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IRIDOIDS FROM *MENTZELIA CORDIFOLIA*

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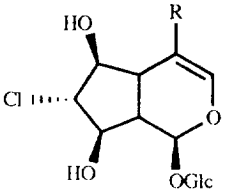
Abstract—From the aerial parts of *Mentzelia cordifolia*, 11 known compounds, seven phenolics and four iridoids have been identified. In addition, two new iridoids, i.e. mentzefoliol and glucosylmentzefoliol, have been isolated and characterized. Their structures have been elucidated mainly by means of spectroscopic data.

INTRODUCTION

Mentzelia cordifolia Dombay is a shrub which is widespread in Peru and Bolivia, where it grows up to 3000 m above sea-level. The plant is widely traded in Peruvian markets: the decoction of the aerial parts is considered an excellent cicatrizant in gastric ulcers and it is also used for its choleretic and anthelminthic properties [1].

No phytochemical investigation has been reported for this species, though previous studies have shown the presence of iridoids in the genus [2–4]. This paper deals with the isolation from *M. cordifolia* of 13 metabolites, two of which are new iridoids, whose structure elucidation was performed mainly by spectroscopic methods.



	R
1	Me
2	CH_2OH
3	CH_2OGlc

RESULTS AND DISCUSSION

Dried aerial parts of the plant were defatted with *n*-hexane and exhaustively extracted first with acetone in a Soxhlet apparatus and then with methanol at room temperature. The acetone residue contained seven phenolic constituents (i.e. scopoletin, isoscopoletin, rutin, hyperin, quercetin, and ferulic and chlorogenic acids). Gel filtration and subsequent separation by CC of the methanolic residue allowed the isolation of the iridoid constituents: mentzeloside, epoxydecaloside, glucosyldecaloside, and 7-chlorodeutziol (**1**), already found in *Mentzelia* spp. [2, 3], and mixtures containing the two new compounds **2** and **3**, which we have named mentzefoliol and glucosylmentzefoliol, respectively.

Compound **1**, an amorphous powder, gave a brown colour with vanillin–hydrochloric acid and $Ce(SO_4)_2$ reagents. The D/CI-mass spectrum ($[M]^+$ peak at *m/z* 382 and $[M + NH_4]^+$ peak at *m/z* 400) and the DEPT ^{13}C NMR data accounted for the molecular formula of 7-chlorodeuteziol ($C_{15}H_{23}O_9Cl$). The nature and the site of linkage of the hexosyl moiety suggested by the MS peak at *m/z* 220 $[M - 162]^+$ was supported by the ^1H and ^{13}C NMR spectra (Table 1).

The ^1H NMR spectral data including COSY and decoupling experiments led to the complete and unambiguous assignments of all the resonances of the aglycone moiety of **1** [5], apart from the stereochemical assignments. El-Naggar *et al.* [5] established the absolute configuration of C-6, C-7 and C-8 only by means of the chemical interconversion of **1** to deutzioside. We have elucidated the complete stereochemical structure for 7-chlorodeutziol by means of spectral data (see below) and without recourse to chemical experiments, i.e. a simpler and faster way for structure elucidation.

Treatment of **1** with pyridine–acetic anhydride afforded the hexaacetyl derivative **1a**, whose ^1H NMR spectrum showed the typical acetylation downfield shift for the two carbinolic aglucone protons and led to the unambiguous assignment of the two resonances and *J*-couplings (see Experimental). The signal at δ4.06 remained practically unaffected and was assigned to H-7 by selective decouplings.

Dedicated to Prof. G. C. Berti on the occasion of his 70th birthday.

Table 1. ^{13}C NMR of **1** (CD_3OD) and **1a**–**3a** ($CDCl_3$, 200 MHz,TMS as int. standard)

C	1	1a	2a	3a
1	93.8	91.8	90.9	91.3
3	135.2	140.2	140.1	140.3
4	113.6	109.4	109.9	110.0
5	41.8	40.9	37.0	37.2
6	81.9[a]	77.0[a]	80.1[a]	80.3
7	71.3[a]	64.9[a]	64.5	64.9
8	77.4[a]	81.0[a]	80.6[a]	80.7[a]
9	46.3	45.9	44.8	45.2
11	15.7	16.4	63.4	68.8
1′	99.5	96.3	96.5	96.3
2′	74.5	71.2	71.0	70.9
3′	77.6*	72.8	72.7	72.5[b]
4′	71.3	68.7	68.7	68.8
5′	77.8*	73.1	73.0	73.1
6′	62.4	62.3	62.1	62.3
1″				100.9
2″				71.9
3″				72.8[b]
4″				68.8
5″				73.1
6″				62.5
MeCO		21.4, 21.3 (×2), 21.4 (×2), 21.6, 21.7	20.9, 21.0, 21.4 (×2), 21.6 (×2), 21.8	20.6, 20.8, 21.2 (×2), 21.4 (×2), 21.6 (×2), 21.8, 21.9
MeCO		169.7, 170.1, 170.3 170.8 (×2), 171.3	169.6, 169.9, 170.2 (×2), 170.4, 170.9 (×2), 171.1	169.7, 169.8 (×2), 170.1 (×2), 170.5 (×2), 170.7 (×2), 171.1

[a,b]Assignments can be interchanged in the same column.
*Assignments made by HETCORR experiments.

The NOE effects between H-6 and H-5, and between H-8 and H-9, as well as the absence of NOE effects between H-1 and H-8, H-6 and H-7, and H-7 and H-8 suggested a *trans*-relationship for the substituents in the cyclopentane ring. Assuming the usual β-configuration for H-5 and H-9 and α- for H-1, these effects allowed us to assign β-configuration to the hydroxyls at C-6 and C-8, and an α-configuration to the Cl at C-7.

Compounds **2** and **3** were contaminated with epoxydecaloside and glucosyldecaloside, respectively. The purification was performed by acetylation followed by CC which afforded the pure acetyl derivatives **2a** and **3a**.

When compared with those of **1a**, the NMR data of **2a**, $C_{29}H_{37}O_{17}Cl$, were consistent with the replacement of the methyl group on C-4 by an oxymethylene group. In fact, the DEPT ^{13}C NMR spectra of **2a** showed the presence of an oxymethylene at δ63.4 instead of the methyl group at δ16.4 in **1a** and the downfield shifts of C-3 and C-5 owing to the γ-effect of the hydroxylation at C-11, while the other resonances remained practically unaffected.

The NMR spectral data of **3a**, $C_{41}H_{53}O_{25}Cl$, were consistent with a structure similar to **2a** with an additional β-D-glucopyranosyl moiety at C-11. This assignment was derived from the ^{13}C NMR spectrum, in comparison with **2a**, on the basis of the oxymethylene peak at δ68.8 and of the upfield shifts of C-3 and C-5, owing to the γ-effect of the peracetylated hexose linked to C-11 [3].

The iridoids isolated from *M. cordifolia* fully confirm the characteristic occurrence in *Mentzelia* of iridoid glycosides devoid of C-10, and having a hydrogenated function at C-11 [2, 6] and a Cl at C-7.

EXPERIMENTAL

General. D/CI-MS: Finnigan Matt TSQ700; NMR: 500 and 200 MHz (^1H and ^{13}C), assignments by 1D and 2D experiments; HPLC: LiChrospher 100 RP-18 column, detection by photodiode array detector.

Plant material. Mentzelia cordifolia Dombay was collected in the Department of Tumbes (North Peru) in September 1988 and identified by E. Cerrate. Voucher specimens are deposited in the Dipartimento di Chimica delle Sostanze Naturali, University of Napoli (Italy) and in the Herbarium of the Museo de Historia Natural "Javier Prado", University of San Marcos, Lima (Peru) (N° BF89346).

Extraction and separation. Air-dried ground aerial parts (340 g) were defatted with *n*-hexane and extracted with Me_2CO in a Soxhlet apparatus followed by MeOH at room temp.

The Me_2CO residue (3.9 g) was dissolved in MeOH–H_2O (2:1) and extracted with EtOAc. The hydro-alcoholic layer was submitted to purification by Polyclar AT CC (MeOH–H_2O mixtures of increasing polarity as eluents) to give rutin (13 mg) and hyperin (24 mg). The EtOAc layer was purified by Polyamide SC6 CC (C_6H_6–MeCOEt–MeOH 2:1.5:1.5) to yield scopoletin (32 mg), isoscopoletin (21 mg), ferulic acid (8 mg), chlorogenic acid (8 mg), and quercetin (15 mg). These compounds were identified by comparison of HPLC-UV DAD with authentic samples.

The MeOH residue (7.6 g) was filtered and fractionated on a Sephadex LH-20 column using MeOH as eluent. 21 fractions (20 ml each) were collected. Fraction 8 (3.76 g) was chromatographed over an Amberlite XAD-2 column using H_2O and MeOH as eluents. The alcoholic fraction contained cordifoliol (**1**) (0.12 g).

A part (300 mg) of fr. 5 (600 mg) was further fractionated by flash CC over silica gel using $CHCl_3$–MeOH–H_2O (6:4:1) to give several iridoid fractions, i.e. glucosyldecaloside (5 mg), mentzelioside (14 mg), a mixture of epoxydecaloside and mentzefoliol (**2**), and a mixture of glucosyldecaloside and glucosylmentzefoliol (**3**).

Separate reactions of the last two mixtures with Ac_2O–pyridine (1:2) for 24 hr at room temp. and subsequent CC on silica gel with toluene–Me_2CO–$CHCl_3$ (2:1:1) gave pure **2a** (8 mg) and **3a** (6 mg) respectively. Compound **1a** was obtained by acetylation of **1** under the same conditions. Known compounds were identified by comparison of their ^1H and ^{13}C NMR data with those reported in the literature [6].

7-Chlorodeutziol (**1**). $[\alpha]_D^{20}$ −44.3° (MeOH; *c* 0.6); UV λ_{max}^{MeOH} nm: 218; IR ν_{max}^{NaCl} cm^{-1}: 3540, 3200, 1730, 1640, 1378–1363, 1065–1030, 900; elem. anal. found: C, 46.7; H, 6.3; Cl, 9.2. $C_{15}H_{23}O_9Cl$ requires: C, 47.1; H, 6.1; Cl, 9.3%. ^1H NMR (200 MHz, CD_3OD): δ 1.51 (3H, *br s*, H_3-11), 2.20 (1H, *dt*, *J* = 10.2 and 2.8 Hz, H-9), 2.34 (1H, *m*, H-5), 3.12 (1H, *dd*, *J* = 8.0 and 7.9 Hz, H-2′), 3.22 (1H, *m*, H-5′), 3.24 (1H, *m*, H-4′), 3.34 (1H, *m*, H-3′), 3.6–3.8 (5H, *m*, H-5, H-6, H-7, H_2-6′), 4.60 (1H, *d*, *J* = 7.6 Hz, H-1′), 5.19 (1H, *d*, *J* = 2.6 Hz, H-1), 5.87 (1H, *br s*, H-3); ^{13}C NMR: Table 1.

Cordifoliol hexaacetate (**1a**). $[\alpha]_D^{20}$ −41.3° ($CHCl_3$; *c* 1.5); ^1H NMR (200 MHz, $CDCl_3$): δ 1.65 (3H, *br s*, H_3-11), 1.96, 2.01, 2.03, 2.09, 2.11, 2.13, (3H each, *s*, MeCO × 6), 2.56 (1H, *dddd*, *J* = 8.1, 1.5, 1.3, and 0.8 Hz, H-5), 2.64 (1H, *ddd*, *J* = 8.1, 2.2 and 0.7 Hz, H-9), 3.69 (1H, *ddd*, *J* = 2.2, 4.7 and 9.5 Hz, H-5′), 4.06 (1H, *ddd*, *J* = 1.5, 2.6 and 5.2 Hz, H-7), 4.13 (1H, *dd*, *J* = 2.2 and 12.5 Hz, H-6′a), 4.30 (1H, *dd*, *J* = 4.7 and 12.5 Hz, H-6′b), 4.83 (1H, *d*, *J* = 8.1 Hz, H-1′), 4.92 (1H, *dd*, *J* = 8.1 and 9.5 Hz, H-2′), 5.07 (1H, *t*, *J* = 9.5 Hz, H-4′), 5.16 (1H, *t*, *J* = 9.5 Hz, H-3′), 5.19 (1H, *br s*, H-6), 5.26 (1H, *d*, *J*-2.2 Hz, H-1), 5.28 (1H, *dd*, *J* = 5.2, 0.7 Hz, H-8), 5.98 (1H, *br s*, H-3); ^{13}C NMR: Table 1.

Mentzefoliol heptaacetate (**2a**). $[\alpha]_D^{20}$ −39.3° ($CHCl_3$; *c* 1.7); elem. anal. found: C, 49.8; H, 5.3; Cl, 5.0. $C_{29}H_{37}O_{17}Cl$ requires: C, 50.3; H, 5.4; Cl, 5.1%. ^1H NMR (200 MHz, $CDCl_3$): δ 1.97, 1.98, 2.01, 2.03, 2.05, 2.06, 2.07 (3H each, *s*, MeCO × 7), 2.41 (*dddd*, *J* = 8.7, 1.6, 1.3, and 0.8 Hz, H-5), 2.53 (*ddd*, *J* = 8.7, 2.2 and 0.9 Hz, H-9), 3.88 (*ddd*, *J* = 2.2, 5.4 and 9.6 Hz, H-5′), 4.09 (*ddd*, *J* = 1.6, 2.6 and 5.2 Hz, H-7), 4.18 (*dd*, *J* = 2.2 and 12.5 Hz, H-6′a), 4.31 (*dd*, *J* = 5.4 and 12.5 Hz, H-6′b), 4.83 (*d*, *J* = 8.6 Hz, H-1′), 4.96 (*dd*, *J* = 8.6 and 9.6 Hz, H-2′), 5.05 (*t*, *J* = 9.6 Hz, H-4′), 5.19 (*t*, *J* = 9.6 Hz, H-3′), 5.21 (*br s*, H-6), 5.25 (*d*, *J* = 2.2 Hz, H-1), 5.30 (*dd*, *J* = 5.2, 0.9 Hz, H-8), 6.48 (*br s*, H-3); ^{13}C NMR: Table 1.

Glucosylmentzefoliol decaacetate (**3a**). $[\alpha]_D^{20}$ −19.3° ($CHCl_3$; *c* 1.1); elem. anal. found: C, 49.8; H, 5.5; Cl, 3.5. $C_{41}H_{53}O_{25}Cl$ requires: C, 50.2; H, 5.4; Cl, 3.6%. ^1H NMR (200 MHz, $CDCl_3$): δ 1.92, 1.94, 1.95, 1.96 (× 2), 1.97, 2.01, 2.02, 2.03, 2.07 (3H, each *s*, MeCO × 10), 2.64 (1H, *dddd*, *J* = 8.5, 1.5, 1.3, and 0.5 Hz, H-5), 2.73 (1H, *ddd*, *J* = 8.5, 2.4 and 0.8 Hz, H-9), 3.63 and 3.67 (1H each, 1 *ddd* each, *J* = 2.3, 4.5 and 9.5 Hz, and *J* = 2.2, 4.6 and 9.7 Hz, respectively, H-5′ and H-5″), 3.99 (1H, *ddd*, *J* = 1.5, 2.6 and 5.4 Hz, H-7), 4.08 (2H, *m*, H-6′a and H-6″a), 4.17 (2H, *m*, H-6′b and H-6″b), 4.80 and 4.82 (1H, each, *d*, *J* = 8.2 and 8.6 Hz, respectively, H-1′ and H-1″), 4.91–5.17 (6H, H-2′, H-2″, H-3′, H-3″, H-4′, H-4″), 5.20 (1H, *br s*, H-6), 5.23 (1H, *dd*, *J* = 5.4 and 0.8 Hz, H-8), 5.28 (1H, *d*, *J* = 2.4 Hz, H-1), 6.26 (1H, *br s*, H-3); ^{13}C NMR: Table 1.

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