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FULL PAPER

Synthesis of *C*-Analogues of β-Glucogallin and Aldose Reductase Inhibition Studies.

Mannem Rajeswara Reddy,[a] Indrapal Singh Aidhen,*[a] Karnam Shruthi,[b] Geereddy Bhanuprakash Reddy*[b]

Abstract: β-Glucogallin **1** (BGG), a major component isolated from the Indian gooseberry (*Emblica officinalis*) medicinal plant, is a potent and selective inhibitor of aldose reductase (AKR1B1). Structurally, BGG is a glucosyl-1-ester, wherein gallic acid is linked to the β-D-glucose ring through ester functionality. Susceptibility of the easily hydrolysable ester functional group in aqueous solution has been the cause of concern. Isosteric replacement of glucosyl-*O*- with -*NH*- has offered the more stable and potent analogue **2**, the *C*-analogue **3**, wherein a –CH_2- unit replaces the glucosyl-*O* however remains unexplored. Synthesis of *C*-analogues **3** and **4** and their aldose reductase inhibition (ARI) constitutes the work presented herein.

Introduction

The number of people with diabetes rose to 422 million in 2014 from 108 million in 1980.[1a] Diabetes can lead to macrovascular complications like stroke and cardiovascular diseases and microvascular complications like retinopathy, nephropathy, cataract and neuropathy. The plant *Emblica officinalis* (gooseberry) has been used for thousands of years as traditional Indian Ayurvedic medicine for the treatment of diabetes in human. Extracts from this plant have been shown to be efficacious against the progression of cataract in a diabetic rat model.[1b] Aldose reductase (ALR2 or AKR1B1) is implicated in the development of secondary complications of diabetics including cataract. The enzyme, ALR2 has been a major drug target for the development of therapies to treat diabetic complications.[2] The compound 1-*O*-galloyl-β-glucose (β-glucogallin) (BGG) **1** extracted as a major component from the fruit of the gooseberry displays selective as well as relatively potent inhibition of AKR1B1.[3] Structurally BGG **1** is a D-glucosyl-1-ester and therefore susceptible to easy hydrolysis in aqueous solution. LaBarbera [4] has synthesized and explored hydrolytically more stable, *N*-analogue of BGG, compound **2** for aldose reductase inhibition activity. The promising results obtained therein, inspired us to undertake synthesis of *C*-analogues **3** and **4** towards the same objective. The envisaged compounds are essentially ketones, resulting from isosteric replacement of glucosyl-O atom in BGG with a -CH_2- unit. The findings of these studies are reported herein.

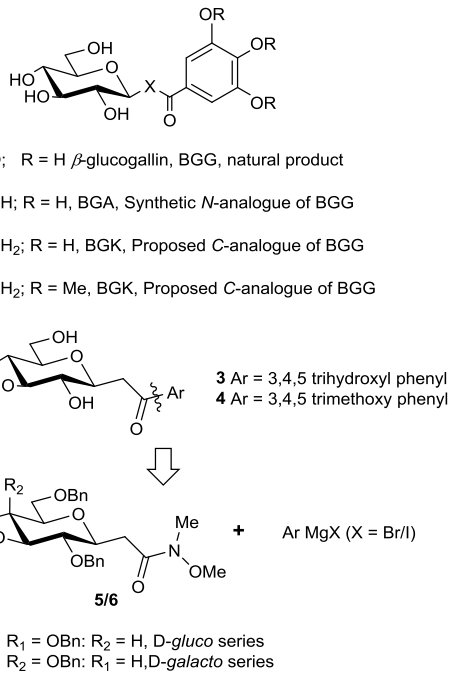

Figure 1. Isosteric replacement D-glucosyl-*O*-of β-glucogallin.

The synthesis of the targeted compounds **3** and **4** through the disconnection depicted in figure 1 banked on the use of Weinreb amide (WA) functionality.[5] The WA based building block **5**, would afford not just the desired targets **3** and **4**, but also enable access to several other analogues through variation in the nature of the aryl residue. Same disconnection and a similar building block **6** is capable of bringing variation in the glycosyl part. With the use of **6**, as an illustration, the corresponding D-galacto configured aryl ketones can be obtained with the same ease.

Results and Discussion

The synthesis of building blocks **5** and **6** required convenient access to the corresponding acids **7** and **8** respectively. Literature known method for the synthesis of **7** [6] which involves addition of lithiumethylacetate [7] on 2, 3, 4, 6-tetra-*O*-benzylgluconolactone **9** [8] for the addition of two carbons on the anomeric position, was

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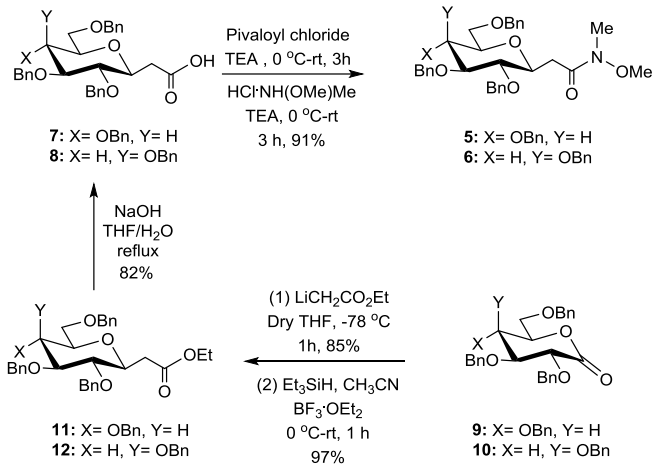
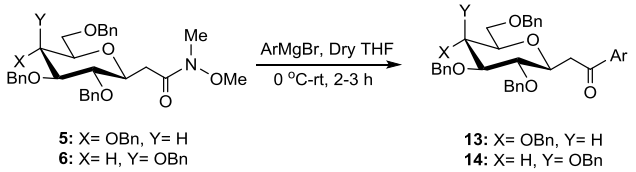
used for the synthesis of both **7** and **8**. The requisite D-galacto configured lactone **10** required for the synthesis of acid **8** was prepared from commercially available D-galactose using literature reported method.[9] Addition of 2, 3, 4, 6-tetra-*O*-benzylgluconolactone **9** onto a freshly prepared lithiumethylacetate followed by reduction of resulted hemiketal with Et_3SiH in presence of $BF_3{\cdot}OEt_2$ provided known ethyl ester **11**. Base hydrolysis of **11** with LiOH in presence of H_2O/THF gave the carboxylic acid **7** in good yield. Activation of acid **7** with pivaloyl chloride followed by treatment of the mixed anhydride, formed insitu with *N*, *O*-dimethyl hydroxylamine hydrochloride (DMHA·HCl) in anhydrous CH_2Cl_2 at 0 °C gave the amide **5** in 91% yield (Scheme 1). The same reaction sequence on D-galacto lactone **10** afforded the corresponding D-galacto-configured WA based building block **6**.



Scheme 1. Synthesis of Building Blocks **5** and **6**

Both the building blocks, **5** and **6**, when subjected to reaction with various arylmagnesium bromides afforded the corresponding glycosyl aryl ketones **13a-e** and **14a-e** respectively, in good yields (Table 1).

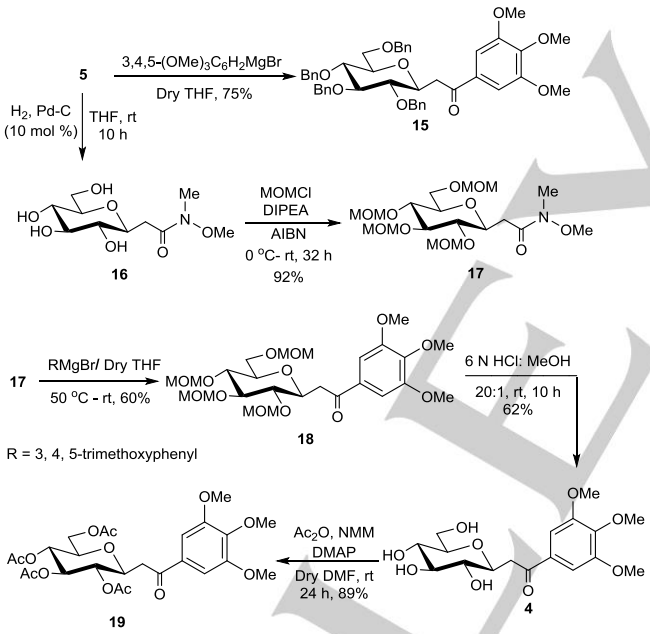
Table 1. Addition of various Grignard reagents on building block **5** and **6**.



Entry	X=OBn,Y=H (D-Gluco)	Yield[a]	Ar	Yield[a]	X=H,Y=OBn (D-Galacto)
1	**13a**	77%	4-(Me)C_6H_4	81%	**14a**
2	**13b**	75%	4-(F)C_6H_4	74%	**14b**
3	**13c**	76%	4-(Cl)C_6H_4	79%	**14c**
4	**13d**	81%	4-(OMe)C_6H_4	73%	**14d**
5	**13e**	86%	Thiophenyl	83%	**14e**

[a] isolated yield.

For the synthesis of 3, 4, 5-trimethoxyphenyl substituted glucosyl ketone **4**, 3,4,5-trimethoxyphenylmagnesium bromide was prepared according to the literature known procedure,[10] and added to the building block **5**. The reaction afforded the benzyl ether protected ketone **15** in good yield. Synthesis of targeted final product **4** needed debenzylation on the glucosyl moiety alone, whereas complete deprotection was required for the access to target **3**. The hydrogenation method for debenzylation using 10% Pd/C as catalyst in THF on compound **15** resulted in additional concomitant reduction of carbonyl group and such observations have been reported at other occasions too.[11] The combined benzyl-ether and methyl-ether deprotection on compound **15**, for the synthesis of the target **3**, using BBr_3[12] in dry dichloromethane or trimethylsilyl iodide[13] in acetonitrile resulted in degradation and formation of a complex products mixture. In order, to circumvent these difficulties, for obtaining **4**, and several of its analogues, envisaged through variation in the aryl residue, change in the nature of protection in the glucosyl residue was invoked. Given the fact that *O*-methoxymethyl ether protection (O-MOM) group has widespread utility in synthetic organic chemistry in general,[14] and also in carbohydrate chemistry,[15] we envisaged another building block **17** as an attractive alternative. The conversion of compound **5** to corresponding MOM protected building block **17** was accomplished in two steps. Debenzylation through hydrogenolysis with catalytic Pd/C**,** and subsequent treatment of tetrol **16** with chloro methyl methyl ether in presence of Hunigs base in anhydrous CH_2Cl_2 afforded the MOM protected Weinreb amide based building block **17** as a pale-yellow color gummy material in good yield. Successful addition of 3, 4, 5-trimethoxyphenylmagnesium bromide onto amide **17** afforded the desired trimethoxyphenyl ketone **18** in good yield. The aqueous acidic condition, enabled facile removal of MOM protection and the formation of target molecule **4**. (Scheme 2)



Scheme 2. Synthesis of MOM protected Building Block **17** and target **4**.

The β orientation of the *C*-residue at the anomeric position was confirmed through the observed coupling constant for C1-proton in the peracetylated derivative **19** and single crystal X-ray analysis of the same **(**Figure 2). Several glucosyl ketones **21a-h**, were prepared by the same scheme in good yield and convenience (Table 2). On observing the significance of MOM protection in the synthetic scheme, we envisaged possible use of MOM protected arylmagnesium bromide **23** for the synthesis of target compound **3**. Synthesis of this Grignard reagent from the corresponding 5-bromo-1, 2, 3-tris (methoxymethyl ether) benzene **22**[16] is not reported earlier and conventional activation procedures[17] (entry 1-3, Table 3) did not enable formation of the desired arylmagnesium derivative **23**.

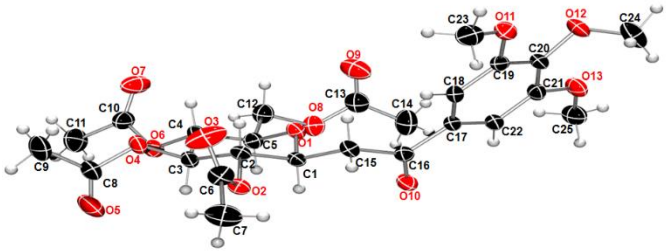
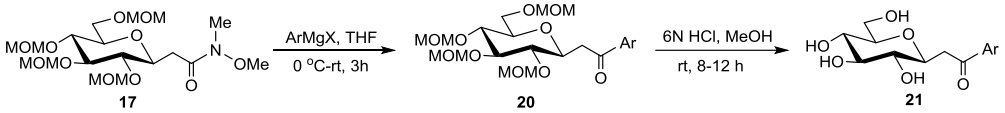


Figure 2. ORTEP diagram of compound **19**.

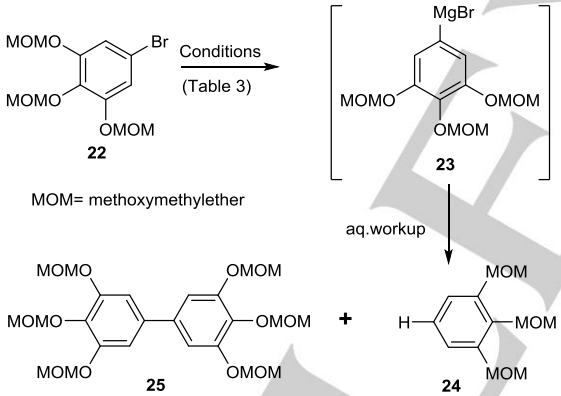
Table 2. Addition of various Grignard reagents on amide **17**, synthesis of glycosyl aryl ketones.



Entry	Ar	**20**	Yield[a]	Ar	**21**	Yield[a]
1	4-(OMe)C_6H_4	**20a**	68%	4-(OMe)C_6H_4	**21a**	79%
2	4-(Cl)C_6H_4	**20b**	70%	4-(Cl)C_6H_4	**21b**	72%
3	4-(OMOM)C_6H_4	**20c**	68%	4-(OH)C_6H_4	**21c**	62%
4	4-(F)C_6H_4	**20d**	61%	4-(F)C_6H_4	**21d**	56%
5	3,4-$(Cl)_2C_6H_3$	**20e**	68%	3,4-$(Cl)_2C_6H_3$	**21e**	75%
6	3,4-$(OMe)_2C_6H_3$	**20f**	61%	3,4-$(OMe)_2C_6H_3$	**21f**	62%
7	3,5-$(F)_2C_6H_3$	**20g**	60%	3,5-$(F)_2C_6H_3$	**21g**	72%
8	3,4,5-$(Cl)_3C_6H_2$	**20h**	66%	3,4,5-$(Cl)_3C_6H_2$	**21h**	41%

[a] isolated yield.

With the use of 1, 2-dibromoethane for activation of magnesium at 50 °C, substantial amount of homo coupling product **25** was obtained after aqueous acidic work up. The observation that addition of 5-12 mol% of diisobutylaluminum hydride (DIBALH) activates the magnesium metal surface[18] and LiCl in conjunction facilitates the insertion[19] of the same into functionalized aryl bromides, we ventured into use of this method for preparation of **23**. Indeed, quantitative formation of **23** was realized, as evidenced by formation of **24** in quantitative yield, after aqueous acidic work up (Scheme 3). Although, formation of **23** was now achieved, it failed to add onto WA functionality in the MOM protected building block **17**. Presuming low reactivity of WA as a possible reason, the WA was reduced and addition of **23** was attempted on aldehyde **26**. Clean addition reaction occurred and afforded the corresponding product **27** as a diastereomeric mixture**.** Oxidation of alcohol **27** with IBX indeed afforded the MOM protected target molecule **28** (Scheme 4). Although fully protected compound **28** was repeatedly and conveniently amenable by this approach, the obtainment of the target **3**, through deprotection remained elusive. The deprotection of compound **28** with aq.6N HCl only led to extensive decomposition.

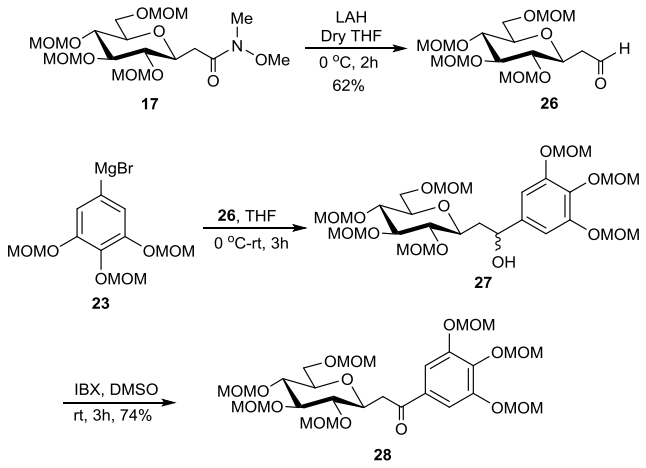


Scheme 3. Preparation of MOM protected arylmagnesium bromide **23**.

Table 3. Reaction condition for the synthesis of Grignard reagent **23.**

Entry	Condition	Ar-H **24** [a]	Dimer **25**[a]
1	I_2/ Mg/ rt or reflux	0	0
2	MeI/ I_2/ Mg/ rt or reflux	0	0
3	1,2-dibromoethane/ Mg/ 50 °C	10%	90%
4	Mg/ LiCl/ DIBAL-H/ rt	100%	0%

[a] isolated yield.



Scheme 4. Addition of more functionalized Grignard reagent **23**, synthesis of desired glycosyl aryl ketone **28.**

Biological Study:

Crude aldose reductase (AR) was isolated from rat lens. Eyeballs were removed from 12-week-old Wistar male rats obtained from National Center for Laboratory Animal Services, National Institute of Nutrition, Hyderabad. AR activity was assayed according to the reported method [20]. The synthesized ketones, **4, 21a-h,** *C*-analogues of β-Glucogallin derivatives were screened for aldose reductase inhibition at different concentrations. Among these synthesized compounds, with extensive variation of substituent's in the aryl ring, compound **21c** alone showed partial inhibition, ~ 30% at 200µM concentration. The conjecture that increased electrophilicity of the carbonyl may be an important factor in AR inhibition, seems to be invalid, as compounds with inductively, electron withdrawing substituents, such as chloro, fluoro substiutents, substrates **20b** and **20d**, respectively did not show any promising activity. Compounds with multiple chlorine atoms (**20e**, **20h)** or two fluorine atoms (**20g**), presumably with increased carbonyl electrophilicity, also showed poor AR inhibition. Apparently the observed inhibition with compound **21c** seems to indicate some other parameter, such as H-bonding with amino acid residue on the protein structure to be more relevant for good substrate binding.

Table 4. *In vitro* biological activity of synthesized glucosyl aryl ketones with Wister male rat lens.

Entry	Compound	Concentration[a]	% Inhibition
1	**1 (BGG)**	15	32
		30	46
		60	62
2	**4**	25	7
		50	9
		200	12
3	**21a**	10	11
		100	12
		200	8
4	**21b**	25	7
		100	8
		250	10
5	**21c**	15	21
		25	19
		150	22
		200	29
6	**21d**	15	11
		25	10
		150	8
7	**21e**	25	6
		100	5
		200	6
8	**21f**	25	7
		100	5
		250	17
9	**21g**	25	5
		100	5
		200	2
10	**21h**	25	6
		100	13
		250	8

[a] micro molar.

Conclusions

In conclusion, synthesis of several D-glucosyl-aryl ketones, **4** and **21a-h**, bridged through a methylene unit at anomeric position has been achieved. All these compounds are new *C*-analogues of BGG, a natural product known for aldose reductase inhibition. Among the synthesized *C*-analogues, compound **21c** indeed showed promising aldose reductase inhibition activity.

Experimental Section

All reactions were carried out in oven dried glassware. Solvents used for column chromatography were laboratory reagent grade. Solvents were distilled from CaH_2 (CH_2Cl_2, DMF), Na/Benzophenone for THF, Mg/I_2 (MeOH). Reactions were performed under nitrogen atmosphere. NMR

spectra were recorded at 293 K, unless stated otherwise Thin layer chromatography was performed on aluminum plates coated with silica gel 60. Visualization was observed by U.V. light or by dipping into a solution of cerium(IV) sulfate (2.5 g) and ammonium molybdate (6.25 g) in 10 % sulfuric acid (250 mL) followed by charring on a hot plate. Melting points were determined for compounds **4, 21a-h** purified by silica gel column chromatography using MeOH:CH_2Cl_2 (1:9), compound **19** was recrystallized from EtOAc: hexane. ^1H (400 MHz and 500 MHz) and ^{13}C (100 MHz and 125 MHz) high resolution NMR experiments were recorded on BRUKER AV 400 and 500 FT NMR spectrometer using tetramethylsilane (TMS) as an internal standard. ^1H NMR spectra were referenced to $CDCl_3$ (δ =7.26 ppm), MeOH [D_4] (δ = 3.34 ppm) and central line of DMSO [D_6] (δ =2.5 ppm), whereas ^{13}C NMR spectra were referenced to the central line of $CDCl_3$ (δ =77.16 ppm), MeOH [D_4] (δ = 49.15 ppm) and [D_6] DMSO (δ =39.5 ppm). Multiplicities are given as, s = singlet, d = doublet, t = triplet, dd = doublet of doublet, m = multiple, and br. s = broad singlet. IR spectra was recorded with a JASCO-FT/IR-4100 Spectrometer with a NaCl cell. Elemental analyses was determined with Perkin–Elmer Instruments series II CHNS/O analyzer. HRMS were recorded with a MICRO-QTOF mass spectrometer by using the ESI technique at 10 eV.

1-N-methoxy-N-methyl-2-(2′, 3′, 4′, 6′-tetra-*O*-benzyl-*β*-D-glucopyranosyl) acetamide (5): The oven dried round bottom flask was charged with acid **7** (2.72 g, 4.68 mmol) in anhydrous CH_2Cl_2 followed by pivaloyl chloride (0.744 ml, 6.08 mmol) and triethyl amine (0.98 ml, 7.49 mmol) at 0°C for 10 min. The reaction mixture was warmed to rt and stirred for 3 h. Then, *N,O*-dimethylhydroxlamine hydrochloride (0.735 g, 7.40 mmol) and triethylamine (0.98 ml, 7.49 mmol) were added slowly at 0 °C, and the mixture was stirred for 3h at rt. The reaction mixture was quenched with water. The organic layer was extracted with CH_2Cl_2, dried over Na_2SO_4 and concentrated under reduced pressure to give crude product, which was further purified by column chromatography on silica. Eluting with ethyl acetate : hexane (1:2), gave the title compound as a light yellow color solid (2.54 g, 87%); m.p. = 86-88 °C, R_f = 0.1 (EtOAc/Hexane 3:7); $[\alpha]^{27}_D$ 113° (c 0.5, $CHCl_3$); ^1H NMR: ($CDCl_3$, 400 MHz) δ = 2.64–2.74 (m, 2H), 3.13 (s, 3H, *NCH*$_3$), 3.48-3.38 (m, 2H), 3.60 (s, 3H, *OMe*), 3.75-3.65 (m, 4H), 3.87-3.82 (m, 1H), 4.48 (d, 1H, *J* =12 Hz), 4.55 (d, 1H, *J*=10 Hz), 4.58 (d,1H, *J* = 8.8 Hz), 4.67 (d,1H, *J* = 11.6 Hz), 4.81 (d, 1H, *J* = 10.8 Hz), 4.86-4.93 (m, 3H), 7.16-7.30 (m, 20H).^{13}C NMR (100 MHz, $CDCl_3$) δ = 34.2 (CH_2), 68.8 (CH_2), 73.3 (CH_2), 74.8 (CH_2), 74.9 (CH_2), 75.5 (CH_2), 75.7 (CH), 78.4 (CH), 78.7 (CH), 81.4 (CH), 87.3 (CH), 127.6 (CH), 127.7 (CH), 127.7 (CH), 127.9 (CH), 127.9 (CH), 128.3 (CH), 128.4 (CH), 128.4 (CH), 128.5 (CH), 138.2 (C), 138.3 (C), 138.6 (C), 171.7 (CO). IR ($CHCl_3$): 1214, 1428, 1640, 2926, 3021, cm^{-1}. HRMS: calcd for $C_{38}H_{44}O_7N$ $(M+H)^+$ 626.3118, found 626.3120.

General procedure A for the addition of arylmagnesium bromide onto the Weinreb amide building blocks 5, 6 and 17: The oven dried two necked round bottom flask was charged with magnesium turnings (3 eq) and a catalytic amount of molecular iodine was added under nitrogen atmosphere. The reaction flask was pre-heated under vacuum to activate the magnesium. Substituted aryl bromide (3 eq) in anhydrous THF was added under stirring into the activated magnesium. After complete consumption of magnesium, the requisite amide (1 eq) in anhydrous THF was added to the reaction mixture at 0 ℃. After 3h, saturated NH_4Cl solution was added and the aqueous layer was extracted with EtOAc. The organic layer was dried over Na_2SO_4 and concentrated in vacuum. The product obtained was purified by silica-gel column chromatography to yield the corresponding ketones.

1-(4-methylphenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-benzyl-*β*-D-glucopyranosyl) ethanone (13a): Same procedure as described above is adopted. Magnesium turnings (0.035 g, 1.44 mmol), 4-bromotoluene (0.18 ml, 1.44 mmol) was converted to the corresponding ArMgBr and amide **5** (0.3 g, 0.48 mmol) was added, to give the compound **13a** after column chromatography on silica gel (EtOAc : hexane 1:9) yielded a white solid (0.078 mg, 76 %); m.p. = 72-74 °C; R_f = 0.5 (EtOAc/Hexane 1:4); $[\alpha]^{25}_D$ 271.3 ° (c 0.4, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ = 2.39 (s, 3H), 3.01–3.10(m, 2H), 3.40–3.46 (m, 2H), 3.64–3.78 (m, 4H), 3.94-3.99 (m, 1H), 4.40 (d, 1H, *J* = 12 Hz), 4.51 (d,1H, *J* = 12.4 Hz), 4.57 (d, 1H, *J* = 10.8 Hz), 4.68 (d, 1H, *J* = 11.2 Hz), 4.81 (d, 1H, *J* = 10.8 Hz), 4.88-4.94 (m, 3H), 7.18-7.33 (m, 22H), 7.75 (d, 2H, *J* = 8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) : δ = 21.6 (CH_3), 40.7 (CH_2), 68.7 (CH_2), 73.4 (CH_2), 74.9 (2 CH_2), 75.5 (CH), 75.5 (CH_2), 78.4 (CH), 79.0 (CH), 81.0 (CH), 87.5 (CH), 127.6 (CH), 127.7 (CH), 127.8 (CH), 127.9 (CH), 127.9 (CH), 128.3 (CH), 128.4 (CH), 128.5 (CH), 128.5 (CH), 128.6 (CH), 129.2 (CH), 135.0 (C), 138.2 (C), 138.3 (C), 138.3 (C), 138.7 (C), 143.8 (C), 197.4 (CO). IR ($CHCl_3$): 1210, 1425**,** 1538, 1684, 2883, 2918 cm^{-1} HRMS: calcd for $C_{43}H_{44}O_6Na$ $(M+Na)^+$ 679.3036, found 679.3025.

1-(4-fluorophenyl)-2-(2′, 3 , 4′, 6′-tetra-*O*-benzyl-*β*-D-glucopyranosyl) ethanone (13b); Building block **5** (0.16 g, 0.256 mmol), magnesium turnings (0.018 g, 0.768 mmol), 1-Bromo-4-Flouro Benzene (0.084 ml, 0.768 mmol) were treated according to the general procedure A to give the title compound **13b**, after column chromatography on silica gel (EtOAc : hexane 1:9) as a semi solid (0.032 g, 77 %); R_f = 0.4 (EtOAc/Hexane 1:4); $[\alpha]^{25}_D$ 8.3 ° (c 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ = 3.02–3.19 (m, 2H), 3.40-3.45 (m, 2H), 3.60-3.80 (m, 5H), 3.942 (m, 1H), 4.426 (t, 1H, *J* = 12.0 Hz), 4.50 (d,1H, *J* = 12.0 Hz), 4.57 (d, 1H, *J* = 10.8 Hz), 4.67 (d, 1H, *J* = 11.2 Hz), 4.81 (d, 1H, *J* = 10.8Hz), 4.88- 4.95 (m, 2H), 7.03-7.31 (m, 22H), 7.85 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.8 (CH_2), 68.7 (CH_2), 73.4 (CH_2), 74.9 (CH_2), 74.9 (CH_2), 75.5 (CH), 75.6 (CH_2), 78.4 (CH), 78.9 (CH), 80.9 (CH), 87.3 (CH), 115.4 (d, CH, J^2 CH-F = 21.5 Hz) , 127.5 (CH), 127.6 (CH), 127.7 (CH), 127.7 (CH), 127.8 (CH), 127.8 (CH), 127.9 (CH), 128.2 (CH), 128.2 (CH), 128.3 (CH), 128.4 (CH), 128.4 (CH), 130.9 (d, J^3 CH-F = 9.2 Hz), 133.7 (C), 137.8 (C), 138.0 (C), 138.1 (C), 138.4 (C), 165.6 (d, J^1 C-F = 253 Hz), 196.1 (CO). IR ($CHCl_3$): 1063, 1231, 1396, 1600, 1665, 2909 cm^{-1}. HRMS: calcd for $C_{42}H_{42}O_6F$ $(M+H)^+$ 661.2965, found 661.2979.

1-(4-chlorophenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-benzyl-*β*-D-glucopyranos-yl) ethanone (13c); Building block **5** (0.3 g, 0.48 mmol), magnesium turnings (0.035 g, 1.44 mmol), 1-bromo-4-chloro benzene (0.275 g, 1.44 mmol) were treated according to the general procedure **A** to give the title compound **13c**, after column chromatography on silica gel (EtOAc : hexane 1:9) as colorless gummy solid (0.081 g, 75 %); R_f = 0.4 (EtOAc/Hexane 1:4); $[\alpha]^{27}_D$ 9.2°(c 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 400MHz): δ = 3.15 (dd, 1H, J^1 = 15.6 Hz, J^2 = 7.6), 3.38 (dd, 1H, J^1 = 15 Hz, J^2 = 5.2 Hz), 3.58-3.68 (m, 4H), 3.75-3.82 (m, 2H), 4.44 (d, 1H, *J* = 12.4 Hz), 4.49 (d, 1H, *J* = 10.8 Hz), 4.57 (dd, 2H, J^1 = 11.6 Hz, J^2 = 5.6 Hz), 4.66 (d, 1H, *J* = 11.6 Hz), 4.78-4.91 (m, 4H), 7.2-7.32 (m, 20H), 7.36 (d, 2H, *J* = 8 Hz), 7.76 (d, 2H, *J*= 8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.8 (CH_2), 68.8 (CH_2), 71.3 (CH), 72.9 (CH), 73.4 (CH_2), 73.5 (CH_2), 74.9 (CH_2), 75.2 (CH_2), 77.6 (CH), 79.3 (CH), 82.0 (CH), 127.9 (CH), 128.0 (CH), 128.0 (CH), 28.1 (CH), 128.2 (CH), 128.2 (CH), 128.5 (CH), 128.6 (CH), 129.1 (CH), 129.8 (CH), 135.6 (C), 138.1 (C), 138.2 (C), 138.4 (C), 138.8 (C), 139.7 (C), 196.0 (CO). IR ($CHCl_3$) 1082, 1274, 1362, 1472, 1588, 1673, 2860, 2907 cm^{-1}. HRMS: calcd for $C_{42}H_{41}O_6ClNa$ $(M+Na)^+$ 699.2489, found 699.2500.

1-(4-methoxyphenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-benzyl-*β*-D-glucopyranosyl) ethanone (13d). Building block **5** (0.1 g, 0.16 mmol), magnesium turning (0.012 g, 0.048 mmol) and 1-bromo-4- methoxy benzene (0.06 g, 0.48 mmol) were treated according to the general procedure **A** to give the title compound **13d**, after column chromatography on silica gel (1:4) as colorless solid (0.80 mg, 75 %), m.p. = 81-83 °C; R_f = 0.3 (EtOAc/Hexane 1:4); $[\alpha]^{27}_D$ -18.2°(c 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ = 3.0-3.11 (m, 2H), 3.41-3.46 (m, 2H), 3.62-3.78 (m,4H), 3.84 (s, 3H, OMe), 3.94-3.99 (m, 1H), 4.41 (d, 1H, *J* = 12.4 Hz), 4.51 (d, 1H, *J* = 12.4 Hz), 4.58 (d, 1H, *J* =10.8 Hz) 4.69 (d, 1H, *J* = 11.2 Hz), 4.81 (d, 1H, *J* = 10.4 Hz), 4.88-4.95 (m, 3H), 6.87 (d, 2H, *J* = 8 Hz), 7.16-7.32 (m, 20H), 7.83-7.85 (m,2H). ^{13}C NMR (100MHz, $CDCl_3$): δ = 40.5 (CH_2), 55.4 (OCH_3), 68.7 (CH_2), 73.4 (CH_2), 74.9 (2xCH_2), 75.5 (CH_2), 75.6 (CH), 78.4 (CH), 79.2 (CH), 81.1 (CH), 87.4 (CH), 113.7 (CH), 127.6 (CH), 127.7 (CH), 127.8 (CH), 127.9 (CH), 127.9 (CH), 127.9 (CH), 128.3 (CH), 128.4 (CH), 128.5 (CH), 128.5

(CH), 130.7 (CH), 138.2 (C), 138.3 (C), 138.7 (C), 163.5 (C), 196.3 (C). IR ($CHCl_3$): 1296, 1426, 1517, 1591, 1653, 2927 cm^{-1} HRMS: calcd for $C_{43}H_{44}O_7Na$ $(M+Na)^+$ 695.2985 found 695.2975.

1-(thiophenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-benzyl-*β*-D-glucopyranosyl) ethanone (13e): building block **5** (0.3 g, 0.48 mmol), magnesium turnings (0.035 g, 1.44 mmol) and 2-bromothiophene (0.140 ml, 1.44 mmol) were treated according to the general procedure **A** to give the title compound **13e**, after column chromatography on silica gel (EtOAc : hexane 1:9) as light yellow color solid (0.130 g, 83 %), m.p. = 95-97 ºC; R_f = 0.4 (EtOAc/Hexane 1:4); $[\alpha]^{27}_D$ 15.3°(c 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400MHz): δ = 2.93 (dd, 1H, J^1 = 15.2 Hz, J^2 = 8 Hz), 3.03 (dd, 1H, J^1 = 15.2 Hz, J^2 = 2 Hz), 3.33-3.38 (m, 2H), 3.57-3.70 (m, 4H), 3.85-3.89 (m, 1H), 4.33 (d, 1H, *J* = 12.4 Hz), 4.43 (d,1H, *J* = 12 Hz), 4.50 (d, 1H, *J* = 10.8 Hz), 4.61 (d, 1H, *J* = 11.2 Hz), 4.74 (d 1H, *J* = 10.8Hz), 4.80-4.87(m, 3H), 7.00 (t, 1H, *J* = 4.4 Hz), 7.09-7.25 (m, 20H),7.52 (d, 2H, *J* = 4.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.7 (CH_2), 68.8 (CH_2), 73.4 (CH_2), 74.9 (CH_2), 74.9 (CH_2), 75.5 (CH_2), 75.6 (CH), 78.4 (CH), 79.0 (CH), 80.9 (CH), 87.3 (CH), 127.5 (CH), 127.6 (CH), 127.7 (CH), 127.7 (CH), 127.8 (CH), 127.9 (CH), 128.1 (CH), 128.2 (CH), 128.3 (CH), 128.4 (CH), 132.3 (CH), 133.6 (CH), 138.2 (C), 138.3 (C), 138.7 (C), 145.0 (C), 190.5 (CO). IR ($CDCl_3$): 1095, 1311, 1451, 1540, 1653, 2843, 2928, 3031 cm^{-1}. HRMS: calcd for $C_{40}H_{40}O_6SNa$ $(M+Na)^+$ 671.2443 found 671.2454.

1-N-methoxy-N-methyl-2-(2′, 3′, 4′, 6′-tetra-*O*-benzyl-*β*-D-galactopyranosyl) acetamide (6). Acid **8** (0.6 g, 1.03 mmol), pivolyl chloride (0.15 ml, 1.23 mmol), *N*,*O* dimethylhydroxyl amine hydrochloride (0.15 g, 1.54 mmol) and triethylamine (0.21 ml, 1.54 mmol) were reacted according to the one step procedure **5**. Purification by column chromatograph on silica, eluting with EtOAc / Hexane (1:3), gave the title compound as a light yellow gum (0.593 g, 92 %). R_f = 0.1 (EtOAc/Hexane 3:7); $[\alpha]^{25}_D$ 189.3° (c 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.64-2.67 (m, 2H), 3.021 (s, 3H, *NMe*), 3.46-3.47 (m, 2H), 3.49 (s, 3H, *OMe*), 3.54 (d, 1H, *J* = 6.4 Hz), 3.58 (dd, 1H, J^1 = 9.2 Hz, J^2 = 2.8 Hz), 3.66 (t, 1H, *J* = 9.2 Hz), 3.75-3.80 (m, 1H), 3.94 (d,1H, *J* = 2.8 Hz), 4.32 (d, 1H, *J* = 12 Hz), 4.37 (d, 1H, *J* = 12 Hz), 4.52-4.60 (m, 3H), 4.66 (d,1H, *J* = 12 Hz), 4.86 (d,1H, *J* = 11.6 Hz), 4.90 (d, 1H, *J* = 11.2 Hz), 7.16-7.28 (m,20H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.8 (CH_2), 61.3 (CH_2), 68.6 (CH_2), 72.22 (CH_2), 73.4 (CH2), 74.0 (CH), 74.6 (CH2), 74.9 (CH2), 76.0 (CH), 76.8 (CH), 78.2 (CH), 84.8 (CH), 127.5 (CH),127.5 (CH), 127.6 (CH), 127.7 (CH), 127.9 (CH), 128.0 (CH), 128.2 (CH), 128.3 (CH), 128.4 (CH), 128.4 (CH), 138.1 (C), 138.4 (C), 138.6 (C), 139.0 (C). IR ($CHCl_3$): 1101, 1370, 1452, 1589, 1649, 2882, 2926 cm^{-1}. HRMS: Calcd for $C_{38}H_{44}O_7N$ $(M+H)^+$ 626.3118, found 626.3107.

1-(4-methylphenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-benzyl-*β*-D-galactopyranosyl) ethanone (14a): Building block **6** (0.08 g, 0.128 mmol), magnesium turnings (0.010 g, 0.384 mmol) and parabromotoluene (0.048 ml, 0.384 mmol) were treated according to the general procedure **A** to give the title compound **14a**, after column chromatography on silica gel (EtOAc : hexane 1:9) as a colorless gum (0.061 g, 73 %); R_f = 0.4 (EtOAc/Hexane 1:4); $[\alpha]^{27}_D$ 7.6° (c 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.37 (S, 3H), 3.10-3.12 (m, 2H), 3.46-3.54 (m,2H, 3.61 (t, 1H, *J* = 6.8 Hz), 3.6 (dd, 1H, J^1 = 9.2 Hz, J^2 = 2.8 Hz), 3.79 (t, 1H, *J* = 9.2 Hz), 3.94-4.02 (m, 2H), 4.34 (d, 1H, *J* = 12 Hz), 4.40 (d, 1H, *J* = 12 Hz), 4.62 (d, 1H, *J* = 11.6 Hz), 4.67 (d, 2H, *J* = 11.2 Hz), 4.75 (d, 1H, *J* = 11.6 Hz), 4.95 (dd, 2H, J^1 = 18.8 Hz, J^2 = 11.6 Hz), 7.18 (d, 2H, *J* = 8 Hz), 7.21-7.37 (m, 20H), 7.73 (d, 2H, *J*= 8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7 (CH_3), 41.2 (CH_2), 68.6 (CH_2), 72.2 (CH_2), 73.4 (CH_2), 73.9 (CH), 74.6 (CH_2), 75,0 (CH_2), 75.8 (CH), 77.0 (CH), 77.9 (CH), 84.9 (CH), 127.7 (CH),127.7 (CH), 128.0 (CH), 128.3 (CH), 128.3 (CH) ,128.5 (CH), 128.5 (CH), 128.5 (CH), 129.2 (CH), 134.9 (C), 138.1 (C) ,138.4 (C), 138.5 (C), 138.9 (C), 143.7 (C), 197.4 (CO). IR ($CHCl_3$): 1113, 1405, 1588, 1644, 2881, 2928 cm^{-1}. HRMS: calcd for $C_{43}H_{44}O_6Na$ $(M+Na)^+$ 679.3036, found 679.3032 .

1-(4-fluorophenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-benzyl-*β*-D-galactopyranosyl) ethanone (14b): Building block **6** (0.08 g, 0.128 m. mol), magnesium turnings (0.010 g, 0.384 m. mol) and 1-bromo-4-flouro benzene (0.042 ml, 0.384 m.mol) were treated according to the general procedure **A** to give the title compound **14b**, after column chromatography on silica gel (EtOAc : hexane 1:9) as a semi solid (0.068 g, 81 %); R_f = 0.4 (EtOAc/Hexane 1:4); $[\alpha]^{27}_D$ 15.3° (c 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.08-3.09 (m, 2H), 3.45-3.53 (m, 2H), 3.61 (t, 1H, *J* = 6.4 Hz), 3.67 (dt, 1H, J^1 = 9.2 Hz, J^2 = 1.2 Hz), 3.79 (t, 1H, J= 9.2 Hz), 3.92-4.02 (m, 2H), 4.35 (d, 1H, *J* = 11.6 Hz), 4.41 (d, 1H, *J* = 12 Hz), 4.62 (d, 1H, *J* = 11.2 Hz), 4.67 (dd, 2H, J^1 = 11.6 Hz , J^2 = 4 Hz), 4.76 (d, 1H, *J* = 11.6 Hz), 4.96 (dd, 2H, J^1 = 22 Hz, J^2 = 11.6 Hz), 7.01-7.06 (m, 2H), 7.21-7.37 (m, 20H), 7.82-7.85 (m,2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.3 (CH_2), 68.7 (CH_2), 72.2 (CH_2), 73.4 (CH_2), 73.9 (CH), 74.6 (CH2), 75.0 (CH2), 75.7 (CH), 77.1 (CH), 77.8 (CH), 84.9 (CH), 115.4 (d, CH, $J^{2CH\text{-}F}$ = 21.6 Hz), 127.6 (CH), 127.73 (CH), 127.8 (CH), 128. 1 (CH), 128.2 (CH), 128.39 (CH), 128.4 (CH), 128.4 (CH), 130.1 (d, CH, $J^{3\ CH\text{-}F}$ = 9.3 Hz), 133.8 (C), 138.1(C), 138.3 (C), 138.4 (C), 138.8 (C), 165.7 (d, C, $J^{1\ C\text{-}F}$ = 253 Hz), 196.2 (CO). IR ($CHCl_3$): 1232, 1320, 1581, 1675, 2909 cm^{-1}. HRMS: calcd for $C_{42}H_{42}O_6F$ $(M+H)^+$ 661.2965, found 661.2956.

1-(4-chlorophenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-benzyl-*β*-D-galactopyranosyl) ethanone (14c): Building block **6** (0.128 g, 0.204 m.mol), magnesium turning (0.015 g, 0.614 mmol) and 1-bromo-4-chloro benzene (0.117 g, 0.614 mmol) were treated according to the general procedure **A** to give the title compound **14c**, after column chromatography on silica gel (EtOAc : hexane 1:9) as a colorless gum (0.110 g, 79%); R_f = 0.4 (EtOAc/Hexane 1:4); $[\alpha]^{26}_D$ 233.4° (c 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400MHz): δ = 3.06-3.08 (m, 2H), 3.44-3.53 (m, 2H), 3.60 (t, 1H, *J* = 6.8 Hz), 3.66 (dd, 1H, J^1 = 9.2 Hz, J^2 = 2.8 Hz), 3.78 (t, 1H, *J* = 9.6 Hz), 3.90-3.95 (m, 1H), 4.01 (d, 1H, *J* = 2 Hz), 4.35 (d, 1H, *J* = 11.6 Hz), 4.40 (d, 1H, *J* = 12 Hz), 4.61 (d, 1H, *J* = 11.6 Hz), 4.66 (dd, 2H, J^1 = 11.6 Hz, J^2 = 6.0 Hz), 4.75 (d, 1H, *J* = 11.6 Hz), 4.92 (d, 1H, *J* = 11.6 Hz), 4.98 (d, 1H, *J* = 11.2 Hz), 7.21—7.35 (m, 22H), 7.74 (d, 2H, *J* = 8.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.5 (CH_2), 68.6 (CH_2), 72.2 (CH2), 73.4 (CH2), 73.9 (CH), 74.6 (CH2), 75.0 (CH2), 75.7 (CH), 77.1 (CH), 77.8 (CH), 84.9 (CH),127.8 (CH), 127.9 (CH), 128.1 (CH), 128.3 (CH),128.4 (CH),128.6 (CH), 128.7 (CH), 128.9 (CH), 129.9 (CH), 135.9 (CH), 138.2 (C), 138.4 (C), 138.5 (C), 138.9 (C), 139.5 (CH), 196.7 (CO). IR ($CHCl_3$): 1095, 1216, 1590, 1679, 2923, 3021 cm^{-1}. HRMS: calcd for $C_{42}H_{41}O_6ClNa$ $(M+Na)^+$ 700.2568, found 700.2581.

1-(4-methoxyphenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-benzyl-*β*-D-galactopyranosyl) ethanone (14d): Building block **6** (0.070 g, 0.112 mmol), magnesium turnings (0.008 g, 0.336 mmol) and 1-bromo-4- methoxy benzene (0.043 ml, 0.336 mmol) were treated according to the general procedure A to give the title compound **14d**, after column chromatography on silica gel (1:4) as a colorless gum (0.034 g, 79 %); $[\alpha]^{25}_D$ 294.7° (c 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.08-3.10 (m, 2H), 3.47-3.53 (m, 2H), 3.61 (t, 1H, *J* = 6.8 Hz), 3.68 (dd, 1H, J^1 = 9.2 Hz, J^2 = 2.8 Hz), 3.79 (d, 1H, *J* = 2.4 Hz), 3.84 (s, 3H, OMe), 3.95-3.98 (m, 1H), 4.03 (d, 1H, *J* = 2.0 Hz), 4.34 (d, 1H, *J* = 11.6 Hz), 4.40 (d, 1H, *J* = 11.6 Hz), 4.63 (d, 1H, *J* = 11.6 Hz), 4.67 (d, 2H, *J* = 11.6), 4.76 (d, 1H, *J* = 11.6 Hz), 4.93 (d, 1H, *J* = 11.6 Hz), 4.98 (d, 1H, *J* = 11.2), 6.86 (d,2H, *J* = 8.8 Hz), 7.23-7.36 (m, 20H), 7.82 (d, 2H, *J* = 9.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.0 (CH2), 55.5 (OMe), 68.7 (CH_2), 72.2 (CH2), 73.4 (CH2), 73.8 (CH), 74.6 (CH2), 75.0 (CH2), 75.8 (CH), 77.0 (CH), 77.9 (CH), 84.9 (CH),113.5 (CH), 127.7 (CH), 127.8 (CH), 128.0 (CH),128.3 (CH), 128.3 (CH), 128.5 (CH),128.5 (CH), 130.7 (CH), 138.1 (C), 138.4 (C), 138.4 (C), 138.8 (C), 163.4 (C), 196.3 (CO). IR ($CHCl_3$): 1248, 1458, 1509, 1599, 1653, 2922 cm^{-1}. HRMS: calcd for $C_{43}H_{44}O_7Na$ $(M+Na)^+$ 695.2985 found 69.2961.

1-(thiophenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-benzyl-*β*-D- galactopyranosyl) ethanone (14e): Building block **6** (0.3 g, 0.48 mmol), magnesium turnings (0.035 g, 1.44 mmol) and 2-bromothiophene (0.140 ml, 1.44 mmol) were treated according to the general procedure **A** to give the title compound **14e**, after column chromatography on silica gel to provide the title compound as a light yellow color gum (0.130 g, 83 %). R_f = 0.4 (EtOAc/ hexane 1:4); $[\alpha]^{25}_D$ 18.4 ° (c 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.05 (dd, 1H, J^1 = 16.0 Hz, J^2 = 8 Hz), 3.12 (dd, 1H, J^1 = 12.0 Hz, J^2 = 2.8 Hz), 3.46-3.54 (m, 2H), 3.59-3.62 (m, 1H), 3.67 (dd, 1H, J^1 = 9.2 Hz, J^2 = 2.8 Hz), 3.78 (t, 1H, *J* = 9.2 Hz), 3.93-3.98 (m, 1H), 4.01-4.02 (m, 1H), 4.60-4.77 (m, 4H), 4.75 (d, 1H, *J* = 11.6 Hz), 4.92 (d,H, *J* = 11.6 Hz),

4.98 (d, 1H, *J* = 11.2 Hz), 7.05 (dd, 1H, J^1 = 4.8 Hz, J^2 = 4.0 Hz), 7.22-7.37 (m, 20H),7.56-7.59 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.0 (CH_2), 68.6 (CH_2), 72.2 (CH_2), 73.4 (CH_2), 73.9 (CH_2), 74.6 (CH_2), 75.0 (CH), 75.9 (CH), 77.1 (CH), 77.8 (CH), 84.9 (CH), 127.6 (CH), 127.7 (CH), 127.9 (CH), 128.1 (CH), 128.2 (CH), 128.3 (CH), 128.4 (CH), 132.3 (2xCH), 133.6 (CH), 138.0 (C), 138.2 (C), 138.3 (C), 138.7 (C), 144.8 (C), 190.4 (CO). IR ($CHCl_3$): 1342, 1400, 1588, 1648, 2921 cm^{-1}. HRMS: calcd for $C_{40}H_{40}O_6SNa$ $(M+Na)^+$ 671.2443 found 671.2454.

1-(3, 4, 5-trimethoxyphenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-benzyl-*β*-D-gluco-pyranosyl) ethanone (15): A oven dried two necked round bottom flask was charged with magnesium turnings (0.063 g, 2.6 mmol), catalytic amount of molecular iodine under nitrogen atmosphere. 1-bromo-3, 4, 5-trimethoxybenzene (0.7 g, 2.6 mmol) in anhydrous THF was added into the activated magnesium. To that solution catalytic amount of MeI was added at 50 ºC, and heating was continued until the colour change of the reaction mixture. After complete consumption of magnesium, building block **5** (0.4 g, 0.71 mmol) in anhydrous THF was added to reaction mixture. After 3h saturated NH_4Cl solution was added and the aqueous layer was extracted with EtOAc, the organic layer was dried over Na_2SO_4 and concentrated in vacuum. The crude residue was purified by column chromatography on silica gel to yield the title compound **15** (0.37g, 75%) as color less gum. R_f = 0.3 (EtOAc:hexane 3:7); $[\alpha]^{26}_D$ 97.5° (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ= 3.04 (dd, 1H, J^1 = 16 Hz, J^2 = 8 Hz), 3.12 (dd, 1H, J^1 = 16 Hz, J^2 = 3.2 Hz), 3.41-3.46 (m, 2H), 3.65- 3.66 (m, 2H), 3.7 (d, 1H, *J* = 9.2 Hz), 3.76 (d, 1H, *J* = 8.8 Hz), 3.82 (s, 6H, 2xOMe), 3.89 (s, 3H, OMe), 3.95-4.0 (m, 1H), 4.41 (d, 1H, *J* = 12.0 Hz), 4.51 (d, 1H, *J* = 12.4 Hz), 4.58 (d, 1H, *J* =10.8 Hz) 4.69 (d, 1H, *J* = 11.2 Hz), 4.81 (d, 1H, *J* = 10.8 Hz), 4.88-4.95 (m, 3H), 7.13 (s, 2H), 7.15-7.18 (m ,2H), 7.23-7.32 (m,18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.7 (CH_2), 56.3 (2xOCH_3), 60.9 (OMe), 68.9 (CH_2), 73.4 (CH_2), 74.8 (2xCH_2), 74.9 (CH_2), 75.5 (CH_2), 75.5 (CH), 78.5 (CH), 79.0 (CH), 81.0 (CH), 87.4 (CH), 106. (CH), 127.6 (CH), 127.7 (CH), 127.7 (CH), 127.8 (CH), 127.9 (CH), 128.2 (CH), 128.3 (CH), 128.4 (CH), 128.5 (CH), 128.6 (CH), 132.6 (C), 138.1 (C), 138.1 (C), 138.2 (C), 138.5 (C), 142.6 (C), 153.0 (C), 196.5 (C). IR ($CHCl_3$): 1217, 1342 1460, 1510, 1568, 1653, 2922 cm^{-1}. HRMS: calcd for $C_{45}H_{49}O_9$ $(M+H)^+$ 733.3377 found 733.3385.

1-*N*-methoxy-*N*-methyl-2-(2′, 3′, 4′, 6′-tetra-*O*-methoxy methyl-*β*-D glu-copyranosyl) acetamide (17): To a stirred solution of building block **5** in THF was added Pd-C (10 mol %) at rt. The reaction mixture was stirred under an atmosphere of H_2 with balloon pressure until starting material was disappeared on TLC. The mixture was filtered through celite and the solvent was removed in vacuo. The resultant tetrol was used for the next step without further purification.

In a flame dried two necked round bottom flask under nitrogen atmosphere, tetrol (0.591 g, 2.238 mmol) was combined with anhydrous dichloromethane (10 mL), upon cooling the suspension on a ice bath (0 ºC) diisopropylethylamine (2.53 ml, 18.0 mmol) was added drop wise. The suspension was stirred at the same temperature for an additional 10 min and then chloromethylmethylether (2.575 mL, 33.59 mmol) was added slowly. After stirring for another 15 min at the same temperature tetrabutylammoniumiodide (3.324 g, 8.9 mmol) was added and then solution was allowed to attain room temperature. The reaction was stirred in darkness for 72 hours, the solution gradually turned red in color and was cooled to 0 ºC, saturated NH_4Cl (50 ml) solution was added and the organic layer was extracted with dichloromethane (3x100 ml), dried over Na_2SO_4, and concentrated to give the **17** as a yellow color oil (0.87 g, 92% yield). R_f = 0.2 (EtOAc/ hexane 1:1, 2,4 DNP active); $[\alpha]^{26}_D$ 233.4° (c 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): 2.76-2.89 (m, 2H), 3.19 (s, 3H, *NMe*), 3.32 (s, 3H, OMe), 3.34-3.38 (m, 1H), 3.39 (s, 3H), 3,41 (s, 3H), 3.44 (s, 3H), 3.51 (t, 1H, *J* = 11.5 Hz), 3.60-3.64 (m, 1H), 3.66 (dd, 1H, J^1 = 10.5 Hz, J^2 = 4.5 Hz), 3.70 (s, 3H, OMe), 3.79-3.87 (m, 2H), 4.61-4.64 (m, 2H), 4.68-4.75 (m, 2H), 4.80-4.84 (m, 2H), 4.86-4.93 (m, 2H), 5.04 (ddd, 1H, J^1 = 31.5 Hz, J^2 = 7.0 Hz, J^3 = 4.0 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 32.1 (*NCH*$_3$), 34.7 (CH_2), 55.3 (OMe), 55.5 (OMe), 56.4 (OMe), 56.5 (OMe), 56.6 (OMe), 61.3 (OMe), 66.6 (CH_2), 75.3 (CH) 77.1 (CH), 78.2 (CH), 80.6 (CH), 84.5 (CH), 96.8 (CH_2), 98.5 (CH_2), 98.8 (2xCH_2): IR ($CHCl_3$): 1053, 1134, 1248, 1458, 1653, 2919 cm^{-1}. HRMS: calcd for $C_{18}H_{35}NO_{11}Na$ $(M+Na)^+$ 464.2108 found 464.2114.

1-(3, 4, 5-trimethoxyphenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*- methoxy methyl-*β*-D-glucopyranosyl) ethanone (18): Building block **17** (0.850 g, 1.9 mmol), magnesium turnings (0.191g, 7.962 mmol), 1-bromo-3, 4, 5-trimethoxybenzene (1.96 g, 7.962 mmol) were treated according to the procedure mentioned for compound **15.** The crude residue was purified by column chromatography on silica gel to yield the title compound **18** (0.65 g, 59.6%) as a colorless gum. R_f = 0.5 (EtOAc/hexane 1:1); $[\alpha]^{26}_D$ 19.5° (c 1.0, $CHCl_3$); ^{1}H NMR (CDCl3, 500 MHz) δ = 3.22-3.29 (m, 4H), 3.31- 3.35 (m, 4H), 3.37-3.41 (m, 4H), 3.43-3.45 (m, 4H), 3.53 (t, 1H, *J* = 12.0 Hz), 3.61-3.68 (m, 2H), 3.76 (dd, 1H, J^1 = 14.0 Hz, J^2 = 2.5 Hz), 3.91 (s, 9H), 3.95-4.02 (m, 1H), 4.57 (dd, 2H, J^1 = 14.0 Hz, J^2 = 8.0 Hz), 4.71-4.74 (m, 2H), 4.83-4.87 (m, 3H), 4.92 (d, 1H, *J* = 8.5 Hz), 7.24 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 40.8 (CH_2), 55.2 (OMe), 56.2 (OMe), 56.3 (2 x OMe), 56.5 (OMe), 56.5 (OMe), 60.9 (OMe), 66.4 (CH_2), 74.9 (CH), 77.0 (CH), 78.2 (CH), 80.7 (CH), 84.4 (CH), 96.8 (CH_2), 98.5 (CH_2), 98.7 (CH_2), 98.8 (CH_2), 105.7(CH), 132.5 (C),142.5 (C),152.99 (C), 196.5 (CO)). IR ($CHCl_3$): 1076, 1143, 1206, 1406, 1509, 1573, 1603, 2879 cm^{-1}. HRMS**:** calcd for $C_{25}H_{40}O_{13}Na$ $(M+Na)^+$ 571.2367 found 571.2347.

1-(4-methoxyphenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-methoxy methyl-*β*-D-gluco pyranosyl) ethanone (20a): An oven dried flask was charged with magnesium turnings (0.100 g, 4.172 mmol), catalytic amount of molecular iodine under nitrogen atmosphere. A solution of 1-bromo-4-methoxybenezene (0.523 g, 4.172 mmol), in anhydrous THF (8 mL) was added under stirring. After 10 min the reaction mixture got strongly self - heated, stirring was continued for further 1 hour, then the solution of crude building block **17** (0.460 g, 1.043 mmol) in anhydrous THF was added to the reaction mixture at 0 ºC. After consumption of starting material (monitored by TLC), the reaction mixture was quenched by adding NH_4Cl (20 mL). The aqueous phase was extracted with EtOAc (3x50 mL), the organic phase was washed with brine (50 mL), dried (Na_2SO_4), concentrated, and purified by silica gel column chromatography to give the title compound **20a** (0.340 g, 68%) as a colorless gum; R_f = 0.3 (EtOAc/hexane 1:1); $[\alpha]^{27}_D$ -21.2° (c 0.5, $CHCl_3$); ^{1}H NMR (CDCl3, 500 MHz): δ= 3.21-3.26 (m, 4H), 3.30-3.33 (m, 4H), 3.36-3.43 (m, 5H), 3.44 (S, 3H), 3.52 (t, 1H, *J* = 9.0 Hz), 3.61 (dd, 1H, J^1 =11.0 Hz, J^2 = 4.5 Hz), 3.65 (t, 1H, *J* = 9.0 Hz), 3.74 (dd, 1H, J^1 = 11.0 Hz, J^2 = 2.0 Hz), 3.86 (S, 3H), 3.97-4.01 (m, 1H), 4.55 (dd, 2H, J^1 = 14.5 Hz, J^2 = 6.5 Hz), 4.73 (dd, 2H, J^1 = 11.5 Hz, J^2 = 6.5 Hz), 4.82-4.85 (m, 3H), 4.91 (d, 1H, J = 6.5 Hz), 6.92 (d, 2H, *J* = 9.0 Hz), 7.95 (d, 2H, *J* = 9.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 40.7 (CH_2), 55.2 (OMe), 55.5 (OMe), 56.4 (OMe), 56.5 (OMe), 56.6 (OMe), 66.5 (CH_2), 75.0 (CH) 77.0 (CH), 78. 2 (CH), 80.9 (CH), 84.4 (CH), 96.7 (CH_2), 98.4 (CH_2), 98.7 (CH_2), 98.8 (CH_2), 113.6 CH), 130.5 (CH), 163.4 (C), 196.4 (CO). IR ($CHCl_3$): 1045, 1160, 1270, 1334, 1441, 1513, 1597, 1631, 2901 cm^{-1}. HRMS: calcd for $C_{23}H_{36}O_{11}Na$ $(M+Na)^+$ 511.2155 found 511.2134.

1-(4-chlorophenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-methoxy methyl-*β*-D-gluco pyranosyl) ethanone (20b): Building block **17** (0.430 g, 0.995 mmol), magnesium turnings (0.093 g, 3.90 mmol), 1-bromo-4-chlorobenzene (0.745 g, 3.90 m. mol) were treated according to the procedure in **20a** to give the title compound **20b**, after column chromatography on silica gel as a color less syrup (0.320g, 70%). R_f = 0.6 (EtOAc/hexane 1:1); $[\alpha]^{27}_D$ 17.7° (c 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): δ= 3.20-3.26 (m, 4H), 3.31-3.34 (m, 4H), 3.36-3.42 (m, 5H), 3.34 (s, 3H), 3.51 (t, 1H, *J* = 9.0 Hz), 3.60 (dd, 1H, J^1 =11.0 Hz, J^2 = 4.5 Hz), 3.64 (t, 1H, *J* = 9.0 Hz), 3.73 (dd, 1H, J^1 = 11.0 Hz, J^2 = 2.0 Hz), 3.94-3.98 (m, 1H), 4.55 (dd, 2H, J^1 = 13.5 Hz, J^2 = 6.5 Hz), 4.71 (dd, 2H, J^1 = 9.0 Hz, J^2 = 6.5 Hz), 4.82-4.86 (m, 3H), 4.90 (d, 1H, *J* = 6.5 Hz), 7.42 (d, 2H, *J* = 8.5 Hz), 7.90 (d, 2H, *J* = 9.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 41.2 (CH_2), 55.3 (OMe), 56.3 (OMe), 56.5 (OMe), 56.6 (OMe), 66.5 (CH_2), 74.9 (CH), 77.0 (CH), 78.3 (CH), 80.8 (CH), 84.3 (CH), 96.7 (CH_2), 98.5 (CH_2), 98.7 (CH_2), 98.9 (CH_2), 128.8 (CH), 129.6 (CH), 135.7 (C), 139.5 (C), 196.8 (CO). IR ($CHCl_3$): 886, 1038,

1167,1276, 1491, 1597, 1687, 2978 cm^{-1}. HRMS: calcd for $C_{22}H_{33}O_{10}ClNa$ $(M+Na)^+$ 515.1600 found 515.1638.

1-(4-*O*-methoxymethylphenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-methoxy methyl-*β*-D glucopyranosyl) ethanone (20c): Into a dried flask heated in an oven was charged with magnesium turnings (0.145 g, 6.009 mmol), activated by molecular iodine and added anhydrous THF (5 mL) with syringe. During stirring the solution of 1-bromo-4-methoxymethyl benzene (0.745 g, 6.01 mmol) in anhydrous THF was added at 50 °C. Reaction flask was strongly self-heated, stirring was continued for 2 h at same temperature, then the solution of crude building block **17** (0.460 g, 1.043 mmol) in anhydrous THF was added to the reaction mixture at 0 ºC. After completed (monitored by TLC), the reaction mixture was quenched by adding NH_4Cl (20 ml). The aqueous phase was extracted with EtOAc (3x50 ml), the organic phase was washed with brine (50 mL), dried (Na_2SO_4), concentrated, and purified by silica gel column chromatography to give the title compound **20c** as colorless syrup (0.380 g, 61%). R_f = 0.5 (EtOAc/hexane 1:1); $[\alpha]^{27}_D$ 31.1° (c 0.5, $CHCl_3$); ^{1} H NMR (CDCl3, 500 MHz): δ = 3.19-3.26 (m, 4H), 3.31-3.39 (m, 5H), 3.41-3.43 (m, 4H), 3.44 (s, 3H), 3.48 (s, 3H), 3.52 (t, 1H, J = 9.5 Hz), 3.62 (dd, 1H, J^1 = 11.5 Hz, J^2 = 4.5 hz), 3.65 (t, 1H, J = 9.0 Hz), 3.74 (dd, 1H,J^1 = 11.5 Hz, J^2 = 2.0 Hz), 3.97-4.01 (m, 1H), 4.57 (dd, 2H, J^1 = 14.5 Hz, J^2 = 6.6 Hz),4.73 (dd, 2H, J^1 = 11.5 Hz, J^2 = 6.5 Hz) 4.82-4.87 (m, 3H), 4.917 (d, 1H, J = 7.0 Hz), 5.23 (s, 2H), 7.06 (d, 2H, J = 9.0 Hz), 7.94 (d, 2H, J = 9.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 40.8 (CH_2), 55.2 (OMe), 56.2 (OMe), 56.3 (OMe), 56.5 (OMe), 56.5 (OMe), 66.4 (CH_2), 75.0 (CH), 77.0 (CH), 78.2 (CH), 80.8 (CH), 84.4 (CH), 94.0 (CH_2), 96.7 (CH_2), 98.5 (CH_2), 98.7 (CH_2), 98.8 (CH_2), 115.7 (CH), 130.4 (CH), 131.4 (C), 161.1 (C), 196.4 (CO). IR ($CHCl_3$): 1038, 1167, 1276, 1491, 1597, 1687, 2978 cm^{-1} HRMS: calcd for $C_{24}H_{38}O_{12}Na$ $(M+Na)^+$ 541.2261 found 541.2261.

1-(4-fluorophenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-methoxy methyl-*β*-D-gluco-pyranosyl) ethanone (20d): Building block **17** (0.440 g, 0.997 mmol), magnesium turnings (0.091 g, 3.99 mmol), 1-bromo-4-fluorobenzene (0.438 mL, 3.99 mmol) were treated according to the procedure in **20a** to give the title compound **20d** as colorless syrup (0.310g, 68.43%) after silica gel column chromatography. R_f = 0.3 (EtOAc:hexane 3:7); $[\alpha]^{26}_D$ 371.1°(c 0.3, $CHCl_3$); ^{1} H NMR (CDCl3, 500 MHz): δ = 3.22-3.26 (m, 4H), 3.33-3.366 (m, 4H), 3.38-3.40 (m, 5H), 3.44 (s, 3H), 3.51 (t, 1H, J = 9.5 Hz), 3.59-3.66 (m, 2H), 3.73 (d, 1H, J = 6.5 Hz), 3.96 (t, 1H, J = 9.0 Hz), 4.56 (dd, 2H, J^1 = 12.5 Hz, J^2 = 6.0 Hz), 4.72 (t, 2H, J = 7.5 Hz), 4.82-4.85 (m, 3H), 4.90 (d, 1H, J = 6.0 Hz), 7.115 (t, 2H, J = 8.0 Hz), 7.99 (t, 2H, J = 6.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 41.0 (CH_2), 55.2 (OMe), 56.3 (OMe), 56.5 (OMe), 56.5 (OMe), 66.4 (CH_2), 74.9 (CH), 77.0 (CH), 78.3 (CH), 80.8 (CH), 84.4 (CH), 96.7 (CH_2), 98.5 (CH_2), 98.7 (CH_2), 98.9 (CH_2), 115.6 (d, CH, J^2 = 21.75 Hz), 130.9 (d, CH, J^3 = 9.3 Hz), 133.8 (C), 165.7 (d, C, J^1 = 253 Hz), 196.3 (CO). IR ($CHCl_3$): 967, 1153, 1298, 1456, 1569, 1653, 2913 cm^{-1}. HRMS: calcd for $C_{22}H_{33}FO_{10}K$ $(M+K)^+$ 515.1695 found 515.1683.

1-(3, 4-dichlorophenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-methoxy methyl-*β*-D-glucopyranosyl) ethanone (20e): Building block **17** (0.460 g, 1.043 mmol), magnesium turnings (0.100 g, 4.172 mmol), 1-bromo-3,4-dichlorobenzene (0.535 g, 4.172 mmol) were treated according to the procedure **20a** to give the title compound **20e**, after column chromatography on silica gel yielded as a colorless syrup (0.350 g, 67.73%). R_f = 0.4 (EtOAc:hexane 3:7); $[\alpha]^{27}_D$ 14.1°(c 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.21 (dd, 1H, J^1 =16.0 Hz, J^2 = 8.0 Hz), 3.27 (s, 3H, OMe), 3.32- 3.36 (m, 5H), 3.38- 3.43 (m, 4H), 3.44 (s, 3H, OMe), 3.52 (t, 1H, J = 9.0 Hz), 3.60 (dd, 1H, J^1 = 11.5 Hz, J^2 = 5.0 Hz), 3.64 (t, 1H, 9.0 Hz), 3.73 (dd, 1H, J^1 = 11.0 Hz, J^2 = 2.0 Hz), 3.91- 3.95 (m, 1H), 4.56 (dd, 2H, J^1 = 14.5 Hz, J^2 = 5.5 Hz), 4.72 (t, 2H, J = 6.5 Hz), 4.82- 4.85 (m, 3H), 4.90 (d, 1H, J = 7.0 Hz), 7.53 (d, 1H, J = 8.5 Hz), 7.78 (dd, 1H, J^1 = 8.0 Hz, J^2 = 2.0 Hz), 8.04 (d, 1H, J = 2.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 41.2 (CH_2), 55.3 (OMe), 56.3 (OMe), 56.6 (2×OMe), 66.5 (CH_2), 74.9 (CH), 76.9 (CH), 78.3 (CH), 80.8 (CH), 84.2 (CH), 96.7 (CH_2), 98.5 (CH_2), 98.7 (CH_2), 98.9 (CH_2), 127.3 (CH), 130.3 (CH), 130.6 (CH), 133.2 (C),137.0 (C),137.6 (C), 195.9 (CO). IR ($CHCl_3$): 886, 961, 1061, 1189,1233, 1481, 1562, 1683, 2952 cm^{-1}. HRMS: calcd for $C_{22}H_{32}O_{10}Cl_2Na$ $(M+Na)^+$ 549.1270 found 549.1268.

1-(3, 4-dimethoxyphenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-methoxy methyl-*β*-D-glucopyranosyl) ethanone (20f): An oven dried two necked flask was charged with magnesium turnings (0.145 g, 6.009 mmol). LiCl (0.153 g in 5 ml anhydrous THF) was added and the magnesium was activated with *i*Bu_2AlH (0.12 ml, 1 M in toluene, 0.12 mmol). After stirring for 10 min, 1-bromo-3, 4-dimethoxybenzene (0.846 ml, 6.009 m.mol) in anhydrous THF (7 ml) was added and stirring was continued for 1h. The suspension was cooled to 0 ºC whereupon the building block **17** (0.530 g, 1.201 mmol) was added in anhydrous THF. The reaction mixture was allowed to warm to 25 ºC and the stirring was continued until the starting material got over (as monitored by TLC). The reaction mixture was quenched with saturated NH_4Cl (50 ml) solution and the resulting mixture was extracted with EtOAc (3x 100 ml). The combined organic layer was dried over Na_2SO_4, concentrated in vacuo and the crude residue was purified by column chromatography on silica gel to give the title compound **20f** (0.380 g, 61%) as a colorless gum. R_f = 0.4 (EtOAc/ hexane 1:1); $[\alpha]^{27}_D$ 19.1°(c 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.1- 3.2 (m, 4H), 3.30- 3.35 (m, 4H), 3.38-3.43 (m, 5H), 3.44 (s, 3H, OMe), 3.52 (t, 1H, J= 9.0 Hz), 3.62 (dd, 1H, J^1 = 12.5 Hz, J^2 = 5.0 Hz), 3.65 (t, 1H, 9.0 Hz), 3.73 (d, 1H, J = 11.5), 3.92-3.93 (m, 6H), 3.9 (t, 1H, J = 9.0 Hz), 4.57 (dd, 2H, J^1 = 14.0 Hz, J^2 = 6.5 Hz), 4.7-4.7 (m, 2H), 4.82- 4.85 (m, 3H), 4.90 (d, 1H, J = 6.5 Hz), 6.8 (d, 1H, J = 8.5 Hz), 7.5 (s, 1H), 7.59 (d, 1H, J = 2.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 40.6 (CH_2), 55.2 (OMe), 55.9 (OMe), 56.1 (OMe), 56.3 (OMe), 56.5 (OMe), 56.5 (OMe), 66.4 (CH_2), 75.0 (CH), 77.0 (CH), 78.2 (CH), 80.8 (CH), 84.4 (CH), 96.7 (CH_2), 98.5 (CH_2), 98.7 (CH_2), 98.8 (CH_2), 109.9 (CH), 110.2 (CH), 123.0 (CH), 130.6 (C),149.0 (C),153.3 (C), 196.414 (CO). IR ($CHCl_3$): 1051, 1125, 1263, 1442, 1589, 1663, 2928 cm^{-1}. HRMS: calc for $C_{24}H_{38}O_{12}Na$ $(M+Na)^+$ 541.2261 found 541.2274.

1-(3, 4-difluorophenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-methoxy methyl-*β*-D-glucopyranosyl) ethanone (20g): Building block **17** (0.550 g, 1.247 mmol), magnesium turnings (0.119 g, 4.98 mmol) and 1-bromo-3,5-difluorobenzene (0.574 mL, 4.172 mmol) were treated according to the procedure **20a** to give the title compound **20g**, after column chromatography on silica gel (EtOAc/hexane 3:7), as a colorless syrup (0.350 g, 60%); $[\alpha]^{26}_D$ 210°(c 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): δ= 3.2 (dd, 1H, J^1 =16.0 Hz, J^2 = 8.0 Hz), 3.2 (s, 3H, OMe), 3.3- 3.3 (m, 4H), 3.37- 3.43 (m, 5H), 3.44 (s, 3H, OMe), 3.52 (t, 1H, J = 9.0 Hz), 3.61 (dd, 1H, J^1 = 11.5 Hz, J^2 = 5.0 Hz), 3.64 (t, 1H, J = 9.0 Hz), 3.74 (dd, 1H, J^1 = 11.0 Hz, J^2 = 2.0 Hz), 3.91-3.95 (m, 1H), 4.58 (dd, 2H, J^1 = 14.5 Hz, J^2 = 5.5 Hz), 4.72 (t, 2H, J = 6.5 Hz), 4.81- 4.87 (m, 3H), 4.90 (d, 1H, J = 7.0 Hz), 7.005 (tt, 1H, J^1 = 8.5 Hz, J^2 = 2.0 Hz), 7.46-7.48 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 41.3 (CH_2), 55.2 (OMe), 56.3 (OMe), 56.5 (2xOMe), 66.4 (CH_2), 74.9 (CH), 76.9 (CH), 78.3 (CH), 80.8 (CH), 84.4 (CH), 96.7 (CH_2), 98.5 (CH_2), 98.7 (CH_2), 98.9 (CH_2), 118.2 (t, CH, J = 25 Hz), 111.2 (dd, CH, J^1 = 19.8 Hz, J^2 = 6.3 Hz), 140.3 (d, C, J = 7.2 Hz), 162.9 (dd, C, J^1 = 249 Hz, J^2 = 11.8 Hz), 195.6 (CO). IR ($CHCl_3$): 971, 1153, 1262, 1413, 1563, 1653, 2913 cm^{-1}. HRMS: calcd for $C_{22}H_{32}O_{10}F_2$ $(M+Na)^+$ 517.1861 found 517.1846.

1-(3, 4, 5-trichlorophenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-methoxy methyl-*β*-D-glucopyranosyl) ethanone (20h):

An oven dried two necked round bottom flask was charged with magnesium turnings (0.216 g, 9.04 mmol), under nitrogen atmosphere. 1-bromo-3,4,5-trichlorobenzene (1.18 g, 4.53 mmol) in anhydrous THF was added into the activated magnesium. To that solution 1,2-dibromoethane (0.390 mL, 4.53 mmol) was added at 50 ºC, heating was continued until the complete consumption of magnesium. Building block **17** (0.5 g, 1.13 mmol) in anhydrous THF was added to reaction mixture. After 3h saturated NH_4Cl solution was added and the aqueous layer was extracted with EtOAc, the organic layer was dried over Na_2SO_4 and concentrated in vacuum. The crude residue was purified by column chromatography on silica gel to yield title compound as a color less gum. R_f = 0.5 (EtOAc:hexane 1:1); $[\alpha]^{27}_D$ -61.5° (c 0.8, $CHCl_3$); ^{1}H NMR (CDCl3, 400

MHz): δ = 3.17-3.23 (m, 1H), 3.28 (s, 3H, OMe), 3.31- 3.68 (m, 4H), 3.41(s, 3H, OMe), 3.44 (s, 3H, OMe), 3.49-3.54 (m, 1H), 3.58-3.66 (m, 2H), 3.71-3.79 (m, 2H), 3.84-3.92 (m, 1H), 4.55-4.65 (m, 2H), 4.69-4.77 (m, 3H), 4.81-4.87 (m, 3H), 4.89-4.93 (m, 1H), 7.95 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.0 (CH_2), 55.2 (OMe), 56.3 (OMe), 56.5 (2 x OMe), 66.4 (CH_2), 74.9 (CH), 76.7 (CH), 78.2 (CH), 80.7 (CH), 84.1 (CH), 96.8 (CH_2), 98.5 (CH_2), 98.7 (CH_2), 98.8 (CH_2), 128.7 (CH), 134.7 (2xC),136.6 (C), 195.1 (CO). IR ($CHCl_3$): 1012, 1162, 1296, 1481, 1549, 1692, 2978 cm^{-1}. HRMS: calcd for $C_{22}H_{31}O_{10}Cl_3K$ $(M+K)^+$ 599.0620 found 599.0620.

General procedure B for the removal of MOM protection: The methoxy methyl ether protected compounds (**18, 20a-h)** dissolved in methanol (2 ml) and were stirred at room temperature for 5 minutes. Aqueous HCl was added and stirring was continued until the starting material disappeared on TLC. The wine-red colored solution was concentrated in vacuum and black colored residual material was purified by silica gel column chromatography to provide the title compounds.

1-(4-methoxyphenyl)-2-(β-D-glucopyranosyl) ethanone (21a): The color less gum **20a** (0.270 g, 0.53 mmol), methanol (2 mL) and HCl (6 N, 20 mL) were treated according to the general procedure B to provide the title compound **21a** (0.105 g, 62%) as a yellow color solid. R_f = 0.3 (MeOH/DCM 1:9); m.p 150-152 ^{o}C; $[\alpha]^{27}_D$ -6.4° (c 1.0, MeOH); ^{1}H NMR (CD_3OD, 500 MHz): δ = 3.14 (dd, 1H, J^1 = 16 Hz, J^2 = 9 Hz), 3.19-3.22 (m, 2H), 3.29-3.36 (m, 2H, one from solvent), 3.35-3.38 (m, 2H), 3.60 (dd, 1H, J^1 =12.0 Hz, J^2 =5.0 Hz), 3.73 (dd, 1H, J^1 = 11.5 Hz, J^2 = 2.5 Hz), 3.82 (td, 1H, J^1 = 9.0 Hz, J^2 = 2.5 Hz), 3.87 (s, 3H), 7.0 (d, 2H, J = 9.0 Hz) , 7.99 (d, 2H, J^1 = 9.0 Hz), ^{13}C NMR (125 MHz, CD_3OD) : δ= 42.9 (CH_2), 62.7 (CH_2), 71.6 (CH), 75.1 (CH), 77.5 (CH), 79.7 (CH), 81.57 (CH), 114.8 (CH), 131.3 (C), 131.8 (CH), 165.3 (C), 198.9 (CO). IR (KBr): 1162, 1481, 1549, 1663, 2921, 3214 cm^{-1}. HRMS: calcd for $C_{15}H_{120}O_7Na$ $(M+Na)^+$ 335.1107 found. 355.1125.

1-(4-chlorophenyl)-2-(β-D-glucopyranosyl) ethanone (21b): The viscous gum **20b** (0.280 g, 0.569 mmol), methanol (2 ml) and HCl (6 N, 20 mL) were treated according to the general procedure B to give the title compound **21b** (0.130 g, 72.22%) as a colorless solid. R_f = 0.7 (MeOH/DCM 1:9); m.p. = 110-112 ^{o}C; $[\alpha]^{27}_D$ -29.1° (c 1.0, MeOH); ^{1}H NMR (CD_3OD, 500 MHz): δ = 3.17-3.23 (m, 3H), 3.30-3.31 (m, 2H), 3.35-3.39 (m, 2H), 3.60 (dd, 1H, J^1 =12.0 Hz, J^2 =5.0 Hz), 3.74 (dd, 1H, J^1 = 11.5 Hz, J^2 = 2.5 Hz), 3.83 (td, 1H, J^1 = 9.0 Hz, J^2 = 2.5 Hz), 7.50 (d, 2H, J = 9.0 Hz) , 7.98 (d, 2H, J = 9.0 Hz).^{13}C NMR (125 MHz, CD_3OD): δ = 40.9 (CH_2), 61.3 (CH_2), 70.2 (CH), 73.6 (CH), 75.9 (CH), 78.3 (CH), 80.2 (CH), 128.5 (CH), 129. 6 (CH), 137.1 (C), 140.5 (C), 199.2 (CO). IR (KBr): 967, 1152, 1393, 1560, 1682, 2991, 3319 cm^{-1}. Elemental analysis calcd (%) for $C_{14}H_{17}O_6$ (316.07): C 53.09, H 5.41; found: C 53.38, H 5.34.

1-(4-hydroxyphenyl)-2-(β-D-glucopyranosyl) ethanone (21c): The colorless gum **20c** (0.280 g, 0.54 mmol), methanol (2 mL) and HCl (6 N, 20 mL) were treated according to the general procedure B to provide the title compound **21c** (0.09 g, 56%) as a yellow colored solid. R_f = 0.65 (MeOH/DCM 2:8); $[\alpha]^{27}_D$ -45.0° (c 0.5, MeOH); ^{1}H NMR (DMSO-D_6, 500 MHz): δ = 2.9-3.0 (m, 3H), 3.07-3.12 (m, 1H), 3.14-3.36 (m, 2H), 3.53-3.58 (m, 2H), 3.68 (td, 1H, J^1 =9.0 Hz, J^2 =2.0 Hz), 4.30 (t, 1H, J = 5.5 Hz), 4.89 (d, 1H, J = 5.0 Hz), 4.97 (d, 1H, J = 4 Hz), 5.08 (d, 1H, J = 5.5 Hz), 6.87 (d, 2H, J = 8.5 Hz), 7.84 (d, 2H, J^1 = 8.5 Hz), 10.44 (s, 1H, OH), ^{13}C NMR (125 MHz, CD_3OD) : δ = 40.6 (CH_2), 61.0 (CH_2), 70.1 (CH), 73.4 (CH), 75.8 (CH), 78.1 (CH), 80.6 (CH), 115.1 (CH), 128.6 (C), 130.5 (CH), 162.0 (C), 196.1 (CO). IR (KBr): 1067, 1421, 1523, 1625, 2991, 3216, 3520 cm^{-1}. HRMS: calcd for $C_{14}H_{18}O_7Na$ $(M+Na)^+$ 321.0950 found. 321.0972.

1-(4-fluorophenyl)-2-(β-D-glucopyranosyl) ethanone (21d): The colorless gum **20d** (0.260 g, 0.546 mmol), methanol (2 mL) and HCl (6 N, 20 mL) were treated according to the general procedure B to provide the title compound **21d** (0.130 g, 79.7%) as a brown colored solid. R_f = 0.7 (MeOH/DCM 1:9); m.p 134-136 ^{o}C; $[\alpha]^{27}_D$ -17.3° (c 1.0, MeOH); ^{1}H NMR (CD_3OD, 500 MHz): δ = 3.17-3.22 (m, 3H), 3.30-3.40 (m, 4H, one from solvent), 3.61 (dd, 1H, J^1 =12.0 Hz, J^2 =5.0 Hz), 3.74 (d, 1H, J = 11.5 Hz), 3.84 (t, 1H, J = 8.5 Hz), 7.21 (t, 2H, J = 9.0 Hz) , 8.07 (dd, 2H, J^1 = 9.0 Hz, J^2 = 5.5 Hz), ^{13}C NMR (125 MHz, CD_3OD) : δ = 40.9 (CH_2), 61.3 (CH_2), 70.2 (CH), 73.6 (CH), 75.9 (CH), 78.3 (CH), 80.2 (CH), 116.5 (d, CH, J = 21.87 Hz), 132..3 (d, CH, J = 9.25 Hz),135.1 (d, C, J = 2.87 Hz), 167.1 (d, C, J = 251.6 Hz) 140.5 (C), 198.9 (CO). IR (KBr): 1160, 1451, 1562, 1637, 2983, 3274 cm^{-1} HRMS: cald for $C_{14}H_{17}O_6FNa$ $(M+Na)^+$ 323.0907 found. 323.0927.

1-(3, 4-dichlorophenyl)-2-(β-D-glucopyranosyl) ethanone (21e). The colorless gum **20e** (0.340 g, 0.646 mmol), methanol (3 mL) and HCl (6 N, 25 mL) were treated according to the general procedure B to provide the title compound **21e** (0.171 g, 75.66%) as a colorless solid. R_f = 0.4 (MeOH/DCM 1:9); m.p 138-140 ^{o}C; $[\alpha]^{27}_D$ -7.9° (c 1.0, MeOH); ^{1}H NMR (CD_3OD, 500 MHz): δ = 3.17-3.23 (m, 4H), 3.32-3.34 (m, 1H), 3.36-3.38 (m, 2H), 3.60 (dd, 1H, J^1 =12.0 Hz, J^2 =5.0 Hz), 3.74 (dd, 1H, J^1 = 12.0 Hz, J^2 = 2.5 Hz), 3.82 (td, 1H, J^1 = 9.0 Hz, J^2 = 2.5 Hz), 7.66 (d, 2H, J = 8.5 Hz) , 7.91 (dd, 1H, J^1 = 8.5 Hz, J^2 = 2.0 Hz), 8.11 (d, 1H, J = 2.0 Hz). ^{13}C NMR (125 MHz, CD_3OD): δ = 42.3 (CH_2), 62.7 (CH_2), 71.6 (CH), 75.0 (CH), 77.2 (CH), 79.7 (CH), 81.6 (CH), 129.0 (CH), 131.2 (C), 131.9 (CH), 133.9 (C), 138.2 (C) 138.6 (C), 198.1 (CO). IR (KBr): 962, 1090, 1219, 1523, 1660, 2991, 3293 cm^{-1} HRMS: calcd for $C_{14}H_{18}O_6Cl_2$ $(M+H)^+$ 352.0480 found. 352.0467.

1-(3, 4-dimethoxyphenyl)-2-(β-D-glucopyranosyl) ethanone (21f): The color less gum **20f** (0.270 g, 0.521 mmol), methanol (2 mL) and HCl (6 N, 25 mL) were treated according to the procedure B to provide the title compound **21f** (0.105 g, 62%) as a yellow colored solid. R_f = 0.3 (MeOH/DCM 1:9); m.p 142-144 ^{o}C; $[\alpha]^{27}_D$ -38.4° (c 1.0, MeOH); ^{1}H NMR (DMSO-D6, 400 MHz): δ = 2.98-3.05 (m, 3H), 3.07-3.10 (m, 2H), 3.15-3.22 (m, 2H), 3.68 (dd, 2H, J^1 =11.6 Hz, J^2 =5.2 Hz), 3.79 (s, 3H), 3.82 (s, 3H), 7.04 (d, 1H, J =8.4 Hz), 7.43 (d, 1H, J = 2.0 Hz), 7.62 (dd, 1H, J^1 =8.4 Hz, J^2 = 2.0 Hz) ^{13}C NMR (100 MHz, DMSO-D6) : δ = 40.9 (CH_2), 55.7 (OMe), 55.9 (OMe), 61.3 (CH_2), 70.4 (CH), 73.6 (CH), 76.2 (CH), 78.3 (CH), 80.8 (CH), 110.5 (CH), 111.0 (CH), 123.1 (CH), 130.1 (C), 148.7 (C), 153.2 (C), 197.0 (CO). IR (KBr): 1063, 1296, 1403, 1523, 1662, 2986, 3219 cm^{-1}. ^{1} Elemental analysis calcd (%) for $C_{16}H_{22}O_8$ (342.13): C 56.14, H 6.48; found: C 56.46, H 6.07.

1-(3, 5-diflurophenyl)-2-(β-D-glucopyranosyl) ethanone (21g): The colorless gum **20g** (0.280 g, 0.566 mmol), methanol (2 mL) and HCl (6 N, 25 mL) were treated according to the general procedure B to provide the title compound **21g** (0.130 g, 72.3%) as colorless solid. R_f = 0.3 (MeOH/DCM 1:9); m.p 142-144 ^{o}C; $[\alpha]^{27}_D$ -8.1° (c 1.0, MeOH); ^{1}H NMR (CD_3OD, 500 MHz): δ = 3.19 (dd, J^1 = 17.0 Hz, J^2 1H), 3.21-3.23 (m, 3H), 3.33-3.38 (m, 2H), 3.60 (dd, 1H, J^1 =12.0 Hz, J^2 =5.0 Hz), 3.74 (d, 1H, J = 11.5 Hz), 3.80 (t, 1H, J = 9.0 Hz), 7.22 (t, 1H, J = 8.5 Hz), 7.58 (d, 2H, J = 7.5 Hz), ^{13}C NMR (100 MHz, CD_3OD): δ = 41.1 (CH_2), 61.2 (CH_2), 70.2 (CH), 73.5 (CH), 75.7 (CH), 78.2 (CH), 80.1 (CH), 107.8 (t. J = 25.7 Hz, CH), 110.9 (dd, CH, J^1 = 20.21 Hz, J^2 = 6.0 Hz) 140.4 (d, J = 7.4 Hz, C), 163.8 (dd, C, J^1 = 248.2 Hz, J^2 = 12.0 Hz), 198.95 (CO). IR (KBr): 1191, 1422, 1569, 1691, 2913, 3295, cm^{-1} Elemental analysis calcd (%) for $C_{14}H_{16}O_6F_2$ (318.09): C 52.83, H 5.07; found: C 52.98, H 4.45.

1-(3, 4, 5-trimethoxy phenyl)-2-(β-D-glucopyranosyl) ethanone (4): The colorless gum **18** (0.555 g, 1.021 mmol), methanol (3 mL) and HCl (6 N, 30 mL) were treated according to the general procedure B to give the title compound **4** (0.30 g, 62%) as light yellow colored solid. R_f = 0.3 (MeOH/DCM 1:9); m.p. 164-166 ^{o}C; $[\alpha]^{27}_D$ -2.5° (c 0.3, MeOH); ^{1}H NMR (CD_3OD, 500 MHz): δ = 3.18-3.23 (m, 1H), 3.24-3.29 (m, 2H), 3.36-3.38 (m, 1H), 3.40-3.44 (m, 1H), 3.45-3.48 (m, 1H), 3.66 (dd, 1H, J^1 =12.0 Hz, J^2 =5.2 Hz), 3.80 (dd, 1H, J^1 = 12.0 Hz, J^2 = 2.4 Hz), 3.85-3.90 (m, 4H), 3.94 (s, 6H), 7.36 (s, 2H) , ^{13}C NMR (125 MHz, CD_3OD): δ = 42.2 (CH_2) 56.8 (2x OMe), 61.2 (OMe), 62.7 (CH_2), 71.6 (CH), 75.0 (CH), 77.6 (CH), 79.7 (CH), 81.6 (CH), 107.2 (CH), 133.9 (C), 143.8 (C), 154.43 (2xC),

199.5 (CO). IR (KBr): 1067, 1133, 1462, 1561, 1656, 2943, 3269 cm^{-1} HRMS: calcd for $C_{17}H_{24}O_9Na$ $(M+Na)^+$ 395.1381 found. 395.1299.

1-(3, 4, 5-trimethoxyphenyl)-2-(2', 3', 4', 6'-tetra-*O*-acetyl-*β*-D-gluco-pyranosyl) ethanone (19): To the tetrol **4** (0.130 g, 0.350 mmol) in DMF (2 mL) were added successively acetic anhydride (0.396 mL, 4.192 mmol), *N, N* diisopropylethylamine (0.77 mL, 7 mmol) and 4-(dimethyl-amino)-pyridine (0.022 g) at 0 °C, and the resultant mixture was stirred at room temperature for 12 h. To the reaction mixture was added water and the organic layer was extracted with EtOAc. The combined organic layer was washed with saturated sodium hydrogen carbonate solution, dried over Na_2SO_4, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to yield title compound **19** (0.169 g, 89.8%), as a colorless solid. R_f = 0.5 (EtOAc:hexane 1:1); m.p. 127-129 °C; $[\alpha]^{27}_D$ 67 ° (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400MHz): δ = 1.97 (s, 3H), 2.0 (s, 6H), 2.03 (s, 3H), 2.9 (dd, 1H, J^1 = 16.4 Hz, J^2 = 3.6 Hz), 3.30 (dd, 1H, J^1 = 16.4 Hz, J^2 = 8.0 Hz), 3.71-3.75 (m, 1H), 3.9 (s, 9H), 3.99 (dd, 1H, J^1 = 12.4 Hz, J^2 = 2.0 Hz), 4.20-4.24 (m, 1H), 4.25-4.29 (m, 1H), 5.04 (t, 1H, J = 9.6 Hz), 5.1 (t, 1H, J =9.6 Hz) 5.25 (t, 1H, J= 9.6 Hz), 7.1 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6 (CH_3), 40.3 (CH_2), 56.3 ((2xOCH3), 60.9 (OMe), 62.0 (CH_2), 68.4 (CH), 71.8 (CH), 74.2 (CH), 74.3 (CH), 75.8 (CH), 105. 8(CH), 132.0 (C), 143.0 (C), 153.0 (C), 169.5 (C), 170.0 (C), 170.2 (C), 170.5 (C), 195.1 (C). IR (KBr): 1033, 1118, 1263, 1409, 1571, 1619, 1637, 1697, 2990, 3216 cm^{-1} HRMS: calc for $C_{25}H_{33}O_{13}$ $(M+H)^+$ 541.1921 found 541.1943.

1-(3, 4, 5-trichlorophenyl)-2-(*β*-D-glucopyranosyl) ethanone (21h): The colorless gum **20h** (0.3 g, 1.021 mmol), methanol (3 mL) and HCl (6 N, 30 mL) were treated according to the general procedure B to give the title compound **21h** (0.07 g, 41%) as a light yellow colored solid. R_f = 0.3 (MeOH/DCM 1:9); m.p. 94-96 °C; $[\alpha]^{27}_D$ -11.7° (c 0.5, MeOH); ^{1}H NMR (CD_3OD, 400 MHz): δ = 3.08-3.10 (m, 1H), 3.12-3.14 (m, 2H), 3.23-3.25 (m, 2H), 3.27-3.29 (m, 1H), 3.50 (dd, 1H, J^1 = 11.6 Hz, J^2 = 7.2 Hz), 3.65 (dd, 1H, J^1 =12.0 Hz, J^2 =2.0 Hz), 3.71 (td, 1H, J^1 = 8.8.0 Hz, J^2 = 2.8 Hz), 7.98 (s, 2H) , ^{13}C NMR (100 MHz, CD_3OD) : δ = 40.9 (CH_2), 61.2 (CH_2), 70.2 (CH), 73.6 (CH), 75.8 (CH), 78.2 (CH), 80.2 (CH), 128.2 (CH), 134.3 (2x C), 135.3 (C), 137.0 (C), 195.6 (CO). IR (KBr): 1067, 1163, 1238, 1444, 1523, 1678, 2991, 3216 cm^{-1}HRMS: cald for $C_{14}H_{15}O_6$ Cl_3Na $(M+Na)^+$ 406.9832 found. 406.9829.

3, 3', 4, 4', 5, 5'-hexakis(methoxymethyl ether)-1, 1'-biphenyl (25): To a two necked round bottom flask fitted with a condenser was added magnesium(0.094 g, 3.93 mmol), the setup was kept on oil bath at 60 °C for five minutes. To this was added the bromo compound **22** (0.67 g, 1.96 mmol) in anhydrous THF (8 ml), and 1,2-dibromoethane (0.17 mL, 1.96 mmol), while maintaining the same temperature. Stirring was continued at 60 °C, until the magnesium was fully consumed. After acidic workup with saturated aq. NH_4Cl, the organic layer was extracted with EtOAc, dried over Na_2SO_4, concentrated under reduced pressure, the resultant crude product was purified by silica gel column chromatography to give the title compound as light yellow colored gummy compound **25** (0.58 g, 58%), R_f = 0.7 (EtOAc:hexane 1:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.44 (s, 12H), 3.55 (s, 6H), 5.1 (s, 4H), 5.2 (s, 8H), 6.9 (s, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 56.3 (CH_3), 57.2 (CH_3), 95.6 (CH_2), 96.6 (CH_2), 109.9 (CH), 136.2 (C), 137.5 (C), 151.1 (C). HRMS: calcd for $C_{24}H_{34}O_{12}Na$ $(M+Na)^+$ 537.1948 found 537.1960.

2-(2', 3', 4', 6'-tetra-*O*-methoxy methyl-*β*-D glucopyranosyl) acetal-dehyde 26: An oven dried round bottom flask was charged with amide **17** (0.350 g, 0.793 mmol) in anhydrous THF under a nitrogen atmosphere. Lithium aluminum hydride (0.40 g, 1.03 mmol), was added to the reaction mixture at 0 ℃. Stirring was continued until the starting material disappeared (on TLC). To the suspension was added H_2O dropwise, and it was filtered through a pad of celite. The organic layer was extracted with EtOAc, dried over Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by column chromatography to yield the title compound **26** as a colorless gum (0.190 g, 62.7%), R_f = 0.3 (EtOAc:hexane 1:1); $[\alpha]^{27}_D$ 53.1° (c 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.65 (dd, 1H, J^1 =8.5 Hz, J^2 = 2.5 Hz), 2.87 (dd, 1H, J^1 = 3.5 Hz, J^2 = 1.5 Hz), 3.34 (s, 3H), 3.36 (s, 3H), 3,43 (s, 3H), 3.44-3.45 (m, 4H), 3.47-3.50 (m, 2H), 3.60-3.65 (m, 2H), 3.79-3.83 (m, 2H), 4.63 (s, 2H), 4.68-4.72 (m,1H), 4.73-4.77 (m, 1H), 4.82-4.84 (m, 2H), 4.85-4.87 (m, 2H), 9.79-9.80 (m, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 45.8 (CH_2), 55.3 (OMe), 55.5 (2xOMe), 56.5 (OMe), 66.5 (CH_2), 73.9 (CH) 77.0 (CH), 78.5 (CH), 80.0 (CH), 84.1 (CH), 96.8 (CH_2), 98.5 (CH_2), 98.8 (2xCH_2), 200.5 (C, -CHO). IR ($CHCl_3$): 1061, 1189, 1233, 1481, 1562, 1757, 2863, 2952 cm^{-1}. HRMS: calcd for $C_{26}H_{30}O_{10}Na$ $(M+Na)^+$ 405.1737 found 405.1754.

1-(3, 4, 5-trimethoxymethylphenyl)-2-(2′, 3′, 4′, 6′-tetra-*O*-methoxy methyl-*β*-D-glucopyranosyl) ethanone (28):

Step 1: Aldehyde **26** (0.120 g, 0.314 mmol), magnesium turnings (0.030g, 1.256 mmol), LiCl (0.026 g, 0.628 mmol), *i*Bu_2AlH (0.031 mL, 1 M in toluene, 0.031 mmo0l) and 1-bromo-3,4,5-trimethoxymethylbenzene **25** (0.423 g, 1.256 mmol) were treated according to the procedure **20f** to give the mixture of diastereomers, after column chromatography on silica gel (EtOAc/hexane 3:2), as a colorless syrup (0.150 g, 71.77%).

Step 2: To the mixture of diastereomers (0.120 g, 0.184 mmol), dimethyl sulfoxide (3 mL) and IBX (0.103 g, 0.369 mmol) were added at room temperature and the solution was kept at 70 °C for 3h. After completed the reaction (monitored by TLC), the solution was allowed to stirr at 25 ° C, then diluted with H_2O (5 ml) and filtered through a pad of celite. The filtrate was extracted with EtOAc (3x50 ml), the organic layer was dried over Na_2SO_4 and concentrated in vacuum. The crude residue was purified by silica gel column chromatography to give the title compound **30** (0.095 g, 79.83%) as a colorless gum. R_f = 0.4 (EtOAc:hexane 1:1); $[\alpha]^{26}_D$ 110.5° (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.22 (dd, 1H, J^1 =17.0 Hz, J^2 = 8.5 Hz), 3.29-3.33 (m, 4H), 3.35- 3.39 (m, 4H), 3.41 (s, 3H), 3.43- 3.46 (m, 4H), 3.50 (s, 6H), 3.52-3.55 (m, 1H), 3.61 (s, 3H, OMe), 3.62-3.67 (m, 2H), 3.77 (dd, 1H, J^1 = 11.5 Hz, J^2 = 2.0 Hz), 3.97-4.01 (m, 1H), 4.59 (dd, 2H, J^1 = 12.5 Hz, J^2 = 6.5 Hz), 4.72 (dd, 2H, J^1 = 18.0 Hz, J^2 = 7.0 Hz), 4.83- 4.87 (m, 3H), 4.91 (d, 1H, J = 7.0 Hz), 5.21 (s, 2H), 5.24 (s, 2H), 5.24 (s, 2H), 7.438 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 40.8 (CH_2), 55.3 (OMe), 56.3 (OMe), 56.4 (2 x OMe), 56.5 (OMe), 56.6 (OMe), 57.3 (OMe), 66.5 (CH_2), 74. (CH), 77.0 (CH), 78.2 (CH), 80.5 (CH), 84.5 (CH), 95.3(2 x CH_2), 96.8 (CH_2), 98.5 (2 x CH_2), 98.7 (CH_2), 98.7 (CH_2), 110.4 (CH), 133.2 (C),140.9 (C),150.8 (C), 196.1 (CO). IR ($CHCl_3$): 1031, 1162, 1276, 1438, 1561, 1623, 2923 cm^{-1} HRMS: calcd for $C_{28}H_{46}O_{16}$ $(M+Na)^+$ 661.2684 found 661.2692.

Crystal data for compound 19: Formula: $C_{25}H_{32}O_{13}$; unit cell parameters: a = 9.2676 (5), b = 15.6349 (12), c = 18.7223 (4), space group P21; CCDC 1588605 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Biological assay:

Rat lens aldose reductase: Crude aldose reductase (AR) was prepared from rat lens. Eyeballs were removed from 12-week-old Wistar strain (WNIN) male rats obtained from National Center for Laboratory Animal Services, National Institute of Nutrition, Hyderabad. Animal care and protocols were in accordance with and approved by Institutional Animal Ethics Committee. Lenses were dissected by posterior approach and homogenized in 9 volumes of 100 mM potassium phosphate buffer pH 6.2. The homogenate was centrifuged at 12,000x g for 30 min at 4 °C and the resulting supernatant was used as the source of AR.

Aldose reductase assay: AR activity was assayed according to the reported method.[20] Briefly, the assay mixture in 1 ml contained 50 µM potassium phosphate buffer pH 6.2, 0.2 M lithium sulfate, 5 µM 2-mercapto ethanol, 10 µM DL-glyceraldehyde, 0.1 µM NADPH, and enzyme preparation (rat lens). Appropriate blanks were employed for corrections. The assay mixture was incubated for 5 min at 37 °C and initiated by the

addition of NADPH at 37 °C. The change in the absorbance at 340 nm due to NADPH oxidation was followed in a Simadzu spectrophotometer.

Inhibition studies: For inhibition studies concentrated stocks of compounds were prepared in water. Various concentrations of inhibitors were added to the assay mixture and incubated for 5 min before initiating the reaction by NADPH as described above. The percent of inhibition with test compounds was calculated considering the AR activity in the absence of inhibitor as 100%.

Results: Among the synthesized C-analogues of β-Glucogallin, compounds **4, 21a-h,** substrate **21c** alone, showed partial inhibition, 30% at 200µM concentration.

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Keywords: *β*-Glucogallin • Aldose reductase • Weinreb amide • Glycosyl ketones • *C*-analogues

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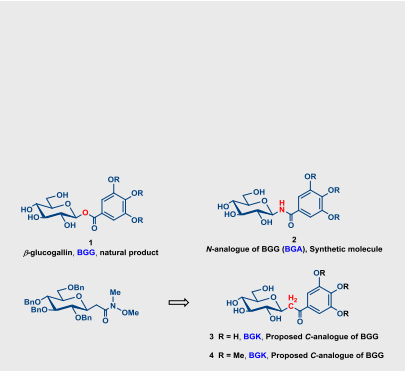

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