NEW SECOIRIDOIDS FROM ISERTIA HAENKEANA

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Abstract- Eight new secoiridoid glycosides (7R)- and (7S)-haenkeanoside (8) and (9), (7R)- and (7S)-isohaenkeanoside (10) and (11), (7R)- and (7S)-O-methylhaenkeanoside (12) and (13), and (7R)- and (7S)-O-methylisohaenkeanoside (14) and (15), were isolated from leaves of Isertia haenkeana, and their structures have been established on the basis of spectral data and chemical transformations. These compounds are the first report of any coumaroyl secoiridoid morroniside type with a trans- and cis-configuration at acyl double bond. Moreover, compounds 12, 13, 14, and 15 exhibit a methoxy group (C-7) in the aglycone part.

The genus Isertia belongs to the Rubiaceae family, most of the species occurring in tropical and subtropical South America.[1] The only species studied of this genus have been the Isertia hypoleuca Benth,[2] from which several alkaloids of quinamine type have been isolated and distinguished,[3,4] as well as the sterols and triterpenes -amyrin, -sitosterol and taraxasterol.[5]

Due to the scarce phytochemical work realizad on this genus we decided to realize a deep study on a second species of the same genus, the Isertia haenkeana D.C.

In this work we discuss the isolation and characterization of a series of new secoiridoid glycosides of one sample of Isertia haenkeana D.C. collected in Costa Rica.

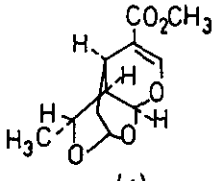
RESULTS AND DISCUSSION.

Fractionation of the chloroform to methanol extracts of dry leaves of Isertia haenkeana D.C. on a silica gel chromatography column followed by HPLC afforded fifteen secoiridoid glycosides, seven of which, namely sarracenin (1),[6] kingiside (2),[7] alpigenoside (3),[7] (7R)- and (7S)-morronisides (4) and (5),[7-10] and (7R)- and (7S)-7-O-methylmorronisides (6) and (7)[11] were known substances, and were identified by means of physical constants and spectral data.

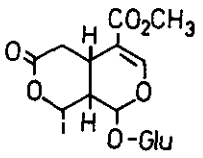
Spectral data of the new secoiridoids reveal that they have a common skeleton of a

morroniside type, esterified through the C-6' hydroxy group of the glucose with a rest of coumaric acid. They constitute a mixture of C-7 epimers and C(2") C(3") double bond isomers. Their elucidation was based principally in the comparison of the ^{1}H- and ^{13}C-nmr spectra of the corresponding acetylated morroniside epimers (4) and (5) with those of their methylmorroniside derivatives 7-O-(6) and (7).

For the structural elucidation, the mixture of epimers was separated by acetylation. However, we were unable to separate cis-trans isomers.



(1)



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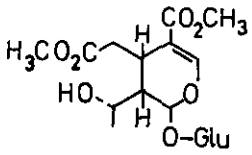

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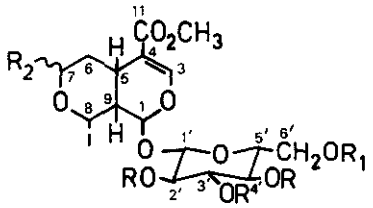
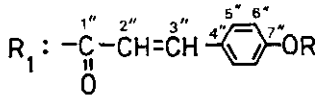




A = coumaroyl

(4) R=R_1=H, R_2=α-OH
(5) R=R_1=H, R_2=β-OH
(6) R=R_1=H, R_2=α-OMe
(7) R=R_1=H, R_2=β-OMe
(8) R=H, R_1=t-A, R_2=α-OH
(9) R=H, R_1=t-A, R_2=β-OH
(10) R=H, R_1=c-A, R_2=α-OH
(11) R=H, R_1=c-A, R_2=β-OH
(12) R=H, R_1=t-A, R_2=α-OMe
(13) R=H, R_1=t-A, R_2=β-OMe
(14) R=H, R_1=c-A, R_2=α-OMe
(15) R=H, R_1=c-A, R_2=β-OMe

(4a) R=R_1=Ac, R_2=α-OAc
(5a) R=R_1=Ac, R_2=β-OAc
(6a) R=R_1=Ac, R_2=α-OMe
(7a) R=R_1=Ac, R_2=β-OMe
(8a) R=Ac, R_1=t-A, R_2=α-OAc
(9a) R=Ac, R_1=t-A, R_2=β-OAc
(10a) R=Ac, R_1=c-A, R_2=α-OAc
(11a) R=Ac, R_1=c-A, R_2=β-OAc
(12a) R=Ac, R_1=t-A, R_2=α-OMe
(13a) R=Ac, R_1=t-A, R_2=β-OMe
(14a) R=Ac, R_1=c-A, R_2=α-OMe
(15a) R=Ac, R_1=c-A, R_2=β-OMe

(7R)-Haenkeanoside pentaacetate (8a) was obtained as an amorphous compound (512 mg) of molecular formula $C_{36}H_{42}O_{18}$ (elemental analysis); $[\alpha]_D^{20}$ -57° ($CHCl_3$). (7S)-Haenkeanoside pentaacetate (9a) was also an amorphous compound (160 mg); $[\alpha]_D^{20}$ -58°

($CHCl_3$). These two epimers showed similar uv absorptions at 231 (ϵ 18,936) and 296 (ϵ 16,085) nm (methanol), and their ir spectra showed bands at ν_{max} (KBr) 1760 (CO), 1715 (CO), 1640 (C=C) and 1605 cm^{-1} (C=C).

On the basis of the 1,3-diaxial interactions,[8] the ^{1}H-nmr spectra (Tables 1 and 2) showed that the more significative δ_H values for the study of the configuration in C-7 are the corresponding signals for the protons attached to C-5, C-7 and C-8. The δ_H for C-5H in the 7R- epimer (8a) appears at 2.85 ppm (dt, $J_{5,6ax}$=12 Hz, $J_{5,6eq}$=4 Hz and $J_{5,9}$=4 Hz) and in the 7S- epimer (9a) at 3.07 ppm. The major differences between both compounds are the chemical shifts for C-7H. Thus, in the 7R- epimer δ_H 5.75 (dd, $J_{7,6ax}$=10 Hz and $J_{7,6eq}$=2.5 Hz) and in the 7S- epimer (9a) δ_H is a broad signal at 6.14 ppm. Finally, δ_H for C-8H in compound (8a) appears at 3.95 (dq, $J_{8,9}$=3 Hz and $J_{8,10\text{-}Me}$=7 Hz) and in the isomer (9a) at δ_H 4.25 ppm. These assignments were supported by the ^{13}C-nmr spectra[9] (Table 3) which showed that δ_C for C-5 is 29.9 ppm for the 7R- epimer (8a) and 25.8 ppm for the 7S- isomer (9a). The chemical shift for C-7 in the isomer (8a) was found at 93.7 ppm and at 91.2 ppm for the epimer (9a). Finally, δ_C for C-8 appeared at 73.4 and 67.2 ppm for the 7R- and 7S- epimers (8a) and (9a), respectively.

Table 1. ^{1}H-Nmr spectral data of compounds 8a-15a ($CDCl_3$, 200 MHz, δ ppm)

	8a	9a	10a	11a	12a	13a	14a	15a
C-1H	5.72 d	5.70 d	5.68 d	5.67 d	5.63 d	5.70 d	5.59 d	5.67 d
C-3H	7.45 s	7.44 s	7.45 s	7.45 s	7.48 s	7.42 s	7.42 s	7.42 s
C-5H	2.85 dt	3.07 dt	2.85 dt	3.07 dt	2.69 dt	3.05 dt	2.69 dt	3.05 dt
C-6H_{ax}	1.35 m	1.55 m	1.35 m	1.55 m	1.35 m	1.42 m	1.35 m	1.42 m
C-6H_{eq}	2.10 m	2.00 m	2.10 m	2.00 m	2.05 m	1.92 m	2.05 m	1.92 m
C-7H	5.75 dd	6.14 d	5.75 dd	6.14 d	4.40 dd	4.68 d	4.40 dd	4.68 d
C-8H	3.95 dq	4.25 dq	3.95 dq	4.25 dq	3.82 m	4.20 dq	3.82 m	4.20 dq
C-9H	1.71 m	1.79 m	1.72 m	1.79 m	1.70 m	1.69 m	1.70 m	1.69 m
C-10H	1.36 d	1.28 d	1.34 d	1.31 d	1.34 d	1.30 d	1.35 d	1.31 d
C-2"H	6.41 d	6.40 d	5.98 d	5.96 d	6.35 d	6.38 d	5.92 d	5.95 d
C-3"H	7.68 d	7.68 d	6.98 d	6.98 d	7.67 d	7.67 d	6.90 d	6.96 d
C-5"H	7.56 d	7.57 d	7.67 d	7.67 d	7.55 d	7.55 d	7.56 d	7.56 d
C-6"H	7.13 d	7.14 d	7.10 d	7.10 d	7.06 d	7.12 d	7.02 d	7.09 d
C-11-OCH_3	3.72 s	3.72 s	3.72 s	3.72 s	3.70 s	3.70 s	3.70 s	3.70 s
C-7-OCH_3					3.47 s	3.31 s	3.49 s	3.31 s

Table 2. Coupling constants for the protons in compounds 8a-15a.

Compound	$J_{1,9}$	$J_{5,6ax}$	$J_{5,6eq}$	$J_{5,9}$	$J_{7,6ax}$	$J_{7,6eq}$	$J_{8,9}$	$J_{8,10}$	$J_{2",3"}$	$J_{5",6"}$
8a	8.8	12.6	4.6	4.6	9.8	2.3	2.5	6.8	16	8.5
9a	8.8	12.6	4.6	4.6	3	0	3	7	16	8.6
10a	8.8	12.6	4.6	4.6	9.8	2.3	2.5	6.8	12.7	8.5
11a	8.8	12.6	4.6	4.6	3	0	3	7	12.8	8.4
12a	8.5	12.5	4.5	4.5	10	2.5	-	-	16	8.6
13a	8.7	12.5	4.5	4.5	3	0	3	7	16	8.6
14a	8.5	12.5	4.5	4.5	10	2.5	-	-	12.6	8.6
15a	8.7	12.5	4.5	4.5	3	0	3	7	12.7	8.6

Table 3. ^{13}C- Nmr spectral data of compounds 8a-15a ($CDCl_3$, 50.32 MHz, δ ppm).

Carbon	8a	9a	10a	11a	12a	13a	14a	15a
1	94.7	94.4	94.7	94.4	95.2	94.5	95.2	94.5
3	152.4	152.5	152.3	152.5	152.3	152.1	152.3	152.1
4	110.2	111.1	110.2	111.1	110.4	111.3	110.3	111.3
5	29.9	25.8	29.9	25.8	29.9	25.8	29.9	25.8
6	32.9	31.2	32.9	31.2	33.9	32.2	33.9	32.2
7	93.7	91.2	93.7	91.2	102.6	97.5	102.6	97.5
8	73.4	67.2	73.4	67.2	72.5	63.9	72.5	63.9
9	38.8	39.1	38.8	38.6	39.1	39.0	38.7	38.7
10	18.7	18.8	18.7	19.0	18.7	18.6	19.1	18.9
11	166.4	166.5	166.3	166.5	166.5	166.4	166.5	166.4
1'	96.6	96.8	96.6	96.8	96.8	96.6	96.8	96.6
2'	70.9	71.0	70.9	71.0	70.8	70.8	70.8	70.8
3'	72.0	72.1	71.8	72.1	72.0	71.8	72.1	71.7
4'	68.5	68.6	68.5	68.6	68 4	68.4	68.1	68.1
5'	72.5	72.6	72.5	72.6	72.2	72.4	72.2	72.4
6'	61.9	61.8	61.9	61.8	61.8	61.8	61.6	61.8
1"	166.1	166.1	165.0	166.1	166.1	165.9	166.1	165.9
2"	117.3	117.3	118.6	118.7	117.3	117.2	118.1	118.7
3"	144.4	144.6	143.7	143.9	144.3	144.2	143.9	143.9
4"	131.8	131.3	132.0	132.0	131.8	131.7	132.4	132.2
5"	129.2	129.4	131.1	130.8	129.1	129.1	130.8	130.8
6"	122.0	122.1	121.0	121.2	121.9	121.9	121.9	121.2
7"	157.1	152.1	151.0	151.0	152.0	152.1	152.0	152.1
11-OCH_3	51.3	51.4	51.3	51.4	51.2	51.0	51.2	51.0
7-OCH_3					56.0	54.3	56.0	54.3

A comparison of the ^{1}H-nmr spectral data of the haenkeanosides (7R) (8) and (7S) (9) and of the morronisides (7R) (4) and (7S) (5) indicates that the esterification with p-coumaric acid takes place at the C-6' hydroxy group of glucose moiety since the signals due to the protons attached to C-6' are shifted downfield. Thus, δ_H is 4.35 (m) in (8) and (9), and 3.87 in (4) and (5), whereas all other glucose signals are almost unchanged.[12] The p-coumaric acid subunit in these compounds shows to be the trans- isomer: δ_H (C-2"H) 6.40, J=16 Hz and δ_H (C-3"H) 7.68, J=16 Hz.

Further confirmation of the proposed structure came from the ^{13}C-nmr spectra of (8) and (9) which were very similar to the spectra of morronisides (4) and (5), except for the signals due to the trans-p-coumaroyl group, so that the ester linkage cannot be on the secoiridoid moiety. The chemical shifts of the four glucose C-atoms (C-1', C-2', C-3', and C-4') were identical in these compounds, so that the linkage of the p-coumaric acid can only be at the C-6' hydroxy group.

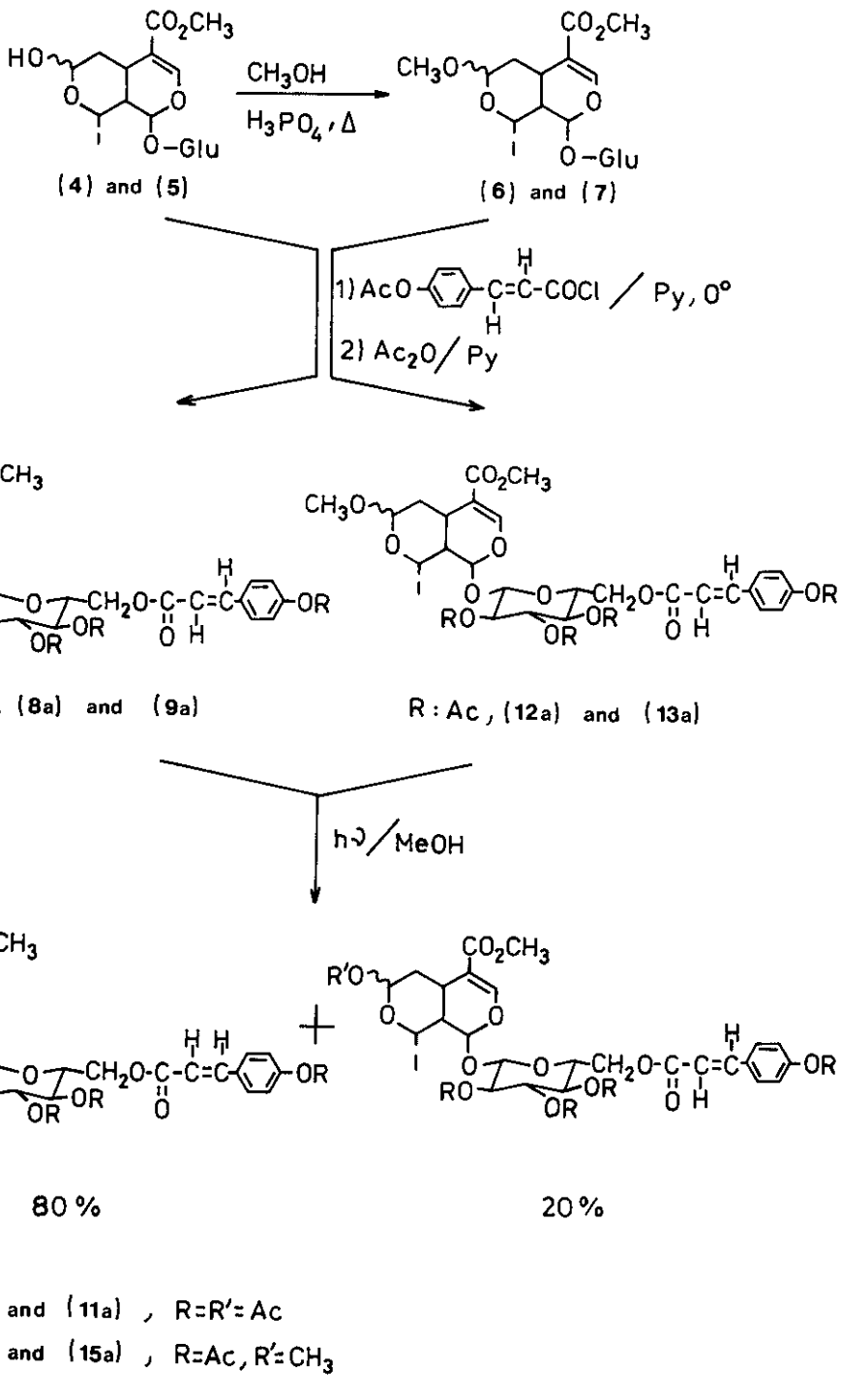
The signal for C-6'is shifted downfield by 1.4 ppm and the corresponding of the carbon atom at the β-position, C-5', is shifted upfield by 2.8 ppm. In fact, the downfield shift of the α-C-signal and the upfield shift of the β-C-signal upon acylation is well documented.[13]

(7R)- and (7S)-Isohaenkeanoside pentaacetates (10a) and (11a). Due to the impossibility to separate both isomers either by TLC or HPLC (total amount: 168 mg), the nmr spectral data of these compounds were deduced from the data of isomers 8a and 9a, obtained by synthesis. The only difference of these secoiridoids with the previous ones is that the p-coumaroyl residue was now in the cis- form. According to this structural fact, the ^{1}H-nmr spectra (Tables 1 and 2) showed δ_H (C-2"H) 5.98 (J=13 Hz) and δ_H (C-3"H) 6.98 (J=13 Hz) for compound 10a, and δ_H (C-2"H) 5.96 (J=13 Hz) and δ_H (C-3"H) 6.98 (J=13 Hz) for compound 11a. On the other hand, the ^{13}C-nmr spectra showed only a sligth difference between the chemical shifts for the C-2" and C-3" ($\Delta\delta$= +1.4 and -0.7 ppm, respectively), which is the usual feature for this class of cis-trans isomers.

(7R)-O-Methylhaenkeanoside tetraacetate (12a) was obtained as an amorphous compound (1.024 g) with molecular formula $C_{35}H_{42}O_{17}$ (elemental analysis); $(\alpha)_D^{20}$ -33° ($CHCl_3$).

(7S)-O-Methylhaenkeanoside tetraacetate (13a) was also an amorphous compound (952 mg); $(\alpha)_D^{20}$ -59° ($CHCl_3$). These two epimers showed similar uv absorptions at 231 (ϵ 17,703) and 296 (ϵ 14,444) nm in methanol and their ir spectra showed bands at ν_{max} 1760 (CO), 1715 (CO), 1640 (C=C) and 1605 cm^{-1} (C=C). On the basis of the ^{1}H- and ^{13}C-nmr spectral data, these natural products were found to be methyl derivatives at C-7 of

SCHEME



(10a) and (11a), R=R'=Ac

(14a) and (15a), R=Ac, R'=CH_3

the corresponding haenkeanosides. ^{1}H-Nmr spectra showed singlet signals at 3.47 ppm for the 7R- epimer (12a) and at 3.31 ppm for 7S-epimer (13a), assigned to the methoxycarbonyl group at C-7. The C-7H chemical shift for the 7R- epimer (8a) was 5.57 ppm, whereas their methyl derivative 12a was 4.40 ppm. In the 7S- epimer (9a), this signal was observed at 6.14 ppm, and in its corresponding methyl derivative 13a at 4.68 ppm. The ^{13}C-nmr spectra showed quaternary carbon signals at 55.5 and 54.3 ppm for the 7R- (12a) and 7S- (13a) epimers, respectively, which were assigned to the methoxycarbonyl group at C-7. The chemical shift for C-7 in compound 8a was 93.7 ppm, but 102.4 ppm for its methyl derivative 12a. For the 7S- epimer (9a) this carbon signal was present at δ_C 91.2 and at δ_C 97.7 for its methyl derivative (13a).
Further evidence supporting these structures (12a) and (13a) was provided by the methylation of haenkeanosides (8) and (9) with methanol and phosphoric acid.
(7R)- and (7S)-O-Methylisohaenkeanoside tetraacetates (14a) and (15a). These secoiridoids (266 mg and 238 mg, respectively) were the cis- isomers at the p-coumaroyl residue of the corresponding compounds (12a) and (13a). Accordingly, (C-2"H) was found at 5.92 (J=13 Hz) ppm and (C-3"H) at 6.90 (J=13 Hz) ppm in epimer (14a). Similarly, (C-2"H) was found at 5.95 (J=12 Hz) ppm and (C-3"H) at 6.96 (J=13 Hz) ppm in compound (15a). As for the above mentioned isomers (10a) and (11a), the ^{13}C-nmr spectra showed only small differences between the chemical shifts of C-2" and C-3" ($\Delta\delta$= +1.4 and -0.4 ppm, respectively) as expected for these isomers.
Hemisynthesis of the new secoiridoids. To confirm the structure of the new compounds we performed the synthesis of (8a) to (15a) from the morronisides (4) and (5) (see Scheme). Esterification of the C-6' hydroxy group of the glucose moiety with t-acetylcoumaroyl chloride followed by acetylation afforded compounds (8a) and (9a). Compounds (12a) and (13a) were prepared similarly, after methylation of morronisides (4) and (5). Finally, the cis-isomers (10a), (11a), (14a), and (15a) were obtained from their respective trans-isomers by irradiation at 350 nm.

EXPERIMENTAL.

Optical rotations were measured with a Perkin-Elmer 141 polarimeter at 20-25°C (c=1.00). Uv spectra were measured with a Perkin-Elmer 124 double beam spectrophotometer and ir spectra were recorded on a Nicolet 5 DXFTIR spectrophotometer. Mass spectra were obtained with an Hewlett-Packard GC-MS 5985B instrument. ^{1}H- and ^{13}C-nmr spectra were recorded on a Bruker SY-200 spectrometer at

200 MHz and 50.3 MHz, respectively, the chemical shifts being in ppm from $SiMe_4$ (δ=0) as internal standard. The DEPT technique was used in the ^{13}C-nmr spectra. HPLC was performed on a Knauer liquid chromatograph using a polygosil 60-C_{18} column.

Isolation of secoiridoid glucosides. The air-dried plant material (1.5 kg) of Isertia haenkeana collected in July, 1981 in Costa Rica (Palmar Norte), (vouchers of the plant were deposited in the herbarium of Natural History museum of San José, N. 3046), was extracted with chloroform, ethyl acetate, acetone and methanol.

The chloroform fraction (60 g) was chromatographed through silica gel. Elution with benzene-ethyl acetate (4:1) yielded sarracenin (1) (120 mg). The other secoiridoids were isolated from the ethyl acetate (66.82 g), acetone (136.49 g), and methanol (190.28 g) fractions.

The ethyl acetate fraction was chromatographed through silica gel and eluted successively with ethyl acetate-acetone (3:1) and chloroform-methanol (6:1) yielding a mixture of products that were grouped from their R_f values. The later fractions were acetylated with acetic anhydride and pyridine at room temperature for 12 h. The acetylated mixture of compounds (8a), (9a), (10a), and (11a) was chromatographed with chloroform-acetone (1:15) to give the two epimers in C-7 but no the cis-trans isomers. Similarly, elution with chloroform-ethyl acetate (4:1) allowed the separation of epimers at C-7 (12) and (14) from the epimers at C-7 (13) and (15). Compounds (6a) and (7a) were isolated by elution with chloroform-ethyl acetate (2:1).

The remaining products, the already known compounds (2), (3), (4), and (5) were separated by semipreparative HPLC, using a Polygosil 60-C_{18} (5 μm) column; solvent: methanol-water (1:4), 4 ml/min.

Sarracenin (1). 120 mg of white crystalline material mp 127-128°C (benzene-ethyl ether). Uv: (EtOH) λ_{max} 232 (ϵ 9,660) nm. Ir: (KBr) ν_{max} 2970, 1707, 1640, 1440, 1380, 920, 860, and 818 cm^{-1}. Ms: m/z (%) 226 (M^+, 12), 180 (12), 165 (13), 148 (14), 137 (17), 121 (20),109 (16), 96 (19), 69 (100), and 41 (71). ^1H-Nmr: ($CDCl_3$), 1.33 (3H, d, $J_{9,8}$=6.5 Hz, C-9H), 1.68 (2H, m, C-6H), 2.37 (1H, m, C-4H), 2.97 (1H, m, C-5H), 3.76 (3H, s, C-11H), 4.22 (1H, q, $J_{8,9}$=6.5 Hz, C-8H), 4.98 (1H, d, $J_{3,4}$=3 Hz, C-3H), 5.79 (1H, t, $J_{7,6}$=2 Hz, C-7H), and 7.46 (1H, s, C-2H). ^{13}C-Nmr: ($CDCl_3$) 18.62 (C-9), 22.12 (C-4 or C-5), 32.32 (C-4 or C-5), 35.10 (C-6), 51.25 (C-11), 68.94 (C-8), 88.10 (C-3 or C-7), 112.37 (C-1), 91.67 (C-3 or C-7), 149.99 (C-2), and 166.66 (C-10).

Tetraacetylkingiside (2a). Compound (2) was acetylated with Ac_2O/Py at room temperature. Work-up in the usual manner afforded (2a), mp 164-165°C, $[\alpha]_D^{20}$ =-91° ($CHCl_3$). Uv: (MeOH) λ_{max} 233 (ϵ 10,715) nm. Ir: (KBr) ν_{max} 1755, 1715, 1655, and 1450 cm^{-1}. ^{1}H-Nmr: ($CDCl_3$) 1.50 (3H, d, $J_{8,10}$=7 Hz, C-10H), 2.35 (1H, m, $J_{1,9}$=5 Hz, $J_{5,9}$=4.5 Hz and $J_{8,9}$=3 Hz, C-9H), 2.80 (2H, AB system, $J_{6a,6b}$=17 Hz, $J_{5,6a}$=8 Hz and $J_{5,6b}$=5.5 Hz, C-6H), 3.23 (1H, m, C-5H), 3.75 (3H, s, C-11Me), 4.60 (1H, m, C-8H), 5.45 (1H, d, $J_{1,9}$=7 Hz, C-1H), and 7.45 (1H, s, C-3H).

Pentaacetylalpigenoside (3a). Compound (3) was acetylated in the usual manner affording (3a). Uv: (MeOH) λ_{max} 233 (ϵ 10,232) nm. Ir: (KBr) ν_{max} 1750, 1715, 1655, 1440, and 1405 cm^{-1}. ^{1}H-Nmr: ($CDCl_3$) 1.33 (3H, d, $J_{10,8}$=6.5 Hz, C-10H), 2.15 (1H, m, C-9H), 2.58 (2H, AB system, $J_{6a,6b}$=16.5 Hz, $J_{5,6a}$=7.5 Hz and $J_{5,6b}$=5.5 Hz, C-6H), 3.29 (1H, m, C-5H), 3.64 and 3.69 (6H, s, -COOMe), 3.78 (1H, m, C-8H), 5.60 (1H, d, $J_{1,9}$=7 Hz, C-1H), and 7.46 (1H, s, C-3H).

Pentaacetylmorronisides (4a) and (5a). Compounds (4) and (5) afforded both epimers (4a) and (5a) after acetylation in the usual manner.

Compound (4a), mp 144-145°C. Uv: (MeOH) λ_{max} 237 (ϵ 10,471) nm. Ir: (KBr) ν_{max} 1715 and 1640 cm^{-1}.

^{1}H-Nmr: ($CDCl_3$) 1.33 (1H, m, C-6H_{ax}), 1.35 (3H, d, $J_{10,8}$=7 Hz, C-10H), 1.70 (1H, m, C-9H), 2.10 (1H, m, C-6H_{eq}), 2.84 (1H, dt, $J_{5,6ax}$=12 Hz, $J_{5,6eq}$=4 Hz and $J_{5,9}$=4 Hz, C-5H), 3.72 (3H, s, C-11H), 3.95 (1H, dq, $J_{8,9}$=3 Hz and $J_{8,10}$=7 Hz, C-8H), 5.70 (1H, d, $J_{1,9}$=9 Hz, C-1H), 5.75 (1H, dd, $J_{7,6ax}$=10 Hz and $J_{7,6eq}$= 2.5 Hz, C-7H), and 7.43 (1H, s, C-3H). ^{13}C-Nmr: ($CDCl_3$, DEPT) 18.8 (C-10), 30.1 (C-5), 33.1 (C-6), 38.9 (C-9), 51.3 (C-OMe), 61.8 (C-6'), 68.6 (C-4'), 71.0 (C-2'), 72.1 (C-3'), 72.6 (C-5'), 73.6 (C-8), 93.9 (C-7), 94.8 (C-1), 96.8 (C-1'), 110.3 (C-4), 152.5 (C-3), and 166.4 (C-11).

Compound (5a), mp 151-152°C. ^{1}H-Nmr: ($CDCl_3$) 1.28 (3H, d, $J_{10,8}$=7 Hz, C-10H), 1.53 (1H, m, C-6H_{ax}), 1.80 (1H, m, C-9H), 2.0 (1H, m, C-6H_{eq}), 3.09 (1H, dt, $J_{5,6ax}$=12 Hz, $J_{5,6eq}$=4 Hz and $J_{5,9}$=4 Hz, C-5H), 3.72 (3H, s, C-11H), 4.31 (1H, m, C-8H), 5.69 (1H, d, $J_{1,9}$=9 Hz, C-1H), 6.14 (1H, d, $J_{7,6ax}$=3 Hz, C-7H), and 7.43 (1H, s, C-3H). ^{13}C-Nmr: ($CDCl_3$, DEPT), 18.8 (C-10), 26.0 (C-5), 31.3 (C-6), 39.2 (C-9), 51.3 (C-OMe), 61.7 (C-6'), 67.3 (C-8), 68.7 (C-4'), 71.1 (C-2'), 72.1 (C-3'), 72.6 (C-5'), 91.3 (C-7), 94.4 (C-1), 96.8 (C-1'), 111.1 (C-4), 152.5 (C-3), and 166.6 (C-11).

Tetraacetyl-7-O-methylmorronisides (6a) and (7a).

Compound (6a), mp 144-145°C. Uv: (MeOH) λ_{max} 236 (ϵ 16,595) nm. Ir: (KBr) ν_{max} 1760, 1750, 1705, and 1620 cm^{-1}. ^{1}H-Nmr: ($CDCl_3$) 1.34 (3H, d, $J_{10,8}$=7 Hz, C-10H), 1.68 (1H, m, C-9H), 2.78 (1H, dt, $J_{5,6ax}$=12 Hz, $J_{5,6eq}$=4 Hz and $J_{5,9}$=4 Hz, C-5H), 3.49 (3H, s, C-7OMe), 3.71 (3H, s, C-11OMe), 4.41 (1H, dd, $J_{7,6ax}$=10 Hz and $J_{7,6eq}$=2.5 Hz, C-7H), 5.67 (1H, d, $J_{1,9}$=9 Hz, C-1H), and 7.42 (1H, s, C-3H). ^{13}C-Nmr: ($CDCl_3$, DEPT), 18.4 (C-10), 29.9 (C-5), 33.8 (C-6), 38.9 (C-9), 50.9 (C-11OMe), 55.5 (C-7OMe), 61.6 (C-6'), 68.6 (C-4'), 70.7 (C-2'), 71.6 (C-8), 72.0(C-3'), 72.5 (C-5'), 95.1 (C-1), 96.7 (C-1'), 102.4 (C-7), 110.7 (C-4), 152.0 (C-3), and 166.1 (C-11).

Compound (7a), mp 103-104°C. ^{1}H-Nmr: ($CDCl_3$) 1.27 (3H, d, $J_{10,8}$=7 Hz, C-10H), 1.45 (1H, m, C-6H_{ax}), 1.72 (1H, m, C-9H), 1.92 (1H, m, C-6H_{eq}), 3.05 (1H, dt, $J_{5,6ax}$=12 Hz, $J_{5,6eq}$=4 Hz and $J_{5,9}$=4 Hz, C-5H), 3.34 (3H, s, C-7OMe), 3.71 (3H, s, C-11OMe), 4.20 (1H, m, C-8H), 4.73 (1H, d, $J_{7,6ax}$=2.7 Hz, C-7H), 5.70 (1H, d, $J_{1,9}$=9 Hz, C-1H), and 7.43 (1H, s, C-3H). ^{13}C-Nmr: ($CDCl_3$, DEPT), 18.6 (C-10), 26.1 (C-5), 32.6 (C-6), 39.4 (C-9), 51.0 (C-11OMe), 54.3 (C-7OMe), 61.7 (C-6'), 64.1 (C-8), 68.6 (C-4'), 71.0 (C-2'), 72.0 (C-3'), 72.6 (C-5'), 94.7 (C-1), 96.7 (C-1'), 97.7 (C-7), 111.7 (C-4), 152.1 (C-3), and 166.5 (C-11).

Compounds (8a)-(15a). See Tables 1,2, and 3.

7-O-Methylmorronisides (6) and (7). A solution of the mixture of (4) and (5) (250 mg, 0.6 mmol) in methanol (12.5 ml) and phosphoric acid (0.05 ml) was refluxed for 24 h. Evaporation of the solvent afforded compounds (6) and (7). The compounds were identified by acetylation (Ac_2O/py), which gave (6a) and (7a), identical to the above described derivatives.

(7R)- and (7S)-Haenkeanoside pentaacetates (8a) and (9a). To morronisides (4) and (5) (325 mg, 0.8 mmol) in dry pyridine (4 ml) at 0°C was added dropwise a solution of t-acetylcoumaroyl chloride (200 mg, 0.89 mmol) in pyridine (1 ml). The mixture was left standing overnight at -5°C. After usual work up 60 mg of crude mixture was obtained. This mixture was inmediately acetylated (Ac_2O/Py) to (8a) and (9a), identical to the compounds described above.

(7R)- and (7S)-O-Methylhaenkeanoside tetraacetates (12a) and (13a). The preparation of compounds (12a) and (13a) was performed similarly, from (7R)- and (7S)-O-

methylmorronisides.

(7R)- and (7S)-Isohaenkeanoside pentaacetates (10a) and (11a). A solution of the mixture of (8a) and (9a) (500 mg, 0.65 mmol) in methanol (250 ml) was irradiated for 24 h at 350 nm under argon with a HQL 125 W lamp. The solvent was evaporated under vacuum to leave a mixture of the cis and trans isomers, in a 80% yield of cis-isomer (isohaenkeanoside) and 20% of trans-isomer (haenkeanoside). This mixture could not be separated by silica gel cromatography or HPLC.

(7R)- and (7S)-O-Methylisohaenkeanoside tetraacetates (14a) and (15a). The synthesis of these compounds (14a) and (15a) was performed in a similar manner as above, using (7R)- and (7S)-O-methylhaenkeanoside tetraacetates (12a) and (13a).

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