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CARDENOLIDES FROM *ERYSIMUM CHEIRANTHOIDES*

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Key Word Index—*Erysimum cheiranthoides*; Cruciferae; cardenolide; strophadogenin glucoside; , cheiranthoside; erysimoside; olitoriside; boiviose.

Abstract—Three new cardiac glycosides were isolated along with two known cardenolides from the seeds of *Erysimum cheiranthoides*. The new ones were characterized by spectral methods as 16β-hydroxystrophanthidin (strophadogenin) 3-*O*-β-glucopyranosyl-(1 → 4)-β-boiviopyranoside, strophadogenin 3-*O*-α-rhamnopyranosyl-(1 → 4)-β-digitoxopyranoside and strophanthidin 3-*O*-α-rhamnopyranosyl-(1 → 4)-β-digitoxopyranoside, named cheiranthosides I, II and III, respectively.

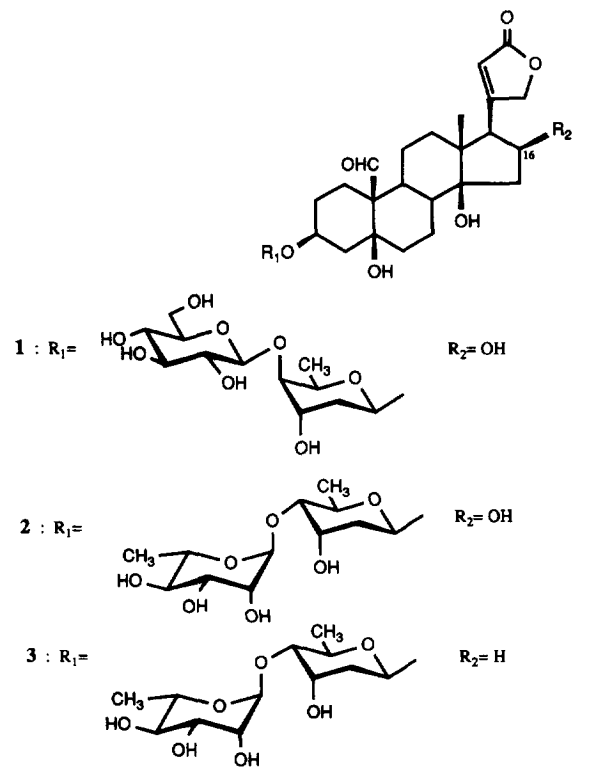
INTRODUCTION

Erysimi Herba, the whole plant of *Erysimum cheiranthoides* (Cruciferae), is a Chinese crude drug used for reducing a high temperature and inducing diuresis [1]. The isolation and structure elucidation of several cardiac glycosides, strophanthin-β, corchonoside A, erysimoside, helveticoside and helveticosol, were reported previously [1, 2]. As a part of our continuing chemical studies on the various glycosides, we have investigated the glycosides of the seeds.

RESULTS AND DISCUSSION

The methanolic extract of the seeds of *E. cheiranthoides* was partitioned between hexane and water. Chromatographic analysis using a combination of MCI gel, silica gel and ODS provided three new glycosides, cheiranthosides I, II and III (**1**, **2** and **3**), along with two known glycosides, olitoriside (strophanthidin 3-*O*-glucosyl boivioside) (**4**) [3] and erysimoside (strophanthidin 3-*O*-glucosyl digitoxoside) (**5**) [3], and rutin.

Cheiranthoside I (**1**) showed a $[M - H]^-$ ion peak at *m/z* 711 and fragment peaks at *m/z* 549 $[M - H -$ hexose$]^-$, and 419 [*m/z* 549 − dideoxyhexose]$^-$ in the negative ion FAB-mass spectrum. By comparing the ^{13}C NMR spectrum of **1** with that of **4**, it was observed that the signals due to C-15, C-16 and C-17 of the aglycone were shifted by + 11.0, + 45.0 and + 8.1 ppm, respectively. In the ^1H–^1H COSY spectrum, the signals due to H-17 (δ3.28, 1H, *d*, *J* = 8.0 Hz) H-16 (δ4.96, 1H, *dt*, *J* = 2.0, 8.0 Hz) and H_2-15 (δ2.70, 1H, *dd*, *J* = 8.0, 14.4 Hz); (δ2.14, 1H, *m*) were assigned. This evidence indicated the occurrence of a hydroxy group attached to C-16 on strophanthidin. The configuration of the hydroxyl group at C-16 was assigned as β, based on the *J* value (8Hz) between H-16 and H-17 [4], and therefore the aglycone was identified to be strophadogenin [5]. Moreover, the carbon signals due to the sugar residue were superimposable on those of **4**. Compound **1** was therefore determined to be strophadogenin 3-*O*-β-glucopyranosyl-(1 → 4)-β-boiviopyranoside, and was named cheiranthoside I.



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Cheiranthoside II (**2**) showed a $[M - H]^-$ ion peak at *m/z* 695 and fragment peaks at 549 $[M - H - rha]^-$ in the negative ion FAB-mass spectrum, which corresponds to the deoxy-compound of **1**. The ^{13}C NMR spectrum for **2** displayed the presence of one mole each of terminal α-rhamnopyranosyl residue and C_4-substituted β-digitoxopyranosyl residue, and the aglycone moiety signals were similar to those of **1**. Therefore, cheiranthoside II (**2**) was characterized as strophadogenin 3-*O*-α-rhamnopyranosyl-(1 → 4)-β-digitoxopyranoside.

Cheiranthoside III (**3**) displayed the molecular ion peak due to $[M - H]^-$, at *m/z* 679 as well as the fragment peak due to $[M - H - hexose]^-$ at *m/z* 533 in the negative ion FAB-mass spectrum. The ^{13}C NMR spectrum of **3** revealed that it had the same aglycone to that of **4** and the sugar moiety was the same as **2** thus indicating that **3** was strophanthidin 3-*O*-α-rhamnopyranosyl-(1 → 4)-β-digitoxopyranoside. The glycosides **1**–**5** were isolated from this plant for the first time.

Table 1. ^{13}C NMR Data for cheiranthosides I (**1**), II (**2**) and III (**3**), olitoriside (**4**) and Erysimoside (**5**) in C_5D_5N

	1	2	3	4	5
C-1	24.7	24.6	24.7	24.7	24.8
2	25.6	25.5	25.5	25.6	25.6
3	74.8	74.9	74.9	74.7	75.2
4	36.2	36.2	36.2	36.1	36.3
5	74.0	73.9	73.9	73.6	74.0
6	36.7	36.7	36.8	36.8	36.9
7	18.5	18.4	18.4	18.5	18.6
8	42.1	42.0	41.8	41.8	41.9
9	39.5	39.5	39.5	39.5	39.6
10	55.3	55.2	55.2	55.3	55.4
11	22.4	22.3	22.6	22.6	22.7
12	39.6	39.6	39.6	39.5	39.6
13	50.2	50.2	49.7	49.7	49.9
14	83.8	83.7	84.4	84.3	84.4
15	43.0	42.9	32.1	32.0	32.2
16	72.1	72.2	27.1	27.1	27.2
17	59.1	59.0	51.0	51.0	51.1
18	16.7	16.6	15.9	15.9	16.0
19	208.5	208.5	208.5	208.5	208.6
20	174.6	174.5	175.7	175.7	175.7
21	76.7	76.6	73.7	73.7	73.7
22	120.3	120.3	117.7	117.7	117.8
23	172.3	172.3	174.4	174.5	174.5
boiv C-1	98.3	97.6	97.6	98.2	97.6
(or dig C-1)					
2	35.1	39.6	39.4	35.0	39.0
3	66.1	68.8	68.8	66.0	69.2
4	76.4	82.3	82.3	76.2	83.4
5	69.5	67.3	67.3	69.4	67.7
6	17.6	18.4	18.3	17.5	18.6
glc c-1	103.2	104.0	104.0	103.1	106.1
(or rha C-1)					
2	74.7	72.4	72.4	74.7	75.0
3	78.4	72.2	72.2	78.3	78.4
4	71.9	73.7	73.7	71.8	71.6
5	78.5	70.3	70.3	78.4	78.5
6	63.0	18.4	18.4	62.9	62.6

EXPERIMENTAL

Optical rotations were taken with a JASCO DIP-360 digital polarimeter ($l = 0.5$). ^1H (400 MHz) and ^{13}C (100 MHz) NMR: with TMS as an internal standard. FAB and EI-MS: JEOL JMS DX-303HF mass spectrometer. TLC was performed on precoated silica gel 60 F_{245} (Merck) and detection was achieved by spraying 10% H_2SO_4 following by heating. CC: silica gel (270–400 mesh, Merck), Chromatorex ODS (30–50 mesh, Fuji Silysia Chemical Ltd.) and MCI gel CHP-20P (Mitsubishi Chemical Ind.).

Extraction and separation. The seeds (2.5 kg) of *E. cheiranthoides* were extracted with MeOH, and the extract (189 g) was partitioned between *n*-hexane and H_2O. The aq. layer (123 g) was subjected to CC over MCI gel CHP-20P, eluting sequentially with H_2O, 40%, 60%, 80%, and 100% MeOH, to provide five frs (fr. 1–5). Fr. 2 (40% MeOH eluate, 10 g) was subjected to CC over Sephadex LH-20 (MeOH) to give olitoriside (**4**) (21 mg), erysimoside (**5**) (8 mg) and rutin (9 mg). Fr. 3 (60% MeOH eluate, 18 g) was subjected to CC over silica gel ($CHCl_3$–MeOH–H_2O, 8:2:0.2) and ODS (50% MeOH) to give cheiranthosides I (**1**, 39 mg), II (**2**, 42 mg), and III (**3**, 91 mg).

Cheiranthoside I (**1**). White amorphous powder, $[\alpha]_D^{27} + 4.1°$ ($c = 0.94$, MeOH). Positive ion FAB-MS (*m/z*): 735.3242 [Calcd for $C_{35}H_{52}O_{15}Na$: 735.3204, $[M + Na]^+$. Negative ion FAB-MS (*m/z*): 711 $[M - H]^-$, 549 $[M - H - glc]^-$, 419 [*m/z* 549 − boi]$^-$. ^1H NMR (pyridine d_5): δ 1.10 (3H, *s*, H_3-18), 1.60 (3H, *d*, $J = 6.6$ Hz, boi H_3-6), 1.90 (1H, *br d*, $J = 16.2$ Hz, H_a-7), 2.43 (1H, *m*, H_b-7), 2.07, 2.43 (each 1H, *m*, boi H-2), 2.30 (1H, *m*, H-8), 2.14 (1H, *m*, H-15), 2.70 (1H, *dd*, $J = 8.0$, 14.3 Hz, H-15), 3.28 (1H, *d*, $J = 8.0$ Hz), 3.85 (1H, *m*, glc H-5), 3.98 (1H, *t*, $J = 8.4$ Hz, glc H-2), 4.02 (1H, *t*, $J = 3.0$ Hz, boi H-4), 4.17 (1H, *br t*, $J = 8.4$ Hz, glc H-4), 4.18 (1H, *br t*, $J = 8.4$ Hz, glc H-3), 4.34 (1H, *dd*, $J = 5.9$, 11.7 Hz, glc H-6), 4.36 (1H, *m*, H-3), 4.48 (1H, *dq*, $J = 1.8$, 6.6 Hz, boi H-5), 4.54 (1H, *dd*, $J = 2.6$, 11.7 Hz, glc H-6), 4.75 (1H, *ddd*, $J = 3.0$, 3.3, 3.3 Hz, boi H-3), 4.90 (1H, *d*, $J = 7.7$ Hz, glc H-1), 4.96 (1H, *br dt*, $J = 2.0$, 8.0 Hz, H-16), 5.38 (1H, *dd*, $J = 1.8$, 9.9 Hz, boi H-1), 5.55, 5.69 (each 1H, *dd*, $J = 1.8$, 18.1 Hz, H_2-21), 6.23 (1H, *t*, $J = 1.8$ Hz, H-23), 10.38 (1H, s, H-19).

Cheiranthoside II (**2**). White amorphous powder, $[\alpha]_D^{27} + 6.9°$ ($c = 1.11$, MeOH). Positive FAB-MS (*m/z*): 719.3254 [Calcd for $C_{35}H_{52}O_{14}Na$: 719.3255, $[M + Na]^+$. Negative ion FAB-MS (*m/z*): 695 $[M - H]^-$, 549 $[M - H - rha]^-$. ^1H NMR (pyridine d_5): δ 1.10 (3H, *s*, H_3-18), 1.35 (3H, *d*, $J = 6.2$ Hz, dig H_3-6), 1.56 (3H, *d*, $J = 6.2$ Hz, rha H_3-6), 1.91 (1H, *br d*, $J = 10.2$ Hz, H_a-7), 2.54 (1H, *m*, H_b-7), 1.94, 2.31 (each 1H, *d*, $J = 13.5$, dig H-2), 2.19, (1H, *m*, H-15), 2.70 (1H, *dd*, $J = 8.6$, 14.4 Hz, H-15), 3.30 (1H, *d*, $J = 8.1$ Hz, H-17), 3.63 (1H, *dd*, $J = 2.9$, 9.5 Hz, dig H-4), 4.34 (1H, *m*, H-3), 4.98 (1H, *dt*, $J = 2.2$, 8.3 Hz, H-16), 5.42 (1H, *dd*, $J = 2.2$, 9.5 Hz, dig H-1), 5.49 (1H, *d*, $J = 1.8$ Hz, rha H-1), 5.57, 5.72 (each 1H, *dd*, $J = 1.8$, 18.3 Hz, H_2-21), 6.26 (1H, *t*, $J = 1.8$ Hz, H-23), 10.43 (1H, *s*, H-19).

Cheiranthoside III (**3**). White amorphous powder, $[\alpha]_D^{27}$ + 7.1° (*c* = 1.07, MeOH). Positive FAB-MS (*m/z*): 703.3312 [Calcd for $C_{35}H_{52}O_{13}Na$: 703.3305, $[M + Na]^+$. Negative FAB-MS (*m/z*):679 $[M - H]^-$, 533 $[M - H - rha]^-$. ^1H NMR (pyridine d_5): δ1.00 (3H, *s*, H_3-18), 1.36 (3H, *d*, *J* = 6.2 Hz, dig H_3-6), 1.65 (3H, *d*, *J* = 5.8 Hz, rha H_3-6), 1.92, 1.97 (each 1H, *d*, *J* = 7.0 Hz, H-7), 2.45, 2.53 (each 1H, *d*, *J* = 11.7 Hz, dig H_2-2), 2.78 (1H, *br d*, *J* = 8.8 Hz, H-17), 4.34 (1H, *m*, H-3), 5.03, 5.29 (each 1H, *dd*, *J* = 1.5, 17.9 Hz, H_2-21), 5.40 (1H, *dd*, *J* = 1.8, 9.5 Hz, dig H-1), 5.49 (1H, *br s*, rha H-1), 6.26 (1H, *br s*, H-23), 10.40 (1H, *s*, H-19).

Olitoriside (**4**). White amorphous powder, $[\alpha]_D^{29}$ + 9.8° (*c* = 0.71, MeOH). Negative ion FAB-MS (*m/z*): 695 $[M - H]^-$, 533, 403, 385. ^1H NMR (pyridine d_5): δ 0.99 (3H, *s*, H_3-18), 1.61 (3H, *d*, *J* = 6.2 Hz, boi H_3-6), 2.78 (1H, *m*, H-17), 3.87 (1H, *m*, glc H-5), 3.98 (1H, *t*, *J* = 7.7 Hz, glc H-2), 4.02 (1H, *t* like, *J* = 3.0 Hz, boi H-4), 4.17 (2H, *m*, glc H-3, 4), 4.33 (1H, *dd*, *J* = 5.9, 11.7 Hz, glc H-6), 4.37 (1H, *m*, H-3), 4.50 (1H, *m*, boi H-5), 4.52 (1H, *dd*, *J* = 2.6, 11.7 Hz, glc H-6), 4.75 (1H, *ddd*, *J* = 2.9, 3.0, 3.3 Hz boi H-3), 4.90 (1H, *d*, *J* = 7.7 Hz, glc H-1), 5.39 (1H, *dd*, *J* = 1.8, 9.9 Hz, boi H-1), 5.03, 5.26 (each 1H, *dd*, *J* = 1.8, 18.3 Hz, H_2-21), 6.13 (1H, *t*, *J* = 1.8 Hz, H-23), 10.39 (1H, *s*, H-19).

Erysimoside (**5**). White amorphous powder, $[\alpha]_D^{27}$ + 7.8° (*c* = 0.50, MeOH). Negative ion FAB-MS (*m/z*): 695 $[M - H]^-$, 533, 403, 365. ^1H-NMR (pyridine d_5): δ1.00 (3H, *s*, H_3-18), 1.63 (3H, *d*, *J* = 6.2 Hz, dig H_3-6), 2.78 (1H, *m*, H-17), 4.71 (1H, *br s*, dig H-3), 4.99 (1H, *d*, *J* = 7.7 Hz, glc H-1), 5.03, 5.29 (each 1H, *d*, *J* = 18.0 Hz, H_2-21), 5.39 (1H, *br d*, *J* = 9.0 Hz, dig H-1), 6.12 (1H, *t*, *J* = 1.8 Hz, H-23), 10.40 (1H, *s*, H-19).

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