Heterocyclic Letters
Vol. 11| No.3|329-334|May-July|2021
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

BANIK'S GLYCOSYLATION REACTION

Bimal Krishna Banik*[1] and Ram N. Yadav[2]

[1]Department of Mathematics and Natural Sciences, College of Sciences and Human Studies, Deanship of Research Development, Prince Mohammad Bin Fahd University, Al Khobar 31952, Kingdom of Saudi Arabia; [2] Department of Chemistry, Faculty of Engineering & Technology, Veer Bahadur Singh Purvanchal University, Jaunpur-222003 (U.P.) INDIA
Email: bimalbanik10@gmail.com; bbanik@pmu.edu.sa
#Dedicated to the Dr. R. R. Gupta on the Occasion on his 80th Birthday

Abstract:
Ferrier rearrangement is one of the most fascinating reactions for installing diverse nucleophiles with high degree of stereoselectivity at the anomeric centre of the carbohydrate system toward the synthesis biologically active natural products. In carbohydrate chemistry, a reaction of glycosyl donor and acceptor catalyzed by various promoters is called glycosylation. Banik's glycosylation describes reaction of diverse hydroxy beta lactams with unsaturated glycals in the presence of iodine or bismuth nitrate as the catalysts.

Definition:
Banik's glycosylation describes the glycosylation of *rac*-β-lactam as glycosyl acceptor with diversely protected D-glucal as glycosyl donor using molecular iodine or bismuth nitrate as potential glycosyl promoter under ambient reaction condition.

Synthetic utility:
Optical resolution of *rac*-β-lactam into its enantiomeric form.
Chemical required:
Rac-β-lactam and protected D-glucal
Reagents: Bismuth (III) nitrate pentahydrate and molecular iodine
Solvent: Dichloromethane and THF
Temperature: 0^0C-RT
Time of the Reaction: 3-5 h
The General and Mechanistic Aspects of Banik's Glycosylation:
Banik's glycosylation is related to Ferrier glycosylation reaction. However, Banik has demonstrated glycosylation with beta lactam derivatives for the first time. It involves the allylic coupling of a nucleophile to a glycal having a leaving group at C-3 position, which leads to the corresponding 2,3-unsaturated glycoside. Initially the delocalized allyloxocarbenium ion **2** is formed by acid activator. This intermediate trapped by *in situ* with nucleophiles which leads to

the anomeric mixtures of α and β **3** and **4** glycosides followed by the double bond migration to the position 3, 4[1][2].

The glycosidic bond is usually formed by the nucleophilic attack of the nucleophile or other partially protected sugars moiety to the electrophilic center of a glycal. The compound that gives the glycosyl moiety is called the *glycosyl donor*, and the nucleophile that receives it is known as *glycosyl acceptor*. The reaction generally is performed in the presence of an activator called "promoter". The role of the promoter is to assist the departure of the leaving group from the anomeric postion of the sugar moiety. Promoters are often used in catalytic amounts, although in some instances they are used stoichiometrically. In some cases, other additives such as molecular sieves or base as acid scavenger are used[3,4].

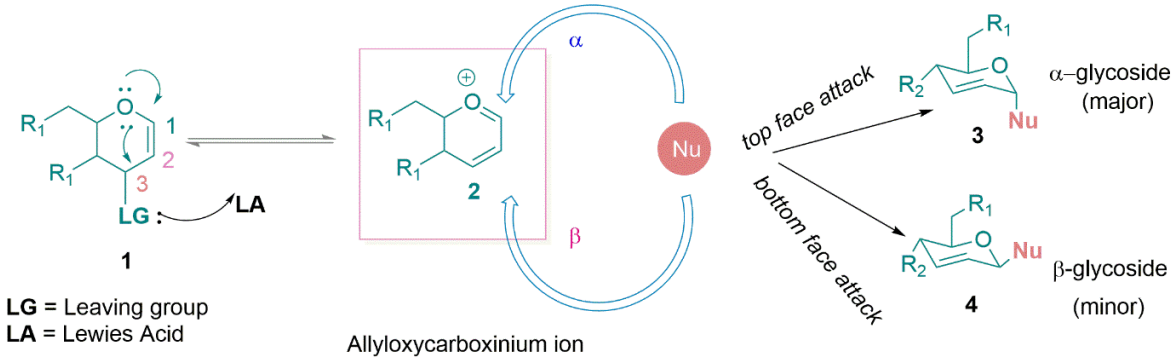


FIG. 1 General reaction mechanism

Challenge and Problem with Glycosidic bond formation:

The success of a coupling reaction between glycals and nucleophiles depends on the donor and acceptor's reactivity and the nature of the protecting groups present in the sugar's structures. It greatly influences the preferred selectivity of the reaction towards the two anomeric forms. The mode of reaction condition and experience of the person conducting the reaction also plays a role. The choice of solvent and temperature also play a crucial role in product distribution[5].

Promotor, solvent, and experimental condition:

The promoters are generally a Lewis acid, transition metal, ionic liquid, organocatalyst, and solid supported resin. These have a significant influence on the reaction as it favors the departure of the leaving group. The solvent also impacts the overall rate of the processes and on the glycosylated products' stereochemistry. Solvents of low polarity such as dichloromethane or diethyl ether are frequently used for the glycosylation reaction. The polar aprotic solvents, such as acetonitrile or nitromethane, have also been used for this purpose. It is known that the coordinating properties of the solvents to form a complex with sugar oxonium cation intermediate influence the approaches of the nucleophiles and influence the anomeric ratio of the products.

β-lactam O-glycosides from Glycal as glycosyl donor

Perhaps, oxygen-glycosides are common, and these can be synthesized from glycals by nucleophilic addition of β-lactam alcohols in the presence of a catalyst. A wide range of O-glycosides of corresponding enantiopure β-lactam alcohols was prepared. The most common catalysts include molecular iodine and bismuth (III) nitrate pentahydrate.

This reaction proceeded with numerous types of β-lactam alcohols, and the products were obtained predominantly as the α-anomers, in good yields. The alteration of the mechanistic

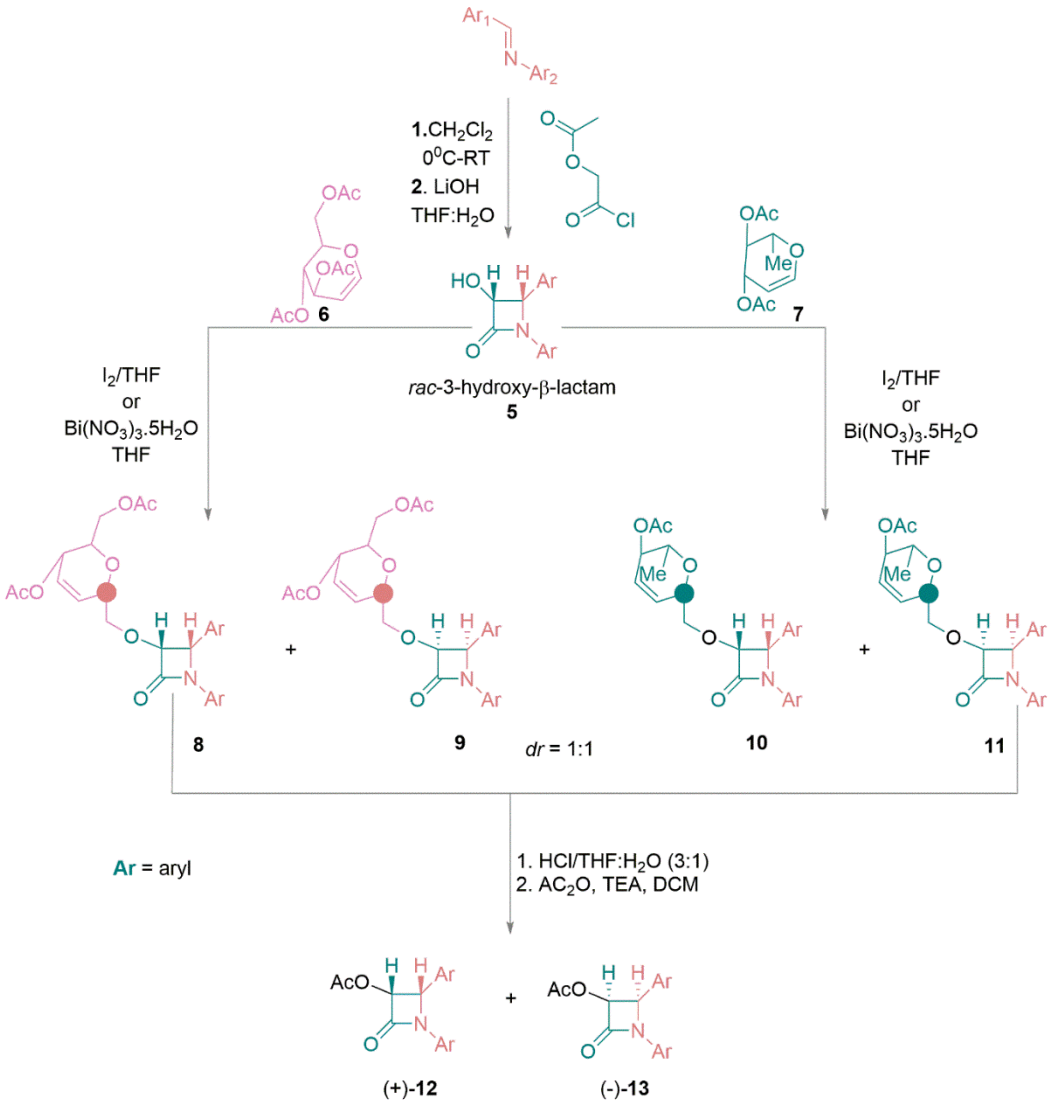
route concerning temperature changes was a very attractive part of this method. Importantly, THF or acetonitrile as solvent failed to demonstrate this switch in a mechanism that was observed only with DCM and 1, 2-dichloroethane.

Glycosylation with *rac*-β-lactam:

The *rac*-β-lactam**s** are synthesized by using thermal ketene-imine [2+2] cycloaddition reaction. The resulting racemic *cis*-acetoxy β-lactams have been transformed into the corresponding cis 3-hydroxy-β-lactam using a mild base at 0^0C.

The racemic *cis*-β-lactam is used as a glycosyl acceptor in Ferrier glycosylation. To this end, glycosyl donors have dissolved in anhydrous dichloromethane, and the reaction flask was placed under the ice bath. After cooling the reaction for five minutes, the molecular iodine (1.equiv.) was added in one slot, and the reaction mixture cooled at the same temperature for additional five minutes with constant stirring.

The racemic beta lactam (1.0 mmole) was dissolved in anhydrous dichloromethane and added to the reaction mixture dropwise with a syringe pump over 5 to 10 minutes. After that, that reaction mixture was allowed to stir for 1h at the same temperature, and the reaction mixture was brought to room temperature and keep stirring 3-5h. The reaction's progress was monitored by checking the TLC of the aliquot of the reaction mixture. After the completion, the reaction mixture was quenched with aq. sodiumthiosulphate and extracted with dichloromethane. The organic layer was washed with water, and the solvent was removed using a rotary evaporator under reduced pressure. The resulting crude mass was purified over silica gel column



SCHEME 1 Chiral resolution of rac-b-lactam using carbohydrate chiron in glycosylation reaction

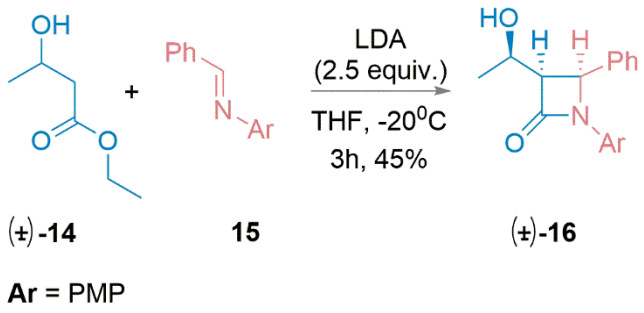
chromatography using hexane, and ethyl acetate as eluent to afford the α-glycoside of the corresponding β-lactam in excellent yield

Glycosylation using *rac*-hydroxymethyl β-lactam:

We envisioned that the *rac*-*cis*-3-(1-hydroxyethyl)-4-phenyl-N-*p*-anisyl-2-azetidinone **16**, is the key component of thienamycin. Towards, this endeavor we have performed the reaction of *rac*- (±)-ethyl-3-hydroxy-butyrate 1**4** and anisylaldimine **5** in anhydrous THF at -20^{0}C to room temperature.

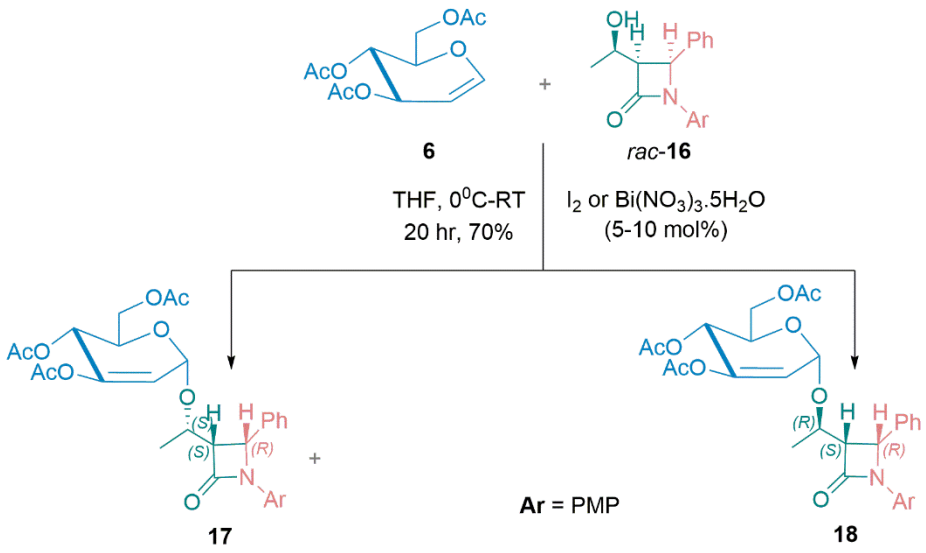
We have noticed that the lithium dianion of ester-enolate at – 20 ^{0}C with 2.5 equivalents of lithium ispropyl amide (LDA) in 1 **M** THF solution with one equivalent of *p*-anisylaldimine **15** gave *cis*-β-lactam **16** in 45% yield as single diastereoisomer. The extensive study in the field of β-lactams chemistry and the stereochemical outcome of cis and trans beta-lactam at C3

and C4 position inevitably depends on the configuration the of lithium enolate (Z/E structure) and spatial arrangement of the substituent of aldimine in transition state (T.S) of the ester-imine enolate intermediate. Based on the literature report the outcome of the *cis* stereochemistry is attributed due to E-enolate followed by the transition state.



SCHEME 2 synthesis of 3-hydroxymethyl β-lactam analog of tthienamycine

Ferrier glycosylation of *cis*-3-(1-hydroxyethyl)-4-phenyl-N-p-anisyl-2 azetidinone **6** using Tri-O-acetyl-D-glucal **7** as model glycosyl donor in presence of Bi $(OTf)_3$. (5-10 mol%) in anhydrous THF at 0^0C to 25^0C was performed for 20 h. Thin layer chromatography was used to follow the course of the reaction using ethyl acetate-hexane (20:80). Two major new spots were appeared in the TLC plate. After work-up and column chromatography of the crude materials, two products corresponding to compounds **17** and **18** were isolated in 70% yield[6].



SCHEME 3 Glycosylation of rac-3-hydroxy β-lactamvia-Ferrier glycosylation of D-glucal

Conclusions:

Banik's glycosylation is extremely versatile to prepare numerous glycosides mostly by a stereoselective pathway. Various catalysts are able to promote the glycosylation reaction

between acceptor-donor. Because of the biological activity of the glycosides, this method as described herein will find a wide range of application in chemistry, biology, medicine and pharmacy.

References:

[1] B.K. Banik, M.S. Manhas, A.K. Bose, Stereospecific Glycosylation via Ferrier Rearrangement for Optical Resolution, J. Org. Chem. 59 (1994) 4714–4716. https://doi.org/10.1021/jo00096a004.

[2] B.K. Banik, C. Mukhopadhyay, C.R. Logan, F.F. Becker, Optical resolution of dibenzo[a,g]fluorenol via glycosylation, Synth. Commun. 37 (2007) 3895–3900. https://doi.org/10.1080/00397910701572209.

[3] D. Crich, Mechanism of a chemical glycosylation reaction, Acc. Chem. Res. 43 (2010) 1144–1153. https://doi.org/10.1021/ar100035r.

[4] P.O. Adero, H. Amarasekara, P. Wen, L. Bohé, D. Crich, The Experimental Evidence in Support of Glycosylation Mechanisms at the SN1-SN2 Interface, Chem. Rev. 118 (2018) 8242–8284. https://doi.org/10.1021/acs.chemrev.8b00083.

[5] Y. Geng, A. Kumar, H.M. Faidallah, H.A. Albar, I.A. Mhkalid, R.R. Schmidt, Cooperative catalysis in glycosidation reactions with o-glycosyl trichloroacetimidates as glycosyl donors, Angew. Chemie - Int. Ed. 52 (2013) 10089–10092. https://doi.org/10.1002/anie.201302158.

[6] B.K. Banik, O. Zegrocka, M.S. Manhas, A.K. Bose, Enantiomerically pure β-lactams with the thienamycin side chain via glycosylation, Heterocycles. (1997) 173–176. https://doi.org/10.3987/com-97-s66.

Received on March 14, 2021.