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Full Paper

Sweet Poisons: Synthetic Strategies towards Tutin Glycosides

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The polycyclic, polyoxygenated picrotoxane tutin was subjected to various glycosylation reaction conditions in an effort to synthesise β-linked tutin glycosides, recently found in toxic honeys. Cationic palladium-mediated glycosylation of tutin was successful; however, the α-linked tutin tetrabenzyl glucoside was obtained as the major product (5 : 1, α : β). Hydrogenolysis of the benzyl ether protecting groups resulted in concomitant tutin double-bond migration. Epoxide opening and rearrangement were observed upon acetylation of the tutin glucoside.

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Introduction

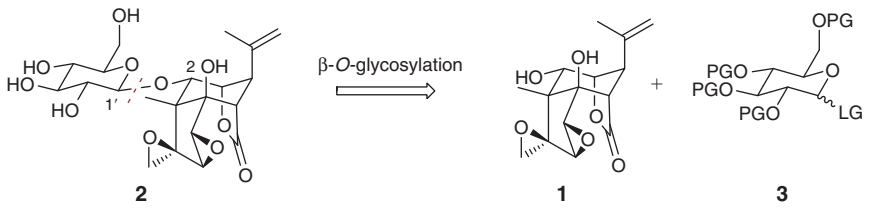
The neurotoxin tutin (**1**),[1] a polyoxygenated, polycyclic sesquiterpene from the picrotoxane family,[1b] has been shown to be present in New Zealand toxic honey (Scheme 1).[2] In fact, until recently, it was thought to be the major toxic component in honey samples and as such its concentration was carefully monitored.[3,4] Concerns about the presence of other unmonitored tutin-based metabolites[2] led to a human pharmacokinetic study of tutin from honey. The study indicated that unknown conjugates of tutin were also present.[4] The structures of two main tutin conjugates were later elucidated to be 2-(β-D-glucopyranosyl)-tutin (**2**; Scheme 1) and 2-[6′-(α-D-glucopyranosyl)-β-D-glucopyranosyl]-tutin (not shown).[5] Due to the difficulty in isolating useful quantities of these compounds from honeys, we sought to develop a synthesis method for preparing tutin glycoside **2**. Larger amounts of this tutin glycoside would allow further examination of its toxicity and pharmacokinetics, and the compound could potentially be used as a standard for food safety analyses.

There has been only one total synthesis study of tutin (**1**) reported to date.[6] Our approach was to use natural tutin (**1**), available in reasonable yields from leaves of the plant tutu, *Coriaria* species,[7] as the substrate for glycosylation efforts. We are not aware of any previous reports of synthetic glycosylation of tutin or of any other picrotoxanes;[1b] however, acylation of the secondary alcohol 2-OH has been achieved,[8] and double acetylation at both the 2-OH and C6-OH has been reported.[9] The highly strained skeleton of tutin (**1**), including two epoxide rings and a lactone, was expected to be susceptible to various rearrangements, as found in previous attempts to solve and interrelate picrotoxane structures.[10]

Assembly of the tutin glucoside **2** could be achieved via the β-*O*-glycosylation reaction between tutin (**1**) and an activated sugar donor of the general structure **3** (Scheme 1). Numerous methods of *O*-glycosylation have been reported towards the synthesis of complex glycosides with anomeric β-stereoselectivity.[11] Strategies to achieve selectivity include using silyl tethering groups,[12] and judicious choice of leaving groups and/or neighbouring group participation,[11e,13] catalyst,[11a] and conformational rigidity[13c,14] of the glycosyl donor.

Results and Discussion

Our first glycosylation efforts, subjecting tutin (**1**) to epoxide **4** (obtained from dimethyldioxirane (DMDO)-mediated glycal



2 1 3

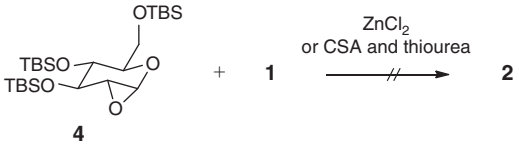
Scheme 1. PG, protecting group; LG, leaving group.

oxidation), activated with $ZnCl_2$ under the conditions reported by Halcomb and Danishefsky[13b] or Bronsted acid–base pair,[15] were unsuccessful (Scheme 2). Our next choice of sugar donor was the known tetraacetylated trichloroacetimidate **6** (Scheme 3).[16] It was anticipated that the neighbouring acetyl group would stabilise the reactive oxocarbenium species **7** and direct the tutin **1** nucleophile to the β face, thereby conferring β-selectivity.

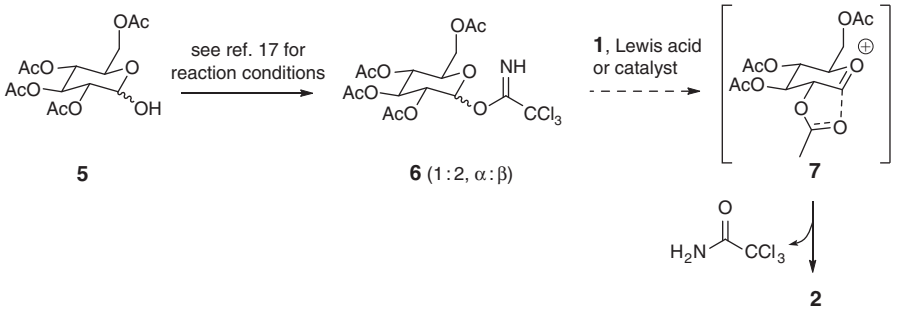
Preparation of the acetimidate **6** was performed using a literature procedure wherein tetra-*O*-acetyl-D-glucose (**5**) was treated with trichloroacetonitrile[17] to provide a mixture of anomers (1 : 2, α : β), which was used without further purification. To our disappointment, despite screening several commonly used Lewis acids (Table 1, entries 1–4) at low-to-ambient temperatures, no evidence for the formation of the desired glycoside was found. In the case of trimethylsilyl trifluoromethanesulfonate (TMSOTf), decomposition of tutin (**1**) was observed. Only starting materials were recovered upon treatment with $AuCl_3$ and $ZnCl_2$, whereas boron trifluoride diethyl etherate ($BF_3{\cdot}Et_2O$) led to a Chapman rearrangement of the sugar donor.[18]

Recently, reports on the use of cationic metal catalysts to facilitate glycosylation have emerged.[19] These metal complexes are proposed to coordinate and promote the departure of the leaving group on the glycosyl donor to generate the corresponding oxocarbenium ion. Thus, we applied the in situ generated $Pd(PPh_3)_2(OTf)_2$ species[19b] and the commercially available $Pd(MeCN)_4(BF_4)_2$[19a] (Table 1, entries 5–7) to our system. Pleasingly, traces of a glycosylated tutin derivative were observed when conducting the reaction in dichloromethane (DCM; Table 1, entry 5), as indicated by electrospray ionisation mass spectrometry (ESI-MS). The spectrum featured a peak at *m/z* 839.3372, assigned as the $[M + Na]^+$. Notably, when MeCN was used as the solvent, no traces of the product were found (Table 1, entry 6). This is consistent with the proposed mechanism as a coordinating solvent is expected to affect the binding of the metal complex to the glycosyl donor. Regardless, no conditions were found to generate the corresponding glycosylated tutin in an appreciable amount. This low conversion could be attributed to the stabilising effect of the acyl-protecting groups, which deactivate the oxacarbenium ion towards glycosylation with the sterically crowded secondary alcohol on tutin (**1**).

These preliminary results prompted us to investigate the transformation using the tetrabenzylated trichloroacetimidate **9** bearing armed protecting groups (Scheme 4).[20] The glycosyl donor **9** was obtained in three steps as described in the literature (Scheme 4).[21] With the more reactive glycosyl donor in hand, we first examined the traditional Lewis acid-mediated process with $BF_3{\cdot}Et_2O$ as this was previously shown to be compatible with tutin (**1**) (Table 2, entry 1). As the glycosyl donor **9** does not possess a participating group, poor stereoselectivity in the glycosylation step may be expected. Furthermore, solvent choice is also well known to affect selectivity. Thus, we examined various reaction conditions to account for such effects (Table 2, entries 1–3).[22] The use of diethyl ether (Et_2O) achieved the highest conversion (10 % by NMR), with the least amount of competing processes such as trichloroacetimidate hydrolysis and diglucoside formation (Table 2, entry 3).



Scheme 2. TBS, *tert*-butyldimethylsilyl; CSA, camphorsulfonic acid.



Scheme 3.

Table 1. Screening of catalysts for the glycosylation of tutin 1 with sugar donor 6
cat., catalytic amount; NP, no product

Sugar donor	Entry	Conditions	Solvent	Temperature	Conversion[A] [%]
6	1	TMSOTf	DCM	0°C–RT	Decomposition
	2	$AuCl_3$ (cat.)	DCM	RT	NP
	3	$ZnCl_2$ (cat. or 1–2.1 equiv.)	DCM	−78°C to RT	NP
	4	$BF_3{\cdot}Et_2O$ (cat.)	DCM/Et_2O/MeCN	0°C or RT	NP
	5	$Pd(MeCN)_4(BF_4)_2$ (cat.)	DCM	RT	Trace
	6	$Pd(MeCN)_4(BF_4)_2$ (cat.)	MeCN	RT	NP
	7	$PdCl_2(PPh_3)_2$, AgOTf	DCM	RT	NP

[A]Determined by NMR.

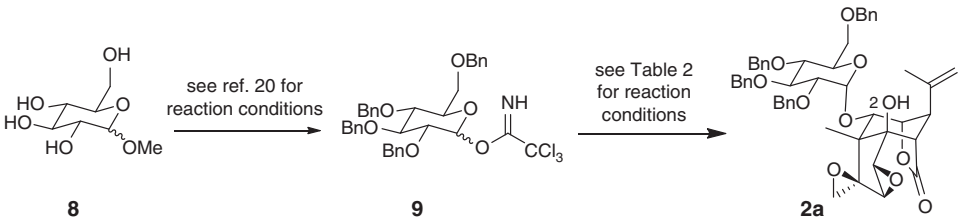
The early observation of glycosylation when $Pd(MeCN)_4(BF_4)_2$ was used (see above) prompted us to further investigate the use of palladium-mediated catalysis. Furthermore, to counteract diglucoside formation, dried powdered molecular sieves were added to the reaction mixture.[23] Though no traces of the desired product were detected with $Pd(MeCN)_4(BF_4)_2$ (Table 2, entry 4), treatment of tutin (**1**) and the glycosyl donor **9** with $Pd(PPh_3)_2(OTf)_2$ was encouraging (Table 2, entries 6–7). Gratifyingly, 20-% conversion was achieved with the more nucleophilic [Pd] species $Pd(PhCN)_2(OTf)_2$ with double catalyst loading (10 mol-% [Pd] and 20 mol-% AgOTf, Table 2, entry 8).

Purification of the tutin tetrabenzyl glucoside product was complicated by co-elution with the hydrolysis product tetrabenzyl glucose (indicated by NMR and ESI-MS) and required acetylation and multiple chromatographic separations. Eventually, we were able to isolate the tutin tetrabenzyl glucoside in a disappointing 9-% yield (41 % based on recovered tutin) as a ~5 : 1 mixture of anomers. The NMR spectra indicated the main anomer to be tutin tetrabenzyl-α-glucoside **2a** (Table 3), as evident by the 4.1-Hz coupling constant of the resonance, attributable to the anomeric H1′ by the 2D NMR correlations (Table 3, the corresponding H1′ in 2-(β-D-glucopyranosyl)-tutin (**2**) showed 8-Hz coupling[5]).

We next examined the effect of the hindered base 2,6-lutidine, which can act as scavenger of the triflic acid generated during the course of the reaction. Although we observed 30-% conversion at best with this modification (Table 2, entry 9), as indicated by NMR analysis of the crude reaction mixture, the procedure was not reproducible on a larger scale. Increasing the amount of catalyst to 20 mol-% did not appear to benefit the transformation (Table 2, entry 10).

The subsequent removal of the benzyl ethers via hydrogenolysis was initially carried out in the presence of Pd/C, under an atmosphere of hydrogen gas, at ambient temperatures (Scheme 5). Monitoring of the reaction with thin layer chromatography (TLC) and mass spectrometry indicated the complete consumption of the starting material, with the emergence of two products after 48 h. The mass spectrum of the crude reaction mixture indicated the presence of a deprotected tutin glucoside as well as traces of the over-reduced dihydrotutin glucoside **11** (Scheme 5). However, the ^{1}H NMR spectrum did not show the coupled H13 olefinic methylene signals of a tutin (Table 3). Instead, the spectrum featured two allylic methyl signals, also observed in the ^{13}C NMR spectrum.[24] Therefore, the structure was assigned as α-neotutin glucoside (**10**) with double-bond isomerisation resulting from the formation of the π-allyl complex with [Pd] catalyst, which has been documented for tutin (**1**) treated with the same catalyst.[9,25] Double-bond isomerisation to the tetra-substituted alkene **10** in conjunction with the considerable steric bulk of the tutin scaffold account for the absence of concomitant double-bond reduction during the hydrogenolysis of the benzyl ethers.

Purification of **10** via silica gel chromatography proved difficult. Thus, the mixture was treated with pyridine and acetic anhydride, with the aim to isolate and characterise the peracetylated neotutin glycoside derivative. This reaction proceeded smoothly, however, affording the unexpected glycoside **12**. The ^{1}H NMR spectrum (Table 4) did not show the coupled H11 epoxide methylene signals of a tutin derivative (Table 3), and the heteronuclear multiple-bond correlation (HMBC) spectrum did not show a correlation between H2 and the anomeric carbon C1′ of the sugar moiety. Instead, a glycosidic linkage was



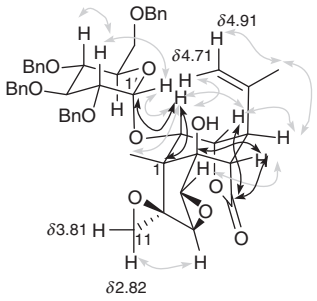
Scheme 4.

Table 2. Screening of catalysts for the glycosylation of tutin 1 with donor 9
NP, no product

Sugar donor	Entry	Conditions	Solvent	Conversion[A] [%]
9	1	$BF_3{\cdot}Et_2O$ (0.1 equiv.), 0°C–RT or −78°C to RT	DCM	Trace
	2	$BF_3{\cdot}Et_2O$ (0.1 equiv.), 0°C–RT or −78°C to RT	MeCN	NP
	3	$BF_3{\cdot}Et_2O$ (0.1 equiv.), 0°C–RT or −78°C–RT	Et_2O	~10
	4	$Pd(MeCN)_4(BF_4)_2$ (cat.)	DCM	NP
	5	$PdCl_2(PPh_3)_2$ (2.5 mol-%), AgOTf (2.5 mol-%), RT, 24 h	DCM	NP, hydrolysis and dimerisation of **9**
	6	$PdCl_2(PPh_3)_2$ (2.5 mol-%), AgOTf (2.5 mol-%), 4-Å sieves, RT, 24 h	DCM	<5, hydrolysis and dimerisation of **9**
	7	$PdCl_2(PPh_3)_2$ (5 mol-%), AgOTf (5 mol-%), 4-Å sieves, RT, 24–48 h	DCM	≈10
	8	$PdCl_2(PhCN)_2$ (10 mol-%), AgOTf (20 mol-%), 4-Å sieves, RT, 24–48 h	DCM	20
	9	$PdCl_2(PhCN)_2$ (10 mol-%), AgOTf (20 mol-%), 4-Å sieves, 2,6-lutidine, RT, 24–48 h	DCM	30
	10	$PdCl_2(PhCN)_2$ (20 mol-%), AgOTf (40 mol-%), 4-Å sieves, (+/–)-2,6 lutidine, RT, 24–48 h	DCM	Trace

[A]Determined by NMR.

Table 3. NMR data for tutin tetrabenzyl-α-glucoside 2a



2a

#	δ_H [ppm]	δ_C [ppm]	#	δ_H [ppm]	δ_C [ppm]
1		45.78	1′	4.80 (d, *J* 4.1)	101.71
2	4.02 (s)	82.91	2′	3.51 (dd, *J* 9.9, 4.8)	80.11
3	5.17 (br d, *J* 4.8)	81.71	3′	3.84 (t, *J* 9.8, 8.9)	81.41
4	2.92 (br m)	49.34	4′	3.50 (dd, *J* 9.6, 8.6)	77.81
5	3.05 (dd, *J* 4.5, 0.9)	48.8	5′	3.94 (m)	71.36
6		78.05	6′	3.64 (2H, m)	69.18
7	3.73 (d, *J* 3.1)	60.72	6′-CH_2Ph	4.53 (d, *J* 11.9)	73.53
8	3.18 (d, *J* 3.1)	60.32		4.42 (d, *J* 11.9)	
9		64.91	4′-CH_2Ph	4.70 (2H, m)	73.39
10	1.45 (s)	20.44	3′-CH_2Ph	4.80 (2H, m)	75.73
11	2.82 (d, *J* 5.3)	52.42	2′-CH_2Ph	4.48 (d, *J* 11.0)	75.27
	3.81 (d, *J* 5.3)			4.87 (d, *J* 11.0)	
12		140.91	Aromatics	7.17–7.40 (m)	138.51
13	4.71 (br d, *J* 2.6)	112.51			138.41
	4.91 (br m)				138.21
14	1.86 (s)	22.83			137.91
15		174.71			128.51
					128.41[A]
					128.01
					127.91[A]
					127.81[A]

Grey arrow: ROESY correlations; black arrow: HMBC correlations; [A]multiple signals.

indicated between C1′ and an acetal CH (^{1}H: δ 5.73 ppm; ^{13}C: δ 106.6 ppm; Table 4). This acetal proton was further vicinally homonuclear coupled to a neighbouring CH proton (determined by correlation spectroscopy) and heteronuclear coupled to an epoxy CH corresponding to tutin C8 (determined by HMBC). Overall, the 1D and 2D NMR data led us to propose the structure **14**, the aglycone portion of which was previously assigned to an acid rearrangement product of dihydrotutin.[25] Our ^{1}H NMR data (Table 4) agreed with those previously reported,[25] and the couplings and NOESY correlations supported the stereochemistry shown.

The exhaustive debenzylation of **2a** using Pearlman's catalyst was found to proceed at a faster rate, with complete consumption of the starting material after 16 h at room temperature (RT); however, it did not suppress the unwanted double-bond isomerisation.

Conclusions

Though the desired tutin β-glycosides could not be obtained, we have successfully achieved glycosylation of the sterically hindered tutin using palladium catalysis to obtain the tutin tetrabenzylated α-glycoside **2a**, albeit in low yields. Removal of the benzyl ethers resulted in concomitant double-bond migration to produce the tutin analogue **10**. Under standard acetylation reaction conditions, the neotutin glycoside **10** was found to rearrange to provide C11-glycoside **12**.

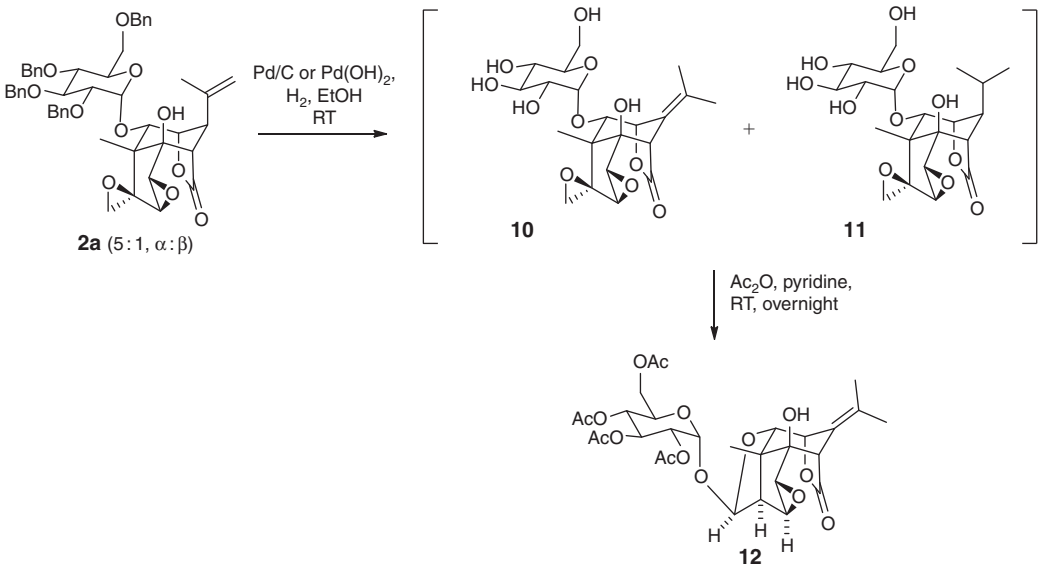
Experimental

General Experimental Methods

TLC was performed on ALUGRAM® aluminium-backed UV254 silica gel 60 (0.2 mm) plates. Compounds were visualised with either *p*-anisaldehyde or 20 % w/w phosphomolybdic acid in ethanol. Column chromatography was performed using silica gel 60. Infrared spectra were recorded on a Bruker Optics Alpha attenuated total reflectance Fourier transform infrared spectrometer. High-resolution mass spectrometry (HRMS) was conducted on a Bruker microTOFQ mass spectrometer using an ESI source in either the positive or the negative mode. ^{1}H NMR spectra were recorded at either 400 MHz on a Varian 400-MR NMR system or 500 MHz on a Varian 500 MHz AR premium shielded spectrometer. All spectra were recorded from samples in $CDCl_3$ at 25°C in 5-mm NMR tubes. Chemical shifts (δ) were reported relative to the residual chloroform singlet at 7.26 ppm. Resonances were assigned as follows: chemical shift (number of protons, multiplicity, coupling constant(s), assigned proton(s)). Multiplicity abbreviations are reported by the conventions: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). Proton decoupled ^{13}C NMR spectra were recorded at either 100 MHz on a Varian 400-MR NMR system or 125 MHz on a Varian 500 MHz AR premium shielded spectrometer under the same conditions as those used to record the ^{1}H NMR spectra. Chemical shifts were reported relative to the $CDCl_3$ triplet at 77.16 ppm. DCM was dried using a PURE SOLV MD-6 solvent purification system. All other solvents and reagents were used as received. Tutin (**1**) used in this study was isolated from leaves of the plant tutu, *Coriaria* species.[7,26]

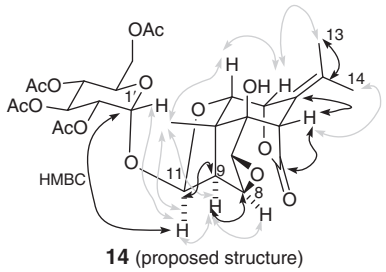
*α-2,3,4,6-Tetra-O-benzyl Tutin Glucoside (**2a**)*

A solution of the anomeric mixture of 2,3,4,6-tetra-O-benzyl-D-glucopyranosyl trichloroacetimidate (465 mg, 0.680 mmol, 1.0 equiv.) in anhydrous DCM (3.0 mL) was transferred via a syringe to an oven-dried reaction flask containing pre-activated 4-Å sieves (1.0 g, 500 wt-%). To this suspension was added tutin (200 mg, 0.680 mmol, 1 equiv.), and the light yellow suspension was stirred at RT for 10 min. To a separate flask containing a solution of $Pd(PhCN)_2Cl_2$ (26 mg, 0.07 mmol, 0.1 equiv.) in DCM (1 mL) was added AgOTf (35 mg, 0.14 mmol, 0.2 equiv.), and the resulting dark red suspension was allowed to stir at RT for 10 min. This suspension of pre-formed $Pd(PhCN)_2(OTf)_2$ was then transferred dropwise to the reaction flask and the light yellow suspension was allowed to stirred at RT for 48 h. Then, the reaction mixture was passed through a plug of Celite, rinsed with ethyl acetate (EtOAc), and the solvent was removed under vacuum. The crude residue was purified by silica gel chromatography (0–30 % EtOAc/petroleum ether) to remove the unreacted acetimidate **9** and tutin (**1**) (16–20-% conversion) to afford the *title compound* as a (5 : 1, α/β) mixture of anomers. The fractions containing the product and co-eluted hydrolysed sugar were redissolved in pyridine (2 mL), and acetic anhydride (3 drops) was added and the mixture was stirred overnight at RT. Then, the solvent was removed under vacuum, and the residue was subjected to silica gel chromatography to separate



Scheme 5.

Table 4. NMR data for acetylated rearranged neotutin glucoside 12



#	δ_H [ppm]	δ_C [ppm]	#	δ_H [ppm]	δ_C [ppm]
1		55.21	1′	5.24 (d, *J* 3.8)	97.61
2	3.87 (d, *J* 4.7)	89.94	2′	4.95 (dd, *J* 3.9, 10.2)	71.68
3	5.17 (d, *J* 4.7)	77.55	3′	5.74 (t, *J* 9.8)	70.49
4		124.02	4′	5.11 (dd, *J* 9.6, 10.2)	68.59
5	3.54 (s)	49.45	5′	4.76 (br m)	68.32
6		81.44	6′	4.27 (dd, *J* 3.9, 12.4)	62.05
7	4.04 (d, *J* 2.6)	65.93		4.15 (dd, *J* 2.3, 12.5)	
8	3.59 (d, *J* 2.5)	58.39	2′-OAc	1.98 (s)	20.9
9	2.87 (d, *J* 7.3)	60.03	3′-OAc	2.03 (s)	20.95
10	1.07 (s)	30.33	4′-OAc	2.03 (s)	20.95
11	5.42 (d, *J* 7.3)	106.6	6′-OAc	2.08 (s)	20.99
12		130.21	2′-(CO)		169.81
13	1.77 (s)	20.21	3′-(CO)		169.83
14	1.82 (s)	20.69	4′-(CO)		170.51
15		172.43	6′-(CO)		171.02

Grey arrow: NOESY correlations; black arrow: HMBC correlations.

1-*O*-acetyl-2,3,4,6-tetra-O-benzyl-D-glucopyranoside from the product, which was eluted with 25–30 % EtOAc/petroleum ether as a colourless gum (55 mg, 9 %, 41 % based on recovered tutin). NMR assignments for the major isomer **2a** are provided in Table 3. ν_{max} (film)/cm^{-1} 3449, 3062, 2918, 2865, 1780, 1496, 1068, 735, 696. *m/z* (HRMS ESI) 839.3372; $[M + Na]^+$ requires 839.3407.

*α-Neotutin Glucoside (**10**)*

A solution of the anomeric mixture of α-2,3,4,6-tetra-*O*-benzyl tutin glucoside (**2a**) (α : β, 5 : 1) (15.0 mg, 0.018 mmol) was dissolved in ethanol (EtOH; 2 mL), followed by the addition of a catalytic amount of $Pd(OH)_2$ (5 mg). The reaction flask was evacuated and refilled with N_2 twice before it was purged with H_2. The reaction mixture was allowed to stir overnight (16 h) at RT. TLC analysis indicated the complete consumption of the starting material. The reaction mixture was filtered through a plug of Celite to remove the catalyst, rinsed with EtOAc, and concentrated. The resultant colourless oil was taken up in D_2O, and the aqueous layer was washed once with $CDCl_3$. The aqueous layer was freeze-dried overnight to obtain the *title compound* **10** as a colourless oil (8 mg, quantitative, but with minor impurities of reduced product **11**). ν_{max} (film)/cm^{-1} 3422, 2954, 1736, 1056. δ_H (D_2O, 400 MHz) 5.45 (1H, s, H3), 4.89 (1H, d, *J* 3.9, H1′), 3.87 (1H, d, *J* 3.2, H8), 3.81 (2H, m, H6′), 3.72 (1H, *J* 4.5, H11), 3.66 (2H, m, overlap, H3′, H4′), 3.63 (1H s, H5), 3.49 (1H, br s, H2), 3.39 (1H, d, *J* 3.8, H2′), 3.29 (1H, *J* 3.2, overlap, H7), 3.29 (1H, m, overlap, H5′), 2.97 (1H, d, *J* 4.5, H11), 1.65 (6H, s, 13-CH_3, 14-CH_3, overlap), 1.25 (3H, s, 10-CH_3). δ_C (D_2O, 125 MHz) 179.47, 104.82, 89.30, 85.96, 82.39, 76.04, 75.15, 74.40, 72.25, 69.36, 63.26, 61.60, 61.42, 56.17, 53.93, 48.39, 22.45, 22.14, 21.57. *m/z* (HRMS ESI) 479.1524; $[M + Na]^+$ requires 479.1529.

*2,3,4,6-Tetra-O-acetyl-α-neotutin Acetal-Glucoside (**12**)*

A solution of the α-2,3,4,6-tetra-*O*-benzyl tutin glucoside (20 mg, 0.018 mmol) was dissolved in EtOH (2 mL), followed by the addition of a catalytic amount of Pd/C (5 mg). The reaction flask was evacuated and refilled with N_2 twice before it was purged with H_2 for 48 h at RT. TLC analysis indicated the complete removal of the benzyl groups. The reaction mixture was filtered through a plug of Celite, rinsed with EtOAc, and concentrated to give a colourless gum. Mass spectrometry analysis indicated the presence of tutin glycoside and dihydrotutin glucoside. The crude residue was taken up in D_2O and washed with $CDCl_3$. The sample in D_2O was freeze-dried (5 mg) and the resultant white solid crude residue was dissolved in

pyridine (1 mL). Acetic anhydride (2 drops) was added, and the reaction mixture was stirred overnight at RT. Then, pyridine was removed under vacuum, and the residue was purified with a small plug of silica (gradient elution, 10–60 % EtOAc/petroleum ether) to give the glycoside with the proposed structure **12** (1 mg). ν_{max} (film)/cm^{-1} 2958, 2924, 1744, 1367, 1224, 1035, 996. The NMR data of the isolated glycoside are provided in Table 4. *m/z* HRMS ESI 647.2009; $[M+Na]^+$ requires 647.1952.

Supplementary Material

^{1}H NMR and ^{13}C NMR spectra of all compounds are available on the Journal's website.

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