount of AcCl was directly added to the crude product **14** and stirred under an atmosphere of H_2 effects the reductive cleavage of the benzyl protection group. The three step one pot reaction produced compound **18** in an excellent yield of 90%.

2.1.4 Summary

With respect to the methods reported in literature, several changes were made to the processes, which resulted in increased yield and scalability of the reactions. Preparation of compound **3** was done using two step one pot reaction in comparison to the two separate reactions reported in the literature.[40,43] Oxidation of the pyranosides to uronates was done using TEMPO/BAIB reagents instead of PtO_2/molecular O_2 method reported in the literature. On the contrary to the literature report, the TEMPO oxidation of the primary hydroxyl group was found to undergo selectively with out any over oxidation of the secondary hydroxyl group at C-4 position.[54] Finally, the improvements made in the synthetic strategy by performing the oxidation reaction prior to the conversion of the azido group in to acetamido group resulted not only in remarkable improvement in the yield and scalability of the oxidation reaction but also of the subsequent steps of benzoylation and reduction reactions. The reduction of azido group in to amino group, conversion of the amino group in the acetamido group and reductive cleavage of anomeric benzyl protection group was carried out as one pot reaction with excellent yield and scalability.

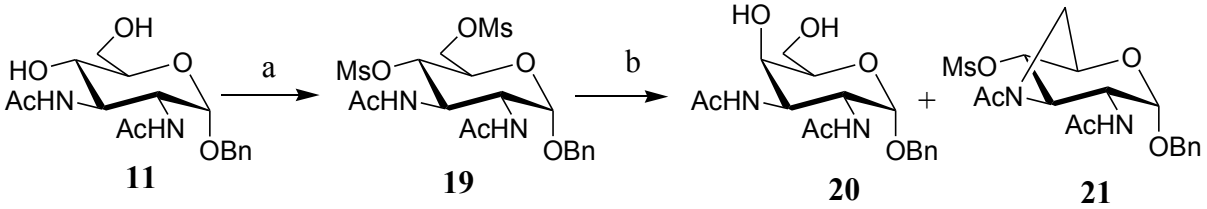
2.2 Improved synthesis of Methyl 2,3-diacetamido-2,3-dideoxy-D-galacturonate (18)

2.2.1 Synthesis of 2,3-diacetamido-2,3-dideoxy-D-galactopyranoside

Procedures described in the literature

Benzyl 2,3-diacetamido-2,3-dideoxy-D-galactopyranoside was prepared from its glucose isomer (benzyl 2,3-diacetamido-2,3-dideoxy-D-glucopyranoside), by inversion of configuration of hydroxyl group at C-4 position (from equatorial to axial position). The method was also reported by Wolfgang Meyer Zu Reckendorf in 1970.[55]

Proven methods and their optimization



Scheme 7. Inversion of configuration at C-4. (**a**) MsCl, pyridine, 0 °C, 79% (**b**) H_2O, CH_3COONa, ethylene glycol monomethyl ether, reflux, 65%.

As mentioned above, the conversion of the glucose isomer to galactose isomer was achieved by inversion of configuration of the hydroxyl group at C-4 position. For this reason both hydroxyl groups of compound **11** (at C-4 and C-6 positions) were converted in to mesyl groups using MsCl in pyridine at 0 °C to provide the dimesyl compound **19** in 79% yield. The following nucleophilic substitutions at C-4 and C-6 positions was carried out by using CH_3COONa in ethylene glycol mono methyl ether and water under reflux to get the galactose derivative **20** in 65% yield. Intramolecular substitution of the mesylate at C-6 position by the acetamido group at C-4 position produced the bicyclic side product **21** in 15% yield.[55]

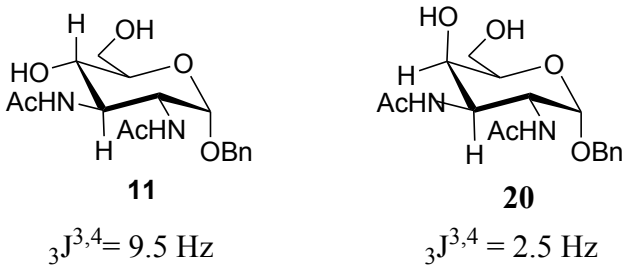


Figure 7. ^{1}H NMR coupling constants: Comparison of coupling constants at positions 3 and 4 of compounds **11** and **20**.

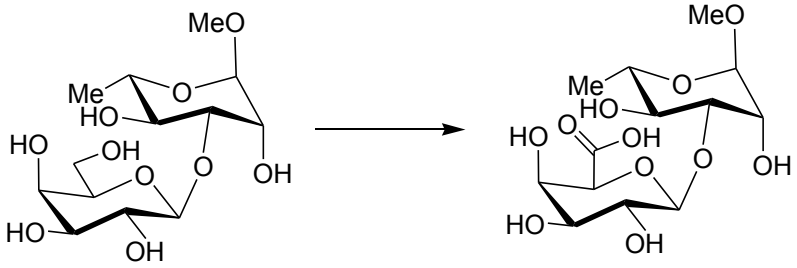
The change of configuration from compound **11** to *galacto*-configurated **20** (Fig 7.) was evident by ^{1}H NMR coupling constants. The proton at C-4 position of glucose compound **11** showed a *trans-axial* coupling constant of $^{3}J_{3,4}$= 9.5 Hz while the galactose isomer **20** coupled at a lower frequency of $^{3}J_{3,4}$ = 2.5 Hz due to less intense *cis*-coupling.

2.2.2 Synthesis of methyl 2,3-diacetamido-2,3-dideoxy-D-galacturonate

Similar to the preparation of methyl-2,3-diacetamido-2,3-dideoxy-D-glucuronate **13**, methyl-2,3-diacetamido-2,3-dideoxy-D-galacturonate was prepared by oxidation of benzyl 2,3-diacetamido-2,3-dideoxy-α-D-galactopyranoside **20**.

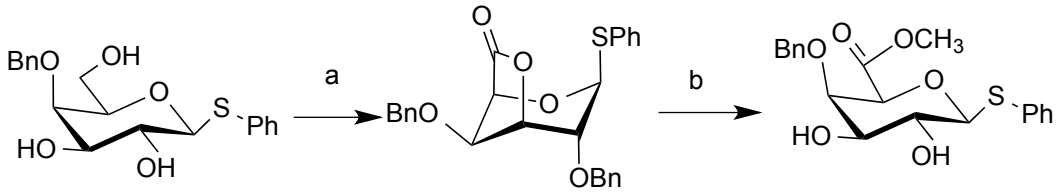
Procedures described in the literature

Selective oxidation of primary hydroxyl group of galactose which was was connected with a rhamnopyranoside to form a disaccharide (Fig 8), was reported by R.A.Field et al.[56] The oxidation was carried out by using TEMPO-NaOCl system in 73% yield.

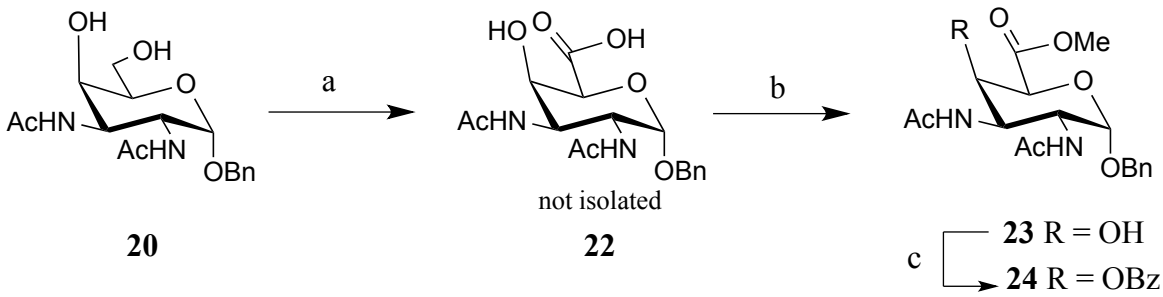


Scheme 8. (**a**) Oxidation of plant cell wall disacharides: TEMPO, NaOCl, KBr, H_2O, 73%.

Furthermore, G.A.Van der Marel et al reported the oxidation of the primary hydroxyl group of a galactose thioglycoside with TEMPO-BAIB sytem.[46,47] Interestingly, the primary alcohol is first oxidised to a lactone, which on stirring with methanol undergoes transesterification to produce the required uronate.



Scheme 9. Oxidation and lactone formation: (**a**) TEMPO, BAIB, H_2O, DCM, (**b**) CH_3OH, 75% (2 steps).



20 **22**

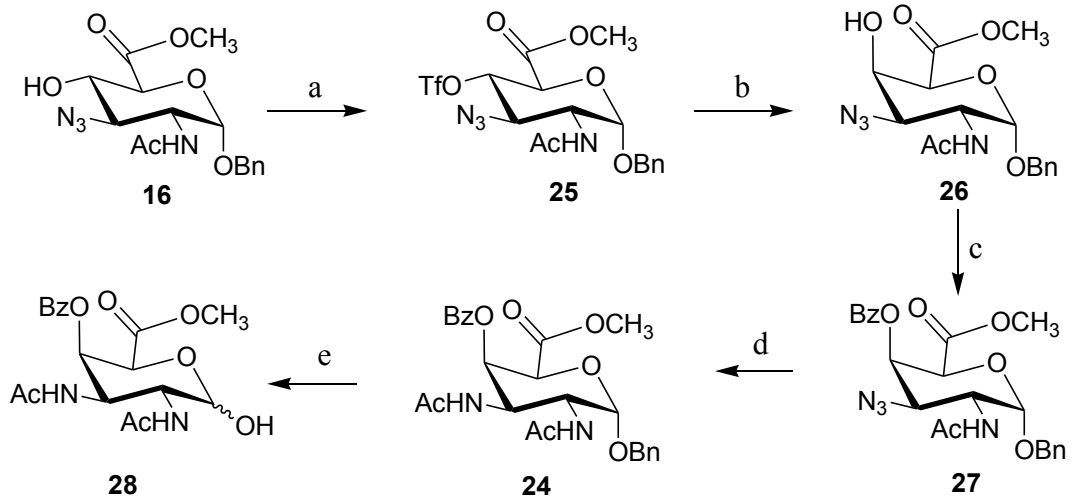
Scheme 10. (**a**) TEMPO, BAIB, H_2O, DCM, (**b**) CH_2N_2, CH_3OH, 68% (2 steps) (**n**) BzCl, pyridine, DCM, –5 °C, 62%

Proven methods and their optimization

The transformation of the *galacto*-configurated pyranoside **20** to uronic acid **22** was achieved by selective oxidation of the primary hydroxyl group in the presence of a secondary hydroxyl group using catalytic amount of TEMPO radical (primary oxidant) and stochiometric amount of BAIB (secondary oxidant). Importantly, the duration of the reaction was strictly controlled by TLC, because the reaction gives lower yields if prolonged for longer than the time of complete conversion of the starting material. Also, the duration of the reaction has to be optimized depending on the scale of the reaction. Treatment of the crude carboxylic acid product **22** with diazomethane in methanol resulted in the methyl ester **23** in 68% yield. In comparison to the oxidation reaction of the glucose isomer **11**, the reaction of galactose isomer takes longer time, subjectively due to the steric effects produced by the axially configurated C-4 hydroxyl group. Oxidation with TEMPO and NaOCl did not result in conversion of the starting material. Subsequent benzoylation with BzCl in pyridine at –10 °C produced compound **24** in 62% yield. In comparison, the same reaction with the glucose isomer resulted in a slightly better yield of 68%.

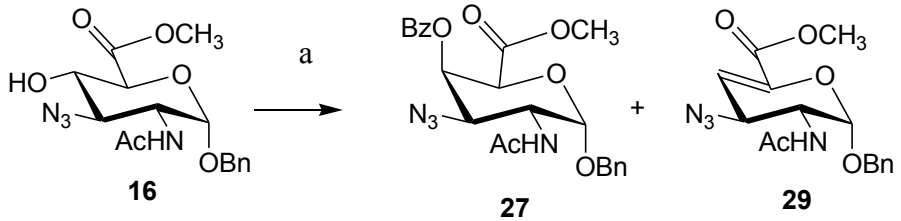
2.2.3 Improvements in the synthesis of methyl 2,3-diacetamido-2,3-dideoxy-D-galacturonate

Similar to 2,3-diacetamido-2,3-dideoxy-glucopyranoside, upscaling of the oxidation procedure applied to 2,3-diacetamido-2,3-dideoxy-galactopyranoside leads to decreased yields.



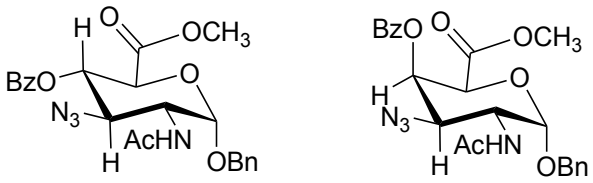
Scheme 11. (**a**) Tf_2O, pyridine, DCM, –10 °C (**b**) $NaNO_2$, DMF 69% (2 steps) (**c**) BzCl, pyridine, DCM, –5 °C 89% (**d**) Pd/C, H_2, Ac_2O, MeOH (**e**) Pd/C, H_2, AcCl, MeOH, 87%. (2 steps)

Therefore, methyl(benzyl 2-acetamido-3-azido-2,3-dideoxy-α-D-glucopyranoside)uronate **16** obtained by a improved oxidation procedure (Sec. 2.1.3 Improvements of oxidation reactions) was used as starting material for the preparation of methyl 2,3-diacetamido-2,3-dideoxy-D-galacturonate. In order to convert glucuronate **16** into the corresponding galacturonate **26** triflate intermediate **25** was prepared by using triflic anhydride, pyridine in DCM at –10 °C which was then used without further purification for the next step. Treatment of **25** with $NaNO_2$ in DMF gave after 48 hours compound **26** in 78% yield (over 2 steps). Benzoylation of galacturonate **26** with BzCl in pyridine and DCM at –5 °C resulted in compound **27** in 89% yield. Similar to the glucose isomer, benzoylation of the 3-azido derivative **26** compared to the corresponding 3-acetamido derivative **23** leads to improved yields (62% to 89%). Next, the conversion of the azido group in to acetamido group at C-3 position and the reductive cleavage of the benzyl group at the anomeric position of compound **27** were carried out as described for glucuronate **18**. The three step one pot reaction produced compound **28** in an excellent 87% yield.



Scheme 12. Mitsunobu esterification (**a**) Diisopropyl azodicarboxylate, benzoic acid, PPh_3, DMF

To reduce synthetic steps, direct benzoylation with inversion of configuration at C-4 under Mitsunobu reaction conditions was proved on compound **16**. Unfortunately, the major product of the reaction was compound **29** as result of elimination. The desired product **27** was obtained in minor amount.



17 **27**

$^3J_{3,4}$ = 9.6 Hz $^3J_{3,4}$ = 2.8Hz

Figure 8. ^{1}H NMR coupling constants: Comparison of coupling constants at positions 3 and 4 of compounds **17** and **27**.

As in previous case, the change in configuration at C-4 position was confirmed by the NMR coupling constants (Figure 8). The glucose isomer **17** gave a *trans-axial* coupling constant of $^3J_{3,4}$= 9.6 Hz while the galactose isomer **27** coupled with a lower frequency of $^3J_{3,4}$ = 2.8 Hz due to less intense *cis*-coupling.

2.3 Improved synthesis of Methyl 2,3-diazido-4-benzoyl-2,3-dideoxy-D-mannouronate

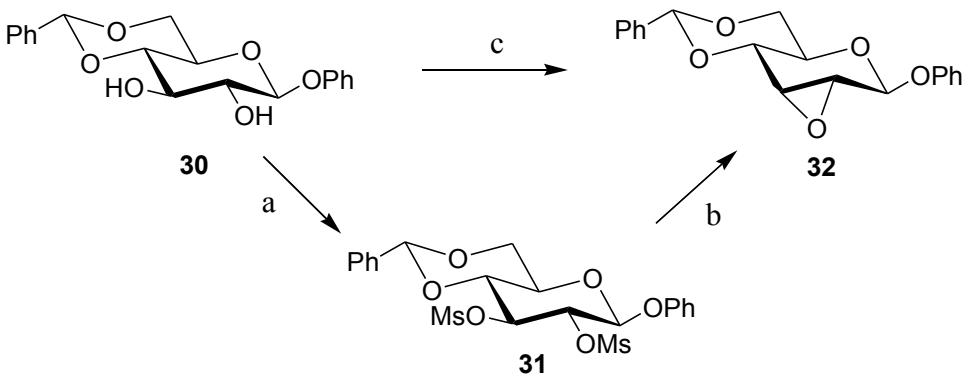
2.3.1 Synthesis of phenyl 2,3-diacetamido-2,3-dideoxy-mannopyranoside

Procedures described in the literature

For the preparation of phenyl 2,3-diacetamido-2,3-dideoxy mannopyranoside the key intermediate is the epoxide phenyl 2,3-anhydro-4,6-O-benzylidene-β-D-allopyranoside. Several variations has been reported in the literature to get epoxides by using basic hydrolysis (aq.KOH) or methanolysis (NaOMe) of disulfonate sugars (mesyl or tosyl) over a range of temperatures from RT to 80 ºC.[57-59] However, the preparation of epoxide directly from the sugar diols using Mitsunobu reagent was found to be better than all the other reported methods.[60-65] Furthermore, T. Norberg et al. described the synthesis and ring opening of epoxides by substitution reactions that facilitates the formation of 2,3-diazido manno pyranoside.[66] As shown before, several methods are available in the literature for the conversion of the azido group to acetamido group and cleavage of benzylidene protection group to produce the required 2,3-diacetamido-2,3-dideoxy mannopyranoside.[40,43]

Proven methods and their optimization

As reported in the literature, various methods were attempted for the preparation of epoxide sugars.



Scheme 13. Formation of epoxides (**a**) MsCl, pyridine, 0 °C, 84% (**b**) CH_3ONa(0.5 M), CH_3OH/THF, reflux, 45% (**c**) dialkyl azodicarboxylate, PPh_3, DMF, 80 °C, 77%.

Initially, a couple of methods for the preparation of epoxide from the dimesyl compound **31** were tried. The reactions proceeded through in situ nucleophile generation (at the C-2 position) and a substitution reaction (at the C-3 position), generating the epoxide at the 2,3 position. The reactions were performed using either 30% aq KOH solution or methanolic CH_3ONa (0.5 M) in CH_3OH/THF (1:1 v/v) under reflux conditions. However, both reactions resulted in poor yields with the generation of unwanted isomeric mannose epoxide **33** (Fig 9).

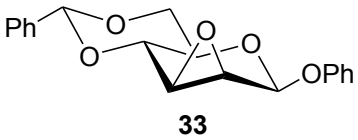
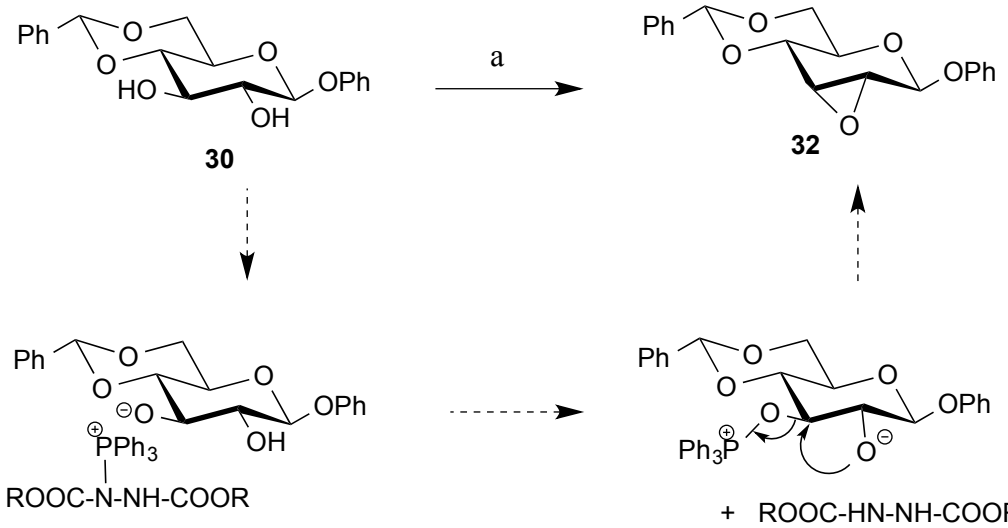


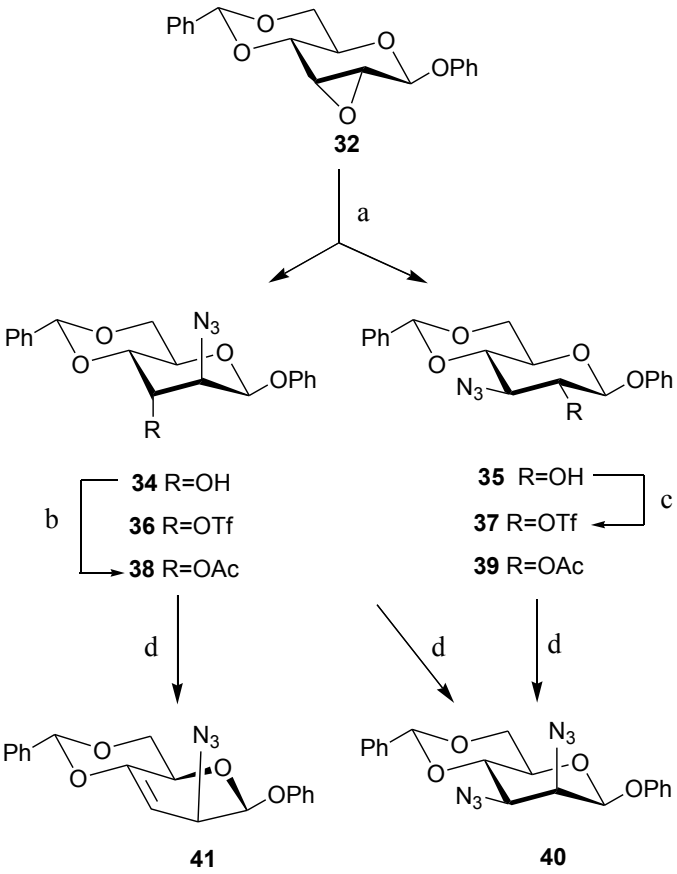
Figure 9. Structure of phenyl 2,3-anhydro-4,6-O-benzyliden-β-D-mannopyranoside



Scheme 14. Mechanism of epoxide formation[67] (**a**) Dialkyl azodicarboxylate, PPh_3, DMF.

Finally, epoxide **32** was prepared directly from diol **30** by Mitsunobu reaction using PPh_3 and dialkyl azodicarboxylate (i-propyl, t-butyl or ethyl) at 80°C in dry DMF. After completion of the reaction, direct evaporation of the reaction mass followed by simple crystallisation of the syrupy crude residue in ethanol resulted in the crystalline epoxide product **32** in 77% yield

(using DIAD, diisopropyl diazocarboxylate).[68] Using the above process, reactions up to 20 g scale were performed without any trouble. Nevertheless, due to the explosive nature of azocarboxylates,[69] an alternative procedure was developed using the t-butyl variant (DBAD) of the azocarboxylate. After the reaction, a simple work-up decomposes the explosive azocarboxylate (DBAD) in to safer byproducts.[70,71] Preliminary reactions with DEAD (ethyl azodicarboxylate, 40% in toluene) proceeded with a moderate yield of 65%, but considering the hazardous nature of DEAD, further optimisation of the reaction conditions was not carried out. The ideal solvent for the reaction was found out to be DMF, after obtaining negative results with DCM and 1,4-dioxane. Initially the purification of the crude reaction mass was tried with column chromatography, but due to the presence of a high amount of PPh_3, the separation of the product from PPh_3 was not possible. However, this problem could be averted by the conversion of PPh_3 to polar PPh_3O by means of a mild work-up with H_2O_2.[72] Another important change to the reaction could be to minimise the usage of toxic azocarboxylates by using a catalytic amount and regenerating it in situ with an oxidant (stoichiometric amount) such as BAIB.[73]



Scheme 15. (**a**) NaN_3, H_2O, NH_4Cl, DMF, 120 °C, 95 % (**b**) Ac_2O, pyridine, 0° C (**c**) Tf_2O, pyridine, DCM, - 10 °C, (**d**) NaN_3, DMF, 65 % (2 Steps)

The opening of the epoxide ring in compound **32** by nucleophilic substitution was carried out with NaN_3, NH_4Cl and H_2O in DMF at 120°C to give an isomeric mixture of products **34** and **35** (ratio 40:60) in 95% combined yield. The ratio observed for the isomeric products was against the prediction of the Fürst-Plattner rule which predicts the transdiaxial isomer **34** to be the predominant product.[74,75] The reason for the unexpected ratio could be due to the difference in the stability of transient positive charges formed in the carbon atoms present at the C-2 and C-3 positions during the nucleophilic substitution process. The positive charge at the C-2 position (formed by N_3^- ion attack at the C-2 carbon atom producing the diaxial isomer **34**) would be less stable relative to the positive charge on the C-3 carbon atom (formed by N_3^- ion attack at C-3 carbon atom producing the diequatorial isomer **35**) because of the proximity of the C-2 carbon to the anomeric centre. Another hindrance to nucleophilic attack at the C-2 position could be the orientation of the phenyl group in the anomeric position, which would create steric strain on the incoming azide nucleophile. Nevertheless, the unexpected major product, the diequatorial isomer **26**, happened to be more amenable to the subsequent reactions. So, the reaction was optimised to get a maximum ratio of the diequatorial isomer **35** considering its advantages over the other isomer **34** in the subsequent substitution reaction (see scheme 15). In the process of obtaining more of the gluco isomer **35**, several variations in reagents and reaction conditions were tried. The introduction of CsF.[76] and tetraethyl ammonium chloride (TEAC) did not increase the ratio of the desired isomer. Reactions with NaN_3 or LiN_3[77] (20% in water) without using any catalyst were also tried but were not successful. The ideal temperature of the reaction (with NaN_3, NH_4Cl, H_2O) was found to be 120 ºC after the reactions at low temperatures (80-110 ºC) failed to produce full conversion while the reactions at higher temperatures (130-150 ºC) produced an undesired ratio. So, the isomeric products (**34** and **35**, which can be used as a mixture for the subsequent reaction) were eluted as a mixture using flash chromatography. However, for the analytical characterisation, the mixture was separated and the individual isomers were acetylated. See Figures 10, 11 and 12 for the X-ray structures of the acetylated products **38** and **39** and the triflate **37**, respectively.

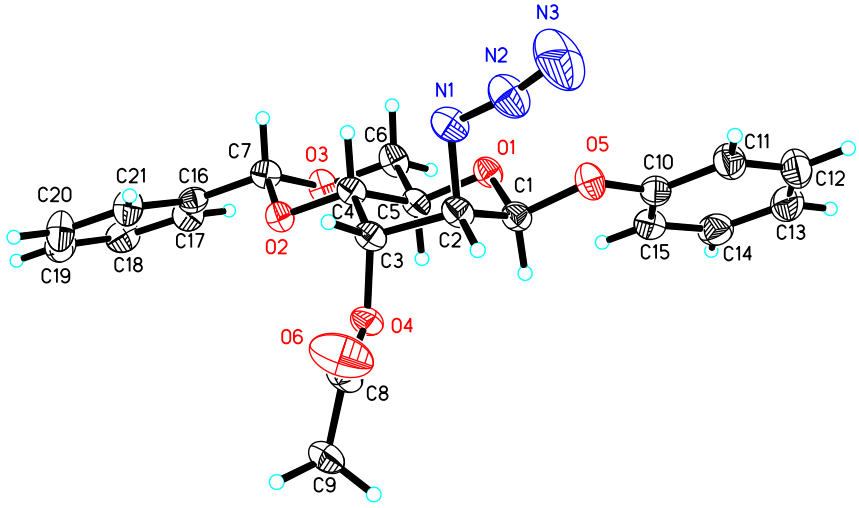


Figure 10. Crystal structure of 38

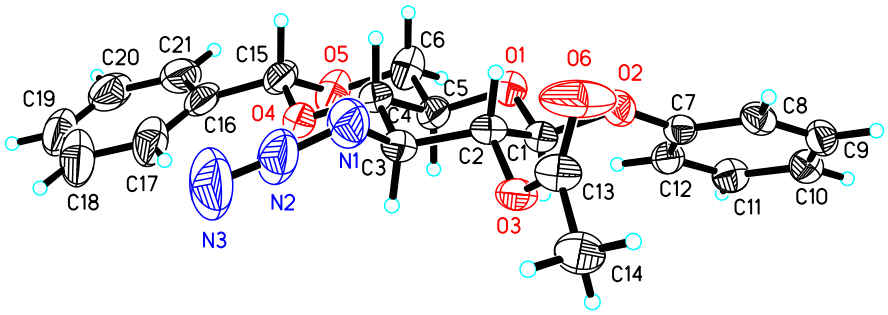


Figure 11. Crystal structure of 39

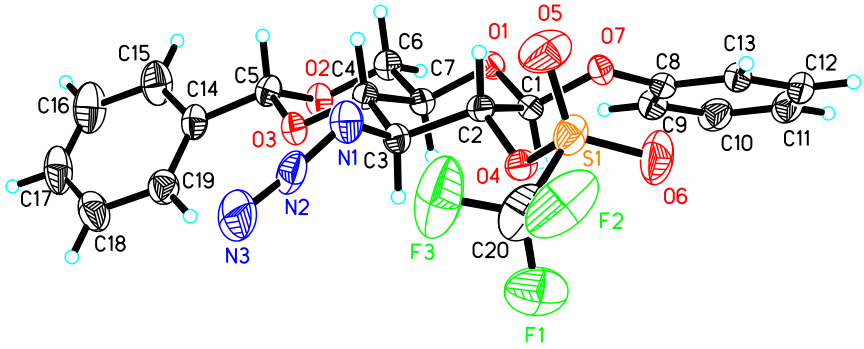


Figure 12. Crystal structure of 37

The mixture of isomeric products containing the *altro* configured sugar **34** and the *gluco* configured sugar **35** were converted into trifluoromethanesulfonyl (triflate) derivatives **36** and **37** using Tf_2O and pyridine in DCM at –10 ºC. For analytical purposes, triflate compounds **36** and **37** were separately prepared and characterised. For subsequent reactions, the crude triflate mixture was directly used in the next step, i.e. azidation with NaN_3 in DMF at RT. Interestingly, upon nucleophilic substitution, both triflate isomers were converted into 2,3-dizido mannose configured sugar **40** in 65% yield. Besides the desired substitution product **40**, a minor elimination product **41** was obtained.[78] As theoretically expected, the elimination product originated from the triflate isomer **36**, which possesses an anti-periplanar hydrogen atom. Incidentally, it was observed by TLC that the rate of nucleophilic substitution of the diaxial triflate was higher than that of the diequatorial isomer. Variations in reaction conditions such as changes in temperature, solvents (DCM and 1,4-dioxane) and the mode of addition of NaN_3 did not alter the substitution-elimination ratio of the reaction. Both product **40** and **41** were characterised by means of X-ray diffraction crystallography (see Fig 13 and 14).

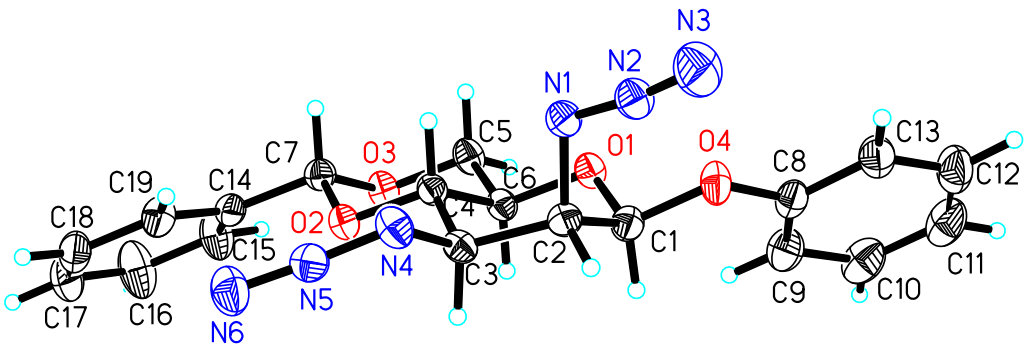


Figure 13. Crystal structure of 40

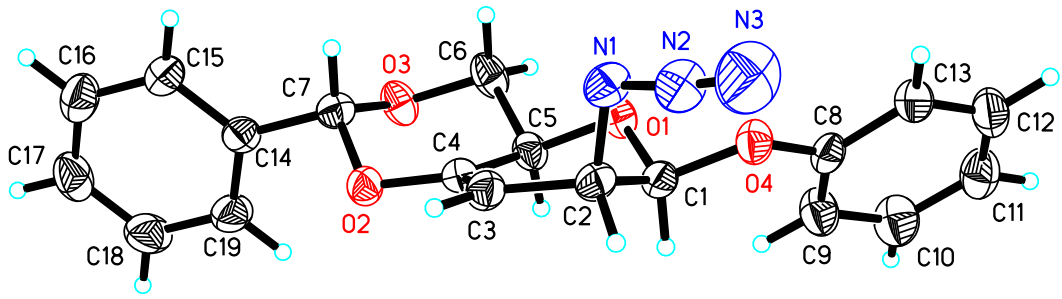
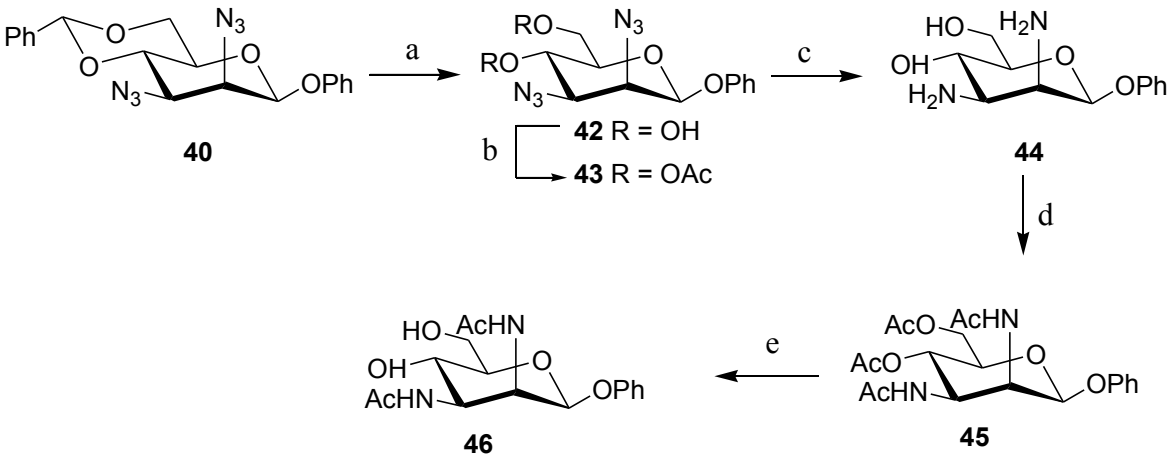


Figure 14. Crystal structure of 41



Scheme 16. (**a**) CH_3COOH, H_2O, 90 °C, 80% (**b**) Ac_2O, pyridine, 0°C, 93 % (**c**) Pd/C, H_2, CH_3OH (**d**) Ac_2O, pyridine, 0°C (**e**) CH_3ONa(0.5 M),CH_3OH (45 %, 3 steps)

After successful preparation of 2,3-diazido-2,3-dideoxy mannopyranoside **40**, it was used in a series of simple protection group modifications. Hydrolysis of the benzylidene acetal group in compound **40** was carried out using 80% aqueous acetic acid. Stirring the reaction at 90 °C provided the unprotected sugar **42** in 79% yield.[43] (See Fig. 15 for the X-ray structure of the acetylated product **43)**. Next, the transformation of azido groups in compound **42** in to acetamido groups was carried out in three steps. First, reduction of the azido groups with a Pd (10% on activated charcoal) catalyst over an atmosphere of H_2 gave the free diamino compound **44**. Subsequent acetylation with acetic anhydride in pyridine at 0 °C provided the completely acetylated product **45** which was selectively de-acetylated with 0.5 M CH_3ONa to get 2,3-diacetamido-2,3-dideoxy mannopyranoside **46** in 45% overall yield (in three steps). Similar reactions for the glucose isomer described in Chapter 1 provided better yield.

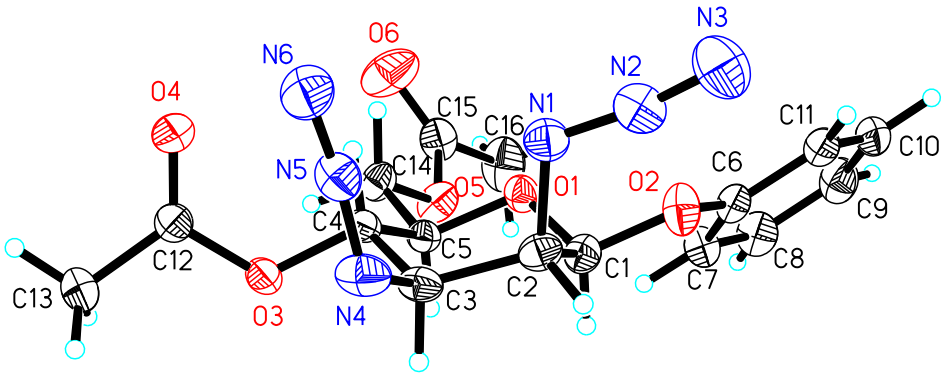


Figure 15. Crystal structure of 43

2.3.2 Synthesis of Methyl 2,3-diacetamido-2,3-dideoxy mannouronate

Procedures described in the literature

Oxidation of the primary hydroxyl group in 2,3-diacetamido-2,3-dideoxy mannopyranoside in to an aldehyde group before conversion into a carboxylic acid was reported by Nilsson et al.[66] For some reason, the carboxylic acid group was not converted in to an ester, which would have been much more easier to handle in the purification and characterisation process.

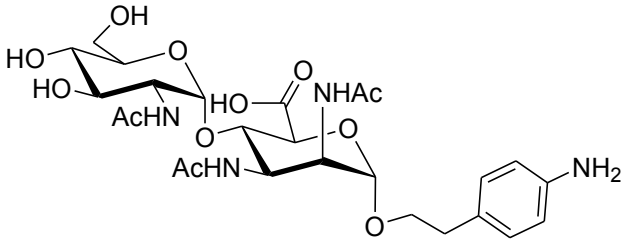
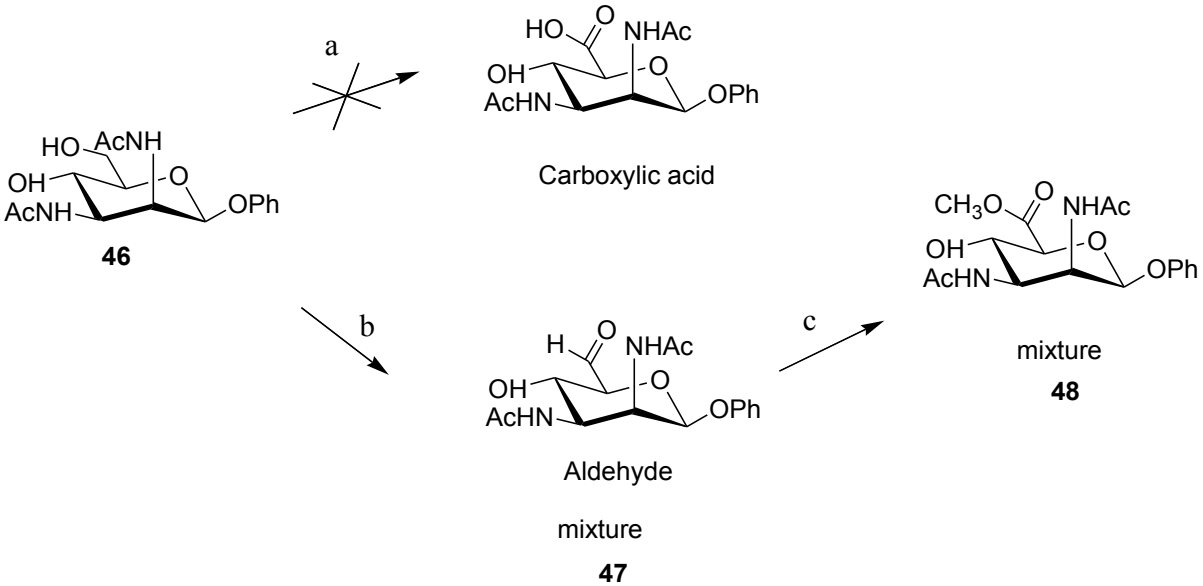


Figure 16. M.Nilsson et al: Preparation of diacetamido manno uronic acid

Proven method and their optimization



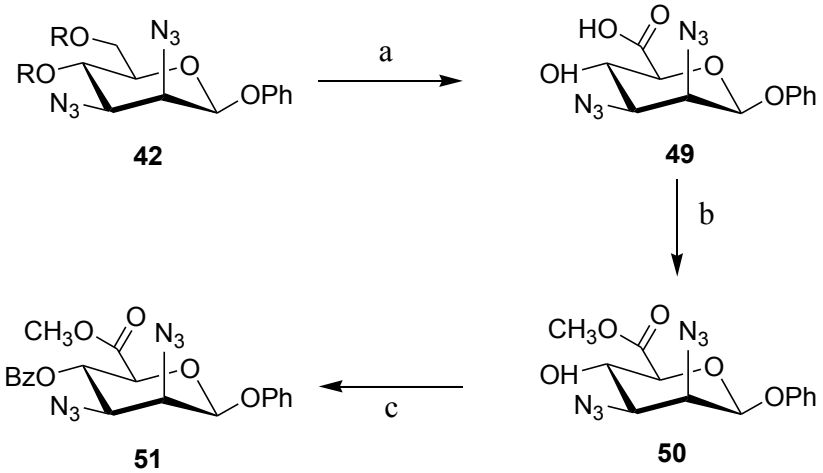
Scheme 17. (**a**)TEMPO, BAIB, DCM, H_2O (**b**) TEMPO, TCCA, pyridine, -40 °C (**c**) Br_2, H_2O, CH_3OH.

Oxidation of **46** under conditions similar to those used for the corresponding glucose and galactose derivatives (TEMPO, BAIB and H_2O) did not result in the formation of desired carboxylic acid product.[79] The conversion of the starting material to the product was seen by TLC, but after work-up, the product could not be isolated. Attempts made to isolate the organic product from the aqueous layer were unsuccessful. TEMPO oxidation with different secondary oxidants like NaOCl and $Ca(OCl)_2$ also produced negative results. So a different

reaction to prepare the ester **48** through the aldehyde product **47** was developed. TEMPO/BAIB[80] oxidation in absolute DCM failed to produce the desired aldehyde product. TEMPO oxidation with NCS (*N*-chlorosuccinimide) in the presence of TBACl did not result in any conversion of the starting material.[81] The reaction with TEMPO and TCCA (trichloroisocyanuric acid) using DCM as the solvent showed very little conversion. So, using TEMPO and TCCA as an oxidation system, a variety of solvents and temperature conditions were tried. Finally, the reaction showed complete conversion of the starting material when the reaction was carried out with pyridine at –35°C.[82] After work-up and isolation (column chromatography) of the product, it was characterised as a mixture by NMR spectroscopy. But, the observation of an aldehyde proton peak in the spectrum confirmed the formation of the aldehyde product. So, after completion of the reaction, without purification, the next step, i.e. an oxidative esterification reaction using Br_2/H_2O and $NaHCO_3$[83] was also tried, but it also gave a mixture of products **48** which could not be isolated or characterised

2.3.3 Improvement in the synthesis of 2,3-diacetamido-2,3-dideoxy-D- mannouronate

Following the failure of the oxidation reactions of phenyl 2,3-diacetamido-2,3-dideoxy-β-D-mannopyranoside, a modification to the present scheme was followed. Instead of performing the oxidation reaction with 2,3-diacetamido compound **46** as the starting material; compound **42** carrying two azido groups instead of the acetamido groups at the C-2 and C-3 positions was used. Due to the successful usage of the TEMPO/BAIB system in the previous chapters, it was selected as the reagent of choice for the oxidation reaction.



42 **49** **50** **51**

Scheme 18. (**a**) TEMPO, BAIB, DCM, H_2O (**b**) CH_2N_2, CH_3OH, 79 % (2 steps) (**c**) BzCl, pyridine, DCM, –5 °C, 87 %

Remarkably, the TEMPO/BAIB oxidation of diazide **42** to carboxylic acid **49**, which was directly converted in to ester **50** using CH_2N_2 in absolute methanol, proceeded with a excellent yield of 79%. Unlike the earlier TEMPO/BAIB oxidation of acetamido sugars (**8**, **11** and **20**), the reaction did not have a critical time limit and furthermore it was highly reproducible and scalable (up to 5 g). Benzoylation was done with the addition of BzCl into a mixture of compound **50** in pyridine and DCM at 0 °C to get compound **51** in a good yield of 87%. (See Fig. 17 for the X-ray structure of the compound **51**.)

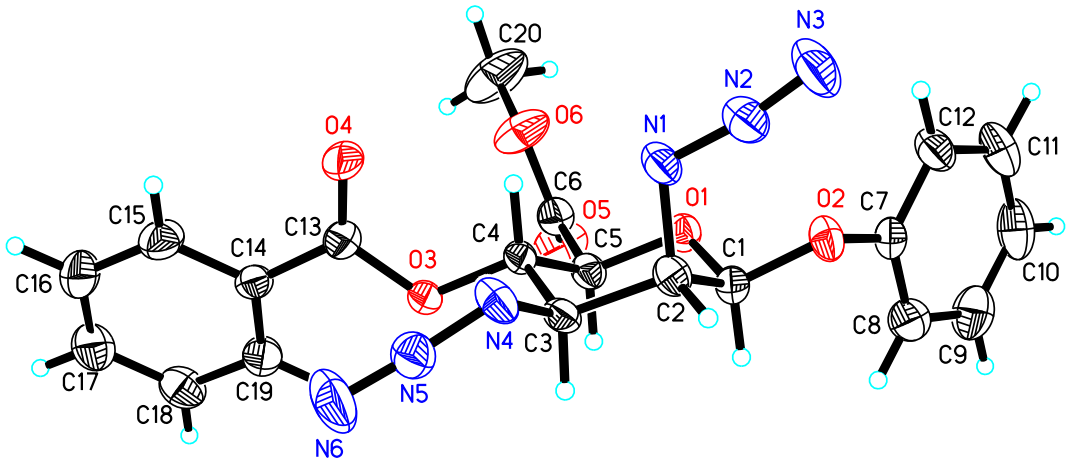
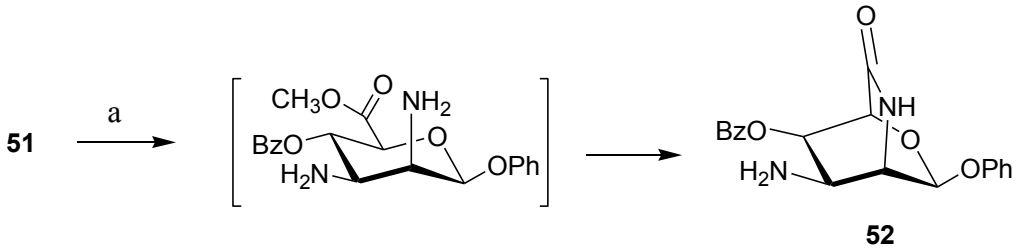
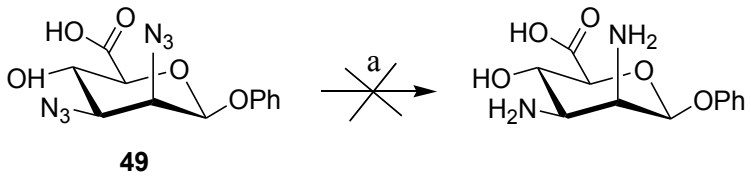


Figure 17. Crystal structure of 51



Scheme 19. Scheme (**a**) Pd/C, H_2,CH_3OH

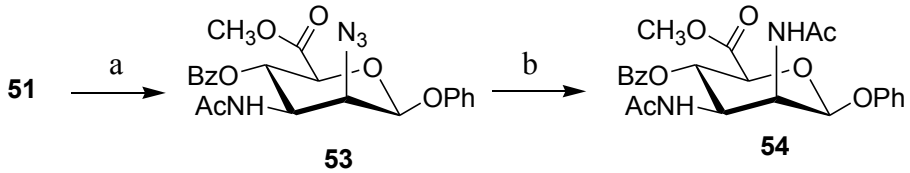
The reduction of **51** using Pd/C and H_2 resulted in cyclisation of the diamine product in to δ-lactam **52**. The side reaction proceeded by simple displacement of the methoxy group by the amino group at the C-2 position.



49

Scheme 20. (**a**) Pd/C, H_2,CH_3OH

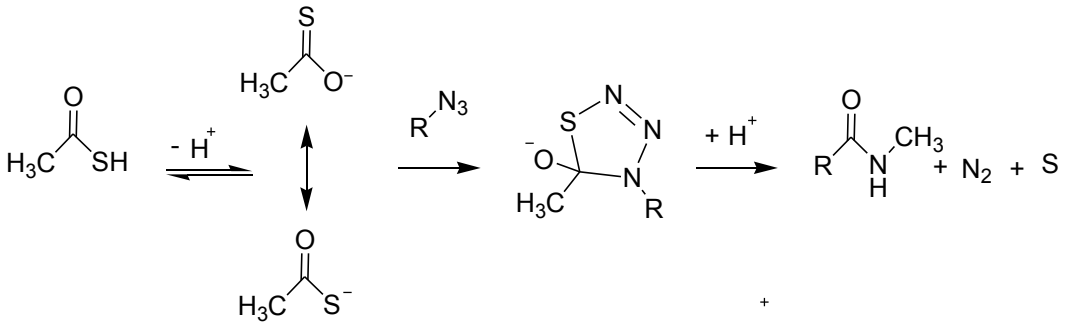
To avoid this problem, direct reduction of the carboxylic acid **49** was tried to reduce the chance of cyclisation due to the poor leaving group ability of the OH group in the carboxylic acid. However, the reaction, which was carried out using Pd on activated charcoal in an H_2 atmosphere, was non-reactive. Another problem with the reaction was the purification of its starting material **49**. The carboxylic acid compound could not be completely purified even after repeated attempts using column chromatography (three times). So, considering the practical difficulty in the whole process, further trials of the reaction were not continued.



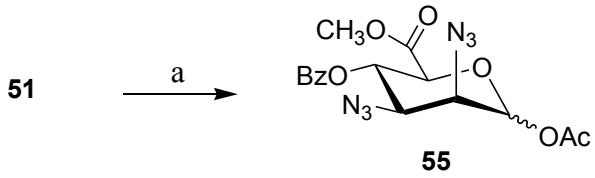
53 **54**

Scheme 21. (**a**) Thioacetic acid, 2,6-lutidine, 1,4-dioxane, 100 °C, 70 % (**b**) Raney Ni, H_2, Ac_2O, EtOAc/MeOH, 83 %

To overcome the problem of cyclisation, the azido group at the C-3 position of compound **51** was directly and selectively converted to an acetamido group by heating the substance with thioacetic acid, 2,6-lutidine in 1,4-dioxane at 100 °C for 24 hours.[84] The reaction proceeded through a cyclo addition mechanism, where the azido group was directly converted to the acetamido group without the formation of the free amino group (Scheme 21). The azido group at the C-2 position was non-reactive, probably due to inadequate space for the cyclo addition mechanism to take place. The reaction proceeded with a yield of 70%, producing compound **53** with about 10% of the recovered starting material **51** along with 10% of compound **54** (product of the next reaction). The partially reduced product **53** could be used as a glycosyl donor for glycosylation reactions with a non-participating azido group at the C-2 position. Finally, the conversion of the azido group into an acetamido group[85] was carried out using Raney nickel,[86] H_2 and Ac_2O (in situ reduction-acetylation) in a mixture of EtOAc/MeOH to give compound **53** in 83% yield. Surprisingly, the reaction without the use of Ac_2O did not show any conversion (to the amine).



Scheme 22. Mechanism of thioacid cyclo addition.



Scheme 23. (**a**) Ac_2O, $HClO_4$ (70%), 25 %

Finally, acetolysis of the phenyl group at the anomeric position was performed using a catalytic amount of $HClO_4$ (70%) in Ac_2O to give the final product **55** in 25% yield. Different catalysts, such as 0.3% H_2SO_4, 10% H_2SO_4 with silica, 10% PTSA, TMSCl, $BF_3.Et_2O$ and TFA,[87] as reported in literature,[88] were tried to improve the yield, but were not successful.

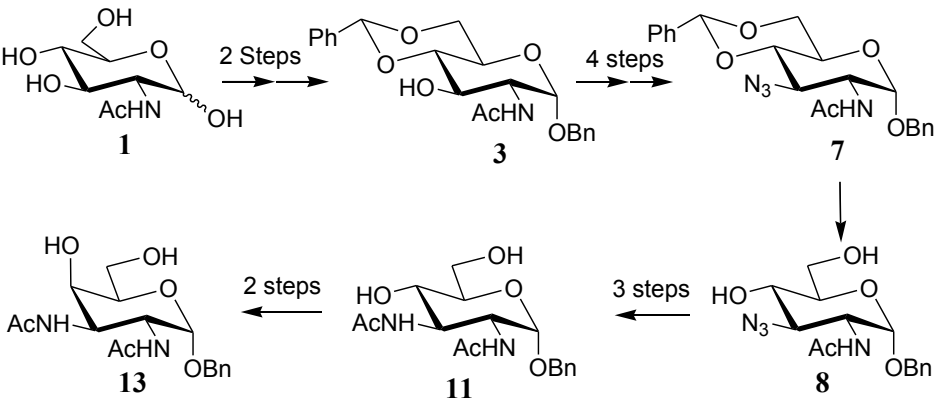
2.3.4 Summary

Overall, the preparation of methyl(acetyl 2,3-diazido-2,3-dideoxy-4-benzoyl-β-D-mannopyranoside)uronate proceeded with good novelty and outcomes. The preparation of an epoxide ring system in sugars, which is a challenging task, was achieved through many initial probing reactions. The preparation was performed in high yield and in a large scale in comparison to the literature methods. Subsequent epoxide ring opening reactions were also performed with good novelty by using both compounds of the isomeric mixture as the raw material for subsequent reactions. The most challenging of all, the oxidation reaction, was dealt with carefully, with the knowledge acquired from earlier reactions of glucose and galactose isomers.

3. Summary and outlook

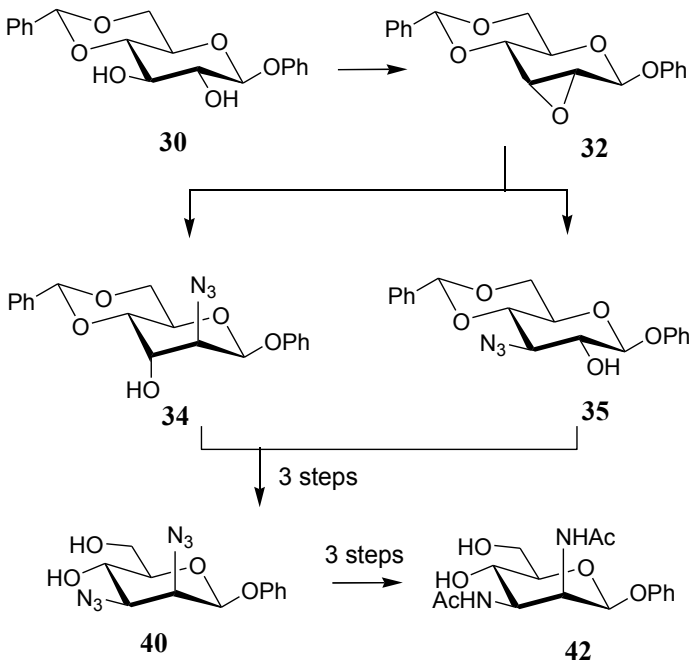
The synthesis of *glucose*, *galactose* and *mannose* derivatives of 2,3-diacetamido uronates was initiated with the preparation of the corresponding 2,3-diacetamido pyranoside derivatives which were subjected to the crucial oxidation reaction.

3.1 Synthesis of 2,3-diacetamido pyranosides



Scheme 24. Synthesis of 2,3-diacetamido *gluco* and *galacto* pyranosides

With careful consideration of the existing methods available in the literature, the preparation of 2,3-diacetamido-2,3-dideoxy-α-D-glucopyranoside was improved by modifications of the existing reaction conditions. The 2,3-diacetamido-2,3-dideoxy-α-D-galactopyranoside was directly prepared from the glucose isomer by simple inversion of the configuration at the C-4 position.

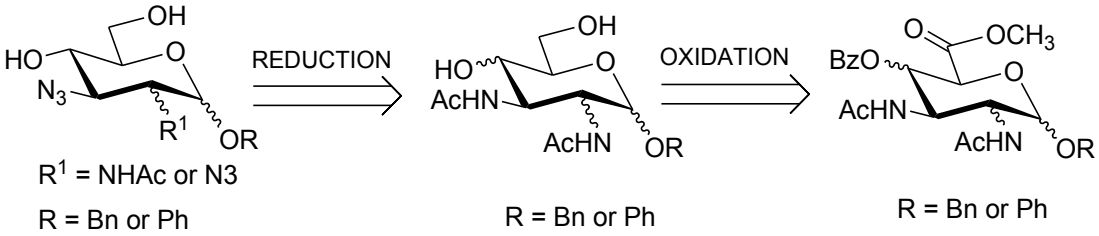


Scheme 24. Synthesis of 2,3-diacetamido mannopyranoside

The synthesis of 2,3-diacetamido mannopyranoside was carried out via the preparation and opening of the crucial epoxide intermediate. The reactions proceeded with good yield and are prepared in good scale.

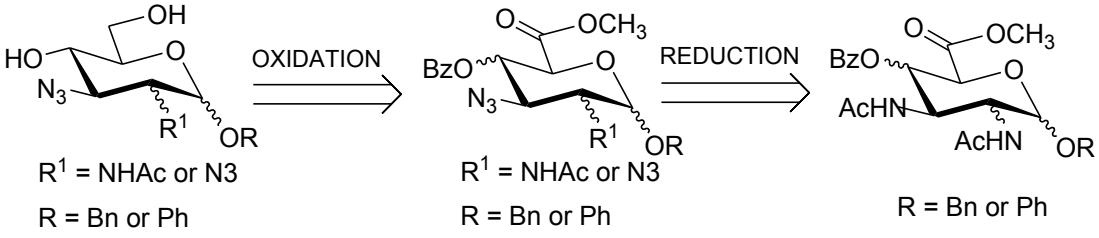
3.2 Oxidation of 2,3-diacetamido pyranosides to uronates

As reported in literature, the crucial oxidation reactions were carried out using the selective TEMPO/BAIB reagent system. After careful optimisation of the reaction conditions, the 2,3-diacetamido glucose and galactose pyranosides underwent the oxidation with good yields, but the scale up of the reactions were only up to 400 mg. Moreover, the reactions in case of 2,3-diacetamido mannose pyranosides were not successful.



Scheme 24. Literature method

After extensive optimisation of the reaction conditions and choice of substrates, improvements were achieved according to the yield and the scale up of the oxidation reactions. Unlike the methods reported in literature, where diacetamido pyranosides were used as substrates for the oxidation, we performed the reactions using mono azido derivatives (for glucose and galactose) and diazido derivative (for mannose). The following reactions of benzoylation and reductive cleavage of anomeric groups also proceeded with good yields. The scale up of the reactions was also good and the total number of steps required to prepare the final compound was also minimized by the modified method. (see Table 1). In general, it was found that the azido groups were better groups for the oxidation reactions than the corresponding acetamido groups



Scheme 25. Modified method

So, herewith, we report an efficient synthetic method for the preparation of 2,3-diacetamido pyranosides, which can be used to prepare biologically important oligosaccharides.

	Literature method			Modified method		
	Yield %	Steps	Scale up (g)	Yield %	Steps	Scale up (g)
Glucose derivative	5.6	11	0.4	12.2	8	2
§Galactose derivative	2.6	13	0.4	9.5	10	2
Mannose derivative	-	-	-	15.3	9	5

Table 1. Comparison of overall yields and total number of steps.

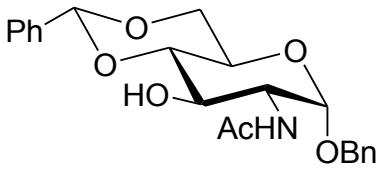
4. Experimental Part

4.1. General methods

Melting points were determined with a Boetius micro-heating plate BHMK 05 (Rapido, Dresden) and were not corrected. Optical rotation was measured for solutions in a 2-cm cell with an automatic GYROMAT polarimeter (Dr.Kernchen Co.). ^{1}H NMR spectra (250.13 MHz, 300.13 MHz, and 500.13 MHz) and ^{13}C NMR spectra (62.9 MHz, 75.5 MHz and 125.8 MHz) were recorded on Bruker instruments AC 250, ARX 300, and AVANCE 500 with $CDCl_3$ or DMSO-d_6 as solvents. The calibration of spectra was carried out on solvent signals ($CDCl_3$: δ^{1}H 7.25, δ^{13}C 77.0; DMSO-d_6: δ^{1}H 2.50, δ^{13}C 39.7). ^{1}H and ^{13}C NMR signals were assigned by DEPT and two-dimensional ^{1}H, ^{1}H COSY, and ^{1}H, ^{13}C correlation spectra (HMBC and HSQC). Mass spectra were recorded on an AMD 402/3 spectrometer (AMD Intectra GmbH). Elemental analysis was performed on a CHNS-Flash-EA-1112 instrument (Thermoquest)**.** For the X-ray structural determination of compounds **37, 38**, **39**, **40**, **41**, **43** and **51** in X8Apex system with CCD area detector was used (λ = 0.71073 Å, graphite monochromator). The structures were deduced by direct methods (Bruker-SHELXTL). The refinement calculations were carried out using the full-matrix least-squares method of Bruker SHELXTL, Vers.5.10, Copyright 1997, Bruker Analytical X-ray Systems. All non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were put into theoretical positions and refined using the riding model. All washing solutions were cooled to 5°C. Reactions were monitored using thin-layer chromatography (TLC, Silica Gel 60, F_{254}, MerckKGaA). The spots were made visible by immersing the TLC plates into a methanolic 5 % v/v H_2SO_4 solution and charring with a heat gun up to 1 min. Preparative flash chromatography was performed by elution from columns of slurry-packed Silica Gel 60 (Merck, 63–200 μm). All solvents and reagents were purified and dried according to standard procedures.[89] After workup, solvents were evaporated at reduced pressure with a rotary evaporator. For low boiling organic solvents (B.P below 120°C), a water bath with 40 °C temperature was used and for higher boiling solvents (such as DMF and DMSO) higher temperatures up to 60 °C was used.

4.2 Synthesis of methyl 2,3-diacetamido-2,3-dideoxy-D-glucuronate

4.2.1. Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (3)



N-Acetyl-D-glucosamine (**1**, 5.09 g, 23.0 mmol) was dissolved in a solution of hydrochloric acid in benzyl alcohol (1.28 M, 43.7 ml, prepared by adding 3.7 mL of acetyl chloride to 40 ml dry benzyl alcohol). After stirring for 3–4 h at 55–60 °C (monitored by TLC, $CHCl_3$-MeOH 3:1)[90,91] the temperature was reduced to 35 °C. Benzaldehyde dimethyl acetal (6.0 mL, 40 mmol) was then added and after stirring overnight at 35 ºC, the reaction mixture was completely solidified. The solid was filtered off and dissolved in a minimum amount of pyridine. Addition of ice cold water gave rise to crystallisation. Finally, the crystalline precipitate was filtered off and co-distilled several times with a mixture of toluene and ethanol (5:1, v/v) until the odour of pyridine disappeared. Recrystallization from ethanol provided **3** (5.05 g, 55%) as colourless crystals.

mp 263–264 °C (EtOH); lit.[92] 263–264 °C.

[α] $^{22}_{D}$ +151.9 ° (*c* 1.0, $CHCl_3$: MeOH 1:1 v/v), **[α]** $^{22}_{D}$ +117 (*c* 1.0, pyridine); Lit.[93] **[α]** $^{20}_{D}$ +108,0 (*c* 1.0, pyridine).

R_f 0.48 (solvent: $CHCl_3$-MeOH 6:1).

^{1}H NMR (300.13 MHz, DMSO-d$_6$) δ = 8.01 (d, 1H, $^3J_{2,NH}$ = 8.0 Hz, NH); 7.48-7.29 (m, 10H, Ph); 5.62 (s, 1H, H-7); 4.81 (d, 1H, $^3J_{1,2}$ = 3.7 Hz, H-1); 4.70 (d, 1H, ^2J = 12.5 Hz), 4.49 (d, ^2J= 12.5 Hz) (CH_2Ph); 4.15 (m, 1H, H-6eq); 3.86 (ddd, 1H, $^3J_{2,3}$ = 10.2 Hz, $^3J_{2,NH}$ = 8.0 Hz, $^3J_{1,2}$ = 3.7 Hz, H-2); 3.79-3.65 (m, 3H, H-3, H-5, H-6ax); 3.52 ('t', 1H, $^3J_{3,4}$ = $^3J_{4,5}$ = 8.8 Hz, H-4); 1.85 (s, 3H, CH_3CO).

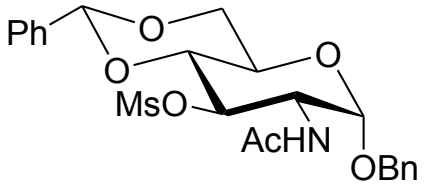
^{13}C NMR (75.5 MHz, DMSO-d$_6$) δ = 169.3 (*C*OCH_3); 137.90, 137.87 (*i*-Ph(7), *i*-CH_2Ph); 129.0 (*p*-Ph(7)); 128.4, 128.2 (*m*-Ph(7), *m*-CH_2Ph); 127.8 (*o*-CH_2Ph); 127.7 (*p*-CH_2Ph); 126.5 (*o*-Ph(7)); 101.0 (C-7); 97.1 (C-1); 82.2 (C-4); 68.7 (*C*H_2Ph); 68.2 (C-6); 67.4 (C-3); 63.0 (C-5); 54.4 (C-2); 22.7 (CO*C*H_3).

$C_{22}H_{25}NO_6$(399.44):

Calcd.: C, 66.15; H, 6.31; N, 3.51.

Found: C, 65.41; H, 5.80; N 3.25.

4.2.2. Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-mesyl-α-D-glucopyranoside (4)



Over the course of 1 h methanesulfonyl chloride (13.9 mL, 180 mmol) was added dropwise to a stirred soln of compound **3** (23.97 g, 60 mmol) in dry pyridine (315 mL) at 0 °C. After stirring for 12 h at that temperature (monitored by TLC, $CHCl_3$-MeOH 6:1), the reaction mixture was slowly poured into ice-water (300 mL). The precipitate was filtered, washed with cold water, and dried. Crystallisation from ethanol provided **4** (23.49 g, 82%) as colourless crystals.

mp 198–199 °C (EtOH); lit.[94] 198–199 °C.

[α] $^{22}_{D}$ +60.5(*c* 1.0, DMSO); Lit.[95] **[α]** $^{25}_{D}$ +76.0 (*c* 1.0, pyridine).

R_f 0.71 ($CHCl_3$-MeOH 6:1).

^{1}H NMR (300.13 MHz, DMSO-d$_6$) δ = 8.21 (d, 1H, $^3J_{2,NH}$ = 9.8 Hz, NH); 7.47-7.30 (m, 10H, Ph); 5.72 (s, 1H, H-7); 4.87 (d, 1H, $^3J_{1,2}$ = 3.7 Hz, H-1); 4.75 (d, 1H, ^2J = 12.5 Hz), 4.56 (d, ^2J = 12.5 Hz) (CH_2Ph); 4.74 (dd, 1H, $^3J_{2,3}$ = 10.5 Hz, $^3J_{3,4}$ = 9.2 Hz, H-3); 4.31 (ddd, 1H, $^3J_{2,3}$ = 10.5 Hz, $^3J_{2,NH}$ = 9.8 Hz, $^3J_{1,2}$ = 3.7 Hz, H-2); 4.21 (m, 1H, H-6eq); 3.95 ('t', 1H, $^3J_{3,4}$ = $^3J_{4,5}$ = 9.2 Hz, H-4); 3.87-3.72 (m, 2H, H-5, H-6ax); 3.12 (s, 3H, SO_2CH_3); 1.88 (s, 3H, CH_3CO).

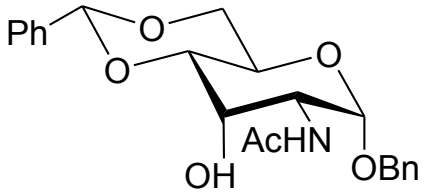
^{13}C NMR (75.5 MHz, DMSO-d$_6$) δ = 169.8 (*C*OCH_3); 137.38, 137.36 (*i*-Ph(7), *i*-CH_2Ph); 129.0 (*p*-Ph(7)); 128.5, 128.29, 128.27 (*m*-Ph(7), *o*-CH_2Ph, *m*-CH_2Ph); 128.0 (*p*-CH_2Ph); 126.1 (*o*-Ph(7)); 100.3 (C-7); 97.6 (C-1); 78.8 (C-4); 78.4 (C-3); 69.3 (*C*H_2Ph); 67.8 (C-6); 63.1 (C-5); 51.2 (C-2); 38.8 (SO_2CH_3); 22.5 (CO*C*H_3).

$C_{23}H_{27}NO_8S$ (477.53)

Calcd.: C, 57.85; H, 5.70; N, 2.93; S, 6.71.

Found: C, 57.49; H, 5.69; N, 2.88; S, 6.80.

4.2.3. Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-allopyranoside (5)



A mixture of mesyl compound **4** (20.06 g, 42.0 mmol) and water free (anhydrous) sodium acetate (20.02 g, 244 mmol) in a solution of ethylene glycol monomethyl ether and water (95: 5, v/v; 250 mL) was stirred under gentle reflux for 48 hours (avoid overheating! TLC: $CHCl_3$-MeOH 6:1). The mixture was then poured into ice water (ca. 300 mL) and the precipitate was filtered off, washed with ice water, co-distilled with toluene (3 x 100 mL) and dried. Crystallisation from ethanol provided **5** (13.01 g, 78%) as colourless crystals.

mp 203–206 °C (EtOH); lit.[95] 203–206 °C;

[α] $_{D}^{22}$ +118.0 (*c* 1.0, DMSO);Lit.[41] **[α]** $_{D}^{20}$ +118.5 (*c* 1.0, DMSO);

R_f 0.66 ($CHCl_3$-MeOH 6:1);

^{1}H NMR (300.13 MHz, DMSO-d$_6$) δ = 7.72 (d, 1H, $^3J_{2,NH}$ = 9.2 Hz, NH); 7.49-7.26 (m, 10H, Ph); 5.65 (s, 1H, H-7); 4.92 (d, 1H, $^3J_{3,OH}$ = 4.2 Hz, OH); 4.73 (d, 1H, $^3J_{1,2}$ = 4.2 Hz, H-1); 4.69 (d, 1H, ^2J = 12.5 Hz), 4.49 (d, ^2J = 12.5 Hz) (C*H*$_2$Ph); 4.20-4.04 (m, 3H, H-2, H-5, H-6eq); 3.96 (br m, 1H, H-3); 3.74-3.65 (m, 2H, H-4, H-6ax); 1.90 (s, 3H, CH_3CO).

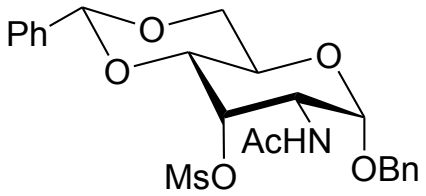
^{13}C NMR (75.5 MHz, DMSO-d$_6$) δ = 169.2 (*C*OCH$_3$); 138.2, 137.9 (*i*-Ph(7), *i*-CH$_2$Ph); 129.0 (*p*-Ph(7)); 128.3, 128.1 (*m*-Ph(7), *m*-CH$_2$Ph); 127.9 (*o*-CH$_2$Ph); 127.6 (*p*-CH$_2$Ph); 126.6 (*o*-Ph(7)); 100.8 (C-7); 96.7 (C-1); 78.4 (C-4); 69.2 (*C*H$_2$Ph); 68.5 (C-6); 66.7 (C-3); 57.4 (C-5); 49.9 (C-2); 22.6 (CO*C*H$_3$).

$C_{22}H_{25}NO_6$ (399.44):

Calcd.: C, 66.15; H, 6.31; N, 3.51.

Found: C, 65.89; H, 6.39; N, 3.09.

4.2.4. Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-mesyl-α-D-allopyranoside (6)



Over the course of 1 h methanesulfonyl chloride (13.7 mL, 138.0 mmol) was added dropwise to a stirred soln of compound **5** (9.19 g, 23.0 mmol) in dry pyridine (140 mL) at 0 °C. After stirring for 12 h at that temperature (monitored by TLC, EtOAc -MeOH 40:1), the reaction mixture was slowly poured into ice-water (150 mL). The aqueous phase was extracted with DCM (3 x 100 mL) and the combined organic phases were washed successively with aq 20% H_2SO_4 (3 x 150 mL); cold water (2 x 100 mL), aq $NaHCO_3$ (3 x 150 mL), ice-water (100 mL), dried, and concentrated. Syrupy crude mesyl derivative **6** was dried under high vacuum for 12 h and then used for the next step without further purification.

Analytical data was obtained by crystallisation of the crude product in ethanol.

mp 118–120 °C (EtOH);

$[\alpha]_D^{22}$ +75.3 (*c* 1.0 $CHCl_3$);

R_f 0.3 (Tol- EtOAc 1.5:1);

^{1}H NMR (500.13 MHz, DMSO-d$_6$) δ = 7.53 (d, 1H, $^3J_{2,NH}$ = 8.7 Hz, NH); 7.47-7.44 (m, 4H, Ph); 7.41-7.35 (m, 5H, Ph); 7.30 (m, 1H, Ph); 5.69 (s, 1H, H-7); 5.04 ('t', 1H, $^3J_{2,3} = {}^3J_{3,4}$ = 2.8 Hz, H-3); 4.85 (d, 1H, $^3J_{1,2}$ = 4.1 Hz, H-1); 4.76 (d, 1H, ^3J = 12.5 Hz); 4.62 (d, 1H, ^2J = 12.5 Hz), (C*H*$_2$Ph); 4.36 (m, 1H, H-2); 4.14 (dd, 1H, $^2J_{6eq,6ax}$ = 10.0 Hz, $^3J_{5,6eq}$ = 5.0 Hz, H-6$_{eq}$); 4.04 (dd, 1H, $^3J_{4,5}$ = 10.0 Hz, $^3J_{3,4}$ = 2.8 Hz, H-4); 3.99 (d't', 1H, $^3J_{4,5} = {}^3J_{5,6ax}$ = 10.0 Hz, $^3J_{5,6eq}$ = 5.0 Hz, H-5); 3.72 ('t', 1H, $^2J_{6eq,6ax} = {}^3J_{5,6ax}$ = 10.0 Hz, H-6$_{ax}$); 3.09 (s, 3H, SO_2CH_3); 1.92 (s, 3H, CH_3CO).

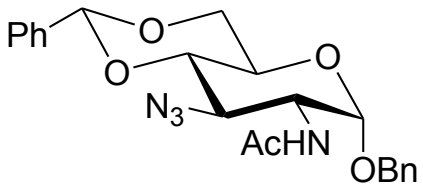
^{13}C NMR (125.8 MHz, DMSO-d$_6$) δ = 169.8 (*C*OCH_3); 137.9, 137.5 (*i*-Ph(7), *i*-CH_2Ph); 129.0, 127.5 (*p*-Ph(7), *p*-CH_2Ph); 128.3, 128.2, 127.5, 126.3 (*o*-Ph(7), *o*-CH_2Ph, *m*-Ph(7), *m*-CH_2Ph); 95.6 (C-1); 76.2 (C-3); 74.8 (C-4); 69.1 *C*H$_2$Ph); 68.1 (C-6); 58.0 (C-5); 48.5 (C-2); 38.6 (SO_2CH_3); 22.5 (CO*C*H$_3$).

$C_{23}H_{27}NO_8S$ (477.53):

Calcd.: C, 57.85; H, 5.70; N, 2.93; S, 6.71.

Found: C, 57.52; H, 5.64; N, 2.91; S, 6.75.

4.2.5. Benzyl 2-acetamido-3-azido-4,6-*O*-benzylidene-2,3-dideoxy-α-D-glucopyranoside (7)



Carefully dried crude compound **6** (10.03 g; 21.0 mmol) was dissolved in dry DMF (140 mL) and sodium azide (13.65 g, 210 mmol) and TBAHS (tetrabutylammonium hydrogen sulphate) (7.13 g, 21.0 mmol) was added. The suspension was stirred vigorously at 120 ºC for two hours (monitored by TLC: Tol-EtOAc 1:2). The reaction mass was concentrated and the residue was dissolved in DCM (400 mL). The organic solution was washed with water (3 x 150 mL), dried and concentrated. Crystallisation from ethanol provided compound **7** (5.79 g, 65%, 2 steps) as colourless crystals.

mp 244–245 °C (EtOH); lit.[41] 244–245 °C; lit.[96] 248–249 °C;

$[\alpha]_D^{22}$ +97.0(*c* 0.9, DMSO); lit. [41] $[\alpha]_D^{20}$ +97.0 (*c* 1.0, DMSO);

R_f 0.69 ($CHCl_3$-MeOH 6:1);

^{1}H NMR (500.13 MHz, DMSO-d$_6$) δ = 8.28 (d, 1H, $^3J_{2,NH}$ = 8.2 Hz, NH); 7.45-7.35 (m, 9H, Ph); 7.31 (m, 1H, Ph); 5.73 (s, 1H, H-7); 4.83 (d, 1H, $^3J_{1,2}$ = 3.2 Hz, H-1); 4.74 (d, 1H, ^2J = 12.3 Hz), 4.53 (d, 1H, ^2J = 12.3 Hz), (CH_2Ph); 4.19 (m, 1H, H-6eq); 3.95-3.86 (m, 2H, H-2, H-5); 3.82-3.75 (m, 3H, H-3, H-4, H-6ax); 1.86 (s, 3H, CH_3CO).

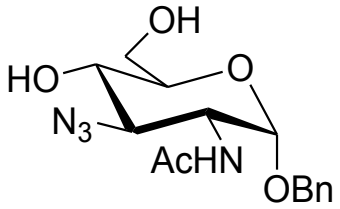
^{13}C NMR (125.8 MHz, DMSO-d$_6$) δ = 169.4 (*C*OCH_3); 137.6, 137.4 (*i*-CH_2Ph, *i*-Ph(7)); 129.1 (*p*-Ph(7)); 128.4, 128.3, 127.9, 126.1 (*o*-CH_2Ph, *m*-CH_2Ph, *o*-Ph(7), *m*-Ph(7)); 127.8 (*p*-CH_2Ph); 100.6 (C-7); 96.5 (C-1); 79.7 (C-4); 68.0 (C-6); 63.1 (C-3); 60.0 (C-5); 51.8(C-2); 22.6 (CO*C*H_3).

$C_{22}H_{24}N_4O_5$ (424.45):

Calcd.: C, 62.25; H, 5.70; N, 13.20.

Found: C, 62.03; H, 5.26; N, 13.08.

4.2.6. Benzyl 2-acetamido-3-azido-2,3-dideoxy-α-D-glucopyranoside (8)



Compound **7** (4.24 g, 10 mmol) was dissolved in aq 80% acetic acid (150 mL) and stirred at 90 ºC. After 45 min (monitored by TLC: $CHCl_3$-MeOH 6:1), the reaction mixture was diluted with toluene (100 mL) and concentrated. Following repeated co-distillation with toluene (3 x 100 mL) the residue was purified by flash chromatography (eluent gradient MeOH 0→ 25% in $CHCl_3$) to provide **8** (2.65g, 79%) as colourless crystals.

mp 195-196 °C; lit. [97] 195–197 °C;

[α]$_D^{22}$ +130 (*c* 1.0, $CHCl_3$-MeOH 1 :1 v/v), lit.[97] **[α]**$_D^{20}$ +128 (*c* 1.0, $CHCl_3$-MeOH 1 :1);

R_f 0.16 ($CHCl_3$-MeOH 6:1);

^{1}H NMR (300.13 MHz, DMSO-d$_6$) δ = 8.21 (d, 1H, $^3J_{2,NH}$ = 8.0 Hz, NH); 7.43-7.76 (m, 5H, Ph); 5.68 (d, 1H, $^3J_{4,OH}$ = 7.0 Hz, OH(4)); 4.72 (d, 1H, $^3J_{1,2}$ = 2.7 Hz, H-1); 4.69 (d, 1H, ^2J = 12.4 Hz), 4.45 (d, 1H, ^2J = 12.4 Hz), (CH_2Ph); 4.65 (t, 1H, $^3J_{6,OH}$ = 5.7 Hz OH(6)); 3.75-3.60 (m, 3H, H-2, H-3, H-6a); 3.57-3.48 (m, 2H, H-5, H-6b); 3.32 (m, 1H, H-4); 1.85 (s, 3H, CH_3CO).

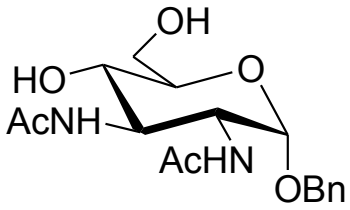
^{13}C NMR (75.5 MHz, DMSO-d$_6$) δ = 169.4 (*C*OCH_3); 137.8 (*i*-Ph); 128.4 (*m*-Ph); 127.8 (*o*-Ph); 127.7 (*p*-Ph); 95.5 (C-1); 73.2 (C-5); 69.4 (C-4); 68.2 (*C*H_2Ph); 64.0 (C-3); 60.5 (C-6); 51.5 (C-2); 22.6 (CO*C*H_3).

$C_{15}H_{20}N_4O_5$ (336.34):

Calcd.: C, 53.56; H, 5.99; N, 16.66.

Found: C, 53.29; H, 5.35; N, 16.42.

4.2.7. Benzyl 2,3-diacetamido-2,3-dideoxy-α-D-glucopyranoside (11)



A solution of compound **7** (4.24 g, 10.0 mmol) in aq 80% acetic acid (150 mL) was heated at 90 ºC for 45 min (monitored by TLC: $CHCl_3$-MeOH 6:1). The reaction mixture was diluted with toluene (100 mL) and concentrated. After repeated co-distillation with toluene (3 x 100 mL) the crude compound **7** was used without further purification for the next step. To a solution of crude **8** in methanol (250 mL) 10% palladium-on charcoal (ca. 1.0 g) was added. The suspension was stirred for 2 h at room temperature under an atmosphere of hydrogen (monitored by TLC: $CHCl_3$-MeOH 5:1). Then, the reaction mixture was filtered over Celite, eluted with MeOH and the combined filtrates were concentrated. Freshly distilled acetic anhydride (12.0 mL, 115 mmol) was added at 0 °C to a stirred soln of the residue **9** in dry pyridine (36 mL). After stirring for 2 h at 0 °C (monitored by TLC: $CHCl_3$-MeOH 10:1), the reaction mixture was poured into ice water (200 mL). The aqueous layer was extracted with DCM (3 x 50 mL). The combined extracts were washed successively with aq 15% $NaHSO_4$ (3 x 50 mL), water (70 mL), aq NaHCO3 (3 x 50 mL), water (70 mL), dried and concentrated. After drying under high vacuum for 3 h the residue **10** was dissolved in dry methanol (30 mL) and sodium methoxide (0.5 M in methanol, 2 mL) was added. After stirring for 2 h at RT (monitored by TLC: $CHCl_3$-MeOH 5:1), the reaction mixture was neutralised with IRC-120 (H^+) resin, filtered and concentrated. Flash Chromatography (eluent gradient MeOH 0 → 15% in $CHCl_3$) provided compound **11** (1.93 g, 55%) as colourless crystals.

mp 267–268 °C (EtOH); lit.[40] 267–268 °C (EtOH);

$[\alpha]_D^{22}$ +146.3 (*c* 1.0, DMSO); lit.[40] $[\alpha]_D^{20}$ +146.5 (*c* 1.0, DMSO);

R_f 0.4 ($CHCl_3$-MeOH 5:1);

^{1}H NMR (500.13 MHz, DMSO-d$_6$) δ = 7.71 (d, 1H, $^3J_{3,NH}$ = 9.0 Hz, NH(3); 7.44 (d, 1H, $^3J_{2,NH}$ = 8.5 Hz, NH(2)); 7.42 (m, 2H, *o*-Ph); 7.38 (m, 2H, *m*-Ph); 7.30 (m, 1H, *p*-Ph); 4.96 (d, 1H, $^3J_{4,OH}$ = 6.3 Hz, OH(4)); 4.71 (d, 1H, $^3J_{1,2}$ = 3.5 Hz, H-1); 4.70 (d, 1H, ^2J = 12.3 Hz, CH_2Ph); 4.56 (t, 1H, $^3J_{6,OH}$ = 6.0 Hz, OH(6)); 4.45 (d, 1H, ^2J = 12.3 Hz CH_2Ph); 4.00 (d‘t’, 1H, $^3J_{2,3}$ = 11.7 Hz, $^3J_{3,4}$ = 9.5 Hz, $^3J_{3,NH}$ = 9.0 Hz, H-3); 3.81 (ddd, 1H, $^3J_{2,3}$ = 11.7 Hz, $^3J_{2,NH}$

= 8.5 Hz, $^3J_{1,2}$ = 3.5 Hz, H -2); 3.65 (m, 1H, H-6a); 3.55-3.48 (m, 2H, H-5, H-6a); 3.29 (d't', 1H, $^3J_{3,4}$ = $^3J_{4,5}$ = 9.5 Hz, $^3J_{4,OH}$ = 6.3 Hz, H-4); 1.80 (s, 3H, CH_3CO).

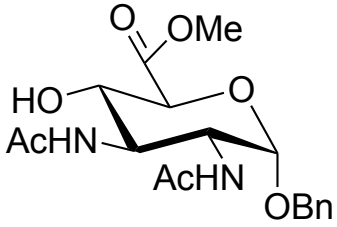
^{13}C NMR (125.8 MHz, DMSO-d$_6$) δ = 170.5, 169.7 (*C*OCH$_3$); 138.0 (*i*-Ph); 128.4 (*m*-Ph); 128.4 (*o*-Ph); 127.7 (*p*-Ph); 95.6 (C-1); 73.7 (C-5); 68.4 (C-4); 68.1 (*C*H$_2$Ph); 60.9 (C-6); 52.4 (C-2); 51.7 (C-3); 23.1, 22.6 (CO*C*H$_3$).

$C_{17}H_{24}N_2O_6$ (352.38):

Calcd.: C, 57.94; H, 6.86; N, 7.95.

Found: C, 57.61; H, 6.97; N, 7.79.

4.2.8. Methyl(benzyl 2,3-diacetamido-2,3-dideoxy-α-D-glucopyranoside)uronate (13)



BAIB (bis(acetoxy)iodobenzene) (330 mg, 1.0 mmol)was added to a mixture of **11** (100 mg, 0.28 mmol) and TEMPO (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl) (8.8 mg, 0.06mmol) in 3 mL DCM/H_2O (ratio 3:1) at RT under stirring. The reaction was stirred for another 6 hours (monitored by TLC: $CHCl_3$-MeOH-AA 10:4:1). After the reaction was complete, under ice cooling, 1 mL CH_3OH and further 2.5 mL 1 M $Na_2S_2O_3.5H_2O$ was added slowly. The layers were separated and the aqueous phase was acidified to P_H 3 with 1M HCl and extracted with ethyl acetate. Then, the combined organic layer was dried with $MgSO_4$ and evaporated under vacuum. The crude product **12** was taken directly to the next step with CH_2N_2 in MeOH. After completion of the reaction (monitored by TLC: $CHCl_3$-MeOH-AA 10:4:1), the excess CH_2N_2 was quenched with acetic acid and the reaction mass was concentrated and purified by column chromatography (Eluent Gradient: MeOH 0 → 20% in $CHCl_3$) to provide **13** (75.5mg, 68.14 %) as colourless crystals.

mp 258-260 °C;

***R*f** 0.27 (EtOAC-MeOH 5:1);

[α] $^{22}_{D}$ 127.7 ° (*c* 1.0, $CHCl_3$);

^{1}H NMR (300.13 MHz, DMSO-d$_6$) δ = 7.77 (d, 1H, $^3J_{3,NH}$ = 8.8 Hz, NH(3)); 7.58 (d, 1H, $^3J_{2,NH}$ = 8.5 Hz, NH(2)); 7.45-7.27 (m, 5H, Ph); 5.41 (d, 1H, $^3J_{4,OH}$ = 7.0 Hz, OH); 4.76 (d, 1H, $^3J_{1,2}$ = 3.1 Hz, H-1); 4.69 (d, 1H, ^2J = 12.5 Hz), 4.49 (d, ^2J = 12.5 Hz), (C*H*$_2$Ph); 4.09-3.84 (m,

3H, H-2, H-3, H-5); 3.69 (s, 3H, OCH_3); 3.58 (d't', 1H, $^3J_{3,4} = {}^3J_{4,5} = 9.8$ Hz, $^3J_{4,OH} = 7.0$ Hz, H-4); 1.80, 1.80 (2s, 6H, CH_3CO).

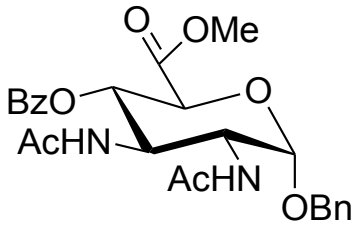
^{13}C NMR (75.5 MHz, DMSO-d_6) δ = 170.2 (COO); 169.85, 169.82 (*C*OCH_3); 137.5 (*i*-Ph); 128.4 (*m*-Ph); 128.0 (*o*-Ph); 127.9 (*p*-Ph); 96.4 (C-1); 72.6 (C-5); 69.7 (C-4); 68.9 (*C*H_2Ph); 52.2 (OCH_3); 51.8 (C-2); 51.1 (C-3); 23.1, 22.6 (CO*C*H_3).

$C_{18}H_{24}N_2O_7$(326.12):

Calcd.:C, 56.83; H, 6.36; N, 7.36;

Found: C, 56.67; H, 6.27; N, 7.24;

4.2.9. Methyl(benzyl 2,3-diacetamido-4-*O*-benzoyl-2,3-dideoxy-α-D-glucopyranoside)uronate (14)



Over the course of 1 h benzoyl chloride (0.3 mL, 2.5 mmol) was added dropwise to a stirred soln of compound **13** (380 mg, 1.0 mmol), dry pyridine (6 mL) in dry DCM(6 mL) at -10 °C. After stirring for 2 h at -5 °C (monitored by TLC, $CHCl_3$: MeOH 5:1), the reaction mixture was slowly poured into ice-water (15 mL). The aqueous phase was extracted with DCM (3 x 6 mL), and the combined organic phases were washed successively with aq 15% $NaHSO_4$ (3 x 6 mL); aq $NaHCO_3$ (3 x 6 mL) and ice-water (6 mL). The crude solution was dried, concentrated and purified by column chromatography (Eluent Gradient: MeOH 0 → 5 % in $CHCl_3$) to give **14** (324.28 mg, 67 %) as colourless crystals.

mp.: 126-127°C (EtOAc/Heptane);

***R*f**: 0.37 ($CHCl_3$-MeOH 6:1);

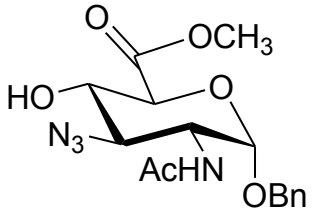
[α] $^{22}_{D}$ +29.2° (*c* 1.0, $CHCl_3$);

^{1}H NMR (500.13 MHz, DMSO-d_6) δ = 7.95 (d, 1H, $^3J_{2,NH}$ = 8.8 Hz, NH; 7.93 (d, 1H, $^3J_{3,NH}$ = 9.8 Hz, NH; 7.88 (m, 2H, *o*-Bz); 7.66 (m, 1H, *p*-Bz); 7.52 (m, 2H, *m*-Bz); 7.44 (m, 2H, *o*-CH_2Ph); 7.37 (m, 2H, *m*-CH_2Ph); 7.31 (m, 1H, *p*-CH_2Ph); 5.03 ('t', 1H, $^3J_{3,4} = J_{4,5} = 10$ Hz, H-4); 4.93 (d, 1H, $^3J_{1,2}$ = 3.5 Hz, H-1); 4.76 (d, 1H, ^2J= 12.5 Hz), 4.57 (d, 1H, ^2J= 12.5 Hz), (C*H*$_2$Ph); 4.49 (d't', 1H, $^3J_{2,3}$ = 12.0 Hz, $^3J_{3,4}$ = 10.0 Hz, $^3J_{3,NH}$ = 9.8 Hz, H-3); 4.34 (d, 1H, $^3J_{4,5}$ = 10.0 Hz, H-5); 4.14 (ddd, 1H, $^3J_{2,3}$ = 12.0 Hz, $^3J_{2,NH}$ = 8.5 Hz, $^3J_{1,2}$ = 3.5 Hz, H-2); 3.53 (s, 3H, OCH_3); 1.83, 1.66 (2s, 6H, CH_3CO).

^{13}C NMR (125.8 MHz, DMSO-d$_6$) δ = 170.0, 169.8 (CH_3CO); 168.4 ($COOCH_3$); 165.3 (PhCOO9; 137.4 (*i*-CH_2Ph); 129.4 (*o*-Bz); 129.2 (*i*-Bz); 128.9 (*m*-Bz); 128.4 (*m*-CH_2Ph); 128.0 (*o*-CH_2Ph); 127.9 (*p*-CH_2Ph); 71.6 (C-4); 69.4 (CH_2Ph); 69.1 (C-5); 52.4 (OCH_3); 50.9 (C-2); 48.2 (C-3); 22.9, 22.5 ($CO CH_3$).

$C_{25}H_{28}N_2O_8$(484.18):
Calcd.: C, 61.97; H, 5.83; N, 5.78;
Found: C, 62.23; H, 5.91; N, 5.75;

4.2.10. Methyl(benzyl 2-acetamido-3-azido-2,3-dideoxy-α-D-glucopyranoside)uronate (16)



BAIB (bis(acetoxy)iodobenzene) (2.37 g, 7.38 mmol) was added to a mixture of **8** (1 g, 2.97 mmol) and TEMPO (2,2,6,6-tetramethyl piperidinyloxy) (92.5 mg, 0.59 mmol) in 30 mL DCM/H_2O (ratio 3:1) at 0 ºC under stirring. The reaction was stirred for 8 hours at RT (monitored by TLC: $CHCl_3$:MeOH:AA 20:1:0.5). 10 mL MeOH and further 25 mL 1 M $Na_2S_2O_3.5H_2O$ was added slowly at 0 ºC. The layers were separated and the aqueous phase was acidified to P_H 3 with 1M HCl and extracted with ethyl acetate. Then, the combined organic layers were dried with Na_2SO_4 and evaporated under vacuum. The crude product **15** was taken directly to the next step with CH_2N_2 in MeOH. After completion of the reaction (monitored by TLC: $CHCl_3$:MeOH:AA 20:1:0.5), excess CH_2N_2 was quenched with acetic acid, the reaction mass was evaporated and co-distilled with toluene and purified by column chromatography (eluent gradient MeOH 0 → 2.5% in $CHCl_3$) to provide **16** (853.2 mg, 79 %) as colourless crystals.

mp: 156-157°C;

***R*f**: 0.3; ($CHCl_3$:MeOH 30:1);

[α] $^{22}_{D}$ + 122.8 ° (*c* 1.0, $CHCl_3$);

^{1}H NMR (500.13 MHz, DMSO-d$_6$) δ = 8.26 (d, 1H, $^3J_{2,NH}$ = 8.0 Hz, NH); 7.40-7.30 (m, 5H, Ph); 6.06 (d, 1H, $^3J_{4,OH}$ = 7.6 Hz, OH); 4.81 (d, 1H, $^3J_{1,2}$ = 3.2 Hz, H-1); 4.69 (d, 1H, ^2J = 12.5

Hz), 4.51 (d, ^{2}J = 12.5 Hz), (CH_2Ph); 4.07 (d, 1H, $^{3}J_{4,5}$ = 9.8 Hz, H-5); 3.74 (ddd, 1H, $^{3}J_{2,3}$ = 11.3 Hz, $^{3}J_{2,NH}$ = 8.0 Hz, $^{3}J_{1,2}$ = 3.2 Hz, H-2); 3.71 (s, 3H, OCH_3); 3.69 (dd, 1H, $^{3}J_{2,3}$ = 11.3 Hz, $^{3}J_{3,4}$ = 9.1 Hz H-3); 3.53 (d't', 1H, $^{3}J_{4,5}$ = 9.8 Hz, $^{3}J_{3,4}$ = 9.1 Hz, $^{3}J_{4,OH}$ = 7.6 Hz, H-4); 1.84 (s, 3H, CH_3CO).

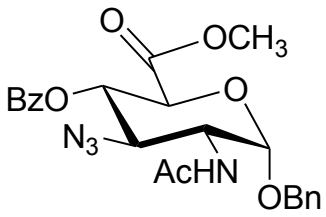
^{13}C NMR (125.8 MHz, DMSO-d_6) δ = 169.4 (*C*OCH_3); 169.2 (*C*$OOCH_3$); 137.4 (*i*-Ph); 128.5 (*m*-Ph); 127.9 (*p*-Ph); 127.8 (*o*-Ph); 96.2 (C-1); 71.8 (C-5); 71.0 (C-4); 69.1 (*C*H_2Ph); 63.1 (C-3); 52.3 (OCH_3); 51.2 (C-2); 22.6 (CO*C*H_3).

$C_{16}H_{20}N_4O_6$(364.35):

Calcd.: C, 52.74; H, 5.53; N, 15.38;

Found:C, 52.31 H, 5.17; N, 15.03;

4.2.11 Methyl(benzyl 2-acetamido-3-azido-4-*O*-benzoyl-2,3-dideoxy-α-D-glucopyranoside)uronate (17)



In the course of 1 h benzoyl chloride (0.88mL, 7.56 mmol) was added dropwise to a stirred soln of compound **16** (1.13 g, 3.09 mmol) in dry pyridine (11.25 mL) in DCM (22.5 mL) at 0 °C. After stirring for 4 h at 0 °C (monitored by TLC: $CHCl_3$:MeOH40:1). DCM (20 mL) was added to the reaction mass and the organic solution was washed with 15% cold $NaHSO_4$ (3 X 15 mL), aq $NaHCO_3$ (3 x 15 mL), brine solution (15 mL) and concentrated under vacuum. After repeated co-distillation with toluene (3 x 20 mL) to remove adhering pyridine the residue was purified by flash chromatography (Eluent Gradient: EtOAc 0 → 120 % in PE) to provide **17** (1.14 g, 89 %) as colourless crystals.

mp: 160-162 °C;

***R*f**: 0.2 (PE-EtOAc 1:1);

[α] $^{22}_{D}$ + 25.4 ° (*c* 1.0, $CHCl_3$);

^{1}H NMR (250.13 MHz, DMSO-d$_6$) δ = 8.36 (d, 1H, $^3J_{2,NH}$ = 8.2 Hz, NH); 8.02 (m, 2H, *o*-Bz); 7.71 (m, 1H, *p*-Bz); 7.56 (m, 2H, *m*-Bz); 7.48-7.30 (m, 5H,Ph(1); 5.13 ('t', 1H, $^3J_{4,5}$ = 10.0 Hz, $^3J_{3,4}$ = 9.6 Hz, H-4); 4.98 (d, 1H, $^3J_{1,2}$ = 3.3 Hz, H-1); 4.77 (d, 1H, ^2J = 12.4 Hz), 4.58 (d, 1H, ^2J = 12.4 Hz), CH_2Ph); 4.46 (d, 1H, $^3J_{4,5}$ = 10.0 Hz, H-5); 4.16 (dd, 1H, $^3J_{2,3}$ = 11.4 Hz, $^3J_{3,4}$ = 9.6 Hz, H-3); 4.02 (ddd, 1H, $^3J_{2,3}$ = 11.4 Hz, $^3J_{2,NH}$ = 8.2 Hz, $^3J_{1,2}$ = 3.3 Hz, H-2); 3.53 (s, 3H, OCH_3); 1.88 (s, 3H, CH_3CO).

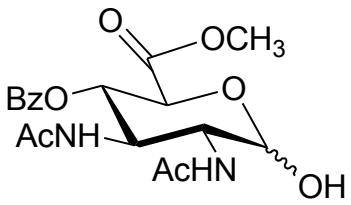
^{13}C NMR (62.9 MHz, DMSO-d$_6$) δ = 169.6 (*C*OCH_3); 168.0 (*C*$OOCH_3$); 164.9 (Ph*C*OO); 137.3 (*i*-Ph(1)); 134.2 (*p*-Bz); 129.7 (*o*-Bz); 129.1 (*m*-Bz); 128.6 (*i*-Bz); 128.5 (*m*-Ph(1)); 127.9 (*o*-Ph(1)); 127.9 (*p*-Ph(1)); 96.1 (C-1); 71.0 (C-4); 69.6 (CH_2Ph); 68.3 (C-5); 60.4 (C-3); 52.6 (OCH_3); 51.2 (C-2); 22.6 (CO*C*H_3).

$C_{23}H_{24}N_4O_7$(468.46):

Calcd.: C, 58.97; H, 5.16; N, 11.96;

Found: C, 58.22; H, 4.62; N, 11.45;

4.2.12 Methyl(2,3-diacetamido-4-*O*-benzoyl-2,3-dideoxy-D-glucopyranoside)uronate 18αβ



To a solution of **17** (200 mg, 0.427 mmol) in dry methanol (3 mL), 10% palladium-on charcoal (ca. 88 mg) and freshly distilled Ac_2O (0.13 mL, 1.359 mmol) was added and the suspension was stirred for 4 hours (monitored by TLC: $CHCl_3$-MeOH 30:1). After completion of the reaction, to the reaction mixture containing the crude product **14**, acetyl chloride (44µL) was added and the suspension was stirred for another 4 hours at room temperature under an atmosphere of hydrogen (monitored by TLC: $CHCl_3$-MeOH 10:1).The reaction mass was filtered through celite, concentrated and purification by column chromatography (MeOH 0→ 7.5 % in $CHCl_3$) provided **18αβ** (151.5 mg, 90 %) as colourless crystals. Analytical data for **14** can be found under Sec. **4.2.9**

mp: 98-100 °C;

***R*f**: 0.59 (C_3:MeOH 6:1);

$[\alpha]_D^{22}$ +57.2° (*c* 1.0, DMSO);

α:

^{1}H NMR (300.13 MHz, DMSO-d$_6$) δ = 7.95-7.81 (m, 3H, *o*-Bz, NH(3); 7.70 (d, 1H, $^3J_{2,NH}$ = 8.9 Hz, NH(2)); 7.66 (m, 1H, *p*-Bz); 7.52 (m, 2H, *m*-Bz); 7.24 (d, 1H, $^3J_{1,OH}$ = 4.0 Hz, OH); 5.10 ('t', 1H, $^3J_{1,OH}$ = 4.0 Hz, $^3J_{1,2}$ = 3.2 Hz, H-1); 5.01 ('t', 1H, $^3J_{3,4}$ = $^3J_{4,5}$ = 10.0 Hz, H-4); 4.48 (d, 1H, $^3J_{4,5}$ = 10.0 Hz, H-5); 4.46-4.40 (m, 1H, H-3); 4.05 (ddd, 1H, $^3J_{2,3}$ = 11.7 Hz, $^3J_{2,NH}$ = 8.9 Hz, $^3J_{1,2}$ = 3.2 Hz, H-2); 3.52 (s, 3H, OCH_3); 1.83, 1.65 (2s, 6H, CH_3CO).

^{13}C NMR (75.5 MHz, DMSO-d$_6$) δ = 169.9, 169.8 (CH_3CO); 168.9 ($COOCH_3$); 165.3 (Ph*C*OO); 133.7 (*p*-Bz); 129.4 (*o*-Bz); 129.4 (*i*-Bz); 128.9 (*m*-Bz); 90.8 (C-1); 71.8 (C-4); 68.4 (C-5); 52.3 (OCH_3); 51.5 (C-2); 48.2 (C-3); 22.9, 22.6 $CO*C*H_3$).

β:

^{1}H NMR (300.13 MHz, DMSO-d$_6$) δ = 7.07 (d, 1H, $^3J_{1,OH}$= 6.6 Hz, OH); 4.79 (dd, 1H, $^3J_{1,2}$ = 8.3 Hz, $^3J_{1,OH}$ = 6.6 Hz, H-1); 3.51 (s, 3H, OCH_3); 1.77, 1.65 (2s, 6H, CH_3CO) (not all signals are given).

^{13}C NMR (75.5 MHz, DMSO-d$_6$) δ = 169.6, 169.4 (CH_3CO); 168.4 ($COOCH_3$); 96.0 (C-1); 72.9, 71.4 (C-4, C-5); 54.5, 52.4 (C-2, C-3); 52.3 (OCH_3); 23.0, 22.8 ($CO*C*H_3$) (not all signals are given).

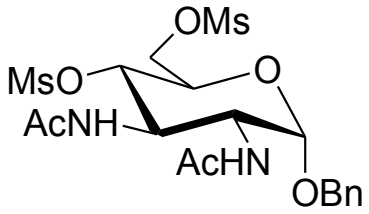
$C_{18}H_{22}N_2O_8$(394.38)

Calcd.: C, 54.82; H, 5.62; N, 7.10;

Found C, 54.39; H, 5.31; N, 6.87;

4.3 Synthesis of Methyl 2,3-diacetamido-2,3-dideoxy-D-galacturonate

4.3.1. Benzyl 2,3-diacetamido-2,3-dideoxy-4,6-*O*-dimesyl-α-D-glucopyranoside (19)



In the course of 30 min methanesulfonyl chloride (4.5 mL, 45.0 mmol) was added dropwise to a stirred soln of compound **11** (1.76 g, 5.0 mmol) in dry pyridine (30 mL) at 0 °C. After stirring for 45 min at 0 °C (monitored by TLC, $CHCl_3$-MeOH 5:1), the reaction mixture was slowly poured into ice-water (100 mL). The aqueous phase was extracted with DCM (3 x 40 mL), and the combined organic phase was washed with aq $NaHCO_3$ (3 x 50 mL), dried and concentrated. After repeated co-distillation with toluene (3 x 50 mL) to remove pyridine, the residue was purified by flash chromatography (eluent gradient MeOH 0 → 15% in $CHCl_3$) to provide **19** (2.01 g, 79%) as colourless crystals

mp 207–208 °C (EtOH); lit.[55] 206–207 °C;

$[\alpha]_D^{22}$ +108.8(*c* 1.0, $CHCl_3$); lit.[55] $[\alpha]_D^{20}$ +108.5(*c* 1.0, DMSO);

R_f 0.52 ($CHCl_3$-MeOH 5:1);

^{1}H NMR (500.13 MHz, DMSO-d$_6$) δ = 7.92 (d, 1H, $^3J_{3,NH}$ = 9.5 Hz, NH(3)); 7.84 (d, 1H, $^3J_{2,NH}$ = 9.1 Hz, NH(2)); 7.45-7.29 (m, 5H, Ph); 4.83 (d, 1H, $^3J_{1,2}$ = 3.3 Hz, H-1); 4.73 (d, 1H, ^2J = 12.0 Hz), 4.52 (d, 1H, ^2J = 12.0 Hz), (C*H*$_2$Ph); 4.50 (br t, 1H, H-4); 4.41 (dd, 1H, ^2J= 11.4 Hz, $^3J_{5,6a}$ = 2.3 Hz, H-6a); 4.31 (dd, 1H, ^2J= 11.4 Hz, $^3J_{5,6b}$ = 4.7 Hz, H-6b); 4.31-4.25 (m, 1H, H-3); 4.09-4.04 (m, 1H, H-2); 4.03 (ddd, 1H, $^3J_{4,5}$ = 10.0 Hz, $^3J_{5,6b}$ = 4.7 Hz, $^3J_{5,6a}$ = 2.3 Hz, H-5); 3.19, 3.17 (2s, 6H, SO_2CH_3); 1.82, 1.79 (2s, 6H, CH_3CO).

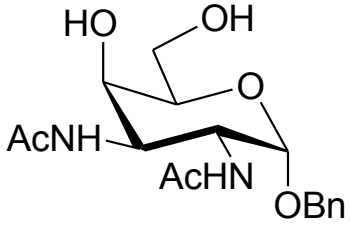
^{13}C NMR (125.8 MHz, DMSO-d$_6$) δ = 170.0, 169.9 (*C*OCH_3); 137.3 (*i*-Ph); 128.4, 128.3 (*o*-Ph, *m*-Ph); 128.0 (*p*-Ph); 95.6 (C-1); 76.1 (C-4); 69.0 (*C*H$_2$Ph); 68.1 (C-6); 67.9 (C-5); 51.2 (C-2); 49.0 (C-3); 38.5, 37.1 (SO_2CH_3); 23.1, 22.4 (CO*C*H$_3$).

$C_{19}H_{28}N_2O_{10}S_2$(508.12):

Calcd.:C, 44.87; H, 5.55; N, 5.51; S, 12.61;

Found: C, 44.99; H, 5.27; N, 5.16; S, 12.33;

4.3.2. Benzyl 2,3-diacetamido-2,3-dideoxy-α-D-galactopyranoside (20)



A mixture of dimesyl compound **19** (2.54 g, 5.0 mmol) and anhydrous sodium acetate (2.46 g, 30 mmol) in a solution of ethylene glycol monomethyl ether and water (95: 5, v/v; 65 mL) was stirred under gentle reflux for 48 hours (avoid overheating! TLC: $CHCl_3$-MeOH 8:1). The mixture was co-distilled with toluene and concentrated. Purification by flash chromatography (eluent gradient MeOH 0 → 15% in $CHCl_3$) provided **13** (1.15 g, 65%) as colourless crystals.

mp 253 °C (EtOH); lit. [55] 250-252 °C (EtOH);

[α] $^{22}_{D}$ +185.1(*c* 1.0, DMSO); lit. [55] **[α]** $^{20}_{D}$ +186.5(*c* 1.0, DMSO);

R_f 0.21 ($CHCl_3$-MeOH 8:1);

^{1}H NMR (500.13 MHz, DMSO-d$_6$) δ = 7.63 (d, 1H, $^3J_{2,NH}$ = 8.5 Hz, NH(2)); 7.55 (d, 1H, $^3J_{3,NH}$ = 8.2 Hz, NH(3)); 7.40 (m, 2H, *o*-Ph); 7.35 (m, 2H, *m*-Ph); 7.29 (m, 1H, *p*-Ph); 4.95 (br s, 1H, OH); 4.74 (d, 1H, $^3J_{1,2}$ = 3.5 Hz, H-1); 4.69 (d, 1H, ^2J = 12.3 Hz, CH_2Ph); 4.63 (br s, 1H, OH); 4.44 (d, 1H, ^2J = 12.3 Hz, CH_2Ph); 4.18 (ddd, 1H, $^3J_{2,3}$ = 12.3 Hz, $^3J_{2,NH}$ = 8.5 Hz, $^3J_{1,2}$ = 3.5 Hz, H-2); 4.09 (ddd, 1H, $^3J_{2,3}$ = 12.3 Hz, $^3J_{3,NH}$ = 8.2 Hz, $^3J_{3,4}$ = 2.5 Hz, H-3); 3.77 (br s, 1H, H-4); 3.72 (dt, 1H, $^3J_{5,6}$ = 6.3 Hz, $^3J_{4,5}$ = 1.0 Hz, H-5); 3.54-3.44 (m, 2H, H-6); 1.81, 1.80 (2s, 6H, CH_3CO).

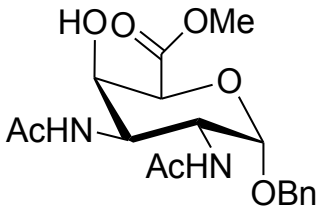
^{13}C NMR (125.8 MHz, DMSO-d$_6$) δ = 170.0, 169.7 (*C*OCH_3); 138.1 (*i*-Ph); 128.4 (*o*-Ph); 127.8 (*m*-Ph); 127.6 (*p*-Ph); 96.0 (C-1); 71.7 (C-5); 68.1 (*C*H_2Ph); 66.2 (C-4); 60.7 (C-6); 49.0 (C-3); 47.3 (C-2); 22.9, 22.7 (CO*C*H_3).

$C_{17}H_{24}N_2O_6$ (352.38):

Calcd.: C, 57.94; H, 6.86; N, 7.95.

Found: C, 57.58; H, 6.72; N, 7.84.

4.3.3. Methyl(benzyl 2,3-diacetamido-2,3-dideoxy-α-D-galactopyranoside)uronate (23)



This compound was prepared from **20** (100 mg, 0.28 mmol) by a procedure similar to that used for the preparation of compound **13**. Purification by column chromatography (Eluent Gradient: MeOH 0 → 20% in $CHCl_3$) provided **23** (75mg, 67.69 %) as colourless crystals.

mp: 257-258 °C;

R_f: 0.26 (EtOAc-MeOH 5:1);

[α] $^{22}_{D}$ +159.5 ° (*c* 1.0, $CHCl_3$);

^{1}H NMR (300.13 MHz, DMSO-d$_6$) δ = 7.77 (d, 1H, $^3J_{CH,NH}$ = 7.5 Hz, NH); 7.67 (d, 1H, $^3J_{CH,NH}$ = 7.0 Hz, NH); 7.40-7.25 (m, 5H, Ph); 5.40 (d, 1H, $^3J_{4,OH}$ = 5.7 Hz, OH); 4.87 (d, 1H, $^3J_{1,2}$ = 2.8 Hz, H-1); 4.67 (d, 1H, ^2J = 12.5 Hz), 4.48 (d, ^2J = 12.5 Hz), (CH_2Ph); 4.23-4.08 (m, 3H, H-2, H-3, H-4); 4.40 (d, 1H, $^3J_{4,5}$ = 1.2 Hz, H-5); 3.65 (s, 3H, OCH_3); 1.81, 1.80 (2s, 6H, CH_3CO).

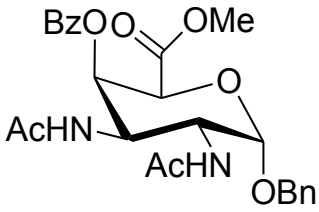
^{13}C NMR (75.5 MHz, DMSO-d$_6$) δ = 170.0 (COO); 169.9, 169.0 (*C*OCH_3); 137.0 (*i*-Ph); 128.4 (*m*-Ph); 127.8 (*o*-Ph); 127.7 (*p*-Ph); 96.5 (C-1); 71.0 (C-5); 69.0 (*C*H_2Ph); 67.1 (C-4); 51.8 (OCH_3); 48.4, 46.5 (C-2, C-3); 22.9, 22.7 (CO*C*H_3).

$C_{18}H_{24}N_2O_7$ (326.12):

Calcd.: C, 56.83; H, 6.36; N, 7.36;

Found: C, 56.97; H, 6.42; N, 7.53;

4.3.4. Methyl(benzyl 2,3-diacetamido-4-*O*-benzoyl-2,3-dideoxy-α-D-galactopyranoside) uronate (24)



This compound was prepared from **23** (380 mg, 0.1 mmol) by a procedure similar to that used for the preparation of compound **14** (reaction monitored by TLC:$CHCl_3$-MeOH 5:1). Purification by flash chromatography (Eluent Gradient: MeOH 0 → 5 % in $CHCl_3$) afforded compound **24** (305.23 mg, 62 %) as a colourless syrup.

mp.: 59 - 61°C (EtOAc/Heptane);

***R*f**: 0.60 ($CHCl_3$-MeOH 6:1);

[α] $^{22}_{D}$ +77.8° (*c* 1.0, $CHCl_3$);

^{1}H NMR (500.13 MHz, DMSO-d$_6$) δ = 8.09 (d, 1H, $^3J_{3,NH}$ = 7.8 Hz, NH(3)); 8.05 (d, 1H, $^3J_{2,NH}$ = 8.2 Hz, NH(2)); 7.94 (m, 2H, *o*-Bz); 7.68 (m, 1H, *p*-Bz); 7.56 (m, 2H, *m*-Bz); 7.42 (m, 2H, *o*-CH_2Ph; 7.37 (m, 2H, *m*-CH_2Ph); 7.31 (m, 1H, *p*-CH_2Ph); 5.72 (dd, 1H, $^3J_{3,4}$ = 2.8

Hz, $^3J_{4,5}$ = 1.6 Hz, H-4); 5.05 (d, 1H, $^3J_{1,2}$ = 3.4 Hz, H-1); 4.78 (d, 1H, $^3J_{4,5}$ = 1.6 Hz, H-5); 4.76 (d, 1H, ^2J = 12.3 Hz), 4.55 (d, 1H, ^2J = 12.3 Hz), (CH_2Ph); 4.47 (ddd, 1H, $^3J_{2,3}$ = 12.5 Hz, $^3J_{3,NH}$ = 7.8 Hz, $^3J_{3,4}$ = 2.8 Hz, H-3); 4.27 (ddd, 1H, $^3J_{2,3}$ = 12.5 Hz, $^3J_{2,NH}$ = 8.2 Hz, $^3J_{1,,2}$ = 3.4 Hz, H-2); 3.52 (s, 3H, OCH_3); 1.81, 1.71 (2s, 6H, CH_3CO).

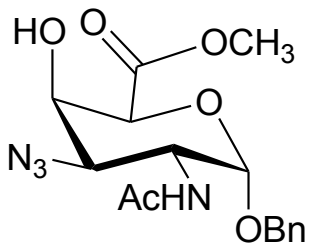
^{13}C NMR (125.8 MHz, DMSO-d$_6$) δ = 170.2, 170.0 (CH_3CO); 168.0 ($COOCH_3$); 165.0 (PhCO); 137.6 (*i*-CH_2Ph); 133.5 (*p*-Bz); 129.7 (*i*-Bz); 129.6 (*o*-Bz); 128.8 (*m*-Bz); 128.4 (*m*-CH_2Ph); 127.9 (*o*-CH_2Ph); 127.8 (*p*-CH_2Ph); 96.4 (C-1); 70.0 (C-4); 69.4 (CH_2Ph); 69.0 (C-5); 52.1 (OCH_3); 46.9 (C-2); 46.4 (C-3); 22.6, 22.5 ($COCH_3$).

$C_{25}H_{28}N_2O_8$ (484.18):

Calcd.: C, 61.97; H, 5.83; N, 5.78;

Found: C, 62.41; H, 5.80; N, 5.74;

4.3.5. Methyl(benzyl 2-acetamido-3-azido-2,3-dideoxy-a-D-galactopyranoside)uronate (26)



Trifluoromethanesulfonic anhydride (577 µL, 3.43 mmol) was added dropwise at - 10ºC over a period of 30 minutes to a solution of compound **16** (500 mg,1.37 mmol) and pyridine (387.4 µL 4.79 mmol) in dry DCM (7.5 mL). The reaction was maintained at - 5ºC for another 30 minutes (monitored by TLC $CHCl_3$:MeOH 40:1). DCM (7.5 mL) was added to the reaction mass and the organic solution was washed with 15% cold $NaHSO_4$ (3 X 5 mL) and water (5 mL). The organic layer was dried with Na_2SO_4 and evaporated under vacuum. The crude product **25** was taken to the next step in DMF (2.5 mL) with $NaNO_2$ (74.6 mg, 10.82 mmol). The mixture was stirred overnight at RT (monitored by TLC: Tol (100%)) and diluted with DCM (10 mL). The organic solution was washed with water (3 X 3 mL), concentrated and purification by flash column chromatography (MeOH 0 → 5 % in $CHCl_3$) provided **26** (538 mg, 78 %) as colourless crystals. For analytical purpose **25** was purified and characterized.

mp: 183-185°C

***R*f:** 0.3; ($CHCl_3$:MeOH 30:1),

$[\alpha]_D^{23}$ + 169.2° (*c* 1.0, $CHCl_3$)

^{1}H NMR (500.13 MHz, DMSO-d$_6$) δ = 8.12 (d, 1H, $^3J_{2,NH}$ = 9.1 Hz, NH); 7.39 (m, 2H, *o*-Ph); 7.34 (m, 2H, *m*-Ph); 7.29 (m, 1H, *p*-Ph); 5.82 (d, 1H, $^3J_{4,OH}$ = 6.4 Hz, OH); 4.84 (d, 1H, $^3J_{1,2}$ = 3.5 Hz, H-1); 4.66 (d, 1H, ^2J = 12.6 Hz), 4.49 (d, 1H, ^2J = 12.6 Hz), (CH_2Ph); 4.43 (d, 1H, $^3J_{4,5}$ = 1.3 Hz, H-5); 4.35 (ddd, 1H, $^3J_{2,3}$ = 12.0 Hz, $^3J_{2,NH}$ = 9.1 Hz, $^3J_{1,2}$ = 3.5 Hz, H-2); 4.28 (dd, 1H, $^3J_{4,OH}$ = 6.4 Hz, $^3J_{3,4}$ = 2.8 Hz, $^3J_{4,5}$ = 1.3 Hz, H-4); 3.67 (s, 3H, OCH_3); 3.66 (dd, 1H, $^3J_{2,3}$ = 12.0 Hz, $^3J_{3,4}$ = 2.8 Hz, H-3); 1.85 (s, 3H, CH_3CO).

^{13}C NMR (125.8 MHz, DMSO-d$_6$) δ = 169.6 (*C*OCH_3); 168.7 (*C*$OOCH_3$); 137.7 (*i*-Ph); 128.3 (*m*-Ph); 127.8 (*o*-Ph); 127.7 (*p*-Ph); 96.5 (C-1); 71.1 (C-5); 69.0 (*C*H_2Ph); 68.5 (C-4); 58.6 (C-3); 51.9 (OCH_3); 46.3 (C-2); 22.6 (CO*C*H_3).

$C_{16}H_{20}N_4O_6$(364.35):

Calcd.:C, 52.74; H, 5.53; N, 15.38;

Found:C, 52.91 H, 5.64; N, 15.55;

51

***R*f**: 0.2 (PE:EtOAc 1:1);

$[\alpha]_D^{25}$ +376.2 ° (*c* 1.0, $CHCl_3$);

^{1}H NMR (500.13 MHz, $CDCl_3$) δ = 7.43-7.37 (m, 3H, *m*-Ph, *p*-Ph); 7.32 (m, 2H, *o*-Ph); 5.72 (d, 1H, $^3J_{2,NH}$ = 9.8 Hz, NH); 4.95 (d, 1H, $^3J_{1,2}$ = 3.7 Hz, H-1); 4.77 (d, 1H, ^2J = 11.7 Hz), 4.56 (d, 1H, ^2J = 11.7 Hz), (CH_2Ph); 4.77 ('t', 1H, $^3J_{3,4}$ = $^3J_{4,5}$ = 9.8 Hz, H-4); 4.46 (d, 1H, $^3J_{4,5}$ = 9.8 Hz, H-5); 4.46 (ddd, 1H, $^3J_{2,3}$ = 10.7 Hz, $^3J_{2,NH}$ = 9.8 Hz, $^3J_{1,2}$ = 3.7 Hz, H-2); 3.83 (s, 3H, OCH_3); 3.79 (dd, 1H, $^3J_{2,3}$ = 10.7 Hz, $^3J_{3,4}$ = 9.8 Hz, H-3); 1.97 (s, 3H, CH_3CO).

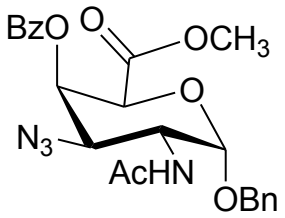
^{13}C NMR (125.8 MHz, $CDCl_3$) δ = 169.9 (*C*OCH_3); 166.5 (*C*$OOCH_3$); 135.6 (*i*-Ph); 128.9 (*m*-Ph); 128.9 (*p*-Ph); 128.5 (*o*-Ph); 118.3 (q, $J_{C,F}$ = 320 Hz, CF_3); 96.2 (C-1); 80.7 (C-4); 71.1 (CH_2Ph); 68.9 (C-5); 62.0 (C-3); 53.1 (OCH_3); 51.5 (C-2); 23.0 (CO*C*H_3).

$C_{17}H_{19}F_3N_4O_8S$ (496.41)**:**

Calcd.: C, 41.13; H, 3.86; N, 11.29; S, 6.46

Found: C, 40.58; H, 3.37; N, 11.02; S, 6.13

4.3.6. Methyl(benzyl 2-acetamido-3-azido-2,3-dideoxy-4-*O*-benzoyl-α-D-galactopyranoside)uronate) 27



In the course of 1 h benzoyl chloride (0.88mL, 7.56 mmol) was added dropwise to a stirred soln of compound **26** (1.13 g, 3.09 mmol) in dry pyridine (11.25 mL) in DCM (22.5 mL) at 0 °C. After stirring for 4 h at 0 °C (monitored by TLC: $CHCl_3$:MeOH 40:1), DCM (20 mL) was added to the reaction mass and the organic solution was washed with 15% cold $NaHSO_4$ (3 X 15 mL), aq $NaHCO_3$ (3 x 15 mL) and brine solution (15 mL). After concentration under vacuum and repeated co-distillation with toluene (3 x 20 mL) to remove adhering pyridine the residue was purified by flash chromatography (Eluent Gradient: EtOAc 0 → 120 % in PE) to provide **27** (1.14 g, 89 %)as colourless crystals.

mp: 196-198°C;

***R*f**: 0.2 (PE:EtOAc 1:1);

[α] $^{23}_{D}$ 189.3 ° (*c* 1.0, $CHCl_3$);

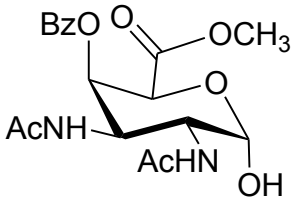
^{1}H NMR (500.13 MHz, DMSO-d$_6$) δ = 8.29 (d, 1H, $^3J_{2,NH}$ = 8.5 Hz, NH); 7.93 (m, 2H, *o*-Bz); 7.70 (m, 1H, *p*-Bz); 7.57 (m, 2H, *m*-Bz); 7.43 (m, 2H, *o*-Ph(1)); 7.38 (m, 2H, *m*-Ph(1)); 7.32 (m, 1H, *p*-Ph(1)); 5.95 (dd, 1H, $^3J_{3,4}$ = 2.8 Hz, $^3J_{4,5}$ = 1.3 Hz, H-4); 5.03 (d, 1H, $^3J_{1,2}$ = 3.2 Hz, H-1); 4.80 (d, 1H, $^3J_{4.5}$ = 1.3 Hz, H-5); 4.74 (d, 1H, ^2J = 12.2 Hz), 4.57 (d, 1H, ^2J = 12.2 Hz), (C*H*$_2$Ph); 4.32 (dd, 1H, $^3J_{2,3}$ = 12.0 Hz, $^3J_{3,4}$ = 2.8 Hz, H-3); 4.26 (ddd, 1H, $^3J_{2,3}$ = 12.0 Hz, $^3J_{2,NH}$ = 8.5 Hz, $^3J_{1,2}$ = 3.2 Hz, H-2); 3.50 (s, 3H, OCH_3); 1.85 (s, 3H, CH_3CO).

^{13}C NMR (125.8 MHz, DMSO-d$_6$) δ = 169.7 (*C*OCH_3); 167.6 (*C*$OOCH_3$); 164.8 (Ph*C*OO); 137.4 (*i*-Ph(1)); 134.0 (*p*-Bz); 129.4 (*o*-Bz); 129.1 (*m*-Bz); 129.0 (*i*-Bz); 128.4 (*m*-Ph(1)); 127.9 (*o*-Ph(1)); 127.8 (*p*-Ph(1)); 96.6 (C-1); 70.1 (C-4); 69.5 (*C*H_2Ph); 68.8 (C-5); 57.4 (C-3); 52.2 (OCH_3); 47.6 (C-2); 22.6 (CO*C*H_3).

$C_{23}H_{24}N_4O_7$(468.46):

Calcd.:C, 58.97; H, 5.16; N, 11.96; **Found:** C, 58.45; H, 4.74; N, 11.75;

4.3.7. Methyl(2,3-diacetamido-2,3-dideoxy-4-*O*-benzoyl-α-D-galactopyranoside)uronate 28



To a solution of **27** (200 mg, 0.427 mmol) in dry methanol (3 mL), 10% palladium-on charcoal (ca. 88 mg) and freshly distilled Ac_2O (0.13 mL, 1.359 mmol) was added and the suspension was stirred for 4 hours (monitored by TLC: $CHCl_3$-MeOH 30:1). After completion of the reaction, to the reaction mixture containing the crude product **24**, acetyl chloride (44μL) was added and the suspension was stirred for another 4 hours at room temperature under an atmosphere of hydrogen (monitored by TLC: $CHCl_3$-MeOH10:1).The reaction mass was filtered through celite, concentrated and purification by column chromatography (MeOH 0→ 7.5 % in $CHCl_3$) provided **28** (146.5 mg, 87 %) as colourless crystals. Analytical data of **24** can be found under section **4.3.4.**

mp 107-108 °C;

***R*f**: 0.55 ($CHCl_3$:MeOH 6:1);

[α] $^{22}_{D}$ +102.6° (*c* 1.0, $CHCl_3$);

^{1}H NMR (500.13 MHz, DMSO-d$_6$) δ = 7.98 (d, 1H, $^3J_{3,NH}$ = 7.8 Hz, NH(3)); 7.93 (m, 2H, *o*-Bz); 7.84 (d, 1H, $^3J_{2,NH}$ = 8.4 Hz, NH(2)); 7.67 (m, 1H, *p*-Bz); 7.55 (m, 2H, *m*-Bz); 7.07 (d, 1H, $^3J_{1,OH}$ = 4.2 Hz, OH); 5.68 (dd, 1H, $^3J_{3,4}$ = 3.2 Hz, $^3J_{4,5}$ = 1.5 Hz, H-4); 5.22 (dd, 1H, $^3J_{1,OH}$ = 4.2 Hz, $^3J_{1,2}$ = 3.2 Hz, H-1); 4.86 (d, 1H, $^3J_{4.5}$ = 1.5 Hz, H-5); 4.41 (ddd, 1H, $^3J_{2,3}$ = 12.3 Hz, $^3J_{3,NH}$ = 7.8 Hz, $^3J_{3,4}$ = 3.2 Hz, H-3); 4.19 (ddd, 1H, $^3J_{2,3}$ = 12.3 Hz, $^3J_{2,NH}$ = 8.4 Hz, $^3J_{1,2}$ = 3.2 Hz, H-2); 3.51 (s, 3H, OCH_3); 1.82, 1.70 (2s, 6H, 2 CH_3CO).

^{13}C NMR (125.8 MHz, DMSO-d$_6$) δ = 170.2, 170.0 (*C*OCH_3); 168.5 (*C*$OOCH_3$); 165.0 (Ph*C*OO); 133.5 (*p*-Bz); 129.9 (*i*-Bz); 129.6 (*o*-Bz); 128.8 (*m*-Bz); 90.7 (C-1); 70.2 (C-4); 68.3 (C-5); 52.0 (OCH_3); 47.5 (C-2); 46.4 (C-3); 22.7, 22.5 (CO*C*H_3).

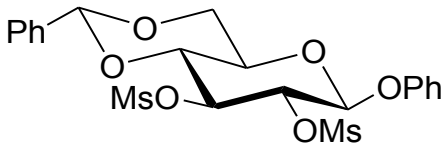
29

^{1}H NMR (500.13 MHz, DMSO-d$_6$) δ = 8.33 (d, 1H, $^3J_{2,NH}$ = 8.4 Hz, NH); 7.36-7.28 (m, 5H, Ph); 6.03 (d, 1H, $^3J_{3,4}$ = 2.7 Hz,H-4); 5.20 (d, 1H, $^3J_{1,2}$ = 2.7 Hz, H-1); 4.75 (d, 1H, ^2J = 12.3 Hz), 4.68 (d, 1H, ^2J = 12.3 Hz), (C*H*$_2$Ph); 4.05 (ddd, 1H, $^3J_{2,3}$ = 10.0 Hz, $^3J_{2,NH}$ = 8.4 Hz, $^3J_{1,2}$ = 2.7 Hz, H-2); 3.73 (s, 3H, OCH$_3$); 3.35 (dd, 1H, $^3J_{2,3}$ = 10.0 Hz, $^3J_{3,4}$ = 2.7 Hz, H-3); 1.87 (s, 3H, CH$_3$CO).

^{13}C NMR (125.8 MHz, DMSO-d$_6$) δ = 169.9 (*C*OCH$_3$); 161.6 (*C*OOCH$_3$); 141.3 (C-5); 137.2 (*i*-Ph); 128.3 (*m*-Ph); 127.8 (*p*-Ph); 127.7 (*o*-Ph); 109.1 (C-4); 97.2 (C-1); 70.2 (*C*H$_2$Ph); 54.8 (C-3); 52.5 (OCH$_3$); 49.5 (C-2); 22.5 (CO*C*H$_3$).

4.4 Synthesis of Methyl (acetyl-2,3-diazido-2,3-dideoxy-β-D-mannuronate)

4.4.1. Phenyl 2,3-*O*-dimesyl-4,6-*O*-benzylidene-β-D-glucopyranoside (31)



In the course of 30 min methanesulfonyl chloride (4.25 mL, 45.0 mmol) was added dropwise to a stirred soln of 4,6-*O*-benzylidene-β-D-glucopyranoside (**30)** (1.72 g, 5.0 mmol) in dry pyridine (30 mL) at 0 °C. After stirring for 45 min at 0 °C (monitored by TLC: Tol-EtOAc 5:1), the reaction mixture was slowly poured in to cold water (100 mL). The crude product was filtered and washed with water and further purification was done by re-crystallisation with ethanol to provide **31** (2.10 g, 84 %) as colourless crystals.

mp 117-118°C (EtOH);

***R*$_f$** 0.78 (CHCl$_3$-MeOH 6:1);

[α] $^{22}_{D}$ +37.8 ° (*c* 1.02, CHCl$_3$)

^{1}H NMR (500.13 MHz, CDCl$_3$) δ = 7.29-7.54 (m, 5H, Ph(1)); 7.06-7.35 (m, 5H, Ph(7));

5.58 (s, 1H, H-7); 5.17 (d, 1H, $^3J_{1,2}$= 7.37 Hz, H-1); 4.98 (t, 1H, $^3J_{2,3}$ = $^3J_{3,4}$ = 9.25 Hz, H-3);

4.92 (dd, 1H, $^3J_{2,3}$ = 9.25 Hz, $^3J_{1,2}$ = 7.37 Hz, H-2); 4.45 (dd, 1H, $^2J_{6ax,6eq}$ = 10.25 Hz, $^3J_{5,6eq}$ = 4.91 Hz, H-6eq); 3.87 (t, 1H, $^3J_{3,4}$ = $^3J_{4,5}$ = 9.25 Hz, H-4); 3.86 (t, 1H, $^2J_{6ax,6eq}$ = $^3J_{5,6ax}$ = 10.25

Hz, H-6ax); 3.64 (dd, 1H, $^{3}J_{5,6ax}$ = 10.25 Hz, $^{3}J_{4,5}$ = 9.25 Hz, $^{3}J_{5,6eq}$ = 4.91 Hz, H-5); 3.22, 3.06 (2s, 6H, 2 CH_3SO_2)

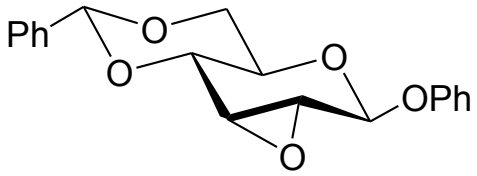
^{13}C NMR (125.8 MHz, $CDCl_3$) δ = 156.44, 136.1, 129.76, 129.5, 128.46, 126.0, 124.02, 117.44 Ph; 102.02 (C-7); 99.79 (C-1); 78.95 (C-3); 78.05 (C-4); 78.03 (C-2), 68.24 (C-6); 66.09 (C-5); 39.24, 39.77 (CH_3SO_2)

$C_{21}H_{24}O_{10}S_2$ (500.08):

Calcd.: C, 50.39; H, 4.83; S 12.81;

Found: C, 50.58; H 4.92; S 12.94.

4.4.2. Phenyl 2,3-anhydro-4,6-*O*-benzylidene-β-D-allopyranoside(32)



0.5 M Sodium methoxide (75 mL) was added at 60 °C drop wise over a period of 1 h to a stirred solution of **31** (5 g,10.0 mmol) in dryTHF/CH_3OH (1:1 mixture) (100 mL). After stirring at 75 °C for additional 12 h (monitored by TLC: Tol-EA 12:1), the reaction mixture was neutralised with IRC-120 (H^+) resin, filtered, dried and concentrated. Purification by flash chromatography (eluent gradient: EtOAc 0 → 20 % in PE) provided **32** (1.46 g, 45 %) as colourless crystals. The side product **33** was also isolated and characterised by NMR.

mp154-155°C;

***R*f** 0.47 (PE:EtOAc 2.5:1);

[α] $^{22}_{D}$ -45.626° (*c* 1.0, $CHCl_3$);

^{1}H NMR (300.13 MHz, $CDCl_3$) δ = 7.54 (m, 2H, *o*-Ph(7)); 7.44-7.30 (m, 5H, *m*-Ph(1), *m*-Ph(7), *p*-Ph(7)); 7.11-7.05 (m, 3H, *o*-Ph(1), *p*-Ph(1)); 5.68 (d, 1H, $^{4}J_{1,3}$ = 0.9 Hz, H-1); 5.60 (s, 1H, H-7); 4.30 (ddd, 1H, ^{2}J= 10.3 Hz, $^{3}J_{5,6eq}$ = 4.9 Hz, $^{5}J_{3,6eq}$ = 0.9 Hz, H-6eq); 4.22 (dd, 1H, $^{3}J_{4,5}$ = 9.1 Hz, $^{3}J_{3,4}$ = 1.0 Hz, H-4); 3.95 (ddd, 1H, $^{3}J_{5,6ax}$ = 10.2 Hz, $^{3}J_{4,5}$ = 9.1 Hz, $^{3}J_{5,6eq}$ = 4.9 Hz, H-5); 3.75 ('t', 1H, ^{2}J= 10.3 Hz, $^{3}J_{5,6ax}$ = 10.3 Hz, H-6ax); 3.66 (br d, 1H, $^{3}J_{2,3}$ = 4.3 Hz, H-3); 3.60 (d, 1H, $^{3}J_{2,3}$ = 4.3 Hz, H-2).

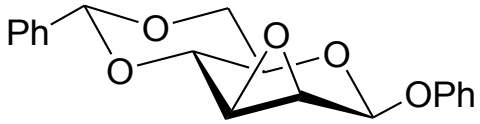
^{13}C NMR (75.5 MHz, $CDCl_3$) δ = 156.5 (*i*-Ph(1)); 137.0 (*i*-Ph(7)); 129.6 (*m*-Ph(1)); 129.3 (*p*-Ph(7)); 128.4 (*m*-Ph(7)); 126.3 (*o*-Ph(7)); 122.9 (*p*-Ph(1)); 116.3 (*o*-Ph(1)); 102.7 (C-7); 94.6 (C-1); 77.2 (C-4); 69.0 (C-6); 61.3 (C-5); 55.1, 51.2 (C-2, C-3).

$C_{19}H_{18}O_5$(326.34):

Calcd. C, 69.93; H, 5.56

Found C, 69.82; H, 5.51.

4.4.3. Phenyl 2,3-anhydro-4,6-*O*-benzyliden-β-D-mannopyranoside (33)



R_f 0.44 (PE-EtOAc 2.5:1).

$[\alpha]_D^{23}$ + 35.2 (*c* 0.9, $CHCl_3$).

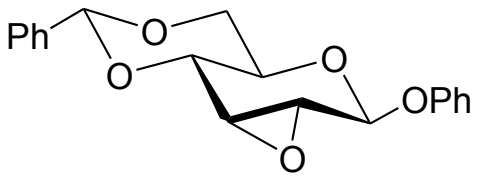
^{1}H NMR (500.13 MHz, DMSO-d_6) δ = 7.46 (m, 2H, *o*-Ph(7)); 7.41-7.38 (m, 3H, *m*-Ph(7), *p*-Ph(7)); 7.33 (m, 2H, *m*-Ph(1)); 7.11 (m, 2H, *o*-Ph(1)); 7.04 (m, 1H, *p*-Ph(1)); 5.94 (d, 1H, $^3J_{1,2}$ = 1.0 Hz, H-1); 5.71 (s, 1H, H-7); 4.41 (dd, 1H, ^2J = 10.0 Hz, $^3J_{5,6eq}$ = 4.7 Hz, H-6eq); 3.77 (d, 1H, $^3J_{4,5}$ = 9.8 Hz, H-4); 3.75 ('t', 1H, ^2J = $^3J_{5,6ax}$ = 10.0 Hz, H-6ax); 3.59 (d, 1H, $^3J_{2,3}$ = 3.8 Hz, H-3); 3.57 (ddd, 1H, $^3J_{5,6ax}$ = 10.0 Hz, $^3J_{4,5}$ = 9.8 Hz, $^3J_{5,6eq}$ = 4.7 Hz, H-5); 3.53 (dd, 1H, $^3J_{2,3}$ = 3.8 Hz, $^3J_{1,2}$ = 1.0 Hz, H-2).

^{13}C NMR (125.8 MHz, DMSO-d_6) δ = 156.6 (*i*-Ph(1)); 137.5 (*i*-Ph(7)); 129.7 (*m*-Ph(1)); 129.2 (*p*-Ph(7)); 128.3 (*m*-Ph(7)); 126.4 (*o*-Ph(7)); 122.5 (*p*-Ph(1)); 116.2 (*o*-Ph(1)); 101.5 (C-7); 95.9 (C-1); 73.7 (C-4); 68.4 (C-6); 68.1 (C-5); 54.9 (C-3); 50.3 (C-2). $C_{19}H_{18}O_5$(326.12):

Calcd. C, 69.93; H, 5.56;

Found C, 69.46; H, 5.32;

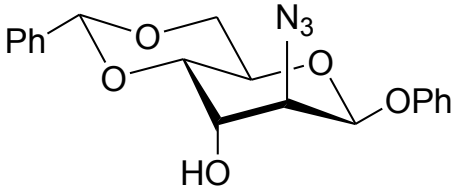
4.4.4. Phenyl 2,3-anhydro-4,6-*O*-benzylidene-β-D-allopyranoside (32)



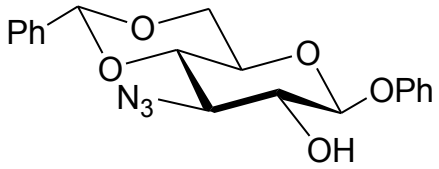
Di-*iso*-propylazo-1,2-dicarboxylate (DIAD, 21.84 g, 108.0 mmol) was added at 85 °C portion wise over 1 h to a stirred solution of phenyl4,6-*O*-benzylidene-β-D-glucopyranoside[98-100] (**30**,12.40 g, 36.0 mmol) and triphenylphosphine (33.05 g, 126.0 mmol) in dry DMF (180 mL). After stirring for another 12 hat 85 °C (monitored by TLC: Tol-Acetone 5:1), 20 mL MeOH was added and the reaction mixture was concentrated under high-vacuum and the residue was purified by crystallisation from Ethanol to provide **32** (9.05 g, 77 %) as colourless crystals.

Analytical data available in section 4.4.2.

4.4.5. Phenyl 2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-altropyranoside (34) and phenyl 3-azido-4,6-*O*-benzylidene-3-deoxy-β-D-glucopyranoside (35)



34



35

NaN_3 (10.27g, 158 mmol), NH_4Cl (2.43g, 45.42 mmol) and water (12.69 mL, 705 mmol) was added to a solution of compound **32 (**9 g, 27.61 mmol) in 135 mL DMF. The mixture was stirred at 120ºC for 90 minutes (monitored by TLC: Tol-EtOAc30 :1) and diluted with DCM (300 mL). The organic solution was washed with water (3 X 100 mL), concentrated and purification of the crude product by flash chromatography (eluent gradient EtOAc 0 → 20% in PE) provided the isomer mixture (**34** and **35** together, 9.67 g, 95 % yield, isomer ratio 60:40) as colourless crystals.

34:

mp 149-151°C,

Rf: 0.255 (Tol-EtOAc12:1)

$[\alpha]_D^{23}$ -98.2 ° (*c* 1.0, $CHCl_3$)

^{1}H NMR (500.13 MHz, $CDCl_3$) δ = 7.50 (m, 2H, *o*-Ph(7)); 7.41 (m, 3H, *m*-Ph(7), *p*-Ph(7)); 7.33 (m, 2H, *m*-Ph(1)); 7.10-7.05 (m, 3H, *o*-Ph(1), *p*-Ph(1)); 5.69 (d, 1H, $^3J_{1,2}$ = 1.6 Hz, H-1);

5.63 (s, 1H, H-7); 4.39 (dd, 1H, $^{2}J_{6ax,6eq}$ = 10.4 Hz, $^{3}J_{5,6eq}$ = 5.0 Hz, H-6eq); 4.15 (br 't', 1H, H-3); 4.09 (ddd, 1H, $^{3}J_{5,6ax}$ = 10.4 Hz, $^{3}J_{4,5}$ = 9.8 Hz, $^{3}J_{5,6eq}$ = 5.0 Hz, H-5); 3.94 (dd, 1H, $^{3}J_{1,2}$ = 1.6 Hz, $^{3}J_{2,3}$ = 3.5 Hz, H-2); 3.89 (dd, 1H, $^{3}J_{4,5}$ = 9.8 Hz, $^{3}J_{3,4}$ = 2.7 Hz, H-4); 3.86 ('t', 1H, $^{2}J_{6ax,6eq}$ = $^{3}J_{5,6ax}$ = 10.4 Hz, H-6ax); 2.64 (s, 1H, OH).

^{13}C NMR (125.8 MHz, $CDCl_3$) δ = 156.2 (*i*-Ph(1)); 136.8 (*i*-Ph(7)); 129.5 (*m*-Ph(1)); 129.4 (*p*-Ph(7)); 128.4 (*m*-Ph(7)); 126.2 (*o*-Ph(7)); 123.0 (*p*-Ph(1)); 116.3 (*o*-Ph(1)); 102.1 (C-7); 96.7 (C-1); 75.9 (C-4); 68.6 (C-3); 68.6 (C-6); 63.8 (C-5); 62.7 (C-2).

$C_{19}H_{19}N_3O_5$(369.13):

Calcd.:C, 61.78; H, 5.18 N, 11.38

Found C, 61.55; H, 5.02 N, 11.21

35:

mp: 205-207°C;

Rf: 0.23 (Tol-EtOAc 12:1);

[α] $^{24}_{D}$ -33.3 ° (*c* 1.0, $CHCl_3$);

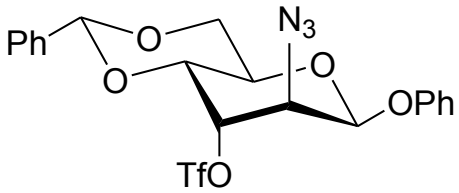
^{1}H NMR (500.13 MHz, $CDCl_3$) δ = 7.51 (m, 2H, *o*-Ph(7)); 7.42-7.37 (m, 3H, *m*-Ph(7), *p*-Ph(7)); 7.33 (m, 2H, *m*-Ph(1)); 7.10 (m, 1H, *p*-Ph(1)); 7.05 (m, 2H, *o*-Ph(1)); 5.60 (s, 1H, H-7); 5.04 (d, 1H, $^{3}J_{1,2}$ = 7.5 Hz, H-1); 4.40 (dd, 1H, $^{2}J_{6ax,6eq}$ = 10.5 Hz, $^{3}J_{5,6eq}$ = 4.4 Hz, H-6eq); 3.85-3.76 (m, 2H, H-3, H-6ax); 3.74 ('t', 1H, $^{3}J_{2,3}$ = 8.0 Hz, $^{3}J_{1,2}$ = 7.5 Hz, H-2); 3.66-3.60 (m, 2H, H-4, H-5); 2.70 (s, 1H, OH). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ = 156.6 (*i*-Ph(1)); 136.6 (*i*-Ph(7)); 129.7 (*m*-Ph(1)); 129.2 (*p*-Ph(7)); 128.3 (*m*-Ph(7)); 126.0 (*o*-Ph(7)); 123.5 (*p*-Ph(1)); 116.9 (*o*-Ph(1)); 101.6 (C-7); 101.4 (C-1); 79.2 (C-4); 73.3 (C- 2); 68.6 (C-6); 67.5 (C-5); 64.4 (C-3).

$C_{19}H_{19}N_3O_5$ (369.13) :

Calcd.:C, 61.78; H, 5.18; N, 11.38;

Found C, 61.91; H, 4.98; N, 11.52;

4.4.6. Phenyl 2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-trifluoromethanesulfonyl-β-D-altropyranoside (36)



Trifluoromethanesulfonic anhydride (382.29 mg, 0.23 mL, 1.35 mmol) was added, at - 10ºC drop wise over a period of 30 minutes to compound **34** (200 mg, 0.542 mmol) and pyridine (0.15 mL, 1.90 mmol) in dry CH_2Cl_2 (4 mL). The reaction was maintained at -5ºC for another 30 minutes (monitored by TLC Tol-EtOAc 60:1). CH_2Cl_2 (4mL) was added to the reaction mass and the organic solution was washed with 15% cold $NaHSO_4$ (3 X 3 mL) and water (3mL). The organic layer was dried with Na_2SO_4, evaporated under vacuum and purification by column chromatography (EtOAc 0 – 15 % in PE) provided **36** (206.88 mg, 77%) as colourless syrup.

***R*f** 0.61(Tol-EtOAc 20:1);

[α] $^{22}_{D}$ -73.5° (*c* 1.0, $CHCl_3$);

^{1}H NMR (500.13 MHz, $CDCl_3$) δ = 7.49-7.44 (m, 2H, *o*-Ph(7)); 7.41-7.32 (m, 5H, *m*-Ph(1), *m*-Ph(7), *p*-Ph(7)); 7.15-7.04 (m, 3H, *o*-Ph(1), *p*-Ph(1)); 5.67 (d, 1H, $^3J_{1,2}$ = 1.6 Hz, H-1); 5.62 (s, 1H, H-7); 5.23 (dd, 1H, $^3J_{2,3}$ = 3.5, $^3J_{3,4}$ = 1.5 Hz, H-3); 4.41 (dd, 1H, $^2J_{6ax,6eq}$ = 10.6 Hz, $^3J_{5,6eq}$ = 4.0 Hz, H-6eq); 4.26 (dd, 1H, $^3J_{2,3}$ = 3.5 Hz, $^3J_{1,2}$ = 1.6 Hz, H-2); 4.12-4.03 (m, 2H, H-4, H-5); 3.93-3.82 (m, 1H, H-6ax).

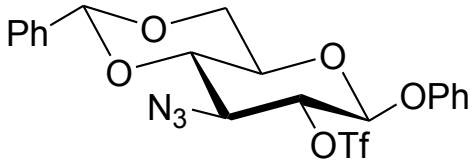
^{13}C NMR (125.8 MHz, $CDCl_3$) δ = 156.8 (*i*-Ph(1)); 136.3 (*i*-Ph(7)); 129.8 (*m*-Ph(1)); 129.4 (*p*-Ph(7)); 128.3 (*m*-Ph(7)); 126.1 (*o*-Ph(7)); 123.6 (*p*-Ph(1)); 118.4 (q, $J_{C,F}$ = 320 Hz, CF_3); 116.3 (*o*-Ph(1)); 102.6 (C-7); 97.3 (C-1); 81.7 (C-3); 72.5 (C-4); 68.6 (C-6); 64.1 (C-5); 61.3 (C-2).

$C_{20}H_{18}F_3N_3O_7S$(501.08):

Calcd.:C, 47.91; H, 3.62; N, 8.38; S, 6.39

Found: C, 47.69; H, 3.54; N, 8.29 S, 6.24

4.4.7. Phenyl 3-azido-4,6-*O*-benzylidene-3-deoxy-2-*O*-trifluoromethanesulfonyl-β-D-glucopyranoside (37)



This compound was prepared from **35** (200 mg, 0.542 mmol) by a procedure similar to that used for the preparation of compound **36** (monitored by TLC: Tol-EtOAc 60:1).Purification by flash chromatography (EtOAc 0 – 15 % in PE) afforded compound **37** (220.32 mg, 82 %) as colourless crystals.

mp Decompose on melting

***R*f** 0.57(Tol-EtOAc 20:1),

[α] $^{22}_{D}$ -59.8 ° (*c* 1.0, $CHCl_3$)

^{1}H NMR (500.13 MHz, $CDCl_3$) δ = 7.50 (m, 2H, *o*-Ph(7)); 7.44-7.38 (m, 3H, *m*-Ph(7), *p*-Ph(7)); 7.38-7.30 (m, 2H, *m*-Ph(1)); 7.13 (m, 1H, *p*-Ph(1)); 7.06 (m, 2H, *o*-Ph(1)); 5.63 (s, 1H, H-7); 5.17 (d, 1H, $^3J_{1,2}$ = 7.8 Hz, H-1); 4.70 (d, 1H, $^3J_{1,2}$ = 7.8 Hz, H-2); 4.42 (dd, 1H, $^2J_{6ax,6eq}$ = 10.6 Hz, $^3J_{5,6eq}$ = 4.9 Hz, H-6eq); 3.96 ('t', 1H, $^3J_{2,3}$ = $^3J_{3,4}$ = 9.8 Hz, H-3); 3.84 (dd, 1H, $^2J_{6ax,6eq}$ = 10.6 Hz, $^3J_{5,6ax}$ = 9.8 Hz, H-6ax); 3.74 ('t', 1H, $^3J_{3,4}$ = 9.8 Hz, $^3J_{4,5}$ = 9.3 Hz, H-4); 3.62 (ddd, 1H, $^3J_{5,6ax}$ = 9.8 Hz, $^3J_{4,5}$ = 9.3 Hz, $^3J_{5,6eq}$ = 4.7 Hz, H-5).

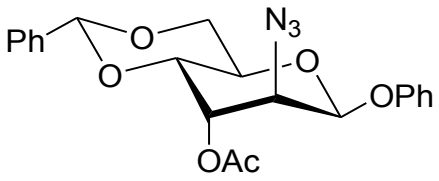
^{13}C NMR (125.8 MHz, $CDCl_3$) δ = 156.1 (*i*-Ph(1)); 136.1 (*i*-Ph(7)); 129.8 (*m*-Ph(1)); 129.4 (*p*-Ph(7)); 128.4 (*m*-Ph(7)); 125.9 (*o*-Ph(7)); 124.1 (*p*-Ph(1)); 118.4 (q, $J_{C,F}$ = 319 Hz, CF_3); 117.2 (*o*-Ph(1)); 101.6 (C-7); 98.8 (C-1); 82.2 (C-2); 79.4 (C-4); 68.3 (C-6); 67.4 (C-5); 62.7 (C-3).

$C_{20}H_{18}F_3N_3O_7S$(501.08):

Calcd.: C, 47.91; H, 3.62; N, 8.38; S, 6.39

Found: C, 47.61; H, 3.49; N, 8.22; S, 6.18

4.4.8. Phenyl 3-*O*-acetyl-2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-altropyranoside (38)



Freshly distilled acetic anhydride (1.0 mL) was added at 0 °C to a stirred soln of compound **34** (400 mg, 1.08 mmol)in dry pyridine (4.0 mL). After stirring for1 h at RT (monitored by TLC: Tol-EtOAc 40:1), the reaction mixture was diluted with toluene and concentrated. Traces of acetic acid and pyridine were removed by repeated co-distillation with toluene. Purification by flash chromatography (eluent gradient EtOAc 0 → 10% in PE) afforded compound **38** (369 mg, 83%) as colourless crystals.

mp 129-131°C;

Rf: 0.25 (Tol-EtOAc 40:1);

$[\alpha]_D^{22}$ -80.3° (*c* 1.02, $CHCl_3$);

^{1}H NMR (500.13 MHz, $CDCl_3$) δ = 7.45 (m, 2H, *o*-Ph(7)); 7.39-7.35 (m, 3H, *m*-Ph(7), *p*-Ph(7)); 7.34 (m, 2H, *m*-Ph(1)); 7.11-7.07 (m, 3H, *o*-Ph(1), *p*-Ph(1)); 5.59 (s, 1H, H-7); 5.58 (d, 1H, $^3J_{1,2}$ = 1.6 Hz, H-1); 5.43 ('t', 1H, $^3J_{2,3}$ = 3.5, $^3J_{3,4}$ = 3.0 Hz, H-3); 5.13-4.06 (m, 2H, H-2, H-5); 4.40 (dd, 1H, $^2J_{6ax,6eq}$ = 10.4 Hz, $^3J_{5,6eq}$ = 5.0 Hz, H-6eq); 4.02 (dd, 1H, $^3J_{4,5}$ = 9.8 Hz, $^3J_{3,4}$ = 3.0 Hz, H-4); 3.87 ('t', 1H, $^2J_{6ax,6eq}$ = 10.4 Hz, $^3J_{5,6ax}$ = 10.0 Hz, H-6ax); 2.15 (s, 3H, CH_3CO).

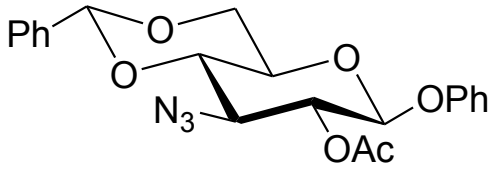
^{13}C NMR (125.8 MHz, $CDCl_3$) δ = 169.4 (COCH$_3$); 156.3 (*i*-Ph(1)); 136.9 (*i*-Ph(7)); 129.6 (*m*-Ph(1)); 129.1 (*p*-Ph(7)); 128.3 (*m*-Ph(7)); 126.1 (*o*-Ph(7)); 123.2 (*p*-Ph(1)); 116.3 (*o*-Ph(1)); 102.0 (C-7); 97.1 (C-1); 73.7 (C-4); 69.1 (C-3); 68.9 (C-6); 64.7 (C-5); 61.1 (C-2); 20.9 (COCH$_3$).

$C_{21}H_{21}N_3O_6$(411.14):

Calcd.: C, 61.31; H, 5.14 N, 10.21

Found: C, 61.17; H, 5.07 N, 10.09

4.4.9. Phenyl 2-*O*-acetyl-3-azido-4,6-*O*-benzylidene-3-deoxy-β-D-glucopyranoside (39)



This compound was prepared from **35** (200 mg, 0.542 mmol)) by a procedure similar to that used for the preparation of compound **38** (monitored by TLC: Tol-EtOAc 40:1). Purification by flash chromatography (eluent gradient EtOAc 0 → 10% in PE) afforded compound **39** (396 mg, 89%) as colourless crystals.

mp 160-162°C;

***R*f** 0.24 (Tol-EtOAc 40:1);

$[\alpha]_D^{22}$ -61.7° (*c* 1.0, $CHCl_3$);

^{1}H NMR (500.13 MHz, $CDCl_3$) δ = 7.51 (m, 2H, *o*-Ph(7)); 7.41-7.35 (m, 3H, *m*-Ph(7), *p*-Ph(7)); 7.31 (m, 2H, *m*-Ph(1)); 7.09 (m, 1H, *p*-Ph(1)); 6.99 (m, 2H, *o*-Ph(1)); 5.62 (s, 1H, H-7); 5.18 (dd, 1H, $^3J_{2,3}$ = 9.8 Hz, $^3J_{1,2}$ = 7.9 Hz, H-2); 5.11 (d, 1H, $^3J_{1,2}$ = 7.9 Hz, H-1); 4.42 (dd, 1H, $^2J_{6ax,6eq}$ = 10.7 Hz, $^3J_{5,6eq}$ = 5.0 Hz, H-6eq); 3.86 ('t', 1H, $^3J_{2,3}$ = $^3J_{3,4}$ = 9.8 Hz, H-3); 3.85 ('t', 1H, $^2J_{6ax,6eq}$ = 10.7 Hz, $^3J_{5,6ax}$ = 10.0 Hz, H-6ax); 3.74 ('t', 1H, $^3J_{3,4}$ = 9.8 Hz, $^3J_{4,5}$ = 9.3 Hz, H-4); 3.65 (ddd, 1H, $^3J_{5,6ax}$ = 10.0 Hz, $^3J_{4,5}$ = 9.3 Hz, $^3J_{5,6eq}$ = 5.0 Hz, H-5); 2.15 (s, 3H, CH_3CO).

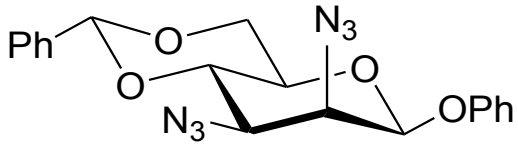
^{13}C NMR (125.8 MHz, $CDCl_3$) δ = 169.1 (COCH_3); 156.8 (*i*-Ph(1)); 136.5 (*i*-Ph(7)); 129.7 (*m*-Ph(1)); 129.2 (*p*-Ph(7)); 128.4 (*m*-Ph(7)); 126.0 (*o*-Ph(7)); 123.4 (*p*-Ph(1)); 116.9 (*o*-Ph(1)); 101.6 (C-7); 99.9 (C-1); 79.1 (C-4); 71.5 (C-2); 68.5 (C-6); 67.4 (C-5); 63.1 (C-3); 20.7 (COCH$_3$).

$C_{21}H_{21}N_3O_6$(411.14):

Calcd.: C, 61.31; H, 5.14 N, 10.21

Found: C, 61.11; H, 5.01 N, 10.02

4.4.10. Phenyl 2,3-diazido-4,6-*O*-benzylidene-2,3-dideoxy-β-D-mannopyranoside (40)



Trifluoromethanesulfonic anhydride (9.89 mL, 58.8 mmol) was added dropwise at – 10 ºC over a period of 1.5 h to a mixture of compounds **34** and **35** (8.68 g, 23.52 mmol) and pyridine (6.65 mL, 82.32 mmol) in dry DCM (180 mL). The reaction was maintained at - 5ºC for another 1 hour (monitored by TLC Tol-EtOAc 30:1). DCM(125 mL) was added to the reaction mass and the organic solution was washed with 15% cold $NaHSO_4$ (3 X 80 mL) and water (80 mL). The organic layer was dried with Na_2SO_4 and evaporated under vacuum. The crude product was taken to the next step in DMF (135 mL) with NaN_3 (4.58 g, 70.56 mmol). The mixture was stirred overnight at RT (monitored by TLC: Tol) and diluted with DCM (300 mL). The organic solution was washed with water (3 X 100 mL), concentrated and purification by flash column chromatography (EtOAc 0 → 15 % in PE) provided **40** (6.051 g, 65.29 %) as colourless crystals. The side product **41** (1.65 g, 20 %) a colourless crystal compound was also isolated and characterized.

40

mp 152-154°C;

***R*f** 0.44 (Tol);

[α] $^{23}_{D}$ -70.7° (*c* 1.02, $CHCl_3$);

^{1}H NMR (500.13 MHz, $CDCl_3$) δ = 7.50 (m, 2H, *o*-Ph(7)); 7.41-7.36 (m, 3H, *m*-Ph(7), *p*-Ph(7)); 7.35-7.31 (m, 2H, *m*-Ph(1)); 7.10 (m, 1H, *p*-Ph(1)); 7.04 (m, 1H, *o*-Ph(1)); 5.65 (s, 1H, H-7); 5.27 (d, 1H, $^3J_{1,2}$ = 1.4 Hz, H-1); 4.39 (dd, 1H, $^2J_{6ax,6eq}$ = 10.7 Hz, $^3J_{5,6eq}$ = 5.0 Hz, H-6eq); 4.12 (dd, 1H, $^3J_{2,3}$ = 3.6 Hz, $^3J_{1,2}$ = 1.4 Hz, H-2); 4.07 (dd, 1H, $^3J_{3,4}$ = 10.2 Hz, $^3J_{4,5}$ = 9.2 Hz, H-4); 3.92 (dd, 1H, $^2J_{6ax,6eq}$ = 10.7 Hz, $^3J_{5,6ax}$ = 10.0 Hz, H-6ax); 3.81 (dd, 1H, $^3J_{3,4}$ = 10.2 Hz,$^3J_{2,3}$ = 3.6, H-3); 3.55 (ddd, 1H, $^3J_{5,6ax}$ = 10.0 Hz, $^3J_{4,5}$ = 9.2 Hz, $^3J_{5,6eq}$ = 5.0 Hz, H-5).

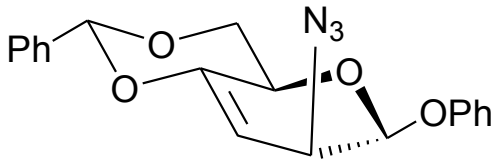
^{13}C NMR (125.8 MHz, $CDCl_3$) δ = 156.0 (*i*-Ph(1)); 136.6 (*i*-Ph(7)); 129.7 (*m*-Ph(1)); 129.2 (*p*-Ph(7)); 128.3 (*m*-Ph(7)); 125.9 (*o*-Ph(7)); 123.5 (*p*-Ph(1)); 116.5 (*o*-Ph(1)); 101.7 (C-7); 98.4 (C-1); 76.6 (C-4); 68.4 (C-6); 68.2 (C-3); 63.2 (C-5); 60.4 (C-2).

$C_{19}H_{18}N_6O_4$(394.14):

Calcd.: C, 57.86; H, 4.60; N, 21.31;

Found: C, 57.66; H, 4.49; N, 4.51;

41



mp 98-100°C;

***R*f** 0.47 (Tol);

[α] $^{23}_{D}$ + 177.1 ° (*c* 1.03, $CHCl_3$);

^{1}H NMR (300.13 MHz, $CDCl_3$) δ = 7.55-7.51 (m, 2H, *o*-Ph(7)); 7.45-7.40 (m, 3H, *m*-Ph(7), *p*-Ph(7)); 7.34 (m, 2H, *m*-Ph(1)); 7.12-7.06 (m, 3H, *p*-Ph(1), *o*-Ph(1)); 5.64 (s, 1H, H-7); 5.49 (dd, 1H, $^3J_{2,3}$ = 5.3 Hz, $^4J_{3,5}$ = 1.8 Hz H-3); 4.54 (dd't', 1H, $^3J_{5,6ax}$ = 10.0 Hz, $^3J_{5,6eq}$ = 6.4 Hz, $^5J_{2,5}$ = $^4J_{3,5}$ = 1.8 Hz, H-5); 4.48 (dd, 1H, ^2J= 10.0 Hz, $^3J_{5,6eq}$ = 6.4 Hz, H-6eq); 3.84 ('t', 1H, ^2J= $^3J_{5,6ax}$ = 10.0 Hz, H-6ax).

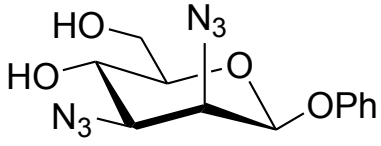
^{13}C NMR (75.5 MHz, $CDCl_3$) δ = 156.4, 156.0 (*i*-Ph(1), C-4); 136.0 (*i*-Ph(7)); 129.7 (*p*-Ph(7)); 129.6 (*m*-Ph(1)); 128.5 (*m*-Ph(7)); 126.2 (*o*-Ph(7)); 123.1 (*p*-Ph(1)); 116.7 (*o*-Ph(1)); 103.8 (C-7); 100.9 (C-3); 97.8 (C-1); 69.7 (C-6); 66.4 (C-5); 56.1 (C-2).

$C_{20}H_{20}N_3O_4$(351.12):

Calcd.: C, 65.56; H, 5.50; N, 11.47;

Found: C, 65.43; H, 5.39; N, 11.41;

4.4.11. Phenyl 2,3-diazido-2,3-dideoxy-β-D-mannopyranoside (42)



Compound **40** (5.9 g, 0.0149 mol) was dissolved in aq 80% acetic acid (300 mL) and stirred at 90 ºC. After 45 min (TLC: Tol-EtOAc 5:1), the reaction mixture was diluted with toluene (200 mL) and evaporated. After repeated co-distillation with toluene (3 x 150 mL) the residue was purified by flash chromatography (eluent gradient EtOAc 0 → 70% in PE) to provide **42** (3.73g, 80%) as colourless crystals.

mp 122-124°C;

***R*f** 0.22 (PE-EtOAc1:1);

[α] $^{24}_{D}$ -73.1 ° (*c* 1.02, $CHCl_3$);

^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 7.33 (m, 2H, *m*-Ph; 7.07-6.99 (m, 3H, *o*-Ph, *p*-Ph); 5.74 (d, 1H, $^3J_{4,OH}$ = 6.5 Hz, OH(4)); 5.51 (d, 1H, $^3J_{1,2}$ = 1.2 Hz, H-1); 4.73 (t, 1H, $^3J_{6,OH}$ = 5.8 Hz, OH(6)); 4.33 (dd, 1H, $^3J_{2,3}$ = 3.6 Hz, $^3J_{1,2}$ = 1.2 Hz, H-2); 3.80 (dd, 1H, $^3J_{3,4}$ = 9.8 Hz, $^3J_{2,3}$ = 3.6 Hz, H-3); 3.73-3.38 (m, 4H, H-4, H-5, H-6).

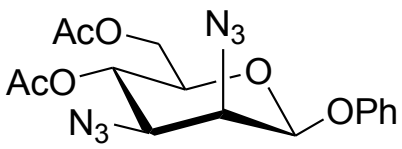
^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 156.3 (*i*-Ph); 129.7 (*m*-Ph); 122.4 (*p*-Ph); 116.0 (*o*-Ph); 96.9 (C-1); 78.2 (C-5); 65.3 (C-4); 63.6 (C-3); 62.7 (C-2); 60.3 (C-6).

$C_{12}H_{14}N_6O_4$(306.11):

Calcd.: C, 47.06; H, 4.61; N, 27.44;

Found: C, 46.78; H, 4.52; N, 27.27;

4.4.12. Phenyl 4,6-O-diacetyl-2,3-diazido-2,3-dideoxy-β-D-mannopyranoside (43)



This compound was prepared from **42** (100 mg, 0.327 mmol) by a procedure similar to that used for the preparation of compound **38** (monitored by TLC: Tol-EtOAc 5:1). Purification by flash chromatography (eluent gradient EtOAc 0 → 20% in PE) provided compound **43** (119 mg, 93.77 %) as colourless crystals.

mp: 85-86°C;

***R*f**: 0.37 (Tol-EtOAc 5:1);

[α] $^{23}_{D}$ -83.3 ° (*c* 1.0, $CHCl_3$);

^{1}H NMR (300.13 MHz, $CDCl_3$) δ = 7.31 (m, 2H, *m*-Ph); 7.08 (m, 1H, *p*-Ph); 7.02 (m, 2H, *p*-Ph); 5.25 ('t', 1H, $^3J_{3,4}$ = 10.0 Hz, $^3J_{4,5}$ = 9.8 Hz, H-4); 5.22 (d, 1H, $^3J_{1,2}$ = 1.2 Hz, H-1); 4.27 (dd, 1H, ^2J = 12.3 Hz, $^3J_{5,6a}$ = 6.0 Hz, H-6a); 4.18 (dd, 1H, $^3J_{2,3}$ = 3.5 Hz, $^3J_{1,2}$ = 1.2 Hz, H-2); 4.17 (dd, 1H, ^2J= 12.3 Hz, $^3J_{5,6b}$ = 2.8 Hz, H-6b); 3.74 (ddd, 1H, $^3J_{4,5}$ = 9.8 Hz, $^3J_{5,6a}$ = 6.0 Hz, $^3J_{5,6b}$ = 2.8 Hz, H-5); 3.65 (dd, 1H, $^3J_{3,4}$ = 10.0 Hz, $^3J_{2,3}$ = 3.5 Hz, H-3); 2.14, 2.07 (2s, 6H, CH_3CO).

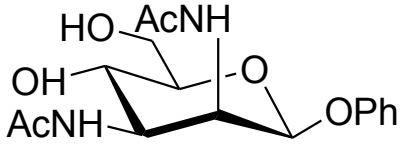
^{13}C NMR (75.5 MHz, $CDCl_3$) δ = 170.6, 169.3 ($COCH_3$); 156.1 (*i*-Ph); 129.6 (*m*-Ph); 123.4 (*p*-Ph); 116.6 (*o*-Ph); 98.1 (C-1); 73.3 (C-5); 66.7 (C-4); 62.7 (C-2); 62.3 (C-6); 61.6 (C-3); 20.6, 20.6 ($COCH_3$).

$C_{16}H_{18}N_6O_6$(390.13):

Calcd.: C, 49.23; H, 4.65; N, 21.53;

Found: C, 49.55; H, 4.72; N, 21.89;

4.4.13. Phenyl 2,3-diacetamido-2,3-dideoxy-β-D-mannopyranoside (37)



To a solution of **40** (2g, 6.53 mmol) in methanol (20 mL) 10% palladium-on charcoal (ca. 0.44 g) was added. The suspension was stirred for 5 h at room temperature under an atmosphere of hydrogen (monitored by TLC: ACN-Pyridine-Water 8:1:1).Then, the reaction mixture was filtered over Celite, eluted with MeOH and the combined filtrates were

concentrated. Freshly distilled acetic anhydride (6.0 mL, 54.5 mmol) was added at 0 °C to a stirred soln of the residue in dry pyridine (30 mL). After stirring for 2 h at that temperature (TLC: $CHCl_3$-MeOH 10:1), the reaction mixture was poured into ice water (30 mL). The aqueous layer was extracted with DCM (3 x 20 mL). The combined extracts were washed successively with aq 15% $NaHSO_4$ (3 x 25 mL), aq NaHCO3 (3 x 20 mL), water (20 mL), dried and concentrated. After drying under high vacuum for 3 h the residue was dissolved in dry methanol (20 mL) and sodium methoxide (0.5 M in methanol, 0.5 mL) was added. Afters stirring for 1 h at r.t., the reaction mixture was neutralised with IRC-120 (H^+) resin, filtered, dried and concentrated. Flash Chromatography (eluent gradient Methanol 0 → 20% in$CHCl_3$) gave compound **46** (0.74 g, 45 %) as colourless powder.

Rf: 0.37 ($CHCl_3$-MeOH 5:1);

[α] $^{23}_{D}$ -106.3 ° (*c* 1.0, $CHCl_3$: MeOH 1:1 v/v),

^{1}H NMR (500.13 MHz, DMSO-d$_6$)

δ = 7.64 (d, 1H, $^3J_{3,NH}$ = 8.2 Hz, NH(2); 7.43 (d, 1H, $^3J_{2,NH}$ = 9.77 Hz, NH(2)); 7.28 (m, 2H, *o*-Ph); 6.96-1.01 (m, 4H, *m*-Ph, *p*-Ph); 5.38 (d, 1H, $_3J^{1,2}$ = 1.58 Hz, H-1); 4.88 (d, 1H, $_3J^{4,OH}$ =5.79 Hz, OH(4)); 4.45 (m, 1H, H-2); 4.35 (t, 1H, $^3J_{6,OH}$ = 5.04 Hz, OH(6));3.97 (ddd, 1H, $^3J_{2,3}$ = 3.97 Hz, $^3J_{3,4}$ = 8.58 Hz, $^3J_{3,NH}$ = 9.77 Hz, H-3); 3.73 (ddd, 1H, ^3J= 1.58, $^3J_{5,6eq}$=3.78 Hz, $^3J_{ax,eq}$=12.25, H-6$_{eq}$); 3.57 (d't'd, 1H, $^3J_{ax,OH}$= 5.0, $^3J_{5,6ax}$=7.55 Hz, $^3J_{ax,eq}$=12.25, H-6$_{ax}$); 4.40-3.51 (m, 2H, H-4, H-5); 1.96, 1.79 (2S, 6H, 2 CO*C*H$_3$)

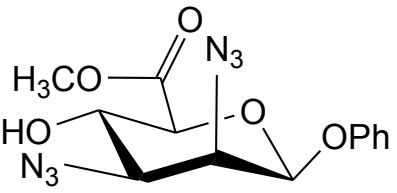
^{13}C NMR (125.8 MHz, DMSO-d$_6$) δ = 170.02, 169.50 (*C*OCH$_3$); 156.5, 129.4, 121.87, 116.21, (Ph); 79.0, 63.9 (C-4, C-5), 60.88 (C-6); 53.49 (C-3); 50.25 (C-2); 23.01, 22.71 (CO*C*H$_3$)

$C_{16}H_{22}N_2O_6$ (338.15)

Calcd. :C, 56.80; H, 6.55; N, 8.28;

Found: C, 56.21; H, 6.12; N, 7.59;

4.4.14. Methyl(phenyl 2,3-diazido-2,3-dideoxy-β-D-mannopyranoside)uronate (50)



BAIB (bis(acetoxy)iodobenzene) (2.63 g, 8.17 mmol) was added to a mixture of **42** (1 g, 3.27 mmol) and TEMPO (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl) (102 mg, 0.65 mmol) in 30 mL DCM/H_2O (ratio 3:1) at 0 ºC under stirring. The reaction was stirred for another 12 hours at RT (monitored by TLC: Tol-EtOAc-AA 16:4:1). 10 mL MeOH and further 25 mL 1 M $Na_2S_2O_3.5H_2O$ was added slowly at 0 ºC. The layers were separated and the aqueous phase was acidified to P_H 3 with 1M HCl and extracted with ethyl acetate. Then, the combined organic layer was dried with Na_2SO_4 and evaporated under vacuum. The crude product was taken directly to the next step with CH_2N_2 in MeOH. After completion of the reaction (monitored by TLC: Tol-EtOAc-AA 16:4:1), excess CH_2N_2 was quenched with acetic acid, the reaction mass was co-distilled with toluene and purified by column chromatography (eluent gradient EtOAc 0 → 40 % in PE) to provide **50**(852mg, 79 %) as a colourless syrup.

$\boldsymbol{R_f}$: 0.3 (PE-EtOAc 1:1);

$[\alpha]_D^{24}$ -95.7 ° (*c* 1.0, $CHCl_3$)

^{1}H NMR (300.13 MHz, DMSO-d$_6$) δ = 7.34 (m, 2H, *m*-Ph); 7.05 (m, 1H, *p*-Ph); 7.03 (m, 2H, *o*-Ph); 6.14 (d, 1H, $^3J_{4,OH}$ = 6.5 Hz, OH); 5.70 (d, 1H, $^3J_{1,2}$ = 1.3 Hz, H-1); 4.46 (dd, 1H, $^3J_{2,3}$ = 3.4 Hz, $^3J_{1,2}$ = 1.3 Hz, H-2); 4.17 (d, 1H, $^3J_{4,5}$ = 9.3 Hz, H-5); 3.87 (dd, 1H, $^3J_{3,4}$ = 10.0 Hz, $^3J_{2,3}$ = 3.4 Hz, H-3); 3.78 (ddd, 1H, $^3J_{3,4}$ = 10.0 Hz, $^3J_{4,5}$ = 9.3 Hz, $^3J_{4,OH}$ = 6.5 Hz, H-4); 3.69 (s, 3H, CH_3CO).

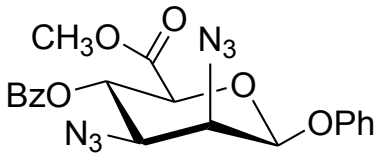
^{13}C NMR (75.5 MHz, DMSO-d$_6$) δ = 168.4 (COO); 155.8 (*i*-Ph); 129.8 (*m*-Ph); 122.8 (*p*-Ph); 116.0 (*o*-Ph); 96.5 (C-1); 76.0 (C-5); 66.8 (C-4); 62.7 (C-3); 62.2 (C-2); 52.4 (OCH_3).

$C_{13}H_{14}N_6O_5$(334.29):

Calcd.: C, 46.71; H, 4.22; N, 25.14;

Found: C, 46.41; H, 4.13; N, 25.05;

4.4.15. Methyl(phenyl 2,3-diazido-4-*O*-benzoyl-2,3-dideoxy-β-D-mannopyranoside)uronate (51)



In the course of 1 h benzoyl chloride (0.743 mL, 6.34 mmol) was added dropwise to a stirred soln of compound **50** (846 g, 2.52 mmol) in dry pyridine (9 mL) in DCM(9 mL) at 0 °C. After stirring for 12 h at 0 °C (monitored by TLC: Tol-EtOAc 5:1). DCM (20 mL) was added to the reaction mass and the organic solution was washed with 15% cold $NaHSO_4$ (3 X 10 mL), aq $NaHCO_3$ (3 x 10 mL), brine solution (15 mL) and concentrated. After repeated co-distillation with toluene (3 x 10 mL) to remove pyridine the residue was purified by flash chromatography (Eluent Gradient: EtOAc 0 → 90% in PE) to provide **51** (965mg, 87 %) as colourless crystals.

mp: 119-121°C;

***R*f**: 0.54 (Tol-EtOAc 5:1);

[α] $^{22}_{D}$ -119.8 ° (*c* 1.0, $CHCl_3$);

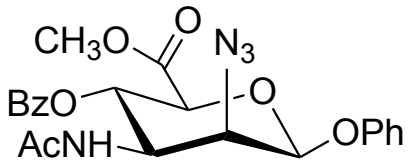
^{1}H NMR (300.13 MHz, DMSO-d$_6$) δ = 8.00 (m, 2H, *o*-Bz); 7.73 (m, 1H, *p*-Bz); 7.59 (m, 2H, *m*-Bz); 7.37 (m, 2H, *m*-Ph(1); 7.11-7.05 (m, 3H, *o*-Ph(1), *p*-Ph(1)); 5.81 (d, 1H, $^3J_{1,2}$ = 1.3 Hz, H-1); 5.25 (dd, 1H, $^3J_{3,4}$ = 10.2 Hz, $^3J_{4,5}$ = 9.8 Hz, H-4); 4.76 (dd, 1H, $^3J_{2,3}$ = 3.5 Hz, $^3J_{1,2}$ = 1.3 Hz, H-2); 4.69 (d, 1H, $^3J_{4,5}$ = 9.8 Hz, H-5); 4.49 (dd, 1H, $^3J_{3,4}$ = 10.2 Hz, $^3J_{2,3}$ = 3.5 Hz, H-3); 3.51 (s, 3H, OCH_3). **^{13}C NMR** (75.5 MHz, DMSO-d$_6$) δ = 167.3 (*C*$OOCH_3$); 165.1 (Ph*C*OO); 155.8 (*i*-Ph(1)); 134.3 (p-Bz); 129.9 (*m*-Ph(1)); 129.5 (*o*-Bz); 129.2 (*m*-Bz); 128.5 (*i*-Bz); 123.0 (*p*-Ph(1)); 116.1 (*o*-Ph(1)); 96.3 (C-1); 72.2 (C-5); 68.1 (C-4); 61.9 (C-2); 60.5 (C-3); 52.6 (OCH_3).

$C_{20}H_{18}N_6O_6$(438.39):

Calcd.:C, 54.79; H, 4.14; N, 19.17;

Found: C, 55.01; H, 4.25; N, 20.27;

4.4.16. Methyl(phenyl 2-azido-3-acetamido-4-benzoyl-2,3-dideoxy-β-D-mannopyranoside)uronate (53)



Thioacetic acid (0.4 mL, 5.7 mmol) and 2,6-lutidine (0.66 mL, 5.7 mmol)was added to a solution of **51** (500 mg, 1.14 mmol)in dry 1,4-dioxane (12.5 mL)and stirred for 24 hours at 100 °C(monitored by TLC, Tol-EtOAc 2:1). The reaction mass was filtered through a column of charcoal (packed over a layer of celite), concentrated and purified by column chromatography (Eluent Gradient: Ethyl acetate 0 → 50% in PE) providing **53** (362 mg, 70 %) as colourless crystals.

mp: 217-218°C;

***R*f**: 0.26 (PE-EtOAc 1:1);

[α] $^{22}_{D}$ -123.6 ° (*c* 1.04, $CHCl_3$);

^{1}H NMR (300.13 MHz, DMSO-d$_6$) δ = 8.32 (d, 1H, $^3J_{3,NH}$ = 9.0 Hz, NH); 7.88 (m, 2H, *o*-Bz); 7.69 (m, 1H, *p*-Bz); 7.54 (m, 1H, *m*-Bz); 7.35 (m, 2H, *m*-Ph(1)); 7.09-7.03 (m, 3H, *o*-Ph(1), *p*-Ph(1)); 5.99 (d, 1H, $^3J_{1,2}$ = 1.3 Hz, H-1); 5.05 (dd, 1H, $^3J_{3,4}$ = 10.4 Hz, $^3J_{4,5}$ = 9.8 Hz, H-4); 4.80 (ddd, 1H, $^3J_{3,4}$ = 10.4 Hz, $^3J_{3,NH}$ = 9.0 Hz, $^3J_{2,3}$ = 3.5 Hz, H-3); 4.65 (d, 1H, $^3J_{4,5}$ = 9.8 Hz, H-5); 4.42 (dd, 1H, $^3J_{2,3}$ = 3.5 Hz, $^3J_{1,2}$ = 1.3 Hz, H-2); 3.50 (s, 3H, OCH_3); 1.78 (s, 3H, CH_3CO).

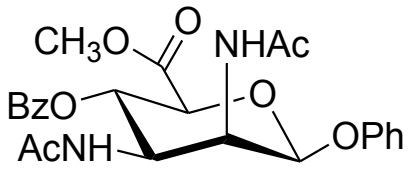
^{13}C NMR (75.5 MHz, DMSO-d$_6$) δ = 169.9 (*C*OCH_3); 167.8 (*C*$OOCH_3$); 165.5 (Ph*C*OO); 155.8 (*i*-Ph(1)); 133.9 (*p*-Bz); 129.8 (*m*-Ph(1)); 129.3 (*o*-Bz); 129.1 (*i*-Bz); 129.0 (*m*-Bz); 122.8 (*p*-Ph(1)); 116.1 (*o*-Ph(1)); 96.5 (C-1); 72.8 (C-5); 68.2 (C-4); 62.9 (C-2); 52.5 (OCH_3); 49.5 (C-3); 22.5 (CO*C*H_3).

$C_{22}H_{22}N_4O_7$(454.43):

Calcd.:C, 58.15; H, 4.88; N, 12.33;

Found: C, 57.92; H, 4.79; N, 12.18;

4.4.17. Methyl(phenyl 2,3-diacetamido-4-*O*-benzoyl-2,3-dideoxy-β-D-mannopyranoside)uronate (54)



To a solution of **53** (200 mg, 0.44 mmol) in EtOAc/MeOH 3:1 v/v mixture (4 mL), raney nickel (ca. 100 mg) and freshly distilled Ac_2O (0.13mL, 1.359 mmol) was added and the suspension was stirred overnight at room temperature under an atmosphere of hydrogen (monitored by TLC: $CHCl_3$-MeOH 20:1).The reaction mass was filtered through celite, concentrated and purification by column chromatography (MeOH 0→ 5% in $CHCl_3$) provided **44** (172.5 mg, 83 %) as colourless foam.

Rf: 0.3 ($CHCl_3$-MeOH 20:1);

$[\alpha]_D^{22}$ -135.8° (*c* 1.04, $CHCl_3$);

^{1}H NMR (300.13 MHz, DMSO-d$_6$) δ = 8.08 (d, 1H, $^3J_{2,NH}$ = 9.8 Hz, NH(2)); 7.90 (m, 2H, *o*-Bz); 7.79 (d, 1H, $^3J_{3,NH}$ = 9.1 Hz, NH(3)); 7.68 (m, 1H, *p*-Bz); 7.54 (m, 2H, *m*-Bz); 7.31 (m, 2H, *m*-Ph(1)); 7.05-7.00 (m, 3H, *o*-Ph(1), *p*-Ph(1)); 5.79 (d, 1H, $^3J_{1,2}$ = 2.0 Hz, H-1); 5.29 (dd, 1H, $^3J_{3,4}$ = 10.4 Hz, $^3J_{4,5}$ = 9.5 Hz, H-4); 4.72 (ddd, 1H, $^3J_{3,4}$ = 10.4 Hz, $^3J_{3,NH}$ = 9.1 Hz, $^3J_{2,3}$ = 4.1 Hz, H-3); 4.65 (d, 1H, $^3J_{4,5}$ = 9.5 Hz, H-5); 4.60 (dd, 1H, $^3J_{2,3}$ = 4.1 Hz, $^3J_{1,2}$ = 2.0 Hz, $^3J_{2,NH}$ = 9.8 Hz, H-2); 3.50 (s, 3H, OCH_3); 2.02, 1.71 (2s, 6H, CH_3CO).

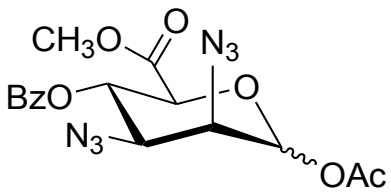
^{13}C NMR (75.5 MHz, DMSO-d$_6$) δ = 170.8, 169.7 (*C*OCH_3); 167.9 (*C*$OOCH_3$); 165.4 (Ph*C*OO); 156.2 (*i*-Ph); 133.7 (*p*-Bz); 129.7 (*m*-Ph(1)); 129.5 (*i*-Bz); 129.3 (*o*-Bz); 129.0 (*m*-Bz); 122.5 (*p*-Ph(1)); 116.4 (*o*-Ph(1)); 96.3 (C-1); 72.8 (C-5); 68.3 (C-4); 52.3 (OCH_3); 50.3 (C-3); 50.0 (C-2); 23.1, 22.6 (CO*C*H_3).

$C_{24}H_{26}N_2O_8$(470.47):

Calcd.: C, 61.27; H, 5.57; N, 5.95;

Found: C, 61.44; H, 5.45; N, 6.03;

4.4.18. Methyl(acetyl 2,3-diazido-4-*O*-benzoyl-2,3-dideoxy-β-D-mannopyranoside)uronate (55)



Perchloric acid (70 %) (12.5 µL) was added to a solution of **51** (100 mg, 0.22 mmol) in freshly distilled acetic anhydride (1 mL) at 0 °C and stirred for 24 hours at that temperature. (monitored by TLC Tol-EtOAc10:1). The reaction mass was diluted with EtOAc (2mL) and washed with water (1 mL), $NaHCO_3$ (3 x 1 mL), water (1 mL). Traces of acetic acid were removed by co-distillation with toluene. The crude product was concentrated and purified by column chromatography (Eluent Gradient: EtOAc 0 → 50% in PE) providing **55** (23 mg, 25 %) as colourless glassy syrup.

$[\alpha]_D^{22}$ = + 35.9. (*c* 1.0, $CHCl_3$);

^{1}H NMR (300.13 MHz, DMSO-d$_6$) δ = 8.05 (m, 2H, *o*-Bz); 7.73 (m, 1H, *p*-Bz); 7.58 (m, 2H, *m*-Bz); 6.09 (d, 1H, $^3J_{1,2}$ = 2.8 Hz, H-1); 5.33 ('t', 1H, $^3J_{3,4}$ = 9.2 Hz, $^3J_{4,5}$ = 8.8 Hz, H-4); 4.70 (dd, 1H, $^3J_{3,4}$ = 9.2 Hz, $^3J_{2,3}$ = 3.5 Hz, H-3); 4.59 (d, 1H, $^3J_{4,5}$ = 8.8 Hz, H-5); 4.48 (dd, 1H, $^3J_{2,3}$ = 3.5 Hz, $^3J_{1,2}$ = 2.8 Hz, H-2); 3.55 (s, 3H, OCH_3); 2.17 (s, 3H, CH_3CO).

^{13}C NMR (75.5 MHz, DMSO-d$_6$) δ = 168.4 (*C*OCH_3); 167.4 (*C*$OOCH_3$); 165.0 (Ph*C*OO); 134.3 (*p*-Bz); 129.7 (*o*-Bz); 129.1 (*m*-Bz); 128.5 (*i*-Bz); 90.0 (C-1); 70.7 (C-5); 68.2 (C-4); 60.2 (C-2); 59.2 (C-3); 52.6 (OCH_3); 20.8 (CO*C*H_3).

$C_{16}H_{16}N_6O_7$(404.33):

Calcd. C, 47.53; H, 3.99; N, 20.78;

Found C, 47.29; H, 3.63; N, 20.40;

5. References

1. J. Davies, J. *Nature* **1996**, *383*, 219–220.
2. Levy, S. B.; *Sci. Am*. **1998**, *278*, –53.
3. Sevag, N. G.; Ashton, B. *Nature*, **1964**, 203, 1323–1326
4. Ritossa, F. M. *Expl. Cell. Res*., **1964**, *35,* 601–607
5. Walsh, C. *Nature*, **2000**, *406*, 775–781.
6. Ashburner, M.; Boner, H. J. *Cell*, **1979**, *17,* 241–254.
7. Walsh, C.T.; Fischer, S.L.; Park, S.; Prahlad, M.; Wu, Z. *Chemistry & Biology*, **1996**, *3*, 21–28.
8. **National Nosocomial Infections Surveillance System.** National Nosocomial Infections Surveillance (NNIS) System report, Am. J. Infect. Control **27**:520-532
9. Itokazu, G. S.; Quinn, J.P.; Bell-Dixon, C.; Kahan, F.M.; Weinstein, R.A. *Clin. Infect. Dis*, **1996**, *23***,** 779-784.
10. Schweizer, M.; IIindennach, I.; Garten, W.; Henning, U. *Eur. J. Biochem*., **1978,** *82*, 211– 217.
11. Andersson, J.; Schreier, M. H.; Melchers, F. *Proc. Natl. Acad. Sci.*, **1980**, *77*, 612–616.
12. Hoffmann, M. K.; Koenig, S.; Mittler, R. S.; Oettgen, H. F.; Ralph, P.; Galanos, C.; Hammerling, U. *The Journal of Immunology*, **1979**, *122*, 497–502.
13. J. M. Cruse, J.M.; Lewis, R. E.; Karger, S. Conjugate Vaccines, Basel 1989.
14. Okuda, S.; Murata, S.; Suzuki, N. *Biochem. J.*, **1986**, *239*, 733–738.
15. Erin L. Westman, E. L.; McNally, D.J.; Rejzek, M.; Miller, W.L.; Kannathasan, V. S.; Preston, A.; Maskell, D.J.; Field, R.A.; Brisson, J.R.; Lam,J.S. *Biochem. J.,* **2007**, *405*, 123–130.
16. Thoden, J.B.; Holden, H.M.; *Biochemistry,* **2011**, *50*, 1483–1491
17. Caro, M.; Brissonb, J.R.; Martin, A.; Karibiana, D. *FEBS Letters*, **2000**, *477*, 8–14.

18. Paulsen, H. *Angew. Chem. Int. Ed.*, **1982**, *21*, 155–173.

19. Christ , W.J.; McGuinness , P.D.; Asano , O.; Wang, .Y.; Mullarkey ,M.A.; Perez , M.; Hawkins , L.D.; Blythe ,T.A.; Dubuc , G.R.; Robidoux,. A.L.; *J. Am. Chem. Soc.*, **1994**, 116, 3637–3638 ,

20. O Holst, O.; Brade, L.; Kosma, P.; Brade, H.; *J. Bacteriol.,* **1991**, *173*, 1862.

21. Ritter, T.K.; Wong, C.H.; *Angew. Chem. Int. Ed.*, **2001**, *40*, 2508–3533.

22. Seltmann, G.; Holst, O. *The Bacterial Cell Wall*, Springer **2002**.

23. Wang, L.; Wang, Q.; Reeves, P.R. *Subcellular Biochemistry*, **2010**, *53*, 123–152.

24. Raetz, C.; Whitfield, C. *Lipopolysaccharide Endotoxins Annu. Rev. Biochem.,* **2002**, *71*, 635–700.

25. Caroff, M.; Karibian, D. *Carbohydrate Research*, **2003**, *338,* 2431–2447.

26. Williams, P. *Methods in Microbiology*, Volume 27

27. Knirel, Y.A.; Vinogradov, E.V.; Shashkov, A.S.; Dmitriev, B. A.; Kochetkov, N. K. Carbohydr. Res. **1982**, 104, C4-C7.

28. Knirel, Y. A., and Kochetkov, N. K. (1994) Structure of lipopoly- saccharides from Gram-negative bacteria. III. Structure of O-specific polysaccharides. Biokhimiya 59, 1784–1851.

29. Sadovskaya, I.; Brisson, J.R.; Thibault, P.; Richards, J.C.; Lam, J.S.;

30. Altman, E.; *Eur. J. Biochem.*, **2000**, *267*,1640–1650.

31. Coyne, M. J.; Russell, K. S.; Coyle. C. L.; Goldberg, J. B., *J. Bacteriol.*, **1994**, *176*, 3500.

32. Loutet, S.A.; Flannagan, R.S.; Kooi, C.; Sokol, P.A.; Valvano, M.A. *J. Bacteriol.*, **2006**, *188,* 2073–2080.

33. Qureshi, N.; Takayama, K.; Mascagni, P.; Honovich, J.; Wong, R.; Cotter, R. J. *The Journal of Biological Chemistry*, **1988**, *263*, 11971-11976.

34. Ashley S Beasley, A.; Cotter, R.J.; Vogel, S.N.; Inzana, T.J.; Qureshi, A.A.; Qureshi, N. *Innate Immunity*, **2012**, *18*, 268–278.

35. Knirel, Y.A; Kocharova, N. A.; Shashkov, A.S.; Dmitriev, B.A.; Kochetkov, N.K. *Carbydr. Res*., **1981**, *93*, C12-C13.

36. Cummins, C. S.; White, R. H. *J.Bacteriol*., **1983**, *153*, 1388-1393.

37. Fabio1, J.L.D.; Caroff, M.; Karibian, D.; Richards, J.C.; Perry, M.B. *FEMS, Microbiology letters*, **1992**, *97*, 275–282.

38. Paulsen, H. *Angew. Chem. Int. Ed.*, **1982**, *21*, 155–173.

39. Harvill, E. T.; Preston, A.; Cotter, P. A.; Allen, A. G.; Maskell, D. J.; Miller, J. F. *Infect. Immun*., **2000**, *68*, 6720–6728.

40. Rejzek, M.; Kannathasan, V. S.; Wing, C.; Preston, A.; Westman, E. L.; Lam, J. S.; Naismith, J. H.; Maskell, D .J.; Field, R. A. *Org. Biomol. Chem* ., **2009**, *7*, 1203–1210.

41. Meyer zu Reckendorf, W. *ChemischeBerichte*, **1969**, *102,* 4207- 4208.

42. Meyer zuReckendorf, W. *ChemischeBerichte*, **1968**, *101***,** 3802–3807.

43. Berger, I.; Nazarov, A.A.; Hartinger, C.G.; Groessl, M.; Valiahdi, S.M.; Jakupec, M.A.; Keppler, B.K. *ChemMedChem,* **2007**, *2*, 505 – 514

44. Code, J.D.C.; Stubba, B.; Schiattarella, M.; Overkleeft, H.S.; van Boeckel,‡C.A.A.; van Boom, J.H.; van der Marel, G.A. *J. Am. Chem. Soc*., **2005**, *27*, 3767-3773.

45. Mico, A.D.; Margarita, R.; Parlanti, L.; Vescovi, A; Piancatelli, G.; *J. Org. Chem.***1997**, *62*, 6974-6977

46. van den Bos, L.J.; Litjens, R.E.J.N.; Overkleeft, H.S.; van der Marel, G.A.; *Org. Lett.,* **2005**, *7*, 2007-2010.

47. Jung, M.E.; Toyota, A.; *J. Org. Chem.* **2001**, *66*, 2624-2635.

48. Miao, C.X.; He,L.N.; Wang, J,Q; Wang, J.L. *Adv. Synth. Catal. 2009*, *351*, 2209 – 2216.

49. Lin, F.; Peng, W.; Xu, W.; Hanb, X.; Yua, B. *Carbohydr. Res* 339 (2004) 1219–1223

50. Chauvin, A.L.; Nepogodiev, S.A.; Field, R.A. *J. Org. Chem.* **2005**, *70*, 960-966

51. Söderman, P.; Widmalm,G.; *Eur. J. Org. Chem.* **2001**, 3453-3456

52. Ikunaka,M.; Matsumoto,J.; Nishimoto,Y. *Tetrahedron Asymmetry,* **2002**, *13,* 1201–1208

53. Calderón, F. *Synlett*, **2006**, 4, 657–658.

54. Rejzek, M.; Mukhopadhyay, B.; Wenzel. C.Q.; Lamb, J.S.; Field, R.A. *Carbohydrate Research,* **2007**, *342*, 460–466.

55. Meyer zuReckendorf, W. *ChemischeBerichte*, **1970**, *103*, 995–996.

56. Chauvin, A.L.; Nepogodiev, S.A.; Field, R.A. *J. Org. Chem*. **2005**, *70*, 960–966.

57. Inch, T.D.; Lewis, G.J. *Carbohyd. Res*., **1972**, *22,* 91-101.

58. Sum, P.E.; Weiler, M., *Can. J. Chem*., **1982**, *60*, 327-334

59. Walvoort, M. T.C.; Moggre, G. J.; Lodder, G.; Overkleeft, H. S.; Codee, J. D. C.; and van der Marel, G. A. *J. Org. Chem*. **2011**, 76, 7301–7315

60. Helferich, B.; Schmitz-Hillebrecht, E. *Berichte der Deutschen Chemischen Gesellschaft* **1933,***66*, 378-383.

61. Gent, P. A.; Gigg, R.; Penglis, A. A. E. *Journal of the Chemical Society, Perkin Transactions 1,* **1976**, 1395-1404.

62. Murphy, P. V.; O'Brien, J. L.; Smith III, A. B. *Carbohydr. Res.,* **2001**, *334*, 327-335.

63. Guthrie, R. D.; Jenkins, I. D.; Yamasaki, R. *Journal of the Chemical Society*, *Chemical Communications*, **1980**, 784-785.

64. Capek, K.; Capkova, J.; Jary, J.; Knirel, Y. A. *Collection of Czechoslovak Chemical Communications*, **1987**, *52*, 2248−2259.

65. Mengel, R.; Bartke, M. *Angew. Chem. Int. Ed.*, **1978**, 17, 679−680.

66. Nilsson, M.; Norberg, T. *Carbohydrate Research,* **2000**,327, 261–267.

67. Hughes, D. L. *Organic preparations and procedures int.,***1996,** 28 (2), 127-164.

68. Guthrie, R. D.; Jenkins, I. D.; Yamasaki, R. *Journal of the Chemical Society, Chemical Communications*, **1980**, 784−785.

69. Kumara Swamy, K. C.; Bhuvan Kumar, N. N.; Balaraman, E.; Pavan Kumar, K. V. P.; *Chem. Rev.* **2009**, *109,* 2551–2651

70. Kiankarimi, M.; Lowe, R.; McCarthy, J.R.; Whitten, J.P. *Tetrahedron Letters*, **1999**, *40*, 4497−4500.

71. Pelletier, J.C.; Kincaid, S.; *Tetrahedron Letters*, **2000**, *41*, 797–800.

72. Proctor, A.J.; Beautement, K.; Clough, J,.M.; Knight, D.W.; Li, Y. *Tetrahedron Letters,* **2006,** *47* 5151–5154.

73. But, T. Y. S.; Toy, P. H. *J. Am. Chem. Soc*., **2006**, *128*, 9636.

74. Fürst, A.; Plattner, P. A., *Helv.Chim.Acta*, **1949**, *32*, 275.

75. Stevens, C.L.; Glinski, R.P.; Taylor, K.G.; Blumbergs, P.; Gupta, S.K. *J. Am. Chem. Soc*., **1970**, *92*, 3160–3168.

76. Tsuda, T.; Furuike, T.; Shin-Nishimura, I. *Bull. Chem. Soc. Jpn*., **1996,** *69*, 411-416.

77. Deshpande, S.G.; Pathak. T., *Tetrahedron,* **2007**, *63*, 602–608

78. Williams, D.R.; Klingler, F.D.; Allen, E.E.; Lichtenthaler, F.W.; *Tetrahedron Letters*, **1988**, *29*, 5087-5090

79. Gnichtel, H.; Rebentisch, D. *J. Org. Chem.* **1982**, *47*, 2691−2697.

80. Hansen, T. M.; Florence, G.J.; Mas, P.L.; Chen, J.; Abrams, J. N.; Forsyth, C.J. *Tetrahedron Letters,* **2003**, *44,* 57–59.

81. Einhorn, J.; Einhorn, C.; Ratajczak, F.; Pierre, J.L. *J. Org. Chem*., **1996**, *61*, 7452–7454.

82. Angelin, M.; Hermansson, M.; Dong, H.; Ramström, O. *Eur. J. Org. Chem.,* **2006**, 4323–4326.

83. Williams, D.R.; Klingler, F.D.; Allen, E.E.; Lichtenthaler, F.W.; *Tetrahedron Letters*, **1988**, *29*, 5087-5090

84. Shangguan, N.; Katukojvala, S.; Greenberg, R.; Williams, L.J.; *J. Am. Chem. Soc*., **2003**, 125, 7754−7755.

85. Afonso, C. A. M. *Tetrahedron Lett*., **1995**, *36*, 8857.

86. Wu, B.; Zhang, J.; Yang, M.; Yue, Y.; Ma, L.J.; Yu, X. Q. *Arkivoc*, **2008**, 95-102.

87. Comegna, D.; Bedini, E.; Parrilli, M. *Tetrahedron* **2008,** *64,* 3381−3391.

88. Shah, R.N.; Baptista, J.; Perdomo, G.R.; Carver, J.P.; Krepinsky, J.J. J. Carbohydrate chemistry, **1987**, *6*, 645-660.

89. Amarego, W. L. F.; Chai, C. L. L. „Purification of Laboratory Chemicals“, **2003**, 5th Ed.; Butterworth-Heinemann: Elsevier Science.

90. Shulman, M. L.; Khorlin, A. Y. *Carbohydr. Res.***1973**, *27*, 141–147

91. Babič, A.; Pečar, S. *Tetrahedron Lett.***2007**, *48*, 4403–4405.

92. Lee, H. H.; Congson, L. N.; Whitfield, D. M.; Radics, L. R.; Krepinsky, J. J. *Can. J. Chem.***1992**, *70*, 2607–2617.

93. Lee, H. H.; Congson, L. N.; Whitfield, D. M.; Radics, L. R.; Krepinsky, J. J. *Can. J. Chem.***1992**, *70*, 2607–2617.

94. Gross, P. H.; Jeanloz, R. W. *J. Org. Chem.***1967**, *32*, 2759–2763.

95. Gross, P. H.; Jeanloz, R. W. *J. Org. Chem.***1967**, *32*, 2759–2763.

96. Calvo-Mateo, A.; de las Heras, F. G. *Carbohydr. Res.***1986**, *155*, 266−271.

97. Meyer zu Reckendorf, W.; Wassiliadou-Micheli, N. *Chem. Ber.***1974**, *107*, 1188-1194.

98. Helferich, B.; Schmitz-Hillebrecht, E. *Berichte der Deutschen Chemischen Gesellschaft* **1933,***66*, 378-383.

99. Gent, P. A.; Gigg, R.; Penglis, A. A. E. *Journal of the Chemical Society, Perkin Transactions 1***1976**, 1395-1404.

100. Murphy, P. V.; O'Brien, J. L.; Smith III, A. B. *Carbohydr. Res.***2001**, *334*, 327-335

Appendix

Crystal Data and Structural refinement

Phenyl-2-O-triflyl-3-azido-3-deoxy-4-6-O-benzylidene-β-D-glucopyranoside (28)

Identification code	is_e400colrc	
Empirical formula	$C_{20}H_{18}F_3N_3O_7S$	
Formula weight	501.43	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group (H.-M.)	P 21	
Space group (Hall)	P 2yb	
Unit cell dimensions	a = 10.6222(4) Å	α = 90.00°.
	b = 8.0316(3) Å	β = 98.5100(10)°.
	c = 13.0546Å	γ = 90.00°.
Volume	1101.47(7) $Å^3$	
Z	2	
Density (calculated)	1.512 Mg/m^3	
Absorption coefficient	0.220 mm^{-1}	
F(000)	516	
Crystal size	0.99 x 0.22 x 0.12 mm^3	
Θ range for data collection	1.94 to 30.99°.	
Index ranges	-15≤h≤15, -10≤k≤11, -18≤l≤18	

APPENDIX

Reflections collected	14532
Independent reflections	6277 [R(int) = 0.0186]
Completeness to Θ = 30.99°	99.7%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8113 and 0.9740
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5636 / 0 / 307
Goodness-of-fit on F^2	1.046
Final R indices [I>2σ(I)]	R1 = 0.0335, wR2 = 0.0811
R indices (all data)	R1 = 0.0401, wR2 = 0.0854
Largest diff. peak and hole	0.214 and -0.231 e.$Å^{-3}$

Phenyl-2-azido-2-deoxy-3-O-acetyl-4,6-O-benzylidene-β-D-altropyranoside (29)

Identification code	e221colrc
Empirical formula	$C_{21}H_{21}N_3O_6$
Formula weight	411.41
Temperature	173(2) K
Wavelength	0.71073Å
Crystal system	orthorhombic
Space group (H.-M.)	'P 21 21 21'
Space group (Hall)	'P 2ac 2ab'
Unit cell dimensions	
	a = 9.9405(3)Å α = 90.00°.

	b = 13.2647(4)Å β = 90.00°.
	c = 15.3743(4)Å γ = 90.00 °.
Volume	2027.22(10) $Å^3$
Z	4
Density (calculated)	1.348Mg/m^3
Absorption coefficient	0.100mm^{-1}
F(000)	864
Crystal size	0.38 x 0.33 x 0.17 mm^3
Θ range for data collection	2.44to 30.00°.
Index ranges	-13≤h≤13, -18≤k≤17, -21≤l≤21
Reflections collected	23088
Independent reflections	5888 [R(int) = 0.0231]
Completeness to Θ = 30.00°	99.9%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9629and 0.9831
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5139 / 0 / 272
Goodness-of-fit on F^2	1.045
Final R indices [I>2σ(I)]	R1 = 0.0360, wR2 = 0.0911
R indices (all data)	R1 = 0.0450, wR2 = 0.0958
Largest diff. peak and hole	0.249 and -0.231 e.$Å^{-3}$

APPENDIX

Phenyl-2-O-acetyl-3-azido-3-deoxy-4-6-O-benzylidene-β-D-glucopyranoside (30)

Identification code	is_e222colrc	
Empirical formula	$C_{21}H_{21}N_3O_6$	
Formula weight	411.41	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group (H.-M.)	'P 21'	
Space group (Hall)	'P 2yb'	
Unit cell dimensions	a = 8.2456(4)(4) Å	α = 90.00°.
	b = 5.6605(2) Å	β = 90.134(2).
	c = 21.8434(10) Å	γ = 90.00°.
Volume	1019.52(8) $Å^3$	
Z	2	
Density (calculated)	1.340 Mg/m^3	
Absorption coefficient	0.100 mm^{-1}	
F(000)	432	
Crystal size	0.99 x 0.16 x 0.12 mm^3	
Θ range for data collection	2.47to 29.96°.	
Index ranges	-11≤h≤11, -7≤k≤5, -30≤l≤28	
Reflections collected	10243	
Independent reflections	4350 [R(int) = 0.0194]	
Completeness to Θ = 29.96°	98.5 %	

APPENDIX

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9077and 0.9881
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3454/ 0 / 272
Goodness-of-fit on F^2	1.024
Final R indices [I>2σ(I)]	R1 = 0.0373, wR2 = 0.0805
R indices (all data)	R1 = 0.0526, wR2 = 0.0869
Largest diff. peak and hole	0.264and -0.226 e.$Å^{-3}$

Phenyl-2,3-diazido-2,3-dideoxy-4,6-O-benzylideneβ-D-*manno*pyranoside (31)

Identification code	is_e240col	
Empirical formula	$C_{19}H_{18}N_6O_4$	
Formula weight	394.39	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group (H.-M.)	P 21	
Space group (Hall)	P 2yb	
Unit cell dimensions	a = 4.9198(2) Å	α = 90.00°.
	b = 9.8840(4) Å	β = 90.529(2)°.
	c = 19.0156(7) Å	γ = 90.00°.
Volume	924.64(6) $Å^3$	
Z	2	

Density (calculated)	1.417 Mg/m^3
Absorption coefficient	0.103 mm^{-1}
F(000)	412
Crystal size	0.68 x 0.36 x 0.07 mm^3
Θ range for data collection	1.07 to 30.98°.
Index ranges	$-6 \leq h \leq 7$, $-13 \leq k \leq 14$, $-27 \leq l \leq 27$
Reflections collected	11543
Independent reflections	5694 [R(int) = 0.0196]
Completeness to Θ = 30.98°	99.9%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9331 and 0.9928
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4833 / 0 / 262
Goodness-of-fit on F^2	1.017
Final R indices [$I>2\sigma(I)$]	R1 = 0.0381, wR2 = 0.0951
R indices (all data)	R1 = 0.0495, wR2 = 0.1007
Largest diff. peak and hole	0.297 and -0.210e.$Å^{-3}$

32

Identification code	is_e269c1_2
Empirical formula	$C_{19}H_{17}N_3O_4$
Formula weight	351.36
Temperature	173(2) K

APPENDIX

Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	P 1	
Space group (Hall)	P 1	
Unit cell dimensions	a = 10.2247(5) Å	α = 81.448(2)°.
	b = 10.5323(5) Å	β = 79.037(3)°.
	c = 16.8949(8) Å	γ = 75.623(2)°.
Volume	1720.38(14) $Å^3$	
Z	4	
Density (calculated)	1.357 Mg/m^3	
Absorption coefficient	0.097 mm^{-1}	
F(000)	736	
Crystal size	0.55 x 0.27 x 0.01 mm^3	
Θ range for data collection	2.25 to 29.00°.	
Index ranges	-13≤h≤13, -14≤k≤14, -23≤l≤21	
Reflections collected	43164	
Independent reflections	15585 [R(int) = 0.0265]	
Completeness to Θ = 29.00°	99.6%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9099 and 0.9865	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	12409 / 0 / 207	
Goodness-of-fit on F^2	1.006	

Final R indices [I>2σ(I)]	R1 = 0.0399, wR2 = 0.0828
R indices (all data)	R1 = 0.0589, wR2 = 0.0895
Largest diff. peak and hole	0.143 and -0.214 e.Å^{-3}

Phenyl-2,3-diazido-2,3-dideoxy-β-D-mannopyranoside (33)

Identification code	is_e306col	
Empirical formula	C_{16} H_{18} N_6 O_6	
Formula weight	390.36	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group (H.-M.)	P 21	
Space group (Hall)	P 2yb	
Unit cell dimensions	a = 9.6731(14) Å	α = 90.00°.
	b = 5.2485(7) Å	β = 103.678(7)°.
	c = 18.712(3) Å	γ = 90.00°.
Volume	923.1(2) Å^3	
Z	2	
Density (calculated)	1.404 Mg/m^3	
Absorption coefficient	0.110 mm^{-1}	
F(000)	408	
Crystal size	0.99 x 0.10 x 0.03 mm^3	
Θ range for data collection	2.66 to 28.99°.	
Index ranges	-13≤h≤13, -7≤k≤7, -25≤l≤25	

APPENDIX

Reflections collected	10831
Independent reflections	4520 [R(int) = 0.0359]
Completeness to Θ = 28.99°	99.9%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8989 and 0.9967
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3609 / 0 / 255
Goodness-of-fit on F^2	1.014
Final R indices [I>2σ(I)]	R1 = 0.0402, wR2 = 0.0815
R indices (all data)	R1 = 0.0586, wR2 = 0.0886
Largest diff. peak and hole	0.209 and -0.168 e.$Å^{-3}$

Methyl-(phenyl-2,3-diazido-2,3-dideoxy-4-benzoyl-β-D-mannopyranoside)uronate (42)

Identification code	ch_OB2	
Empirical formula	$C_{20}\ H_{18}\ N_6\ O_6$'	
Formula weight	438.40	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group (H.-M.)	'P 21'	
Space group (Hall)	'P 2yb'	
Unit cell dimensions	a = 13.2002(11)Å	α= 90.00 (15)°.
	b = 5.8944(6)Å	β= 91.944(6)°.
	c = 26.554(3)Å	γ = 90.00 (14)°.

APPENDIX

Volume	2064.9(3)Å^3
Z	4
Density (calculated)	1.410Mg/m^3
Absorption coefficient	0.107mm^{-1}
F(000)	912
Crystal size	1.00 x 0.07 x 0.04 mm^3
Θ range for data collection	1.53 to 25.50°.
Index ranges	-15≤h≤15, -6≤k≤7, -32≤l≤32
Reflections collected	16188
Independent reflections	7396 [R(int) = 0.0547]
Completeness to Θ = 25.50°	100 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9003 and 0.9957
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4921 / 0 / 579
Goodness-of-fit on F^2	1.000
Final R indices [I>2σ(I)]	R1 = 0.0486, wR2 = 0.0864
R indices (all data)	R1 = 0.0917, wR2 = 0.1037
Largest diff. peak and hole	0.193 and -0.198e.Å^{-3}

Curriculum Vitae

Jaya Shanmuga Prakash Jegannathan

- Ph.D (Carbohydrate Chemistry, 2009-Oct 2013), University of Rostock, Germany
- M.Sc., Chemical Sciences (Pondicherry University, India)

Research

Feb 2009-till date **Ph.D University of Rostock, Germany.**

Synthetic Carbohydrate Chemistry.

Total Synthesis of gluco, galacto and mannose derivatives of 2,3-acetamido uronates.

June 2006-Jan 2009 **Research Associate, SRF Ltd, R & D, India**

Fluorine Chemistry.

Synthesis of Ethyl trifluoroacetoacetate, Ethyl amino crotonate. Synthesis of fluorinating agents such as SF_4, DAST, F_2.

Education

2004 –2006 **Master of Science (M.Sc) in Chemical Sciences**

Organic, Inorganic, Physical and Theoritical Chemistry
Grade - First Class

Pondicherry University (central university), Pondicherry, India.

2000-2003 **Bachelor of Science (B.Sc) in Chemistry**

Major Chemistry, Ancillary Physics, Allied Mathematics
Grade - First Class

Madras Christian College (Autonomous), University of Madras, Chennai, India.

Publications

Sep 2011	*Presented a poster* "Synthesis of Diacetamido-Dideoxy-uronic Acids which Represent Rare Modules of Bacterial Envelope", in JCF-fruehjahrssymposium, Rostock, Germany.
Mar 2012	*Presented a poster* " 2,3-acetamido-2,3-dideoxymannouronate: a bacterial cell wall constituent.", in Tagung Iminiumsalze Conference, Bartholomä/Ostalbkreis, Germany.

Credentials

2004	Secured 2nd rank in all India entrance examination of Pondicherry University**.**
2008	TOEFL Score 97/120

References

Prof. Christian Vogel,

Department for Organic Chemistry,

University of Rostock,

18059 Rostock , Germany

Email: christian.vogel@uni-rostock.de Tel.: +49 381 498 6430

Prof. S.Baskaran,

Department of Chemistry,

Indian Institute of Technology, Madras,

Chennai 605014, India.

Email: sbhaskar@iitm.ac.in Tel.: +91 44 2257 5218

Erklärung

Ich versichere hiermit an Eides statt, dass ich die vorliegende Arbeit selbstständig angefertigt und ohne fremde Hilfe verfasst habe, keine außer den von mir angegebenen Hilfsmitteln und Quellen dazu verwendet habe und die den benutzten Werken inhaltlich und wörtlich entnommenen Stellen als solche kenntlich gemacht habe.

Jaya Shanmuga Prakash