Phenyl β-D-Glucopyranoside Derivatives from the Fruits of *Idesia polycarpa*

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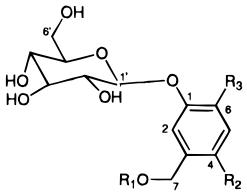
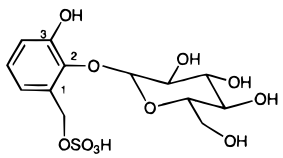
Integrated spectroscopic analysis has led to the characterization of a novel 2-(hydroxymethyl)-phenyl β-D-glucopyranoside derivative from the fruits of *Idesia polycarpa*. This compound, which has been given the trivial name idescarpin, was identified as 6-hydroxy-2-[[[(1-hydroxy-6-oxo-2-cyclohexen-1-yl)carbonyl]oxy]methyl]phenyl β-D-glucopyranoside (**1**). Three other compounds were identified as salirepin (**2**), 2-(β-D-glucopyranosyloxy)-3-hydroxybenzyl hydrogen sulfate [idesin hydrogen sulfate (**3**)], and idesin (**4**). Both **1** and **3** are new compounds.

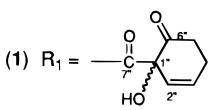
Idesia polycarpa Maxim. is a deciduous tree of the Flacourtiaceae family and is the only *Idesia* species found in Taiwan. It is distributed in forests at medium and, rarely, at low altitudes.[1] A variety of compounds has been found in this plant, including phenazine derivatives;[2] pyrocatechol, benzyl alcohol, phenethyl alcohol, and fatty acids,[3] idesin,[4] and flavonoids.[5] In the course of our search for physiologically active substances in nature, we found that the EtOH extract from the fruits of *I. polycarpa* possessed platelet aggregation inhibitory activity in vitro. This observation led us to reinvestigate the constituents of the fruits. In the present paper, we describe the isolation, identification, and/or structure elucidation of four phenyl glucopyranosides not previously reported from the fruits, namely two novel substances, 6-hydroxy-2-[[[(1-hydroxy-6-oxo-2-cyclohexen-1-yl)carbonyl]oxy]methyl]phenyl β-D-glucopyranoside (**1**) and 2-(β-D-glucopyranosyloxy)-3-hydroxybenzyl hydrogen sulfate (idesin hydrogen sulfate) (**3**), as well as two known compounds, salirepin and idesin.

The *n*-BuOH and H_2O fractions of *I. polycarpa* were fractionated by a combination of Si gel column chromatography, gel filtration on Sephadex LH-20, and Diaion HP-20. 6-Hydroxy-2-[[[(1-hydroxy-6-oxo-2-cyclohexen-1-yl)carbonyl]oxy]methyl]phenyl β-D-glucopyranoside (**1**) was isolated from the *n*-BuOH-soluble fraction, while salirepin (**2**), idesin hydrogen sulfate (**3**), and idesin (**4**) were isolated from the H_2O-soluble part.





(**3**)



(**1**) R_1 = , R_2 = H, R_3 = OH

(**2**) R_1 = H, R_2 = OH, R_3 = H

(**4**) R_1 = H, R_2 = H, R_3 = OH

Compound **1** was obtained as a syrup. The FABMS (neg) of **1** gave a quasi-molecular ion $[M - H]^-$ peak at *m/z* 439.4 (100) and an HRFABMS $[M + H]^+$ ion at *m/z* 441.1390, which agreed with the formula $C_{20}H_{25}O_{11}$. As cited in Table 1, the assignment and connectivities of protons were derived from an H−H COSY experiment. The protons could be grouped into four spin-coupling systems—(a) HC(4)/HC(5)/HC(6); (b) $H_aC(7)/H_bC(7)$; (c) HC(1′)/HC(2′)/HC(3′)/HC(4′)/HC(5′)/$H_2C(6')$, and (d) $H_2C(5'')/H_2C(4'')$/HC(3″)/HC(2″)—that were attributable to a 6-hydroxy-2-(hydroxymethyl)phenyl group, β-glucosyl moiety, and a 1-hydroxy-6-oxo-2-cyclohexenecarboxylate group, respectively. The assignment of the β-configuration to D-glucose at the anomeric carbon was based on the C-1′ chemical shift value at δ 107.2. This assignment was further supported by the chemical shift and large coupling constant of the anomeric proton (δ 4.61, J = 6.7 Hz). The linkage of the glucose through an ether group from C-1′ of the sugar unit to C-1 of phenyl group was established unambiguously by analysis of the ^3J-heteronuclear couplings visualized through a COLOC experiment. The benzylic oxymethylene signals were deshielded in the proton domain, indicating the presence of an ester group. Analyses of these NMR data indicated that this ester contained two carbonyls, one tertiary oxygen-bearing carbon, one ethylene group, and two cis-substituted olefinic protons. An analysis of the COLOC spectrum (Table 2) allowed extension of the COSY spin system interpretation to encompass the six-membered ring, the sixth carbon being the oxygen-bearing quaternary one. This ester was identified as a 1-hydroxy-6-oxo-2-cyclohexenecarboxylate group by the ^{13}C- and ^1H-NMR experiments (Table 1), which were in agreement with published data for homaloside D.[6] Thus, the structure of **1** was elucidated as 6-hydroxy-2-[[[(1-hydroxy-6-oxo-2-cyclohexen-1-yl)carbonyl]oxy]-methyl]phenyl β-D-glucopyranoside. Recently a position isomer of **1**—poliothrysin, 4-hydroxy-2-[[[(1-hydroxy-6-oxo-2-cyclohexen-1-yl)carbonyl]oxy]methyl]phenyl β-D-glucopyranoside—has been reported from the leaves of *Poliothrysis sinensis*.[7]

Both the ^1H- and ^{13}C-NMR data of salirepin (**2**) compared well with the published in the literature.[8]

Compounds **3** and **4** were easily identified by comparing their NMR spectra with those of **1**. (Table 1). Except for the chemical shifts of the cyclohexenone carboxylic acid ester in the ^1H- and ^{13}C-NMR spectra of **1**, there was a striking resemblance in these NMR spectra with those of the 6-hydroxy-2-(hydroxymethyl)-phenyl β-D-glucopyranoside moiety in **1**.

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Table 1. ^{1}H- and ^{13}C-NMR Chemical Shift Assignments of Compounds **1**, **3**, and **4**[a]

	compound					
	1		**4**		**3**	
positon	δ ^{13}C	δ ^{1}H	δ ^{13}C	δ ^{1}H	δ ^{13}C	δ ^{1}H
1	144.7 (s)		144.2 (s)		132.0 (s)	
2	131.1 (s)		136.2 (s)		144.1 (s)	
3	121.0 (d)	6.79 (dd,2.0,7.8)	121.3 (d)	6.86 (d,8.4)	150.6 (s)	
4	126.8 (d)	7.01 (t,7.8)	126.7 (d)	6.99 (t,7.8)	117.6 (d)	6.86 (dd,2.0,7.5)
5	118.3 (d)	6.87 (dd,2.0,7.8)	117.4 (d)	6.86 (d,8.4)	126.6 (d)	7.01 (t,7.5)
6	151.0 (s)		150.3 (s)		121.1 (d)	6.96 (dd,2.0,7.5)
7	64.9 (t)	5.48 (d,12.5)a; 5.29 (d,12.5)b	60.5 (t)	4.79 (d,12.5)a; 4.63 (d,12.5)b	66.2 (t)	5.32 (d,12.0)a; 5.19 (d,12.0)b
1′	107.2 (d)	4.61 (d,6.7)	106.3 (d)	4.62 (d,7.5)	106.9 (d)	4.63 (d,7.5)
2′	75.3 (d)	3.50−3.45 (m)	75.0 (d)	3.60 (t,8.4)	75.3 (d)	3.55 (m)
3′	77.7 (d)	3.50−3.45 (m)	77.5 (d)	3.53−3.43 (m)	77.7 (d)	3.45−3.36 (m)
4′	70.9 (d)	3.50−3.45 (m)	70.9 (d)	3.53−3.43 (m)	70.9 (d)	3.45−3.36 (m)
5′	78.3 (d)	3.35 (m)	77.9 (d)	3.35 (m)	78.3 (d)	3.32 (m)
6′	62.3 (t)	3.85 (dd,2.2,12.5); 3.73 (dd,4.8,12.5)	62.2 (t)	3.90 (dd,2.0,9.5); 3.73 (dd,4.8,9.5)	62.1 (t)	3.88 (dd,2.3,12.3); 3.75(dd,5.0,12.3)
1″	79.2 (s)					
2″	129.2 (d)	5.74 (dt,1.5,8.5)				
3″	133.3 (d)	6.13 (m)				
4″	27.1 (t)	2.65−2.41 (m)				
5″	36.8 (t)	2.93−2.85 (m)a; 2.65−2.41 (m)b				
6″	207.3 (s)					
7″	171.4 (s)					

[a] Assignments were based on ^{13}C−DEPT, ^{13}C−^{1}H COSY, and ^{1}H−^{1}H COSY spectra.

Table 2. Long-Range C−H Connectivities in Compound **1** and **4**, Established by COLOC

	compound			
	1		**4**	
position	δ ^{13}C	^2J; ^3J	δ ^{13}C	^2J; ^3J
1	144.7 (s)	H-1′; H-4; H-6; Ha,Hb-7	144.2 (s)	H-1′; H-4; Ha-7
2	131.1 (s)	Ha,Hb-7	136.2 (s)	H-5; Ha,Hb-7
3	121.0 (d)	H-4; Ha,Hb-7	121.3 (d)	H-4; Ha,Hb-7
5	118.3 (d)	H-6	117.4 (d)	H-6
6	151.0 (s)	H-4	150.3 (s)	H-4
1′			106.3 (d)	H-2′
1″	79.2 (s)	H-5″		
2″	129.2 (d)	H-4″		
3″	133.3 (d)	Hb-3″; H-4″		
4″	27.1 (t)	H-6″		
5″	36.8 (t)	H-4″; H-5″		
6″	207.3 (s)	H-6″		
7″	171.4 (s)	Ha,Hb-7		

The FABMS (neg) of **3** showed a quasi-molecular ion $[M - H]^-$ at m/z 381 and an HRFABMS $[M - H]^-$ ion at m/z 381.0471, which agreed with the formula $C_{13}H_{17}O_{11}S$. Fragment peak at m/z 139 $[M - H - 80 - 162]^-$ indicated the losses of $[HSO_3]^-$ and a glucosyl moiety mass unit from the quasi-molecular ion.[9] The IR spectrum of **3** exhibited distinctive absorptions at ν_{max} 1235 and 1221 cm^{-1} due to the S−O bond stretching vibration.[10,11] On the basis of the above analyses, the structure of **3** was identified as 2-(*β*-D-glucopyranosyloxy)-3-hydroxybenzyl hydrogen sulfate (idesin hydrogen sulfate).

The FABMS (neg.) of **4** gave a quasi-molecular ion peak at m/z 301, which, together with the DEPT results, were consistent with the molecular formula $C_{13}H_{18}O_8$. On the basis of these data, **4** was described as 6-hydroxy-2-(hydroxymethyl)phenyl *β*-D-glucopyranoside (idesin).

Experimental Section

General Experiment Procedures. Mps were determined with a Yanagimoto micro-melting point apparatus and are uncorrected. Optical rotations were measured using a JASCO DIP-370 polarimenter in MeOH. IR spectra were taken on a Perkin-Elmer 781 IR spectrometer. The UV spectrum was obtained on a Hitachi U-3200 spectrophotometer in MeOH. FABMS and HRFABMS spectra were recorded on a JEOL JMX-HX 110 spectrometer. ^{1}H-, ^{13}C-, and 2D NMR measurements were recorded on a Bruker ACP-300 spectrometer with deuterated MeOH as internal standard.

Plant Material. The fruits of *Idesia polycarpa* were collected at Juili, Chiayi Hsien, Taiwan, in September 1992. A voucher specimen has been deposited in the herbarium of the Department of Botany of the National Taiwan University.

Extraction And Isolation. The dried fruits (2.2 kg) were extracted with 95% EtOH (20 L × 3). The solvent was evaporated *in vacuo* at ca. 50 °C to give 458.5 g of residue. The crude extract was partitioned in succession between H_2O and Et_2O, followed by *n*-BuOH, yielding 61.2, 192, and 125 g, respectively. The *n*-BuOH extract was subjected to Si gel column chromatography with a gradient of MeOH in $CHCl_3$, and 14 fractions (1−14) were collected. Fraction 9 (24.5 g) gave compound **1** (3.5 g) after successive chromatographic separations on a Sephadex LH-20 column (MeOH) and Si gel MPLC (MeOH gradient in EtOAc).

Diaion HP-20 column chromatography of the H_2O extract gave six fractions (A−F). The column was eluted initially with H_2O and then with increasing amounts of MeOH in H_2O. Fractions were collected in 450-mL portions and pooled according to their TLC profile in $CHCl_3$−MeOH−H_2O (7:3:0.3). Sequential chromatography of fraction B (4.0 g) on Si gel (EtOAc−MeOH gradient) and Sephadex LH-20 (MeOH) afforded compounds **2** (201 mg) and **3** (160 mg). Compound **4** (1.50 g) was obtained from fraction C (13.8 g) in the same manner as described above.

Idescarpin [6-hydroxy-2-[[[(1-hydroxy-6-oxo-2-cyclohexen-1-yl)carbonyl]oxy]methyl]phenyl *β*-D-glucopyranoside] (1): syrup; $[\alpha]^{26}_D$ −79° (*c* 3.55, MeOH); IR (KBr) ν_{max} 3350, 1730, 1590, 1460, 1250, 1050, 740 cm^{-1}; UV(MeOH) λ_{max} (log ϵ) 326 (2.56), 277

(3.35), 213 (3.76) nm; FABMS (neg mode) m/z $[M - 1]^-$ 439.4; HRFABMS m/z $[M + H]^+$ 441.1390 (calcd 441.1397 for $C_{20}H_{25}O_{11}$); ^{1}H- and ^{13}C-NMR, see Table 1.

Salirepin [4-hydroxy-2-(hydroxymethyl)phenyl β-D-glucopyranoside] (2): amorphous white solid; mp 110−112 °C [lit.[7] mp 101−103 °C]; physical and spectroscopic data comparable to these reported in the literature.[8]

Idesin hydrogen sulfate [2-β-(D-glucopyranosyloxy)-3-hydroxybenzyl hydrogen sulfate] (3): syrup; $[\alpha]^{26}_D$ +6.5° (*c* 2.0, MeOH); IR (KBr) ν_{max} 3395, 2890, 1651, 1596, 1474, 1253, 1221, 1064 cm^{-1}; UV(MeOH) λ_{max} (log ϵ) 277 (3.33), 206 (3.93) nm; FABMS (neg mode) m/z 381 $[M - H]^-$, 139 $[M - H - HSO_3 - 162]^-$, 97 $[HSO_4]^-$; FABMS (pos mode) m/z 427 $[M - H + 2Na]^+$, 405 $[M + Na]^+$; HRFABMS m/z $[M - H]^-$ 381.0471 (calcd 381.0492 for $C_{13}H_{17}O_{11}S$); ^{1}H- and ^{13}C-NMR, see Table 1.

Idesin [6-hydroxy-2-(hydroxymethyl)phenyl β-D-glucopyranoside] (4): amorphous white powder; mp 103−105 °C (lit.[4] mp 98−100 °C); $[\alpha]^{26}_D$ −11° (*c* 1.35, MeOH); IR (KBr) ν_{max} 3300, 1685, 1460, 1415, 1385, 1365, 1260, 1185, 1050, 935, 830, 780, 765, 740 cm^{-1}; FABMS (neg mode) m/z 301 $[M - H]^-$, 139 $[M - H - 162]^-$; ^{1}H- and ^{13}C-NMR, see Table 1.

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