**C-Glycosyl Amino-Substituted Hydro- and Benzoquinones: Synthesis and Preliminary Biological Evaluation**

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Received 20 June 2007; revised 18 July 2007

**Abstract:** Reaction of C-β-D-glycopyranosyl-1,4-dimethoxybenzenes with acetyl nitrate afforded 2-(β-D-glycopyranosyl)-1,4-dimethoxy-5-nitrobenzenes in high yields. These were converted smoothly (reduction to amines, N-acylation, oxidation, and reduction) into the corresponding C-glycosyl-hydro(benzo)quinone derivatives, with different amide-based substituents at C-5. Reduction of the nitro compounds to amines proceeded smoothly by catalytic hydrogen transfer with HCO2NH4.

**Key words:** glycosides, electrophilic aromatic substitution, hydrogen transfer, reduction, amines, amides

Even though C-glycosyl flavonoids constitute a specific class of natural products, carbohydrates directly bound to an aromatic moiety through a C–C bond are rare, as compared to common sugars. However, glycosyl arenes (also termed C-aryl glycosides) are currently attracting increasing interest, as regard to their synthesis and because of bioactivities anticipated for such glycomimics, based on possible interactions with sugar-processing enzymes and on their resistance to both acid- and enzyme-catalyzed hydrolysis.

Our interest in this field stems from earlier studies devoted to the synthesis of 5-thio-β-D-xylopyranosides and C-5-thio-β-D-xylopyranosyl compounds as orally active venous antithrombotics. C-5-Thio-β-D-xylopyranosyl derivatives of phenol, resorcinol, phloroglucinol were obtained by aromatic electrophilic substitution, or by O → C-glycoside rearrangement, showing the reactivity of electron-rich aryls, in agreement with studies aiming at preparing C-glycosyl flavonoids, or D-glycosyl derivatives (furanose or pyranose type) of dimethyldihydroquinone. By such a coupling and subsequent oxidation and reduction, Kalvoda first obtained various glycosyl derivatives of dimethyldihydroquinone.

**Scheme 1** Recent synthetic developments with 2-C-β-D-glycopyranosyl-1,4-dimethoxybenzenes

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**SYNTHESIS** 2007, No. 22, pp 3473–3488
Advanced online publication: 29.10.2007
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nosyl-hydro(1,4-benzo)quinones, a class of simple compounds with only few synthetic representatives. Because glycosyl-hydro(benzo)quinones correspond to a stable scaffold amenable to various functionalizations or modifications, resulting in possible bioactivities, the synthesis of glycopyranosyl derivatives was carried out, using 1,4-dimethoxybenzene, and its 2,3-, and 2,6-dimethyl derivatives. While enzymatic and crystallographic studies showed that the glucosyl-hydro(benzo)quinones were weak inhibitors of glycogen phosphorylase (GP) due to binding at the active site, the o- and m-dimethyl analogues opened the first access to C-glycosyl-tocopherols, as unprecedented antioxidants. This encouraged us to further investigate the potential of such glycosyl-arenes, in particular by electrophilic substitution (halogenation, formylation, nitration; Scheme 1). We herein report on the synthesis of 2-glycosyl-1,4-dimethoxy-5-nitrobenzenes. After reduction, they gave access to a library of sugar-based amide-linked aromatics, which have been tested against A375 human melanoma cell lines.

Because of the lability of acetyl protecting groups, nitration of 2-(2,3,4,6-tetra-O-acetyl-D-glycopyranosyl)-1,4-dimethoxybenzenes (1,2) was envisaged under mild conditions and in particular with acyl nitrates, because such nitrating agents are accessible by simple methods avoiding harsh acidic conditions. Acetyl nitrate [ca. 2.1 equiv prepared in situ in anhyd MeCN from NH₄NO₃ (2.4 equiv) and AcCl (2.1 equiv)] was found effective to achieve the regioselective nitration of 1 and 2 within 2 hours, to afford 3 and 5 in 81% and 75% yield, respectively (Scheme 2). The substrates were reactive enough for

Scheme 2 Reagents and conditions: (a) NH₄NO₃, AcCl, MeCN, 0 °C to r.t., 2 h; (b) Na₂S₂O₄ (H₂O–MeOH) or HCO₂NH (MeOH), 10% Pd/C, r.t.; (c) RCOCl, pyridine, CH₂Cl₂; (d) BaO, MeOH; (e) CAN, MeCN–H₂O; (f) Na₂S₂O₄, CHCl₃/H₂O.
the nitration to proceed with limited amounts of an hazardous reagent (caution: AcONO\textsubscript{2} may explode upon heating).\textsuperscript{18} The grade of NH\textsubscript{4}NO\textsubscript{3} appeared to be critical since limited drying led to incomplete nitration of 1, while extensive drying in the presence of P\textsubscript{2}O\textsubscript{5} favored dinitration (see experimental section). Minor side-products, to be fully described in a forthcoming paper, were separated by column chromatography and identified as chlorinated regioisomers (see Scheme 2 for numbering). Not surprisingly, the C-5 chloro isomers were more abundant \[\text{4 (5-Cl): 11\%, 6 (5-Cl): 13\%}\] as compared to the C-6 analogues (D-Glc: 3\%, D-Gal: 2\%). Regarding their formation, we assumed that, because NO\textsubscript{2}\textsuperscript{+} ions or acetyl nitrate are oxidizing agents,\textsuperscript{19} chloride anions, still present in the medium even after filtration of precipitated NH\textsubscript{4}Cl (see experimental) may undergo oxidation, thus forming reactive species (e.g., chlorine atom, chloronium ion) capable of aromatic substitution with activated substrates. This is reminiscent of reported halogenations, occurring together with nitration,\textsuperscript{20a} or favored by the electrophilic fluorination agent Selectfluor,\textsuperscript{20b} or dimethyldioxirane.\textsuperscript{20c} While more complete removal of precipitated NH\textsubscript{4}Cl appeared difficult, few attempts to minimize chlorination by reducing the quantity of AcCl (NH\textsubscript{4}NO\textsubscript{3}/AcCl ratio changed from 2.4/2.1 to 2.7/1.8) were not encouraging, since the reaction was slower (3.5 h) while the chloro isomers were again detected. Probably, use of silver nitrate would allow a more efficient elimination of chloride anions, as insoluble silver chloride. Moreover, attempts to achieve nitrosation or nitration of glycosyl hydroquinone failed, mainly due to oxidation to glycosyl-benzoquinone under the conditions applied (NaNO\textsubscript{2}/AcCl, NH\textsubscript{4}NO\textsubscript{3}/AcCl in varying amounts \textasciitilde1.1 equiv, 1.5 equiv, 2.1 equiv, CAN–NaHCO\textsubscript{3}).\textsuperscript{21}

In order to prepare the corresponding amino derivatives, reduction of compounds 3 and 5 was attempted in the presence of Raney nickel in EtOH,\textsuperscript{22} but not surprisingly this led to deacetylation and other unwanted transformations. Other reductive conditions applicable to nitro compounds were not tried because of limited efficiency (NaBH\textsubscript{4}) or possible side reactions (LiAlH\textsubscript{4}, NH\textsubscript{2}NH\textsubscript{2}), but catalytic hydrogen transfer was considered. Sodium dithionite/hydrosulfite (Na\textsubscript{2}S\textsubscript{2}O\textsubscript{4}),\textsuperscript{23} currently used in our group for reducing glycosyl benzoquinones\textsuperscript{13f,14f} was envisaged, although it usually requires heating under basic conditions. Compound 3 was reduced within 13 minutes in the presence of Na\textsubscript{2}S\textsubscript{2}O\textsubscript{4} and Pd/C 10\% in H\textsubscript{2}O–MeOH to afford 7 in 60\% yield, together with a polar by-product. Another experiment with HCO\textsubscript{2}NH\textsubscript{2} as the hydrogen donor in MeOH with Pd/C 10\% afforded within 75 minutes 7 as the sole product in 82\% yield. Use of a combination of Na\textsubscript{2}S\textsubscript{2}O\textsubscript{4} and HCO\textsubscript{2}NH\textsubscript{2} with Pd/C in H\textsubscript{2}O–MeOH led within 15 minutes to 7 in 54\% yield, in addition to a polar by-product, assumed to be a salt of 7.

To the best of our knowledge, catalytic hydrogen transfer with Na\textsubscript{2}S\textsubscript{2}O\textsubscript{4} has not been reported previously,\textsuperscript{24} although nitroarenes have been reduced with Na\textsubscript{2}S\textsubscript{2}O\textsubscript{4} in aqueous or biphasic medium in the presence of an electron transfer catalyst.\textsuperscript{25} Interestingly, a bacterial cellulose with a palladium deposit was recently shown to catalyze the generation of hydrogen when incubated with sodium dithionite.\textsuperscript{26}

Compounds 7,8 were acylated in high yields with 13 acyl chlorides to afford \textsuperscript{9a–n} and \textsuperscript{10f} (D-Gal) which display various substituents bound by a fairly stable amide linkage (Scheme 3). 2,6-Bis(chloroformyl)pyridine (0.53 equiv) was used to prepare compounds \textsuperscript{9n} (87\%) and \textsuperscript{9m} (6\%, an ethyl ester formed most probably during extrac-

Scheme 3 Reagents and conditions: (a) Na\textsubscript{2}S\textsubscript{2}O\textsubscript{4} (H\textsubscript{2}O–MeOH) or HCO\textsubscript{2}NH\textsubscript{2} (MeOH), 10\% Pd/C, r.t.; (b) acyl chloride, pyridine, CH\textsubscript{2}Cl\textsubscript{2}; (c) oxidation by air.
tion with CH₂Cl₂ containing EtOH as stabilizer). Compounds 9f and 10f were deacetylated cleanly by BaO in anhydrous MeOH; at 0–4 °C to afford 11f and 12f. Meanwhile 9a and 9n were oxidized to the benzoquinone analogues 13a–l and 13n with ceric ammonium nitrate (CAN) in aqueous acetonitrile solution in good to excellent yields. Then hydroquinone analogues 14a–l and 14n were obtained upon reduction with Na₂S₂O₄ in good to excellent yields.

Further work (Scheme 3) demonstrated the efficiency and the mildness of the reduction of nitro compounds by catalytic hydrogen transfer. For example, 9f was reduced to afford 15 in high yield (86%) which was then converted by acylation into 16–18. Interestingly, upon treatment with Na₂S₂O₄, benzoquinone 13f was reduced as mentioned before to hydroquinone 14f, without modification of the nitro group. However, the aniline derivative 19 was formed upon reduction with Na₂S₂O₄, HCO₂NH₄, 10% Pd/C in H₂O–MeOH. This compound proved to be highly sensitive to oxidation, since it was converted during work-up and chromatography into the benzoquinone 20 (71%), probably because of air oxidation. The smooth and selective reduction of both polyfunctional nitro compounds 9f and 14f to the corresponding anilines showed again the interest of catalytic hydrogen transfer conditions.

While assays showed no inhibition of GP by deacetylated compound 11f, the antitumor activities in vitro of some of the compounds synthesized were evaluated by MTT tetrazolium dye assay against A375 cell line (human melanoma cell), on consideration of structural similarities (benzoquinone, amido moieties) with anticancer agents as antracyclines or naphthalimides. Each compound was tested at five different concentrations to determine IC₅₀ (m/L) required to inhibit cell growth by 50%. The results revealed that compounds derived from 1,4-dimethoxybenzene had low activities, as 17, 18 were found to be inactive, while 10f and 16 had IC₅₀ = 260, 160 µg/mL, respectively. The benzoquinones have IC₅₀ (µg/mL) values as follows: 13b: 74; 13c: 110; 13e: 57; 13f: 20; 13g: 23; 13i: 40 (mean value for 2 assays); 13l: 146; 13n: no activity. The hydroquinones tested showed the following IC₅₀ (µg/mL): 14b: 20; 14c: 87; 14g: 107.

CH₂Cl₂ was washed three times with H₂O, dried (CaCl₂), and distilled over CaH₂ before use. Other organic solvents were distilled. Petroleum ether (PE) used had bp 45–60 °C. TLC was carried out on aluminum sheets coated with silica gel 60 F₂54 (Merck, Darmstadt, Germany). TLC plates were inspected under 254 and 312 nm UV light, and/or developed by treatment with a mixture of 5% H₂SO₄ in EtOH followed by heating. Silica gel column chromatography was performed with Geduran® silica gel Si 60 (40–63 µm) purchased from Merck. ¹H and ¹³C NMR spectra were recorded at 25 °C using Bruker AC200, DRX300 or DRX500 spectrometers with the residual solvent as the internal standard. The ¹H NMR spectra, the coupling constants for pyranosyl rings have been assigned and listed without duplication. NMR solvents were purchased from Euriso-Top (Saint Aubin, France). HRMS (LSIMS) mass spectra were recorded in the positive mode (unless stated otherwise) using a Thermo Finnigan Mat 95 XL spectrometer. MS (ESI) mass spectra were recorded in the positive mode using a Thermo Finnigan LCQ spectrometer. Optical rotations were measured using a PerkinElmer polarimeter. Elemental analyses were performed at the Service Central d’Analyses du CNRS (Vernaison, France).

2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-1,4-dimethoxy-5-nitrobenzene (3) A mixture of NH₄NO₃ (previously dried under vacuum for 2–3 days) (175 mg, 2.18 mmol, 2.4 equiv) and AcCl (140 mL, 1.97 mmol, 2.1 equiv) in anhyd MeCN (5 mL) was stirred at 0 °C for 40 min. Due to the limited solubility of NH₄Cl, a precipitate appeared meanwhile in the turbid solution. After removal of the insoluble materials by filtration, 1,4-dimethoxy-2-(2,3,4,6-tetra-oxo-β-D-glucopyranosyl)benzene (1; 450 mg, 0.96 mmol) was added to the filtrate obtained. Upon stirring at r.t. for 2 h, TLC showed that compound 1 was converted into three compounds (R₉ = 0.53, 0.49, 0.40, PE–EtOAc, 1:1). The more polar spot was easily visible under daylight. H₂O (10 mL) was added to the mixture, which was extracted with CH₂Cl₂ (3 × 15 mL). The extracts were combined and washed with brine (15 mL), H₂O (15 mL), dried (MgSO₄), and evaporated. The residue was purified by chromatography (PE–EtOAc, 3:1) on silica gel to afford successively the C-6 chlorinated compound (13 mg, 3%), its C-5 isomer (53 mg, 11%) (found to be identical to analytical samples obtained by other routes), and the nitro compound 3 (400 mg, 81%).

Other experiments suggested that the content of H₂O in NH₄NO₃ was critical as regard to the nitration outcome. An assay similarly carried out with 1 (20 mg), NH₄NO₃ (previously dried under vacuum for 1 day, 2.4 equiv) and AcCl (2.1 equiv) led, after 5 days, to incomplete conversion of 1, with formation of 3 and chloro isomers (TLC). Use of NH₄NO₃ (7.2 equiv) dried for 24 h in the presence of P₂O₅ and AcCl (6.3 equiv) resulted in complete conversion of 1 after 40 min and afforded 3 (39%), the chloro isomer 4 (6.5%), and a 5,6-dichloro product (23%) (MS, NOE 1D). If the nitration was carried out with NH₄NO₃, dried for one week under vacuum in the presence of P₂O₅, 1 was not completely transformed but a dinitro compound (MS) was found predominantly among the products. Attempted nitration of 1 (60 mg) in MeCN at r.t. with NH₄NO₃, dried for one week under vacuum in the presence of P₂O₅, 2.4 and 3.0 equiv (10 mL), and trifluoroacetic anhydride led (6 equiv) led, even after 3–4 days, to partial conversion of 1 (ca 60%) and formation of separable dinitro isomers (MS). They were identified by NMR spectroscopy based on NOE 1D as the 3,6-dinitro (minor isomer) and the 5,6-dinitro (major isomer) derivatives.

Yellow-green solid; mp 142.5–143 °C (CH₂Cl₂–PE); R₉ = 0.40 (PE–EtOAc, 1:1); [α]₁₇₀ = −25.0 (c 0.75 CH₂Cl₂).

¹H NMR (300.13 MHz, CDCl₃): δ = 7.38 (s, 1 H, Ar), 7.17 (s, 1 H, Ar), 5.37 (t, J = 9.3 Hz, 1 H, H-5), 4.97 (d, J = 9.9 Hz, 1 H, H-2), 5.23 (t, J = 9.3 Hz, 1 H, H-4), 4.97 (d, J = 9.9 Hz, 1 H, H-1), 2.07, 2.06, 2.01, 1.82 (4 s, 12 H, OCOCH₃).

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2-(2,3,4,6-Tetra-O-acetyl-b-D-galactopyranosyl)-1,4-dimethoxy-5-nitrobenzene (5)

Treatment of 2 (350 mg, 0.75 mmol), according to the above procedure for the synthesis of 3, afforded 5 (288 mg, 75%), as well as minor products chlorinated at C-10 (6 mg, 3%) and at C-5 (51 mg, 13%) \([R_f = 0.55, 0.52\ (PE-\text{EtOAc, 1:1}); \text{yellow-green crystals (PE-CH}_2\text{Cl}_2-\text{Et}_2\text{O);} \text{mp 156–157 °C; } R_f = 0.41\ (\text{PE-\text{EtOAc, 1:1});} \text{[a]_D^{20} = -10.0 (c 0.9, CH}_2\text{Cl}_2).}\]

1H NMR (300 MHz, CDCl3): \(\delta = 7.40\ (s, 1\ \text{H, Ar}), 7.23\ (s, 1\ \text{H, Ar}), 5.54\ (br\ d, J_{4,3} = 3.3\ \text{Hz, 1\ H, H-4}), 5.43\ (t, J_{3,2} = 9.9\ \text{Hz, 1\ H, H-2}), 5.24\ (dd, 1\ H, H-3), 4.96\ (d, J_{1,2} = 9.9\ \text{Hz, 1\ H, H-1}), 4.18–4.08\ (m, 3\ \text{H, H-5}, H-6, H-7), 3.97\ (3\ \text{H, OCH}_3), 3.87\ (3\ \text{H, OCH}_3), 2.22, 2.04, 2.00, 1.84\ (4\ \text{s, 12\ H, OCOCH}_3).\]

MS (EL 70 eV): \(m/z\% = 290\ (100), 483\ (85, [M^+]).\]

MS (ESI+): \(m/z\% = 483.9\ (100, [M + H]^+), 965.6\ (40, [2\ M + H]^+).\)

HRMS (EI, 70 eV): \(m/z\% = 483.9\ [M + H]^+\) calecd for C_{25}H_{25}NO_{12}, 483.1741; found: 483.1735.

The other polarn compound formed with Na_2S_2O_4 as the hydrogen donor was poorly soluble in CHCl_3, but was soluble in DMSO and MeOH; \(R_f = 0.40\ (PE-\text{EtOAc, 1:1}); R_f = 0.26\ (\text{MeOH-\text{EtOAc, 1:6)}; [a]_D^{20} = -12.8\ (c 0.75, \text{MeOH}).\)

MS data as for 7.

MS (ESI+): \(m/z\% = 484.0\ (95, [M + H]^+), 506.1\ (100, [M + Na]^+), 586.1\ (10, [M + H]^+), 608.2\ (52, [M' + Na]^+), 966.6\ (30, [2\ M + H]^+), 989.0\ (35, [2\ M + Na]^+), 1091.0\ (72, [2M + M' + Na]^+), 1193.1\ (75, [2M' + Na]^+).\]

2-(2,3,4,6-Tetra-O-acetyl-b-D-galactopyranosyl)-2,5-dimethoxyaniline (8)

Treatment of 5 (205 mg, 0.4 mmol) with HCO_2NH according to the previous procedure, afforded 8 (158 mg, 82%) as a pale-yellow syrup; \([a]_D^{20} = 0.9\ (c 0.8, \text{CHCl}_3).\)

1H NMR (300.13 MHz, CDCl3): \(\delta = 6.82\ (s, 1\ \text{H, Ar}), 6.28\ (s, 1\ \text{H, Ar}), 5.55–5.54\ (m, 2\ \text{H, H-2, H-4}), 5.19\ (d, J = 3.3, 9.9\ \text{Hz, 1\ H, H-3}), 4.85\ (d, J_{2,1} = 9.9\ \text{Hz, 1\ H, H-1}), 4.20–4.03\ (m, 3\ \text{H, H-5, H-6, H-7}), 3.93–3.82\ (br\ s, 2\ \text{H, NH}_2, \text{exch D}_2\text{O}), 3.82\ (3\ \text{H, OCH}_3), 3.74\ (3\ \text{H, OCH}_3), 2.20, 2.01, 1.98, 1.79\ (4\ \text{s, 12\ H, OCOCH}_3).\]

HRMS (EI, 70 eV): \(m/z\% = 483.1\ (100, [M + H]^+), 965.6\ (40, [2\ M + H]^+).\)

MS (EL 70 eV): \(m/z\% = 483.8\ (100, [M + H]^+).\)

HRMS (EI, 70 eV): \(m/z\% = 483\ (85, [M^+]).\)

Acylation of 7 and 8 to 9a–n and 10f; General Procedure A

4-C-Glycosyl-2,5-dimethoxyaniline 7 or 8 (1 equiv) was dissolved in anhyd CHCl_3 (3 mL), and anhyd pyridine (20.3 mL, 1.2 equiv) was added. Acyl chloride (0.218 mmol, 1.05 equiv) was then added. After the above mixture had been stirred at r.t. for \(~2\) h, TLC showed the complete conversion of the starting material into a new more mobile compound. Then the mixture was concentrated under vacuum and purified using PE-\text{EtOAc (1:1)} as eluent to yield the desired compound.

1H NMR (300.13 MHz, CDCl3): \(\delta = 8.27\ (s, 1\ \text{H, Ar}), 8.01\ (s, 1\ \text{H, CONH}), 6.92\ (s, 1\ \text{H, Ar}), 6.43\ (dd, J = 1.2, 16.8\ \text{Hz, J}_{\text{H3-16k}} = 16.8\ \text{Hz, 1\ H}_{\text{H16k}}), 6.31\ (dd, J_{\text{H16k-5k}} = 9.6\ \text{Hz, J}_{\text{H16k-5k}} = 16.8\ \text{Hz, 1\ H}_{\text{H16k}}), 5.77\ (dd, J = 1.5, 9.9\ \text{Hz, 1\ H}_{\text{H16k}}), 5.30\ (t, J_{\text{H16k-5k}} = 9.3\ \text{Hz, 1\ H, H-3}), 5.28\ (t, J_{\text{H16k-5k}} = 9.6\ \text{Hz, 1\ H, H-2}), 5.22\ (t, J_{\text{H16k-5k}} = 9.3\ \text{Hz, 1\ H, H-4}), 4.99\ (dd, J_{\text{H16k-5k}} = 9.9\ \text{Hz, 1\ H, H-1}), 4.29\ (dd, J_{\text{H16k-5k}} = 4.8\ \text{Hz, J}_{\text{H16k-5k}} = 12.6\ \text{Hz, 1\ H, H-6}), 4.13\ (dd, J_{\text{H16k-5k}} = 2.1\ \text{Hz, 1\ H, H-6}), 3.87\ (3\ \text{H, OCH}_3), 3.87–
(E)-2-(3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-1,4-di- methoxy-5-(cinnamamido)benzene (9b)

Treatment of 7 (119 mg) according to procedure A afforded 9b (151 mg, 93%); pale yellow green syrup; \( R_f = 0.36 \) (PE–EtOAc, 1:1); \( \mu \alpha \) (%) = 614 (100, \([M + H]^+\)).

HRMS (CI, isotopomer): \( m/z \) ([M + H]^+) calcld for C_{31}H_{37}NO_{14}: 618.2187; found: 618.2187.

2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-1,4-dimethoxy-5-(3,5-dinitrobenzamido)benzene (9e)

Treatment of 7 (102 mg) according to procedure A afforded 9e (122 mg, 89%); white crystals; mp 181–182 °C; \( R_f = 0.36 \) (PE–EtOAc, 1:1); \( \mu \alpha \) (%) = 12.8 (c 0.8, CHCl_3).

HRMS (CI, isotopomer): \( m/z \) ([M + H]^+) calcld for C_{30}H_{39}NO_{14}: 602.2237; found: 602.2240.

2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-1,4-dimethoxy-5-(4-methoxybenzamido)benzene (9d)

Treatment of 7 (111 mg) according to procedure A afforded 9d (129 mg, 93%); colorless syrup; \( R_f = 0.39 \) (EtOAc–PE, 1:1); \( \mu \alpha \) (%) = 14.0 (c 1.0, CHCl_3).

HRMS (CI, isotopomer): \( m/z \) ([M + H]^+) calcld for C_{30}H_{39}NO_{14}: 602.2237; found: 602.2239.

2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-1,4-dimethoxy-5-(4-nitrobenzamido)benzene (9c)

Treatment of 7 (111 mg) according to procedure A afforded 9c (129 mg, 93%); pale yellow syrup; \( R_f = 0.34 \) (PE–EtOAc, 1:1); \( \mu \alpha \) (%) = 16.7 (c 1.0, CHCl_3).

HRMS (CI, isotopomer): \( m/z \) ([M + H]^+) calcld for C_{30}H_{39}NO_{14}: 602.2237; found: 602.2239.

2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-1,4-dimethoxy-5-(3,5-dimethoxybenzamido)benzene (9f)

Treatment of 7 (111 mg) according to procedure A afforded 9f (129 mg, 93%); colorless syrup; \( R_f = 0.39 \) (EtOAc–PE, 1:1); \( \mu \alpha \) (%) = 14.0 (c 1.0, CHCl_3).

HRMS (CI, isotopomer): \( m/z \) ([M + H]^+) calcld for C_{30}H_{39}NO_{14}: 602.2237; found: 602.2239.
HRMS (CI, isobutane): [M + H]+ calcd for C_{27}H_{32}NO_{13}: 633.1932; found: 633.1933.

2-(3,4,6-Tetra-O-acetyl-b-D-glucopyranosyl)-1,4-dimethoxy-5-(4-biphenylcarboxamido)benzene (9g)

Treatment of 7 (114 mg) according to procedure A afforded 9g (148 mg, 95%); colorless syrup; R_f = 0.42 (PE-EtOAc, 1:1); [a]_D^{25} = -20.3 (c 0.9, CH_2Cl_2).

1^H NMR (300.13 MHz, CDCl_3): δ = 8.69 (s, 1 H, CONH), 8.36 (s, 1 H, Ar), 7.95 (d, J = 8.4 Hz, 2 H, Ar), 7.71 (d, J = 8.1 Hz, 2 H, Ar), 7.62 (d, J = 8.4 Hz, 2 H, Ar), 7.44 (m, 3 H, Ar), 6.98 (s, 1 H, Ar), 5.40 (t, J = 9.3 Hz, 1 H, H-3), 5.32 (t, J = 9.6 Hz, 1 H, H-2), 5.25 (t, J = 9.9 Hz, 1 H, H-4), 5.03 (d, J = 9.6 Hz, 1 H, H-1), 4.31 (dd, J = 4.8 Hz, J = 12.3 Hz, 1 H, H-6), 4.16 (dd, J = 2.1 Hz, 1 H, H-5), 3.92 (s, 3 H, OCH_3), 3.92–3.88 (hidden, 1 H, H-5), 3.88 (s, 3 H, OCH_3), 2.07, 2.06, 2.02, 1.82 (4 s, 12 H, OCH_3).

MS (CI, isobutane): m/z (%) = 638 (100, [M + H]+).

HRMS (CI, isobutane): m/z [M + H]+ calcd for C_{27}H_{32}NO_{13}: 638.2237; found: 638.2237.

2-(3,4,6-Tetra-O-acetyl-b-D-glucopyranosyl)-1,4-dimethoxy-5-(2-furylcarboxamido)benzene (9j)

Treatment of 7 (81 mg) according to procedure A afforded 9j (94 mg, 97%); pale yellow syrup; R_f = 0.29 (PE-EtOAc, 1:1); [a]_D^{25} = -138.6 (c 1.05, CH_2Cl_2).

1^H NMR (300.14 MHz, CDCl_3): δ = 8.82 (s, 1 H, CONH), 8.28 (s, 1 H, Ar), 7.55 (br, J = 1.9 Hz, 1 H, py), 7.22 (d, J = 4.2 Hz, 1 H, py), 6.95 (s, 1 H, Ar), 6.56 (q, J = 18 Hz, J = 3.0 Hz, 1 H, py), 5.38 (t, J = 9.3 Hz, 1 H, H-3), 5.30 (t, J = 9.6 Hz, 1 H, H-2), 5.24 (t, J = 9.3 Hz, 1 H, H-4), 5.00 (d, J = 9.6 Hz, 1 H, H-1), 4.29 (dd, J = 4.8 Hz, J = 12.3 Hz, 1 H, H-6), 4.15 (dd, J = 18 Hz, J = 1.8 Hz, 1 H, H-5), 3.93 (s, 3 H, OCH_3), 3.89 (d, J = 12 Hz, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 2.08, 2.07, 2.01, 1.80 (4 s, 12 H, OCH_3).

HRMS (CI, isobutane): m/z [M + H]+ calcd for C_{27}H_{32}NO_{13}: 578.1874; found: 578.1874.

2-(3,4,6-Tetra-O-acetyl-b-D-glucopyranosyl)-1,4-dimethoxy-5-(2-thienylcarboxamido)benzene (9k)

Treatment of 7 (52 mg) according to procedure A afforded 9k (61 mg, 96%); pale yellow syrup; R_f = 0.41 (PE-EtOAc, 1:1); [a]_D^{25} = -12.6 (c 0.9, CH_2Cl_2).

1^H NMR (300.13 MHz, CDCl_3): δ = 8.47 (s, 1 H, CONH), 8.23 (s, 1 H, Ar), 7.59 (dd, J = 3.9 Hz, J = 0.9 Hz, 1 H, H-5), 7.54 (dd, J = 4.8 Hz, J = 0.9 Hz, 1 H, H-3), 7.11 (dd, J = 3.9 Hz, J = 4.8 Hz, 1 H, H-1), 6.93 (s, 1 H, Ar), 5.37 (t, J = 9.3 Hz, 1 H, H-3), 5.27 (t, J = 9.6 Hz, 1 H, H-2), 5.02 (t, J = 9.2 Hz, 1 H, H-8), 4.98 (d, J = 9.6 Hz, 1 H, H-3), 4.28 (dd, J = 4.8 Hz, J = 12.3 Hz, 1 H, H-6), 4.14 (dd, J = 18 Hz, J = 1.2 Hz, 1 H, H-5), 3.90 (s, 3 H, OCH_3), 3.85 (d, J = 12 Hz, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 2.06, 2.05, 2.00, 1.78 (4 s, 12 H, OCH_3).

HRMS (CI, isobutane): m/z (%) = 594 (100, [M + H]+).

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6.98 (s, 1 H, Ar), 5.40 (t, J = 9.3 Hz, 1 H, H-3), 5.30 (t, J = 9.3 Hz, 1 H, H-2), 5.25 (t, J = 9.6 Hz, 1 H, H-4), 5.02 (d, J = 9.9 Hz, 1 H, H-1), 4.30 (dd, J = 4.8 Hz, J = 12.3 Hz, 1 H, H-6), 4.16 (dd, J = 3.9 Hz, 1 H, H′-6), 3.93–3.87 (hidden, 1 H, H-5), 3.87 (s, 3 H, OCH3), 2.08, 2.07, 2.02, 1.81 (4 s, 12 H, OCOCH3).

MS (Cl-isobutane): m/z (%): 589 (100, [M + H]+).

HRMS (Cl-isobutane): m/z [M + H]+ calcd for C28H33N2O14: 589.2033; found: 589.2031.

-N-Carbonyl-(6-ethoxycarbonyl-2-pyrild)-4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2,5-dimethoxyaniline (9m) and 2,6-(bis-2,5-dimethoxy-4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)anilinono-N-carbonyl)piperidine (9n)

Treatment of 7 (102 mg) according to procedure A (note: 0.53 equiv of pyridine-2,6-dicarboxylic chloride was added) afforded 9m (8 mg, 6%) and 9n (101 mg, 87%).

9m

Yellow-green syrup; Rf = 0.55 (PE- EtOAc 1:1, UV 312 nm orange, 254 nm black).

1H NMR (300.13 MHz, CDCl3): δ = 10.75 (s, 1 H, CONH), 8.43 (dd, J = 1.2 Hz, J = 7.8 Hz, 1 H, pyridine H-3′ or H-5′), 8.37 (s, 1 H, Ar), 8.29 (dd, J = 1.2, 7.8 Hz, 1 H, pyridine H-5 or H-3), 8.06 (J, t = 7.8 Hz, 1 H, H-5′), 6.97 (s, 1 H, Ar), 5.39 (t, J = 9.3 Hz, 1 H, H-3), 5.32 (t, J = 9.3 Hz, 1 H, H-2), 5.25 (t, J = 9.6 Hz, 1 H, H-4), 5.01 (d, J = 9.6 Hz, 1 H, H-1), 4.51 (q, J = 7.0, 2 H, OCH3), 4.30 (dd, J = 5.1 Hz, J = 12.6 Hz, 1 H, H-6), 4.16 (dd, J = 2.1 Hz, J = 12.6 Hz, 1 H, H-6′), 3.98 (s, 3 H, OCH3), 3.89 (m, 1 H, H-5′), 3.89 (s, 3 H, OCH3), 2.09, 2.07, 2.01, 1.79 (4 s, 12 H, OCOCH3), 1.52 (t, J = 7.0 Hz, 3 H, CH(CH3)2).

MS (Cl-isobutane): m/z (%): 661 (100, [M + H]+).

HRMS (Cl-isobutane): m/z [M + H]+ calcd for C31H34N2O13: 661.2245; found: 661.2248.

9n

Yellow-green syrup; [α]D 17−27.2 (c 1.0, CHCl3); Rf = 0.34 (PE- EtOAc 1:1, UV 312 nm orange, 254 nm black).

1H NMR (300.13 MHz, CDCl3): δ = 10.37 (s, 2 H, CONH), 8.48 (d, J = 7.8 Hz, 2 H, Ar), 8.38 (s, 2 H, Ar), 8.17 (t, J = 7.8 Hz, 1 H4), 7.06 (s, 2 H, Ar), 5.41 (t, J = 9.0 Hz, 2 H, H-3), 5.33 (t, J = 9.6 Hz, 2 H, H-2), 5.27 (t, J = 9.3 Hz, 2 H, H-4), 5.05 (d, J = 9.6 Hz, 2 H, H-1), 4.28 (dd, J = 4.8 Hz, J = 12.3 Hz, 2 H, H-6), 4.14 (dd, J = 1.8 Hz, 2 H, H-6′), 3.95 (s, 3 H, 2 OCH3), 3.87 (hidden, 2 H, H-5), 3.92 (s, 6 H, 2 OCH3), 2.11, 2.08, 2.03, 1.82 (4 s, 24 H, OCOCH3).

13C NMR (75.5 MHz, CDCl3): δ = 171.1, 170.7, 170.0, 169.7 (4 C=O, acetyl), 164.8 (CO=O), 161.8 (CONH), 152.1, 150.4, 147.3, 143.4 (4 C=O, Ar), 139.3 (CH, pyridine C-4), 127.8, 125.5 (CH, pyridine C-3′ and C-5′), 119.3 (C=O, Ar), 110.2 (CHAr), 103.9 (CHAr), 76.5 (C-5), 74.9 (C-3′), 73.6 (C-4′), 72.4 (C-2), 69.3 (C-6′), 62.9 (C-6), 59.6, 59.8 (2 OCH3), 21.2, 21.1, 21.1, 20.8 (4 CH2, acetyl), 14.7 (CH2CH2O).

2-(β-D-Galactopyranosyl)-1,4-dimethoxy-5-(4-nitrobenzamido)benzene (12)

Treatment of 10f (88 mg) according to the above procedure afforded 12f (61 mg; 94%) as an orange-red solid; mp 214–216 °C; \( R_f = 0.44 \) (MeOH–CH₂Cl₂, 1:5); \([\alpha]_D^{21} = -2.6 \) (c 0.53, DMSO).

1H NMR (300.13 MHz, DMSO-\( d_6 \)): \( \delta = 9.90 \) (s, 1 H, CONH), 8.36 (d, \( J = 8.7 \) Hz, 2 H, Ar), 8.19 (d, \( J = 8.7 \) Hz, 2 H, Ar), 7.44 (s, 1 H, Ar), 7.10 (s, 1 H, Ar), 4.73 (br s, 1 H, OH excl. D₂O), 4.58 (br s, 2 H, OH excl. D₂O), 4.46 (d, \( J = 9.6 \) Hz, 1 H, H-1), 4.37 (br s, 1 H, OH excl. D₂O), 3.80 (s, 3 H, OCH₃), 3.80–3.73 (hidden, 2 H, H-2 and H-3), 3.73 (s, 3 H, OCH₃), 3.51–3.41 (m, 4 H, H-4, H-5, H-6, H-6').

13C NMR (75.5 MHz, DMSO-\( d_6 \)): \( \delta = 163.6 \) (CONH), 151.1, 149.1, 145.8 (3 C\(_\alpha\), Ar), 129.5, 129.5 (2 CH\(_\alpha\)), 126.3, 126.0 (2 C\(_\gamma\), Ar), 123.5, 123.5 (2 CH\(_\alpha\)), 114.1 (C\(_\gamma\), Ar), 111.8, 108.9 (2 CH\(_\alpha\)), 79.8, 75.1, 74.4 (C-1), 70.6, 69.9 (C-2 to C-5), 60.8 (C-6), 56.5, 52.2 (2 OCH₃).

MS (ESI+): \( m/z \ (%) = 950.8 \) (100, [M + Na]⁺).


Oxidation of 9a–9l and 9n to 13a–13l and 13n; General Procedure B

The C-glycosyl amidobenzene (1 equiv) dissolved in MeCN (2 mL) was reacted with ceric ammonium nitrate (400 mg, 0.73 mmol, 4 equiv) dissolved in H\(_2\)O (5 mL) at r.t. After ~2 h, TLC (PE–EtOAc, 1:1) or similar showed that the starting material had been consumed, to afford a more mobile compound. H\(_2\)O (10 mL) was poured into the mixture which was extracted with CH\(_2\)Cl\(_2\) (3 x 15 mL). The extracts were combined and washed with brine (15 mL), H\(_2\)O (15 mL), dried (MgSO\(_4\)), and concentrated. The residue was chromatographed (PE–EtOAc, 3:2) or similar on silica gel. Concentration of the homogeneous fractions led to the desired benzoquinone.

2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(4-methyl-benzamido)-1,4-benzoquinone (13a)

Treatment of compound 9a (98 mg) according to procedure B afforded 13a (62 mg, 67%) as a yellow-green syrup; \( R_f = 0.44 \) (PE–EtOAc, 1:1); \([\alpha]_D^{19} = -19.0 \) (c 1.0, CHCl₃).

1H NMR (300.13 MHz, CDCl₃): \( \delta = 8.21 \) (s, 1 H, CONH), 7.64 (s, 1 H, Ar), 6.93 (s, 1 H, Ar), 6.47 (d, \( J = 16.2 \) Hz, 1 H, H\(_{\text{ex}}\)), 6.32 (dd, \( J = 16.2, 10.2 \) Hz, 1 H, H\(_{\text{ex}}\)), 5.37 (t, \( J = 9.3 \) Hz, 1 H, H-3), 5.14 (t, \( J = 9.6 \) Hz, 1 H, H-4), 4.93 (t, \( J = 9.3 \) Hz, 1 H, H-1), 4.72 (q, \( J = 9.6 \) Hz, 1 H, H-1), 4.26 (dd, \( J = 5.1, 16.6 \) Hz, 1 H, H-6), 4.15 (dd, \( J = 5.1, 16.6 \) Hz, 1 H, H-6'), 3.82 (dq, 1 H, H-5), 2.10, 2.06, 2.01, 1.91 (4 x, 12 H, OCOCH₃).

13C NMR (75.5 MHz, CDCl₃): \( \delta = 186.4, 182.9 \) (2 C=O, benzoinone), 171.0, 170.3, 170.0 (4 C=O, acetyl), 164.6 (CONH), 146.4, 138.7 (2 C\(_\gamma\), Ar), 130.7 (CH\(_{\text{ex}}\)), 130.7 (CH\(_{\text{ex}}\)), 115.1, 104.6 (2 CH\(_\alpha\)), 76.6 (C-5), 73.9 (C-3), 73.2 (C-2), 72.0 (C-1), 68.7 (C-4), 62.5 (C-6), 21.1, 21.0, 21.0, 20.9 (4 CH₃, acetyl).

MS (ESI, isobutane): \( m/z \ (%) = 540 (100, [M + H]^+) \), 506 (20, [M + Na]⁺).


2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(4-methoxy-benzamido)-1,4-benzoquinone (13d)

Treatment of compound 9d (100 mg) according to procedure B afforded 13d (81 mg, 85%) yellow crystals; mp 141–142 °C (CH\(_2\)Cl\(_2\)–PE–Et\(_2\)O); \( R_f = 0.48 \) (EtOAc–PE, 1:1); \([\alpha]_D^{21} = -20.5 \) (c 0.88, CHCl₃).

1H NMR (300.13 MHz, CDCl₃): \( \delta = 8.78 \) (s, 1 H, CONH), 7.85 (d, \( J = 8.7 \) Hz, 2 H, Ar), 7.69 (s, 1 H, Ar), 7.00 (d, \( J = 8.7 \) Hz, 2 H, Ar), 6.96 (s, 1 H, Ar), 5.39 (t, \( J = 9.6 \) Hz, 1 H, H-3), 5.15 (t, \( J = 9.9 \) Hz, 1 H, H-4), 4.95 (t, \( J = 9.3 \) Hz, 1 H, H-1), 4.75 (dd, \( J = 9.9, 16.2 \) Hz, 1 H, H-6), 4.25 (dd, \( J = 5.1, 16.6 \) Hz, 1 H, H-6'), 3.86 (s, 3 H, OCH₃), 3.84 (dq, 1 H, H-5), 2.11, 2.06, 2.02, 1.92 (4 x, 12 H, OCOCH₃).

13C NMR (75.5 MHz, CDCl₃): \( \delta = 186.5, 183.2 \) (2 C=O, benzoinone), 171.0, 170.4, 170.0 (4 C=O, acetyl), 165.6 (CONH), 163.8, 146.5, 138.9 (3 C\(_\gamma\), Ar), 130.6 129.8, 129.8 (3 C\(_\gamma\), Ar).
1H NMR (300.13 MHz, CDCl$_3$): $\delta$ = 8.89 (s, 1 H, CONH), 7.94 (d, $J$ = 8.1 Hz, 2 H, Ar), 7.73 (d, $J$ = 8.4 Hz, 3 H, Ar), 7.73 (s, 1 H, Ar), 7.44 (m, 3 H, Ar), 6.99 (s, 1 H, Ar), 5.40 (t, $J_{d,9} = 9.3$ Hz, 1 H, H-$3$), 5.16 (t, $J_{d,9} = 9.6$ Hz, 1 H, H-$4$), 4.96 (t, $J_{d,3} = 9.1$ Hz, 1 H, H-$2$), 4.75 (d, $J_{d,3} = 9.6$ Hz, 1 H, H-$1$), 4.26 (dd, $J_{d,9,6} = 5.1$ Hz, $J_{d,9,6} = 12.6$ Hz, 1 H, H-$6$), 4.16 (dd, $J_{d,9,6} = 1.8$ Hz, 1 H, H-$6\text{'}$), 3.84 (dq, 1 H, H-$1$, H-$5$), 2.11, 2.06, 2.02, 1.93 (4 s, 12 H, OCOCH$_3$).

13C NMR (75.5 MHz, CDCl$_3$): $\delta$ = 186.6, 183.1 (2 C=O, benzoquinone), 171.0, 170.4, 170.4, 170.0 (4 C=O, acetyl), 165.9 (CONH), 146.6, 146.2, 139.8, 138.8, 131.9 (5 C$_{ar}$, Ar), 130.7, 129.5, 128.9, 128.3, 128.0, 128.0, 127.7, 127.7, 117.4 (11 CH$_{ar}$), 76.6 (C-5), 73.9 (C-3), 73.2 (C-2), 72.1 (C-1), 68.7 (C-4), 62.5 (C-6), 21.2, 21.0, 21.0, 20.9 (4 CH$_3$, acetyl).

MS (CI, isobutane): $m/z$ (%) = 636 (100, [phenol + H$^+$]), 634 (60, [M + H$^+$]).

HRMS: $m/z$ [M + H]$^+$ calc for C$_{29}$H$_{26}$N$_2$O$_{13}$: 634.1924; found: 634.1924.

2-(2,3,4,6-Tetra-o-acetyl-b-D-glucopyranosyl)-5-(3,5-dimethoxybenzamido)-1,4-benzoquinone (13h)

Treatment of compound 9b (43 mg) according to procedure B afforded 13h (36 mg, 88%); yellow-green syrup: $R_f$ = 0.54 (PE–EtOAc, 1:1); $[\alpha]_{D}^{23}$ = 30.7 (c 0.2, CHCl$_3$).

1H NMR (300.13 MHz, CDCl$_3$): $\delta$ = 8.86 (s, 1 H, CONH), 8.36 (dd, $J_{d,7} = 7.5$ Hz, $J_{d,1} = 1.5$ Hz, 1 H, Ar), 8.04 (d, $J$ = 8.4 Hz, 1 H, Ar), 7.93 (s, 1 H, Ar), 7.76 (dd, $J = 0.9$ Hz, 7.2 Hz, 1 H, Ar), 7.65–7.52 (m, 3 H, Ar), 6.96 (d, $J$ = 6.9 Hz, 1 H, Ar), 5.40 (t, $J_{d,9} = 9.3$ Hz, 1 H, H-$3$), 5.15 (t, $J_{d,3} = 9.9$ Hz, 1 H, H-$4$), 4.96 (t, $J_{d,3} = 9.6$ Hz, 1 H, H-$2$), 4.75 (dd, $J_{d,9,6} = 9.6$ Hz, 1 H, H-$1$), 4.09 (s, 12 H, OCOCH$_3$), 3.84 (dq, 1 H, H-$1$, H-$5$), 2.10, 2.06, 2.02, 1.94 (4 s, 12 H, OCOCH$_3$).

13C NMR (75.5 MHz, CDCl$_3$): $\delta$ = 186.6, 182.9 (2 C=O, benzoquinone), 171.0, 170.4, 170.4, 170.0 (4 C=O, acetyl), 168.3 (CONH), 146.5, 138.9, 134.2 (3 C$_{ar}$, Ar), 133.0 (CH$_{ar}$), 132.5 (C$_{ar}$, Ar), 130.7 (CH$_{ar}$), 130.4 (C$_{ar}$, Ar), 129.0, 128.4, 127.3, 126.3, 125.3, 125.0, 115.0 (7 CH$_{ar}$), 76.6 (C-5), 73.9 (C-3), 73.2 (C-2), 72.1 (C-1), 68.7 (C-4), 62.5 (C-6), 21.2, 21.0, 21.0, 20.9 (4 CH$_3$, acetyl).

MS (CI, isobutane): $m/z$ (%) = 601 (50), 600 (100, [M + H]$^+$).

HRMS (CI, isobutane): $m/z$ [M + H]$^+$ calc for C$_{29}$H$_{26}$N$_2$O$_{13}$: 608.1768; found: 608.1767.

2-(2,3,4,6-Tetra-o-acetyl-b-D-glucopyranosyl)-5-(2-naphthamido)-1,4-benzoquinone (13i)

Treatment of compound 9i (56 mg) according to procedure B afforded 13i (46 mg, 86%); yellow-green crystals; $m$ = 165–166 °C (CH$_2Cl_2$–PE–Et$_2$O); $R_f$ = 0.54 (PE–EtOAc, 1:1); $[\alpha]_{D}^{23}$ = –28.3 (c 0.8, CHCl$_3$).

1H NMR (300.14 MHz, CDCl$_3$): $\delta$ = 9.01 (s, 1 H, CONH), 8.41 (s, 1 H, Ar), 7.95 (m, 4 H, Ar), 7.78 (s, 1 H, Ar), 7.63 (m, 2 H, Ar), 7.00 (s, 1 H, Ar), 5.39 (t, $J_{d,9} = 9.3$ Hz, 1 H, H-$3$), 5.15 (t, $J_{d,9} = 9.6$ Hz, 1 H, H-$4$), 4.96 (t, $J_{d,3} = 9.1$ Hz, 1 H, H-$2$), 4.76 (d, $J_{d,3} = 9.6$ Hz, 1 H, H-$1$), 4.28 (dd, $J_{d,9,6} = 4.8$ Hz, $J_{d,9,6} = 12.3$ Hz, 1 H, H-$6$), 4.16 (dd, $J_{d,9,6} = 1.8$ Hz, 1 H, H-$6\text{'}$), 3.84 (dq, 1 H, H-$1$, H-$5$), 2.11, 2.06, 2.02, 1.93 (4 s, 12 H, OCOCH$_3$).

13C NMR (75.5 MHz, CDCl$_3$): $\delta$ = 186.5, 183.2 (2 C=O, benzoquinone), 171.0, 170.4, 170.3, 170.0 (4 C=O, acetyl), 166.3 (CONH), 146.6, 138.9, 135.8, 132.9 (4 C$_{ar}$, Ar), 130.7 (CH$_{ar}$), 130.6 (C$_{ar}$, Ar), 129.7, 129.6, 129.1, 128.8, 128.3, 127.7, 127.6, 114.8 (8 CH$_{ar}$), 76.7 (C-5), 74.0 (C-3), 73.2 (C-2), 72.1 (C-1), 68.7 (C-4), 62.5 (C-6), 21.2, 21.0, 21.0, 20.9 (4 CH$_3$, acetyl).

MS (ESI+): $m/z$ (%) = 1236.6 (75, [2 M + Na]$^+$), 607.9 (100, [M + H]$^+$).

2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(2-furylcarbamoxy)-1,4-benzoquinone (13j)

Treatment of compound 9j (62 mg) according to procedure B afforded 13j (52 mg, 89%); golden-yellow needles; mp 89–91°C (CHCl3–PE–Et2O); Rf = 0.42 (PE–EtOAc, 1:1); [α]D23 = −21.7° (c 0.78, CH2Cl2).

1H NMR (300.14 MHz, CDCl3): δ = 8.98 (s, 1 H, CONH), 7.65 (s, 1 H, Hquinone), 7.61 (dd, J = 1.8 Hz, Jα = 0.6 Hz, 1 H, Hα), 7.31 (dd, Jα = 0.6 Hz, Jα = 3.6 Hz, 1 H, Hα), 6.96 (d, J = 0.9 Hz, 1 H, Hα), 6.61 (dd, J = 1.8 Hz, Jα = 3.6 Hz, 1 H, Hα), 5.38 (t, Jα = 9.3 Hz, 1 H, H-3), 5.14 (t, Jα = 10.2 Hz, 1 H, H-4), 4.94 (t, Jα = 9.6 Hz, 1 H, H-2), 4.73 (dd, Jα = 9.6, 0.9 Hz, 1 H, H-1), 4.27 (dd, Jα = 5.1 Hz, Jα = 12.6 Hz, 1 H, H-6), 4.15 (dd, Jα = 2.1 Hz, 1 H, H-6), 3.83 (dq, 1 H, H-5), 2.10, 2.06, 2.01, 1.92 (4s, 2 H, OCH2).

13C NMR (75.5 MHz, CDCl3): δ = 186.3, 182.7 (2 C=O, benzoquinone), 171.0, 170.4, 170.0 (170.0 (4 C=O, acetyl), 156.7 (CONH), 147.0, 146.4 (2 C=O, Ar), 146.0 (CHO), 138.5 (C=O, Ar), 130.7 (CHO), 117.7, 114.7, 113.5 (3 CH2), 76.6 (C-5), 73.9 (C-3), 73.2 (C-2), 72.1 (C-1), 68.7 (C-4), 62.4 (C-6), 21.2, 21.0, 21.0, 20.9 (4 CH3, acetyl).

MS (CI, isobutane): m/z (%) = 548 (100, [M + H]+).


2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(2-thienylcarbamoxy)-1,4-benzoquinone (13k)

Treatment of compound 9k (60 mg) according to procedure B afforded 13k (54 mg) as golden-yellow crystals; mp 168–169°C (CHCl3–Et3O–PE); Rf = 0.44 (EtOAc–PE, 1:1); [α]D30 = −20.1° (c 1.0, CH2Cl2).

1H NMR (300.13 MHz, CDCl3): δ = 8.64 (s, 1 H, CONH), 7.68 (dd, J = 3.9 Hz, Jα = 0.9 Hz, 1 H, Hquinone), 7.65 (dd, Jα = 5.1 Hz, Jα = 0.9 Hz, 1 H, Hquinone), 7.61 (s, 1 H, Ar), 7.16 (dd, J = 3.9 Hz, Jα = 5.1 Hz, 1 H, Hquinone), 6.94 (d, J = 0.9 Hz, 1 H, H-9), 5.36 (t, Jα = 9.3 Hz, 1 H, H-3), 5.12 (t, Jα = 9.3 Hz, 1 H, H-4), 4.92 (t, Jα = 9.3 Hz, 1 H, H-2), 4.98 (dd, Jα = 9.6 Hz, Jα = 0.9 Hz, 1 H, H-1), 4.25 (dd, Jα = 4.8 Hz, Jα = 12.3 Hz, 1 H, H-6), 4.13 (dd, Jα = 2.1 Hz, 1 H, H-6), 3.81 (dq, 1 H, H-5), 2.09, 2.04, 1.99, 1.90 (4s, 4 CH3, acetyl).

13C NMR (75.5 MHz, CDCl3): δ = 186.3, 182.9 (2 C=O, benzoquinone), 171.1, 171.0, 170.4, 170.0, 170.0 (170.0 (4 C=O, acetyl), 162.2, 162.2 (2 CONH), 148.3, 148.3, 146.5, 146.5 (4 C=O, Ar), 140.6 (CHO), 138.3, 138.3 (2 C=O, Ar), 131.0, 131.0, 127.2, 127.2, 115.5, 115.5 (6 CH3), 76.5, 76.5 (2 C-5), 73.9, 73.9 (2 C-3), 73.3 (2 C-2), 72.2 (2 C-1), 68.6 (C-4), 62.3 (C-6), 21.2, 21.0, 21.0, 21.0, 20.9, 20.9 (8 CH3, acetyl).

MS (ESI+): m/z (%) = 1060.2 (35, [M + Na]+), 1037.9 (100, [M + H]+).

Reduction of 13a–l and 13n to 14a–l and 14n; General Procedure C

The C-glycosyl benzoquinone (1 equiv) was dissolved in CHCl3 (1 mL). A solution of NaN3 (85% tech., 400 mg, 0.978 mmol, 6 equiv) in H2O (3 mL) was added to the solution. After stirring the mixture vigorously for 45 min at r.t., TLC showed the starting material was still present while a new more polar compound appeared. Another portion of NaN3 (132 mg, 2 equiv) was added to the mixture and after 1 h, TLC showed the complete conversion of the starting material. After extracting the mixture with CHCl3 (3 × 15 mL), the combined organic phases were washed with brine (15 mL), H2O (15 mL), and dried (MgSO4). After filtration and concentration, the residue was chromatographed (PE–EtOAc, 1:1) on silica gel to afford the desired hydroquinone.

2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(acrylamido)hydroquinone (14a)

Treatment of compound 13a (45 mg) according to procedure C afforded 14a (29 mg, 65%); yellow-green syrup; Rf = 0.17 (PE–EtOAc, 1:1); [α]D25 +14.6 (c 0.57, CHCl3).

1H NMR (300.13 MHz, CDCl3): δ = 8.34, 8.07 (2s, 2 H, CONH and OH, exch. D2O), 6.93 (s, 1 H, Ar), 6.65 (s, 1 H, Ar), 6.40 (d, J = 17.1 Hz, 1 H, H1k), 6.23 (dd, J = 10.8, 17.1 Hz, 1 H, H1k), 5.76 (d, J = 10.8 Hz, 1 H, H-2), 5.29 (t, Jα = 9.3 Hz, 1 H, H-3), 5.24 (t, Jα = 9.0 Hz, 1 H, H-2), 5.18 (t, Jα = 9.3 Hz, 1 H, H-1), 4.57 (d, Jα = 9.3 Hz, 1 H, H-1), 4.26 (dd, Jα = 4.2 Hz, Jα = 12.6 Hz, 1 H, H-6), 4.09 (dd, Jα = 1.8 Hz, 1 H, H-6), 3.81 (dq, 1 H, H-5), 2.02, 2.00, 1.94, 1.80 (4s, 12 H, OCH2).

13C NMR (75.5 MHz, CDCl3): δ = 170.8, 170.0, 170.0, 169.7 (4 C=O, acetyl), 165.3 (CONH), 150.8, 148.9, 141.5, 129.0 (4 C=O, Ar), 127.5 (CH2_alkene), 127.4 (CH2_alkene), 110.4, 110.2 (2 CH3), 76.5, 74.5, 74.2,
Treatment of compound 13b (95 mg) according to procedure C afforded 14b (89 mg, 93%); pale yellow foam; \( R_f = 0.11 \) (PE–EtOAc, 1:1); \( {\text{t}}_{R f}^{1} = 29.9 \) (c 0.7, CHCl\(_3\)).

\( 1^H \) NMR (300.13 MHz, CDCl\(_3\)): \( \delta = 8.54 \) (s, 1 H, OH exch. D\(_2\)O), 8.45 (s, 1 H, CONH, exch. D\(_2\)O), 7.72 (d, \( J = 15.6 \) Hz, 1 \( H_{\text{Ar}} \)), 7.69 (s, 1 H, OH exch. D\(_2\)O), 7.51–7.48 (m, 2 H, Ar), 7.35 (s, 1 H, Ar), 7.33–7.29 (m, 3 H, Ar), 6.79 (s, 1 H, Ar), 6.61 (d, \( J = 15.6 \) Hz, 1 \( H_{\text{Ar}} \)), 5.38 (t, \( J_{\text{H,Ar}} = 9.3 \) Hz, 1 H, Ar), 5.31 (t, \( J_{\text{H,Ar}} = 9.6 \) Hz, 1 H, Ar), 5.24 (t, \( J_{\text{H,Ar}} = 9.5 \) Hz, 1 H, Ar), 4.74 (d, \( J_{\text{H,Ar}} = 9.6 \) Hz, 1 H, H-1), 4.30 (dd, \( J_{\text{H,Ar}} = 4.5 \) Hz, \( J_{\text{H,Ar}} = 12.6 \) Hz, 1 H, H-6), 4.15 (br d, \( J_{\text{H,Ar}} = 1.5 \) Hz, 1 H, H-6), 3.86 (dq or dd, 1 H, H-5), 2.06, 2.03, 2.00, 1.844 (4 s, 12 H, OCOCH\(_3\)).

\( 1^C \) NMR (75.5 MHz, CDCl\(_3\)): \( \delta = 171.4, 170.8, 170.3, 170.1 \) (4 Cq, acetyl), 165.9 (CONH), 148.8 (Cq, Ar), 148.3 (CHAr), 141.1, 134.8 (2 Cq, Ar), 130.7, 129.4, 129.0, 128.5, 128.1 (5 CHAr), 127.8 (Cq, Ar), 127.5 (CHAr), 121.0 (CH\(_2\)), 119.2 (Cq, Ar), 110.0 (CH\(_2\)), 77.2 (C-1), 76.5 (C-5), 74.5 (C-3), 72.0 (C-2), 68.9 (C-4), 62.6 (C-6), 21.1, 21.1, 21.1, 21.0 (4 CH\(_3\), acetyl).

Treatment of compound 13e (75 mg) according to procedure C afforded 14e (68 mg, 90%); pale yellow foam; \( R_f = 0.12 \) (PE–EtOAc, 1:1); \( {\text{t}}_{R f}^{1} = 21.1 \) (c 0.97, CHCl\(_3\)).

\( 1^H \) NMR (300.13 MHz, CDCl\(_3\)): \( \delta = 8.67 \) (s, 1 H, CONH, exch. D\(_2\)O), 7.98, 7.80 (2 s, 2 H, OH exch. D\(_2\)O), 7.35 (J = 4.2 Hz, 2 H, Ar), 6.98 (d, \( J = 1.5 \) Hz, 1 H, Ar), 6.78 (s, 1 H, Ar), 6.61 (br s, 1 H, Ar), 5.34 (t, \( J_{\text{H,Ar}} = 9.3 \) Hz, 1 H, H-1), 5.26 (t, \( J_{\text{H,Ar}} = 9.0 \) Hz, 1 H, H-2), 5.22 (t, \( J_{\text{H,Ar}} = 9.3 \) Hz, 1 H, H-4), 4.79 (d, \( J_{\text{H,Ar}} = 9.3 \) Hz, 1 H, H-1), 4.30 (dd, \( J_{\text{H,Ar}} = 4.2 \) Hz, \( J_{\text{H,Ar}} = 12.3 \) Hz, 1 H, H-6), 4.16 (br d, \( J_{\text{H,Ar}} = 1.2 \) Hz, 1 H, H-6), 3.90 (dq, 1 H, H-5), 3.84 (s, 6 H, OCH\(_3\)), 2.08, 2.05, 2.00, 1.82 (4 s, 12 H, OCOCH\(_3\)).

\( 1^C \) NMR (75.5 MHz, CDCl\(_3\)): \( \delta = 171.4, 170.8, 170.2, 170.1 \) (4 Cq, acetyl), 167.1 (CONH), 161.3, 149.2, 141.1, 140.3, 136.3 (5 Cq, Ar), 129.0, 128.1 (2 CHAr), 127.9 (CH\(_2\)), 118.6 (Cq, Ar), 105.7, 104.6 (2 CH\(_2\)), 76.5 (C-5 and C-1), 74.5 (C-3), 72.0 (C-2), 70.3 (C-4), 62.6 (C-6), 56.0, 56.0 (2 OCH\(_3\)), 21.1, 21.1, 21.1, 20.9 (4 CH\(_3\), acetyl).

HRMS (CI, isobutane): \( m/z \) (%): 1260.9 (45, [M + Na]*) 1238.9 (100, [M + 2H]*), 620.0 (60, [M + H]*).

Treatment of compound 13f (63 mg) according to procedure C afforded 14f (57 mg, 90%); yellow-green foam; \( R_f = 0.20 \) (PE–EtOAc, 1:1); \( {\text{t}}_{R f}^{1} = 26.8 \) (c 1.27, CHCl\(_3\)).

\( 1^H \) NMR (300.13 MHz, CDCl\(_3\)): \( \delta = 8.69 \) (s, 1 H, CONH, 8.29 (d, \( J = 8.7 \) Hz, 2 H, Ar), 8.01 (d, \( J = 8.7 \) Hz, 2 H, Ar), 7.59 (br s, 1 H, Ar) 7.09 (s, 1 H, Ar, exch. D\(_2\)O), 7.78 (s, 1 H, Ar) 7.24 (br s, 1 H, OH exch. D\(_2\)O), 6.76 (s, 1 H, Ar) 5.57 (t, \( J_{\text{H,Ar}} = 9.3 \) Hz, 1 H, H-3), 5.30 (t, \( J_{\text{H,Ar}} = 9.6 \) Hz, 1 H, H-2) 5.24 (t, \( J_{\text{H,Ar}} = 9.6 \) Hz, 1 H, H-1), 4.71 (d, \( J_{\text{H,Ar}} = 9.3 \) Hz, 1 H, H-1), 4.31 (dd, \( J_{\text{H,Ar}} = 4.5 \) Hz, \( J_{\text{H,Ar}} = 1.5 \) Hz, 1 H, H-6), 4.19 (dd, \( J_{\text{H,Ar}} = 1.8 \) Hz, 1 H, H-6), 3.91 (dq, 1 H, H-5), 2.07, 2.07, 2.01, 1.86 (4 s, 12 H, OCOCH\(_3\)).

HRMS (CI, isobutane): \( m/z \) (%): 605.10 (100, [M + H]*), 498 (100).

HRMS (CL, isobutane): \( m/z \) (%): 605.10 (100, [M + H]*), 498 (100).

HRMS (CL, isobutane): \( m/z \) ([M + H]+) calcéd for C\(_{27}H\(_{32}\)NO\(_{12}\): 586.1924; found: 586.1924.

HRMS (CL, isobutane): \( m/z \) ([M + H]+) calcéd for C\(_{27}H\(_{32}\)NO\(_{13}\): 584.1924; found: 584.1924.

HRMS (CL, isobutane): \( m/z \) ([M + H]+) calcéd for C\(_{29}H\(_{32}\)NO\(_{13}\): 590.1873; found: 590.1875.

HRMS (CL, isobutane): \( m/z \) ([M + H]+) calcéd for C\(_{29}H\(_{32}\)NO\(_{13}\): 590.1873; found: 590.1875.

HRMS (CL, isobutane): \( m/z \) ([M + H]+) calcéd for C\(_{29}H\(_{32}\)NO\(_{13}\): 590.1873; found: 590.1875.
\[ \text{H NMR (300.13 MHz, CDCl}_3\]): \delta = 8.70 \text{ (s, 1 H, CONH)}, 7.98 \text{ (s, 1 H, OH exch. D}_2\text{O)}, 7.91 \text{ (d, J = 8.4 Hz, 2 H, Ar)}, 7.66 \text{ (d, J = 8.1 Hz, 2 H, Ar)}, 7.59–7.51 \text{ (m, 3 H, Ar)}, 7.44–7.36 \text{ (m, 4 H, 3 Ar and OH exch. D}_2\text{O)}, 6.82 \text{ (s, 1 H, Ar)}, 5.38 \text{ (t, J = 9.3 Hz, 1 H, H-3)}, 5.32 \text{ (t, J = 9.6 Hz, 1 H, H-2)}, 5.25 \text{ (t, J = 9.3 Hz, 1 H, H-4)}, 4.75 \text{ (d, J = 9.0 Hz, 1 H, H-1)}, 4.31 \text{ (dd, J = 4.2 Hz, J = 12.6 Hz, 1 H, H-6)}, 4.15 \text{ (dd, J = 1.5 Hz, 1 H, H-6\text{'}), 3.89 \text{ (m, 1 H, H-5)}, 2.06, 1.99, 1.84 (4 s, 12 H, OCOCH}_3\text{).} \\
\text{13C NMR (75.5 MHz, CDCl}_3\): \delta = 171.3, 170.8, 170.2, 170.1 \text{ (4 C=O, acetyl), 167.2 (CONH), 149.1, 145.5, 141.0, 140.0, 132.6 (5 C\_Ar), 129.9, 129.0, 128.7, 128.4, 128.4, 127.8 (7 CH\_Ar), 127.8 (C\_Ar), 127.6, 127.6 (2 CH\_Ar), 119.0 C\_Ar), 117.6, 110.2 (2 CH\_2), 77.4 (C\_-1), 76.5 (C\_-5), 74.4 (C\_-3), 71.8 (C\_-2), 68.9 (C\_-4), 62.5 (C\_-6), 21.1, 21.1, 21.1, 20.9 (4 CH\_4, acetyl).} \\
\text{MS (ESI+): m/z (%) = 1927.6 (25, [M + Na\text{\textsuperscript{+}}], 1906.20 (20, [M + H\text{\textsuperscript{+}}]), 1292.97 (70, [2 M + Na\text{\textsuperscript{+}}]), 1270.84 (100, [2 M + H\text{\textsuperscript{+}])}. 658.2 (20, [M + Na\text{\textsuperscript{+}}]), 636.00 (85, [M + H\text{\textsuperscript{+}]})}. \\
\text{HRMS (ESI+): m/z [M + H\text{\textsuperscript{+}}] calc for C\text{\textsubscript{3}H\text{\textsubscript{12}}N\text{\textsubscript{2}}O\text{\textsubscript{12}}: 636.2081; found: 636.2079.} \]

2-2,3,4,6-Tetra-O-acetyl-ß-D-glucopyranosyl-5-(1-naphthalamido)hydroquinone (14b)

Treatment of compound 13a (37 mg) according to procedure C afforded 14h (32 mg, 86%); yellow syrup: \( R_f = 0.20 \) (EtOAc–PE, 1:1; \([\alpha]_D^{23} = -21.6 \text{ (c 0.75 CH\_Cl)}\). 

\[ \text{HRMS (ESI+): m/z [M + H\text{\textsuperscript{+}}] calc for C\text{\textsubscript{3}H\text{\textsubscript{12}}N\text{\textsubscript{2}}O\text{\textsubscript{12}}:} 650.1561; \text{found: 650.1561.} \]

2-2,3,4,6-Tetra-O-acetyl-ß-D-glucopyranosyl-5-(2-thienylcarboxamido)hydroquinone (14k)

Treatment of compound 13k (52 mg) according to procedure C afforded 14k (38 mg, 76%); pale yellow syrup: \( R_f = 0.16 \) (EtOAc–PE, 1:1; \([\alpha]_D^{23} = -28.9 \text{ (c 0.9, CH\_Cl)}\). 

\[ \text{HRMS (ESI+): m/z [M + H\text{\textsuperscript{+}}] calc for C\text{\textsubscript{3}H\text{\textsubscript{12}}N\text{\textsubscript{2}}O\text{\textsubscript{12}}:} 550.1561; \text{found: 550.1561.} \]

2-2,3,4,6-Tetra-O-acetyl-ß-D-glucopyranosyl-5-(2-furylcarboxamido)hydroquinone (14j)

Treatment of compound 13j (44 mg) according to procedure C afforded 14j (37 mg, 84%); yellow-green foam; \( R_f = 0.13 \) (EtOAc–PE, 1:1; \([\alpha]_D^{23} = -22.5 \text{ (c 1.0, CH\_Cl)}\). 

\[ \text{HRMS (ESI+): m/z [M + H\text{\textsuperscript{+}}] calc for C\text{\textsubscript{3}H\text{\textsubscript{12}}N\text{\textsubscript{2}}O\text{\textsubscript{12}}:} 610.1924; \text{found: 610.1923.} \]

C-Glycosyl Amino-Substituted Hydro- and Benzoquinones
2-(2,3,4,6-Tetra-o-acetyl-β-D-glucopyranosyl)-1,4-dimethoxy-5-(4-nicotinamidobenzamido)benzene (18)

Treatment of 15 (90 mg) according to procedure A afforded 18 (75 mg, 71%); white syrup; Rf = 0.07 (PE–EtOAc, 1:1); [α]d21 = –18.1 (c 0.68, CH2Cl2).

1H NMR (300.13 MHz, CDCl3); δ = 9.13 (s, 1 H, Ar), 9.06 (br s, 1 H, CONH), 8.73 (br s, 1 H, Ar), 8.60 (s, 1 H, CONH), 8.26 (s, 1 H, Ar), 8.23 (d, J = 7.8 Hz, 1 H, Ar), 7.85 (m, 4 H, Ar), 7.40 (br s, 1 H, Ar), 6.94 (s, 1 H, Ar), 5.38 (t, J8,9 = 9.3 Hz, 1 H, H-9), 5.27 (t, J8,9 = 9.3 Hz, 1 H, H-8), 5.22 (t, J6,7 = 9.6 Hz, 1 H, H-1), 4.99 (d, J6,7 = 9.6 Hz, 1 H, H-6), 4.28 (dd, J8,9 = 4.8 Hz, J6,7 = 12.6 Hz, 1 H, H-6), 4.06 (d, J6,7 = 1.2 Hz, 1 H, H-6), 3.95 (s, 3 H, OCH3), 3.89 (s, 3 H, OCH3), 2.07, 2.06, 2.01, 1.81 (4 s, 12 H, OCH2).

HRMS (ESI+): m/z (%) = 1446.7 (40 [M + Na]+), 1424.8 (100 [M + H]+), 713.0 (50 [M + H]+).

HRMS (ESI+): m/z [M + H]+ calec for C38H41N2O13: 713.2609; found: 713.2609.
References