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# Synthesis of 2,3,6-trideoxy sugar triazole hybrids as potential new broad spectrum antimicrobial agents

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ABSTRACT

Here, we describe a molecular hybridization inspired design and synthesis of novel 6-triazolyl 2,3,6-trideoxy sugars as promising new broad-spectrum antimicrobial agents using click chemistry in key step. These compounds showed MIC between 0.39 and 50 μg/mL against different native and resistant bacteria and fungi with no toxicity. Among them, compound **29** was the most active molecule with MIC 0.78 μg/mL against *Staphylococcus aureus* and *Klebsiella pneumoniae* and 3.12 μg/mL against methicillin- and vancomycin-resistant *S. aureus*. Compound **26** was the most potent anti-fungal candidate with MIC 0.39 μg/mL against *Trichophyton mentagrophytes*. Compound **46** was found to be promising with broad-spectrum activity against both bacterial and fungal strains. The bioinformatic studies involving bacteria's protein co-crystals prompted penicillin binding protein-2 as the most likely target of these compounds.


## 1. Introduction

The discovery of antibiotics revolutionized the treatment of surgical and non-surgical infections [1]. Their overwhelming benefits carried away almost everyone to believe that the infectious diseases would soon be a thing of the past [2]. However the accumulation of drug resistant bacterial strains and slow pace of new antibiotics development turned the situation from one of exhilarating optimism to growing pessimism with a warning of impending return to pre-antibiotic era [2]. The falling numbers of FDA approved antibiotics since 1980 substantiate this scenario [3]. The situation is dim as limited new leads are added to give diversity to the search of potential drugs [4]. Out of the twenty antibiotics approved since 2000, only three – linezolid, daptomycin and retapamulin – originated from new scaffolds [1]. The picture is more grim in case of drugs of Gram-negative bacteria. Adding to the woes, now they are posing more threat than Gram-positive bacteria [5]. Furthermore, recently bedaquiline, a novel diarylquinoline based analogue, is approved by the FDA for multidrug resistant tuberculosis [6].

Fungal infections are another serious health concern. They are mounting pressure on health-care system over the past two decades. The ever increasing immuno-compromised patients and emergence of drug resistance fungal strains has led to this scenario. The existing antifungal drugs e.g., amphotericin-B, flucytosine, azoles etc suffer from severe side effects and/or resistance [7]. Thus, the situation is warranting discovery of alternative drugs involving new molecules with broad-spectrum activity [8]. Natural products with some desirable activity, pathogens' metabolites and/or their critical functional components often serve as good starting point for exploring new prototypes as drug leads. Nevertheless, merging or joining two or more such skeletons, also referred to as molecular hybridization, offer scope for scaffold hopping and open avenues for discovering novel drug molecules [9–12].

The cell walls of bacteria and fungi respectively carry large proportion of peptidoglycan and glucosamine moieties which share similarity in their sugar units. During the past two decades different sugar like scaffolds which include hex-2-enopyranosid-4-ulose [13–15], 4,6-*O*-butylidene-β-D-glucopyraosyl-3-phthalimido-4-styryl-azetidin-2-one [16] and 9-chloro-8-hydroxy-8,9-deoxyspyrone [17] have been recognized as privileged structure in antibacterial and antifungal drug discovery.

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We recently synthesized 2,3-dideoxy hex-2-enopyranosid-4-uloses which showed very mild antibacterial and antifungal activity in *in vitro* screening [18,19]. Furthermore, in medicinal chemistry heterocycles have drawn considerable attention at all times. Here, 1,2,3-triazoles have attracted us due to their facile synthesis through click chemistry [20] and wide biological profiles which include antibacterial and antifungal activities [21–23]. It also mimics the amide features of penicillin antibiotics [24].

Glycoconjugates having a carbohydrate and traizoles moieties are involved in important biological functions, including those on the cell surface, such as the recognition of host compounds, immunological responses, inflammation, cell–cell recognition, bacterial and viral infection, cell communication, metastasis, and many important functions inside cells [25]. Also, many recent reports suggested that different triazole carbohydrate conjugates are endowed with antimicrobial activity [26–30]. In this gamut, we conceptualized the hybridization of our previously reported 2,3-dideoxy hex-2-enopyranosid-4-uloses and 1,2,3-triazole derivatives to result in a new lead to serve as probable broad-spectrum agent with antibacterial and antifungal properties. The synthesis was implemented by choosing the C-6 position of the 2,3,6-trideoxy hex-2-enopyranosid-4-ulose for integration with the 1,2,3-triazole moiety to result in 2,3,6-trideoxy sugar–triazole conjugates [31,32].

## 2. Chemistry

The synthesis of the target molecules are envisaged as shown in Scheme 1. The intermediates 2,3-dideoxy hex-2-enopyranosid-4-uloses **1a**–**c** were synthesized from D-glucal as reported in our earlier work [18]. Tosylation of the hydroxy group at C-6 led to the 6-*O*-tosyl derivative **2a**–**c**. Luche reduction of **2a**–**c** furnished their 4-hydroxy derivatives **3a**–**c** which were then treated with $NaN_3$ in DMF at 120 °C to obtain 6-azido-4-*O*-hydroxy 2,3,6-trideoxy hex-2-enopyranosides **4a**–**c** in near quantitative yield. The 6-azido derivatives were now reacted with different terminal alkynes using click chemistry to afford 6-triazolo derivatives **5**–**23**. Oxidation of the 4-hydroxy group of the 6-triazolo derivatives furnished the target sugar triazole conjugates (Table 1).

The intermediates 2,3-dideoxy hex-2-enopyranosid-4-uloses **1a**–**c** were synthesized from D-glucal as reported in our earlier work [15]. Tosylation of the hydroxy group at C-6 led to the 6-*O*-tosyl derivative **2a**–**c**. Luche reduction of **2a**–**c** furnished their 4-hydroxy derivatives **3a**–**c** which were then treated with $NaN_3$ in DMF at 120 °C to obtain 6-azido-4-O-hydroxy 2,3,6-trideoxy hex-2-enopyranosides **4a**–**c** in near quantitative yield. The 6-azido derivatives were now reacted with different terminal alkynes using click chemistry to afford their 6-triazolo derivatives **5**–**23**. Oxidation of the 4-hydroxy group of the 6-triazolo derivatives furnished the target sugar triazole conjugates **24**–**42** (Table 1).

## 3. Biological evaluation

The synthesized sugar triazole conjugates **10**, **24**–**42**, **46**, **50**, **51** and **53** were evaluated for *in vitro* antibacterial activity (MIC; the minimum concentration of drug/compound that produced 90% of growth inhibition) by Muller-Hinton broth dilution method against Gram-positive bacteria *Staphylococcus aureus* (Sa) (ATCC 25923) and Gram-negative bacteria *Klebsiella pneumoniae* (Kp) (ATCC 27736), *Escherichia coli* (Ec) (ATCC 9637), and *Pseudomonas aeruginosa* (Pa) (ATCC BAA-427). They showed activity in the range of 0.78–50 μg/mL against the mentioned bacterial strains.

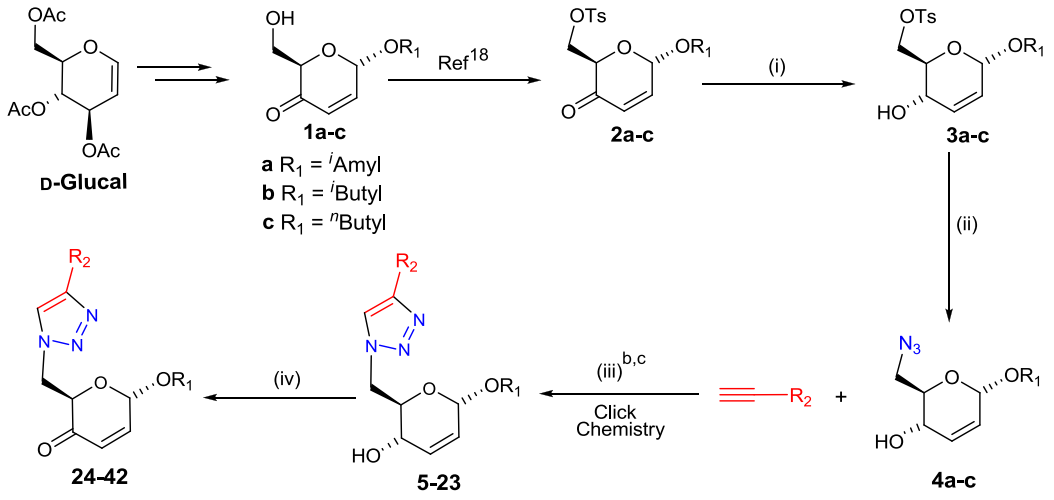
## 4. Result and discussion

### 4.1. Antimycobacterial activity

Among the compounds, **29**, **38** and **53** showed MIC 0.78 μg/mL against Sa which make them sixteen-folds more active than standard drugs ampicillin and vancomycin (Table 1). For Kp the MIC of compounds **29** and **46** is 0.78 μg/mL. It makes them as sixteen-, eight- and two-folds more active than ampicillin (also vancomycin), methicillin and gentamycin, respectively (Table 1).

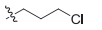
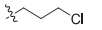
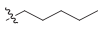
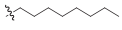
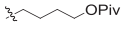
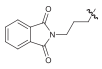
In these analogues structure–activity relationships (SARs) revealed that the antibacterial activity against Sa and Kp improved by increasing the number of carbons in the alkyl chain at C-4 position of triazole ring (compounds **27** to **29**, 3.12 μg/mL to 0.78 μg/mL; Table 1).

In comparison to compound **29**, compound **30** showed eight- and sixty-four-folds less activity against Sa and Kp, respectively, and suggested the unfavourable nature of n-butyl substituent at anomeric position for the activity. Compound **29** with a high CLog*P* value (4.164) showed better activity indicating that lipophilicity as an important parameter for antibacterial activity, though




**Scheme 1.** General synthetic strategy[a]. [a]Reagents and Conditions: (i) $NaBH_4$, $CeCl_3.7H_2O$, EtOH, 1 h, 0 → 10 °C (ii) $NaN_3$, DMF, 2–5 h, 80–120 °C, yield:~60% (iii) Sodium ascorbate, $CuSO4{\cdot}5H_2O$, tBuOH: $H_2O$, yield:~75% ([b]For compound **22** and **23** MeOH:$H_2O$ was used as solvent. [c]In case of preparation of compound **23** $K_2CO_3$ was also used along with other reagents) (iv) DMP, DCM, 3–6 h, −5–10 °C, yield: ~50%; for compound **6**, **25** $R_1$ = $^i$Butyl, **7**, **11**, **26**, **30** $R_1$ = $^n$Butyl and for remaining $R_1$=$^i$Amyl.

**Table 1**
Sugar–triazole conjugates, their CLog*P* values and antibacterial activities.

| Comp | $R_2$ | CLog*P*[a] | Sa[b] | Sa (MR and VR)[b] | Kp[b] | Ec[b] | Pa[b] |
|---|---|---|---|---|---|---|---|
| **10** |  | 4.658 | >50 | >50 | >50 | >50 | >50 |
| **24** |  | 1.232 | 1.56 | 6.25 | 3.12 | 50 | 50 |
| **25** |  | 0.703 | 12.5 | >50 | 50 | >50 | >50 |
| **26** |  | 0.833 | 12.5 | >50 | >50 | >50 | >50 |
| **27** |  | 2.577 | 3.12 | 6.25 | 3.12 | >50 | >50 |
| **28** |  | 3.106 | 3.12 | 6.25 | 1.56 | >50 | >50 |
| **29** |  | 4.164 | 0.78 | 3.12 | 0.78 | >50 | >50 |
| **30** |  | 3.765 | 6.25 | >50 | >50 | >50 | >50 |
| **31** |  | 0.601 | >50 | >50 | 50 | >50 | >50 |
| **32** |  | 0.124 | 50 | >50 | 50 | 50 | 50 |
| **33** |  | 2.244 | 12.5 | >50 | 12.5 | 50 | 50 |
| **34** |  | 0.843 | 12.5 | >50 | 50 | >50 | >50 |
| **35** |  | 1.788 | 1.56 | 12.5 | >50 | >50 | >50 |
| **36** |  | 2.290 | 6.25 | 12.5 | 3.12 | 50 | 50 |
| **37** |  | 1.175 | 6.25 | 12.5 | 6.25 | >50 | >50 |
| **38** |  | 2.470 | 0.78 | 3.12 | >50 | >50 | >50 |
| **39** |  | 2.023 | 50 | >50 | 50 | 50 | 50 |
| **40** |  | 0.905 | 6.25 | >50 | >50 | >50 | >50 |
| **41** |  | 1.810 | 6.25 | 25 | >50 | >50 | >50 |
| **42** | H | 0.192 | 25 | >50 | >50 | 50 | >50 |
| **46** |  | 4.168 | 1.56 | 3.12 | 0.78 | 50 | 50 |
| **50** |  | 0.1002 | 25 | >50 | >50 | >50 | >50 |
| **51** |  | 1.485 | 50 | >50 | >50 | >50 | >50 |
| **53**[c] |  | 4.164 | 0.78 | 12.5 | 50 | >50 | >50 |
| Ciprofloxacin | | | 0.09 | 0.38 | 0.01 | 0.01 | 0.09 |
| Gentamycin | | | 0.39 | 1.56 | 1.56 | 1.56 | 0.39 |
| Ampicillin | | | 12.5 | 0.78 | 12.5 | 50 | >50 |
| Vancomycin | | | 12.5 | – | 12.5 | 12.5 | >50 |
| Methicillin | | | 0.04 | – | 6.25 | 50 | >50 |

[a] CLog*P* calculated by Chemdraw Ultra 10.0 software.
[b] *Staphylococcus aureus* (Sa), methicillin- and vancomycin-resistant (MR and VR) Sa, *Klebsiella pneumoniae* (Kp), *Escherichia coli* (Ec), *Pseudomonas aeruginosa* (Pa); Antibacterial activity as MIC in μg/mL.
[c] Compound **53** is 1,5-disubstituted analogue of compound **29**.

exceptions exist. Probably, lipophilicity may facilitate the compound's penetration into bacteria's cell wall to result in its rupture and release of cytoplasmic constituents thus leading to its death [4,33,34].

The aromatic substituted triazoles **36**–**41** showed moderate to high activities. Among them compound **38** having a 4-fluorophenyl substituent was found to be most active at MIC 0.78 μg/mL against Sa which may be attributed to the high electro-negativity of

fluorine atom. It may modify the electronic nature of the molecule, and thereby influence its absorption, distribution and metabolism [23]. The compounds' low activity against Gram-negative bacteria may be due to the additional outer membrane of the organism.

Adamantane derivatives have been reported to show antibacterial and antifungal activities [35,36]. Its cage like structure improves the hydrophobicity of a variety of bioactive molecules [37]. In view of this, we synthesized adamantyl moiety containing compound **46**, using Scheme 2A, which showed activity 1.56 μg/mL and 0.78 μg/mL against Sa and Kp, respectively. We also probed the role of C-4 keto group towards antibacterial activity of these compounds. Reduction of this group in the most active compound **29** yielded corresponding 4-hydroxy derivative **10**, which was found to be inactive against Gram-positive and Gram-negative bacteria.

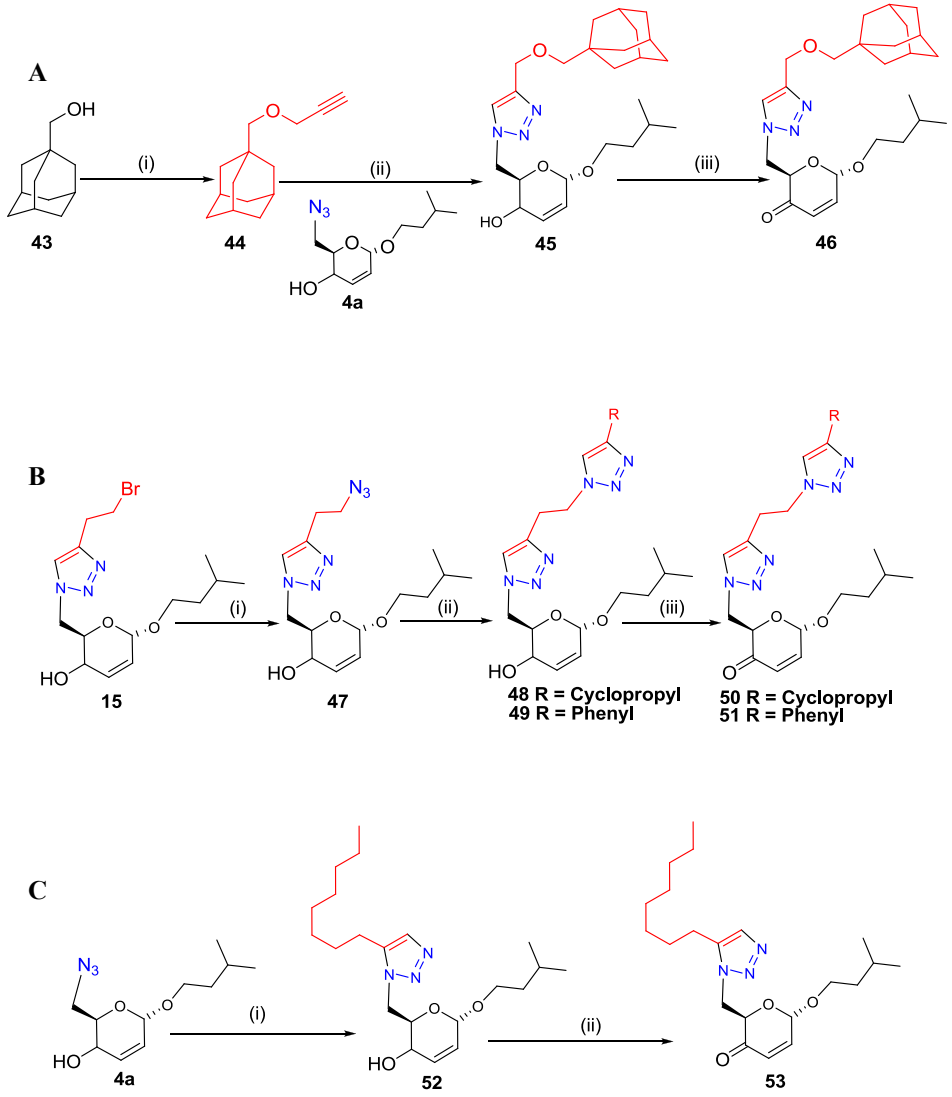
The role of triazole ring in the antibacterial activity was explored with the synthesis of two bis-triazolyl compounds **50** and **51** following Scheme 2B. They showed activity only against Sa with MIC 25 μg/mL and 50 μg/mL.

The affect of substituent position of triazole ring on antibacterial activity was scrutinized with 1,5-disubstituted triazole analogue of compound **29** (Compound **53**) synthesized following Scheme 2C by using ruthenium (II) catalysed cycloaddition reaction [38]. It showed activity of 0.78 μg/mL and 50 μg/mL against Sa and Kp, respectively. This suggests that while the position of the substituent on the triazole ring has no effect on the activity of Gram-positive bacteria, it does have a role in case of Gram-negative bacteria.

All the synthesized compounds were evaluated *in vitro* against methicillin-resistant *S. aureus* (MRSA) and Vancomycin-resistant *S. aureus* (VRSA) strains. Of there, compounds **29**, **38** and **46** showed MIC 3.12 μg/mL against MRSA and VRSA.

### 4.2. Antifungal activity

The synthesized compounds were also evaluated against fungal strains *Candida albicans* (Ca), *Aspergillus fumigatus* (Af), *Cryptococcus neoformans* (Cn), *Sporothrix schenckii* (Ss) and *Trichophyton mentagrophytes* (Tm) and the results were summarized in Table 2. For Ca, these compounds' MICs values have spread from 6.25 μg/mL to 50 μg/mL. Among these, compounds **30** and **38** showed highest




**Scheme 2.** Synthesis of adamantyl (A), bis triazole (B) and 1,5-disubstituted triazole (C) containing sugar-triazole conjugates[a]. [a]Reagents and conditions: A (i) NaH, THF, TBAI,  , 24–48 h (ii) $C_6H_7NaO_6$, $CuSO_4.5H_2O$, tBuOH: $H_2O$, yield: 80% (iii) DMP, DCM, 3–6 h, 0–20 °C, yield: 54%; B (i) $NaN_3$, DMF, 2–5 h, 80 °C–120 °C, yield: ~49% (ii) $C_6H_7NaO_6$, $CuSO_4 \cdot 5H_2O$, tBuOH: $H_2O$, yield: ~60% (iii) DMP, DCM, 3–6 h, 0–20 °C, yield: ~50%; C (i) Cp*RuCl $(PPh_3)_2$, toluene, 3 h, 80 °C, yield: 81% (iii) DMP, DCM, 3–6 h, 0–20 °C, yield: 61%.

**Table 2**
Sugar–triazole conjugates and their antifungal activities.

| Comp | Ca[a] | Af[a] | Cn[a] | Ss[a] | Tm[a] |
|---|---|---|---|---|---|
| **10** | >50 | >50 | 25 | >50 | 50 |
| **24** | 25 | 50 | 50 | 12.5 | 50 |
| **25** | 50 | >50 | >50 | 50 | >50 |
| **26** | 25 | >50 | 50 | 3.12 | 0.39 |
| **27** | >50 | >50 | >50 | 12.5 | 3.12 |
| **28** | >50 | >50 | >50 | 25 | 12.5 |
| **29** | >50 | >50 | >50 | 50 | 3.12 |
| **30** | 6.25 | >50 | 25 | 25 | 6.25 |
| **31** | >50 | >50 | >50 | 12.5 | 25 |
| **32** | >50 | 25 | 50 | 25 | 3.12 |
| **33** | >50 | 25 | 50 | 12.5 | 25 |
| **34** | 12.5 | 50 | 12.5 | 25 | 6.25 |
| **35** | 25 | >50 | 25 | 12.5 | >50 |
| **36** | 12.5 | 50 | 25 | 12.5 | 50 |
| **37** | >50 | >50 | >50 | 25 | 12.5 |
| **38** | 6.25 | 50 | 50 | 6.25 | 1.56 |
| **39** | 25 | 50 | 50 | 50 | 50 |
| **40** | 12.5 | >50 | 25 | 12.5 | 6.25 |
| **41** | 25 | >50 | 50 | 50 | 25 |
| **42** | 50 | >50 | 50 | >50 | >50 |
| **46** | >50 | 1.56 | 50 | 50 | 1.56 |
| **50** | 50 | >50 | 50 | >50 | >50 |
| **51** | 50 | >50 | 50 | 50 | 50 |
| **53** | 50 | >50 | 25 | 6.25 | 25 |
| Clotrimazole | 0.25 | 8 | 0.25 | 4 | 2 |
| Flucanazole | 1.00 | >32 | 2.00 | 4 | 16 |
| 5-Fluorocytosine | 0.25 | >32 | 0.13 | >32 | >32 |
| Miconazole | 25 | 12.5 | 12.5 | 3.12 | 0.78 |

[a] *Candida albicans* (Ca); *Cryptococcus neoformans* (Cn); *Sporothrix schenckii* (Ss); *Trichophyton mentagrophytes* (Tm); *Aspergillus fumigatus* (Af); Antifungal activity as MIC in μg/mL.

activity (6.25 μg/mL) which was four-folds more active than standard drug miconazole. The MICs of these compounds against Af were between 1.56 and 50 μg/mL. Here, compound **46** showed the best activity (1.56 μg/mL). It was five- and eight-folds more active than clotrimazole and miconazole, respectively. In Cn, compound **34** was found to be the most active with an MIC value of 12.5 μg/mL. It is equipotent to miconazole. Compound **26** showed highest activity against Ss (3.12 μg/mL) and Tm (0.39 μg/mL). Its activity against Tm is two- and forty-folds more than miconazole and flucanazole, respectively. Compounds **38** and **46** also showed promising activity (1.56 μg/mL) against Tm. The SARs of these compounds revealed that the antifungal activity was enhanced by the introduction of halogen or adamantyl group at C-4 position of the triazole ring.

### 4.3. Molecular modelling

The plausible binding modes and mechanism of action of the synthesized compounds in the bacterial cells were explored using bioinformatics tools and compounds' structural/functional similarities with different ligands of bacteria's protein co-crystals. From these studies, it appeared that penicillin binding protein-2 (PBP-2) as the most likely target of these compounds. Thus in SYBYL X 1.3, PBP-2 of *S. aureus* (PDB code: 4DKI) were used for docking experiments to investigate the binding interactions of these compounds with the protein. In these experiments, the new compounds occupied the binding space of the protein in a way comparable to that of ceftobiprole (ligand in 4DKI) and ampicillin [39]. Furthermore, the docking scores of the new compounds were found to be almost parallel to the reported activities. To maintain brevity, the details of mode of interactions of compound **29** were discussed in comparison to ampicillin. In binding with PBP-2 protein, ampicillin showed interactions with Ser-403, Ser-462, Thr-600 and Tyr-446. Of these former three are directed to its acyl side chain and the fourth one was directed to the carbonyl oxygen of its β-lactam (Fig. 1).

In compound **29**, the ethereal and pyran oxygens have mimicked parts of acyl side chain and β-lactam moieties of ampicillin. They showed interaction with Ser-403, Ser-462 and Tyr-446. Apart from these, N2 and N3 of triazole moiety satisfied part of acyl side chain of ampicillin by interacting with Thr-600 (Fig. 1). PBP-2 is also common to *Klebsiella pneumonia*, *E. coli* and *P. aeruginosa* and with respect to *S. aureus* they showed an identity of 67%, 32% and 27%, respectively. The activity profiles of the compounds between *S. aureus* and *K. pneumonia* is in agreement with the high identity of their PBP-2 enzymes. In case of *E. coli* and *P. aeruginosa*, the compounds' low order of activity may be due to the altered binding pocket environment along with other reasons. Thus the foregoing offers a rationale for the activities.

Among the synthesized compounds, several have shown potent antifungal activity. The structure similarity between standard drugs and the synthesized compounds suggested that triazole moiety may be the key component for antifungal activity. These types of compounds may inhibit the fungal cytochrome P450 enzyme 14α-demethylase [40]. In brief, 2,3,6-trideoxy sugar–triazole conjugates reported here showed very good *in vitro* antibacterial and antifungal activities (Table 1) as compared to that of 2,3-dideoxy hex-2-enopyranosid-4-ulose alone [18,19]. This clearly showed the advantage of coupling of 2,3-dideoxy hex-2-enopyranosid-4-uloses with 1,2,3-triazoles, thus justifying the designed compounds [18,19].

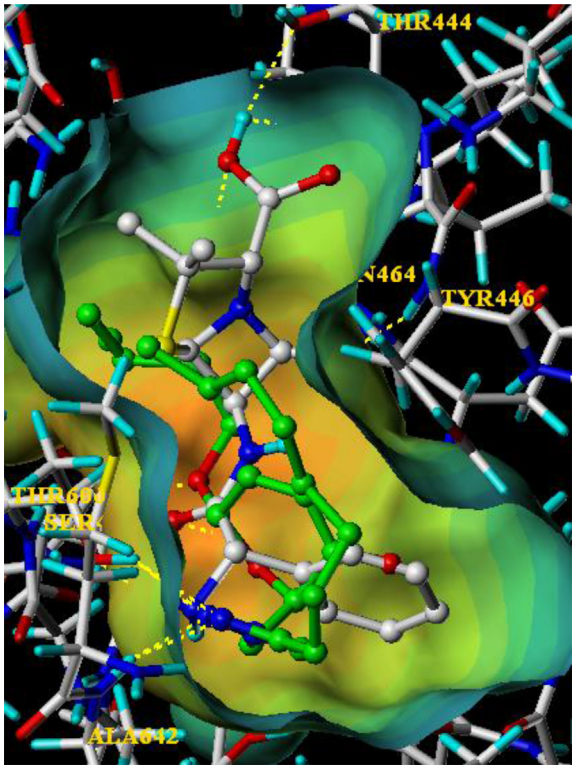



**Fig. 1.** Binding Poses of ampicillin (grey) and compound **29** (green) in ball-and-stick mode in the active site of PBP-2 (4DKI). The residues (Ser-403, Thr 444, Tyr-446, Ser-462, Thr-600, Ala 642 and Asn 464) surrounding the pocket are shown in stick mode. The dashed yellow lines represent selected H-bond interactions between the residues and the ligand/compound. In order to signify the binding pocket, it is shown in surface view mode with cavity depth. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

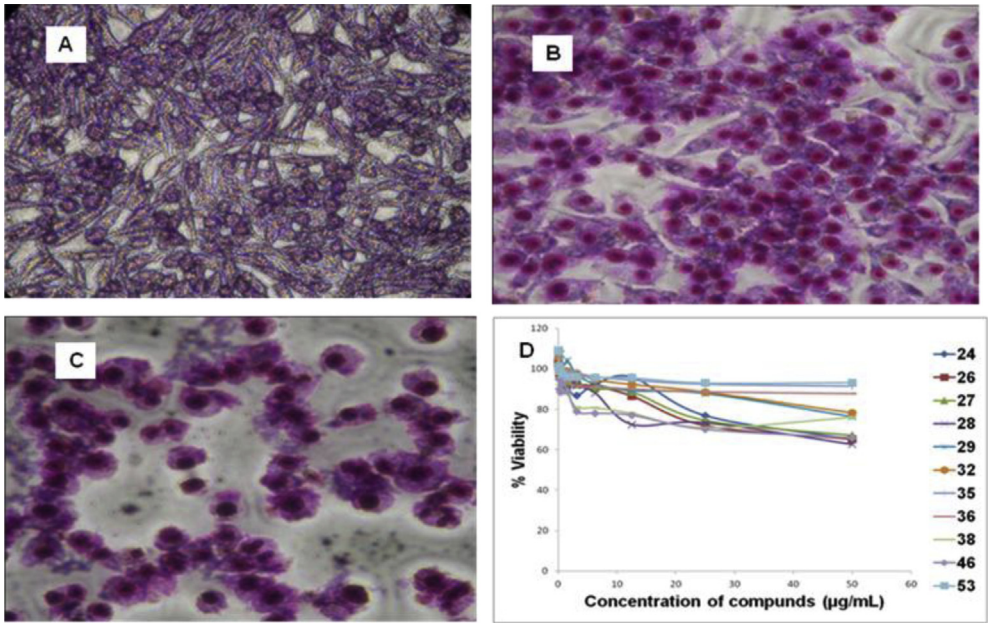



**Fig. 2.** (A) Normal growth of mammalian cell L929. (B) Morphological changes in mammalian cells L929 at MIC of compounds (MIC ≤ 3.12 μg/mL). (C) Morphological changes in mammalian cells L929 at 50 μg/mL of compounds. (D) Viability (determined by MTT assay) of mammalian cells L929 exposed to compounds **24**, **26**, **27**, **28**, **29**, **32**, **35**, **36**, **38**, **46** and **53**.

### 4.4. Toxicity study

Detailed toxicology of the compounds (**24**, **26**, **27**, **28**, **29**, **32**, **35**, **36**, **38**, **46** and **53**) showing low MIC (≤3.12 μg/mL) against the bacterial or fungal strains were done on mammalian cell L929. The morphological anomalies in the cells were examined under phase contrast microscope. In control, the cells were fairly transparent and attached to wall of the tissue culture plate (Fig. 2a). The compounds at MIC dose did not exhibit any toxicity to L929 cells and showed normal morphology (Fig. 2b). However, when the cells exposed to 50 μg/mL of the compound for 24 h, they lost normal morphology (Fig. 2c). The MTT assay revealed that the viability of the cells was inversely proportional to the concentration of the compounds (Fig. 2d).

## 5. Conclusion

In conclusion, we designed and synthesized a series of novel 6-triazolyl 2,3,6-trideoxy sugar–triazole conjugates using the concept of molecular hybridization. These compounds showed moderate to excellent *in vitro* activities against different Gram-positive, Gram-negative as well as resistant bacterial strains and fungi with MIC values between 0.39 and 50 μg/mL. Compound **29** was found to be the most active with MIC 0.78 μg/mL against Gram-positive (*S. aureus*) and Gram-negative (*K. pneumoniae*) bacteria and 3.12 μg/mL against methicillin- and vancomycin-resistant *S. aureus*. Compounds **38**, **46** and **53** were the other promising antibacterial molecules from this series. Compounds **26**, **38** and **46** showed high activity (MIC, 0.39–1.56 μg/mL) against *T. mentagrophytes* and high to threshold activity (MIC, 3.25–50 μg/mL) against *S. schenckii*. Of these, compound 46 was found to be the most promising one due to its broad spectrum activity against both bacterial and fungal strains. Exploration of bacterial cell enzymes with bioinformatics tools and compounds' structural/functional similarities with different ligands of bacteria's protein co-crystals led to suggest penicillin binding protein-2 as the most likely target of these compounds. All high active compounds (MIC ≤ 3.12 μg/mL) did not show any toxicity to mammalian cell L929. Further optimization of high active compounds would be taken up soon.

## 6. Experimental section

### 6.1. Chemistry

#### 6.1.1. General remarks

The chemicals used in synthesis were purchased from Sigma–Aldrich Co and Spectrochem (India). The organic solvents used in synthesis were dried by standard methods. All the reactions were monitored by thin layer chromatography over basic alumina coated TLC plates and the spots were visualized with the help of $CeSO_4$ or 10% $H_2SO_4$/EtOH on hot plate. The pure compound was isolated by column chromatography using silica gel of mesh size 60–120, 100–200 and 230–400. All the products were characterized by $^1H$, $^{13}C$, DEPT pulse sequence, two-dimensional homonuclear COSY (Correlation Spectroscopy), Heteronuclear Single Quantum Correlation (HSQC), Heteronuclear Multiple Bond Correlation (HMBC), IR, MS (ESI), HRMS (ESI) and HRMS (DART). All NMR spectra were recorded on Bruker Avance DPX 200FT, Bruker DRX 300 Spectrometers at 200, 300 MHz ($^1H$) and 50, 75, MHz ($^{13}C$). The chemical shifts ($\delta$) are given in ppm, related to tetramethylsilane (TMS) as an internal standard. For $^{13}C$ NMR reference $CDCl_3$ appeared at 77.10 ppm unless otherwise stated. Electron spray ionization Mass Spectra (ESIMS) were obtained on Micromass quadro II spectrometer. HRMS were recorded on JEOL, JMS T100LC Accu TOF. IR spectra were recorded on Perkin–Elmer 881 and FTIR-8210 PC Shimadzu Spectrophotometers either as KBr disc or neat and value are expressed in $cm^{-1}$. Optical rotations were determined on an Autopol III polarimeter (Rudolph Research) and using a 1 dm cell in chloroform as solvent at 25 °C unless otherwise stated; concentrations mentioned are in g/100 mL.

### 6.2. General procedure for the preparation of compounds *2a–2c*

To a solution of the enone **1a** (1500 mg, 7.01 mmol) in dry DCM (25 mL) was added dry pyridine (8 mL) and the temperature of the

reaction mixture was kept at −30 °C followed by drop wise addition of *p*-toluenesulphonyl chloride (2268 mg, 11.9 mmol) dissolved in dry dichloromethane (DCM) (10 mL) for 1 h. After the addition was complete, the reaction mixture was stirred at the same temperature for an additional 1 h and finally kept in a refrigerator at 5 °C for overnight. On completion of reaction (TLC), the reaction mixture was poured into ice cold water (excess) and the organic layer was separated. The aqueous layer was extracted with dichloromethane (4 × 5 mL). The combined organic layers were washed successively with water and brine, dried over sodium sulphate and evaporated *in vacuo* using co-distillation with toluene to remove pyridine. The crude product so obtained was purified by column chromatography to give the pure compound **2a** as viscous oil; yield (75%); $R_f = 0.45$ (hexane-ethyl acetate, 10:3); eluent for column chromatography (hexane-ethyl acetate, 50:3); $[\alpha]_D^{31} = -31.44$ (c 0.20, $CHCl_3$); IR (neat, $cm^{-1}$): 3025, 1699, 1599, 1364, 1179; $^1H$ NMR ($CDCl_3 + CCl_4$, 300 MHz): $\delta$ 7.75 (d, 2H, H-2′ and H-6′, $J = 8.1$ Hz), 7.32 (d, 2H, H-3′ and H-5′, $J = 8.0$ Hz), 6.82 (dd, 1H, H-2, $J = 10.3$ Hz & $J = 3.4$ Hz), 6.02 (d, 1H, H-3, $J = 10.3$ Hz), 5.16 (d, 1H, H-1, $J = 3.3$ Hz), 4.59 (dd, 1H, H-5, $J = 5.8$ Hz & $J = 2.0$ Hz), 4.44 (dd, 1H, H-6a, $J = 10.8$ Hz & $J = 2.1$ Hz), 4.25 (dd, 1H, H-6b, $J = 10.8$ Hz & $J = 6.1$ Hz), 3.86–3.78 (m, 1H, H-1′a), 3.58–3.50 (m, 1H, H-1′b), 2.44 (s, 3H, $CH_3$ of OTs), 1.72–1.61 (m, 1H, H-3′), 1.54–1.41 (m, 2H, H-2′), 0.91(s, 3H, $CH_3$ of $^i$amyl), 0.89 (s, 3H, $CH_3$ of $^i$amyl); $^{13}C$ NMR ($CDCl_3 + CCl_4$,50 MHz): $\delta$ 191.9(C-4), 144.6 (Ar*q*C), 144.3 (C-2), 133.1 (Ar*q*C), 129.8 (C-3′ and C-5′), 128.2 (C-2′ and C-6′), 127.2 (C-3), 93.1 (C-1), 72.3 (C-5), 68.1 (C-1′), 68.0 (C-6), 38.4 (C-2′), 25.0 (C-3′), 22.8 and 22.5 (2 $CH_3$ of $^i$amyl) 21.7 ($CH_3$ of OTs); MS (ESI): *m/z* 368; found 386 $[M+NH_4]^+$, 391 $[M+Na]^+$; HRMS (ESI): Calc for $C_{18}H_{24}O_6S$ $[M]^+$ 368.1294, found 368.1302.

Compounds **2b** and **2c** were prepared using the same procedure as described above for **2a.** However they were not isolated by column chromatography and crude product was used as such for the next step.

### 6.3. General procedure for the preparation of compounds *4a–4c*

To a stirred solution of **2a** (1934 mg, 5.25 mmol) in ethanol were added $CeCl_3.7H_2O$ (1174.49 mg, 3.15 mmol) and $NaBH_4$ (116.66 mg, 3.15 mmol) at 0 °C and the reaction mixture was stirred continuously for 40 min keeping the temperature of the reaction mixture below 10 °C. After completion of the reaction (TLC control), excess $NaBH_4$ was neutralized with acetone and the solvent was concentrated (rotary evaporator) to obtain the crude product **3a**. To the dried crude product **3a** dissolved dimethyl formamide (DMF) was added $NaN_3$ (847.6 mg, 13.04 mmol) and the reaction mixture was refluxed at 90–100 °C for 3 h. The cooled reaction mixture was poured into excess of ice-cold water and extracted with DCM (5 × 8 mL). The combined organic layers were washed with brine, dried over sodium sulphate and evaporated under reduced pressure to yield the crude product. It was then purified by column chromatography to give the pure compound **4a** as viscous oil; yield (64%); $R_f = 0.57$ (hexane-ethyl acetate, 3:2); eluent for column chromatography (hexane-ethyl acetate, 50:3); $[\alpha]_D^{31} = -35.27$ (c 0.40, $CHCl_3$); IR (neat, $cm^{-1}$): 3396, 3021, 2102, 1461, 1218; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 5.92 (d, 1H, H-3, $J = 15.3$ Hz), 5.77 (dd, 1H, H-2, $J = 15.3$ Hz & $J = 6.9$ Hz), 4.98 (s, 1H, H-1), 4.12–4.04 (m, 1H, H-4), 3.92–3.76 (m, 1H, H-5), 3.92–3.76 (m, 2H, H-5 & H-6a), 3.60–3.42 (m, 3H, H-6a & H-6b), 1.76–1.59 (m, 1H, H-3′), 1.56–1.45 (m, 2H, H-2′), 0.93 (s, 3H, $CH_3$ of $^i$amyl), 0.90 (s, 3H, $CH_3$ of $^i$amyl); $^{13}C$ NMR ($CDCl_3$,75 MHz): $\delta$ 132.6 (C-3), 127.1 (C-2), 94.2 (C-1), 71.4 (C-5), 67.4 (C-1′), 65.1 (C-4), 52.0 (C-6), 38.5 (C-2′), 25.1 (C-3′), 22.7 & 22.4 (2 $CH_3$ of $^i$amyl); MS (ESI): *m/z* 241; found 259 $[M+NH_4]^+$, 242 $[M+H]^+$; HRMS (ESI): Calc for $C_6H_8NO_2$ $[M-C_5H_{11}O + N_2]^+$ 126.0555; found 126.0544.

Compounds **4b** and **4c** were prepared using the same procedure as described above for **4a.** However they were not isolated by column chromatography and crude product was used as such for the next step.

### 6.4. General procedure for the preparation of compounds *6–9, 11–12, 14–23*

#### 6.4.1. Compound *6*

To a vigorously stirred solution of azide **4b** (250 mg, 1.111 mmol) in *tert*-butyl alcohol was added the 5 chloropentyne (0.173 mL, 1.66 mmol). The reaction was initiated by the addition of a solution of $CuSO_4.5H_2O$ (49.38 mg, 0.22 mmol) and sodium ascorbate (87.16 mg, 0.44 mmol) in distilled water. The coloured suspension formed and the reaction mixture was stirred at room temperature till the disappearance of the starting material on TLC. After the completion of reaction, ice-cold distilled water was added to the reaction mixture and the aqueous layer was extracted 3–4 times with $CHCl_3$. The combined organic extracts were dried *in vacuo* and purified using column chromatography to afford pure triazolyl 2,3,6 trideoxy hex-2-enopyranoside **6**; yield (78%); $R_f = 0.47$ (hexane-ethyl acetate, 3:2); eluent for column chromatography (hexane-ethyl acetate, 4:1); $[\alpha]_D^{31} = -5.44$ (c 0.08, $CHCl_3$); IR (neat, $cm^{-1}$): 3855, 3353, 2928, 2361, 1651, 1219, 768; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.50 (s, 1H, H-5′), 5.93 (d, 1H, H-3, $J = 9.9$ Hz), 5.71 (d, 1H, H-2, $J = 9.7$ Hz), 4.90 (s, 1H, H-1), 4.72 (d, 1H, H-6a, $J = 14.3$ Hz), 4.56 (dd, 1H, H-6b, $J = 14.4$ Hz & $J = 6.7$ Hz), 3.97 (d, 1H, H-4, $J = 6.9$ Hz), 3.85 (d, 1H, H-5, $J = 9.1$ Hz), 3.57 (t, 2H, H-1′, $J = 6.0$ Hz), 3.15 (t, 2H, H-3‴, $J = 7.0$ Hz), 2.88 ( t, 2H, H-1‴, $J = 7.0$ Hz), 2.16 (t, 2H, H-2‴, $J = 6.7$ Hz), 1.77–1.68 (m, 1H, H-2′), 0.83–0.78 (m, 6H, $2CH_3$ of $^i$ butyl); $^{13}C$ NMR ($CDCl_3$,75 MHz): $\delta$ 146.3 (C-4′), 133.1 (C-3), 126.4 (C-2), 123.1 (C-5′), 94.6 (C-1), 75.5 (C-1′), 70.7 (C-5), 64.5 (C-4), 51.3 (C-6), 44.2 (C-3‴), 32.0 (C-1‴), 28.4 (C-2′), 22.7 (C-2‴), 19.3 & 19.4 ($2CH_3$ of $^i$ butyl). MS (ESI): *m/z* 329; found 330 $[M+H]^+$; HRMS (ESI): Calc for $C_{15}H_{25}$ $ClN_3O_3$ $[M+H]^+$; 330.1584; found 330.1618.

Compounds **7**, **8**, **9**, **11**, **12**, **14**, **15**, **16**, **17**, **18**, **19**, **21**, **22**, **23** were prepared following the procedure as described above for compound **6**. While compounds **8**, **9**, **12**, **14**, **15**, **16**, **17**, **18**, **19**, **21**, **22**, **23** were synthesized from precursor 6-azido hex-2-enopyranoside **4a,** compound 7 and **11** were synthesized from precursor **4c**.

#### 6.4.2. Compound *7*

This compound was obtained as a viscous oil; yield (86%); $R_f = 0.47$ (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 3:1); $[\alpha]_D^{31} = -43.75$ (c 0.032, $CHCl_3$); IR (neat, $cm^{-1}$): 3759, 2364, 1655, 1576, 1218; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.50 (s, 1H, H-5′), 5.93 (d, 1H, H-3, $J = 10.1$ Hz), 5.69 (d, 1H, H-2, $J = 10.0$ Hz), 4.90 (s, 1H, H-1), 4.72 (dd, 1H, H-6a, $J = 14.3$ Hz & $J = 2.1$ Hz), 4.57 (dd, 1H, H-6b, $J = 14.3$ Hz and $J = 6.6$ Hz), 3.98 (dd, 1H, H-4, $J = 6.8$ Hz & $J = 8.9$ Hz), 3.85 (d, 1H, H-5, $J = 8.6$ Hz), 3.56 (t, 2H, H-3‴, $J = 6.3$ Hz), 3.44–3.31 (m, 2H, H-1′), 2.87 (t, 2H, H-1‴, $J = 7.2$ Hz), 2.14 ( dd, 2H, H-2‴, $J = 20.3$ Hz & $J = 6.5$ Hz), 1.46–1.40 (m, 2H, H-3′), 1.28–1.25 (m, 2H, H-2′), 0.86 (t, 3H, H-4′, $J = 7.3$ Hz); $^{13}C$ NMR ($CDCl_3$,75 MHz): $\delta$ 146.3 (C-4′), 133.2 (C-3), 126.4 (C-2), 123.0 (C-5′), 94.5 (C-1), 70.7 (C-5), 68.6 (C-4), 64.5 (C-1′), 51.3 (C-6), 44.2 (C-3‴), 32.0 (C-2′), 31.7 (C-1‴), 22.7 (C-2‴), 19.4 (C-3′), 13.9 (C-4′). MS (ESI): *m/z* 329; found 330 $[M+H]^+$; HRMS (ESI): Calc for $C_{15}H_{25}Cl_1N_3O_4$ $[M+H]^+$; 330.1584; found 330.1586.

#### 6.4.3. Compound *8*

This compound was obtained as a viscous oil; yield (73%); $R_f = 0.55$ (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 4:1); $[\alpha]_D^{31} = -3.08$ (c 0.14, $CHCl_3$); IR (neat, $cm^{-1}$): 3779, 3346, 2924, 2364, 1461, 1050; $^1H$ NMR ($CDCl_3$,

300 MHz) : δ 7.43 (s, 1H, H-5′), 5.93 (d, 1H, H-3, $J$ = 10.2 Hz), 5.72–5.67 (m, 1H, H-2), 4.91 (s, 1H, H-1), 4.71–4.55 (m, 2H, H-6), 4.00–3.94 (m, 1H, H-4), 3.83 (d, 1H, H-5, $J$ = 9.0 Hz), 3.52–3.46 (m, 1H, H-1′a), 3.40–3.35 (m, 1H, H-1′b), 2.69 (t, 2H, H-1‴, $J$ = 7.5 Hz), 1.82 (s, 1H, H-3′), 1.68–1.57 (m, 2H, H-2′), 1.41–1.34 (m, 6H, H-2‴, H-3‴ & H-4‴), 0.91–0.82 (m, 9H, 2$CH_3$ of $^i$amyl & 1$CH_3$ of H-5‴); $^{13}$C NMR ($CDCl_3$,75 MHz) : δ 148.5 (C-4′), 133.1 (C-3), 126.5 (C-2), 122.4 (C-5′), 94.6 (C-1), 70.8 (C-5), 67.2 (C-1′), 64.6 (C-4), 51.2 (C-6), 38.5 (C-2′), 31.6 (C-1‴), 29.8 (C-2‴), 29.3 (C-3‴), 25.7 (C-4‴), 25.1 (C-3′), 22.7 & 22.5 (2$CH_3$ of $^i$amyl), 14.2 ($CH_3$ of C-5‴). MS (ESI): $m/z$ 337; found 338$[M+H]^+$ HRMS (DART): Calc for $C_{18}H_{32}N_3O_3[M+H]^+$; 338.2443; found 338.2457.

### 6.4.4. Compound **9**

This compound was obtained as a viscous oil; yield (78%); $R_f$ = 0.51 (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 4:1); $[\alpha]_D^{31}$ = −3.91 (c 0.10, $CHCl_3$); IR (neat, $cm^{-1}$): 3411, 3019, 2928, 2364, 1589, 1217, 767; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.43 (s, 1H, H-5′), 5.93 (d, 1H, H-3, $J$ = 10.2 Hz), 5.69 (d, 1H, H-2, $J$ = 10.1 Hz), 4.91 (s, 1H, H-1), 4.71–4.53 (m, 2H, H-6), 3.98 (t, 1H, H-4, $J$ = 9.0 Hz), 3.84 (d, 1H, H-5, $J$ = 8.9 Hz), 3.53–3.32 (m, 2H, H-1′), 2.69 (t, 2H, H-1‴, $J$ = 7.3 Hz), 1.64–1.57 (m, 3H, H-3′ & H-2′), 1.40–1.30 (m, 8H, H-2‴–H-5‴), 0.87–0.82 (m, 9H, 2$CH_3$ of $^i$amyl & 1$CH_3$ of H-6‴); $^{13}$C NMR ($CDCl_3$,75 MHz): δ 148.4 (C-4′), 133.1 (C-3), 126.4 (C-2), 122.4 (C-5″), 94.5 (C-1), 70.8 (C-5), 67.2 (C-1′), 64.56 (C-4), 51.2 (C-6), 38.4 (C-2′), 31.64 (C-1‴), 29.8 (C-2‴), 29.5 (C-3‴), 29.0 (C-4‴), 25.7 (C-5‴), 25.1 (C-3′), 22.6 and 22.5 (2$CH_3$ of $^i$amyl), 14.1 ($CH_3$ of C-6‴); MS (ESI): $m/z$ 351; found 352 $[M+H]^+$; HRMS (DART): Calc for $C_{19}H_{34}N_3O_3$ $[M+H]^+$; 352.2600; found 352.2613.

### 6.4.5. Compound **11**

This compound was obtained as a viscous oil; yield (66%); $R_f$ = 0.47 (hexane-ethyl acetate, 3:2); eluent for column chromatography (hexane-ethyl acetate, 7:3); $[\alpha]_D^{31}$ = +18.22 (c 0.06, $CHCl_3$); IR (neat, $cm^{-1}$): 3908, 3762, 3455, 2927, 2365, 1631, 1220, 1041, 770; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.42 (s, 1H, H-5′), 5.93 (d, 1H, H-3, $J$ = 10.2 Hz), 5.69 (d, 1H, H-2, $J$ = 10.1 Hz), 4.90 (s, 1H, H-1), 4.70 (d, 1H, H-4, $J$ = 12.4 Hz), 4.56 (dd, 1H, H-6a, $J$ = 14.43 Hz and $J$ = 6.72 Hz), 3.98 (t, 1H, H-6b, $J$ = 7.2 Hz), 3.86 (s, 1H, H-5), 3.47–3.33 (m, 2H, H-1′), 2.68 (t, 2H, H-1‴, $J$ = 7.53 Hz), 1.66–1.61 (m, 4H, H-2′ & H-3′), 1.49–1.40 (m, 12H, H-2‴-H-7‴), 0.88–0.84 (m, 6H, H-4′ & H-8‴); $^{13}$C NMR ($CDCl_3$,75 MHz): δ 148.5 (C-4′), 133.1 (C-3), 126.5 (C-2), 122.4 (C-5′), 94.5 (C-1), 70.8 (C-5), 68.5 (C-1′), 64.6 (C-4), 51.2 (C-1′), 31.9 (C-1‴), 31.8 (C-2′), 29.6 (C-6‴), 29.5 (C-4‴), 29.4 (C-5‴), 29.3 (C-3‴), 25.8 (C-2‴), 25.7 (C-7‴), 19.4 (C-3′), 14.2 (C-4′), 13.9 (C-8‴). MS (ESI): $m/z$ 365; found 366 $[M+H]^+$; HRMS (ESI): Calc for $C_{20}H_{36}N_3O_3$ $[M+H]^+$; 366.2757; found 366.2742.

### 6.4.6. Compound **12**

This compound was obtained as a viscous oil; yield (83%); $R_f$ = 0.57 (chloroform-methanol 24:1); eluent for column chromatography (chloroform-methanol 10:0.1); $[\alpha]_D^{31}$ = −21.13 (c 0.08, $CHCl_3$); IR (neat, $cm^{-1}$): 3749, 3427, 2930, 2363, 1640, 1218; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.47 (s, 1H, H-5″), 5.92 (d, 1H, H-3, $J$ = 10.1 Hz), 5.68 (d, 1H, H-2, $J$ = 10.2 Hz), 4.91 (s, 1H, H-1), 4.71–4.56 (m, 2H, H-6), 4.00–3.95 (m, 1H, H-4), 3.83 (d, 1H, H-5, $J$ = 9.2 Hz), 3.66 (t, 2H, H-1′, $J$ = 6.3 Hz), 3.54–3.46 (m, 1H, H-4‴a), 3.40–3.33 (m, 1H, H-4‴b), 2.73 (t, 2H, H-1‴, $J$ = 7.2 Hz), 1.78–1.71 (m, 2H, H-2‴), 1.67–1.56 (m, 2H, H-3‴), 1.40–1.34 (m, 3H, H-3′ & H-2′), 0.86–0.82 (m, 6H, 2$CH_3$ of $^i$amyl). $^{13}$C NMR ($CDCl_3$,75 MHz): δ 147.9 (C-4′), 133.2 (C-3), 126.3 (C-2), 122.6 (C-5′), 94.5 (C-1), 70.7 (C-5), 67.2 (C-1′), 64.3 (C-4), 62.3 (C-4‴), 51.2 (C-6), 38.4 (C-1‴), 32.1 (C-3‴), 25.6 (C-2′), 25.2 (C-2‴), 25.0 (C-3′), 22.6 & 22.4 (2$CH_3$ of $^i$amyl). MS (ESI): $m/z$ 339; found 340 $[M+H]^+$; HRMS (DART): Calc for $C_{17}H_{30}N_3O_4$ $[M+H]^+$ 340.2236; found 340.2219.

### 6.4.7. Compound **14**

This compound was obtained as a viscous oil; yield (89%); $R_f$ = 0.47 (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 15:7); $[\alpha]_D^{31}$ = +13.71 (c 0.04, $CHCl_3$); IR (neat, $cm^{-1}$):3752, 3423, 2925, 2363, 1722, 1463, 1287, 1161, 1045; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.45 (s, 1H, H-5′), 5.92 (d, 1H, H-3, $J$ = 10.1 Hz), 5.70–5.66 (m, 1H, H-2), 4.90 (s, 1H, H-1), 4.69 (dd, 1H, H-6a, $J$ = 14.4 Hz & $J$ = 2.4 Hz), 4.58 (dd, 1H, H-6b, $J$ = 14.4 Hz & $J$ = 6.7 Hz), 4.05 (t, 2H, H-4 & H-5, $J$ = 6.12 Hz), 3.96 (t, 1H, H-4‴a, $J$ = 2.43 Hz), 3.84 (d, 1H, H-4‴a, $J$ = 8.97 Hz), 3.52–3.44 (m, 1H, H-1′a), 3.35 (dd, 1H, H-1′b, $J$ = 6.7 Hz & $J$ = 2.6 Hz), 2.72 (t, 2H, H-1‴, $J$ = 6.75 Hz), 1.71 (d, 4H, H-2‴ & H-3‴), 1.64–1.53 (m, 1H, H-3′), 1.39–1.32 (m, 2H, H-2′), 1.23 (s, 9H, OCOC($CH_3$)$_3$), 0.85–0.80 (m, 6H, 2$CH_3$ of $^i$amyl). $^{13}$C NMR ($CDCl_3$,75 MHz): δ 178.7 (C-5‴), 147.6 (C-4′), 133.2 (C-3), 126.3 (C-2), 122.6 (C-5′), 94.5 (C-1), 70.7 (C-5), 67.1 (C-1′), 64.4 (C-4‴), 64.1 (C-4), 51.2 (C-6), 38.4 (C-2′), 29.7 (C of Piv), 28.3 (C-1‴), 27.2 (3$CH_3$ of Piv), 25.9 (C-2‴), 25.2 (C-3‴), 25.0 (C-3′), 22.7 & 22.4 (2$CH_3$ of $^i$amyl). MS (ESI): $m/z$ 423; found 424 $[M+H]^+$; HRMS (ESI):Calc for $C_{22}H_{38}N_3O_5$ $[M+H]^+$; 424.2811; found 424.2797.

### 6.4.8. Compound **15**

This compound was obtained as a viscous oil; yield (86%); $R_f$ = 0.53 (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 7:3); $[\alpha]_D^{31}$ = −20.68 (c 0.03, $CHCl_3$); IR (neat, $cm^{-1}$): 3419, 3021, 2930, 2366, 1706, 1217; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.61 (s, 1H, H-5′), 5.92 (d, 1H, H-3, $J$ = 10.0 Hz), 5.71 (d, 1H, H-2, $J$ = 10.1 Hz), 4.92 (s, 1H, H-1), 4.72 (dd, 1H, H-6a, $J$ = 14.4 Hz & $J$ = 6.3 Hz), 4.61 (dd, 1H, H-6b, $J$ = 14.4 Hz & $J$ = 6.3 Hz), 3.99 (t, 1H, H-4, $J$ = 6.5 Hz), 3.83 (d, 1H, H-5, $J$ = 8.9 Hz), 3.64 (t, 2H, H-2‴, $J$ = 6.8 Hz), 3.55–3.47 (m, 1H, H-1′a), 3.38 (m, 1H, H-1′b, $J$ = 13.5 Hz & $J$ = 6.7 Hz), 3.29 (t, 2H, H-1‴, $J$ = 6.8 Hz), 1.68–1.55 (m, 1H, H-3′), 1.41–1.32 (m, 2H, H-2′), 0.87–0.82 (m, 6H, 2$CH_3$ of $^i$amyl). $^{13}$C NMR ($CDCl_3$,75 MHz): δ144.8 (C-4‴), 132.9 (C-3), 126.6 (C-2), 123.6 (C-5′), 94.5 (C-1), 70.7 (C-4), 67.3 (C-1′), 64.6 (C-5), 51.4 (C-6), 38.4 (C-2′), 29.8 (C-2‴), 29.5 (C-1‴), 25.1 (C-3′), 22.7 & 22.5 (2$CH_3$ of $^i$amyl). MS (ESI): $m/z$ 373; found 374 $[M+H]^+$; HRMS (ESI): Calc for $C_{15}H_{25}BrN_3O_3$ $[M+H]^+$; 374.1079; found 374.1061.

### 6.4.9. Compound **16**

This compound was obtained as a viscous oil; yield (64%); $R_f$ = 0.53 (hexane-ethyl acetate, 3:2); eluent for column chromatography (hexane-ethyl acetate, 4:1); $[\alpha]_D^{31}$ = −4.38 (c 0.06, $CHCl_3$); IR (neat, $cm^{-1}$): 3916, 3774, 3373, 2956, 2370, 1598, 1220; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.41 (s, 1H, H-5′), 5.92 (d, 1H, H-3, $J$ = 10.2 Hz), 5.61 (d, 1H, H-2, $J$ = 10.1 Hz), 4.85 (s, 1H, H-1), 4.77 (d, 1H, H-6a, $J$ = 13.7 Hz), 4.39 (t, 1H, H-4, $J$ = 7.1 Hz), 3.96 (d, 2H, H-6b & H-5, $J$ = 13.7 Hz), 3.37–3.20 (m, 2H, H-1′), 1.59–1.46 (m, 1H, H-3′), 1.31–1.27 (m, 11H, 2H of H-2′ & 9H of C($CH_3$)$_3$), 0.81–0.76 (2$CH_3$ of $^i$amyl). $^{13}$C NMR ($CDCl_3$,75 MHz): δ 157.3 (C-4′), 133.5 (C-3), 125.9 (C-2), 120.3 (C-5′), 94.3 (C-1), 70.1 (C-5), 66.8 (C-4), 64.5 (C-1′), 51.4 (C-6), 38.3 (C-2′), 30.3 (qC or C-1‴′), 29.6 (C($CH_3$)$_3$) 24.9 (C-3′), 22.6 & 22.4 (2$CH_3$ of $^i$amyl). MS (ESI): $m/z$ 323; found 324 $[M+H]^+$; HRMS (DART): Calc for $C_{17}H_{30}$ $N_3O_3$ $[M+H]^+$; 324.2250; found 324.2287.

### 6.4.10. Compound **17**

This compound was obtained as a viscous oil; yield (86%); $R_f$ = 0.47 (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 3:1); $[\alpha]_D^{31}$ = −29.17 (c 0.15, $CHCl_3$); IR (neat, $cm^{-1}$): 3419, 3020, 1758, 1630, 1216; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.94 (s, 1H, H-5′), 7.82 (d, 2H, H-2‴ & H-6‴, $J$ = 7.1 Hz),

7.43–7.29 (m, 3H, H-3‴, H-4‴ & H-5‴) 5.94 (d, 1H, H-3, $J$ = 10.2 Hz), 5.71 (dd, 1H, H-2, $J$ = 10.2 Hz & $J$ = 6.4 Hz), 4.93 (s, 1H, H-1), 4.81–4.76 (m, 1H, H-6a), 4.69 ( dd, 1H, H-6b, $J$ = 14.2 Hz & $J$ = 2.1 Hz), 4.04 (dd, 1H, H-4, $J$ = 6.4 Hz & $J$ = 2.4 Hz), 3.91 (d, 1H, H-5, $J$ = 9.2 Hz), 3.53–3.47 (m, 1H, H-1′a), 3.41–3.36 (m, 1H, H-1′b), 1.58–1.45 (m, 1H, H-3′), 1.41–1.31 (m, 2H, H-2′), 0.78 (d, 3H, $CH_3$ of $^i$amyl, $J$ = 1.8 Hz), 0.76 (d, 3H, $CH_3$ of $^i$amyl, $J$ = 1.8 Hz); $^{13}$C NMR ($CDCl_3$,50 MHz): δ 147.8 (*q*C), 133.0 (C-2), 130.5 (*q*C), 128.8 (C-3‴ & C-5‴), 128.2 (C-4‴), 126.5 (C-3), 125.7 (C-2‴ & C-6‴), 121.4 (C-4‴), 94.5 (C-1), 70.7 (C-5), 67.4 (C-1′), 64.6 (C-4), 51.4 (C-6), 38.3 (C-2′), 25.0 (C-3), 22.6 & 22.3 (2 $CH_3$ of $^i$amyl); MS (ESI): *m*/*z* 343; found 344 $[M+H]^+$; HRMS (ESI): Calc for $C_{19}H_{25}N_3O_3$ $[M]^+$ 343.1896; found 343.1928.

### 6.4.11. Compound **18**

This compound was obtained as a viscous oil; yield (89%); $R_f$ = 0.51 (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 13; 7); $[\alpha]_D^{31}$ = −25.02 (c 0.06, $CHCl_3$); IR (neat, $cm^{-1}$): 3752, 3417, 2928, 2367, 1637, 1218; $^1$H NMR ($CDCl_3$, 300 MHz): δ 8.59 (s, 1H, H-3‴), 8.38 (s, 1H, H-5″), 8.19 (d, 1H, H-6‴, $J$ = 7.7 Hz), 7.80 (t, 1H, H-5‴, $J$ = 6.5 Hz), 7.28–7.25 (m, 1H, H-4‴), 5.95 (d, 1H, H-3, $J$ = 10.0 Hz), 5.72 (d, 1H, H-2, $J$ = 10.2 Hz), 4.95 (s, 1H, H-1), 4.81 (dd, 2H, H-4 & H-6a, $J$ = 12.2 Hz & $J$ = 21.2 Hz), 4.11 (d, 1H, H-6b, $J$ = 20.1 Hz), 3.95 (d, 1H, H-5, $J$ = 8.5 Hz), 3.52–3.35 (m, 2H, H-1′), 1.58–1.49 (m, 1H, H-3′), 1.39–1.32 (m, 2H, H-2′), 0.89–0.75 (m, 6H, 2$CH_3$ of $^i$amyl). $^{13}$C NMR ($CDCl_3$,75 MHz): δ 150.3 (C-1‴), 149.4 (C-3‴), 148.3 (C-4″), 137.1 (C-5‴), 133.0 (C-3), 126.7 (C-2), 124.0 (C-6‴), 123.0 (C-4‴), 120.4 (C-5″), 94.6 (C-1), 70.7 (C-4), 67.5 (C-1′), 64.6 (C-5), 51.5 (C-6), 38.4 (C-2′), 25.1 (C-3′), 22.6 & 22.4 (2$CH_3$ of $^i$amyl). MS (ESI): *m*/*z* 344; found 345 $[M+H]^+$; HRMS (DART): Calc for $C_{18}H_{25}N_4O_3$ $[M+H]^+$; 345.1926; found 345.1907.

### 6.4.12. Compound **19**

This compound was obtained as a viscous oil; yield (69%); $R_f$ = 0.57 (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 3:7); $[\alpha]_D^{31}$ = −73.02 (c 0.06, $CHCl_3$); IR (neat, $cm^{-1}$): 3746, 3420, 2365, 1642, 1220; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.91 (s, 1H, H-5″), 7.78 (dd, 2H, H-3‴ & H-2‴, $J$ = 8.61 Hz & $J$ = 5.4 Hz), 7.09 (t, 2H, H-3‴ & H-5‴, $J$ = 8.6 Hz), 5.94 (d, 1H, H-3, $J$ = 10.2 Hz), 5.70 (d, 1H, H-2, $J$ = 10.2 Hz), 4.93 (s, 1H, H-1), 4.80 (dd, 1H, H-6a, $J$ = 14.3 Hz & $J$ = 2.0 Hz), 4.66 (dd, 1H, H-6b, $J$ = 14.3 Hz & $J$ = 6.5 Hz), 4.05 (t, 1H, H-4, $J$ = 6.9 Hz), 3.93 (d, 1H, H-5, $J$ = 9.1 Hz), 3.49–3.32 (m, 3H, H-1′ & H-3′), 1.56–1.47 (m, 1H, H-2a′), 1.38–1.25 (m, 2H, H-2b′), 0.87–0.74 (m, 6H, 2$CH_3$ of $^i$amyl). $^{13}$C NMR ($CDCl_3$,75 MHz): δ 164.4 (C-4‴), 161.1 (C-4″), 146.9 (C-3), 133.1 (C-2), 127.6 (C-6‴), 127.5 (C-2‴), 126.5 (C-3‴), 121.2 (C-5″), 116.02 (C-4‴), 115.7 (C-5‴), 94.6 (C-1), 70.8 (C-5), 67.4 (C-4), 64.6 (C-1′), 51.5 (C-6), 38.4 (C-2′), 25.1 (C-3′), 22.6 & 22.3 (2$CH_3$ of $^i$amyl). MS (ESI): *m*/*z* 361; found 362 $[M+H]^+$; HRMS (ESI): Calc for $C_{19}H_{25}FN_3O_3$ $[M+H]^+$; 362.1880; found 362.1870.

### 6.4.13. Compound **21**

This compound was obtained as a viscous oil; yield (70%); $R_f$ = 0.56 (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 13:7); $[\alpha]_D^{31}$ = −100.67 (c 0.02, $CHCl_3$); IR (neat, $cm^{-1}$): 3298, 2926, 2369, 1657,1219; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.39 (s, 1H, H-5″), 5.92 (dd, 1H, H-3, $J$ = 10.1 Hz), 5.67 (d, 1H, H-3, $J$ = 10.1 Hz), 4.89 (s, 1H, H-1), 4.68 (d, 1H, H-4, $J$ = 12.45 Hz), 4.52 (dd, 1H, H-6a, $J$ = 14.4 Hz & $J$ = 6.6 Hz), 3.94 (d, 1H, H-6b, $J$ = 6.6 Hz), 3.86 (d, 1H, H-5, $J$ = 9.09 Hz), 3.47–3.33 (m, 2H, H-1′), 1.91 (s, 1H, H-1‴), 1.59 (t, 1H, H-3′, $J$ = 6.63 Hz), 1.34 (t, 4H, H-2′, H-2‴a & H-3‴a $J$ = 6.81 Hz), 0.93–0.80 (m, 8H, H-2‴a, H-3‴b, & 2$CH_3$ of $^i$amyl). $^{13}$C NMR ($CDCl_3$,75 MHz): δ 150.1 (C-4″), 133.3 (C-3), 126.2 (C-2), 121.5 (C-5″), 94.5 (C-1), 70.8 (C-5), 67.2 (C-4), 64.4 (C-1′), 51.2 (C-6), 38.4 (C-2′), 25.1 (C-3′), 22.7 & 22.4 (2$CH_3$ of $^i$amyl), 7.77 (C-1‴), 6.66 (C-2‴ & C-3‴). MS (ESI): *m*/*z* 307; found 308 $[M+H]^+$; HRMS (ESI): Calc for $C_{16}H_{26}$ $N_3O_3$ $[M+H]^+$; 308.1974; found 308.1962.

### 6.4.14. Compound **22**

This compound was obtained as a viscous oil; yield (58%); $R_f$ = 0.53 (chloroform: methanol 49:1); eluent for column chromatography (chloroform:methanol, 10:0.1); $[\alpha]_D^{31}$ = −7.93 (c 0.04, $CHCl_3$); IR (neat, $cm^{-1}$): 3769, 3379, 2928, 2362, 1710, 1398, 1030; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.81 (dd, 2H, H-6‴ & H-9‴, $J$ = 5.49 Hz & $J$ = 3.06 Hz), 7.69 (dd, 2H, H-7‴ & H-8‴, $J$ = 5.37 Hz & $J$ = 3.03 Hz), 7.57 (s, 1H, H-5″), 5.91( d, 1H, H-3, $J$ = 10.2 Hz), 5.69–5.65 (m, 1H, H-2), 4.90 (s, 1H, H-1), 4.70–4.60 (m, 2H, H-4 & H-6a), 3.95(d, 1H, H-6b, $J$ = 6.06 Hz), 3.83 (d, 1H, H-5, $J$ = 8.97 Hz), 3.72 ( t, 2H, H-3‴, $J$ = 6.9 Hz), 3.52–3.46 (m, 1H, H-1′a), 3.38–3.33 (m, 1H, H-1′b), 2.62 (t, 2H, H-1‴, $J$ = 7.32 Hz), 2.14–2.02 (m, 2H, H-2‴), 1.62–1.53 (m, 1H, H-3′), 1.37–1.31 (m, 2H, H-2′), 0.82–0.78 (m, 6H, 2$CH_3$ of $^i$amyl). $^{13}$C NMR ($CDCl_3$,75 MHz): δ 168.5 (C-5‴ & C-10‴), 134.0 (2 × *q*C),133.2 (C-7‴ & C-8‴), 132.1 (C-4″), 126.3 (C-6‴, C-9‴& C-2), 123.3 (C-5″ & C-3), 94.5 (C-1), 70.8 (C-5), 51.23 (C-4), 38.4 (C-1′ & C-6), 37.4 (C-3‴), 28.2 (C-2′ & C-1‴), 25.0 (C-3′), 23.0 (C-2‴), 22.7 & 22.4 (2$CH_3$ of $^i$amyl). MS (ESI): *m*/*z* 454; found 455 $[M+H]^+$; HRMS (ESI): Calc for $C_{24}H_{31}$ $N_4O_5$ $[M+H]^+$; 455.2294; found 455.2292.

### 6.4.15. Compound **23**

This compound was obtained as a viscous oil; yield (72%); $R_f$ = 0.53 (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 3:2); $[\alpha]_D^{31}$ = −20.20 (c 0.02, $CHCl_3$); IR (neat, $cm^{-1}$): 3962, 3768, 3322, 2930, 2365, 1568, 1035; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.71 (d, 2H, H-4″ & H-5″, $J$ = 10.65 Hz), 5.93 (d, 1H, H-3, $J$ = 10.1 Hz), 5.69 (d, 1H, H-2, $J$ = 10.1 Hz), 4.90 (s, 1H, H-1), 4.79 (dd, 1H, H-6a, $J$ = 14.4 Hz & $J$ = 2.3 Hz), 4.65 (dd, 1H, H-6b, $J$ = 14.2 Hz & $J$ = 6.5 Hz),4.00 (t, 1H, H-4, $J$ = 6.87 Hz), 3.85 (d, 1H, H-5, $J$ = 8.91 Hz), 3.49–3.30 (m, 2H, H-1′), 1.66–1.53 (m, 1H, H-3′), 1.38–1.31 (m, 2H, H-2′), 0.85–0.81 (m, 6H, 2$CH_3$ of $^i$amyl). $^{13}$C NMR ($CDCl_3$,75 MHz): δ 133.7 (C-3), 133.1 (C-5″), 126.5 (C-2), 125.2 (C-4″), 94.5 (C-1), 70.7 (C-4), 67.3 (C-5), 64.6 (C-6), 51.2 (C-1′), 38.4 (C-2′), 25.1 (C-3′), 22.7 & 22.5 (2 $CH_3$ of $^i$amyl). MS (ESI): *m*/*z* 267; found 268 $[M+H]^+$; HRMS (DART): Calc for $C_{13}H_{22}N_3O_3$ $[M+H]^+$; 268.1661; found 268.1643.

## 6.5. General procedure for the preparation of compounds **25**–**28**, **30**–**31**, **14**–**23**

### 6.5.1. Compound **25**

To a solution of **6** (285 mg, 0.8662 mmol) in dry DCM (20 mL) was added Dess–Martin periodinane (DMP) reagent (556 mg, 1.299 mmol) at −5 °C. Subsequently the reaction was allowed to warm to 5 °C and stirred till all the starting material was converted into the oxidised product (4 h). The reaction was quenched by the addition of saturated aqueous solution of $NaHCO_3$ maintaining the temperature of the reaction mixture at 5 °C. The organic layer was separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over sodium sulphate and evaporated *in vacuo* to obtain the crude product. The crude product was chromatographed over silica gel to yield the pure 6-triazolyl-2,3,6-trideoxy hex-2-enopyranosid-4-ulose **25**; yield (63%); $R_f$ = 0.52 (hexane-ethyl acetate, 7:3); eluent for column chromatography (hexane-ethyl acetate, 17:3); $[\alpha]_D^{31}$ = −24.82 (c 0.04, $CHCl_3$); IR (neat, $cm^{-1}$): 3754, 2925, 2368, 2102, 1721, 1219; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.51 (d, 1H, H-2, $J$ = 5.89 Hz), 7.41 (s, 1H, H-5″), 6.26 (d, 1H, H-3, $J$ = 6.09 Hz), 4.67–4.49 (m, 3H, H-6 & H-5), 3.58–3.46 (m, 5H, H-1, H-3‴ & H-1′), 2.87 (t, 2H, H-1‴, $J$ = 7.1 Hz), 2.15 (dd, 2H, H-2‴, $J$ = 13.4 Hz & $J$ = 6.6 Hz), 2.02–1.92 (m, 1H, H-2′), 0.97–0.84 (m, 6H, 2$CH_3$ of $^i$butyl); $^{13}$C NMR ($CDCl_3$,75 MHz): δ 192.9

(C-4), 172.2 (C-4″), 168.1 (C-3), 141.1 (C-2), 132.6 (C-5″), 94.3 (C-1), 88.03 (C-1′), 62.6 (C-6), 53.5 (C-3‴), 41.2 (C-1‴), 39.1 (C-2‴), 38.2 (C-5), 28.7 (C-2′), 19.3 & 19.4 (2$CH_3$ of $^{i}$ butyl). MS (ESI): *m*/*z* 327; found 328 $[M+H]^+$; HRMS (ESI): Calc for $C_{15}H_{23}ClN_3O_3$ $[M+H]^+$; 328.1428; found 328.1410.

Compounds **26**, **27**, **28**, **30**, **31**, **33**, **34**, **35**, **36**, **37**, **38**, **40**, **41**, **42** were prepared using the same procedure as for compound **25**.

### 6.5.2. Compound **26**

This compound was obtained as a viscous oil; yield (63.7%); $R_f$ = 0.47 (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 3:1); $[\alpha]_D^{31}$ = −174.25 (c 0.012, $CHCl_3$); IR (neat, $cm^{-1}$): 3751, 2925, 3406, 2362, 1697,1219; $^1$H NMR ($CDCl_3$, 300 MHz): 7.43 (s, 1H, H-5″), 6.86 (dd, 1H, H-2, *J* = 10.2 Hz & *J* = 3.4 Hz), 6.10 ( d, 1H, H-3, *J* = 10.3 Hz), 5.19 (d, 1H, H-1, *J* = 3.3 Hz), 5.02 (dd, 1H, H-6a, *J* = 14.4 Hz and *J* = 3.0 Hz), 4.81 (dd, 1H, H-5, *J* = 7.6 Hz and *J* = 3.0 Hz), 4.53 (dd, 1H, H-6b, *J* = 14.4 Hz & *J* = 7.6 Hz), 3.56–3.43 (m, 2H, H-1′), 2.87 (t, 2H, H-3‴, *J* = 7.2 Hz), 2.16 (t, 2H, H-1‴, *J* = 6.6 Hz), 1.49–1.40 (m, 2H, H-2‴), 1.31–1.16 (m, 4H, H-2′ & H-3′), 0.85 (t, 3H, H-4′, *J* = 7.3 Hz); $^{13}$C NMR ($CDCl_3$,75 MHz): δ 193.1 (C-4), 146.3 (C-4″), 144.5 (C-3), 127.1 (C-2), 122.6 (C-5″), 93.2 (C-1), 72.8 (C-5), 69.6 (C-6), 49.5 (C-1′), 44.1 (C-3‴), 32.0 (C-2′), 29.7 (C-1‴), 22.7 (C-2‴), 19.3 (C-3′), 13.8 (C-4′). MS (ESI): *m*/*z* 327; found 328 $[M+H]^+$; HRMS (ESI): Calc for $C_{15}H_{23}ClN_3O_4$ $[M+H]^+$; 328.1428; found 328.1421.

### 6.5.3. Compound **27**

This compound was obtained as a viscous oil; yield (57%); $R_f$ = 0.5 (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 7:3); $[\alpha]_D^{31}$ = −127.56 (c 0.13, $CHCl_3$); IR (neat, $cm^{-1}$): 3380, 2932, 2365, 1699, 1218; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.35 (s, 1H, H-5″), 6.85 (dd, 1H, H-2, *J* = 10.3 Hz & *J* = 3.5 Hz), 6.09 (d, 1H, H-3, *J* = 10.3 Hz), 5.19 (d, 1H, H-1, *J* = 3.4 Hz), 5.02 (dd, 1H, H-6a, *J* = 14.5 Hz & *J* = 3.0 Hz), 4.80 (dd, 1H, H-5, *J* = 7.8 Hz and *J* = 3.0 Hz), 4.51 (dd, 1H, H-6b, *J* = 14.5 Hz & *J* = 7.8 Hz), 3.58–3.44 (m, 2H, H-1′), 2.68 ( t, 2H, H-1‴, *J* = 7.6 Hz), 1.69–1.59 (m, 3H, H-3′ and H-2′), 1.41–1.27 (m, 6H, H-2‴, H-3‴ & H-4‴), 0.88–0.81(m, 9H, 1$CH_3$ of H-5‴& 2$CH_3$ of $^{i}$amyl); $^{13}$C NMR ($CDCl_3$,75 MHz): δ 193.2 (C-4), 148.5 (C-4″), 144.5 (C-2), 127.2 (C-3), 122.0 (C-5″), 93.2 (C-1), 72.9 (C-5), 68.2 (C-1′), 49.4 (C-6), 38.2 (C-2′), 31.5 (C-1‴), 29.3 (C-2‴), 25.7 (C-3‴), 25.0 (C-3′), 22.6 (C-4‴), 22.5 & 22.4 (2$CH_3$ of $^{i}$amyl), 14.1 ($CH_3$ of C-5‴); MS (ESI): *m*/*z* 335; found 336 $[M+H]^+$; HRMS (DART): Calc for $C_{18}H_{30}N_3O_3$ $[M+H]^+$; 336.2287; found 336.2275.

### 6.5.4. Compound **28**

This compound was obtained as a viscous oil; yield (61%); $R_f$ = 0.52 (hexane-ethyl acetate, 7:3); eluent for column chromatography (hexane-ethyl acetate, 9:1); $[\alpha]_D^{31}$ = −136.6794 (c 0.12, $CHCl_3$); IR (neat, $cm^{-1}$): 3772, 3455, 2925, 1685, 1463, 1031; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.35 (s, 1H, H-5″), 6.85 (dd, 1H, H-2, *J* = 10.3 Hz & *J* = 3.5 Hz), 6.09 (d, 1H, H-3, *J* = 10.3 Hz), 5.19 (d, 1H, H-1, *J* = 3.4 Hz), 5.02 ( dd, 1H, H-6a, *J* = 14.4 Hz and *J* = 3.0 Hz), 4.80 (dd, 1H, H-5, *J* = 7.8 Hz & *J* = 3.0 Hz), 4.51 (dd, 1H, H-6b, *J* = 14.5 Hz & *J* = 7.8 Hz), 3.58–3.44 (m, 2H, H-1′), 2.68 (t, 2H, H-1‴, *J* = 7.6 Hz), 1.65–1.57 (m, 3H, H-3′& H-2′), 1.41–1.30 (m, 8H, H-2‴-H-5‴), 0.89–0.80 (m, 9H, 2$CH_3$ of $^{i}$amyl & 1$CH_3$ of H-6‴); $^{13}$C NMR ($CDCl_3$,75 MHz): δ 193.2 (C-4), 148.5 (C-4″), 144.5 (C-2), 127.2 (C-3), 122.0 (C-5″), 93.2 (C-1), 73.0 (C-5), 68.2 (C-1′), 49.5 (C-6), 38.23 (C-2′), 31.7 (C-1‴), 29.8 (C-2‴), 29.6 (C-3‴), 29.0 (C-4‴), 25.7 (C-5‴), 25.0 (C-3′), 22.6 & 22.3 ( 2$CH_3$ of $^{i}$amyl), 14.1 ($CH_3$ Of C-6‴). MS (ESI): *m*/*z* 349; found 350 $[M+H]^+$; HRMS (DART): Calc for $C_{19}H_{32}N_3O_3$ $[M+H]^+$, 350.2443; found 350.2424.

### 6.5.5. Compound **30**

This compound was obtained as a viscous oil; yield (56%); $R_f$ = 0.47 (hexane-ethyl acetate, 7:3); eluent for column chromatography (hexane-ethyl acetate, 9:1); $[\alpha]_D^{31}$ = −15.67 (c 0.04, $CHCl_3$); IR (neat, $cm^{-1}$): 3755, 3693, 3374, 2928, 2363, 1660, 1591, 1217; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.35 (s, 1H, H-5″), 6.86 (dd, 1H, H-2, *J* = 10.1 Hz & *J* = 3.1 Hz), 6.10 (d, 1H, H-3, *J* = 10.2 Hz), 5.19 (d, 1H, H-1, *J* = 2.9 Hz), 5.03 (dd, 2H, H-6, *J* = 14.4 Hz & *J* = 2.3 Hz), 4.81 (dd, 1H, H-5, *J* = 7.6 Hz & *J* = 2.6 Hz), 4.50 (dd, 2H, H-1′, *J* = 14.3 Hz & *J* = 8.0 Hz), 3.52–3.43 (m, 2H, H-1‴), 2.69 (t, 2H, H-2′, *J* = 7.5 Hz), 1.62 (d, 2H, *J* = 6.8 Hz), 1.49–1.42 (m, 12H, H-2‴-H-7‴), 0.87–0.85 (m, 6H, 2$CH_3$ of H-8‴ & H-4′); $^{13}$C NMR ($CDCl_3$,75 MHz): δ 193.2 (C-4), 148.5 (C-4″), 144.4 (C-2), 127.2 (C-3), 122.0 (C-5″), 93.2 (C-1), 72.9 (C-5), 69.6 (C-1′), 49.4 (C-6), 31.9 (C-2′), 31.6 (C-1‴), 29.6 (C-2‴), 29.4 (C-3‴), 29.32 (C-4‴), 29.3 (C-5‴), 25.7 (C-6‴), 22.7 (C-7‴), 19.3 (C-3′), 14.2 (C-4′), 13.8 (C-8‴). MS (ESI): *m*/*z* 363; found 364 $[M+H]^+$; HRMS (ESI): Calc for $C_{20}H_{34}N_3O_4$ $[M+H]^+$; 364.2600; found 364.2602.

### 6.5.6. Compound **31**

This compound was obtained as a viscous oil; yield (63%); $R_f$ = 0.47 (hexane-ethyl acetate 1:1); eluent for column chromatography (hexane-ethyl acetate, 16:9); $[\alpha]_D^{31}$ = +4.95 (c 0.27, $CHCl_3$); IR (neat, $cm^{-1}$): 3754, 3432, 2923, 2372, 1646, 1464, 1220; $^1$H NMR ($CDCl_3$, 300 MHz): δ 9.74 (s, 1H, H-1‴′), 7.40 (s, 1H, H-5″), 6.85 (dd, 1H, H-2, *J* = 10.3 Hz & *J* = 3.5 Hz), 6.09 ( d, 1H, H-3, *J* = 10.3 Hz), 5.19 (d, 1H, H-1, *J* = 3.5 Hz), 5.00 (dd, 1H, H-6a, *J* = 14.4 Hz & *J* = 3.1 Hz), 4.79 (dd, 1H, H-5, *J* = 7.5 Hz & *J* = 3.1 Hz), 4.54 (dd, 1H, H-6b, *J* = 14.4 Hz & *J* = 7.5 Hz), 3.62–3.42 (m, 2H, H-1′), 2.73 (t, 2H, H-1‴, *J* = 7.5 Hz), 2.51 (t, 2H, H-3‴, *J* = 7.2 Hz), 2.03–1.95 (m, 2H, H-2‴), 1.62–1.53 (m, 1H, H-3′), 1.40–1.33 (m, 2H, H-2′), 0.84–0.78 (m, 6H, 2$CH_3$ of $^{i}$amyl); $^{13}$C NMR ($CDCl_3$,75 MHz): δ 202.0 (C-1‴′), 193.1 (C-4), 147.0 (C-4″), 144.5 (C-2), 127.1 (C-3), 122.4 (C-5″), 93.2 (C-1), 72.8 (C-5), 68.2 (C-1′), 49.5 (C-6), 43.1 (C-3‴), 38.2 (C-2′), 24.9 (C-2‴), 24.8 (C-3′), 22.6 (C-2‴), 22.3 & 21.9 (2$CH_3$ of $^{i}$amyl); MS (ESI): *m*/*z* 335; found 336 $[M+H]^+$; HRMS (DART): Calc for $C_{17}H_{26}N_3O_4[M+H]^+$; 336.1923; found 336.1904.

### 6.5.7. Compound **33**

This compound was obtained as a viscous oil; yield (59%); $R_f$ = 0.53 (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 7:3); $[\alpha]_D^{31}$ = −33.35 (c 0.02, $CHCl_3$); IR (neat, $cm^{-1}$): 3750, 3422, 2364, 1642, 1218; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.37 (s, 1H, H-5″), 6.85 (dd, 1H, H-2, *J* = 10.2 Hz & *J* = 3.2 Hz), 6.09 (d, 1H, H-3, *J* = 10.3 Hz), 5.19 (d, 1H, H-1, *J* = 3.03 Hz), 5.01 (dd, 1H, H-6a *J* = 14.3 Hz & *J* = 2.7 Hz), 4.80 (dd, 1H, H-6b, *J* = 7.44 Hz, *J* = 2.79 Hz), 4.53 (dd, 1H, H-5, *J* = 14.4 Hz, & *J* = 7.4 Hz), 4.07 (d, 2H, H-4‴, *J* = 5.9 Hz), 3.61–3.42 (m, 2H, H-1′), 2.72 (d, 2H, H-1‴, *J* = 6.8 Hz), 1.70–1.53 (m, 4H, H-2‴, H-3‴), 1.40 (m, 1H, H-3′), 1.24–1.18 (m, 11H, H-2′ & 9H OCOC($CH_3$)$_3$), 0.89–0.88 (m, 6H, 2$CH_3$ of $^{i}$amyl); $^{13}$C NMR ($CDCl_3$,75 MHz): δ 193.2 (C-4), 178.7 (C-5‴), 147.7 (C-4″), 144.5 (C-2), 127.1 (C-3), 122.2 (C-5″), 93.2 (C-1), 72.8 (C-5), 68.2 (C-1′), 64.1 (C-4‴), 49.5 (C-6), 38.2 (C-2′), 29.7 (C of OCO*C*($CH_3$)$_3$), 28.3 (C-1‴), 27.3 ($CH_3$ of OCOC(*C*$H_3$)$_3$), 25.98 (C-2‴), 25.3 (C-3‴), 25.0 (C-3′), 22.6 & 22.3 (2$CH_3$ of $^{i}$amyl). MS (ESI): *m*/*z* 421; found 422 $[M+H]^+$; HRMS (ESI): Calc for $C_{22}H_{36}N_3O_5$ $[M+H]^+$; 422.2655; found 422.2639.

### 6.5.8. Compound **34**

This compound was obtained as a viscous oil; yield (74%); $R_f$ = 0.53 (hexane-ethyl acetate 7:3); eluent for column chromatography (hexane-ethyl acetate, 17:3); $[\alpha]_D^{31}$ = −0.34 (c 0.17, $CHCl_3$); IR (neat, $cm^{-1}$): 3880, 3751, 3444, 2364, 1655, 1220; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.56 (s, 1H, H-5″), 6.87 (dd, 1H, H-2, *J* = 10.3 Hz & *J* = 3.5 Hz), 6.11 (d, 1H, H-3, *J* = 10.2 Hz), 5.21 (d, 1H, H-1,

$J$ = 3.4 Hz), 5.06 (dd, 1H, H-6a, $J$ = 14.4 Hz & $J$ = 2.94 Hz), 4.82 (dd, 1H, H-5, $J$ = 7.7 Hz & $J$ = 3.1 Hz), 4.59–4.50 (m, 1H, H-6b), 3.64 (t, 2H, H-2‴, $J$ = 6.7 Hz), 3.51–3.43 (m, 1H, H-1′a), 3.29 (t, 3H, H-1‴& H-1′b, $J$ = 6.75 Hz), 1.65–1.54 (m, 1H, H-3′), 1.42–1.36 (m, 2H, H-2′), 0.86–0.80 (m, 6H, $2CH_3$ of $^i$amyl); $^{13}$C NMR ($CDCl_3$,75 MHz): δ 193.1 (C-4), 144.8 (C-4″), 144.5 (C-2), 127.1 (C-3), 123.3 (C-5″), 93.2 (C-1), 72.8 (C-5), 68.3 (C-1′), 49.6 (C-6), 38.2 (C-2′), 31.7 (C-2‴), 29.2 (C-1‴), 25.0 (C-3′), 22.6 & 22.3 ($2CH_3$ of $^i$amyl). MS (ESI): $m/z$ 371; found 372 $[M+H]^+$; HRMS (DART): Calc for $C_{15}H_{23}BrN_3O_3$ $[M+H]^+$; 372.0922; found 372.0932.

### 6.5.9. Compound **35**

This compound was obtained as a viscous oil; yield (86%); $R_f$ = 0.52 (hexane-ethyl acetate, 7:3); eluent for column chromatography (hexane-ethyl acetate, 9:1); $[\alpha]_D^{31}$ = +5.84 (c 0.10, $CHCl_3$); IR (neat, $cm^{-1}$): 3420, 2926, 2365, 1700, 1217; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.34 (s, 1H, H-5″), 6.84 (dd, 1H, H-2, $J$ = 10.3 Hz & $J$ = 3.45 Hz), 6.07 (d, 1H, H-3, $J$ = 10.3 Hz), 5.18 (d, 1H, H-1, $J$ = 3.3 Hz), 5.04 (dd, 1H, H-6a, $J$ = 14.5 Hz & $J$ = 2.9 Hz), 4.78 (dd, 1H, H-5, $J$ = 8.8 Hz & $J$ = 2.82 Hz), 4.42 (dd, 1H, H-6b, $J$ = 14.5 Hz & $J$ = 8.3 Hz), 3.51–3.39 (m, 2H, H-1′), 1.58–1.51 (m, 1H, H-3′), 1.33–1.25 (m, 11H, H-2′, & C($CH_3$)$_3$), 0.88–0.78 (m, 6H, $2CH_3$ of $^i$amyl); $^{13}$C NMR ($CDCl_3$,75 MHz): δ 193.1 (C-4), 157.6 (C-4″), 144.4 (C-2), 127.1 (C-3), 120.2 (C-5″), 96.5 (C-1), 72.9 (C-5), 68.0 (C-1′), 49.3 (C-6), 38.2 (C-2′), 30.4 (C($CH_3$)$_3$), 29.3 (C($CH_3$)$_3$) 24.9 (C-3′), 22.6 & 22.3 ($2CH_3$ of $^i$amyl). MS (ESI): $m/z$ 321; found 322 $[M+H]^+$; HRMS (ESI): Calc for $C_{17}H_{28}N_3O_3$ $[M+H]^+$; 322.2131; found 322.2122.

### 6.5.10. Compound **36**

This compound was obtained as a Glassy solid; yield (81%); $R_f$ = 0.43 (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane-ethyl acetate, 89:11); $[\alpha]_D$ = −147.80 (c 0.24, $CHCl_3$); IR (neat, $cm^{-1}$): 3423, 3020, 1633, 1426, 1216; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.86 (s, 1H, H-5″), 7.83–7.80 (m, 2H, H-2‴ & H-6‴), 7.43–7.32 (m, 3H, H-3‴, H-4‴ & H-5‴) 6.86 ( dd, 1H, H-2, $J$ = 10.3 Hz & $J$ = 3.5 Hz), 5.21 (d, 1H, H-1, $J$ = 3.4 Hz), 5.10 (dd, 1H, H-6a, $J$ = 14.4 Hz & $J$ = 3.1 Hz), 4.87 (dd, 1H, H-5, $J$ = 7.6 Hz & $J$ = 3.1 Hz), 4.63 ( dd, 1H, H-6b, $J$ = 14.4 Hz & $J$ = 7.6 Hz), 3.63–3.55 (m, 1H, H-1′a), 3.51–3.36 (m, 1H, H-1′b), 1.58–1.45 (m, 1H, H-3′), 1.41–1.31 (m, 2H, H-2′), 0.78(d, 3H, $CH_3$ of $^i$amyl, $J$ = 1.8 Hz), 0.76 (d, 3H, $CH_3$ of $^i$amyl, $J$ = 1.8 Hz); $^{13}$C NMR ($CDCl_3$,75 MHz): δ 193.1 (C-4), 147.8 ($q$C), 144.5 (C-2), 130.6 ($q$C), 128.8 (C-3‴ & C-5‴), 128.2 (C-4‴), 127.1 (C-3), 125.8 (C-2‴ & C-6‴), 121.0 (C-4‴), 93.3 (C-1), 72.8 (C-5), 68.4 (C-1′), 49.6 (C-6), 38.2 (C-2′), 25.0 (C-3), 22.5 & 22.3 (2 $CH_3$ of $^i$amyl); MS (ESI): $m/z$ 341; found 342 $[M+H]^+$; HRMS (ESI): Calc for $C_{19}H_{23}N_3O_3$ $[M]^+$ 341.1739; found 341.1741.

### 6.5.11. Compound **37**

This compound was obtained as a viscous oil; yield (89%); $R_f$ = 0.51 (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 13; 7); $[\alpha]_D^{31}$ = −25.02 (c 0.06, $CHCl_3$); IR (neat, $cm^{-1}$): 3752, 3417, 2928, 2367, 1637, 1218; $^1$H NMR ($CDCl_3$, 300 MHz): δ 8.56 (d, 1H, H-3‴, $J$ = 4.2 Hz), 8.25 (s, 1H, H-5″), 8.16 (d, 1H, H-6‴, $J$ = 7.9 Hz), 7.75 (t, 1H, H-5‴′, $J$ = 7.56 Hz), 7.22–7.18 (m, 1H, H-4‴′), 6.85 (dd, 1H, H-2, $J$ = 10.3 Hz & $J$ = 3.4 Hz), 6.11 (d, 1H, H-3, $J$ = 10.3 Hz), 5.20 (d, 1H, H-1, $J$ = 3.3 Hz), 5.12 (dd, 1H, H-6a, $J$ = 14.4 Hz & $J$ = 2.9 Hz), 4.86 (dd, 1H, H-5, $J$ = 7.8 Hz & $J$ = 2.8 Hz), 4.63 (dd, 1H, H-6b, $J$ = 14.34 Hz & $J$ = 7.92 Hz), 3.60–3.41 (m, 2H, H-1′), 1.56–1.44 (m, 1H, H-3′), 1.37–1.33 (m, 2H, H-2′), 0.75–0.72 (m, 6H, $2CH_3$ of $^i$amyl); $^{13}$C NMR ($CDCl_3$,75 MHz): δ 192.9 (C-4), 150.4 (C-1‴), 149.4 (C-3‴), 148.4 (C-5‴), 144.5 (C-2), 136.9 (C-3), 127.2 (C-6‴), 123.6 (C-4‴), 122.9 (C-4‴), 120.3 (C-5″), 93.3 (C-1), 72.7 (C-5), 68.5 (C-6), 49.8 (C-1′), 38.2 (C-2′), 25.0 (C-3′), 22.5 & 22.3 ($2CH_3$ of $^i$amyl). MS (ESI): $m/z$ 342; found 343 $[M+H]^+$; HRMS (DART): Calc for $C_{18}H_{23}N_4O_3$ $[M+H]^+$; 343.1770; found 343.1780.

### 6.5.12. Compound **38**

This compound was obtained as a viscous oil; yield (66%); $R_f$ = 0.57 (hexane-ethyl acetate, 7:3); eluent for column chromatography (hexane-ethyl acetate, 9:1); $[\alpha]_D^{31}$ = −94.93(c 0.08, $CHCl_3$); IR (neat, $cm^{-1}$): 3733, 3437, 2955, 1695, 1367, 1222; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.79 (dd, 3H, H-5″, H-3‴ & H-2‴, $J$ = 9.27 Hz & $J$ = 6.21 Hz), 7.10 (t, 2H, H-5‴ & H-6‴, $J$ = 8.64 Hz), 6.87 (dd, 1H, H-2, $J$ = 10.3 Hz & $J$ = 3.4 Hz), 6.12 (d, 1H, H-3, $J$ = 10.3 Hz), 5.22 (d, 1H, H-1, $J$ = 3.27 Hz), 5.09 (dd, 1H, H-6a, $J$ = 14.4 Hz & $J$ = 3.1 Hz), 4.87 (dd, 1H, H-5, $J$ = 7.4 Hz & $J$ = 3.1 Hz), 4.63 (dd, 1H, H-6b, $J$ = 14.3 Hz & $J$ = 7.4 Hz), 3.63–3.44 (m, 2H, H-1′), 1.60–1.53 (m, 1H, H-3′), 1.41–1.34 (m, 2H, H-2′), 0.87–0.76 (m, 6H, $2CH_3$ of $^i$amyl); $^{13}$C NMR ($CDCl_3$,75 MHz): δ193.1 (C-4), 147.0 (C-4‴), 144.6 (C-4″), 127.6 (C-2), 127.5 (C-3), 127.2 (C-6‴& C-2‴), 120.8 (C-5″), 116.0 (C-1‴), 115.7 (C-5‴ & C-3‴), 93.4 (C-1), 72.8 (C-5), 68.4 (C-1′), 49.7 (C-6′), 38.2 (C-2′), 25.0 (C-3′), 22.6 & 22.3 ( $2CH_3$ of $^i$amyl). MS (ESI): $m/z$ 359; found 360 $[M+H]^+$; HRMS (ESI): Calc for $C_{19}H_{23}FN_3O_3$ $[M+H]^+$; 360.1723; found 360.1710.

### 6.5.13. Compound **40**

This compound was obtained as a viscous oil; yield (75%); $R_f$ = 0.47 (hexane-ethyl acetate, 7:3); eluent for column chromatography (hexane-ethyl acetate, 4:1); $[\alpha]_D^{31}$ = −122.58 (c 0.014, $CHCl_3$); IR (neat, $cm^{-1}$): 3752, 2957, 2361, 1697, 1219; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.31 (s, 1H, H-5″), 6.84 (dd, 1H, H-2, $J$ = 10.3 Hz and $J$ = 3.5 Hz), 6.09 (d, 1H, H-3, $J$ = 10.3 Hz), 5.19 (d, 1H, H-1, $J$ = 3.3 Hz), 4.99 (dd, 1H, H-6a, $J$ = 14.4 Hz & $J$ = 2.9 Hz), 4.77 (dd, 1H, H-5, $J$ = 7.68 Hz and $J$ = 2.97 Hz), 4.51–4.46 (m, 1H, H-6b), 3.60–3.42 (m, 2H, H-1′), 1.96–1.87 (m, 1H, H-1‴), 1.63–1.52 (m, 1H, H-3′), 1.38 (dd, 2H, H-2′, $J$ = 13.47 Hz & $J$ = 6.75 Hz), 0.94-0.79 (m, 10H, 6H of $^i$amyl & 4H of H-2‴ & H-3‴); $^{13}$C NMR ($CDCl_3$,75 MHz): δ 193.1 (C-4), 150.3 (C-4″), 144.4 (C-2), 127.1 (C-3), 121.0 (C-5″), 93.2 (C-1), 72.9 (C-5), 68.3 (C-1′), 38.2 (C-6), 34.0 (C-2′), 25.0 (C-3′), 22.6 & 22.4 ($2CH_3$ of $^i$amyl), 7.7 (C-1‴), 6.7 (C-2‴ & C-3‴). MS (ESI): $m/z$ 305; found 306 $[M+H]^+$; HRMS (ESI): Calc for $C_{16}H_{24}N_3O_3$ $[M+H]^+$; 306.1818; found 306.1806.

### 6.5.14. Compound **41**

This compound was obtained as a viscous oil; yield (59%); $R_f$ = 0.53 (chloroform-methanol, 97:3); eluent for column chromatography (chloroform-methanol, 99:1); $[\alpha]_D^{31}$ = −18.30 (c 0.15, $CHCl_3$); IR (neat, $cm^{-1}$): 3458, 2358, 1696, 1217; $^1$H NMR ($CDCl_3$, 300 MHz): δ 7.82 (dd, 2H, H-8‴& H-7‴, $J$ = 5.4 Hz & $J$ = 3.1 Hz), 7.70 (dd, 2H, H-9‴& H-6‴, $J$ = 5.37 Hz & $J$ = 3.09 Hz), 7.50 (s, 1H, H-5″), 6.85 (dd, 1H, H-2, $J$ = 10.3 Hz & $J$ = 3.48 Hz), 6.09 (d, 1H, H-3, $J$ = 10.3 Hz), 5.20 (d, 1H, H-1, $J$ = 3.39 Hz), 4.99 (dd, 1H, H-6a, $J$ = 14.4 Hz & $J$ = 3.0 Hz), 4.80 (dd, 1H, H-5, $J$ = 7.71 Hz & $J$ = 3.06 Hz),4.53 (d, 1H, H-6b, $J$ = 14.4 Hz & $J$ = 7.7 Hz), 3.72 (t, 2H, H-1′, $J$ = 6.93 Hz), 3.60–3.35 (m, 2H, H-3′), 2.75 (t, 2H, H-2‴, $J$ = 7.5 Hz), 2.09–2.0 (m, 2H, H-1‴), 1.61–1.50 (m, 1H, H-3′), 1.39–1.33 (m, 2H, H-2′), 0.82–0.76 (m, 6H, $2CH_3$ of $^i$amyl). $^{13}$C NMR ($CDCl_3$,75 MHz): δ 193.1 (C-4), 168.4 (C-5‴ & C-10‴), 146.8 (C-2), 144.5 (C-3), 134.0 (2 × qC), 132.1 (C-7‴& C-8‴), 127.1 (C-4″), 123.3 (C-6‴& C-9‴), 122.5 (C-5″), 93.2 (C-1), 72.8 (C-5), 68.2 (C-1′), 49.5 (C-6), 38.2 (C-3‴), 37.3 (C-2′), 28.3 (C-1‴), 25.0 (C-3′), 23.1 (C-2‴), 22.6 & 22.3 ($2CH_3$ of $^i$amyl). MS (ESI): $m/z$ 452; found 453 $[M+H]^+$; HRMS (ESI): Calc for $C_{24}H_{29}N_4O_5$ $[M+H]^+$; 453.2138; found 453.2314.

### 6.5.15. Compound **42**

This compound was obtained as a viscous oil; yield (62%); $R_f$ = 0.46 (hexane-ethyl acetate, 3:2); eluent for column

chromatography (hexane-ethyl acetate, 21:4); $[\alpha]_D^{31} = -54.69$ (c 0.017, $CHCl_3$); IR (neat, $cm^{-1}$): 3957, 3453, 2926, 2366, 1697,1225, 1101 . $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.66 (d, 2H, H-5″ & H-4″, $J = 4.11$ Hz), 6.85 (dd, 1H, H-2, $J = 10.3$ Hz and $J = 3.5$ Hz), 6.09 (d, 1H, H-2, $J = 10.3$ Hz), 5.18 (d, 1H, H-1, $J = 3.33$ Hz), 5.08 (dd, 1H, H-6a, $J = 14.4$ Hz & $J = 2.91$ Hz), 4.81 (dd, 1H, H-5, $J = 7.71$ Hz & $J = 2.97$ Hz), 4.59 (dd, 1H, H-6b, $J = 14.37$ Hz & $J = 7.74$ Hz), 3.55–3.42 (m, 2H, H-1′), 0.91–0.80 (m, 9H, $2CH_3$ of $^i$amyl); $^{13}C$ NMR ($CDCl_3$,75 MHz): $\delta$ 193.0 (C-4), 144.5 (C-5″), 133.8 (C-4″), 127.1 (C-2), 124.9 (C-3), 93.2 (C-1), 72.8 (C-5), 68.3 (C-6), 49.4 (C-1′), 38.1 (C-2′), 25.0 (C-3′), 22.5 & 22.4( $2CH_3$ of $^i$amyl). MS (ESI): $m/z$ 265; found 266 $[M+H]^+$; HRMS (ESI): Calc for $C_{13}H_{20}N_3O_3$ $[M+H]^+$; 266.1505; found 266.1495.

### 6.6. General method for one pot two step procedure for the preparation of compounds **24**, **29**, **32** and **39**

#### 6.6.1. Compound **24**

To a vigorously stirred solution of azide **4a** (200 mg, 0.829 mmol) in *tert*-butyl alcohol was added the 5-chloropentyne (0.104 mL, 0.994 mmol). The reaction was initiated by the addition of a solution of $CuSO_4.5H_2O$ (41.19 mg, 0.165 mmol) and sodium ascorbate (65.57 mg, 0.331 mmol) in distilled water. The coloured suspension formed was stirred at the room temperature till the formation of triazole. After the completion of reaction ice-cold distilled water was added and the aqueous layer was extracted 3–4 times with $CHCl_3$. The combined organic extracts were evaporated *in vacuo* to afford the crude product mixture of **5** which was dissolved in dry DCM followed by the addition of Dess–Martin periodinane (392 mg, 0.918 mmol) at 0 °C. Subsequently the reaction was allowed to warm to 5 °C and stirred till all the starting material was converted into the oxidised product (4 h). The reaction was quenched by addition of saturated aqueous solution of $NaHCO_3$ maintaining the temperature of the reaction mixture at 5 °C. The organic layer was separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over sodium sulphate and evaporated *in vacuo* to obtain the crude product. The crude product was chromatographed over silica gel to yield the pure 6-triazolyl-2,3,6-trideoxy hex-2-enopyranosid-4-ulose **24** as a white solid in 64% over 2 steps. Mp 61 °C - 64 °C; $R_f = 0.44$ (hexane-ethyl acetate, 3:2); eluent for column chromatography (hexane-ethyl acetate, 22:3); $[\alpha]_D^{31} = -42.14$ (*c* 0.20, $CHCl_3$); IR ( neat, $cm^{-1}$): 3021, 1701, 1216; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.43 (s, 1H, H-5"), 6.86 (dd, 1H, H-2, $J = 10.3$ Hz & $J = 3.5$ Hz), 6.11 (d, 1H, H-3, $J = 10.3$ Hz), 5.20 (d, 1H, H-1, $J = 3.2$ Hz), 5.03 (dd, 1H, H-6a, $J = 14.4$ Hz & $J = 3.0$ Hz), 4.81 (dd, 1H, H-5, $J = 7.6$ Hz & $J = 3.0$ Hz), 4.54 (dd, 1H, H-6b, $J = 14.4$ Hz & $J = 7.6$ Hz), 3.62–3.43 (m, 4H, H-3″, H-1′a & H-1′b), 2.87 (t, 2H, H-1″, $J = 7.3$ Hz), 2.20–2.11 (m, 2H, H-2″) 1.60 (pent., 1H, H-3′, $J = 6.7$ Hz), 1.43–1.36 (m, 2H, H-2′), 0.85 (d, 3H, $CH_3$ of $^i$amyl, $J = 6.7$ Hz), 0.82 (d, 3H, $CH_3$ of $^i$amyl, $J = 6.6$ Hz); $^{13}C$ NMR ($CDCl_3$, 50 MHz): $\delta$ 193.0 (C-4), 146.3 (*q*C), 144.4 (C-2), 127.1 (C-3), 122.5 (C-5"), 93.2 (C-1), 72.8 (C-5), 68.2 (C-1′), 49.5 (C-6), 44.1 (C-3″), 38.2 (C-2′), 31.9 (C-2″), 24.9 (C-3′), 22.7 (C-1″), 22.6 & 22.3 (2 $CH_3$ of $^i$amyl); MS (ESI): $m/z$ 341; found 342 $[M+H]^+$. HRMS (DART): Calc for $C_{16}H_{25}ClN_3O_3$ $[M+H]^+$ 342.1584; found 342.1600.

6-triazolyl 2,3,6 trideoxy hex-2- enopyranosid-4-uloses **29, 32** and **39** were likewise prepared from **4a** via intermediates **10, 13** and **20** respectively using the same two step procedure as described above for compound **24**.

#### 6.6.2. Compound **29**

This compound was obtained as a viscous oil; yield (63% in 2 steps); $R_f = 0.57$ (hexane-ethyl acetate, 7:3); eluent for column chromatography (hexane-ethyl acetate, 4:1); $[\alpha]_D^{31} = -18.30$ (c 0.13, $CHCl_3$); IR (neat, $cm^{-1}$): 3749, 3458, 2358, 1696, 1217; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.35 (s, 1H, H-5″), 6.85 (dd, 1H, H-2, $J = 10.3$ Hz & $J = 3.5$ Hz), 6.10 (d, 1H, H-3, $J = 10.3$ Hz), 5.19 (d, 1H, H-1, $J = 3.3$ Hz), 5.03 (dd, 1H, H-6a, $J = 14.5$ Hz & $J = 3.0$ Hz), 4.80 (dd, 1H, H-5, $J = 7.7$ Hz & $J = 3.0$ Hz), 4.51 (dd, 1H, H-6b, $J = 14.5$ Hz & $J = 7.7$ Hz), 3.58–3.44 (m, 2H, H-1′), 2.68 (t, 2H, H-1‴, $J = 7.5$ Hz), 1.64–1.57 (m, 3H, H-2′ & H-3′), 1.33–1.25 (m, 12H, H-2‴-H-7‴), 0.91–0.80 (m, 9H, $2CH_3$ of $^i$amyl and $1CH_3$ of H-8‴); $^{13}C$ NMR ($CDCl_3$,75 MHz): $\delta$ 193.2 (C-4), 148.5 (C-4″), 144.4 (C-2), 127.2 (C-3), 122.0 (C-5″), 93.2 (C-1), 72.9 (C-5), 68.2 (C-1′), 49.4 (C-6), 38.2 (C-2′), 31.9 (C-1‴), 29.7 (C-2‴), 29.6 (C-3‴), 29.4 (C-4‴), 29.3 (C-5‴ & C-6‴), 25.7 (C-7‴), 25.0 (C-3′), 22.7 & 22.5 ($2CH_3$ of $^i$amyl), 14.2 (C-8‴); MS (ESI): $m/z$ 377; found 378 $[M+H]^+$; HRMS (DART): Calc for $C_{21}H_{36}N_3O_3$ $[M+H]^+$; 378.2756; found 378.2758.

#### 6.6.3. Compound **32**

This compound was obtained as a viscous oil; yield (48% in 2 steps); $R_f = 0.51$ (hexane-ethyl acetate, 7:3); eluent for column chromatography (hexane-ethyl acetate, 17:3); $[\alpha]_D^{31} = -153.09$ (c 0.02, $CHCl_3$); IR (neat, $cm^{-1}$): 3904, 3778, 3388, 3020, 1701, 1217; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 10.13 (s, 1H, H-1‴), 8.22 (s, 1H, H-5″), 6.88 (dd, 1H, H-2, $J = 10.3$ Hz and $J = 3.4$ Hz), 6.12 (d, 1H, H-3, $J = 10.3$ Hz), 5.21 (d, 1H, H-1, $J = 3.2$ Hz), 5.11 (dd, 1H, H-6a, $J = 14.3$ Hz & $J = 3.0$ Hz), 4.85 (dd, 1H, H-5, $J = 7.5$ Hz & $J = 3.03$ Hz), 4.67 (dd, 1H, H-6b, $J = 14.3$ Hz, & $J = 7.56$ Hz), 3.58–3.44 (m, 2H, H-1′), 1.63–1.54 (m, 1H, H-3′), 1.41–1.34 (m, 2H, H-2′), 0.84–0.79 (m, 6H, $2CH_3$ of $^i$amyl); $^{13}C$ NMR ($CDCl_3$,75 MHz): $\delta$ 192.5 (C-4), 185.1 (C-1‴), 147.9 (C-4″), 144.6 (C-2), 127.1 (C-3), 126.7 (C-5″), 93.4 (C-1), 72.3 (C-5), 68.5 (C-6), 49.9 (C-6), 38.2 (C-2′), 25.0 (C-3′), 22.6 & 22.4 ($2CH_3$ of $^i$amyl). MS (ESI): $m/z$ 293; found 294 $[M+H]^+$; HRMS (DART): Calc for $C_{14}H_{20}N_3O_4$ $[M+H]^+$; 294.1453; found 294.1474.

#### 6.6.4. Compound **39**

This compound was obtained as a glassy solid; Yield (57% in 2 steps); $R_f = 0.50$ (hexane-ethyl acetate, 7:3); eluent for column chromatography (hexane-ethyl acetate, 9:1); $[\alpha]_D = -26.42$ (*c* 0.21, $CHCl_3$); IR ( neat, $cm^{-1}$): 3020, 1699, 1520, 1216. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.36 (s, 1H, H-5"), 6.88 (dd, 1H, H-2, $J = 10.3$ Hz & $J = 6.8$ Hz), 6.11 (d, 1H, H-3, $J = 10.3$ Hz), 5.20 (d, 1H, H-1, $J = 3.5$ Hz), 5.05 (dd, 1H, H-6a, $J = 14.5$ Hz & $J = 3.0$ Hz), 4.80 (dd, 1H, H-5, $J = 7.9$ Hz & $J = 3.0$ Hz), 4.49 (dd, 1H, H-6b, $J = 14.5$ Hz & $J = 7.9$ Hz), 3.59–3.42 (m, 2H, H-1′a & H-1′b), 3.23–3.15 (m, 1H, H-1‴), 2.10–2.04 (m, 2H, H-2‴a & H-5‴a), 1.75–1.55 (m, 7H, H-2‴b, H-3‴, H-4‴, H-5‴b and H-3′) 1.42–1.32 (m, 2H, H-2′), 0.86 (d, 3H, $CH_3$ of $^i$amyl, $J = 6.6$ Hz), 0.82(d, 3H, $CH_3$ of $^i$amyl, $J = 6.6$ Hz); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 193.1 (C-4), 152.7 (*q*C), 144.4 (C-2), 127.1 (C-3), 121.0 (C-5"), 93.2 (C-1), 72.9 (C-5), 68.1 (C-1′), 49.4 (C-6), 38.2 (C-2′), 36.7 (C-1″), 33.3 (C-2″), 33.2 (C-5″), 25.1 (C-3″ & C-4″), 24.9 (C-3′), 22.6 & 22.3 (2 $CH_3$ of $^i$amyl); MS (ESI): $m/z$ 333; found 334 $[M+H]^+$; HRMS (DART): Calc for $C_{18}H_{28}N_3O_3$ $[M+H]^+$ 334.2130; found 334.2119.

### 6.7. General procedure for the preparation of compounds **45** and **46**

#### 6.7.1. Compound **45**

To a solution of adamantane methanol **43** (997.56 mg, 6 mmol) in 15 mL of anhydrous THF was added NaH (100.80 mg, 4.2 mmol) at 0 °C. After hydrogen was entirely emitted the catalytic amount of tetrabutylammonium iodide (TBAI) and propargyl bromide (1.3 mL, 14.4 mmol) was added, respectively. The mixture was then warmed to room temperature and stirred for an additional 24 h. The reaction was quenched by ice cold water and then left for stirring for about 15 min. After the completion of reaction it was extracted with ethyl acetate. The combined organic extracts were dried, evaporated and purified by column chromatography to obtain compound

**44** (101.53 mg, 0.4978 mmol, 8%) [41]. To a vigorously stirred solution of isoamyl 6-azido-2,3,6-trideoxy-hex-2-enopyranoside **4a** (80 mg, 0.3319 mmol) in *tert*-butyl alcohol compound **44** (101.53 mg, 0.4978 mmol) was added. The reaction was initiated by the addition of a solution of $CuSO_4.5H_2O$ (16.52 mg, 0.066 mmol) and sodium ascorbate (26.15 mg, 0.132 mmol) in distilled water. The coloured suspension formed was stirred at the room temperature till the formation of triazole. After the completion of reaction ice-cold distilled water was added and the aqueous layer was extracted 3–4 times with $CHCl_3$. The combined organic extracts were dried evaporated and passed through column to afford pure compound **45** as a viscous oil; yield (80%); $R_f = 0.57$ (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 20:7); $[\alpha]_D^{31} = -1.68$ (c 0.03, $CHCl_3$); IR (neat, $cm^{-1}$): 3763, 3626, 3403, 2915, 2360, 1582, 1219; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.67 (s, 1H, H-5″), 5.92 (d, 1H, H-3, $J = 9.7$ Hz), 5.71 (d, 1H, H-2, $J = 10.3$ Hz), 4.92 (s, 1H, H-1), 4.74–4.60 (m, 4H, H-4, H-5 & H-6), 3.98 (d, 1H, H-1‴a), 3.84 (s, 1H, H-1‴b), 3.52 (dd, 1H, H-1′a, $J = 16.3$ Hz & $J = 7.1$ Hz), 3.41–3.30 (m, 1H, H-5), 3.06 (s, 1H, H-2a‴), 1.94 (s, 4H, 3 × $CH_{Ad}$ & H-2b‴), 1.68–1.52 (m, 12H, 6 × $CH_{2Ad}$), 1.41–1.25 (m, 3H, H-2′ & H-3′), 0.87–0.83 (m, 6H, $2CH_3$ of $^i$amyl); $^{13}C$ NMR ($CDCl_3$,75 MHz): $\delta$ 142.6 (C-4″), 132.8 (C-3), 126.7 (C-2), 124.0 (C-5″), 94.6 (C-1), 81.6 (C-2‴), 70.7 (C-5), 67.3 (C-1′), 65.2 (C-4), 64.7 (C-1‴), 51.3 (C-6), 39.8 ($3CH_{2Ad}$), 38.4 (C-2′), 37.3 ($3CH_{2Ad}$), 29.8 ($C_{Ad}$) 28.3 ($3CH_{Ad}$) 25.1 (C-3′), 22.7 & 22.5 ($2CH_3$ of $^i$amyl). MS (ESI): *m*/*z* 445; found 446 $[M+H]^+$; HRMS (ESI): Calc for $C_{25}H_{40}N_3O_4$ $[M+H]^+$; 446.3019; found 446.3006.

### 6.7.2. Compound **46**

Compound **45** (121 mg, 0.270 mmol) was dissolved in dry DCM (20 mL) and the temperature of the reaction mixture was lowered to 0 °C. DMP (173.34 mg, 0.406 mmol) was added to the reaction mixture. Subsequently the reaction mixture was allowed to warm to 5 °C and stirred till all the starting material was converted into the oxidised product (4 h). The reaction was quenched by the addition of saturated aqueous solution of $NaHCO_3$ maintaining the temperature of the reaction mixture at 5 °C. The organic layer was separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over sodium sulphate and evaporated *in vacuo* to obtain the crude product. The crude product was chromatographed over silica gel to yield the pure 6-triazolyl-2,3,6-trideoxy hex-2-enopyranosid-4-ulose **46** as a viscous oil; yield (54%); $R_f = 0.48$ (hexane-ethyl acetate, 7:3); eluent for column chromatography (hexane-ethyl acetate, 4:1); $[\alpha]_D^{31} = -30.95$ (c 0.03, $CHCl_3$); IR (neat, $cm^{-1}$): 3772, 3398, 2927, 2364, 1724,1593, 1219; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.60 (s, 1H, H-5″), 6.86 (dd, 1H, H-2, $J = 10.3$ Hz & $J = 3.5$ Hz), 6.10 (d, 1H, H-3, $J = 10.3$ Hz), 5.20 (d, 1H, H-1, $J = 3.4$ Hz), 5.06 (dd, 1H, H-6a, $J = 14.4$ Hz & $J = 3.0$ Hz), 4.83 (dd, 1H, H-5, $J = 7.71$ Hz & $J = 3.0$ Hz), 4.58 (d, 3H, H-6b & H-1‴, $J = 4.32$ Hz), 3.62–3.54 (m, 2H, H-1′), 3.05 (s, 2H, H-2‴), 1.94 (s, 4H, 3 × $CH_{Ad}$ & 1H of $CH_{2aAd}$) 1.68–1.55 (m, 12H, 1H of $CH_{2bAd}$ & 5 × $CH_{2Ad}$ & H-3′), 1.44–1.32 (m, 2H, H-2′), 0.85–0.80 (m, 6H, $2CH_3$ of $^i$amyl); $^{13}C$ NMR ($CDCl_3$,75 MHz): $\delta$ 193.0 (C-4), 146.1 (C-4″), 144.5 (C-2), 127.1 (C-3), 123.6 (C-5″), 93.3 (C-1), 81.6 (C-2‴), 72.8 (C-5), 68.2 (C-1′), 65.2 (C-1‴), 49.6 (C-6), 39.7 ($3CH_{2Ad}$), 38.2 (C-2′), 37.3 ($3CH_{2Ad}$), 28.3 ($C_{Ad}$ & $3CH_{Ad}$), 25.01 (C-3′), 22.6 & 22.4 ($2CH_3$ of $^i$amyl). MS (ESI): *m*/*z* 443; found 444 $[M+H]^+$; HRMS (DART): Calc for $C_{25}H_{38}N_3O_4$ $[M+H]^+$; 444.2862; found 444.2845.

## 6.8. General procedure for the preparation of bis triazolyl compounds **48**, **50** and **51**

### 6.8.1. Compound **48**

To a solution of compound **15** (250 mg, 0.6702 mmol) in DMF was added $NaN_3$ (174.25 mg, 2.6808 mmol) and the reaction mixture was allowed to stirred under reflux (90 °C-100 °C) for 3 h. The cooled reaction mixture was poured into excess of ice-cold water and extracted with dichloromethane (5 × 8 mL). The combined organic layers were washed with brine, dried over sodium sulphate and evaporated to yield crude product of compound **47** which was used for the next step as such without further purification. To a vigorously stirred solution of azide **47** (108 mg, 0.3214 mmol) in *tert*-butyl alcohol, cyclopropyl acetylene (0.0407 mL, 0.4821 mmol) was added. The reaction was initiated by the addition of a solution of $CuSO_4.5H_2O$ (16.03 mg, 0.064 mmol) and sodium ascorbate (25.35 mg, 0.128 mmol) in distilled water. The coloured suspension was formed and the reaction mixture was stirred at the room temperature till the formation of triazole. After the completion of reaction ice-cold distilled water was added and the aqueous layer was extracted 3-4 times with $CHCl_3$. The combined organic extracts were dried, evaporated and passed through a column to afford pure compound **48**. This compound was obtained as a viscous oil; yield (62%); $R_f = 0.53$ ($CHCl_3$-methanol, 1:10); eluent for column chromatography ($CHCl_3$-methanol, 10:0.1); $[\alpha]_D^{31} = -47.91$ (c 0.02, $CHCl_3$); IR (neat, $cm^{-1}$): 3745, 2923, 2360, 1602, 1219; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.36 (s, 1H, H-5″), 7.14 (s, 1H, H-7‴), 5.91(d, 1H, H-3, $J = 10.0$ Hz), 5.69 (d, 1H, H-2, $J = 10.5$ Hz), 4.91 (s, 1H, H-1), 4.64 (t, 4H, H-6 & H-2‴ $J = 7.44$ Hz), 3.96 (t, 1H, H-5, $J = 4.71$ Hz), 3.75 (d, 1H, H-4, $J = 8.94$ Hz), 3.51 (dd, 1H, H-1′a, $J = 16.38$ Hz & $J = 7.44$ Hz), 3.42–3.29 (m, 3H, H-1′b & H-1‴), 1.90-1.81 (m, 1H, H-8‴), 1.68-1.56 (m, 1H, H-3′), 1.41-1.32 (m, 4H, H-2′, H-9‴a, H-10‴a), 0.92-0.78 (m, 8H, $2CH_3$ of $^i$amyl & 2H of H-9‴b & 10‴b); $^{13}C$ NMR ($CDCl_3$,75 MHz): $\delta$ 150.2 (C-6‴), 143.2 (C-4″), 133.0 (C-3), 126.5 (C-2), 123.9 (C-5″), 120.4 (C-7‴), 94.6 (C-1), 70.5 (C-5), 67.3 (C-1′), 64.3 (C-4), 51.3 (C-2‴), 49.3 (C-6), 38.4 (C-2′), 29.8 (C-1‴), 25.1 (C-3′), 22.7& 22.4 ($2CH_3$ of $^i$amyl), 7.80 (C-8‴), 6.68 (C-9‴ & C-10‴). MS (ESI): *m*/*z* 402; found 425 $[M+Na]^+$; HRMS (ESI): Calc for $C_{20}H_{31}N_6O_3$ $[M+H]^+$; 403.2458; found 403.2448.

### 6.8.2. Compound **50**

To a solution of the compounds **48** (80 mg, 0.199 mmol) in dry chloroform ($CHCl_3$) taken in a round bottom flask fitted with a guard tube was added activated $MnO_2$ (342.28 mg, 3.98 mmol) in 2–3 instalments at intervals of 8–9 h and the reaction mixture was allowed to stir at room temperature for the requisite time (20–30 h). After completion (TLC), the reaction mixture was filtered over a bed of celite. The celite bed was washed with $CHCl_3$ a number of times. The filtrate and washings were then concentrated *in vacuo* to obtain the crude product. The crude product was chromatographed to yield the pure compound **50** as a viscous oil; yield (49%); $R_f = 0.51$ (chloroform-methanol, 1:10); eluent for column chromatography (chloroform-methanol, 10:0.2); $[\alpha]_D^{31} = +1.48$ (c 0.02, $CHCl_3$); IR (neat, $cm^{-1}$): 3957, 3745, 2923, 2360, 1602, 1219; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.30 (s, 1H, H-5″), 7.14 (s, 1H, H-7‴), 6.86 (d, 1H, H-2, $J = 10.3$ Hz & $J = 3.5$ Hz), 6.09 (d, 1H, H-3, $J = 10.3$ Hz), 5.19 (d, 1H, H-1, $J = 3.42$ Hz), 4.79 (dd, 1H, H-6a, $J = 7.08$ Hz & $J = 3.1$ Hz), 4.60 (dd, 1H, H-5, $J = 10.2$ Hz & $J = 6.9$ Hz), 4.55 (t, 3H, H-6b, H-2‴), 3.60–3.46 (m, 2H, H-1′), 3.30 (t, 2H, H-1‴, $J = 6.90$ Hz), 1.91–1.86 (m, 1H, H-8‴), 1.65–1.56 (m, 1H, H-3′), 1.43–1.34 (m, 4H, H-2′, H-9‴a& H-10‴a), 0.95–0.79 (m, 8H, 6H of $^i$amyl & 2H of H-9‴b & H-10‴b); $^{13}C$ NMR ($CDCl_3$,75 MHz): $\delta$ 193.0 (C-4), 151.1 (C-6‴), 144.5 (C-4″), 143.3 (C-2), 127.1 (C-3), 123.5 (C-5″), 120.3 (C-7‴), 93.3 (C-1), 72.7 (C-5), 68.3 (C-1′), 49.6 (C-2‴), 49.3 (C-6), 38.2 (C-1‴), 29.8 (C-2′), 25.0 (C-3′), 22.6 & 22.4 ($2CH_3$ of $^i$amyl), 7.80 (C-8‴), 6.72 (C-9‴ & C-10‴). MS (ESI): *m*/*z* 400; found 401 $[M+H]^+$; HRMS (ESI): Calc for $C_{20}H_{29}N_6O_3$ $[M+H]^+$; 401.2301; found 401.2305.

### 6.8.3. Compound **51**

To a solution of compound **15** (250 mg, 0.6702 mmol) in DMF was added $NaN_3$ (174.25 mg, 2.6808 mmol) and the reaction

mixture was allowed to stirred under reflux (90 °C–100 °C) for 3 h. The cooled reaction mixture was poured into excess of ice-cold water and extracted with dichloromethane (5 × 8 mL). The combined organic layers were washed with brine, dried over sodium sulphate and evaporated to yield crude product of compound **47** which was used for the next step as such without further purification. To a vigorously stirred solution of azide **47** (110 mg, 0.327 mmol) in *tert*-butyl alcohol, Phenyl acetylene (0.053 mL, 0.4905 mmol) was added. The reaction was initiated by the addition of a solution of $CuSO_4.5H_2O$ (16.22 mg, 0.0654 mmol) and sodium ascorbate (25.91 mg, 0.131 mmol) in distilled water. The coloured suspension was formed and the reaction mixture was stirred at the room temperature till the formation of triazole. After the completion of reaction ice-cold distilled water was added and the aqueous layer was extracted 3–4 times with $CHCl_3$. The combined organic extracts were evaporated *in vacuo* to afford the crude product mixture of **49**, which was dissolved in dry chloroform ($CHCl_3$), followed by the addition of activated $MnO_2$ (392.16 mg, 4.56 mmol) in 2–3 instalments at intervals of 8–9 h and the reaction mixture was allowed to stir at room temperature (RT) for the requisite time (20–30 h). After completion (TLC), the reaction mixture was filtered over a bed of celite. The celite bed was washed with $CHCl_3$ a number of times. The filtrate and washings were then concentrated *in vacuo* to obtain the crude product. The crude product was chromatographed to yield the pure compound **51** as a viscous oil; yield (50% in 2 steps); $R_f = 0.55$ (chloroform-methanol, 10:1); eluent for column chromatography (chloroform-methanol, 49:1); $[\alpha]_D^{31} = -7.91$ (c 0.02, $CHCl_3$); IR (neat, $cm^{-1}$): 3872, 3745, 2923, 2360, 1602, 1219; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.77 (d, 2H, H-8‴ & H-13‴, $J = 7.29$ Hz), 7.64 (s, 1H, H-5″), 7.41 (t, 2H, H-10‴ & H-12‴, $J = 7.14$ Hz), 7.32 (t, 2H, H-7‴ & H-11‴), 6.72 (dd, 1H, H-2, $J = 10.3$ Hz & $J = 3.5$ Hz), 5.99 (d, 1H, H-3, $J = 10.3$ Hz), 5.1 (d, 1H, H-1, $J = 3.24$ Hz), 4.89 (dd, 1H, H-6a, $J = 14.4$ Hz & $J = 3.2$ Hz), 4.80–4.74 (m, 3H, H-6b, H-5, & H-2‴a), 4.60 (dd, 1H, H-2‴b, $J = 6.7$ Hz & $J = 14.0$ Hz) 3.60–3.52 (m, 1H, H-1‴a), 3.39 (t, 3H, H-1‴b, H-1′, $J = 6.7$ Hz), 1.61–1.50 (m, 1H, H-3′), 1.42–1.37 (m, 2H, H-2′), 0.87–0.79 (m, 6H, $2CH_3$ of $^i$amyl); $^{13}C$ NMR ($CDCl_3$,75 MHz): $\delta$ 193.0 (C-4), 151.1 (C-6‴), 144.5 (C-4″), 143.3 (C-2), 130.9 (C-3), 128.9 (C-10‴ & C-12‴), 125.7 (C-9‴ & C-13‴), 125.7 (C-8‴), 120.4 (C-5″), 120.3 (C-7″), 114.1 (C-11″), 93.2 (C-1), 73.7 (C-5), 68.2 (C-1′), 58.4 (C-2‴), 49.4 (C-6), 38.2 (C-2′), 29.7 (C-1‴), 25.0 (C-3′), 22.7 & 22.6 ($2CH_3$ of $^i$amyl).). MS (ESI): *m*/*z* 436; found 437 $[M+H]^+$; HRMS (ESI): Calc for $C_{23}H_{29}N_6O_3$ $[M+H]^+$; 437.2301; found 437.2305.

### 6.9. General procedure for the preparation of 1,5 triazolyl compounds **52** and **53**

#### 6.9.1. Compound **52**

To a stirred solution of azide **4a** (150 mg, 0.622 mmol) in dry toluene was added decyne (0.107 mL, 0.9336 mmol). The reaction was initiated by the addition of a catalyst $Cp^*RuCl(PPh_3)_2$ (4.956 mg, 0.00622 mmol) and it continued for 3 h at 80 °C. The combined organic extracts were dried, evaporated & passed through a column to afford pure compound **52** as a viscous oil; yield (81%); $R_f = 0.51$ (hexane-ethyl acetate, 1:1); eluent for column chromatography (hexane-ethyl acetate, 4:1); $[\alpha]_D^{31} = -2.71$ (c 0.08, $CHCl_3$); IR (neat, $cm^{-1}$): 3775, 3399, 2925, 2358, 1634, 1459, 1244, 1030; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.44 (s, 1H, H-5″), 5.94 (d, 1H, H-3, $J = 10.2$ Hz), 5.67 (d, 1H, H-2, $J = 10.2$ Hz), 4.85 (s, 1H, H-1), 4.58 (t, 2H, H-4 & H-6a, $J = 3.39$ Hz), 3.98 (dd, 2H, H-6b & H-5, $J = 12.0$ Hz & $J = 5.3$ Hz), 3.42–3.30 (m, 2H, H-1′), 2.71 (t, 2H, H-1‴, $J = 7.4$ Hz), 1.69–1.53 (m, 1H, H-3′), 1.39–1.25 (m, 14H, H-2‴- H-7‴& H-2′), 0.88–0.83 (m, 9H, $2CH_3$ of $^i$amyl & $1CH_3$ of H-8‴); $^{13}C$ NMR ($CDCl_3$,75 MHz): $\delta$ 146.4 (C-5″), 132.3 (C-4″), 131.9 (C-3), 126.3 (C-2), 94.5 (C-1), 71.3 (C-5), 67.1 (C-1′), 65.0 (C-4), 48.6 (C-6), 38.4 (C-2′), 32.0 (C-1‴), 31.9 (C-2‴), 29.8 (C-3‴), 29.5 (C-4‴), 29.4 (C-5‴), 29.3(C-6‴), 28.2 (C-7‴), 25.1 (C-3′), 22.7 & 22.5 ($2CH_3$ of $^i$amyl), 14.2 (C-8‴). MS (ESI): *m*/*z* 379; found 380 $[M+H]^+$; HRMS (DART): Calc for $C_{21}H_{38}N_3O_3$ $[M+H]^+$; 380.2903; found 380.2913.

#### 6.9.2. Compound **53**

To a solution of **52** (217 mg, 0.5725 mmol) in dry DCM (20 mL) was added Dess–Martin periodinane (DMP) reagent (367 mg, 0.858 mmol) at −5 °C. Subsequently the reaction was allowed to warm to 5 °C and stirred till all the starting material was converted into the oxidised product (4 h). The reaction was quenched by the addition of saturated aqueous solution of $NaHCO_3$ maintaining the temperature of the reaction mixture at 5 °C. The organic layer was separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over sodium sulphate and evaporated *in vacuo* to obtain the crude product. The crude product was chromatographed over silica gel to yield the pure 6-triazolyl-2,3,6-trideoxy hex-2-enopyranosid-4-ulose **53** as a viscous oil; yield (61%); $R_f = 0.57$ (hexane-ethyl acetate, 7:3); eluent for column chromatography (hexane-ethyl acetate, 10:1); $[\alpha]_D^{31} = +24.52$ (c 0.03, $CHCl_3$); IR (neat, $cm^{-1}$): 3951, 3396, 1636, 1220; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.40 (s, 1H, H-5″), 6.83 (dd, 1H, H-2, $J = 10.3$ Hz & $J = 3.4$ Hz), 6.09 (d, 1H, H-3, $J = 10.3$ Hz), 5.12 (d, 1H, H-1, $J = 3.3$ Hz), 4.97–4.91 (m, 2H, H-5 & H-6a), 4.34 (dd, 1H, H-6b, $J = 15.0$ Hz & $J = 9.7$ Hz), 3.34 ( dd, 2H, 2.63, H-1′, $J = 12.3$ Hz & $J = 6.8$ Hz), 2.63 (dd, 2H, H-1‴, $J = 12.8$ Hz & $J = 7.7$ Hz) 1.66–1.57 (m, 2H, H-2′), 1.55–1.51 (m, 1H, H-3′), 1.33–1.22 (m, 12H, H-2‴-H-7‴), 0.85–0.75 (m, 9H, $2CH_3$ of $^i$amyl & $1CH_3$ of H-8‴). $^{13}C$ NMR ($CDCl_3$,75 MHz): $\delta$ 193.3 (C-4), 144.3 (C-2), 138.6 (C-5″), 131.8 (C-4″), 127.1 (C-3), 93.1 (C-1), 73.1 (C-5), 68.1 (C-6), 46.9 (C-1′), 38.1 (C-2′), 31.8 (C-1‴), 29.7 (C-2‴), 29.3 (C-3‴), 29.2 (C-4‴), 29.2 (C-5‴), 28.1 (C-6‴), 25.0 (C-3′), 22.7 (C-7‴), 22.5 & 22.4 ($2CH_3$ of $^i$amyl), 14.1 (C-8‴). MS (ESI): *m*/*z* 377; found 378 $[M+H]^+$; HRMS (ESI): Calc for $C_{21}H_{36}N_3O_3$ $[M+H]^+$; 378.2757; found 378.2755.

### 6.10. Biological assay

#### 6.10.1. In vitro antibacterial and antifungal activity assay

All the prepared 2,3,6-trideoxy sugar–triazole conjugates were evaluated for their *in vitro* antibacterial activity against *S. aureus* (ATCC 25923), *E. coli* (ATCC 9637), *P. aeruginosa* (ATCC BAA-427), *K. pneumoniae* (ATCC 27736) and antifungal activity against *C. albicans* (*Ca*), *A. fumigatus* (*Af*), *C. neoformans* (*Cn*), *S. schenckii* (*Ss*), and *T. mentagrophytes* (*Tm*). In this process, the minimum inhibitory concentration of compounds was tested according to the standard microbroth dilution technique as per guidelines of National Committee for Clinical Laboratory Standards [42,43]. Briefly, testing was performed in flat-bottomed 96-well tissue culture plates (CELLSTAR* Greiner bio-one GmbH, Germany) in RPMI 1640 medium buffered with MOPS (3-[N-morpholino] propanesulfonic acid) (Sigma–Aldrich Chemical Co., St. Louis, MO, USA) for fungal strains and in Muller Hinton broth (Titan Biotech Ltd, India) for bacterial strains. The concentration range of test compounds was 50–0.36 and 32–0.0018 l μg/mL for standard compounds. Initial inocula of fungal and bacterial strains were maintained at 1–5 × $10^3$ cells/mL. These plates were incubated in a moist chamber at 35 °C, and an absorbance at 492 nm was recorded on a Versa Max microplate reader (Molecular devices, Sunnyvale, USA) after 24 h for bacterial strains, 48 h for *C. albicans* (*Ca*) and 72 h for *A. fumigatus* (*Af*), *C. neoformans* (*Cn*), *S. schenckii* (*Ss*) and 96 h for *T. mentagrophytes* (*Tm*). The MICs were determined as 90% inhibition of growth with respect to the growth control as observed using SOFT-max Pro 4.3 Software (Molecular Devices, Sunnyvale, USA).

*6.10.2. Cytotoxicity assay*

The cytotoxicity of compounds **24, 26, 27, 28, 29, 32, 35, 36, 38, 46** and **53** against mammalian cells, mouse fibroblast cell line L929 was tested as follows. Stock solutions (1 mg/mL) of the test compounds were prepared in DMSO. The cell line L929 was grown in DMEM medium supplemented with 10% FBS and 1 × antimycotic and antibacterial solution (sigma USA) at 37 °C in humidified atmosphere having 5% $CO_2$. One hundred ml ($1 \times 10^3$ cells in DMEM) of the confluent fibroblast stock suspension ($1 \times 10^5$ cells/ml) was dispensed in 96-well tissue culture plate. The original medium from the wells was replaced with 100 mL serum free DMEM when the cells reached 90% confluency after 5 h of incubation in a $CO_2$ incubator. Various concentrations of the test compounds (25, 12.5, 6.25, 3.12, 1.56, 0.78, 0.39, 0.19, 0.09 mg/mL) were added to the growing cells and incubated for 24 h. Response of L929 cells to the test compounds was determined spectrophotometrically at 570 and 630 nm. The difference between absorbance at 570 and 630 nm was used as an index of the cell viability. [44]

$$\frac{(A570 - A630)\text{sample}}{(A570 - A630)\text{control}} \times 100$$

The morphology of the cells was observed using Giemsa stain under Phase contrast microscope. After fixation of the cells in the wells of 96-well tissue culture plate, Geimsa stain was added to each well and incubated for 30 min at 37 °C. The excess stain was removed by thorough washing with PBS and the culture plates were air dried and observed under a phase contrast microscope.

*6.11. Bioinformatics and modelling studies*

The structures of the compounds were compared for their similarity with the ligands of well known antibacterial targets. This has led to the identification of hydrolase and penicillin binding proteins (PBPs) as potential enzyme classes for the new compounds. The exploration has included pdbs 3D4F, 3RKJ, 1BLH, 2YZ3 and 1KO3 for hydrolase and pdbs 4DKI, 3VSL, 3HUN, 3MZE and 3PBR for penicillin binding proteins. Trial docking studies with these enzymes suggested that PBP-2 as most appropriate target of these compounds. Also similar to reference compounds, the synthesized compounds showed interaction with conserved serine residues of PBP [45]. Following this Basic Local Alignment Search Tool (BLAST: http://blast.ncbi.nlm.nih.gov/Blast.cgi) were used to find out the similarity of PBP-2 between different strains of bacteria. The molecular docking study was carried out in SYBYLX 1.3 [46]. For docking experiment, the penicillin binding protein 2 of *S. aureus* (PDB: 4DKI) was prepared by adding hydrogen atoms, fixing side chain amides and applying Gastregial–Huckle charges. Followed by this, energy of the protein was minimized by the Powell method using Tripos force field with a distance dependent dielectric constant of 1.0 and non-bonding interaction cut-off of 8.0Å and iterations up to 1000 (convergence criteria 0.001 kcal/mol.Å). Using automated based option procedures, the binding pocket was generated in the Protomol module of SYBYLX 1.3. The energy minimized standard inhibitors and synthesized compounds were docked using Surflex-Dock-Geom X docking mode into the pockets of selected target. The best docking poses of the compounds were selected based on the crash and polar and total scores. The best docked conformation was used for site directed residue interaction analysis and visualization in Pymol and SYBYLX 1.3.

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## Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ejmech.2014.06.048.

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