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ORIGINAL PAPER

Highly efficient glucosylation of flavonoids

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Abstract A highly efficient procedure for glucosylation of flavonoids by acetobromoglucose is described. Glucosylation is carried out in a two-phase system $CHCl_3/H_2O$ over 96 h using tetrabutylammonium bromide as phase-transfer catalyst. A purification procedure can be performed without column chromatography, and the yields of the glucosylated flavonoids are mostly quantitative. Acetylated glucosides were deprotected with sodium methanolate to afford the desired glucosides of flavonoids.

Keywords Heterocycles · Phase-transfer catalysis · Natural products · Carbohydrates · Chromones · Coumarins

Introduction

The flavonoids belong to a class of natural heterocyclic compounds. They are biosynthesized by plants and consumed by humans and by animals, thus being an important component of nutrition. Flavonoids are represented by flavones (2-phenyl-4*H*-chromen-4-ones), isoflavones (3-phenyl-4*H*-chromen-4-ones), neoflavones (4-phenyl-2*H*-chromen-2-ones), coumarins (2*H*-chromen-2-ones), and related compounds [1]. Many biologically active compounds are found among natural and synthetic flavonoids [2–7].

3-Heteroarylchromones are isosteric to isoflavones, but contain two pharmacophoric groups: benzopyrane and a heteroaryl ring at position C-3. Diverse 3-heteroarylchromones show antiallergic, anti-inflammatory, fungicidal, antiblastic, and neuroleptic activity [8–10].

The natural flavonoids are generally hydroxylated, and the hydroxy groups are usually glycosylated by various sugars [1]. The flavonoids are normally not soluble in water, and glycosylation enhances their water-solubility. On the other hand, the flavonoids are insoluble in low-polar organic solvents, and hence insoluble in the lipid phase of membranes. Derivatization of flavonoid glycosides (alkylation or acylation) makes them soluble in solvents such as toluene. The influence of glucosylation of polyphenols on their bioavailability is described in a review [11]. Comparison of bactericidal activity of 7-hydroxy-3-pyrazolylchromones and their glucosides has shown that the latter are more active [12].

Results and discussion

Over the last years we have investigated the chemistry of 6-ethyl-7-hydroxy-3-(4-phenyl-4*H*-1,2,4-triazol-3-yl)-chromone (**1**) [13]. The synthesis of its glucosylated derivatives should increase the pharmacological profile for the reasons mentioned above. First we have applied the technique of Pivovarenko [14–17], which was developed for the synthesis of isoflavone glycosides. This method uses acetobromoglucose, which is one of the best reagents for glucosylation; normally the reaction proceeds with high

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anomeric selectivity. This reagent was widely used for glucosylation of flavonoids, especially in total synthesis [18]. According to the method of Pivovarenko, 1-(5-ethyl-2,4-dihydroxyphenyl)-2-(4-phenyl-4*H*-1,2,4-triazol-3-yl)-ethanone (**2**), which is a precursor of **1**, should be deprotonated by KOH and then glucosylated. The product 1-(5-ethyl-4-hydroxy-2-*O*-(*β*-D-tetraacetylglucopyranosyl) phenyl)-2-(4-phenyl-4*H*-1,2,4-triazol-3-yl)ethanone (**3**) should be further cyclized to afford 6-ethyl-3-(4-phenyl-4*H*-1,2,4-triazol-3-yl)-7-*O*-(*β*-D-tetraacetylglucopyranosyl)-4*H*-chromen-4-one (**4**). Unfortunately, this reaction was too inefficient. Four peaks could be detected by HPLC. We were not able to obtain the product **3** after either the usual silica gel column chromatography or reverse-phase HPLC. Therefore, this approach was given up (Scheme 1).

We investigated the glucosylation of 7-hydroxy-3-(4-phenyl-4*H*-1,2,4-triazol-3-yl)-2*H*-chromen-2-one (**5**) by this method following the procedure described in literature [19]. The glucosylation takes place in aqueous acetone and proved to be unproblematic. 3-(4-Phenyl-4*H*-1,2,4-triazol-3-yl)-7-*O*-(*β*-D-tetraacetylglucopyranosyl)-2*H*-chromen-2-one (**6**) was isolated with 50% yield (based on recovered starting material, 25% raw yield). Since a triazole ring was not deleterious to this reaction, we speculate that our failure to convert **2** to **3** is connected with the 6-ethyl group, which is bulky enough to prevent effective glucosylation. This speculation is in agreement with the successful glucosylation of other 1-hetaryl-2,4-dihydroxyacetophenones, bearing structurally similar electron-accepting heterocycles (1,3-thiazol-4-yl, 2-pyridyl, and 2-quinolyl) and having 6-CH instead of the ethyl group [14, 15]. The coumarin **5** was later glucosylated in quantitative yield according to the general procedure A.

Chromones are unstable towards nucleophiles [10], e.g., **1** is decomposed to **2** under the influence of KOH. This is the reason why the above-mentioned procedure [19] is not applicable for the direct glucosylation of **1**. Instead, we tried to apply the glucosylation under phase-transfer conditions in order to synthesize **4**.

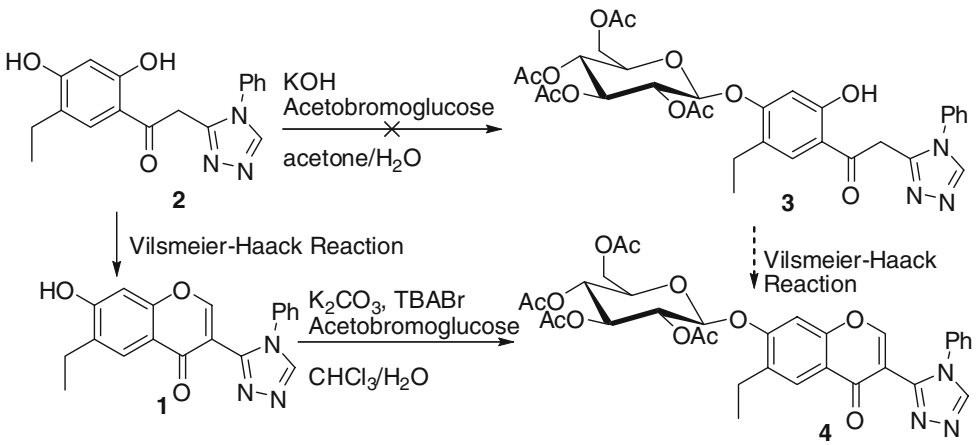
Firstly, we deprotonated **1** with five equivalents of K_2CO_3 by heating. The criterion for complete deprotonation was the formation of a clear solution in water. Prolonged stirring of this solution at r.t. leads to no traces of **2**, since the carbonate anion is a poor nucleophile but a rather good base. According to a method found in literature [19–21], we took $CHCl_3$ and one equivalent each of tetrabutylammonium bromide (TBAB) and acetobromoglucose and let them react with the above-mentioned solution of deprotonated **1**. Although the formation of **4** was detected, the conversion of **1** was not complete. Full separation of glucoside **4** from aglycone **1** was not possible by using silica gel column chromatography. Both compounds adsorb too well on silica gel, leading to "tails" on the column. Only a very small amount of pure **4** could be obtained, then mixed fractions were eluted.

In order to obtain pure **4** a procedure had to be designed which converted **1** into **4** completely, so that no chromatographic purification was necessary.

The NMR spectrum of the organic layer of the reaction mixture showed one equivalent of acetobromoglucose at the beginning. After stirring for 8 h, only 20% of **1** was converted to **4**. The glucosylation seemed to be only a side-reaction of acetobromoglucose accompanied by decomposition. The products of the decomposition were glucals [15, 19], which were also seen by NMR. On the other hand, acetobromoglucose was still detected, which indicated a slow reaction rate.

A breakthrough was the use of five equivalents of acetobromoglucose and running the reaction for 96 h instead of 8 h. Continuous stirring during 96 h was found to be absolutely necessary for full conversion of substrate. On the other hand, prolonged stirring (1 week) resulted in decomposition of the product. For each equivalent of acetobromoglucose one equivalent of K_2CO_3 had to be

Scheme 1



added, since the products of decomposition are glucals and HBr. Using a chloroform extraction (one should closely adhere to this protocol) with subsequent washing of extracts with hexane and further with water, chromatographic purification could be avoided. Compound **4** could be isolated in quantitative yield and in anomerically pure form.

The use of excess glycosylating reagent was suggested previously for solid/solution PTC glucosylation of other isoflavones (threefold excess) [22], flavones (twofold excess) [23], chalcones (1.2-fold excess) [24], and simple phenols (twofold excess) [25]. In conditions of solution-solution PTC, chalcones (2- or 1.2-fold excess) [24] and various flavones and flavonols (1.2-fold excess) [26] were glycosylated. One phenol was glucosylated using an excess of acetobromoglucose with help of autotitration by NaOH solution [27]. Generally the purification required flash chromatography; only two articles report recrystallization of the peracetylated glycosides from MeOH [25] or EtOH [23]. However recrystallization of crude compounds **4**, **6**, and of 2-amino-6-ethyl-3-(4-phenyl-4*H*-1,2,4-triazol-3-yl)-7-*O*-(*β*-D-tetraacetylglucopyranosyl)-4*H*-chromen-4-one (**22**) was not applicable because of fair solubility in alcohols, which was obviously caused by contaminants (in contrast, pure **6** can be recrystallized from *i*-PrOH).

The above-mentioned procedure was successfully applied for the other flavonoids **7**-**10** (Scheme 2). 3-Phenyl-7-*O*-(*β*-D-tetraacetylglucopyranosyl)-4*H*-chromen-4-one (**13**), 2-phenyl-7-*O*-(*β*-D-tetraacetylglucopyranosyl)-4*H*-chromen-4-one (**15**), 3-phenyl-7-*O*-(*β*-D-tetraacetylglucopyranosyl)-2*H*-chromen-2-one (**17**), and 4-phenyl-7-*O*-(*β*-D-tetraacetylglucopyranosyl)-2*H*-chromen-2-one (**19**) are very well soluble in toluene and do not tend to adsorb irreversibly on silica gel, which makes purification simpler, since filtration through silica gel is sufficient (see general procedure B).

The protected glucosides were deacetylated using a very mild modification of Zemplen's protocol [28], which allowed free glucosides to be obtained in quantitative yield without decomposition of the chromone/coumarin ring.

The structures of the synthesized compounds were proven by ^{1}H and ^{13}C NMR spectra and by mass spectra. The use of 2D NMR techniques (COSY, HSQC, and HMBC spectra) allowed us to perform a full assignment of signals for each compound.

Compounds **13** and **14** [29], **15** and **16** [30], and **19** and **20** [31] are already known, but spectral information (^{1}H NMR) has been given only for **19** and 7-*O*-(*β*-D-glucopyranosyl)-4-phenyl-2*H*-chromen-2-one (**20**).

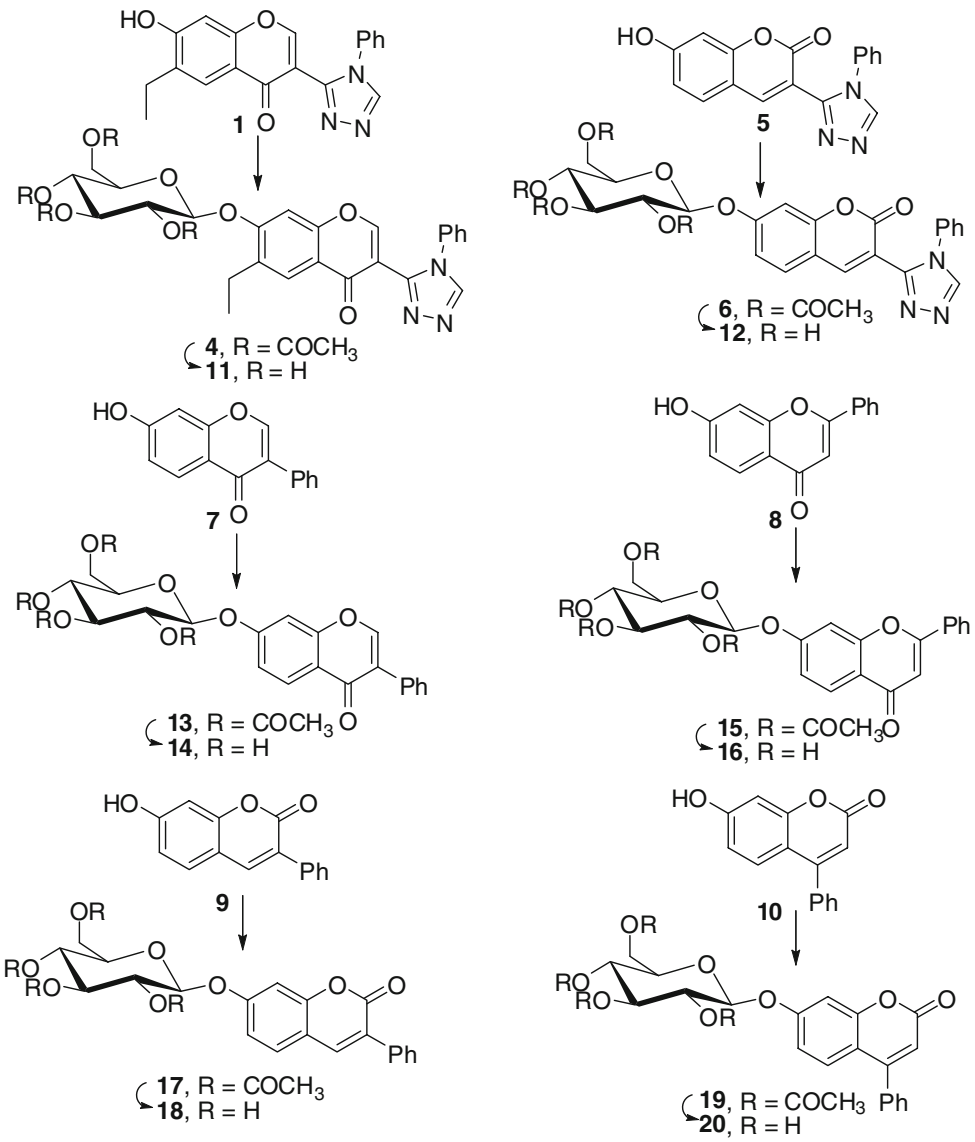
A few words should be said about the NMR spectra of 6-ethyl-7-*O*-(*β*-D-glucopyranosyl)-3-(4-phenyl-4*H*-1,2,4-triazol-3-yl)-4*H*-chromen-4-one (**11**) and 7-*O*-(*β*-D-glucopyranosyl)-3-(4-phenyl-4*H*-1,2,4-triazol-3-yl)-2*H*-chromen-2-one (**12**). The freshly prepared solution in DMSO-d_6 of both compounds showed broad peaks in the ^{1}H NMR spectra, as if paramagnetically broadened. Careful reproduction of deprotection reaction without using a metal spatula, however, reproduced this broadening. By heating to 90 °C the peaks became sharp, and multiplets appeared. After cooling to r.t. the peaks remained sharp. We suppose that a polymeric structure was formed with hydrogen bonds between nitrogen atoms of the triazole ring and OH groups of glucosyl. By heating, the polymeric structure was destroyed, and the molecules of glucoside were solvated by DMSO-d_6. Parent acetylated glucosides **4** and **6** and the other deprotected glucosides have not shown this effect. The signals of the CH protons of the glucosyl moiety of compound **11** were found to be different in "polymeric" and in "solvated" state, e.g., the anomeric proton of **11** resonated at $\delta = 4.88$ ppm as a broad singlet at r.t. in the spectrum with broad peaks. After heating to 90 °C it was shifted to $\delta = 5.07$ ppm (broad doublet, $J = 7.4$ Hz) and remained at this position after cooling. The signals of OH groups were found to be temperature dependent, and in the Experimental Section we provide the chemical shifts for both r.t. (after preheating and cooling) and 90 °C.

We have studied the glucosylation of 2-amino-6-ethyl-7-hydroxy-3-(4-phenyl-4*H*-1,2,4-triazol-3-yl)-4*H*-chromen-4-one (**21**) and found it to form **22** readily in the presence of ten equivalents of acetobromoglucose. Its ^{1}H NMR spectrum showed broad signals, which became sharp after storage of the sample for 1 month or more in DMSO-d_6 at r.t. Surprisingly, the peaks remained broad even at heating to 160 °C. Probably this compound has strong hydrogen bonds between the NH_2 groups and the triazole ring, thus having a polymeric structure. The purity of crude compound could be estimated to be 90% or even higher according to ^{1}H NMR. It could not be further purified by silica gel column chromatography, because of its irreversible adsorption, even in presence of triethylamine in the eluent. Deacetylation of **22** gave crude 2-amino-6-ethyl-7-*O*-(*β*-D-glucopyranosyl)-3-(4-phenyl-4*H*-1,2,4-triazol-3-yl)-4*H*-chromen-4-one (**23**) with a yield of 85%, which was very well soluble in water (Scheme 3). It could not be purified further without the use of HPLC.

Conclusion

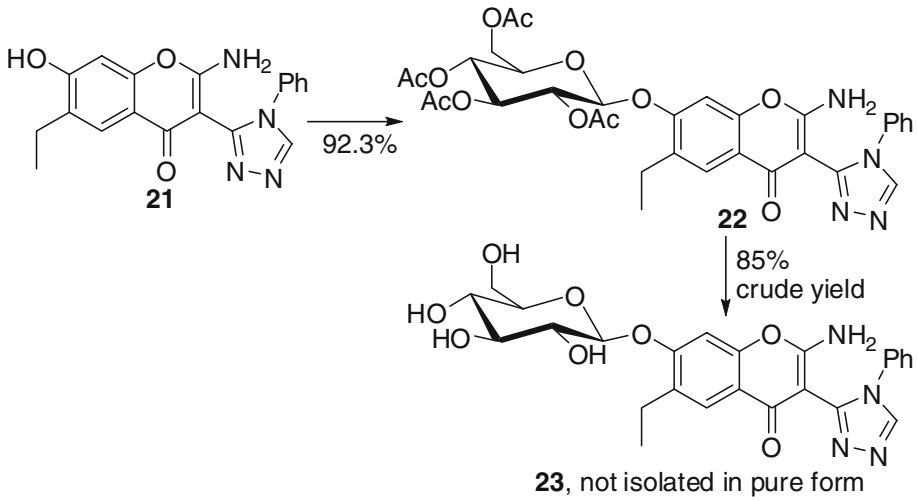
In summary, we have developed a highly efficient procedure for glucosylation of flavonoids (with respect to the efficiency of utilization of such expensive compounds). This has been demonstrated on four model flavonoids and on two 3-heteroarylflavonoids.

Scheme 2



All reactions gave quantitative yield. Glucosylation in PTC conditions, deacetylation by NaOMe in MeOH.

Scheme 3



Experimental

NMR spectra were recorded on Bruker Avance 400 or JEOL JNM-LA 400 with TMS as internal standard. Atom numbers with one prime correspond to atoms of the phenyl ring, with two primes to atoms of the glucosyl moiety. HRMS ESI/TOF were measured on a Bruker Daltonics microTOF II, using Agilent Tune mix for LC/MSD ion trap as external standard, in positive polarization. HRMS ESI/Fourier-transform ion-cyclotrone resonance (FT-ICR) were measured on a Bruker APEX II FT/ICR instrument with a 7-T magnet in positive polarization. Analytical HPLC was performed on Merck RP-18 columns (250 × 4.1 mm) using gradient or isocratic elution by an acetonitrile–water mixture (UV detection at 254 nm). IR spectra were measured on Perkin-Elmer Spectrum 100 IR spectrometer with an attenuated total reflectance (ATR) element. Rotation angles were measured on a Perkin-Elmer 241 polarimeter with 5 s integration time. Syntheses of **1** [13] and **21** [32] have been described previously. 2-(4-Phenyl-4*H*-1,2,4-triazol-3-yl)acetonitrile was synthesized according to the published procedure [33]. Acetobromoglucose was synthesized according to the known procedure [34], stabilized with 2% of $CaCO_3$, precipitated from benzene with hexane (20 cm^3 benzene and 100 cm^3 hexane per 100 g acetobromoglucose) and stored at −20 °C. Methanol was allowed to react with metallic sodium and distilled in nitrogen atmosphere.

7-Hydroxy-3-(4-phenyl-4H-1,2,4-triazol-3-yl)-2H-chromen-2-one (**5**, $C_{17}H_{11}N_3O_3$) [35]

A mixture containing 1.842 g 2-(4-phenyl-4*H*-1,2,4-triazol-3-yl)acetonitrile (10 mmol), 1.381 g 2,4-dihydroxybenzaldehyde (10 mmol), 0.1 cm^3 piperidine, and 40 cm^3 2-propanol was refluxed for 3 min and allowed to stand for 5 h. All volatiles were evaporated in vacuum; 100 cm^3 aqueous 3% H_2SO_4 was added and refluxed for 12 h. The formed precipitate was filtered, washed with water, and dried to give 2.52 g (82%) of **5**. M.p.: 299 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 6.73$ (d, $J = 2.2$ Hz, 1H, 8-H), 6.87 (dd, $J = 8.8$ Hz, $J = 2.2$ Hz, 1H, 6-H), 7.39–7.50 (m, 5H, Ph), 7.70 (d, $J = 8.8$ Hz, 1H, 5-H), 8.48 (s, 1H, 4-H), 8.97 (s, 1H, 5-$H_{triazole}$), 10.92 (s, 1H, OH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 102.1$ (8-CH), 110.18 (3-C), 110.82 (10-C), 113.92 (6-CH), 124.12 (2′-CH_{Ph}), 128.64 (4′-CH_{Ph}), 129.58 (3′-CH_{Ph}), 130.96 (5-CH), 134.53 (1′-C_{Ph}), 144.95 (5-$CH_{triazole}$), 147.41 (4-CH), 148.61 (3-$C_{triazole}$), 156.01 (9-C), 158.00 (2-C), 162.75 (7-C) ppm; IR (ATR): $\bar{\nu} = 688$, 693, 751, 763, 772, 812, 837, 853, 939, 1,117, 1,134, 1,172, 1,205, 1,236, 1,250, 1,274, 1,332, 1,367, 1,393, 1,453, 1,460, 1,501, 1,557, 1,582, 1,597, 1,609, 1,700, 1,724, 3,100–3130 (broad δ_{CH}), 3540 (δ_{OH}) cm^{-1}; HRMS (ESI/TOF): [M + H^+] found (calculated): 306.0887 (306.0873).

*General procedure A for glucosylation of **1**, **5**, and **21***

Substrate (2.5 mmol) and K_2CO_3 (25 mmol) were added to 50 cm^3 water and dissolved with heating, filtered, and more K_2CO_3 (12.5 mmol) was added to the filtrate. Chloroform (50 cm^3) was added to this aqueous solution, followed by acetobromoglucose (12.5 mmol) and tetrabutylammonium bromide (2.5 mmol). The resulting mixture was vigorously stirred for 96 h and then heated to reflux for 1 h (destroying the excess of acetobromoglucose). After cooling to r.t. the two-phase system was separated, and the aqueous phase was washed repeatedly with chloroform (emulsion was always combined with organic extracts). The combined organic extracts were shaken with a saturated solution of K_2CO_3 and diluted with water, and the organic phase was separated. The remaining aqueous phase was reextracted with chloroform, and the combined organic extracts were washed with brine. The chloroform layer was separated, dried with Na_2SO_4, filtered, and evaporated in vacuum. The remaining resin was dissolved or suspended in 20 cm^3 toluene under reflux; after cooling, exactly 100 cm^3 *n*-hexane were added, which resulted in the formation of a brown resin. The solvent was decanted and the residue was washed with hexane and again refluxed in 20 cm^3 of toluene, cooled, treated with 100 cm^3 of hexane, and decanted. The resting gum was dissolved in a minimum amount of acetone and poured into 200 cm^3 water. After 10 min, 200 cm^3 brine was added; this resulted in coagulation and formation of the crude glucoside. It was separated by filtration or decantation, redissolved in acetone and the precipitation described above was repeated (with brine-induced coagulation). Usually after the fourth cycle of such precipitation, a crystalline sediment was formed, which was collected by filtration, washed with distilled water, dried in vacuum, and redissolved in acetone (washed off from the frit, NaCl stays undissolved). The acetone was evaporated and the residue was dried in vacuum (10^{-2} mbar), resulting in a voluminous crystalline mass of the acetylated glucoside. The yield was quantitative.

6-Ethyl-3-(4-phenyl-4H-1,2,4-triazol-3-yl)-7-O-(β-D-tetra-acetylglucopyranosyl)-4H-chromen-4-one (**4**, $C_{33}H_{33}N_3O_{12}$)

M.p.: 117 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 1.04$ (t, $J = 7.3$ Hz, 3H, CH_3CH_2), 1.99–2.04 (m, 12H, OAc), 2.5 (q, $J = 7.3$ Hz, 2H, CH_3CH_2), 4.15 (d, $J = 11$ Hz, 1H, 6″-CH_2), 4.22 (dd, $J = 12.3$ Hz, $J = 5.8$ Hz, 1H, 6″-CH_2), 4.41 (br m, 1H, 5″-CH), 5.06 (t, $J = 9.6$ Hz, 1H, 4″-CH), 5.19 (dd, $J = 8.3$ Hz, $J = 9.3$ Hz, 1H, 2″-CH), 5.44 (d, $J = 9.6$ Hz, 1H, 3″-CH), 5.76 (d, $J = 7.8$ Hz, 1H, 1″-CH), 7.29 (s, 1H, 8-H), 7.42 (m, 5H, Ph), 7.68 (s, 1H, 5-H), 8.79 (s, 1H, 2-H), 8.99 (s, 1H, 5-$H_{triazole}$) ppm; ^{13}C NMR

(100 MHz, DMSO-d_6): $\delta = 13.76$ (CH_3CH_2), 20.25 (2C, CH_3CO), 20.37 (CH_3CO), 20.42 (CH_3CO), 22.19 (CH_3CH_2), 61.64 (6″-CH_2), 67.98 (4″-CH), 70.23 (2″-CH), 71.14 (5″-CH), 71.64 (3″-CH), 96.63 (1″-CH), 102.83 (8-CH), 113.28 (3-C), 117.97 (10-C), 124.11 (2′-CH_{Ph}), 124.95 (5-CH), 128.60 (4′-CH_{Ph}), 129.45 (3′-CH_{Ph}), 132.07 (6-C), 134.48 (1′-C_{Ph}), 145.28 (5-$CH_{triazole}$), 146.34 (3-$C_{triazole}$), 155.56 (9-C), 158.33 (2-CH), 158.58 (7-C), 169.03 (2″-OAc), 169.30 (4″-OAc), 169.58 (3″-OAc), 169.95 (6″-OAc), 172.71 (4-C) ppm; IR (ATR): $\bar{\nu} = 695$, 766, 890, 1,035, 1,066, 1,206, 1,367, 1,454, 1,480, 1,505, 1,616, 1,627, 1,657, 1,746, 2,850–3,000 (broad δ_{CH}) cm^{-1}; $[\alpha]_D^{25} = -20°\ g^{-1}\ cm^3\ dm^{-1}$ ($c = 0.25$, DMF); HRMS (ESI/TOF): [M + H^+] found (calculated): 664.2138 (664.2137).

3-(4-Phenyl-4H-1,2,4-triazol-3-yl)-7-O-(β-D-tetraacetylglucopyranosyl)-2H-chromen-2-one
(**6**, $C_{31}H_{29}N_3O_{12}$)
M.p.: 113 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 1.97$ (s, 3H, 6″-OAc), 1.98 (s, 3H, 3″-OAc), 2.01 (s, 3H, 4″-OAc), 2.02 (s, 3H, 2″-OAc), 4.10 (dd, $J = 12.0$ Hz, $J = 1.8$ Hz, 1H, 6″-CH), 4.19 (dd, $J = 12.0$ Hz, $J = 5.8$ Hz, 1H, 6″-CH), 4.33 (m, 1H, 5″-CH), 5.03 (t, $J = 9.5$ Hz, 1H, 4″-CH), 5.12 (dd, $J = 8.5$ Hz, $J = 8.0$ Hz, 1H, 2″-CH), 5.40 (t, $J = 9.5$ Hz, 1H, 3″-CH), 5.77 (d, $J = 8.0$ Hz, 1H, 1″-CH), 7.06 (dd, $J = 8.8$ Hz, $J = 2.2$ Hz, 1H, 6-CH), 7.08 (d, $J = 2.2$ Hz, 1H, 8-CH), 7.39–7.50 (m, 5H, Ph), 7.87 (d. $J = 8.3$ Hz, 1H, 5-CH), 8.58 (s, 1H, 4-CH), 9.00 (s, 1H, 5-$CH_{triazole}$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 20.23$ (CH_3), 20.28 (CH_3), 20.31 (CH_3), 20.33 (CH_3), 61.53 (6″-CH_2), 67.85 (4″-CH), 70.38 (2″-CH), 71.07 (5″-CH), 71.85 (3″-CH), 96.34 (1″-CH), 103.13 (8-CH), 112.73 (3-C), 113.60 (10-C), 114.21 (6-CH), 124.04 (2′-CH_{Ph}), 128.66 (4′-CH_{Ph}), 129.60 (3′-CH_{Ph}), 130.90 (5-CH), 134.45 (1′-C_{Ph}), 145.05 (5-$CH_{triazole}$), 146.97 (4-CH), 148.28 (3-$C_{triazole}$), 155.32 (9-C), 157.57 (2-C), 159.83 (7-C), 169.07 (2″-OAc), 169.29 (4″-OAc), 169.58 (3″-OAc), 169.88 (6″-OAc) ppm; IR (ATR): $\bar{\nu} = 691$, 753, 765, 907, 934, 991, 1,033, 1,066, 1,131, 1,181, 1,214, 1,366, 1,504, 1,576, 1,613, 1,738, 2,830–3,150 (broad δ_{CH}) cm^{-1}; $[\alpha]_D^{25} = -24°\ g^{-1}\ cm^3\ dm^{-1}$ ($c = 0.25$, acetone); HRMS (ESI/TOF): [M + H^+] found (calculated): 636.1826 (636.1824).

2-Amino-6-ethyl-3-(4-phenyl-4H-1,2,4-triazol-3-yl)-7-O-(β-D-tetraacetylglucopyranosyl)-4H-chromen-4-one
(**22**, $C_{33}H_{34}N_4O_{12}$)
Synthesized according to the general procedure A from 871 mg **21** (2.5 mmol), K_2CO_3 (37.5 + 12.5 mmol), and acetobromoglucose (25 mmol). The crystalline product was found to occlude resting acetone, not removable in vacuum of oil pump (10^{-2} mbar). The product-to-acetone ratio was found to be approximately 1:1 (by NMR). Hence 1.7 g product correspond to 92.3% yield. M.p.: 143 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 1.05$ (t, $J = 7.3$ Hz, 3H, CH_3CH_2), 1.91–2.07 (br m, 12H, OAc), 2.08 (acetone), 2.5 (CH_2CH_3 and DMSO), 4.08 (d, $J = 12.1$ Hz, 1H, 6″-CH_2), 4.23 (dd, $J = 12.1$ Hz, $J = 6.3$ Hz, 1H, 6″-CH_2), 4.33 (m, 1H, 5″-CH), 5.03 (t, $J = 9.5$ Hz, 1H, 4″-CH), 5.17 (dd, $J = 9.5$ Hz, $J = 8.0$ Hz, 1H, 2″-CH), 5.45 (t, $J = 9.5$ Hz, 1H, 3″-CH), 5.73 (d, $J = 7.8$ Hz, 1H, 1″-CH), 6.94 (s, 1H, 8-H), 7.12–7.53 (br m, 5H, Ph), 7.61 (s, 1H, 5-CH), 7.70 (br s, 2H, NH_2), 8.90 (s, 1H, 5-$CH_{triazole}$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 14.01$ (CH_3CH_2), 20.30 (2C, OAc), 20.41 (OAc), 20.47 (OAc), 22.13 (CH_3CH_2), 30.68 (acetone), 61.75 (6″-CH_2), 68.15 (4″-CH), 70.37 (2″-CH), 71.03 (5″-CH), 71.63 (3″-CH), 85.19 (3-C), 96.71 (1″-CH), 101.75 (8-CH), 116.36 (10-C), 124.28 (2′-CH_{Ph}), 124.97 (5-CH), 128.46 (4′-CH_{Ph}), 129.25 (3′-CH_{Ph}), 130.00 (6-C), 134.70 (1′-C_{Ph}), 144.65 (5-$CH_{triazole}$), 147.00 (3-$C_{triazole}$), 152.11 (9-C), 157.10 (7-C), 163.78 (2-CNH_2), 169.05 (2″-OAc), 169.35 (4″-OAc), 169.63 (3″-OAc), 170.06 (6″-OAc), 172.49 (4-C), 206.51 (acetone) ppm; IR (ATR): $\bar{\nu} = 693$, 763, 908, 1,033, 1,062, 1,213, 1,367, 1,460, 1,505, 1,520, 1,562, 1,618, 1,743, 2,910–3,000 (broad δ_{CH}), 3,000–3,670 (broad δ_{NH}) cm^{-1}; $[\alpha]_D^{25} = 0°\ g^{-1}\ cm^3\ dm^{-1}$, $[\alpha]_{546}^{25} = -20.0°\ g^{-1}\ cm^3\ dm^{-1}$ ($c = 0.1$, acetone); HRMS (ESI/TOF): [M + H^+] found (calculated): 679.2237 (679.2246).

*General procedure B for glucosylation of **7**-**10***

The reaction and extraction was performed according to the general procedure A; the chloroform extracts were evaporated without prior drying and 150 cm^3 toluene was added. The obtained heterogeneous mixture was refluxed for 5 min, cooled, and treated with solid Na_2SO_4 to absorb the remaining water, tetrabutylammonium bromide, and some black by-products. The mixture was filtered and washed thoroughly with toluene. The toluene was evaporated, and the remaining gum was dissolved in 10 cm^3 toluene (if necessary, with heating). After cooling, to this solution exactly 50 cm^3 *n*-hexane was added, which resulted in the formation of a brown resin. This was decanted and washed with hexane, and the remaining resin was dissolved in some appropriate solvent (ethyl acetate, acetone, etc.) and adsorbed on 5 g silica gel. Then the silica with the adsorbed peracetylated glucoside was placed on top of a short column (60 g silica) and eluted by ethyl acetate (ca. 0.5 dm^3). The eluate was evaporated and dried in vacuum (10^{-2} mbar), giving pure **15** or not pure **13**, **17** or **19** (more than quantitative yield). The latter were purified by precipitation with water from the acetone solution with brine-induced coagulation (according to the general procedure A). Pure crystalline glucoside came after one (**13**, **17**) or two (**19**) cycles of precipitation. The yield was quantitative.

3-Phenyl-7-O-(β-D-tetraacetylglucopyranosyl)-4H-chromen-4-one (**13**, $C_{29}H_{28}O_{12}$)
M.p.: 145 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 1.99$ (s, 3H, 3″-OAc), 2.03 (s, 6H, 4″- and 5″-OAc), 2.04 (s, 3H, 2″-OAc), 4.12 (dd, $J = 12.3$ Hz, $J = 2.3$ Hz, 1H, 6″-CH_2), 4.22 (dd, $J = 12.3$ Hz, $J = 5.8$ Hz, 1H, 6″-CH_2), 4.36 (m, 1H, 5″-CH), 5.06 (t, $J = 9.5$ Hz, 1H, 4″-CH), 5.15 (dd, $J = 9.5$ Hz, $J = 8.0$ Hz, 1H, 2″-CH), 5.43 (t, $J = 9.5$ Hz, 1H, 3″-CH), 5.83 (d, $J = 8.0$ Hz, 1H, 1″-CH), 7.13 (dd, $J = 8.8$ Hz, $J = 2.3$ Hz, 1H, 6-H), 7.27 (d, $J = 2.3$ Hz, 1H, 8-H), 7.35–7.46 (m, 5H, Ph), 8.10 (d, $J = 8.8$ Hz, 1H, 5-H), 8.51 (s, 1H, 2-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 20.24$ (OAc), 20.30 (OAc), 20.35 (OAc), 20.41 (OAc), 61.56 (6″-CH_2), 67.87 (4″-CH), 70.45 (2″-CH), 71.10 (5″-CH), 71.85 (3″-CH), 96.44 (1″-CH), 103.77 (8-CH), 115.35 (6-CH), 119.24 (10-C), 123.85 (3-C), 127.43 (5-CH), 127.86 (4′-CH_{Ph}), 128.12 (3′-CH_{Ph}), 128.89 (2′-CH_{Ph}), 131.73 (1′-C_{Ph}), 154.47 (2-CH), 156.86 (9-C), 160.13 (7-C), 169.08 (2″-OAc), 169.30 (4″-OAc), 169.59 (3″-OAc), 169.94 (6″-OAc), 174.37 (4-C) ppm; IR (ATR): $\bar{\nu} = 694, 752, 784, 858, 884, 905, 948, 980, 1{,}031, 1{,}055, 1{,}080, 1{,}100, 1{,}124, 1{,}150, 1{,}220, 1{,}371, 1{,}444, 1{,}497, 1{,}620, 1{,}638, 1{,}739, 1{,}750, 2{,}861–3{,}120$ (broad δ_{CH}) cm^{-1}; $[\alpha]_D^{25} = -15.0°$ g^{-1} cm^3 dm^{-1} ($c = 1.03$, acetone); HRMS (ESI/TOF): $[M + H^+]$ found (calculated): 569.1652 (569.1654).

2-Phenyl-7-O-(β-D-tetraacetylglucopyranosyl)-4H-chromen-4-one (**15**, $C_{29}H_{28}O_{12}$)
M.p.: 180 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 1.99$ (s, 3H, OAc), 2.01 (s, 3H, OAc), 2.03 (s, 3H, OAc), 2.04 (s, 3H, OAc), 4.15 (dd, $J = 12.3$ Hz, $J = 2.5$ Hz, 1H, 6″-CH_2), 4.21 (dd, $J = 12.3$ Hz, $J = 5.8$ Hz, 1H, 6″-CH_2), 4.37 (m, 1H, 5″-CH), 5.05 (t, $J = 9.5$ Hz, 1H, 4″-CH), 5.15 (dd, $J = 9.5$ Hz, $J = 8.0$ Hz, 1H, 2″-CH), 5.43 (t, $J = 9.5$ Hz, 1H, 3″-CH), 5.82 (d, $J = 8.0$ Hz, 1H, 1″-CH), 7.00 (s, 1H, 3-H), 7.13 (dd, $J = 8.8$ Hz, $J = 2.3$ Hz, 1H, 6-H), 7.39 (d, $J = 2.3$ Hz, 1H, 8-H), 7.55–7.64 (m, 3H, 3′- and 4′-H_{Ph}), 8.0 (d, $J = 8.8$ Hz, 1H, 5-H), 8.08 (m, 2H, 2′-H_{Ph}) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 20.26$ (OAc), 20.31 (OAc), 20.37 (OAc), 20.40 (OAc), 61.63 (6″-CH_2), 67.89 (4″-CH), 70.48 (2″-CH), 71.14 (5″-CH), 71.82 (3″-CH), 96.58 (1″-CH), 104.28 (8-CH), 106.94 (3-CH), 115.15 (6-CH), 118.80 (10-C), 126.22 (2′-CH_{Ph}), 126.68 (5-CH), 129.07 (3′-CH_{Ph}), 131.01 (1′-C_{Ph}), 131.78 (4′-CH_{Ph}), 156.92 (9-C), 160.31 (7-C), 162.49 (2-C), 169.09 (2″-OAc), 169.31 (4″-OAc), 169.57 (3″-OAc), 169.92 (6″-OAc), 176.33 (4-C) ppm; IR (ATR): $\bar{\nu} = 667, 694, 782, 816, 836, 909, 956, 979, 1{,}032, 1{,}062, 1{,}081, 1{,}129, 1{,}157, 1{,}182, 1{,}216, 1{,}233, 1{,}351, 1{,}370, 1{,}448, 1{,}494, 1{,}571, 1{,}610, 1{,}627, 1{,}653, 1{,}730, 1{,}755, 2{,}860–3{,}100$ (broad δ_{CH}) cm^{-1}; $[\alpha]_D^{25} = -22.3°$ g^{-1} cm^3 dm^{-1} ($c = 1.03$, acetone); HRMS (ESI/TOF): $[M + H^+]$ found (calculated): 569.1653 (569.1654).

3-Phenyl-7-O-(β-D-tetraacetylglucopyranosyl)-2H-chromen-2-one (**17**, $C_{29}H_{28}O_{12}$)
M.p.: 152 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 1.98$ (s, 3H, OAc), 2.02 (s, 3H, OAc), 2.03 (s, 6H, OAc), 4.15 (dd, $J = 12.3$ Hz, $J = 2.3$ Hz, 1H, 6″-CH_2), 4.21 (dd, $J = 12.3$ Hz, $J = 5.6$ Hz, 1H, 6″-CH_2), 4.34 (m, 1H, 5″-CH), 5.04 (t, $J = 9.5$ Hz, 1H, 4″-CH), 5.12 (dd, $J = 9.8$ Hz, $J = 8.0$ Hz, 1H, 2″-CH), 5.42 (t, $J = 9.5$ Hz, 1H, 3″-CH), 5.75 (d, $J = 8.0$ Hz, 1H, 1″-CH), 7.01 (dd, $J = 8.5$ Hz, $J = 2.3$ Hz, 1H, 6-H), 7.10 (d, $J = 2.3$ Hz, 1H, 8-H), 7.37–7.78 (m, 3H, 3′- and 4′-H_{Ph}), 7.71 (m, 2H, 2′-H_{Ph}), 7.75 (d, $J = 8.5$ Hz, 1H, 5-H), 8.23 (s, 1H, 4-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 20.25$ (OAc), 20.31 (OAc), 20.37 (OAc), 20.41 (OAc), 61.58 (6″-CH_2), 67.90 (4″-CH), 70.48 (2″-CH), 71.04 (5″-CH), 71.89 (3″-CH), 96.54 (1″-CH), 102.79 (8-CH), 113.76 (6-CH), 114.79 (10-C), 124.47 (3-C), 128.19 (3′-CH_{Ph}), 128.34 (3C, 2′- and 4′-CH_{Ph}), 129.90 (5-CH), 134.69 (1′-C_{Ph}), 140.41 (4-CH), 154.25 (9-C), 158.65 (7-C), 159.68 (2-C), 169.08 (2″-OAc), 169.30 (4″-OAc), 169.58 (3″-OAc), 169.93 (6″-OAc) ppm; IR (ATR): $\bar{\nu} = 698, 737, 786, 865, 899, 931, 997, 1{,}028, 1{,}044, 1{,}073, 1{,}110, 1{,}127, 1{,}177, 1{,}209, 1{,}241, 1{,}367, 1{,}430, 1{,}502, 1{,}612, 1{,}727, 1{,}741, 2{,}850–3{,}120$ (broad δ_{CH}) cm^{-1}; $[\alpha]_D^{25} = -18.4°$ g^{-1} cm^3 dm^{-1} ($c = 1$, acetone); HRMS (ESI/TOF): $[M + H^+]$ found (calculated): 569.1645 (569.1654).

4-Phenyl-7-O-(β-D-tetraacetylglucopyranosyl)-2H-chromen-2-one (**19**, $C_{29}H_{28}O_{12}$)
This compound tends to form a resin, which solidifies when staying in water for 24 h. ^{1}H NMR data recorded in $CDCl_3$ are reported in Ref. [31]. The ^{1}H NMR spectrum recorded in DMSO-d_6 differs from that mentioned above. ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 1.98$ (s, 3H, OAc), 2.02 (s, 3H, OAc), 2.03 (s, 3H, OAc), 2.08 (s, 3H, OAc), 4.11 (dd, $J = 12.3$ Hz, $J = 2.1$ Hz, 1H, 6″-CH_2), 4.20 (dd, $J = 12.3$ Hz, $J = 5.6$ Hz, 1H, 6″-CH_2), 4.34 (m, 1H, 5″-CH), 5.04 (t, $J = 9.8$ Hz, 1H, 4″-CH), 5.12 (dd, $J = 9.8$ Hz, $J = 8.0$ Hz, 1H, 2″-CH), 5.42 (t, $J = 9.8$ Hz, 1H, 3″-CH), 5.76 (d, $J = 8.0$ Hz, 1H, 1″-CH), 6.31 (s, 1H, 3-H), 6.96 (dd, $J = 8.8$ Hz, $J = 2.5$ Hz, 1H, 6-H), 7.17 (d, $J = 2.5$ Hz, 1H, 8-H), 7.39 (d, $J = 8.8$ Hz, 1H, 5-H), 7.51–7.59 (m, 5H, Ph) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 20.23$ (OAc), 20.27 (OAc), 20.34 (OAc), 20.37 (OAc), 61.57 (6″-CH_2), 67.90 (4″-CH), 70.46 (2″-CH), 71.06 (5″-CH), 71.87 (3″-CH), 96.48 (1″-CH), 103.57 (8-CH), 112.50 (3-CH), 113.58 (10-C), 113.70 (6-CH), 128.10 (5-CH), 128.42 (2′-CH_{Ph}), 128.86 (3′-CH_{Ph}), 129.71 (4′-CH_{Ph}), 134.75 (1′-C_{Ph}), 154.79 (4-C), 154.99 (9-C), 158.84 (7-C), 159.69 (2-C), 169.06 (2″-OAc), 169.29 (4″-OAc), 169.57 (3″-OAc), 169.93 (6″-OAc) ppm; IR (ATR): $\bar{\nu} = 701, 774, 859,$

907, 999, 1,032, 1,068, 1,118, 1,158, 1,210, 1,371, 1,610, 1,734, 2,880–3,120 (broad δ_{CH}) cm^{-1}; $[\alpha]_D^{25} = -18.0°$ g^{-1} cm^3 dm^{-1} ($c = 0.5$, acetone); HRMS (ESI/TOF): $[M + H^+]$ found (calculated): 569.1640 (569.1654).

General procedure C for the deacetylation of protected glucosides

The reaction should be carried out strictly under inert atmosphere. Peracetylated glucoside (0.5 g), 20 cm^3 absolute methanol, and NaOMe (0.1 cm^3, 0.5 N MeOH solution, Fluka) were placed in a weighed flask. The reaction was stirred at r.t. for 24 h and evaporated in vacuum. Conversion was calculated by the difference of mass; in case of insufficient conversion, the procedure was repeated (e.g., for **20**, three cycles of deacetylation were needed). Water was added, and the mixture was filtrated, affording crystalline deprotected glucoside after drying. Ion exchanger Dowex® 50WX8 100–200 mesh (0.5 g) was added to the filtrate and the mixture was stirred for 5 min (controlled by pH), filtrated, and washed with water. Evaporation and drying of the filtrate (in vacuum, 10^{-2} mbar) gave an additional portion of the crystalline glucoside. Yield of the combined fractions was quantitative.

6-Ethyl-7-O-(β-D-glucopyranosyl)-3-(4-phenyl-4H-1,2,4-triazol-3-yl)-4H-chromen-4-one
(**11**, $C_{25}H_{25}N_3O_8$)
M.p.: 203 °C; ^{1}H NMR (400 MHz, DMSO-d_6, r.t.): $\delta = 1.13$ (t, $J = 7.4$ Hz, 3H, CH_3CH_2), 2.66 (q, $J = 7.4$ Hz, 2H, CH_3CH_2), 3.19 (m, 1H, 4″-CH), 3.33 (m, 2H, 2″- and 3″-CH), 3.48 (m, 2H, 5″-CH and 6″-CH_2), 3.72 (m, 1H, 6″-CH_2), 4.68 (br t, $J = 5.5$ Hz, 1H, 6″-OH), 5.08 (br d, $J = 7.5$ Hz, 1H, 1″-CH), 5.16 (d, $J = 4.8$ Hz, 1H, 4″-OH), 5.22 (br s, 1H, 3″-OH), 5.44 (br s, 1H, 2″-OH), 7.29 (s, 1H, 8-H), 7.35–7.45 (m, 5H, Ph), 7.65 (s, 1H, 5-H), 8.76 (s, 1H, 2-H), 8.99 (s, 1H, 5-$H_{triazole}$) ppm; ^{1}H NMR (400 MHz, DMSO-d_6, 90 °C): $\delta = 1.17$ (t, $J = 7.4$ Hz, 3H, CH_3CH_2), 2.70 (q, $J = 7.4$ Hz, 2H, CH_3CH_2), 3.06 (br s, OH + H_2O), 3.27 (m, 1H, 4″-CH), 3.39 (m, 2H, 2″- and 3″-CH), 3.45–3.55 (m, 2H, 5″-CH and 6″-CH_2), 3.77 (br d, $J = 11.3$ Hz, 6″-CH_2), 4.34 (br s, 1H, OH), 4.84 (br s, 1H, OH), 5.06 (m, 2H, 1″-CH and OH), 7.30 (s, 1H, 8-H), 7.36–7.46 (m, 5H, Ph), 7.69 (s, 1H, 5-H), 8.64 (s, 1H, 2-H), 8.85 (s, 1H, 5-$H_{triazole}$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 13.64$ (CH_3CH_2), 22.36 (CH_3CH_2), 60.66 (6″-CH_2), 69.68 (4″-CH), 73.17 (2″-CH), 76.53 (3″-CH), 77.26 (5″-CH), 100.21 (1″-CH), 102.68 (8-CH), 113.15 (3-C), 117.14 (10-C), 124.15 (3C, 5-CH and 2′-CH_{Ph}), 128.60 (4′-CH_{Ph}), 129.45 (3′-CH_{Ph}), 132.24 (6-C), 134.47 (1′-C_{Ph}), 145.22 (5-$CH_{triazole}$), 146.46 (3-$C_{triazole}$), 155.81 (9-C), 158.09 (2-CH), 160.03 (7-C), 172.83 (4-C) ppm; IR (ATR): $\bar{\nu} = 692$, 761, 794, 894, 1,000, 1,041, 1,077, 1,091, 1,207, 1,243, 1,257, 1,284, 1,315, 1,371, 1,429, 1,459, 1,479, 1,506, 1,625, 1,650, 2,850–3,000 (broad δ_{CH}), 3,000–3,600 (broad δ_{OH}) cm^{-1}; $[\alpha]_D^{25} = -41.6°$ g^{-1} cm^3 dm^{-1} ($c = 0.084$, MeOH); HRMS (ESI/FT-ICR): $[M + H^+]$ found (calculated): 496.1727 (496.1720).

7-O-(β-D-Glucopyranosyl)-3-(4-phenyl-4H-1,2,4-triazol-3-yl)-2H-chromen-2-one (**12**, $C_{23}H_{21}N_3O_8$)
M.p.: 180 °C; ^{1}H NMR (400 MHz, DMSO-d_6, r.t.): $\delta = 3.16$ (br s, 1H, 4″-CH), 3.28 (br s, 2H, 2″-CH and 5″-CH), 3.43 (br m, 2H, 3″-CH and 6″-CH_2), 3.69 (br m, 1H, 6″-CH_2), 4.60 (br t, $J = 5.5$ Hz, 1H, 6″-OH), 5.06 (d, $J = 7.0$ Hz, 1H, 1″-CH), 5.08 (br d, $J = 4.5$ Hz, 1H, 4″-OH), 5.17 (br s, 1H, 3″-OH), 5.44 (br s, 1H, 2″-OH), 7.08 (br s, 1H, 8-CH), 7.09 (br d, $J = 8.3$ Hz, 6-H), 7.37–7.50 (m, 5H, Ph), 7.82 (d, $J = 8.3$ Hz, 5-CH), 8.57 (s, 1H, 4-CH), 9.00 (s, 1H, 5-$CH_{triazole}$) ppm; ^{1}H NMR (400 MHz, DMSO-d_6, 90 °C): $\delta = 3.04$ (br s, OH + H_2O), 3.22 (t, $J = 8.4$ Hz, 1H, 4″-CH), 3.33 (m, 2H, 2″-CH and 5″-CH), 3.43 (t, $J = 7.0$ Hz, 1H, 3″-CH), 3.51 (dd, $J = 11.7$ Hz, $J = 5.9$ Hz, 1H, 6″-CH_2), 3.73 (d, $J = 11.3$ Hz, 1H, 6″-CH_2), 4.25 (br s, 1H, OH), 4.71 (br s, 1H, OH), 5.04 (br d, $J = 7.0$ Hz, 2H, 1″-CH and OH), 7.06 (d, $J = 2.0$ Hz, 1H, 8-H), 7.09 (dd, $J = 8.6$ Hz, $J = 2.0$ Hz, 6-H), 7.36–7.52 (m, 5H, Ph), 7.76 (d, $J = 8.6$ Hz, 1H, 5-CH), 8.45 (s, 1H, 4-CH), 8.85 (s, 1H, 5-$CH_{triazole}$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6, r.t.): $\delta = 60.57$ (6″-CH_2), 69.55 (4″-CH), 73.03 (2″-CH), 76.42 (5″-CH), 77.14 (3″-CH), 99.89 (1″-CH), 103.05 (8-CH), 111.96 (3-C), 112.77 (10-C), 114.41 (6-CH), 124.06 (2′-CH_{Ph}), 128.69 (4′-CH_{Ph}), 129.62 (3″-CH_{Ph}), 130.60 (5-CH), 134.47 (1′-C_{Ph}), 145.05 (5-$CH_{triazole}$), 147.20 (4-CH), 148.39 (3-$C_{triazole}$), 155.50 (9-C), 157.81 (2-C), 161.36 (7-C) ppm; IR (ATR): $\bar{\nu} = 690$, 753, 767, 827, 841, 892, 941, 979, 990, 1,021, 1,077, 1,114, 1,128, 1,182, 1,226, 1,250, 1,273, 1,348, 1,364, 1,394, 1,503, 1,612, 1,736, 2,830–2,950 (broad δ_{CH}), 3,000–3,500 (broad δ_{OH}) cm^{-1}; $[\alpha]_D^{25} = -24.5°$ g^{-1} cm^3 dm^{-1} ($c = 1.02$, DMF); HRMS (ESI/FT-ICR): $[M + H^+]$ found (calculated): 468.1422 (468.1407), $[M + Na^+]$ found (calculated): 490.1194 (490.1226).

7-O-(β-D-Glucopyranosyl)-3-phenyl-4H-chromen-4-one
(**14**, $C_{21}H_{20}O_8$)
M.p.: 170 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 3.19$ (br m, 1H, 4″-CH), 3.31 (br m, 2H, 2″- and 3″-CH), 3.44–3.51 (m, 2H, 5″-CH and 6″-CH_2), 3.71 (dd, $J = 10.0$ Hz, $J = 5.5$ Hz, 1H, 6″-CH_2), 4.62 (t, $J = 5.5$ Hz, 1H, 6″-OH), 5.10 (d, $J = 4.7$ Hz, 1H, 4″-OH), 5.11 (d, $J = 7.0$ Hz, 1H, 1″-CH), 5.16 (br d, $J = 4.3$ Hz, 1H, 3″-OH), 5.45 (br d, $J = 4.3$ Hz, 1H, 2″-OH), 7.16 (dd, $J = 8.8$ Hz, $J = 2.3$ Hz, 1H, 6-H), 7.26 (d, $J = 2.3$ Hz, 1H, 8-H), 7.35–7.46 (m, 3H, 3′- and 4′-CH_{Ph}), 7.59 (m, 2H, 2′-CH_{Ph}), 8.06 (d, $J = 8.8$ Hz, 1H, 5-H), 8.49 (s, 1H, 2-H) ppm; ^{13}C

NMR (100 MHz, DMSO-d_6): $\delta = 60.60$ (6″-CH_2), 69.59 (4″-CH), 73.09 (2″-CH), 76.45 (3″-CH), 77.19 (5″-CH), 99.95 (1″-CH), 103.43 (8-CH), 115.70 (6-CH), 118.45 (10-C), 123.73 (3-C), 126.95 (5-CH), 127.82 (4′-CH_{Ph}), 128.12 (3′-CH_{Ph}), 128.91 (2′-CH_{Ph}), 131.87 (1′-C_{Ph}), 154.32 (2-CH), 157.04 (9-C), 161.50 (7-C), 174.43 (4-C) ppm; IR (ATR): $\bar{\nu} = 689$, 697, 756, 780, 831, 840, 883, 898, 954, 1,012, 1,025, 1,044, 1,053, 1,070, 1,105, 1,198, 1,223, 1,236, 1,308, 1,310, 1,329, 1,349, 1,373, 1,381, 1,442, 1,496, 1,600, 1,602, 1,605, 1,623, 1,636, 2,850–2,950 (broad δ_{CH}), 3,000–3,500 (broad δ_{OH}) cm^{-1}; $[\alpha]_D^{25} = -30.4°\ g^{-1}\ cm^3\ dm^{-1}$ ($c = 1.03$, DMF); HRMS (ESI/FT-ICR): [M + H^+] found (calculated): 401.1243 (401.1236), [M + Na^+] found (calculated): 423.1026 (423.1056).

7-O-(β-D-Glucopyranosyl)-2-phenyl-4H-chromen-4-one (**16**, $C_{21}H_{20}O_8$)

M.p.: 281 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 3.20$ (m, 1H, 4″-CH), 3.31 (m, 2H, 2″- and 3″-CH), 3.48 (m, 2H, 5″-CH and 6″-CH_2), 3.72 (m, 1H, 6″-CH_2), 4.63 (t, $J = 5.5$ Hz, 1H, 6″-OH), 5.10 (d, $J = 5.3$ Hz, 1H, 4″-OH), 5.14 (d, $J = 7.0$ Hz, 1H, 1″-CH), 5.17 (br d, $J = 4.0$ Hz, 1H, 3″-OH), 5.45 (br d, $J = 3.8$ Hz, 1H, 2″-OH), 6.99 (s, 1H, 3-H), 7.13 (dd, $J = 8.8$ Hz, $J = 2.3$ Hz, 1H, 6-H), 7.41 (d, $J = 2.3$ Hz, 1H, 8-H), 7.55–7.64 (m, 3H, 3′- and 4′-H_{Ph}), 7.97 (d, $J = 8.8$ Hz, 1H, 5-H), 8.08 (m, 2H, 2′-H_{Ph}) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 60.56$ (6″-CH_2), 69.51 (4″-CH), 73.11 (2″-CH), 76.46 (3″-CH), 77.17 (5″-CH), 99.95 (1″-CH), 103.80 (8-CH), 106.82 (3-CH), 115.53 (6-CH), 117.99 (10-C), 126.33 (3C, 5-CH and 2′-CH_{Ph}), 129.09 (3′-CH_{Ph}), 131.14 (1′-C_{Ph}), 131.72 (4′-CH_{Ph}), 157.10 (9-C), 161.64 (7-C), 162.33 (2-C), 176.43 (4-C) ppm; IR (ATR): $\bar{\nu} = 673$, 774, 823, 861, 870, 910, 1,000, 1,012, 1,065, 1,101, 1,173, 1,248, 1,271, 1,382, 1,450, 1,494, 1,564, 1,571, 1,586, 1,616, 2,830–2,970 (broad δ_{CH}), 3,030–3,590 (broad δ_{OH}) cm^{-1}; $[\alpha]_D^{25} = -43.6°\ g^{-1}\ cm^3\ dm^{-1}$ ($c = 1.02$, DMF); HRMS (ESI/FT-ICR): [M + H^+] found (calculated): 401.1254 (401.1236).

7-O-(β-D-Glucopyranosyl)-3-phenyl-2H-chromen-2-one (**18**, $C_{21}H_{20}O_8$)

M.p.: 228 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 3.19$ (m, 1H, 4″-CH), 3.30 (m, 2H, 2″- and 3″-CH), 3.47 (m, 2H, 5″-CH and 6″-CH_2), 3.72 (m, 1H, 6″-CH_2), 4.62 (t, $J = 5.5$ Hz, 1H, 6″-OH), 5.06 (d, $J = 7.3$ Hz, 1H, 1″-CH), 5.09 (d, $J = 5.3$ Hz, 1H, 4″-OH), 5.16 (br d, $J = 4.5$ Hz, 1H, 3″-OH), 5.43 (br d, $J = 4.5$ Hz, 1H, 2″-OH), 7.05 (dd, $J = 8.8$ Hz, $J = 2.3$ Hz, 1H, 6-H), 7.09 (d, $J = 2.3$ Hz, 1H, 8-H), 7.37–7.48 (m, 3H, 3′- and 4′-H_{Ph}), 7.71 (br d, $J = 8.8$ Hz, 3H, 5-H and 2′-CH_{Ph}), 8.21 (s, 1H, 4-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 60.63$ (6″-CH_2), 69.61 (4″-CH), 73.11 (2″-CH), 76.48 (3″-CH), 77.12 (5″-CH), 99.98 (1″-CH), 102.69 (8-CH), 113.84 (6-CH), 113.96 (10-C), 123.79 (3-C), 128.17 (3′-CH_{Ph}), 128.24 (4′-CH_{Ph}), 128.31 (2′-CH_{Ph}), 129.62 (5-CH), 134.82 (1′-C_{Ph}), 140.67 (4-C), 154.39 (9-C), 159.90 (2-C), 160.09 (7-C) ppm; IR (ATR): = 690, 783, 837, 1,019, 1,042, 1,071, 1,099, 1,113, 1,172, 1,255, 1,363, 1,505, 1,611, 1,622, 1,714, 2,840–2,940 (broad δ_{CH}), 3,000–3,600 (broad δ_{OH}) cm^{-1}; $[\alpha]_D^{25} = -34.6°\ g^{-1}\ cm^3\ dm^{-1}$ ($c = 1.01$, DMF); HRMS (ESI/FT-ICR): [M + H^+] found (calculated): 401.1242 (401.1236), [M + Na^+] found (calculated): 423.1019 (423.1056).

7-O-(β-D-Glucopyranosyl)-4-phenyl-2H-chromen-2-one (***20***)

^{1}H NMR spectrum is consistent with that found in Ref. [31]; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 60.61$ (6″-CH_2), 69.59 (4″-CH), 73.09 (2″-CH), 76.47 (3″-CH), 77.15 (5″-CH), 99.97 (1″-CH), 103.63 (8-CH), 111.87 (3-C), 112.72 (10-C), 113.73 (6-C), 127.75 (5-CH), 128.42 (2′-CH_{Ph}), 128.85 (3″-CH_{Ph}), 129.67 (4″-CH_{Ph}), 134.88 (1″-C_{Ph}), 155.00 (9-C), 155.10 (4-C), 159.93 (2-C), 160.27 (7-C) ppm; IR (ATR): = 707, 781, 796, 816, 893, 991, 1,020, 1,047, 1,071, 1,102, 1,121, 1,161, 1,205, 1,230, 1,257, 1,289, 1,369, 1,382, 1,407, 1,446, 1,552, 1,616, 1,663, 2,840–2,970 (broad δ_{CH}), 3,000–3,600 (broad δ_{OH}) cm^{-1}; $[\alpha]_D^{25} = -37.8°\ g^{-1}\ cm^3\ dm^{-1}$ ($c = 1$, DMF); HRMS (ESI/FT-ICR): [M + H^+] found (calculated): 401.1238 (401.1236), [M + Na^+] found (calculated): 423.1052 (423.1056).

Attempt to synthesize 2-amino-6-ethyl-7-O-(β-D-glucopyranosyl)-3-(4-phenyl-4H-1,2,4-triazol-3-yl)-4H-chromen-4-one (**23**, $C_{25}H_{26}N_4O_8$)

Compound **22** (461 mg, 0.679 mmol) and NaOMe (0.5 cm^3, 0.5 N in MeOH) were stirred in 20 cm^3 absolute MeOH for 72 h (nitrogen atmosphere). All volatiles were removed in vacuum. The difference of mass showed full conversion of **22**. Further operations according to the general procedure C afforded 296 mg (85%) crude **23**, which showed three major peaks by analytical HPLC and could not be further purified by washing with boiling acetone or acetonitrile (23 stays undissolved). HRMS (ESI/TOF): [M + H^+] found (calculated): 511.1810 (511.1823), [M + Na^+] found (calculated): 533.1632 (533.1643).

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