Synthesis and characterization of some biologically active nitrogen containing compounds: Development of new chemotherapeutic agents

ABSTRACT

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Submitted by

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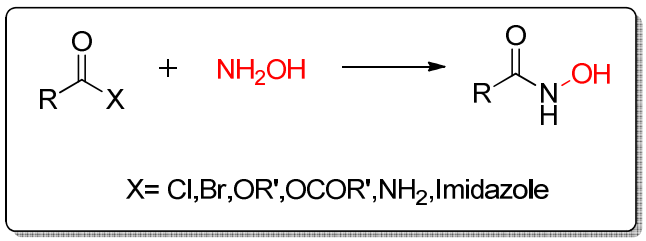
Synthesis and characterization of some biologically active nitrogen containing compounds: Development of new chemotherapeutic agents

The work of the present thesis has been divided into following **four chapters**:

Chapter-1: *Hydroxamate analogues: Recent progress in the synthesis of compound & their therapeutic importance.*

Hydroxamic acids or hydroxamate form a class of compounds which display interesting chemical and biological properties, containing the functional group –CONHOH. They are the amide derivatives, where the hydrogen atom of NH group has been replaced by an OH group. Hydroxamates form a class of compounds which display interesting chemical and biological properties. Among the several possible synthetic methods for the preparation of hydroxamic acids, two approaches, which have been used in most of the cases, are (i) reaction of acyl halides with hydroxylamine and (ii) reactions of acids or esters with hydroxylamine (**Scheme 1**).



Scheme .1 General synthesis of hydroxamates

Both synthetic pathways correspond to acyl substitution where the nucleophile is the hydroxylamine as free base and the leaving group can be either halides X– or the R′O– depending upon the starting compound. These are the most used and reliable methods which are currently applied for the preparation of known as well as new

hydroxamic acids. They mainly have two tautomers: keto-form and oxime-form, as shown in **Figure 1.**

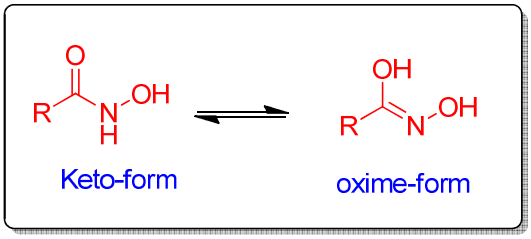


Figure.1 Tautomerism in hydroxamates

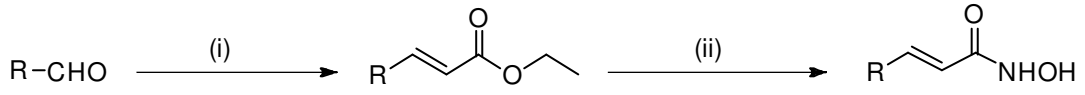
Their carbonyl and *N*-hydroxy groups are capable of forming complex metals in a bidentate fashion, making them excellent ligands for a number of metals of biological significance including zinc, iron, and nickel. Among these metals, zinc is one of the most frequently occurring metals in metalloenzymes (>300 enzymes) particular in zinc-dependent endo-peptidases matrix metalloproteases (MMPs) and histone deacetylases (HDACs) which play substantial roles for cancer therapy in previous decades.

Chapter-2: *Synthesis of N-hydroxycinnamide derivatives and their bio-evaluation*

Cancer is one of the most severe public health issues around the globe according to the World Health Organization (WHO). Among various type of cancers breast cancer is also one of the major causes of cancer death among women worldwide. Due to its complex cancer biology, it is necessary to use multiple therapeutic modalities. So far, the conventional treatments for breast cancer are surgical intervention, hormonal therapy, radiotherapy and chemotherapy. It is merely responsible for 20-25% of all cancer cases and 15-18% of cancer deaths among women.

Hydroxamic acids or hydroxamates are carboxylic acid or aldehyde analogues where –COOH group or –CHO group has been replaced by CONHOH or –CONH-R. Hydroxamic acids are well known effective molecules in the field of cancer chemotherapy and as a mutagenic agent. Several hydroxamates based drugs are functioning very good in clinics for cancer chemotherapy such as SAHA, PXD-101 (Belinostat,Topotarget) and LBH-589 (Panobinostat), which are approved by the U.S. Food and Drug Administration (FDA) in October 2006, July 2014 and February 2015, respectively.

The starting acrylate derivatives (**2a-k**) were prepared by the Horner-Wadsworth-Emmons (HWE) olefination of different aromatic aldehydes (**1a-k**) with triethylphosphonoacetate in the presence of LiOH in THF at ambient temperature. The reaction of acrylate derivatives **(2a-k)** with hydroxylamine hydrochloride in the presence of KOH in methanol at 0-5 °C results in the formation of respective *N*-hydroxy acrylamide (**3a-k**) in moderate to excellent yields (**Scheme 1**).



1a-k **2a-k** **3a-k**

1a, **2a**, **3a, 84 %**; R = 4-chlorophenyl
1b, 2b, 3b, 74 %; R = 2,6-dichlorophenyl
1c, **2c**, **3c, 70 %**; R = pyridin-4-yl
1d, **2d, 3d, 85 %**; R = 4-(1*H*-imidazol-1-yl)phenyl
1e, 2e, 3e, 75 %; R = isophthalaldehyde
1f, 2f, 3f, 79 %; R = terephthalaldehyde
1g, 2g, 3g, 75 %; R= 4-hydroxybenzaldehyde
1h, 2h, 3h, 85 %; R = 3,4,5-trimethoxybenzaldehyde
1i, 2i, 3i, 72 %; R = 4-hydroxybenzaldehyde
1j, 2j, 3j, 80 %; R = 1*H*-indole-3-carbaldehyde
1k, 2k, 3k, 85 %; R = furan-2-carbaldehyde

Scheme 1: **Synthesis of *N*-Hydroxycinnamamide derivatives,**

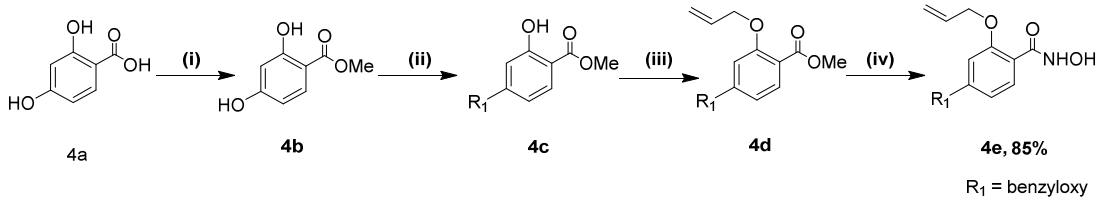
Reagents and conditions (i) LiOH (1.1eq), TEPA (1.1eq), THF, RT (ii) $NH_2OH.HCl$ (5 eq), KOH (10 eq), CH_3OH, 0°C- RT.

Synthesis of 2-*O*-alkyl benzhydroxamic acids:

Following 2-*O*-alkyl benzhydroxamic acids were synthesized in this section:

2-(allyloxy)-4-(benzyloxy)-*N*-hydroxy benzamide (4e),

The compounds methyl 2, 4-dihydroxybenzoate (**4b**) on chemoselective benzylation with benzyl bromide in acetone in the presence of anhydrous K_2CO_3 and catalytic amount of tetra-butyl ammonium bromide **(TBAB)** gave methyl 4-(benzyloxy)-2-hydroxybenzoate (**4c**) in 90% yield. The latter (**4c**) on allylation with allyl bromide in refluxing THF in the presence of anhydrous K_2CO_3 and a catalytic amount of tetra-butyl ammonium bromide (TBAB) resulted in methyl 2-(allyloxy)-4-(benzyloxy) benzoate (**4d**). Finally, the methyl benzoate derivative (**4d**) on reaction with hydroxylamine hydrochloride in the presence of solid KOH in methanol at 0-5 °C led to the formation of desired 2-(allyloxy)-4-(benzyloxy)-*N*-hydroxy benzamide(**4e**) in 85% yield (**Scheme 2**).



Scheme 2: **Synthesis of *O*-alkyl benzamide derivative**

Reagents and conditions (i) MeOH, 20% H_2SO_4, reflux (ii) Benzyloxy bromide, K_2CO_3, Acetone, RT, (iii) allyl bromide, K_2CO_3, TBAB, THF, reflux (iv) $NH_2OH.HCl$, KOH, MeOH, 0-30 °C.

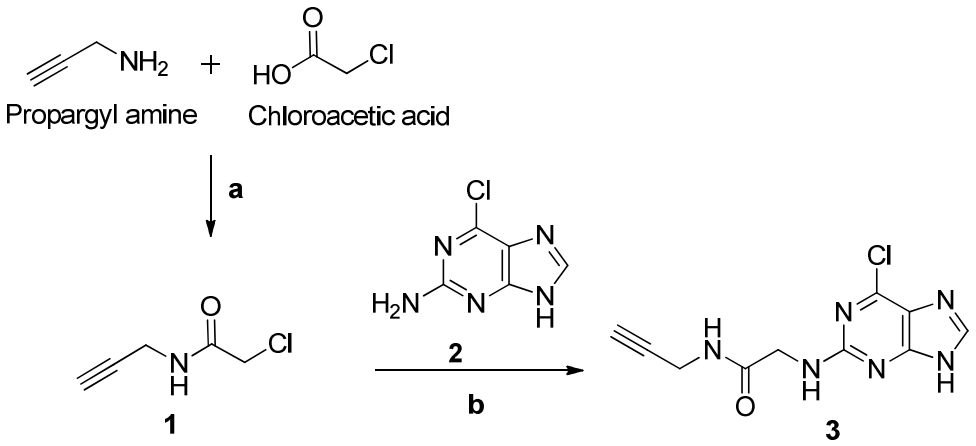
Chapter-3: Synthesis of novel purine nucleoside analogues and their biological evaluation

Nucleosides are considered as fundamental building blocks of nucleic acids and endowed with a broad spectrum of biological activity. These analogues are

synthetically modified compounds which are being synthesized to mimic the natural nucleosides and help in exploiting cellular metabolism and inhibiting cell division and viral replication when incorporated into various cellular processes like DNA and RNA synthesis, cell signaling, enzyme regulation and metabolic process. In addition to this, these analogues can interact with the essential enzymes and inhibit their action as human and viral polymerases, kinases, ribonucleotide reductase, and purine, pyrimidine nucleoside phosphorylase, DNA methyl transferases. Sugar moieties covalently linked with some other biomolecules as proteins, peptides, lipids etc. are of considerable interest due their involvement in complex biological processes and highly selective molecular recognition. They are very crucial in cellular recognition events, including signal transduction, cell adhesion and inflammation, immune response, tumour metastasis and viral & bacterial infections. Consequently multivalent glycohybrids attached with heterocyclic pharmacophore are great importance in medicinal chemistry and drug discovery. Thus Sugar moieties attached with heterocyclic framework opens new doors for the facile and successful construction of wide range of bioactive molecules.

Among the various methodologies reported for synthesis of purine nucleoside analogs, the Cu (I)-catalyzed Huisgen alkyne-azide cycloaddition (CuAAC, also known as 'click reaction') has apparently been one of the most frequently used reactions. The synthesis of triazoles using 'click chemistry' has contributed to a renaissance in the chemistry of azides as building blocks toward higher complexity glycoconjugates. We started our synthetic journey with an objective of synthesis of purine based triazole containing nucleoside analogues, and then corresponding aryl triazole analogues. Primarily, the intermediate 2-chloro-N-propynyl-acetamide was synthesized by coupling of Chloroacetic acid and propargyl amine by reported HOBt

amide-coupling protocol. The second step in the synthetic strategy is the synthesis of purine derived nucleoside analogues employs *N*-alkylation of 2-amino-6-chloropurine **2** at the amino group with the 2-chloro-*N*-propynyl-acetamide **1** by heating these two reactants at 80 °C using strong base sodium hydride in DMF. (**Scheme 1**) Thus, we end up with the intermediate purine derived alkyne **3** in good yield. The synthesized alkyne analogue was further precisely characterized by spectroscopic (^{1}H, ^{13}C NMR) data.

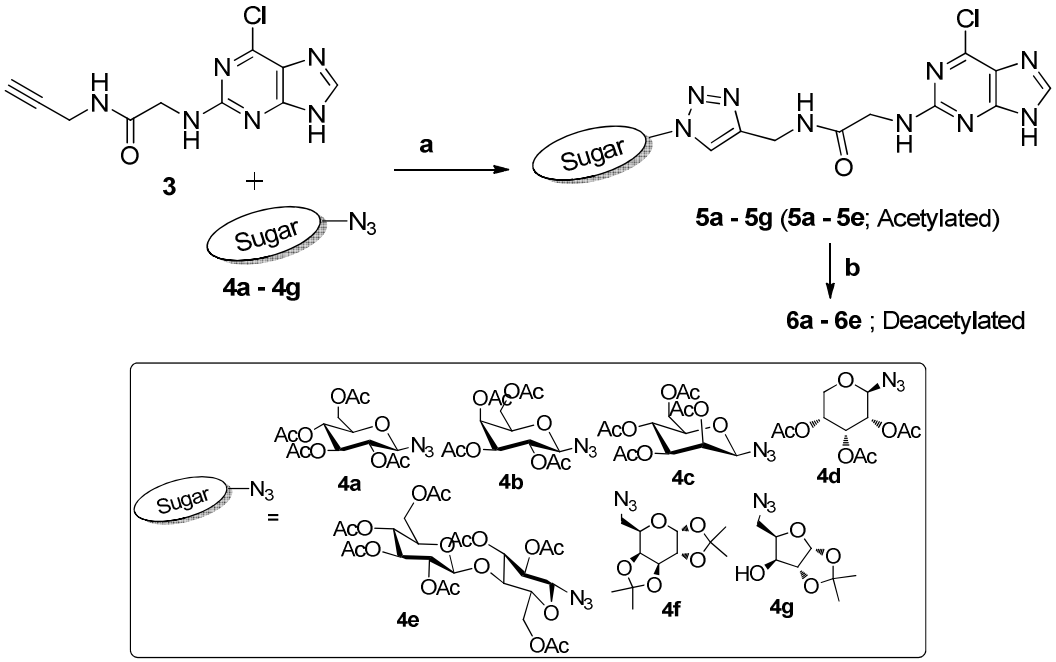


Scheme 1: Synthesis of purine derived alkyne 2-((6-chloro-9*H*-purin-2-yl) amino)-*N*-(prop-2-yn-1-yl) acetamide **a**) HOBT, DIPC, dichloromethane, 0°C to rt, 12 h, 75-86% **b**) 2-amino-6-chloropurine, NaH, DMF, rt (2h) to 80 °C (8h), 90-95%.

Synthesis of purine derived nucleoside analogues

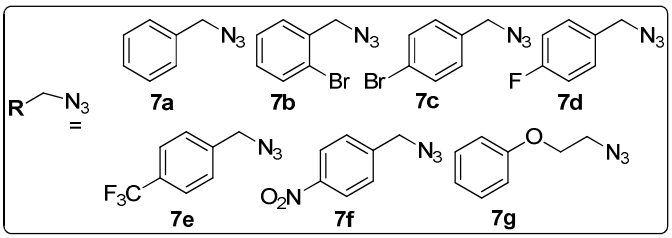
The sugar azides **4a-4g** were prepared and characterized following earlier reported methods. Thus, having purine derived alkyne **3** and sugar azides in hand, the well known 'Click' reaction was performed in solvent system *t*-BuOH/H_2O (1:1) taking equimolar quantities of the reactants, $CuSO_4.5H_2O$ (10 mol%) and sodium ascorbate (20 mol%) at ambient temperature (**Scheme 2**). The reactions were monitored (TLC) up to completion of reaction. Thus various 1, 2, 3-triazole-linked purine nucleoside analogues have been successfully synthesized in high yields. The respective products **5** were isolated and characterized based on their ^{1}H, ^{13}C and Mass spectral data.

Further, the acetylated nucleoside analogues **5a**-**5e** were subjected to Zemplen deacetylation with NaOMe/MeOH at room temperature which led to the formation of the deacetylated purine nucleoside analogues **6a-6e**, respectively in good yields.



Scheme 2: Synthesis of purine derived nucleoside analogues. **a**) $CuSO_4.5H_2O$ (10 mol %), sodium ascorbate (20 mol %), *t*-BuOH**:** H_2O (1:1 v/v), rt, 4 h, 65-75 % **b**) NaOMe, MeOH, rt, 0.5 h, 80-85%.

As described in Scheme 1, similarly the aromatic azides **7a**-**7g** was prepared according to the reported procedure. The respective azide was subjected to CuAAC 1, 3-dipoar cycloaddition with the alkyne **3**. (**Scheme 3**) As described in Scheme 2, Click reaction conditions were maintained which led to the formation of final products **8a-8g** in good yields. The products were isolated and characterized with the help of ^{1}H, ^{13}C and Mass spectral data.



Scheme 3: Synthesis of *N*-9 unprotected 6-chloro-8-arylpurines 2-((6-chloro-9*H*-purin-2-yl) amino)-*N*-(prop-2-yn-1-yl) acetamide. **a**) $CuSO_4.5H_2O$ (10 mol %), sodium ascorbate (20 mol %), *t*-BuOH**:** H_2O (1:1 v/v), RT, 4 h, 75-86%.

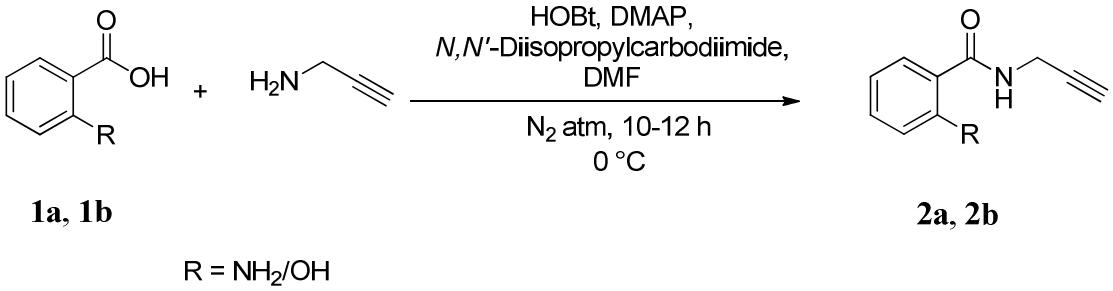
Chapter-4: Synthesis and bioevaluation of novel glycosyl 1, 2, 3-1H-triazolyl methyl benzamide derivatives

Diabetes mellitus (DM) is a chronic disease of global commons, which tends to have problems with adherence. Adherence with medication, diet, and exercise, and blood glucose self–monitoring is quite challenging. Due to consumption of carbohydrate-enriched diet, metabolic and heterogeneous disorder causing high blood-glucose level, leading to hyperglycemia. As per the Global Report on Diabetes (2018) by World Health Organization, diabetes was the seventh major cause of death in 2016. Carbohydrates form the largest group of naturally occurring compounds in nature and also crucial due to their pivotal role in medicinal chemistry and drug discovery. They are also known for their essential function in development, recognition, growth, function and survival of living cells and organisms. Many drug molecules including several antibiotics and few anti-diabetic medicines contain terminal sugar moieties which are necessary for their biological action.

Benzamide moiety is very significant class of nitrogen heterocycles are considered as privileged structures in drug discovery owing to their important roles as key building blocks in the synthesis of a many drugs. This heterocyclic nucleus is linked with diverse range of pharmacological activities such as antihypertensive,

antibacterial, anti-inflammatory, anticancer, analgesic, antihistamine, CNS stimulant and antidiabetic activities. Hence we tried to couple the benzamide nucleus with terminal sugar moieties by applying a suitable and biologically significant linker. 1,2,3-Triazoles are also an essential scaffold in drug discovery and development as several molecules with this moiety exhibited important biological activities such as antifungal, antitubercular, anticancer, anti-HIV, antibacterial, antiviral, anti-Alzheimer, anti-mycobacterial and glycosidase inhibitors.

2-Amino-*N*-propargyl benzamides (**2a** and **2b**) were prepared from commercially available anthranilic acid (**1a**) and 2-hydroxy-benzoic acid (**1b**) following earlier reported protocols as shown in **Scheme 1**. The structures were established on the basis of their spectroscopic data. The flask was degassed and then filled with N_2 (balloon), and HOBt (1mmol), 4- dimethylaminopyridine (DMAP, 1 mmol) were added to the reaction mixture. Then *N*, *N*'-Diisopropylcarbodiimide (DIPC, 1 mmol) was added to the reaction mixture in drop wise manner. After 10 mins, propargyl amine (1.1 mmol) was added and the reaction was stirred overnight at ambient temperature to get the desired 2-amino-*N*-(prop-2-yn-1-yl) benzamide (**2a**) 2-hydoxy-*N*-(prop-2-yn-1-yl) benzamide (**2b**) in good yield (**Scheme 1**).



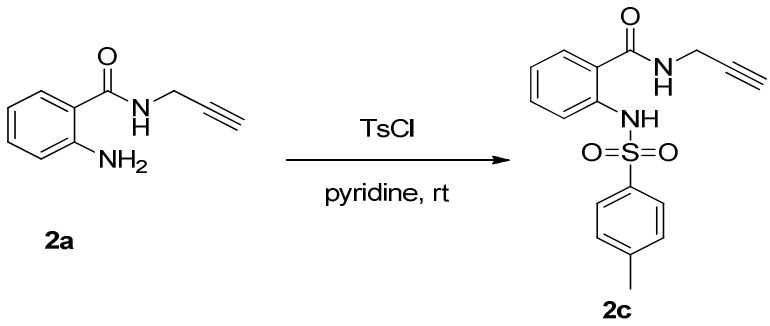
Scheme 1. Synthesis of 2-amino-*N*-propargyl benzamide derivatives.

The structure of the product **2a** was established by their spectroscopic data. ESIMS of the compound displays *m/z* = 175 as $[M+H]^+$ peak corresponding to its molecular

formulae $C_{10}H_{11}N_2O$. In IR spectrum, characteristic absorption peaks observed at 3372 cm^{-1} for amine, 3019 cm^{-1} for -NH, 1648 cm^{-1} for carbonyl (-NHC=O). In the ^1H NMR spectrum, the two exchangeable NH_2 protons were observed at δ 5.43 (bs, 2H, -NH_2) and the amide -NH proton was visible at δ 6.25 (bs, 1H, -NH) while the alkynyl proton was visible at δ 2.16 besides other usual protons at their usual chemical shift. In ^{13}C NMR spectrum, the peaks at δ 168.8 accounted the amide group carbon (-NH-CO-) along with other usual signals. Similarly, the reaction of 2-hydroxy-benzoic acid (**1b**) with propargyl amine the above reaction conditions led to the formation of 2-hydroxy-*N*-(prop-2-yn-1-yl) benzamide (**2b**) in good yield (**Scheme 1**).

Synthesis of 2-(4-methylphenylsulfonamido)-*N*-(prop-2-yn-1-yl) benzamide (2c)

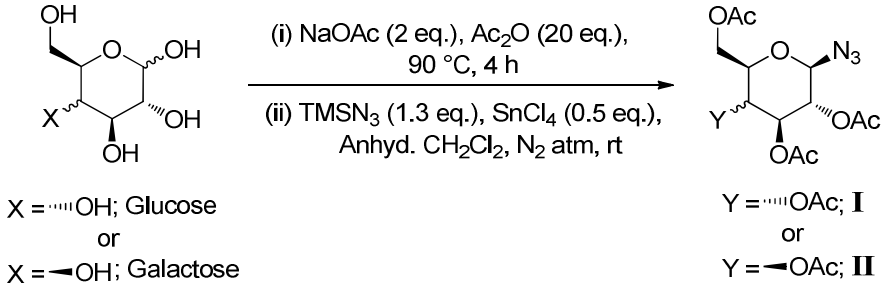
2-(4-methylphenylsulfonamido)-*N*-(prop-2-yn-1-yl) benzamide (**2c**) were prepared by following earlier reported protocols as shown in (**Scheme 2)**. To a solution of the 2-amino-*N*-(prop-2-yn-1-yl) benzamide (**2a**, 1.0 equiv) in pyridine (1 M) at room temperature, *p*-toluenesulfonyl chloride (1.05 equiv) was added. The reaction mixture was allowed to stir at room temperature overnight. The reaction mixture was quenched with water, and the aqueous layer was extracted with dichloromethane. The combined organic extracts were washed with aqueous copper sulphate. The organic layer was then dried over magnesium sulphate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to afford the desired 2-(4-methylphenylsulfonamido)-*N*-(prop-2-yn-1-yl) benzamide (**2c**) in 79% yield (**Scheme 2**).



Scheme2. Synthesis of 2-(4-methylphenylsulfonamido)-*N*-(prop-2-yn-1-yl) benzamide derivative.

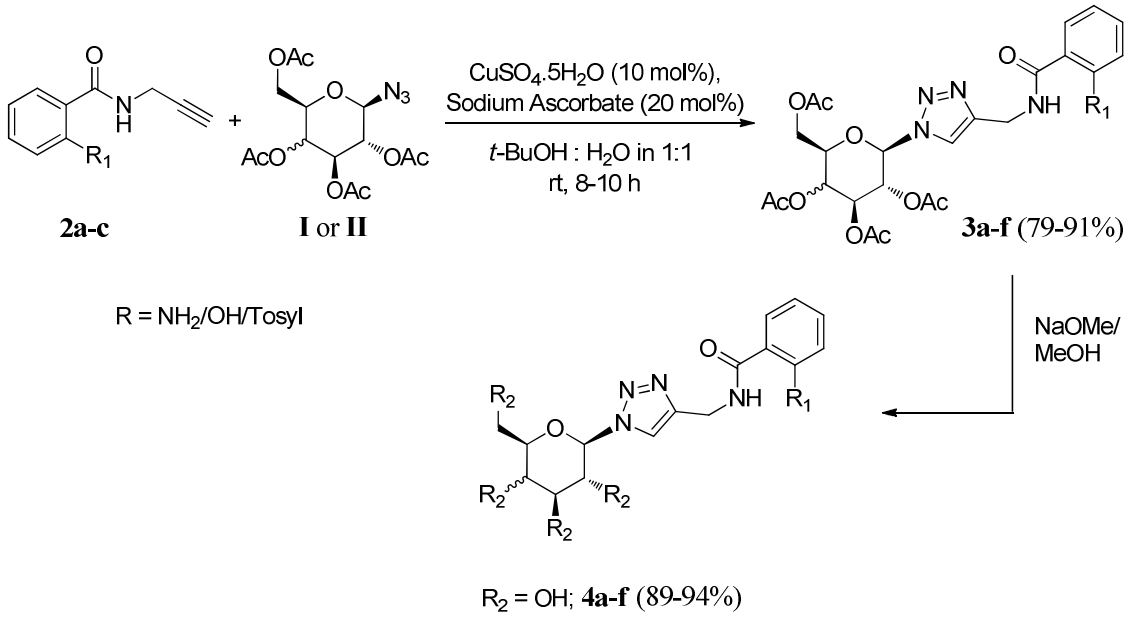
Synthesis of glycosyl triazolyl benzamide

The glycosyl azides (**I** and **II**) were prepared from commercially available glucose and galactose following the methods already reported in the literature as shown in (**Scheme 3**). The structures were established on the basis of their spectroscopic data. These were identical in all respects to those reported earlier.



Scheme 3. Synthesis of the glycosyl azides

The strategy for the synthesis of glycosyl triazolyl benzamide is depicted in **Scheme 4**. Having the 2-phenyl-3-propargyl-benzamide (**2-c**) and glycosyl azides (**I** and **II**) in our hand the CuAAC reactions were performed in *t*-BuOH/H_2O (1:1) using equimolar quantities of the reagents, $CuSO_4.5H_2O$ (10 mol%) and sodium ascorbate (20 mol%) at ambient temperature to afford epimeric mixtures of peracetyl glycosyl-triazolyl benzamide (**3a-f**) in good yields (**Scheme 4**). Propargyl benzamides and glycosyl azides selectively gave only one regioisomer, 1, 4-disubstituted triazole via 1, 3-dipolar cycloaddition reaction.



Scheme 4. Synthesis of glycosyl benzamide

In conclusion, we have synthesized novel glycosyl methyl benzamide analogues with 1, 4-regioselectivity employing the well-known CuAAC reaction of the propylated benzamides with different sugar azides in ambient condition in very good yields. These compounds were evaluated for α-glucosidase enzyme inhibitory activity and three compounds **4f**, **4d** and **4c** exhibited 42.9%, 40.6%, and 39.7% inhibition, respectively as compared to standard drug acarbose having 53.4 % inhibition of the enzyme. Thus, these glycosyl methyl benzamide analogues hold potential to be developed as antidiabetic agents.

List of Research Publications

1. Identification of N-Hydroxycinnamamide analogues and their bio-evaluation against breast cancer cell lines. **Akhilesh Kumar Shukla,** Hamidullah, MK Shrivash, VD Tripathi, R Konwar, J Pandey. ***Biomedicine & Pharmacotherapy*** **(2018)**, 107, 475-483. **ISSN**-07533322
2. Study of developments of biologically active Quinazolinones derivatives: A review. Aniruddh Prasad Chaudhary, **Akhilesh Kumar Shukla**, Jyoti Pandey, Padam Kant ***Chemistry & Biology Interface***, **(2018)**, 8, 2, 62-83. **ISSN-** 22494820
3. Synthesis, characterization and antimicrobial evaluation of N-(4-oxo-2phenyl/thiophenyl quinazoline-3(4*H*)-yl)-1H-indole-2 or 3-carboxamide derivatives. Aniruddh Prasad Chaudhary, **Akhilesh Kumar Shukla**, Padam Kant ***Chemistry & Biology Interface***, **(2018)**, 8, 6, 359-372. **ISSN-** 22494820
4. Design and Synthesis of Novel Heterocyclic Curcumin Analogues as Anticancer Agents and Filarial Topoisomerase II Inhibitors. V.D.Tripathi and **Akhilesh Kumar Shukla.** ***Asian Journal of Organic & Medicinal Chemistry*** **(2018)**, 4, 3,149-153. **ISSN**-24568937
5. Regioselective Three Component Domino Synthesis of Polyhydrospiro [indoline-3, 3'- pyrrolizine]-2-one *via* [3+2] Cycloaddition Reaction. V.D.Tripathi and **Akhilesh Kumar Shukla** and H.S.Mohammed. ***Asian Journal of Organic Chemistry*** **(2019),** 31, 3, 613-616. **ISSN**-09707077
6. Identification of Novel Phenyl Butenonyl *C*-Glycosides with Ureidyl and Sulfonamidyl Moieties as Antimalarial Agents, K. K. G. Ramakrishna, S. Gunjan, **Akhilesh Kumar Shukla**, V. R. Pasam, V. M. Balaramnavar, A. Sharma, S. Jaiswal, J. Lal, R. Tripathi, Anubhooti, R. Ramachandran and Rama Pati Tripathi ***ACS Medicinal Chemistry Letters.*** **(2014)**, *5*, 878-883. **ISSN**-19485875
7. Development of novel glycosyl-1, 2, 3-1*H*-triazolyl methyl benzamide derivatives as inhibitor of α-glucosidase: Synthesis, characterization and *In-silico* study. **Akhilesh Kumar Shukla**, KKG Ramakrishna, MK Shrivash and Jyoti Pandey (Communicated).

8. Design, synthesis and *In-silico* evaluation of novel 1*H*-1, 2, 3-triazolyl-methyl-acetamide-D-glucose conjugates as antifungal agents. **Akhilesh Kumar Shukla**, Ravi. K.Thakur, MK Shrivash and Jyoti Pandey (Communicated).

Book Chapter:

1. Carbohydrates based chemotherapeutics: A frontier in drug discovery and development. S. Mishra, K. Upadhyaya, K. B. Mishra, **Akhilesh Kumar Shukla**, Rama P. Tripathi, and Vinod K. Tiwari. *SNPC **Elsevier book chapter*** **Book: SNPC49C-9780444636010,** Chapter-10, **(2016)**, Page 308-355**, Studies in Natural Products Chemistry, Vol. 49.http://dx.doi.org/10.1016/B978-0-444-63601-0.00010-7.**
2. Hydroxamates based chemotherapeutics: Frontier in drug discovery and development, Jyoti Pandey and **Akhilesh Kumar Shukla** (Under revision).

Presentations in Scientific Conferences:

1. Participation and Poster Presentation in **International Symposium** on "Emerging Frontiers in Carbohydrate Chemistry and Glycobiology" CARBO-XXXIV on **5th-7th December-2019** at Department of Chemistry, University of Lucknow,Lucknow Organised by Association of Carbohydrate Chemists and Technologists, India [**ACCTI**] and NIPER-Raebareli.
2. Participation and Oral Presentation in **Global Conference** On The Control Of Green House Gases At The Source By Physical And Chemical Technology on **22nd-24th**, **April-2019** at Department of Chemistry, School of Physical & Decision Sciences (SPDS) at Babasaheb Bhimrao Ambedkar University (A Central University), Vidya Vihar, Raebareli Road Lucknow-226025, UP, India.
3. Participation and Poster Presentation in **International Symposium** on "CHEMICAL SCIENCES: NATIONAL AND GLOBAL POSPECTIVE" on **29th-31st October-2018** at Lucknow Christian Degree College, Golaganj, Lucknow-226018.

4. Participation and Poster Presentation in **International Symposium** on "International Conference on Emerging Trends in Chemical Sciences (**ICETCS)** on **24th-25th February-2018 at** Deen Dayal Upadhyaya Gorakhpur University,Gorakhpur-273009.
5. Participation and Poster Presentation in **International Symposium** on "International Conference on Updates in Cancer Prevention and Research" [**ICUCPR-2017**] & Satellite Conference on Translational Pharmaceutical Research: Trends and Implication on **14th-16th& 20th February-2017** at Babasaheb Bhimrao Ambedkar University (A Central University), Vidya Vihar, Raebareli Road Lucknow-226025, UP, India.
6. Participation and Poster Presentation in National Seminar on "Role of analytical techniques in advanced scientific research" (**ATASR-2016**) **19-20 March, 2016** at National P.G.College, Lucknow, UP, India.
7. Participation and Poster Presentation in 6th **International Symposium** on "Current Trends in Drug Discovery & Research **25th-28th February 2016** at CSIR-CDRI, Lucknow, UP, India.
8. Participation and Poster Presentation in 3rd Lucknow Science Congress and **National Conference** on "Science for Society: An Interdisciplinary Approach" **31st Oct-2nd November-2015** at Babasaheb Bhimrao Ambedkar University (A Central University), Vidya Vihar, Raebareli Road Lucknow-226025, UP, India.
9. Participation and Poster Presentation in **National Conference** on Innovative Methods in Chemistry Education [IMCE-2015] & National Convention of Chemistry Teachers [**NCCT-2015**], **8th-10th October 2015** at Babasaheb Bhimrao Ambedkar University, Lucknow, UP, India.
10. Participation and Poster Presentation in 21st ISCB **International Conference** (ISCBC-2015), **25th-28th February-2015** at CSIR-Central Drug Research Institute, Lucknow, UP, India.
11. Participation and Poster Presentation in **International Conference** on The Ramanbhai Foundation 7th International Symposium on Current Trends in Pharmaceutical Sciences: "Advances in New Drug Discovery and Development" **2nd-4th February-2015** held at YMCA International Centre, S. G. Highway, Ahmedabad and Gujarat, India.

12. Participation and Poster Presentation in **International Conference** on challenges in chemistry and biology of Carbohydrates CARBO-XXVIII ,**20th-22th, Janaury-2014,** Dehra Dun, India Organised by Association of Carbohydrate Chemists and Technologists [**ACCTI**], India.
13. Participation and Poster Presentation in 5th**International symposium** on Drug Development for Orphan/Neglected Diseases (**CTDDR-2013**), **26th-28th February-2013**, at CSIR-Central Drug Research Institute, Lucknow, UP, India.
14. Participation and Poster Presentation in **International Conference** on Chemistry and Materials Prospects and Perspectives (**ICCMPP-2012**), **14th-16th December-2012**, at Babasaheb Bhimrao Ambedkar University (A Central University), Vidya Vihar, Raebareli Road Lucknow-226025, UP, India.
15. Participation and Poster Presentation in **International Conference**& Humboldt Kolleg on Recent aspects of Organic/Organometallic Compounds and their Usefulness in Materials and Industries on **03rd-06th January-2012** Organised by Chemistry Department, University of Lucknow, Lucknow, UP, India.