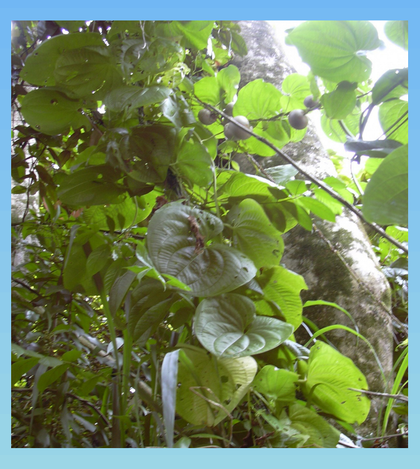
ATTEMPTS OF SYNTHESIS OF DIOSGENYL *N*-(D-GLUCONYL)-2-AMINO-2-DEOXY-β-D-GLUCOPYRANOSIDE

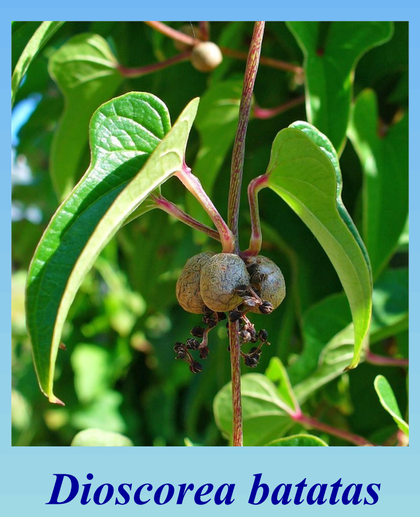
Monika Norkowska, Magdalena Cyman, Dominik Walczak, Damian Trzybiński, Artur Sikorski, Henryk Myszka and Beata Liberek

Faculty of Chemistry, University of Gdańsk, Sobieskiego 18, 80-952 Gdańsk, POLAND
e-mail: myszka@chem.univ.gda.pl



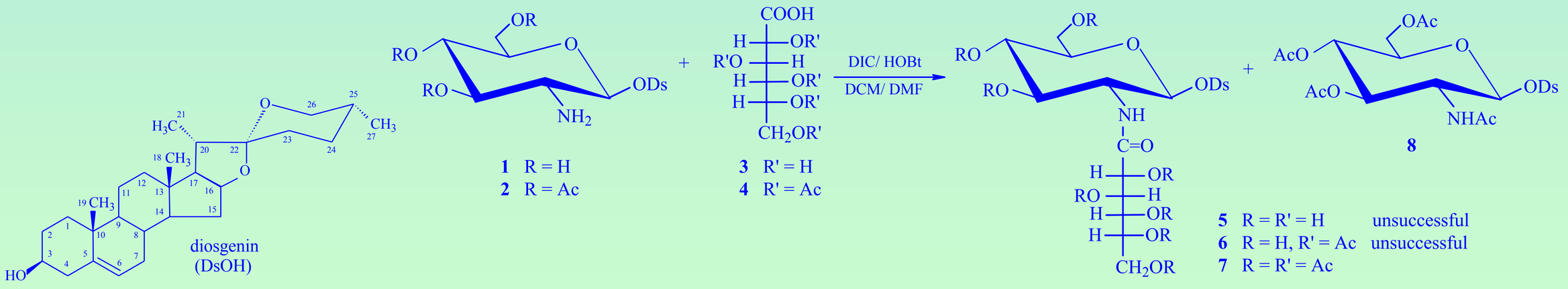
Dioscorea bulbifera

Naturally occurring diosgenyl glycosides belong to the group of saponins. These are steroid or triterpenoid glycosides, widely distributed in plants and in some marine organisms [1]. These glycosides display versatile biological activities, including anti-inflammatory, antibacterial, antiparasitic, antifungal, and antitumor activities [2]. Previously, we reported the synthesis and apoptosis-inducing property in B cell chronic leukemia cells of **diosgenyl 2-amino-2-deoxy-β-D-glucopyranoside hydrochloride** [3]. This compound is also *in vitro* active and *in vivo* efficient against Gram-positive cocci [4]. In search of its *N*-acyl derivatives with a hydrophilic chain we tried to synthesize diosgenyl *N*-(D-gluconyl)-2-amino-2-deoxy-β-D-glucopyranoside.



Dioscorea batatas

To synthesize diosgenyl *N*-(D-gluconyl)-2-amino-2-deoxy-β-D-glucopyranoside three approaches were tested. The first one consists in condensation of diosgenyl 2-amino-2-deoxy-β-D-glucopyranoside (**1**) with D-gluconic acid (**3**) under typical for the liquid-phase peptide synthesis conditions (DIC/HOBT). Unfortunately, desired product **5** was not obtained. The second one consists in analogous reaction of diosgenyl glycoside **1** with 2,3,4,6-tetra-*O*-acetyl-D-gluconic acid (**4**). The latter was obtained according to Braun and Cook procedure [5]. Unfortunately, desired product **6** was also not obtained. The third one consists in condensation of diosgenyl 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranoside (**2**) with acid **4**. This reaction gives diosgenyl 3,4,6-tri-*O*-acetyl-*N*-(2',3',4',6'-tetra-*O*-acetyl-D-gluconyl)-2-amino-2-deoxy-β-D-glucopyranoside (**7**, 17% yield), diosgenyl *N*-acetyl-3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranoside (**8**, 34% yield) and not identified minor byproducts. Such the result indicates that intermolecular acetyl *O*→*N* migration occurs more willingly than coupling of amine **2** with acid **4**.



Structures of the new compounds (**7** and **8**) were established on the basis of IR, ^{1}H and ^{13}C NMR spectroscopy and mass spectrometry. Additionally, crystal structure of the synthesized and used by us 2,3,4,6-tetra-*O*-acetyl-D-gluconic acid (**4**) is presented.

Table 1.
Chemical shifts (ppm) and ^{1}H-^{1}H coupling constants (Hz) in the ^{1}H NMR spectra of **7** and **8** ($CDCl_3$).

No.	Glucosamine									Gluconic acid and diosgenin residues
	H-1	H-2	H-3	H-4	H-5	H-6_a	H-6_b	OAc	NH	
7	4.86 (d) $J_{1,2}$=8.4	3.70 (m)	5.01 (m) $J_{3,4}$=9.2	5.38 (dd) $J_{4,5}$=10.4	3.70 (m) $J_{5,6a}$=2.4 $J_{5,6b}$=4.8	4.09 (dd) $J_{6a,6b}$=12.4	4.25 (dd) $J_{6a,6b}$=12.4	2.00-2.11 (3s)	6.25 (d) $J_{2,NH}$=8.4	2.00-2.11 (4s, 4xOAc); 3.14 (d, OH); 3.83 (m, H-5'); 4.12 (m, 2xH-6'); 5.01 (m, H-4'); 5.15 (d, H-2'); 5.69 (dd, H-3');0.77 (s, H-18_d); 0.78 (d, H-27_d); 0.96 (d, H-21_d); 1.00 (s, H-19_d); 3.36 (t, H-26_d); 3.46 (dd, H-26_d); 3.49 (m, H-3_d); 4.40 (q, H-16_d); 5.28 (d, H-6_d)
8	4.84 (d) $J_{1,2}$=8.4	3.68 (m) $J_{2,3}$=9.6	5.03 (t) $J_{3,4}$=9.6	5.37 (dd) $J_{4,5}$=10.4	3.68 (m) $J_{5,6a}$=2.8 $J_{5,6b}$=5.2	4.10 (dd) $J_{6a,6b}$=12.0	4.25 (dd) $J_{6a,6b}$=12.0	2.01 (s) 2.02 (s) 2.06 (s)	5.46 (d) $J_{2,NH}$=8.4	1.95 (s, NAc); 0.78 (s, H-18_d); 0.79 (d, H-27_d); 0.96 (d, H-21_d); 1.00 (s, H-19_d); 3.37 (t, H-26_d); 3.47 (dd, H-26_d); 3.50 (m, H-3_d); 4.40 (q, H-16_d); 5.34 (d, H-6_d)

Table 2.
Chemical shifts (ppm) in the ^{13}C NMR spectra ($CDCl_3$) of **7**.

C-1	C-2	C-3	C-4	C-5	C-6	CH_3(OAc)	C=O(OAc)	C=O (amide)
98.66	55.78	71.05	71.82	72.09	62.51	20.76-21.05 (3C)	169.66-171.36 (3C)	166.70

Fig. 1.
Structure of 2,3,4,6-tetra-*O*-acetyl-D-gluconic acid (**4**) showing 25% probability displacements for ellipsoids.

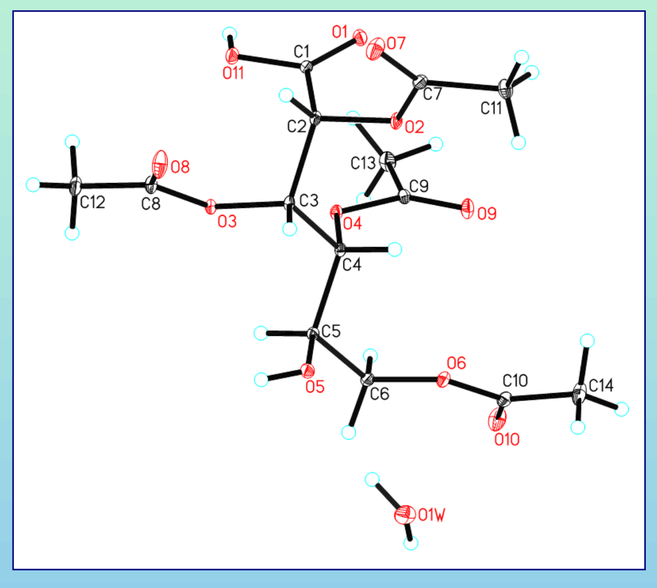


Fig. 2.
Molecular packing of 2,3,4,6-tetra-*O*-acetyl-D-gluconic acid (**4**) (view along c-axis).

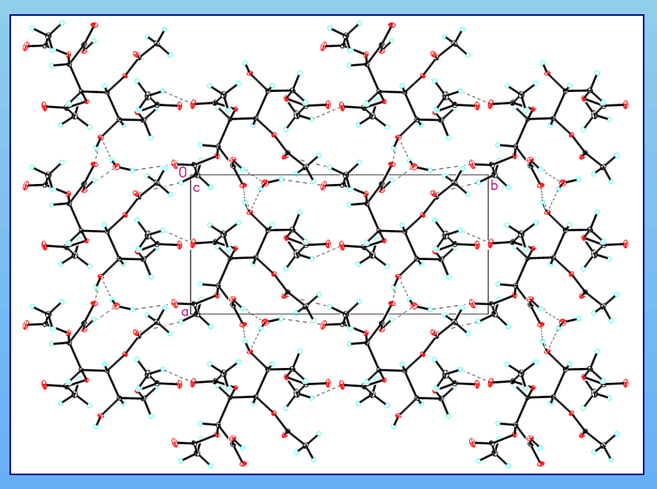


Table 3.
Crystal data and structure refinement for **4**.

Empirical formula	$C_{14}H_{22}O_{12}$
Formula weight	382.32
Temperature (K)	293(2)
Wavelength (Å)	0.71073
Crystal system	monoclinic
Space group	$P2_1$
Unit cell dimensions	a = 7.1732(4) Å b = 15.2991(8) Å c = 8.2095(4) Å α = 90º; β = 94.976(5)º; γ = 90º
V (Å^3)	897.54(8)
Z	2
D_{calcd} (Mg m^{-3})	1.415
Absorption coefficient (mm^{-1})	0.126
F(000)	404
Θ Range for data collection (°)	3.62 - 25.05
Limiting indices	-5 ≤ h ≤ 8; -17 ≤ k ≤ 18 -9 ≤ l ≤ 9
Reflections collected/unique	5721/3118 [R_{int} = 0.0269]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3118/4/249
Flack parameter	-0.1(12)
Final R indices [I>2σ(I)]	R_1 = 0.0450; wR_2 = 0.1075
R indices (all data)	R_1 = 0.0515; wR_2 = 0.1150
Goodness-of-fit on F^2	1.039
Largest diff. peak and hole (e Å^{-3})	0.275 and -0.268

References

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