Knoevenagel condensation between *C*-glycoside and active methylene compounds without catalysts

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A Knoevenagel condensation reaction between a *C*-glycoside based aromatic aldehyde and cyclic active methylene compounds such as barbituric acid, thiobarbituric acid, 1,3-dimethylbarbituric acid, 5,5-dimethyl-1,3-cyclohexanedione, 2,2-dimethyl-1,3-dioxane-4,6-dione and 3-methyl-1-phenyl-2-pyrazolin-5-one has been developed, to give a series of unusual fused heterocyclic compounds. The structures of all the new compounds were established by the spectral data. This method which did not use any catalysts, has the advantages of operational simplicity and minimal environmental impact.

Keywords: Knoevenagel condensation, *C*-glycoside, active methylene compounds

The Knoevenagel condensation reaction between carbonyl compounds and active methylene compounds has largely been studied in heterogeneous media. It is a simple and effective method for forming carbon–carbon bonds.[1,2] Heterocyclic ring systems remain part of many powerful scaffolds holding several pharmacophores, which can act as potent and selective drugs for many diseases.[3,4] Furthermore, Knoevenagel adducts, are also useful intermediates for further transformations, such as Diels–Alder and Michael additions.[5]

C-glycosylation is a rare structural modification of natural products found in microorganisms and higher plants.[6] A major modification of natural products has been focused on glycosylation methods to diversify the functionality of natural products.[7] *C*-glycosides as subunits occur in a variety of biologically important natural products and synthetic compounds.[8–10] Consequently the development of new routes for the synthesis of *C*-glycosides has attracted attention.

In continuation of our research on *C*-glycosides,[11–14] in this paper, we describe the synthesis of novel *C*-glycoside derivatives by a Knoevenagel condensation. The target *C*-glycoside-derived heterocyclic compounds were composed of a sugar ring and a rigid ring-framework.

Results and discussion

Firstly, we needed to synthesise the novel key intermediate of *C*-glycoside **4**. The route is shown in Scheme 1. Starting from D-glucose the β-*C*-glycosidic aryl ketone was synthesised in a one step process.[11] In the next steps, the hydroxyl groups of the sugar were protected as their acetate esters,[15] the carbonyl group was reduced to a methylene[16] and a formyl group was then introduced onto the aromatic ring[17] to give 1-(2,3,4,6-tetra-*O*-acetyl-1-β-D-glucopyranose)-2-(4-formylphenyl)-ethane **4** in an overall yield of 60%.

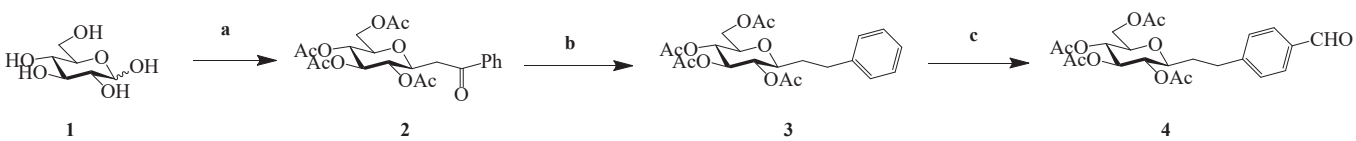
Initially, we chose the reaction of pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione(barbituric acid) with 1-(2,3,4,6-tetra-*O*-acetyl-1-β-D-glucopyranose)-2-(4-formylphenyl)-ethane (**4**) as a model system for an optimisation study. The reaction rate was investigated by measuring the isolated yield of the product, using identical amounts of reactants. It was found that the reaction proceeded under reflux in ethanol without a catalyst to give the desired product **5a** in 85% yield. Next, different catalysts including PTSA, CH_3COOH, NEt_3, and piperidine were examined in the reaction. However, to our surprise, they did not improve the yield. In addition, other solvents, such as dioxane, CH_3OH, CH_3CN, and THF (Table 1, entries 3, 8–11), were also tested but EtOH proved to be superior. Furthermore, the product was collected by filtration when the EtOH solution was cooled to room temperature after completion of the reaction.

With optimised conditions established, we next extended the process to four different cyclic 1,3-dicarbonyl compounds including thiobarbituric acid, 1,3-dimethylbarbituric acid, 5,5-dimethyl-1,3-cyclohexanedione and 2,2-dimethyl-1,3-dioxane-4,6-dione. By selecting the different materials, a new class of compounds was synthesised which may show interesting properties. The results in Table 2 showed that all the reactions proceeded smoothly to afford the derivatives in moderate to excellent yields. The structures of the products were deduced from their ^{1}H NMR, and ^{13}C NMR and elemental analysis.

Next, we planned to utilise 3-methyl-1-phenyl-2-pyrazolin-5-one as the active methylene compound in the above reaction. In this case, an unexpected product namely the 4,4'-(arylmethylene)bis(1*H*-pyrazol-5-ol) derivative **5f** was obtained as a Knoevenagel–Michael adduct in 73% yield instead of a benzylidene–pyrazolinone derivative (Scheme 2). In the ^{1}H NMR spectrum, one singlet appeared at δ 4.72 ppm for methine proton (–CH) and another singlet at δ 1.97 ppm for two methyl protons ($-CH_3$), supporting the formation of compound **5f**.

The literature survey showed that the synthesis of 4,4'-(arylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ols) can be achieved by two methods: (i) successive Knoevenagel synthesis of the corresponding arylidenepyrazolones and its base-promoted Michael reaction;[18,19] and (ii) one-pot tandem Knoevenagel–Michael reaction of aldehydes with two equivalents of 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one performed under various reaction conditions.[20] This is an example of the second case.

Several solvents (MeOH, CH_3CN, acetone, THF, DCM) were also examined with two equivalents of 3-methyl-1-phenyl-2-pyrazolin-5-one. This revealed that DCM was the solvent of



1 **2** **3** **4**

Scheme 1 Synthetic route to the key intermediate **4**.

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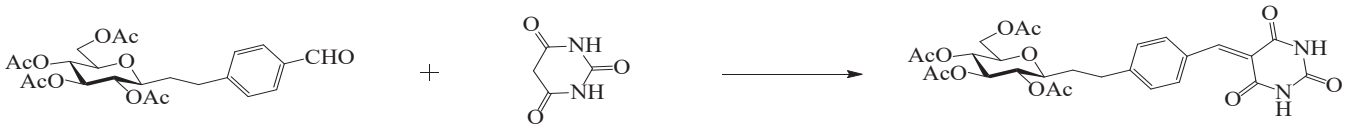
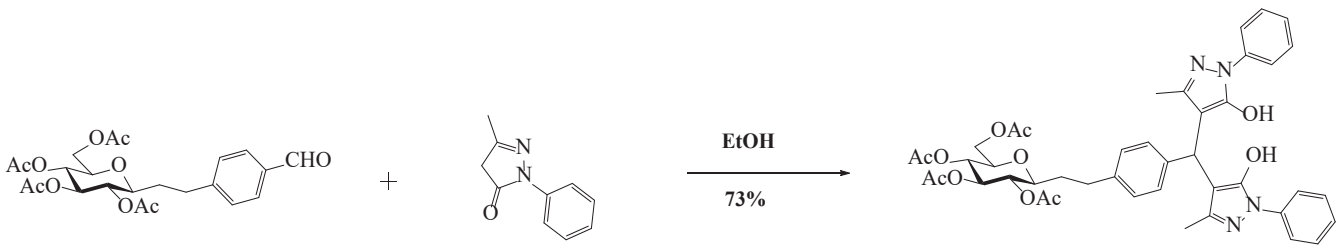
Table 1 Synthetic results of **5a** under different reaction conditions[a]



4 **5a**

Entry	Temperature/°C	Catalyst	Time/h	Solvent	Yield/%[b]
1	r.t.	–	10	EtOH	Trace
2	50 °C	–	10	EtOH	53
3	Reflux	–	10	EtOH	85
4	Reflux	PTSA	10	EtOH	71
5	Reflux	CH_3COOH	8	EtOH	57
6	Reflux	NEt_3	10	EtOH	80
7	Reflux	Piperidine	10	EtOH	75
8	Reflux	–	8	Dioxane	80
9	Reflux	–	16	CH_3OH	82
10	Reflux	–	12	CH_3CN	84
11	Reflux	–	14	THF	82

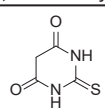
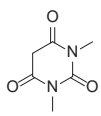
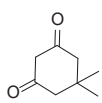
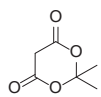
[a]Reagents and conditions: (0.046 g, 0.1 mmol); barbituric acid (0.026 g, 0.2 mmol); and solvent (5 mL).
[b]Isolated yield.



4 **5f**

Scheme 2 Knoevenagel–Michael condensation of 1-(2,3,4,6-tetra-*O*-acetyl-1-β-D-glucopyranose)-2-(4-formylphenyl)-ethane and 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one.

Table 2 The reaction time and yields of the products

Entry	1,3-Dicarbohyl[a]	Time/h	Products	Yield/%
1		10	**5b**	87
2		12	**5c**	92
3		14	**5d**	76
4		13	**5e**	80

[a]Reagents and conditions: (0.046 g, 0.1 mmol); 1,3-dicarbohyl (0.2 mmol); EtOH(5 mL); and reflux.

choice. Incomplete conversion was observed in the other solvents. Decreasing the reaction time to 6 h led to complete conversion in dichloromethane (yield 90%). Good solubility in dichloromethane may be responsible for the higher yields.

Conclusion

In this paper, we have described a strategy for the synthesis of a rigid ring-framework from an aromatic aldehyde containing a sugar unit and several methylene active compounds. The easy availability of the starting materials and the simplicity of the procedure make it a promising approach for the synthesis of heterocyclic compounds containing sugar rings. The synthetic benzylidene derivatives are promising building blocks for drug design, advanced materials, and agricultural chemistry. Further investigations into the scope and synthetic applications of this new approach to complex molecules are now in progress in our laboratory.

Table 3 Condensation of **4** and 3-methyl-1-phenyl-2-pyrazolin-5-one under different solvents

Entry	Solvents	Time/h	Yield/%
1	MeOH	8	72
2	CH_3CN	8	66
3	Acetone	8	60
4	THF	8	65
5	DCM	8	85
6	DCM	6	90
7	DCM	4	77
8	DCM	10	78

Experimental

Melting points were determined in open glass capillaries using a Griffin melting point apparatus. Solvents were distilled and dried by standard methods. All the chemicals used were of analytical grade and used without further purification. The progress of the reactions was monitored by thin-layer chromatography (TLC) on silica gel, and spots

were visualised with UV light or iodine. ^{1}H, ^{13}C NMR and NOESY spectra were recorded in $CDCl_3$ or DMSO-d_6 on a Bruker Avance III 500 MHz spectrometer. Proton chemical shifts are reported in ppm relative to the internal standard tetramethylsilane (δ_{TMS} = 0 ppm) and carbon chemical shifts are reported in ppm relative to the solvents (δ_{CDCl3} = 77.00 ppm). Data were recorded and evaluated using TOPSPIN 3.1 (Bruker Biospin). All chemical shifts are given in ppm relative to tetramethylsilane. The resonance multiplicity is indicated as s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), m (multiplet), or a combination of these. Elemental analyses were performed on a Vario EL III elemental analyser.

2,3,4,6-O-tetra-acety-1-deoxy-1-(2-oxo-2-phenylethyl)-β-D-glucopyranose (**2**)

D-Glucose (50 mmol), dibenzoylmethane (16.8 g, 75 mmol), sodium bicarbonate (6.3 g, 75 mmol), and EtOH–H_2O (4:1, v/v) 100 mL were introduced and microwave irradiation started, the EtOH–H_2O (4:1) began to reflux within 1 h. After the microwave reactor was turned off, the solutions were allowed to cool to room temperature and treated with cation exchange resin (sodium form) to reach pH = 5. The resin was filtered and EtOH was evaporated. The aqueous solution was washed with CH_2Cl_2 and concentrated. The product was used directly without further purification. Sodium acetate (2.46 g, 30 mmol) was added to a solution of 1-phenyl-2-*C*-(β-D-glucopyranosyl) ethanone in acetic anhydride (20 mL, 200 mmol) and the reaction was heated to 135 °C for 4 h. After completion of the reaction (TLC (AcOEt/PE) monitoring), the mixture was cooled to room temperature and ethyl acetate (100 mL) and water (80 mL) were added to the reaction, which was neutralised to pH = 7 by adding sodium carbonate. The extract was then washed with saturated sodium chloride solution three times. Evaporation of the solvent followed by recrystallisation from EtOH gave the crystalline product **2** (8.1 g, 90%), m.p.: 105.5–107 ºC (lit.[21] 104–106 ºC), ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 2H, Ph), 7.56 (t, *J* = 7.3 Hz, 1H, Ph), 7.45 (t, *J* = 7.6 Hz, 2H, Ph), 5.23 (t, *J* = 9.5 Hz, 1H, H3'), 5.07 (t, *J* = 9.5 Hz, 1H, H4'), 5.01 (t, *J* = 9.6 Hz, 1H, H2'), 4.22 (dt, *J* = 10.4, 5.1 Hz, 2H, H1', H6'a), 3.98 (d, *J* = 12.2 Hz, 1H, H6'b), 3.72 (dd, *J* = 9.8, 2.9 Hz, 1H, H5'), 3.33 (dd, *J* = 16.7, 8.3 Hz, 1H, H1'a), 2.93 (dd, *J* = 16.7, 2.7 Hz, 1H, H1'b), 1.98 (dd, *J* = 14.1, 10.0 Hz, 12H, CH_3CO) ppm. ^{13}C NMR (125 MHz, $CDCl_3$), δ 196.1, 170.8, 170.6, 170.1, 169.9, 136.7, 133.6, 128.8, 128.3, 76.4, 73.3, 72.4, 70.3, 66.3, 62.8, 39.5, 20.9 ppm. Anal. calcd for $C_{22}H_{26}O_{10}$: C, 58.66; H, 5.82; found: C, 58.62; H, 6.85%.

2,3,4,6-O-Tetra-acety-1-deoxy-1-(2-phenylethyl)-β-D-glucopyranose (**3**)[15]

2,3,4,6-*O*-Tetra-acety-1-deoxy-1-(2-oxo-2-phenylethyl)-β-D-glucopyranose (**2**) (4.5 g, 10 mmol) was dissolved in methanol (25 mL), trifluoroacetic acid (3 mL) and then Pd/C (0.6 g, 10%) were added. The reaction vessel was purged three times with hydrogen. The reaction was stirred at room temperature for 18 h. After completion of the reaction, it was filtered to recycle the Pd/C, and neutralised with saturated sodium bicarbonate. Evaporation of the solvent followed by column chromatography gave the products as white crystals in 92% yield, m.p.: 142–144 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (t, *J* = 7.5 Hz, 2H, Ph), 7.19 (d, *J* = 7.2 Hz, 1H, Ph), 7.15 (d, *J* = 7.5 Hz, 2H, Ph), 5.11 (t, *J* = 9.5 Hz, 1H, H3'), 5.04 (t, *J* = 9.5 Hz, 1H, H4'), 4.90 (t, *J* = 9.5 Hz, 1H, H2'), 4.25 (dd, *J* = 12.2, 5.3 Hz, 1H, H6'b), 4.13 (dd, *J* = 12.2, 1.7 Hz, 1H, H6'a), 3.59 (ddd, *J* = 9.5, 8.4, 6.8 Hz, 1H, H1'), 3.35–3.30 (m, 1H, H5'), 2.83 (dt, *J* = 13.7, 6.8 Hz, 1H, CH_2CH_2Ph), 2.66 (dt, *J* = 13.7, 8.4 Hz, 1H, CH_2CH_2Ph), 2.10 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO), 2.00 (s, 3H, CH_3CO), 1.97 (s, 3H, CH_3CO), 1.77 (dd, *J* = 13.9, 7.4 Hz, 2H, CH_2CH_2Ph) ppm. ^{13}C NMR (125 MHz, $CDCl_3$), δ 20.5, 30.8, 30.7, 62.4, 68.8, 71.8, 74.3, 75.6, 76.4, 126.0, 128.4, 141.1, 169.4, 169.6, 170.3, 170.6 ppm. Anal. calcd for $C_{22}H_{28}O_9$: C, 60.54; H, 6.47; found: C, 60.58; H, 6.50%.

1-(2,3,4,6-tetra-O-acetyl-1-β-D-glucopyranose)-2-(4-formylphenyl)-ethane (**4**)

A solution of 2,3,4,6-*O*-tetra-acety-1-deoxy-1-(2-phenylethyl)-β-D-glucopyranose **3** (300 mg, 0.69 mmol) and α,α-dichloromethyl methyl ether (2 mL, 2.1 mmol) was dissolved in dry dichloromethane (10 mL), and the solution was cooled to 0 °C under a nitrogen atmosphere. The solution was stirred vigorously as a solution of titanium tetrachloride (2.3 mL, 2.1 mmol) in dry dichloromethane (10 mL) was added *via* syringe pump over a period of 45 min. The dark green mixture was warmed to room temperature and stirred for an additional 2 h. The reaction mixture was poured into ice water (50 mL) and the aqueous layer thoroughly extracted with ether (3 × 15 mL). The combined ether layers were washed with saturated sodium bicarbonate (50 mL), water (60 mL), and saturated sodium chloride (50 mL) and dried over anhydrous magnesium sulfate and the volatile material was evaporated *in vacuo*. The residual blue–green solid was purified by flash chromatography to give the aldehyde **4** (5.56 g, 80%) as white powder, m.p.: 126–128 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.98 (s, 1H, CHO), 7.80 (d, *J* = 8.0 Hz, 2H, Ph), 7.33 (d, *J* = 8.0 Hz, 2H, Ph), 5.13 (t, *J* = 9.3 Hz, 1H, H3'), 5.05 (t, *J* = 9.3 Hz, 1H, H4'), 4.92 (t, *J* = 9.3 Hz, 1H, H2'), 4.25 (dd, *J* = 12.3, 5.2 Hz, 1H, H6'b), 4.14 (dd, *J* = 12.3, 2.0 Hz, 1H, H6'a), 3.60 (ddd, *J* = 9.3, 8.4, 7.0 Hz, 1H, H1'), 3.42–3.28 (m, 1H, H5'), 2.93 (dt, *J* = 13.8, 7.0 Hz, 1H, H1'a), 2.75 (dt, *J* = 13.8, 8.4 Hz, 1H, H1'b), 2.11 (s, 3H, CH_3), 2.07–1.94 (m, 9H, CH_3), 1.86–1.76 (m, 2H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$), δ 20.6, 20.7, 30.1, 31.1, 32.4, 62.4, 68.7, 71.7, 74.2, 75.7, 76.3, 129.1, 130.0, 134.7, 148.6, 169.5, 169.6, 170.3, 170.6, 191.8 ppm. Anal. calcd for $C_{23}H_{28}O_{10}$: C, 59.48; H, 6.08; found: C, 59.45; H, 6.04%.

Synthesis of compounds **5a–f***; general procedure*

A mixture of 1-(2,3,4,6-tetra-*O*-acetyl-1-β-D-glucopyranose)-2-(4-formylphenyl)-ethane (0.046 g, 0.1 mmol), active methylene compounds (0.026 g, 0.2 mmol), in EtOH (5 mL) was stirred under reflux for 10 h. After cooling the reaction mixture to room temperature, the precipitated product was filtered and washed with ethanol (15 mL). The crude product was recrystallised from EtOH to afford the pure product or purified by flash chromatography.

Compound **5a**: Yield 85%, m.p.: 113–115 ºC. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.36 (s, 1H, NH), 11.22 (s, 1H, NH), 8.26 (s, 1H, CH=), 8.11 (d, *J* = 8.0 Hz, 2H, ArH), 7.32 (d, *J* = 8.0 Hz, 2H, ArH), 5.22 (t, *J* = 9.6 Hz, 1H, H3'), 4.89 (t, *J* = 9.6 Hz, 1H, H2'), 4.76 (t, *J* = 9.6 Hz, 1H, H4'), 4.18 (dd, *J* = 12.2, 5.4 Hz, 1H, H6'a), 4.04 (d, *J* = 12.2 Hz, 1H, H6'b), 3.97–3.82 (m, 1H, H1'), 3.63–3.60 (m, 1H, H5'), 2.93–2.75 (m, 1H, H1'a), 2.75–2.59 (m, 1H, H1'b), 2.14–1.88 (m, 12H, CH_3), 1.81 (dd, *J* = 19.0, 9.6 Hz, 1H, CH), 1.64 (dd, *J* = 9.2, 4.6 Hz, 1H, CH) ppm. ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.5, 19.1, 169.0, 168.8, 163.0, 161.2, 154.3, 149.6, 146.4, 133.5, 129.8, 129.2, 128.7, 127.7, 74.8, 73.9, 72.9, 71.0, 68.1, 61.7, 31.4, 30.0, 20.0, 19.9, 19.9, 19.8 ppm. Anal. calcd for $C_{27}H_{30}N_2O_{12}$: C, 56.44; H, 5.26; N, 4.88; found: C, 56.40; H, 5.28, N, 4.87%.

Compound **5b**: Yield 87%, m.p.: 117–119 ºC. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.46 (s, 1H, NH), 12.35 (s, 1H, NH), 8.29 (s, 1H, CH=), 8.18 (d, *J* = 8.2 Hz, 2H, ArH), 7.34 (d, *J* = 8.2 Hz, 2H, ArH), 5.23 (t, *J* = 9.5 Hz, 1H, H3'), 4.91 (t, *J* = 9.5 Hz, 1H, H2'), 4.78 (t, *J* = 9.5 Hz, 1H, H4'), 4.19 (dd, *J* = 12.2, 5.5 Hz, 1H, H6'a), 4.05 (d, *J* = 12.2 Hz, 1H, H6'b), 3.96–3.78 (m, 1H, H1'), 3.71–3.55 (m, 1H, H5'), 2.91–2.76 (m, 1H, H1'a), 2.76–2.63 (m, 1H, H1'b), 2.05 (d, *J* = 10.7 Hz, 3H, CH_3), 2.01 (d, *J* = 9.1 Hz, 6H, CH_3), 1.95 (s, 3H, CH_3), 1.83 (dt, *J* = 16.9, 7.3 Hz, 1H, CH), 1.66 (dt, *J* = 9.2, 6.9 Hz, 1H, CH) ppm. ^{13}C NMR (125 MHz, DMSO-d_6) δ 178.0, 169.6, 169.1, 168.8, 161.4, 159.1, 155.2, 147.1, 133.9, 129.9, 127.8, 117.6, 74.7, 73.9, 72.9, 71.0, 68.0, 61.7, 31.4, 30.1, 20.0, 19.9, 19.9, 19.8 ppm. Anal. calcd for $C_{27}H_{30}N_2O_{11}S$: C, 54.91; H, 5.12; N, 4.74; S, 5.43; found: C, 54.88; H, 5.10; N, 4.76; S, 5.42%.

Compound **5c**: Yield 92%, m.p.: 128–130 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (s, 1H, CH=), 8.07 (d, *J* = 8.2 Hz, 2H, ArH), 7.28 (d, *J* = 8.2 Hz, 2H, ArH), 5.15 (t, *J* = 9.5 Hz, 1H, H3'), 5.06 (t, *J* = 9.5 Hz, 1H, H2'), 4.93 (t, *J* = 9.5 Hz, 1H, H4'), 4.26 (dd, *J* = 12.3, 5.2 Hz, 1H, H6'a), 4.14 (dd, *J* = 12.3, 1.9 Hz, 1H, H6'b), 3.68–3.55 (m, 1H, H1'), 3.42 (d, *J* = 12.5 Hz, 3H, N–CH_3), 3.40–3.36 (m, 1H, H5'), 3.40–3.36 (m, 3H, N–CH_3), 3.01–2.82 (m, 1H, H1'a), 2.82–2.68 (m, 1H, H1'b), 2.12 (s, 3H, CH_3CO), 2.03 (s, 6H, CH_3CO), 2.00 (s, 3H, CH_3CO), 1.83 (s, 2H, CH_2) ppm.^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 169.4, 168.7, 168.6, 161.7, 159.6, 158.2, 150.3, 146.7, 133.4, 129.7, 127.5, 115.8, 75.5,

74.8, 73.3, 70.8, 67.8, 61.5, 31.4, 30.2, 28.1, 27.5, 19.8, 19.8, 19.7, 19.7 ppm. Anal. calcd for $C_{29}H_{34}N_2O_{12}$: C, 57.80; H, 5.69; N, 4.65; found: C, 57.85; H, 5.68; N, 4.67%.

Compound **5d**: Yield 76%, m.p.: 145–147 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.0 Hz, 2H, ArH), 7.16 (d, *J* = 8.0 Hz, 2H, ArH), 5.48 (s, 1H, CH=), 5.12 (t, *J* = 9.6 Hz, 1H, H3'), 5.05 (t, *J* = 9.6 Hz, 1H, H2'), 4.91 (t, *J* = 9.6 Hz, 1H, H4'), 4.26 (dd, *J* = 12.2, 5.3 Hz, 1H, H6'a), 4.14 (dd, *J* = 12.2, 2.2 Hz, 1H, H6'b), 3.66–3.57 (m, 3H, H5', CH_2), 3.57–3.49 (m, 2H, CH_2), 3.39–3.25 (m, 1H, H1'), 2.87–2.81(m, 1H, H1'a), 2.70–2.64 (m, 1H, H1'b), 2.12 (s, 3H, CH_3), 2.04–1.98 (m, 9H, CH_3), 1.90 (s, 6H, CH_3), 1.79–1.75 (m, 2H, CH_2) ppm.^{13}C NMR (125 MHz, $CDCl_3$) δ 198.6, 190.9, 175.2, 169.7, 169.4, 168.7, 168.5, 147.7, 133.8, 129.1, 128.2, 127.3, 125.8, 100.5, 74.8, 73.3, 70.8, 67.9, 63.3, 61.5, 49.8, 42.0, 31.5, 30.1, 28.7, 28.3, 27.3, 26.2, 19.8, 19.6, 14.2, 13.1 ppm. Anal. calcd for $C_{31}H_{38}O_{11}$: C, 63.47; H, 6.53; found: C, 63.44; H, 6.55%.

Compound **5e**: Yield 80%, m.p.: 133–135 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (s, 1H, CH=), 8.10 (d, *J* = 8.2 Hz, 2H, ArH), 7.35 (d, *J* = 8.2 Hz, 2H, ArH), 5.20 (t, *J* = 9.5 Hz, 1H, H3'), 5.12 (t, *J* = 9.5 Hz, 1H, H2'), 4.99 (t, *J* = 9.5 Hz, 1H, H4'), 4.32 (dd, *J* = 12.2, 5.2 Hz, 1H, H6'a), 4.20 (dd, *J* = 12.2, 2.0 Hz, 1H, H6'b), 3.68–3.66 (m, 1H, H1'), 3.47–3.38 (m, 1H, H5'), 2.98 (dt, *J* = 13.9, 7.1 Hz, 1H, H1'a), 2.88–2.76 (m, 1H, H1'b), 2.18 (s, 3H, CH_3), 2.08 (d, *J* = 8.0 Hz, 6H, CH_3), 2.06 (s, 3H, CH_3), 1.88 (d, *J* = 6.9 Hz, 6H, CH_3), 1.31 (d, *J* = 7.2 Hz, 2H, CH_2) ppm.^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 169.4, 168.7, 168.5, 162.5, 159.0, 157.0, 147.5, 133.4, 129.1, 128.8, 128.2, 128.0, 112,9, 103.5, 75.4, 74.8, 73.3, 70.8, 67.8, 61.5, 31.3, 30.1, 26.6, 19.8, 19.7, 19.6, 19.6 ppm. Anal. calcd for $C_{29}H_{34}O_{13}$: C, 58.98; H, 5.80; found: C, 58.89; H, 5.78%.

Compound **5f**: Yield 90%, m.p.: 118–120 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 5.7, 3.3 Hz, 1H, ArH), 7.59 (d, *J* = 8.0 Hz, 4H, ArH), 7.52 (dd, *J* = 5.7, 3.3 Hz, 1H, ArH), 7.26 (dd, *J* = 8.6, 6.5 Hz, 3H, ArH), 7.09 (t, *J* = 7.0 Hz, 3H, ArH), 7.01 (d, *J* = 8.2 Hz, 2H, ArH), 5.09 (t, *J* = 9.6 Hz, 1H, H3'), 5.02 (t, *J* = 9.6 Hz, 1H, H2'), 4.87 (t, *J* = 9.6 Hz, 1H, H4'), 4.72 (s, 1H, CH), 4.23 (dd, *J* = 12.2, 5.2 Hz, 1H, H6'a), 4.14–4.08 (m, 1H, H6'b), 4.07 (d, *J* = 6.7 Hz, 2H, OH), 3.57 (ddd, *J* = 9.6, 5.1, 2.2 Hz, 1H. H1'), 3.38–3.28 (m, 1H, H5'), 2.83–2.70 (m, 1H, H1'a), 2.56 (dt, *J* = 13.5, 5.1 Hz, 1H, H1'b), 2.07 (d, *J* = 2.3 Hz, 6H, CH_3), 2.00 (s, 3H, CH_3), 1.97 (s, 6H, CH_3), 1.71 (dd, *J* = 14.8, 7.5 Hz, 2H, CH_2), 0.98 (d, *J* = 6.7 Hz, 3H, CH_3) ppm.^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 169.4, 168.7, 168.6, 166.8, 157.0, 145.7, 138.2, 137.5, 136.2, 131.4, 130.0, 127.9, 127.5, 126.3, 125.2, 120.3, 105.2, 74.6, 73.4, 70.9, 67.9, 61.5, 32.5, 31.8, 29.4, 26.8, 19.8, 19.7, 18.2, 10.7 ppm. Anal. calcd for $C_{43}H_{46}N_4O_{11}$: C, 64.98; H, 5.83; N, 7.05; found: C, 65.03; H, 5.86; N, 7.02%.

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Electronic Supplementary Information

The ESI are available through:
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