Facile Synthesis of Novel Glycosyl Carboxamide with Sugar in Furanose and Pyranose form Using Benzotriazole Methodology

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Abstract: There is an increased demand for significant amounts of carbohydrate based molecules for complete biological, medicinal, and pharmacological investigations where tremendous efforts have been made to develop novel and facile procedure for the synthesis of glycoconjugates and diverse carboxamides. Limitations with the common approaches for amide bond formation, including use of hazardous chemicals, long reaction times, low reaction yields, frequently require strong basic catalysts, strictly anhydrous conditions, harsh reaction conditions, expensive and limited availability of coupling materials, and moreover the less stability of activated acids warrant the search of a simple, short, and high yielding amide bond synthetic methodology. Herein, a facile and high yielding synthesis of novel glycosyl carboxamide with both furanose and pyranose sugar using benzotriazole methodology has been developed under mild conditions.

Keywords: Acylbenzotriazole, carboxamides, glycoconjugate, amines, benzotriazole.

Amide bond formation, a common basic reaction in organic synthesis is typically mediated by one of the myriad of so-called coupling reagents [1-5]. Amide bond represents the main chemical bonds that link amino acid building blocks together to give proteins where this functionality plays a major role in the elaboration and composition of biological systems. Recently, amide is known for a common functionality found in numerous drugs in therapeutic areas including Atorvastatin, the top selling drug worldwide since 2003 which blocks the production of cholesterol [6a], Lisinopril (a well-known inhibitor of angiotensin converting enzyme) [6b], Valsartan (blocker of angiotensin-II receptors) [6c], Diltiazem (calcium channel blocker used in the treatment of angina or hypertension) [6d] and is indeed present in hundreds of biologically active molecules (Fig. **1**).

Carbohydrate represents an attractive source of readily available, stereochemically defined, highly functionalized moiety, which offers a valuable scaffold in drug discovery research. There is an increased demand for significant amounts of carbohydrate based molecules for complete biological, medicinal, and pharmacological investigations where tremendous efforts have been made to develop novel and facile procedure for the synthesis of diverse carboxamides and glycoconjugates [7]. In general, glycosylations of peptide not only affect their pharmacological parameters e.g. the rate of circulation, solubility, immunogenicity etc, but also influence the wide range of biological functions through modulating their folding, stability and serving as a recognition signal in cell-cell, cell matrix, cell-pathogen interactions and biomarkers in intra- & intercellular communication events. Natural and unnatural glycosylated peptide are known for their important role in these processes and underlies a significant pharmaceutical potential for the development of novel mechanism based drug [8]. Very recently, Pandey *et al.* reported the solution-phase synthesis and in silico screening of a combinatorial library of carbapeptides using glycosyl amino acid scaffolds, where reverse docking calculations involving over 841 protein drug targets have identified two potential targets for these carboxamides which may open a new paradigm basis towards development of second-generation antimicrobial agents [9].

A common approach for amide bond formation usually involves in the treatment of activated derivatives of acids, especially halides, acid anhydrides, or esters with corresponding amines, where the reaction of ammonia or amines with acyl halides is known to be highly exothermic. Reactions of carboxylic acids with ammonia or amines are seldom of preparative value [10]. Acylations of ammonia, primary or secondary amines using esters frequently requires strong basic catalysts and/or high pressure [11]. Synthesis of amides or esters through *in situ* activation of acids using carbodiimide (EDC or DCC or DIC/HOBt) [12], under Mitsunobu conditions (PPh_3/DEAD) [13], several coupling reagents, including HOSu, HONB, HODhbt, CBMIT, DTPC, DPP, HODT, TOTT, TODT, TOTU, CPMA, phosphorous based reagents or CDI mediated coupling reaction are well documented in the literature [1-5]. For mild synthesis of amides, enzymatic catalysis is also investigated where in few cases the method has been introduced as useful alternative as compared to traditional one [14]. Medicinal chemists often generate a library of amides using broad range of substrates with varying reactivities, such as aromatic, aliphatic, heterocyclic, chiral, bulky, sugar based amines etc. and therefore a coupling reagent is needed to be cope with maximum portfolio of reactivity. Although the above described common protocols have successfully employed for the amide bond formation, yet most of them have been associated with one or more limitations, including use of hazardous chemicals, long reaction times, low

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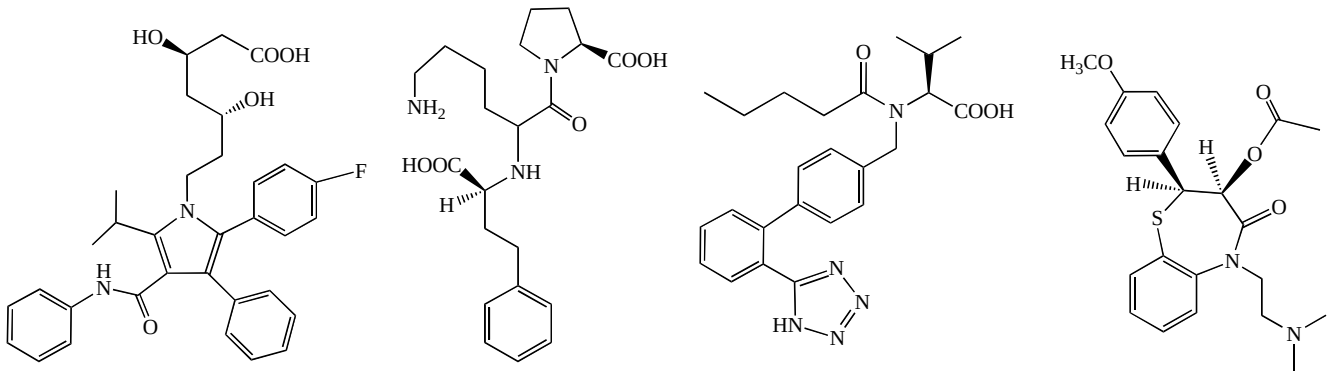


Aorvastatin **Lisinopril** **Valsartan** **Diltiazem**

Fig. (1). Amide group containing some representative known drugs.

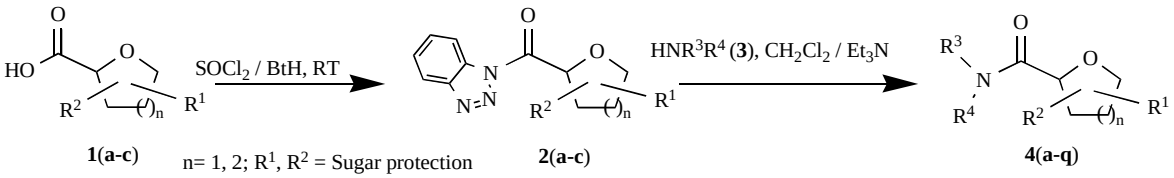
reaction yields, harsh reaction conditions as few methods are highly exothermic and/or high pressure, frequently require strong basic catalysts, required strictly anhydrous conditions, expensive and limited availability of coupling materials, and moreover the less stability of activated acids obtained through *in situ* activation of acids warrants to search a simple, short, and high yielding amide bond methodology.

RESULTS AND DISCUSSION

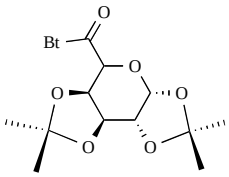
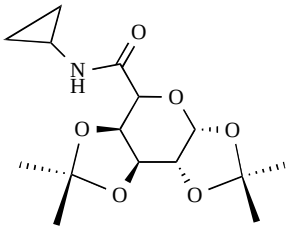
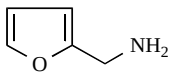
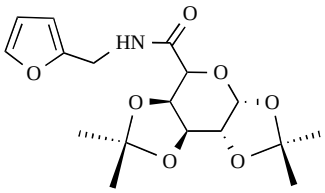
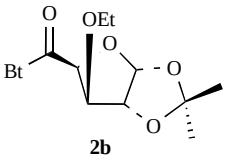
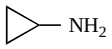
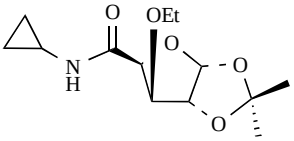
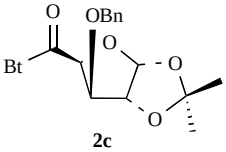
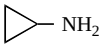
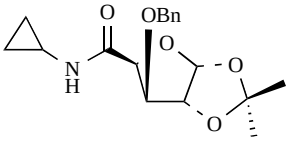
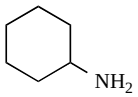
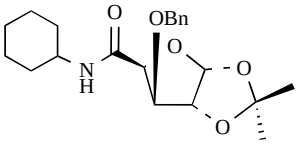
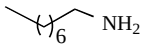
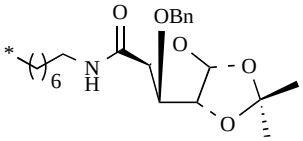
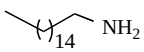
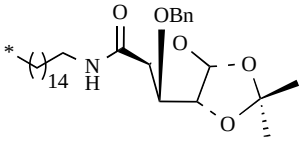
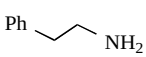
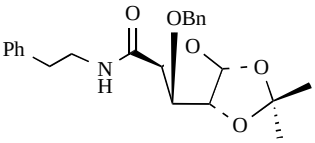
Our ongoing research on benzotriazole mediated novel synthetic methodology [15] and experience in the development of carbohydrate based new chemical entities (NCE's) against some frontline diseases [9, 16] encouraged us to search a simple, facile and high yielding alternate protocol for the synthesis of a variety of carboxamides using *N*-acylbenzotriazole as the stable alternatives of corresponding acid chlorides under mild reaction condition. Because of sufficient stability associated with benzotriazole containing intermediates, the chemistry offers an effective replacement of the corresponding acid chlorides which often found to be unstable and thus benzotriazole methodology has received great interest in organic synthesis, including peptides, heterocycles and other biologically active class of compounds [17]. Katritzky group has enormously explored the *N*-acylbenzotriazole as a stable intermediate in various synthetic methods [18], where appropriate *N*-acylbenzotriazoles have successfully affected formylation [19], triflouacylation [20], regiospecific *C*-acylation of pyrrole or indoles [21] and have also been found to be useful for the synthesis of oxamides [22], 1,3-diketones [23], polycyclic heteroaromatics [24] and Weinreb amides [25]. Despite the many efficient methods and coupling reagents available for the amide bond formation, a simple, convenient and high yielding novel protocol is yet to be developed through intensive research. In a relevant context our main objective was to use the benzotriazole as a coupling reagent for the preparation of amide linkage by activating the carboxylic acids directly to obtain the carbohydrate based novel amide derivatives with both furanose as well as pyranose sugars.

The synthetic strategy begins with commercially available D-(+) galactose and D- glucose. Thus, 1,2;3,4-di-*O*-isopropylidene-α-D-galacturonic acid (**1a**), obtained in two steps from D-galactose *via* well known isopropylidene protection followed by oxidation in basic condition, on one-pot reaction with thionyl chloride and subsequent *in situ* coupling with benzotriazole in anhydrous dichloromethane gave a good yield of 1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranuronosyl benzotriazole (**2a,** 94%) as a white crystalline solid. The chiral acylbenzotriazole **2a** was purified by column chromatography (SiO_2, *n*-hexane-EtOAc) and characterized by spectral data and elemental analysis. Treatment of compound **2a** with cyclopropyl amine in anhydrous dichloromethane afforded *N*-cyclopropyl-1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranuronamide (**4a,** 90%) (Scheme **1**). The crude product was washed with Na_2CO_3 solution (3-4 times) to remove benzotraizole from the reaction mixture. Thus, the obtained compound was found almost pure on TLC and was also evidenced from the ^{1}H NMR spectrum of crude product **4a** (Fig. **2**). Similar reaction of **2a** with furfuryl amine gave desired carboxamide **4b** in 92% yield.

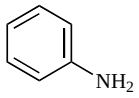
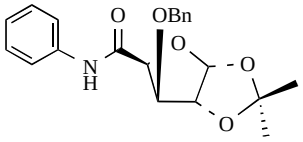
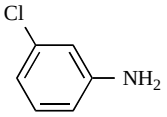
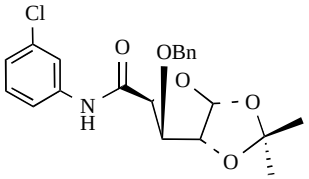
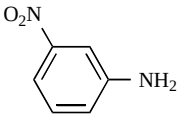
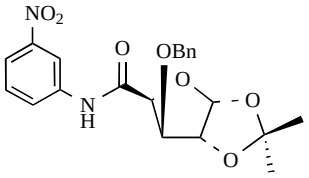
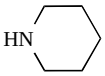
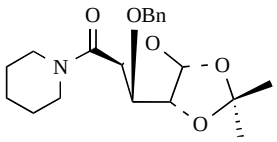
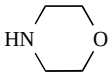
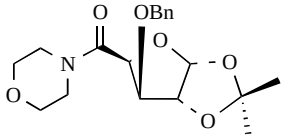
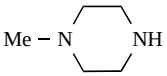
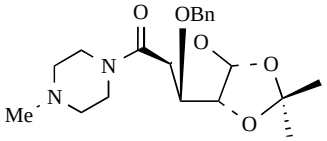
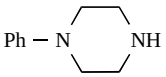
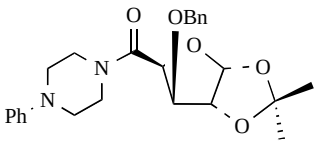
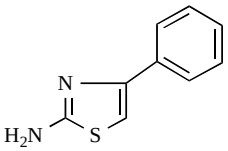
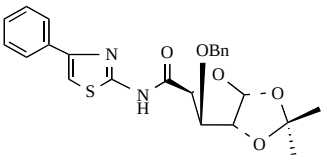
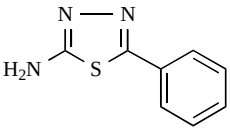
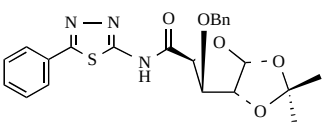
In a similar fashion, acylbenzotriazole (**2b** and **2c**) with sugar in furanose form was obtained in good yield starting from readily available D-glucose in six steps. 1,2;5,6-Di-*O*-isopropylidene glucofuranose on sequential reactions, including 3-*O*-alkylation, selective isopyopylidene deprotection and $NaIO_4$ oxidation afforded good yield of 3-*O*-benzyl (or ethyl)-1,2-*O*-isopropylidene-5-uloses, which was separately subjected to the treatment with freshly prepared $AgNO_3$/KOH, afforded 3-*O*-benzyl (or ethyl)-1,2-*O*-isopropylidene-α-D-xylo-furanuronic acid (**1b, 1c**). Further reaction with thionyl chloride followed by *in situ* coupling with benzotriazole furnished white crystalline solid of 3-*O*-benzyl (or ethyl)-1,2-*O*-isopropylidene-α-D-xylo-furanuronyl benzotriazole (**2b** and **2c** respectively). The one-pot benzotriazole coupling reaction proceeded smoothly (monitored on TLC) to afford the acylbenzotriazole (**2a** and **2b**) in an excellent yield (90 and 92% yield respectively). Pure acylbenzotriazole (**2a** and **2b**) on coupling with variety of amines (**3a-o**), including cyclopropyl amine, cyclohexyl amine, *n*-octyl amine, *n*-hexadecylamine, furfuryl amine, phenylethylamine, aniline, *m*-chloro aniline, *m*-nitro aniline, piperidine, morpholine, *N*-methyl piperazine, *N*-phenyl piperazine, 4-phenyl-thiazol-2-ylamine, and 5-phenyl-



1(a-c) n= 1, 2; R^1, R^2 = Sugar protection **2(a-c)** **4(a-q)**

Entry	RCOBt (2a-c)	Amine (3a-o)	Glycosyl Amide (4a-q)	Time (hrs)	Yield (%)	M. P. (°C)
1	 **2a**			3	90	180- 81
2	**2a**			3	92	122- 123
3	 **2b**			3	88	--
4	 **2c**			3	95	172-173
5	**2c**			3	94	165-166
6	**2c**			3	93	155-156
7	**2c**			3	93	137-138
8	**2c**			3	96	149-150

(Scheme 1). Contd…..

Entry	RCOBt (2a-c)	Amine (3a-o)	Glycosyl Amide (4a-q)	Time (hrs)	Yield (%)	M. P. (°C)
9	**2c**			3	90	169-170
10	**2c**			4	93	145-146
11	**2c**			3.5	91	150-151
12	**2c**			3	91	--
13	**2c**			3	90	--
14	**2c**			3	92	--
15	**2c**			3	92	--
16	**2c**			3	94	168-169
17	**2c**			3	90	160-162

Scheme 1. Synthesis of glycosyl carboxamide in furanose and pyranose sugar.

[1,3,4]thiadiazol-2-ylamine in the presence of triethyl amine at room temperature formed the desired corboxamides (**4c-q**) in high yields (Scheme **1**). All the developed carboxamides (**4a-q**) were purified by SiO_2 column chromatography and characterized by using spectroscopic technique (IR, MS, ^{1}H NMR, and ^{13}C NMR) and CHN elemental analysis.

We tried different solvents eg. toluene, dichloromethane, chloroform, DMF, acetonitrile, where dichloromethane was

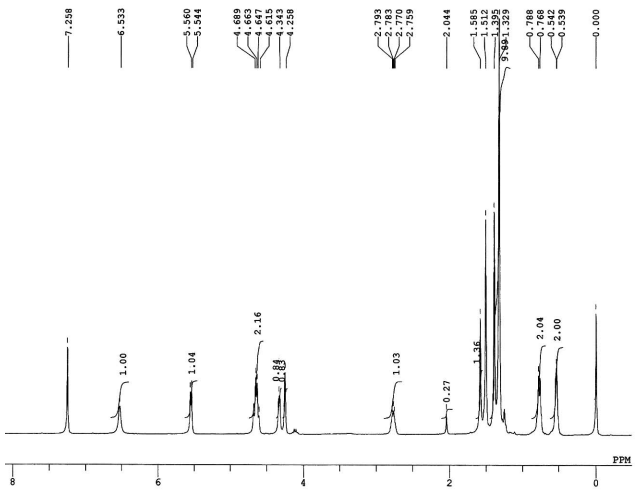


Fig. (2). ^{1}H NMR of crude compound **4a** (washed with Na_2CO_3 solution to remove BtH).

found to be the most suited one. The method is short, high yielding, feasible at room temperature, simple in handling and easy to remove cleaved benzotriazole successfully from reaction mixture through washing with Na_2CO_3 solution.

CONCLUSION

In conclusion, a simple and efficient method for the preparation of secondary and tertiary glycosyl amides has been developed by the treatment of sugar based *N*-acylbenzotriazoles with primary and secondary amines, respectively. Advantages of this procedure are as follows (a) mild reaction condition with activation of carboxylic acid with benzotriazole; (b) the use of acyl chlorides is avoided, (c) *N*-acylbenzotriazoles can be recrystallized and stored for a longer period of time as they are sufficiently stable, and (d) workup procedure is very simple; (e) secondary and tertiary amides were generally obtained in good to excellent yields. The method is useful for the high yielding access of already known carboxamides in a simple way and could further be extended for the development of carbohydrate based novel scaffolds and natural and/or unnatural glycopeptides.

EXPERIMENTAL

General

Thin layer chromatography (TLC) was performed by using silica gel 60 F-254 plates with I_2 vapors as detecting agents followed by spraying with ethanolic H_2SO_4 solution and with *Draggendorff* reagent for carboxamides (**4a-q**). Solvents were evaporated under reduced pressure at temperature <55 ^{0}C. Silica gel (230-400 mesh) was used for column chromatography. *TMS* (0.0 ppm) was used as an internal standard in ^{1}H NMR and $CDCl_3$ (77.0 ppm) in ^{13}C NMR. Infrared spectra were recorded as KBr pelletes by a Perkin Elemer RX-1 spectrometer. Melting points were determined on a Buchi 535 melting point apparatus. Elemental analyses were performed on a Perkin-Elmer 2400 C, H, N analyzer and values were found to be within ±0.5% of the calculated values.

3-O-benzyl-1,2-O-isopropylidene-α-D-xylo-furanuronyl benzotriazole (2c)

$SOCl_2$ (2.98 mmol) was added drop-wise to the stirring solution of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylo-furanuronic acid (**1c**, 2.38 mmol) and benzotriazole (7.74 mmol) in anhydrous CH_2Cl_2 (15 ml). A white solid precipitated within 5 min., the reaction mixture was further stirred for 2 hrs, white solid was filtered off and solvent was removed under vacuum. Thus the crude product obtained was subjected to column chromatography (20% EtOAc in *n*-hexane) to give white solid. Yield: 92 %; m.p. = 160-162 °C; IR (KBr): ν_{max} cm^{-1} 1677.6, 1269.5, 2923.9; MS: m/z = 418 (M+Na); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.40 and 1.57 [each s, each 3H, 2 x >C(C*H*$_3$)], 4.16 (d, *J* = 12 Hz, 1H, *O*CH$_A$Ph), 4.52 (d, *J* = 12 Hz, 1H, *O*CH$_B$Ph), 4.72 (d, *J* = 3.3 Hz, 1H, H-3), 4.78 (d, *J* = 3.6 Hz, 1H, H-2), 6.06 (d, *J* = 3.6 Hz, 1H, H-1), 6.26 (d, *J* = 2.7 Hz, 1H, H-4), 6.71–7.02 (m, 5H, Ar-*H*), 7.55 (t, *J* = 7.5 Hz, 1H), 7.69 (t, *J* = 7.8 Hz, 1H), 8.08 (d, J = 8.1 Hz, 1H), 8.29 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.47, 27.20, 71.95, 81.19, 82.34, 83.14, 105.90, 112.95, 114.23, 120.15, 125.80, 126.39, 127.48, 127.78, 128.02, 128.46, 130.67, 130.90, 135.91, 145.70, and 165.82 ppm.

1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranuronosyl benzotriazole (**2a**, prepared in good yield from compound **1a** using similar procedure). Yield: 94 %, m.p. 174-175 °C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.26, 1.39, 1.50, and 1.62 [each s, each 3H, 4 x >C(C*H*$_3$)$_2$], 4.52 (dd, *J* = 4.8 Hz and 2.7 Hz, 1H), 4.76 (d, *J* = 7.5 Hz, 1H), 5.06 (d, *J* = 7.2 Hz, 1H), 5.79 (d, *J* = 6.3 Hz, 1H), 5.83 (d, *J* = 5.4 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.67 (t, *J* = 7.8 Hz, 1H), 8.13 (d, *J* = 8.7 Hz, 1H), 8.35 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 24.78, 24.90, 25.88, 26.05, 70.06, 70.29, 71.30, 72.61, 96.65, 109.52, 110.77, 114.62, 120.14, 126.47, 130.70, 131.19, 145.82, and 165.78 ppm.

General Experimental Procedure for Sugar Based Carboxamides (4a-q)

To the stirring solution of amine (**3**, 1.33 mmol) and Et_3N (2.53 mmol) in anhydrous dichloromethane (15ml), 1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranuronosyl benzotriazole (**2a**, 1.26 mmol) or compound **2b** (1.26 mmol) was added slowly and reaction mixture was stirred for 3-4 hrs at room temperature. Progress of reaction was monitored through TLC (20% EtOAc in *n*-hexane). On completion of reaction, the reaction mixture was diluted with dichloromethane (20 ml), extracted, washed successively with water (2×10 ml) and 10% Na_2CO_3 (3x10 ml), dried over anhydrous Na_2SO_4 and concentrated under vacuum. Crude product thus obtained on column chromatography (SiO_2) furnished carboxamide (**4**) in good yields (88-96%).

N-Cyclopropyl-1,2;3,4-di-O-isopropylidene-α-D-galacto-pyranuronamide (4a)

Yield 90 %, Colourless solid, m.p.= 180-181 °C; IR (KBr): ν_{max} cm^{-1} 1678.1, 2924.9; MS: m/z = ; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.54 and 0.78 (each m, each 2H, Cyclopropyl C*H*$_2$), 1.32, 1.39, 1.51, and 1.58 [each s, each 3H, 2 × >C(C*H*$_3$)$_2$], 2.77 (m, 1H, Cyclopropyl C*H*), 4.25 and 4.34 (each s, each 1H), 4.61 (d, *J* = 7.8 Hz, 1H), 4.66 (d, *J* =

9.6 Hz, 1H), 5.54 (d, *J* = 4.8 Hz, 1H, H-1), 6.53 (bs, 1H, D_2O exchangeable NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 6.26, 6.43, 22.01, 24.18, 24.81, 25.86, 25.96, 68.72, 70.36, 70.75, 71.55, 96.19, 109.22, 109.34, and 169.67 ppm.

N-Furfuryl-1,2;3,4-di-O-isopropylidene-α-D-galacto-pyranuronamide (4b)

Yield 92 %, Colourless solid, m.p.= 122-123 °C, IR (KBr): ν_{max} cm^{-1} 1676.5, 2926.8; MS: m/z = 376 (M+Na); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.33, 1.38 [each s (two s merged), each 3H, 4 x >C(CH_3)$_2$], 12H), 4.33 (t, *J* = 7.8 Hz, 1H, C_4-H), 4.454 (d, *J* = 5.1 Hz, 1H, C_3-H), 4.52 (d, *J* = 6 Hz, 1H, C_2-H), 4.76 (d, *J* = 5.1 Hz, 1H, C_5-H), 5.56 (d, *J* = 4.5 Hz, 1H, C_1-H), 6.25-6.30 (d, *J* = 16.2 Hz, 2H, furfuryl), 6.84 (bs, 1H, NH), 7.34 (d, 1H, *J* = 7.2 Hz, Furfuryl); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 24.19, 24.78, 25.80, 25.93, 35.93, 68.82, 70.39, 70.72, 71.56, 96.21, 107.26, 109.22, 109.42, 110.31, 142.07, 151.06, and 168.18 ppm.

N-Cyclopropyl-3-O-benzyl-1,2-O-isopropylidene-α-D-xylo-furanuronamide (4d)

Yield: 95%; m.p.= 172-173 °C; IR (KBr): ν_{max} cm^{-1} 1673.6, 2921.1; MS: m/z = 356 (M+Na); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.51 and 0.79 (each m, each 2H, Cyclopropyl CH_2), 1.19 and 1.46 [each s, each 3H, 2 x >C(CH_3)$_2$], 2.74 (m, 1H, cyclopropyl CH), 4.35 (d, *J* = 3.0 Hz, 1H, H-3), 4.57 (two d merged, *J* = 12.0 Hz, 1H, *O*CH_APh and J = 3.6 Hz merged, 1H, H-2), 4.61 (d, *J* = 12.0 Hz, 1H, *O*CH_BPh),), 4.71 (d, *J* = 3.3 Hz, 1H, H-4), 5.96 (d, *J* = 3.3 Hz, 1H, H-1), 6.63 (bs, 1H, NH), 7.31 (m, 5H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 6.32, 6.38, 22.12, 26.26, 26.86, 73.04, 80.94, 82.29, 82.41, 105.44, 112.75, 114.82, 126.09, 127.87, 128.29, 136.95, 138.39, and 169.86 ppm.

N-Cyclohexyl-3-O-benzyl-1,2-O-isopropylidene-α-D-xylo-furanuronamide (4e)

Yield: 94 %; m.p.= 165-166 °C; IR (KBr): ν_{max} cm^{-1} 1677.5, 2943.3; MS: m/z = 376 (M+Na); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.14-1.87 [m, 16H, Cyclohexyl CH_2 and 2 x >C(CH_3)$_2$ merged], 3.81 (m, 1H), 4.34 (d, *J* = 3.0 MHz, 1H, H-3), 4.58 (d, *J* = 8.1 Hz, 1H, *O*CH_APh), 4.63-4.61 (two d merged, *J* = 12.0 Hz, 1H, *O*CH_BPh and *J* = 3.3 Hz, 1H, H-2), 4.71 (d, *J* = 2.7 Hz, 1H, H-4), 5.99 (d, *J* = 3.3 Hz, 1H, H-1), 6.48 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 24.72, 24.76, 25.44, 26.35, 26.92, 32.77, 32.99, 47.79, 73.16, 81.02, 82.41, 82.60, 105.39, 112.63, 127.71, 127.85, 128.31, 137.28, and 166.51 ppm.

N-n-octyl-3-O-benzyl-1,2-O-isopropylidene-α-D-xylo-furanuronamide (4f)

Yield 93 %, m.p.= 155-156 °C; IR (KBr): ν_{max} cm^{-1} 1679.3, 2912.1; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.85 (d, *J* = 6.6 Hz, 3H, CH_3), 1.24 (m, 12H, aliphatic), 1.31 (s, 3H, -CH_3), 1.47 (s, 3H, -CH_3), 3.29 (t, *J* = 6.6 Hz, 2H, CH_2-NH), 4.34 (d, *J* = 3.0 Hz, 1H, H-3), 4.57 (d, *J* = 3.6 Hz, 1H, H-2), 4.57 (d, *J* = 11.7 Hz, 1H, *O*CH_APh), 4.62 (d, *J* = 11.7 Hz, 1H, *O*CH_BPh), 4.74 (d,*J* = 3.0 Hz, 1H, H-4), 5.98 (d, *J* = 3.6 Hz, 1H, H-1), 6.58 (bs, 1H, NH), 7.30 (m, 5H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.05, 22.59, 26.35, 26.82, 26.93, 29.12, 29.19, 29.49, 31.76, 39.03, 73.18, 81.11, 82.41, 82.61, 105.42, 112.63, 127.68, 127.88, 128.36, 137.28, and 167.39 ppm.

N-n-hexadecyl-O-benzyl-1,2-O-isopropylidene-α-D-xylo-furanuronamide (4g)

Yield 93 %, m.p. = 137-138 °C; IR (KBr): ν_{max} cm^{-1} 1671.3, 2918.4; MS: m/z = 554 (M+Na); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.87 (t, *J* = 6.6 Hz, 3H), 1.25 (m, 28H), 1.31 (s, 3H, -CH_3), 1.47 (s, 3H, -CH_3), 3.29 (dt, *J* = 6 Hz and 6.6 Hz, 2H, CH_2) 4.34 (d, *J* = 2.7 Hz, 1H, H-3), 4.56 (d, *J* = 3.3 Hz, 1H, H-2), 4.58 (d, *J* = 12.0 Hz, 1H, *O*CH_APh), 4.60 (d, *J* = 12.0 Hz, 1H, *O*CH_BPh), 4.74 (d, *J* = 2.7 Hz, 1H, H-4), 5.99 (d, *J* = 3.3 Hz, 1H, H-1), 6.59 (bs, 1H, NH), 7.29 (m, 5H, Ar-*H*); ^{13}C NMR (DMSO-D_6, 75 MHz): δ 14.10, 22.65, 26.34, 26.83, 26.92, 29.25, 29.33, 29.489, 29.57, 29.66, 31.88, 39.03, 73.17, 81.09, 82.38, 82.58, 105.40, 112.63, 127.69, 127.88, 128.36, 137.25, and 167.41 ppm.

N-Phenylethyl-3-O-benzyl-1,2-O-isopropylidene-α-D-xylo-furanuronamide (4h)

Yield 96 %, m.p. = 149-150 °C; IR (KBr): ν_{max} cm^{-1} 1672.9, 2932.5; MS: m/z = 398 (M+H); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.31 and 1.47 [each s, each 3H, 2 x >C(CH_3)], 2.76 (t, *J* = 6.6, 2H, CH_2), 3.54 (m, 2H), 4.35 (d, *J* = 3.3 Hz, 1H, H-3), 4.56 (d, *J* = 10.8 Hz, 1H, *O*CH_APh), 4.58 (d, *J* = 10.8 Hz, 1H, *O*CH_BPh), 4.60 (d, *J* = 3.6 Hz, 1H, H-2), 4.74 (d, *J* = 3.0 Hz, 1H, H-4), 5.95 (d, *J* = 3.6 Hz, 1H, H-1), 6.61 (bs, 1H, NH), 7.14-7.29 (m, 10H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.33, 26.93, 35.81, 40.15, 73.19, 81.11, 82.49, 82.51, 105.45, 112.64, 126.41, 127.76, 127.86, 127.95, 128.40, 128.51, 128.62, 128.69, 137.25, 138.68, and 167.56 ppm.

N-Phenyl-O-benzyl-1,2-O-isopropylidene-α-D-xylo-furan-uronamide (4i)

Yield 90 %, m.p. = 169-170 °C; IR (KBr): ν_{max} cm^{-1} 1668.7, 2930.9; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.34 and 1.51 [each s, each 3H, 2 x >C(CH_3)$_2$], 4.42 (d, *J* = 2.7 Hz, 1H, H-3), 4.56 (d, *J* = 3.3 Hz, 1H, H-2), 4.60 (d, *J* = 12.0 Hz, 1H, *O*CH_APh), 4.62 (d, *J* = 12.0 Hz, 1H, *O*CH_BPh), 4.85 (d, *J* = 3.0 Hz, 1H, H-4), 6.08 (d, *J* = 3.3 Hz, 1H, H-1), 7.14-7.58 (m, 10H, Ar-*H*), 8.28 (bs, 1H, NH); ^{13}**C** NMR ($CDCl_3$, 75 MHz): δ 26.38, 27.01, 73.39, 81.35, 82.59, 82.62, 105.69, 112.95, 119.99, 124.59, 127.80, 127.97, 128.39, 128.98, 136.98, 137.02, and 162.83 ppm.

N-m-Chlorophenyl-O-benzyl-1,2-O-isopropylidene-α-D-xylo-furanuronamide (4j)

Yield 93 %, m.p. = 145-146 °C; IR (KBr): ν_{max} cm^{-1} 1674.4, 1271.5, 2924.9; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.26 and 1.51 [each s, each 3H, 2 x >C(CH_3)$_2$], 4.35 (d, *J* = 3.0 Hz, 1H, H-3), 4.57 (d, *J* = 3.6 Hz, 1H, H-2), 4.57 (d, *J* = 11.1 Hz, 1H, *O*CH_APh), 4.60 (d, *J* = 11.7 Hz, 1H, *O*-CH_BPh), 4.72 (d, *J* = 2.7 Hz, 1H, H-4), 5.9 (d, *J* = 3.3 Hz, 1H, H-1), 8.28 (bs, 1H, NH), 7.22-7.56 (m, 9H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.39, 27.02, 73.41, 81.37, 82.62, 82.64, 105.71, 112.96, 120.01, 124.60, 127.67, 127.81, 127.97, 128.39, 128.99, 136.99, 137.03, and 165.85 ppm.

N-m-Nitrophenyl-O-benzyl-1,2-O-isopropylidene-α-D-xylo-furanuronamide (4k)

Yield 91 %, m.p. = 150-151 °C; IR (KBr): ν_{max} cm^{-1} 1675.2, 1271.5, 2924.9; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.25

and 1.51 [each s, each 3H, 2 x >C(CH_3)$_2$], 4.43 (d, *J* = 2.7 Hz, 1H, H-3), 4.57 (d, *J* = 3.3 Hz, 1H, H-2), 4.59 (d, *J* = 11.7 Hz, 1H, *O*CH$_A$Ph), 4.64 (d, *J* = 11.7 Hz, 1H, *O*CH$_B$Ph), 4.85 (d, *J* = 3.0 Hz, 1H, H-4), 6.07 (d, *J* = 3.0 Hz, 1H, H-1), 7.11-7.57 (m, 9H, Ar-*H*), 8.28 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.38, 27.86, 73.40, 81.39, 82.71, 82.86, 105.91, 112.89, 120.01, 124.60, 124.97, 126.67, 127.67, 127.81, 127.97, 128.39, 128.99, 136.99, 137.03, and 165.85 ppm.

3-O-Benzyl-1,2-O-isopropylidene aldotetrose-4-[piperidin-1'-yl]-methanone (4l)

Yield 91 %, IR (KBr): ν_{max} cm^{-1} 1673.8, 1271.5, 2924.9; MS: m/z = 384 (M+Na); ^{1}H NMR ($CDCl_3$, 300 MHz): δ1.13 (m, *J* = 10.5 Hz, 2H) 1.31 and 1.47 [(each s, each 3H, 2 x >C(CH_3)$_2$], 1.58 (m, 6H), 1.78 (m, *J* = 14.4 Hz, 2H), 4.35 (d, *J* = 3.0 Hz, 1H, H-3), 4.57 (d, *J* = 3.6 Hz, 1H, H-2), 4.58 (d, *J* = 11.1 Hz, 1H, *O*CH$_A$Ph), 4.60 (d, *J* = 11.1 Hz, 1H, *O*CH$_B$Ph), 4.71 (d, *J* = 2.7 Hz, 1H, H-4), 5.98 (d, *J* = 3.6 Hz, 1H, H-1), 7.31 (m, 5H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 24.67, 25.39, 26.33, 26.92, 32.73, 32.92, 45.71, 47.97, 73.11, 81.01, 82.41, 82.50, 105.42, 112.70, 115.02, 125.50, 127.69, 127.88, 128.31, 137.17, 139.17, and 166.88 ppm.

3-O-Benzyl-1,2-O-isopropylidene aldotetrose-4-[morpholin-1'-yl]-methanone (4m)

Yield 90%, IR (KBr): ν_{max} cm^{-1} 1669.2, 2928.8; MS: m/z = 386 (M+Na); ^{1}H NMR ($CDCl_3$, 300 MHz): 1.34 and 1.49 [each s, each 3H, 2 x >C(CH_3)$_2$], 3.46 (m, 4H, morpholine), 3.94 (m, 4H, morpholine), 4.26 (d, *J* = 3.6 Hz, 1H, H-3), 4.50 (d, *J* =11.4, Hz, 1H, *O*CH$_A$Ph), 4.65 (d, J = 3.6Hz, 1H, H-2), 4.68 (d, *J* = 12.0 Hz, 1H, *O*CH$_B$Ph), 4.99 (d, *J* = 3.9 Hz, 1H, H-2), 6.10 (d, *J* = 3.9 Hz, 1H, H-1), 7.32 (m, 5H, *Ar-H*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.17, 26.74, 42.76, 45.57, 63.52, 66.47, 72.07, 80.37, 81.63, 82.60, 105.07, 112.24, 125.20, 127.52, 127.71, 128.13, 128.43, 136.68, and 165.69 ppm.

3-O-Benzyl-1,2-O-isopropylidene aldotetrose-4-[N-methyl piperazin-1-yl]-methanone (4n)

Yield 92%, IR (KBr): ν_{max} cm^{-1} 1675.2, 2912.8; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.27 and 1.42 [each s, each 3H, 2 x >C(CH_3)$_2$], 2.14 (s, 3H, CH_3), 2.25 (m, 4H, CH_2), 3.50 (m, 4H, CH_2), 4.19 (d, *J* = 3.0 Hz, 1H, H-3), 4.46 (d, *J* = 11.4 Hz, 1H, *O*CH$_A$Ph), 4.60 (d, *J* = 11.7 Hz, 1H, *O*CH$_B$Ph), 4.58 (d, J =3.3Hz, 1H, H-2), 4.94 (d, *J* = 3.0 Hz, 1H, H-4), 6.05 (d, *J* = 3.3 Hz, 1H, H-1), 7.23 (m, 5H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.13, 26.69, 41.91, 44.37, 45.28, 54.11, 72.03, 80.22, 81.63, 82.78, 104.98, 112.13, 114.90, 125.01, 127.94, 127.97, 128.33, 136.67, 138.00, and 165.31 ppm.

3-O-Benzyl-1,2-O-isopropylidene aldotetrose-4-[N-phenyl-piperazin-1'-yl]-methanone (4o)

Yield 92 %, IR (KBr): ν_{max} cm^{-1} 1670.2, 2921.7; MS: m/z = 461 (M+Na); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.34 and 1.50 [each s, each 3H, 2 x >C(CH_3)$_2$], 2.97 (m, 4H, piperazine CH_2), 3.69 (m, 4H, piperazine CH_2), 4.29 (d, *J* = 3.0 Hz, 1H, H-3), 4.49 (d, *J* = 3.0 Hz, 1H, H-4), 4.66 (d, *J* = 11.4 Hz, 1H, *O*CH$_A$Ph), 4.67 (d, *J* = 11.7 Hz, 1H, *O*CH$_B$Ph), 5.04 (d, *J* = 3.6 Hz, 1H, H-2), 6.13 (d, *J* = 3.9 Hz, 1H, H-1), 6.82-7.40 (m, 10H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.26, 26.85, 49.25, 53.38, 72.15, 80.42, 81.78, 82.64, 105.19, 112.32, 120.37, 121.14, 125.38, 127.65, 128.12, 128.17, 128.49, 129.11, 129.23, 136.70, and 165.66 ppm.

N-2-(4-Phenyl-thiazol-2-yl)-3-O-benzyl-1,2-O-isopropylidene-α-D-xylo-furanuronamide (4p)

Yield: 94 %, m.p. = 168-169 °C; IR (KBr): ν_{max} cm^{-1} 1676.6, 2945.1; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.39 and 1.60 [each s, each 3H, 2 x >C(CH_3)$_2$], 4.42 (d, *J* = 3.0 Hz, 1H, H-3), 4.56 (d *J* = 12.0 Hz, 1H, *O*CH$_A$Ph), 4.58 (d *J* = 12.0 Hz, 1H, *O*CH$_B$Ph), 4.63 (d, *J* = 2.7 Hz, 1H, H-4), 4.96 (d, *J* = 3.3 Hz, 1H, H-2), 6.10 (d, *J* = 3.0 Hz, 1H, H-1), 7.172-7.843 (m, 11H, Aromatic-*H*), 9.71 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): ^{1}H NMR ($CDCl_3$, 75 MHz): δ 26.35, 27.05, 73.14, 80.95, 82.41, 82.58, 105.94, 107.75, 113.09, 126.04, 127.65, 128.00, 128.39, 128.69, 134.27, 136.67, 150.17, 156.31, and 166.11 ppm.

N-(5-Phenyl-[1,34]thiadiazol-2-yl)-3-O-benzyl-1,2-O-isopropylidene-α-D-xylo-furanuronamide (4q)

Yield 90 %, m.p. = 160-162 °C; IR (KBr): ν_{max} cm^{-1} 1673.9, 2934.2; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.35 and 1.52 [each s, each 3H, 2 x >C(CH_3)$_2$], 4.43 (d, *J* = 3.3 Hz, 1H, H-3), 4.52 (d, *J* = 11.7 Hz, 1H, *O*CH$_A$Ph), 4.60 (d, *J* = 12.0 Hz, 1H, *O*CH$_B$Ph), 4.65 (d, *J* = 3.3 Hz, 1H, H-2), 5.00 (d, *J* = 3.3 Hz, 1H, H-4), 6.14 (d, *J* = 3.3 Hz, 1H, H-1), 7.16-7.96 (m, 10H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.35, 27.07, 73.06, 80.99, 82.28, 82.60, 106.07, 113.24, 127.04, 127.36, 127.59, 128.12, 128.39, 128.48, 128.96, 129.15, 130.33, 130.73, 136.53, and 166.26 ppm.

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REFERENCES

[1] Valeur, E.; Bradley, M. Amide bond formation: beyond the mytgh of coupling reagents. *Chem. Soc. Rev*., **2009**, *38*, 606.

[2] Humphrey, J. M.; Chamberlin, A. R. Chemical synthesis of natural product peptides: coupling methods for the incorporation of noncoded amino acids into peptides. *Chem. Rev*., **1997**, *97*, 2243.

[3] Katritzky, A. R.; Suzuki, K.; Singh, S. K. N-acylation in combinatorial chemistry. *ARKIVOC*, **2004**, 12.

[4] Montalbetti, C. A.; G. N.; Falque, V. Amide bond formation and peptide coupling. *Tetrahedron*, **2005**, *61*, 10827.

[5] Najera, C. From α-amino acids to peptides: all you need for the journey. *Synlett*, **2002**, 1388.

[6] (a) Patchett, A. A. Excursions in drug discovery. *J. Med. Chem.*, **1993**, *36*, 2051. (b) Gasparo M. de; Whitebread, S. Binding of valsartan to mammalian angiotensin AT_1 receptors *Regul. Pept.*, **1995**, *59*, 303. (c) Ananthanarayanan, V. S.; Tetreault, S.; Saint-Jean, A. Interaction of calcium channel antagonists with calcium: spectroscopic and modeling studies on diltiazem and its Ca^{2+} complex. *J. Med. Chem*., **1993**, *36*, 1324. (d) Hirschmann, R.; Nicolaou, K. C.; Pietranico, S.; Leahy, E. M.; Salvino, J.; Arison, B.; Cichy, M. A.; Spoors, P. G.; Shakespeare, W. C. *De novo* design and synthesis of somatostatin non-peptide peptidomimetics utilizing .beta.-D-glucose as a novel scaffolding. *J. Am. Chem. Soc*. **1993**, *115*, 12550.

[7] (a) Varki, A. Biological roles of oligosaccharides: all of theories are correct. *Glycobiology*, **1993**, *3*, 97. (b) Gagneau, P.; Varki, A. Evolutionary considerations in relating oligosaccharide diversity to

biological function. *Glycobiology*, **1999**, *9*, 747. (c) Zhu, X.; Schmidt, R. R. New Principles for Glycoside-Bond Formation. *Angew Chem. Int. Ed. Engl.*, **2009**, *48*, 1900.

[8] (a) Kunz, H.; Schultz, M. In *Glycopeptide and related compounds*: *Synthesis, Analysis and Application*, Large, D. G.; Warren, C. D.; Eds: Marcel Dekker Inc New York, **1997**, 23. (b) Wittmann, V.; In Glycoscience, Vol. III, Fraser-Reid, B.; Tatsuta, K.; Theim, J. Eds; Springer-Verlag, Berlag, Berlin, Heidelberg, **2001**, p. 2254.

[9] Pandey, J.; Sharma, A.; Tiwari, V. K.; Dube, D.; Ramachandran, R.; Chaturvedi, V.; Sinha, S. K.; Mishra, N. N.; Shukla, P. K.; Tripathi, R. P. Solution-phase synthesis of a library of carbapeptide analogues based on glycosylamino acid scaffolds and their in silico screening and antimicrobial evaluation. *J. Comb. Chem*, **2009**, *11*, 422.

[10] Wang, W.; McMurray, A selective method for the preparation of primary amides: synthesis of Fmoc-L-4-carboxamidophenylalanine and other compounds. J. S. *Tetrahedron Lett.*, **1999**, *40*, 2501.

[11] Schmidt, M. A.; Movassaghi, M. N-heterocyclic carbene-catalyzed amidation of unactivated esters with amino alcohols. *Org. Lett.*, **2005**, *7*, 2453.

[12] (a) Williams, A.; TIbrahim, I. Carbodiimide chemistry: recent advances. *Chem. Rev.*, **1981**, *81*, 589. (b) Takashiro, E.; Watanabe, T.; Nitta, T.; Kasuya, A.; Miyamoto, S.; Ozawa, Y.; Yagi, R.; Nishigaki, T.; Shibayama, T.; Nakagawa, A.; Iwamoto, A.; Yabe, Y. Structure–activity relationship of HIV-1 protease inhibitors containing AHPBA. Part III: modification of P_2 site. *Bioorg. Med. Chem*. **1998**, *6*, 595.

[13] (a) Furstner, A.; Thiel, O. R.; Blanda, G. Asymmetric synthesis of the fully functional macrolide core of salicylihalamide: remote control of olefin geometry during RCM. *Org. Lett*. **2000**, *2*, 3731. (b) Furstner, A.; Thiel, O. R.; Kindler, N.; Bartkowska, B. Total syntheses of (*S*)-(−)-Zearalenone and lasiodiplodin reveal superior metathesis activity of ruthenium carbene complexes with imidazol-2-ylidene ligands. *J. Org. Chem.* **2000**, *65*, 7990.

[14] Gotor, V. Non-conventional hydrolase chemistry: amide and carbamate bond formation catalyzed by lipases *Bioorg. Med. Chem*., **1999**, *7*, 2189.

[15] (a) Tiwari. V. K.; Singh, A.; Hussain, H. A.; Mishra, B. B.; Tripathi, V. One-pot convenient & high yielding synthesis of dithiocarbamates. *Monatsh Chem.*, **2007**, *138*, 1297. (b) Tiwari, V. K.; Kale, R. R.; Mishra, B. B.; Singh, A. *MW*- assisted one-pot, facile synthesis of 2-Thioxo-2,3-dihydroquinazolin-4(1H)-ones. *ARKIVOC*, **2008**, *xiv*, 27. (c) Tiwari, V. K.; Hussain, H. A.; Mishra, B. B.; Singh, D. D.; Tripathi, V. Benzotriazole mediated one pot convenient synthesis of Thioquinazolinones as potential Antifungal agents. *Med. Chem. Res*., **2007**, *15*, 325. (d) Singh, A.; Kale, R. R.; Tiwari, V. K. Benzotriazole mediated one-pot facile synthesis of N/S-glycosyl dithiocarbamates. *Trends Carbo. Res.*, **2009**, *1*, 80. (e) Tiwari, V. K.; Singh, D. D.; Hussain, H. A.; Mishra, B .B.; Singh, A. One-pot, simple new, and convenient synthesis of 2-thioxo-2,3-dihydroquinazolin-4(1H)-ones. *Monatsh Chem.*, **2008**, *139*, 43.

[16] (a) Yu, H.; Cheng, J.; Ding, L.; Khedri, Z.; Chen, Y.; Chin, S.; Lau, K.; Tiwari, V. K.; Chen, X. Chemoenzymatic synthesis of GD3 oligosaccharides and other disialyl glycans containing natural and non-natural sialic acids. *J. Am. Chem. Soc*., **2009**, *131*, 18467. (b) Pandey, J.; Tiwari, V. K.; Verma, S. S.; Chaturvedi, V.; Bhatnagar, S.; Sinha, S.; Gaikwad, A.; Tripathi, R. P. Synthesis and antitubercular screening of imidazole derivatives. *Eur. J. Med. Chem*., **2009**, *44*, 3350. (c) Cheng, J.; Yu, H.; Lau, K.; Huang, S.; Chokhawala, H. A.; Li, Y.; Tiwari, V. K.; Chen, X. Multifunctionality of *Campylobacter jejuni sialyltransferase-ase CstII*. *Glycobiology*, **2008**, *18*, 686. (d) Katiyar, D.; Tiwari, V. K.; Tiwari, N.; Verma, S. S.; Sinha, S.; Giakwad, A.; Srivastava, A.; Chaturvedi, V.; Srivastava, R.; Srivastava B. S., Tripathi, R. P. Synthesis and antimycobacterial activity of glycosylated b-amino alcohols and amines. *Eur. J. Med. Chem.*,**2005**, *40*, 351. (e) Tripathi, R. P.; Tiwari, V. K.; Tiwari, N.; Giakwad, A.; Sinha, S.; Srivastava, S.; Chaturvedi, V.; Srivastava, B. S. Synthesis of N^1, N^n-diglycosylated beta- diamino alcohols as new class of antitubercular agents. *Bioorg. Med. Chem.*, **2005**, *13*, 5668. (f) Tewari, N.; Tiwari, V. K.; Tripathi, R. P.; Gaikwad, A.; Sinha, S.; Chaturvedi, A. K.; Shukla, P. K.; Srivastava, R.; Srivastava, B. S. Synthesis of Galactopyranosyl amino alcohols as a new class of Antitubercular and antifungal agents. *Bioorg. Med. Chem. Lett.*, **2004**, *14*, 329. (g) Tewari, N.; Katiyar, D.; Tiwari, V. K. Tripathi, R. P. Amberlite IR -120 catalysed efficient synthesis of glycosyl enaminones and their application. *Tetrahedron Lett*., **2003**, *44*, 6639. (h) Tiwari, V. K.; Tewari, N.; Tripathi, R. P.; Arora, K.; Gupta, S.; Srivastava, A. K.; Khan, M. A.; Murthy, P. K.; Walter, R. D. Synthesis and Antifilarial evaluation of N^1, N^n-diglycosylated diaminoalkanes. *Bioorg. Med. Chem.*, **2003**, *11*, 1789. (i) Tewari, N.; Tiwari, V. K.; Mishra, R. C.; Tripathi, R. P.; Srivastava, A. K.; Ahmad, R.; Srivastava, R.; Srivastava B. S. Synthesis and Bioevaluation of glycosyl ureas as alpha-glucosidase inhibitors and their effect on Mycobacteriam. *Bioorg. Med. Chem.*, **2003**, *11*, 2911.

[17] Caprio, V. In *Comprehensive Organic Functional Group Transformations II*; Katritzky, A. R., Taylor, R. J. K., Eds.; Elsevier: New York, **2005**, 135.

[18] Katritzky, A. R.; Suzuki, K.; Wang, Z. Acylbenzotriazoles as Advantageous N-, C-, S-, and O-acylating agnets. *Synlett*, **2005**, 1656.

[19] (a) Katritzky, A. R.; Suzuki, K.; Singh, S. K. Highly diastereoselctive peptide chain extensions of unprotected amino acids with *N*-(Z-α-aminoacyl)benzotriazoles. *Synthesis* **2004**, 2645. (b) Katritzky, A. R.; Angrish, P.; Suzuki, K. The efficient preparation of di-and tripeptides by coupling *N*-(Cbz- or fmoc-α-aminoacyl)benzotriazoles with unprotected amino acids. *Synthesis*, **2006**, p. 411.

[20] Katritzky, A. R.; Zhang, Y.; Singh, S. K. Efficient conversion of carboxylic acids into *N*-acylbenzotriazoles. *Synthesis*, **2003**, 2795.

[21] Katritzky, A. R.; Chang, H.-X.; Yang, B. N-formylbenzotriazole: a stable and convenient N- and O-formylating agent. *Synthesis*, **1995**, 503.

[22] Katritzky, A. R.; Yang, B.; Semenzin, D. Trifluoroacetyl)benzotriazole: a convenient trifluoroacetylating reagent. *J. Org. Chem.*, **1997**, *62*, 726.

[23] Katrizky, A. R.; Suzuki, K.; Singh, S. K.; He, H.-Y. Regiospecific *C*-acylation of pyrroles and indoles using *N*-acylbenzotriazoles. *J. Org. Chem.*, **2003**, *68*, 5720

[24] Katritzky, A. R.; Levell, J. R.; Pleynet, D. P. M. General synthesis of unsymmetrical tetrasubstituted oxamides *via* 1,1'-(1,2-dioxoethane-1,2-diyl)bis-1H-benzotriazole. *Synthesis*, **1998**, 153.

[25] Katritzky, A. R.; Pastor, A. Synthesis of β-dicarbonyl compounds using 1-acylbenzotriazoles as regioselective C-acylating reagents. *J. Org. Chem*., **2000**, *65*, 3679.