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Synthesis of peracetylated *C*-1-deoxyalditol- and *C*-glycoside-dipyrranes via dithioacetal derivatives

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ABSTRACT

Dipyrranes bearing peracetylated mono- or disaccharidic *C*-1-deoxyalditol moieties were prepared from D-galactose, D-glucose, D-mannose, and lactose. A partially hydrolyzed polysaccharide (agarose) was also used as starting material for the synthesis of a disaccharide-containing *C*-glycoside dipyrrane. These compounds were synthesized as follows: the sugar starting materials were first submitted to a mercaptolysis–acetylation one-pot procedure (EtSH/HCl–Ac_2O/pyridine). The resulting peracetylated diethyl dithioacetals were converted into dipyrranes through carbonyl deprotection (H_5IO_6, THF–Et_2O) followed by TFA-catalyzed pyrrole condensation with yields up to 62%. Overall yields from sugar starting materials were up to 49%.

Porphyrin glycoconjugates have become of interest because of the current effort to develop target-specific photosensitizers, which are particularly promising in the photodynamic therapy for cancer.[1] Considering both chemical and enzymatic stabilities of glycoporphyrins, synthetic strategies that lead to a carbon–carbon bond linking the carbohydrate moiety to the porphyrin ring are highly desirable. In this context, dipyrranes (dipyrromethanes)[2] prepared from partially protected 1-hydroxy aldoses[3,4] and *C*-glycosyl aldehydes[5] are important building blocks for the synthesis of *meso*-substituted *C*-1-deoxyalditol- and *C*-glycoside-porphyrins. In the case of the *C*-1-deoxyalditol derivatives, the use of the corresponding carbohydrate-containing dipyrranes can be indispensable for porphyrin synthesis.[3] In previous works dedicated to the synthesis of the aforementioned dipyrranes, only monosaccharides, such as, D-glucose, D-galactose, D- and L-arabinose, D-xylose, and D-gulose have already been utilized as starting materials.[3–5] This could be one of the reasons for the lack of oligosaccharide-containing *C*-1-deoxyalditol- or *C*-glycoside-porphyrins examples in the literature. The presence of higher sugar moieties in glycoconjugates is considered important for the anticipated biological activity and targeting. This is based on the fact that oligosaccharide glycoconjugates have superior binding constants toward carbohydrate-binding proteins than do the monosaccharide ones.[6] Furthermore, dipyrrane synthetic routes known to date are not suitable for the use of unusual starting materials, such as algal galactans, which often present synthetically useful unique structural motifs.[7–9]

As one of our future objectives involves glycoporphyrin synthesis from diverse carbohydrate sources, the present work was devoted to the development of a general strategy for the preparation of dipyrranes from mono-, oligo-, and polysaccharides. Reactions based on mercaptolysis using EtSH/HCl reactant have proven to be efficient for the preparation of protected aldehydes as diethyl dithioacetals from monosaccharides.[10,11] More recently, a multigram production of diethyl dithioacetals containing the rare residue of 3,6-anhydro-L-galactose was performed using commercial agarose as starting material.[8] Here, unmasked aldehydes obtained from peracetylated diethyl dithioacetals were condensed with pyrrole to produce mono- and disaccharide *C*-1-deoxyalditol- and *C*-glycoside-dipyrranes (Table 1). This synthetic strategy was evaluated in terms of its applicability by employing three monosaccharides (D-galactose **1**, D-glucose **2** and D-mannose **3**), a disaccharide (lactose **4**), and a polysaccharide (agarose **5**) as starting materials.

In order to synthesize the peracetylated diethyl dithioacetals shown in Table 1, we developed a one-pot procedure[12] that combines mercaptolysis (EtSH/HCl) and acetylation (Ac_2O/pyridine) to produce **6**,[13] **7**[13], and **8**[13] from monosaccharides **1**, **2**, and **3**, respectively. These reactions were performed by adding the acetylating mixture directly into mercaptolysis reaction after its completion (monitored by TLC analysis). The same approach also provided the lactose-derivative peracetylated dithioacetal **9**.[14]

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0040-4039/$ - see front matter © 2012 Published by Elsevier Ltd.
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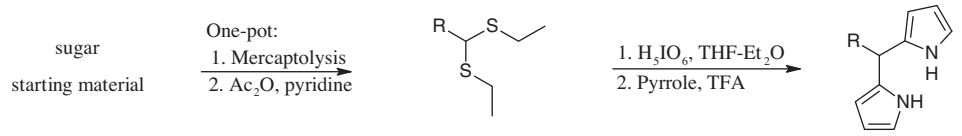
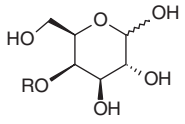
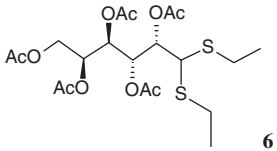
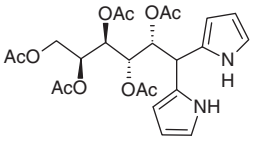
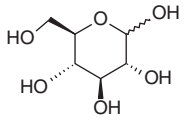
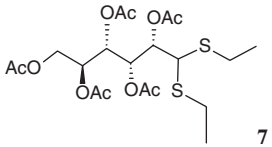
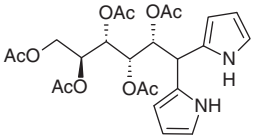
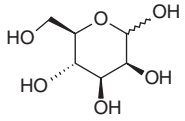
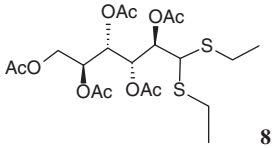
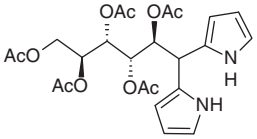
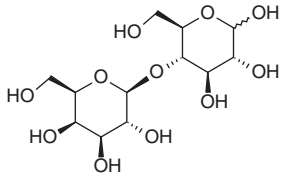
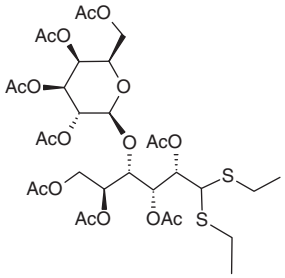
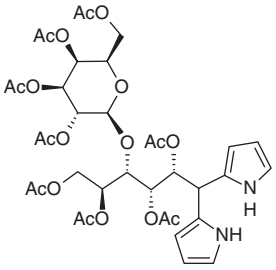
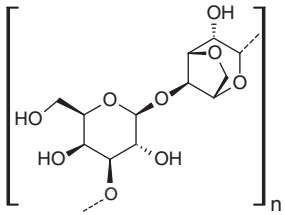
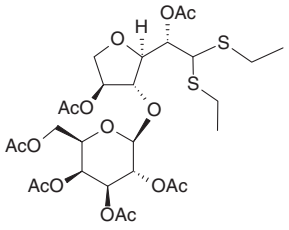
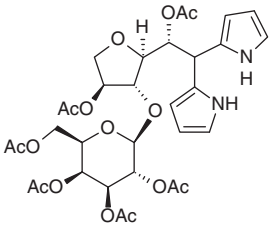
Table 1
Synthesis of dipyrranes from sugar starting materials **1–5**



Entry	Starting material	Mercaptolysis (Time)[a] (min)	Peracetylated diethyl dithioacetal[b] (Yield)[c]	Dipyrrane (Yield)[d]	Overall yield (%)
1	 **1**	30	 **6** (41%)	 **12** (59%)	24
2	 **2**	180	 **7** (98%)	 **13** (50%)	49
3	 **3**	70	 **8** (95%)	 **14** (50%)	48
4	 **4**	240	 **9** (67%)	 **15** (33%)	22
5	 **5**	60	 **10** (46%)	 **16** (62%)	29

[a] Mercaptolysis conditions: HCl/EtSH, 0 °C; for agarose (**5**, entry 5) a partial hydrolysis (1 M TFA, 3 h, 80 °C) was performed before the mercaptolysis step.
[b] Acetylation conditions: Ac_2O/pyridine, 18 h, rt.
[c] Isolated yields calculated from starting materials **1–5**.
[d] Isolated yields calculated from peracetylated diethyl dithioacetals **6–10**.

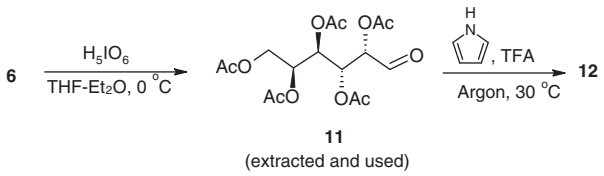
For agarose (**5**), a TFA-mediated partial hydrolysis was necessary before the mercaptolysis step. Agarose is a polysaccharide constituted by 3-linked β-D-Gal*p* and 4-linked 3,6-An-α-L-Gal*p* alternating units, where the glycosidic bonds of the 3,6-anhydrogalactopyranosyl units are significantly more acid-labile than the galactopyranosidic ones.[7,8] Under the specific hydrolysis conditions here utilized, disaccharide agarobiose was then preferentially formed, which resulted in the peracetylated dithioacetal **10**[8] after mercaptolysis–acetylation one-pot reaction.

Table 1 also shows the differences in the mercaptolysis reaction time, accordingly to the starting material employed. For example, mercaptolysis step of **1** had to be interrupted after 30 min, while reaction time for the other starting materials was at least one hour long. As previously noted,[11] the mercaptolysis reaction mixture of **1** became solid in a few minutes, preventing the starting material to be completely consumed. Even though the yield obtained for **6** was consequently lower than for **7–10** (Table 1), we took advantage of the distinct behavior of the galactose derivative to prepare grams of the hydroxyl-unprotected D-galactose dithioacetal by using a crystallization-based purification[11] instead of the use of column chromatography (see Supplementary data).

In order to synthesize dipyrranes from the peracetylated diethyl dithioacetals, we applied a previously stated[8,15] deprotection of carbonyl of dithioacetal derivatives with periodic acid at 0 °C in THF–Et_2O (first step of Scheme 1 reaction). This procedure overcomes the use of toxic heavy metal salts that are traditionally employed in this type of reaction.[16]

Dipyrrane synthesis was then evaluated using aldehyde **11**[10,11] as substrate (Table 2 and second step of Scheme 1 reaction). For these experiments, all condensation reactions were conducted with excess of pyrrole (1:25, aldehyde/pyrrole) in the presence of TFA under solvent-free conditions,[17] for 30 min. Because dipyrranes easily subside to oxidation after its formation, condensation reaction was evaluated in terms of reaction temperature and presence of inert atmosphere. This brief study indicated that the presence of argon atmosphere was essential for reaching fair yields (in Table 2, compare entries 2 and 5). Considering the reaction temperatures evaluated in entries 1, 2, and 3 (Table 2), even though the yields increased by the lowering the temperature, the best yields were reached at higher temperatures when using argon atmosphere (Table 2, entries 4, 5, and 7). These results suggest that the inert atmosphere prevented dipyrrane temperature-mediated degradation.

Sugar-derived aldehydes can be unstable and also cause difficulties during column chromatography. For this reason, most of the condensation conditions evaluated in Table 2 were performed using the aldehyde obtained in the vacuum-dried chloroform extracts of the periodic acid reaction, without further purification. Conditions defined in entry 5 were then reassessed by using a chromatographically purified sample of aldehyde **11** (Table 2, entry 6). This comparison (Table 2, entries 5 and 6) demonstrated that the yield obtained when using the extracted aldehyde (calculated from peracetylated dithioacetal **6**) was higher than that involving an extensively purified sample of aldehyde **11**. This could be explained by losses during the chromatographic procedure. We also noted that the immediate use of the extracted aldehyde was



Scheme 1. Conversion of diethyl dithioacetal **6** into dipyrrane **12**.

Table 2
Synthesis of dipyrrane **12** through pyrrole–aldehyde **11** condensation[a]

Entry	Temperature (°C)	Atmosphere	Aldehyde purification	Yield (%)
1	50	Air	Extraction[b]	27[c]
2	30	Air	Extraction[b]	30[c]
3	0	Air	Extraction[b]	40[c]
4	50	Argon	Extraction[b]	56[c]
5	30	Argon	Extraction[b]	59[c]
6	30	Argon	Chromatography[d]	35[c,e]
7	0	Argon	Extraction[b]	40[c]

[a] Conditions: aldehyde/pyrrole 1:25, TFA 0.1 equiv, 30 min, solvent-free.
[b] Concentrated chloroform extracts from periodic acid reaction.
[c] Isolated yield for dipyrrane **12** calculated from diethyl dithioacetal **6**.
[d] Silica-gel column chromatography of the concentrated chloroform extracts. [b]
[e] 60% (aldehyde **11** yield) and 58% (dipyrrane **12** yield).

important for the success of the more straightforward procedure. In this way, aldehyde–pyrrole condensation conditions were defined in accordance to entry 5 of Table 2.

General procedure[18] for peracetylated dithioacetals conversion into dipyrranes (Scheme 1) was also applied to compounds **7–10** to give dipyrranes **13–16**, as shown in Table 1. Lactose-derivative dipyrrane **15** was obtained with a lower yield (33%) in comparison to the monosaccharide ones (50–59%). However, despite the disaccharide nature of dipyrrane **16**, it presented the highest yield among all dipyrranes here prepared (62%). This result is consistent with the *C*-glycoside-aldehyde being more reactive than the alditol-aldehydes toward dipyrrane formation. This observation is also based on the fact that the periodic acid reaction gives about the same aldehyde yield from either **6** or **10**.[9]

In terms of stability, dipyrranes **12–16** appeared to be indefinitely stable when stored in freezer at −5 °C. During NMR experiments, we also noted that dipyrranes were quite stable in deuterated DMSO solution for, at least, 2 days at room temperature. On the other hand, when employing $CDCl_3$, the originally pale yellow solutions became dark gray in a few hours.

There are only two examples of acetyl protected *C*-1-deoxyalditol dipyrranes described to date in the literature, being both of them synthesized by reacting $SnCl_4$/pyrrolylmagnesium-bromide (1:1) with peracetylated aldoses to give dipyrranes in 35–45% yield.[4] When using protecting groups other than acetyl (benzyl, isopropylidene, or methyl) the same type of dipyrranes were obtained in yields up to 42% from acid-catalyzed pyrrole condensation with partially protected 1-hydroxy aldoses.[3,4] In all cases, the given yields were always calculated from the hydroxyl-protected building block and not from the raw sugar starting material. Independently of the protecting group, the *C*-1-deoxyalditol dipyrranes previously reported[3,4] presented one free hydroxyl group, which was originated from the position involved in the ring closure of the parent pyranoses or furanoses. In contrast, dipyrranes herein synthesized are fully hydroxyl-protected with acetyl groups and the yields obtained in dithioacetals conversion into dipyrromethanes were considerably higher than the previously reported strategies for dipyrrane synthesis.

By observing the peracetylated dipyrrane structures depicted in Table 1, it is noteworthy that the monosaccharide-derivatives **12–14** represent examples of *C*-1-deoxyalditol dipyrranes, while compound **15** corresponds to a *C*-1-deoxyalditol dipyrrane linked to a galactopyranose unit through an *O*-glycosidic bond. Differently, the agarose-derivative dipyrrane **16** constitutes a strict example of a *C*-glycoside where a β-L-threofuranose residue is linked to the dipyrryl unit through a *C*-glycosidic linkage. The β-L-threofuranosyl unit was originated from the fivemembered ring of the 3,6-anhydrogalactopyranosyl units present in agarose structure. In conclusion, we established the use of dithioacetal intermediates to synthesize dipyrranes containing a carbohydrate

moiety attached to the dipyrryl unit through a carbon–carbon bond. This approach allows the use of diverse carbohydrates as starting materials. Dipyrranes **12–16** are currently being employed for the synthesis of *C*-1-deoxyalditol- and *C*-glycoside-*meso*-substituted-porphyrins in our laboratories.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.12.048.

References and notes

1. Zheng, X.; Pandey, R. K. *Anti-Cancer Agents Med. Chem.* **2008**, *8*, 241–268.
2. A recent review proposes the use of the term 'dipyrrane' instead of 'dipyrromethane': Gryko, D. T.; Gryko, D.; Lee, C.-H. *Chem. Soc. Rev.* **2012**, *41*, 3780–3789.
3. Casiraghi, G.; Cornia, M.; Zanardi, F.; Rassu, G.; Ragg, E.; Bortolini, R. *J. Org. Chem.* **1994**, *59*, 1801–1808.
4. Cornia, M.; Capacchi, S.; Del Pogetto, M.; Pelosi, G.; Fava, G. G. *Tetrahedron: Asymmetry* **1997**, *8*, 2905–2912.
5. Štepánk, P.; Dukh, M.; Šaman, D.; Moravcová, J.; Kniežo, L.; Monti, D.; Venanzi, M.; Mancini, G.; Drašar, P. *Org. Biomol. Chem.* **2007**, *5*, 960–970.
6. (a) Leffler, H.; Barondes, S. H. *J. Biol. Chem.* **1986**, *261*, 10119–10126; (b) Hadari, R. H.; Arbel-Goren, R.; Levy, Y.; Amsterdan, A.; Alon, R.; Zakut, R.; Zick, Y. *J. Cell. Sci.* **2000**, *113*, 2385–2397.
7. (a) Gonçalves, A. G.; Noseda, M. D.; Duarte, M. E. R.; Grindley, T. B. *Carbohydr. Res.* **2006**, *341*, 1753–1757; (b) Gonçalves, A. G.; Noseda, M. D.; Duarte, M. E. R.; Grindley, T. B. *J. Org. Chem.* **2007**, *72*, 9896–9904.
8. Ducatti, D. R. B.; Massi, A.; Noseda, M. D.; Duarte, M. E. R.; Dondoni, A. *Org. Biomol. Chem.* **2009**, *7*, 576–588.
9. Ducatti, D. R. B.; Massi, A.; Noseda, M. D.; Duarte, M. E. R.; Dondoni, A. *Org. Biomol. Chem.* **2009**, *7*, 1980–1986.
10. Wolfrom, M. L. *J. Am. Chem. Soc.* **1930**, *52*, 2464–2473.
11. Roberts, J. C.; Nagasawa, H. T.; Zera, R. T.; Fricke, R. F.; Goon, D. J. W. *J. Med. Chem.* **1987**, *30*, 1891–1896.
12. Mercaptolysis–acetylation one-pot procedure: sugar starting material **1–4** (or agarose **5** hydrolyzate) was dissolved to a concentration of 40 g% in a mixture of conc HCl (37%)/EtSH (3:2, v/v) at 0 °C. Mercaptolysis was kept at 0 °C for different reaction times, accordingly to the starting material (see Table 1). The resulting mixture was then directly added of 22 volumes (in relation to HCl/EtSH volume) of pyridine/acetic anhydride (6:5, v/v). Reaction was stirred at 0 °C for an hour and then kept at room temperature for 18 h. Ice water was added to the reaction mixture and the product was extracted with $CHCl_3$. The organic phase was washed with 5% aqueous $CuSO_4$ solution and then water, dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel using ethyl acetate/hexanes as mobile phase (1:3 for compounds **6–8**, 2:3 for **9** and 1:1 for **10**).
13. Khan, A. T.; Khan, M. M. *Carbohydr. Res.* **2010**, *335*, 21392145.
14. Compound **9**: $[\alpha]_D^{22}$ +29.7 (*c* 1.0, DMSO); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.76 (dd, *J* = 5.7, 4.5 Hz, 1H, H-3), 5.48 (t, *J* = 5.3 Hz, 1H, H-2), 5.39 (d, *J* = 3.4 Hz, 1H, H-4′), 5.24–5.17 (m, 1H, H-5), 5.14 (dd, *J* = 10.3, 7.9 Hz, 1H, H-2′), 5.02 (dd, *J* = 10.5, 3.5 Hz, 1H, H-3′), 4.75 (d, 1H, *J* = 7.8 Hz, H-1′), 4.47 (dd, *J* = 12.4, 2.8 Hz, 1H, H-6a), 4.25 (t, *J* = 4.6 Hz, 1H, H-4), 4.21–4.09 (m, 4H, H-1, H-6b, H-6a′, H-6b′), 3.92 (t, *J* = 6.8 Hz, 1H, H-5′), 2.79–2.62 (m, 4H, CH_2CH_3), 2.15, 2.10, 2.09, 2.07, 2.07, 2.06, 2.06, 1.98 (8s, 24H, $COCH_3$), 1.26 (dd, *J* = 14.1, 7.2 Hz, 6H, CH_2CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.5, 170.4, 170.1, 170.1, 169.8, 169.7, 169.7, 169.2 (8C, C=O), 100.5 (1C, C-1′), 75.4 (1C, C-4), 72.4 (1C, C-2), 71.2 (2C, C-3, C-5′), 71.0 (2C, C-5, C-3′), 69.1 (1C, C-2′), 67.0 (1C, C-4′), 62.1 (1C, C-6), 61.4 (1C, C-6′), 51.3 (1C, C-1), 25.5, 24.8 (2C, CH_2CH_3), 20.8 (8C, $COCH_3$), 14.4 (2C, CH_2CH_3). HRMS (ESI): *m*/*z* calcd for $C_{32}H_{48}O_{18}S_2Na^+$: 807.2174; found: 807.2183.
15. Shi, X.-X.; Khanapure, S. P.; Rokach, J. *Tetrahedron Lett.* **1996**, *37*, 4331–4334.
16. (a) Wolfrom, M. L.; Konigsberg, M.; Weisblat, D. I. *J. Am. Chem. Soc.* **1939**, *61*, 574–576; (b) Miljković, M.; Dropkin, D.; Hagel, P.; Habash-Marino, M. *Carbohydr. Res.* **1984**, *128*, 11–20.
17. (a) Lee, C.-H.; Lindsey, J. S. *Tetrahedron* **1994**, *50*, 11427; (b) Littler, B. J.; Miller, M. A.; Hung, C. H.; Wagner, R. W.; O'Shea, D. F.; Boyle, P. D.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 1391–1396.
18. To a cooled (0 °C), stirred mixture of peracetylated diethyl dithioacetal (1 mmol), THF (2 mL), and Et_2O (5 mL), a solution of H_5IO_6 (2 mmol) in THF (1 mL) was added drop wise. The resulting mixture was warmed to room temperature, stirred for 20 min (60 min for **9**), diluted with 0.1 M phosphate buffer, and then extracted with $CHCl_3$. The organic phase containing the freshly prepared aldehyde was washed with 10% aqueous Na_2SO_3 solution, dried (Na_2SO_4), and concentrated. Pyrrole (25 mmol) and TFA (0.1 mmol) were then added to the concentrated extract and the resulting mixture was stirred for 30 min under Argon (see details in Supplementary data). Reaction mixture was then quenched with 0.1 M NaOH and extracted with chloroform. The organic phase was washed with water, dried over Na_2SO_4, concentrated under vacuum, and purified by flash chromatography with ethyl acetate/hexanes as mobile phase (5:7 for compounds **12–14**, 2:1 for **15** and 1:1 for **16**).
Compound **12**: $[\alpha]_D^{22}$ +12.0 (*c* 0.5 , $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.52 (b, 1H, NH), 8.26 (b, 1H, NH′), 6.71 (b, 1H, H-1 pyrrole), 6.68 (b, 1H, H-1′ pyrrole), 6.13 (b, 1H, H-2 pyrrole), 6.12 (b, 1H, H-2′ pyrrole), 6.05 (b, 1H, H-3 pyrrole), 6.02 (b, 1H, H-3′ pyrrole), 5.49–5.40 (m, 2H, H-2, H-3), 5.27 (dd, *J* = 9.5, 1.0 Hz, 1H, H-4), 5.24–5.18 (m, 1H, H-5), 4.32 (d, *J* = 6.6 Hz, 1H, H-1), 4.27 (dd, *J* = 11.8, 4.7 Hz, 1H, H-6a), 3.79 (dd, *J* = 11.8, 7.5 Hz, 1H, H-6b), 2.09, 2.01, 2.01, 2.00, 1.91 (5s, 15H, $COCH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 171.1, 170.6, 170.4, 170.0, 169.9 (5C, C=O), 128.7 (1C, C-4 pyrrole), 127.4 (1C, C-4′ pyrrole), 117.9 (1C, C-1 pyrrole), 117.6 (1C, C-1′ pyrrole),108.8 (1C, C-2, pyrrole), 108.6 (1C, C-3 pyrrole), 108.4 (2C, C-2′ pyrrole), 106.8 (1C, C-3′ pyrrole), 71.7 (1C, C-2), 68.9 (1C, C-3), 68.3 (1C, C-4), 67.9 (1C, C-5), 62.4 (1C, C-6), 39.8 (1C, C-1), 20.9, 20.8, 20.8, 20.7, 20.7 (5C, $COCH_3$). HRMS (ESI): *m*/*z* calcd for $C_{24}H_{30}N_2O_{10}Na^+$: 529.1793; found: 529.1779.
Compound **13**: $[\alpha]_D^{22}$ −15.9 (*c* 1.0 , DMSO); ^{1}H NMR (400 MHz, DMSO) δ = 10.49 (b, 1H, NH), 10.39 (b, 1H, NH′), 6.62 (d, *J* = 1.6 Hz, 1H, H-1 pyrrole), 6.58 (d, *J* = 1.6 Hz, 1H, H-1′ pyrrole), 5.95–5.86 (m, 4H, H-2, H-2′, H-3, H-3′ pyrrole), 5.43 (dd, *J* = 7.3, 5.2 Hz, 1H, H-2), 5.20 (dd, *J* = 6.2, 4.8 Hz, 1H, H-4), 5.00–4.91 (m, 2H, H-3, H-5), 4.27 (d, *J* = 7.4 Hz, 1H, H-1), 4.10 (dd, *J* = 12.2, 3.1 Hz, 1H, H-6a), 4.06–3.99 (m, 1H, H-6b), 2.05 2.00, 1.99, 1.89, 1.88 (5s, 15H, $COCH_3$). ^{13}C NMR (101 MHz, DMSO) δ = 170.0, 169.6, 169.3, 169.1, 169.0 (5C, C=O), 128.7 (1C, C-4 pyrrole), 128.4 (1C, C-4′ pyrrole), 117.2 (1C, C-1 pyrrole), 117.0 (1C, C-1′ pyrrole), 107.3, 106.9, 106.6, 105.6 (4C, C-2, C-3, C-2′, C-3′ pyrrole), 72.3 (1C, C-2), 69.2 (1C, C-3), 68.7 (1C, C-4), 68.6 (1C, C-5), 60.9 (1C, C-6), 38.9 (1C, C-1), 20.4–20.3 (5C, $COCH_3$). HRMS (ESI): *m*/*z* calcd for $C_{24}H_{30}N_2O_{10}Na^+$: 529.1793; found: 529.1768.
Compound **14**: $[\alpha]_D^{22}$ +19.5 (*c* 1.0 , DMSO); ^{1}H NMR (400 MHz, DMSO) δ = 10.64 (b, 1H, NH pyrrole), 10.34 (b, 1H, NH′ pyrrole), 6.63 (b, 1H, H-1 pyrrole), 6.55 (d, *J* = 1.2 Hz, 1H, H-1′ pyrrole), 5.98–5.88 (m, 2H, H-2, H-3 pyrrole), 5.88–5.79 (m, 2H, H-2′, H-3′ pyrrole), 5.56 (dd, *J* = 8.7, 5.7 Hz, 1H, H-2), 5.42 (d, *J* = 8.4 Hz, 1H, H-4), 4.95–4.84 (m, 2H, H-3, H-5), 4.34 (d, *J* = 8.8 Hz, 1H, H-1), 4.08 (dd, *J* = 12.4, 2.6 Hz, 1H, H-6a), 4.04–3.97 (m, 1H, H-6b), 2.07, 1.99, 1.89, 1.82, 1.82 (5s, 15H, $COCH_3$). ^{13}C NMR (101 MHz, DMSO) δ = 170.0, 169.5, 169.2, 169.2, 169.2 (5C, C=O), 129.1 (1C, C-4 pyrrole), 128.5 (1C, C-4′ pyrrole), 117.4 (1C, C-1 pyrrole), 116.9 (1C, C-1′ pyrrole), 107.2 (1C, C-2 pyrrole), 106.9 (1C, C-2′ pyrrole), 106.0 (1C, C-3 pyrrole), 105.8 (1C, C-3′ pyrrole), 72.0 (1C, C-2), 68.8 (1C, C-3), 67.7 (1C, C-5), 66.6 (1C, C-4), 61.3 (1C, C-6), 38.9 (1C, C-1), 20.7, 20.5, 20.4, 20.4, 20.4 ($COCH_3$). HRMS (ESI): *m*/*z* calcd for $C_{24}H_{30}N_2O_{10}Na^+$: 529.1793; found: 529.1773.
Compound **15**: $[\alpha]_D^{22}$ −6.51 (*c* 0.3 , DMSO); ^{1}H NMR (400 MHz, DMSO) δ = 10.31 (b, 1H, NH), 10.27 (b, 1H, NH′), 6.62 (b, 1H, H-1 pyrrole), 6.55 (b, 1H, H-1′ pyrrole), 5.97–5.85 (m, 4H, H-2, H-3, H-2′, H-3′ pyrrole), 5.56 (t, *J* = 6.0 Hz, 1H, H-2), 5.24 (d, *J* = 3.5 Hz, 1H, H-4′), 5.18 (dd, *J* = 9.5, 3.5 Hz, 1H, H-3′), 5.01–4.95 (m, 1H, H-5), 4.93–4.82 (m, 3H, H-3, H-1′, H-2′), 4.40 (d, *J* = 6.8 Hz, 1H, H-1), 4.25 (t, *J* = 6.5 Hz, 1H, H-5′), 4.14 (dd, *J* = 12.0, 2.5 Hz, 1H, H-6a′), 4.08 (t, *J* = 4.8 Hz, 1H, H-4), 4.05–3.89 (m, 3H, H-6a, H-6b, H-6b′), 2.13, 2.00, 1.98, 1.97, 1.97, 1.97, 1.91, 1.89 (8s, 24H, $COCH_3$). ^{13}C NMR (101 MHz, DMSO) δ = 170.0, 169.9, 169.8, 169.5, 169.4, 169.1, 169.1, 168.8 (8C, C=O), 129.0 (1C, C-4 pyrrole), 128.4 (1C, C-4′ pyrrole), 117.2 (1C, C-1 pyrrole), 116.8 (1C, C-1′ pyrrole), 107.2, 106.9, 106.8 (3C, C-2, C-2′, C-3 pyrrole), 105.2 (1C, C-3′ pyrrole), 99.8 (1C, C-1′), 75.8 (1C, C-4), 72.4 (1C, C-2), 70.4 (1C, C-3′), 70.1, 69.9 (2C, C-5, C-5′), 69.9 (1C, C-3), 69.0 (1C, C-2′), 67.2 (1C, C-4′), 61.1 (2C, C-6, C-6′), 38.3 (1C, C-1), 20.5, 20.5, 20.4, 20.4, 20.3, 20.3, 20.3, 20.3 (8C, $COCH_3$). HRMS (ESI): *m*/*z* calcd for $C_{36}H_{46}N_2O_{18}Na^+$: 817.2638; found: 817.2648.
Compound **16**: $[\alpha]_D^{22}$ +16.4 (*c* 1.0 , DMSO); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.47 (b, 1H, NH), 8.44 (b, 1H, NH′), 6.64 (b, 2H, H-1, H-1′ pyrrole), 6.13–6.02 (m, 4H, H-2, H-3, H-2′, H-3′ pyrrole), 5.67 (dd, *J* = 8.5, 3.7 Hz, 1H, H-2), 5.39 (d, *J* = 3.1 Hz, 1H, H-4′), 5.13 (dd, *J* = 10.4, 7.9 Hz, 1H, H-2′), 5.00 (dd, *J* = 10.4, 3.4 Hz, 1H, H-3′), 4.94 (d, *J* = 4.2 Hz, 1H, H-4), 4.60 (d, *J* = 7.9 Hz, 1H, H-1′), 4.53 (d, *J* = 8.5 Hz, 1H, H-1), 4.20 (dd, *J* = 11.4, 6.0 Hz, 1H, H-6a′), 4.13 (dd, *J* = 11.7, 6.7 Hz, 1H, H-6b′), 3.98–3.91 (m, 3H, H-5, H-6a, H-5′), 3.91–3.84 (m, 2H, H-3, H-6b), 2.14, 2.06, 2.03, 1.96, 1.96, 1.91 (6s, 18H, $COCH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.9, 170.6, 170.3, 170.2, 170.0, 169.6 (6C, C=O), 128.9 (1C, C-4 pyrrole), 128.6 (1C, C-4′ pyrrole), 117.4 (2C, C-1, C-1′ pyrrole), 108.7 (1C, C-2 pyrrole), 108.3 (1C, C-2′ pyrrole), 107.4 (1C, C-3 pyrrole), 106.7 (1C, C-3′ pyrrole), 101.6 (1C, C-1′), 85.6 (1C, C-5), 83.6 (1C, C-3), 79.7 (1C, C-4), 73.3 (1C, C-2), 71.1 (1C, C-5′), 71.1 (1C, C-6), 70.8 (1C, C-3′), 68.8 (1C, C-2′), 67.3 (1C, C-4′), 61.5 (1C, C-6′), 39.5 (1C, C-1), 21.0, 20.9, 20.6, 20.6, 20.6, 20.6 (6C, $COCH_3$). HRMS (ESI): *m*/*z* calcd for $C_{32}H_{40}N_2O_{15}Na^+$: 715.2321; found: 715.2300.