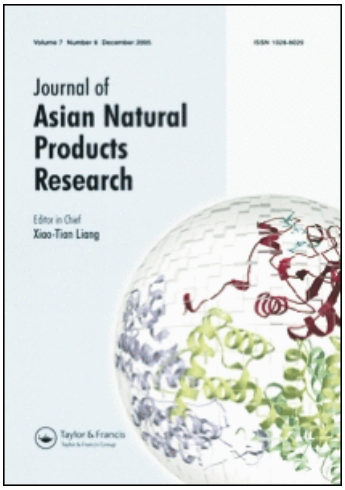

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Synthesis of 6-*O*-methyl ether of Scorzocreticin and Scorzocreticoside I, metabolites from *Sorzonera cretica*

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6-*O*-methyl ether of racemic scorzocreticin (**1a**) and its 8-*O*-β-D-glucoside, scorzocreticoside I (**1b**), isolated from Greek endemic species *Scorzonera cretica* have been synthesized. 6,8-Dimethoxy-3-(4-methoxyphenyl)isocoumarin (**3**) was obtained by reaction of 3,5-dimethoxyhomophthalic acid (**2**) with 4-methoxy-benzoyl chloride at elevated temperature. Hydrolysis of isocoumarin (**3**) to keto acid (**4**) followed reduction and spontaneous cyclodehydration to afford (±)-6,8-dimethoxy-3-(4-methoxyphenyl)-3,4-dihydroisocoumarin (**5**) which was regioselectively demethylated to (±)-6-*O*-methylscorzocreticin (**6**). Glycosylation of the latter using 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide in the presence of silver carbonate in quinoline under Koenigs-Knorr conditions afforded 6-methoxy-8-*O*-glucoside tetraacetate (**7**) as a 1:1 diastereomeric mixture. Finally, deacetylation of (**7**) using sodium methoxide afforded the diastereomeric mixture of R and S 6-*O*-methylscorzocreticin 8-*O*-glucosides (**8**). The 6-*O*-methyl ether of natural scorzocreticoside I (**1b**) was separated and identified on the basis of sign of optical rotation.

Keywords: Isocoumarin glucoside; Scorzocreticin; Scorzocreticoside I

1. Introduction

A-L Skaltsounis isolated three new compounds, the dihydroisocoumarin scorzocreticin (**1a**), its 8-*O*-β-D-glucoside scorzocreticoside I (**1b**) and 8-*O*-β-D-disaccharide scorzocreticoside II, as well as 11 known compounds from the Greek endemic species *Scorzonera cretica* [1]. The genus *Scorzonera* (Compositae) includes 28 European species, 11 of which are found in Greece, four of which, as well as one subspecies, are endemic. *Scorzonera cretica* Willd. is endemic to Crete and the South Aegean region. The plant is commonly used in traditional Cretan cuisine as an ingredient in savory meat dishes. The structures of new compounds were revealed as 6,8-dihydroxy-3-(4-methoxyphenyl)-3,4-dihydro isocoumarin (scorzocreticin) (**1a**), 8-*O*-β-D-glucopyranosylscorzocreticin (scorzo-creticoside I) (**1b**), and 8-*O*-[R-L-rhamnopyranosyl (1–6)-β-D-glucopyrano syl]sco-rzocreticin (scorzocreticoside II). The absolute configuration at stereocentre C-3 was determined by a comparison of their circular dichroism spectra with that of mellein used as reference [2,3]. Scorzocreticin (**1a**) gave

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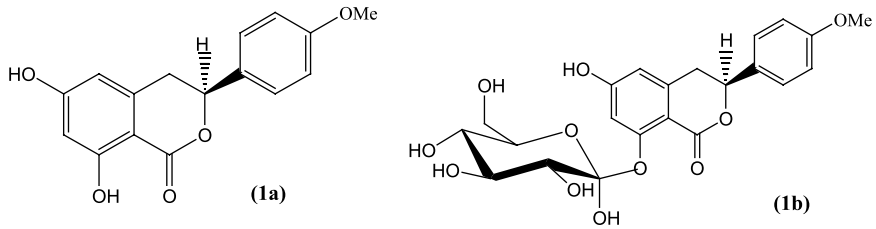


Figure 1. Scorzocreticin (**1a**) and Scorzocreticoside I (**1b**), from Greek endemic species *Scorzonera cretica*.

a positive Cotton effect at 233 nm and a negative Cotton effect at 255 nm, as in the case of mellein. This suggested that the two compounds possess the same absolute configuration at C-3, which in the case of **1a** is *S*. The CD spectrum of (**1b**) was similar to that of (**1a**) which indicated that the absolute configuration at C-3 is identical to (**1a**) (Figure 1).

A synthesis of (±)-6-*O*-methylscorzocreticin and 6-*O*-methylscorzocreticoside I was undertaken as a continuation of our interest towards this class of natural products [4–7].

2. Results and discussion

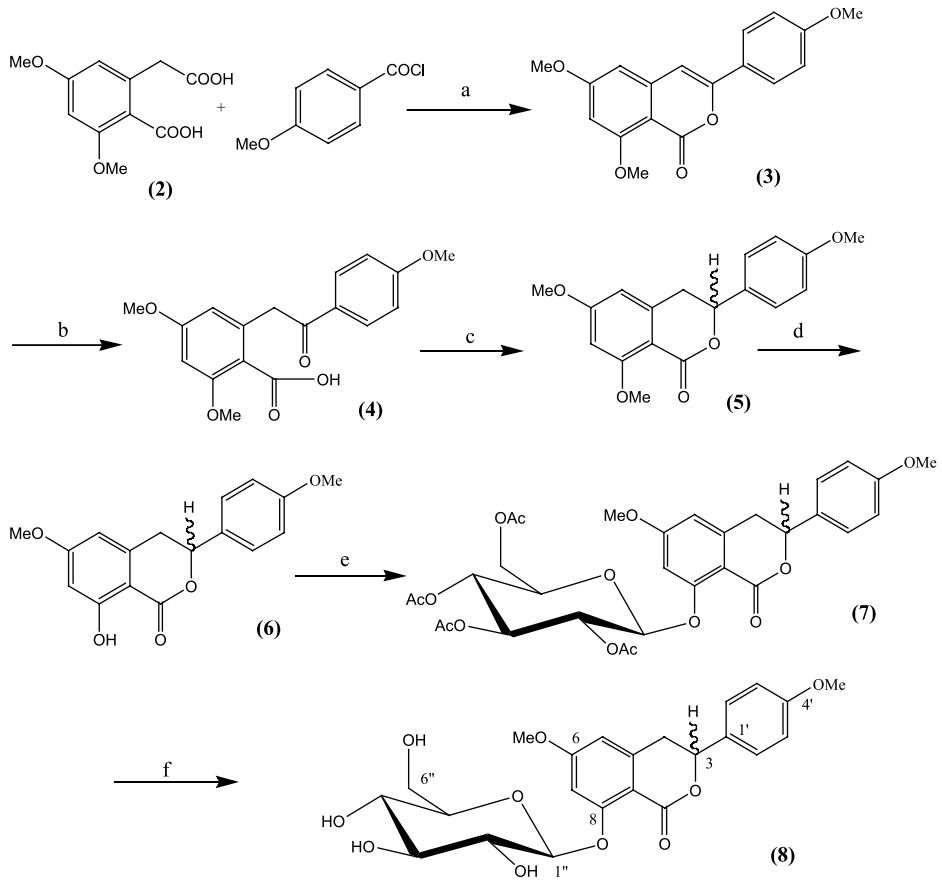
6,8-Dimethoxy-3-(4-methoxyphenyl)isocoumarin (**3**) was obtained in good yield by direct reaction of 3,5-dimethoxyhomophthalic acid (**2**) [8,9] with 4-methoxybenzoyl chloride at elevated temperature [10,11]. The isocoumarin showed the characteristic olefinic proton singlet (H-4) at δ 6.64 in the ^{1}H NMR and signals at δ 100.6 (C-4) and 154.1 (C-3) in the ^{13}C NMR spectrum; the δ-lactonic carbonyl absorption was observed at 1721 cm^{-1}.

Alkaline hydrolysis of the isocoumarin (**3**) furnished the 2-(4-methoxybenzoyl-methyl)-4,6-dimethoxybenzoic acid (**4**). The keto acid showed characteristic two proton singlet at δ 4.02 ($ArCH_2$) in the ^{1}H NMR and that at δ 45.3 (C-4) in ^{13}C NMR spectrum. The ketonic and carboxylic carbonyl absorptions were observed in IR spectrum at 1716 and 1695 cm^{-1}, respectively.

Reduction of the keto acid (**4**) using sodium borohydride [12,13] directly afforded the (±)-6,8-dimethoxy-3-(4-methoxyphenyl)-3,4-dihydroisocoumarin (**5**) *via* spontaneous cyclodehydration of intermediate racemic hydroxy acid [14]. Diastereotopy of methylene protons (C4) adjacent to newly generated stereocentre (C3) in dihydroisocoumarin (**5**) was observed [15,16]. Thus, the double doublet of the hydrogen *cis* to phenyl ring located slightly upfield at δ 3.08 ppm (J_{gem} = 16.3 Hz, J_{cis} = 3.2 Hz) and that of *trans* hydrogen slightly downfield at δ 3.16 ppm (J_{gem} = 16.5, J_{trans} = 12.6 Hz). The double doublet for H-3 appeared at δ 5.52 with J_{vic} = 12.0 Hz (*trans* H4) and J_{vic} = 3.16 Hz. (*cis* H4). ^{13}C NMR spectrum showed signals at δ 80.03 and 35.7 ppm for C-3 and C-4, respectively. The δ-lactonic carbonyl absorption appeared at 1720 cm^{-1} in the IR spectrum.

Regioselective demethylation of the 8-methoxyl in (±)-6,8-dimethoxy-3-(4-methoxyphenyl)-3,4-dihydroisocoumarin (**5**) was accomplished under mild conditions using boron tribromide (−78°C, 15 min) to furnish the (±)-8-hydroxy-6-methoxy-3-(4-methoxyphenyl)-3,4-dihydroisocoumarin (**6**). Characteristic lowering of lactonic carbonyl absorption to 1685 cm^{-1} due to chelation was also observed (Scheme 1).

Glycosylation was carried out using 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide [17] in the presence of silver carbonate in quinoline under Koenigs-Knorr conditions



Scheme 1. Reagents and conditions: (a) 200°C, 4 h, 76%; (b) 5% KOH, EtOH, 4 h reflux, 85%; (c) $NaBH_4$, EtOH 2 h, r.t. 80%; (d) BBr_3, CH_2Cl_2, −78°C, 15 min 70%; (e) D-glucosyl bromide, Ag_2CO_3, quinoline, 3 h r.t., 75%; (f) $NaOCH_3$, CH_3OH-$CHCl_3$ r.t. 2 h, then Dowex 50W-8X (H^+), 85%.

to furnish an inseparable 1:1 diastereomeric mixture of R and S 6-*O*-methylscorzocreticin 8-*O*-glucoside tetraacetate (**7**) [18,19]. The use of 1.5 equivalent of acetobromo glucose relative to phenolic dihydroisocoumarin (**6**) gave (**7**) in 75% yield. The latter was characterized by disappearance of the H-bonded hydroxyl signal, appearance of sharp bands at 1756 cm^{-1} for the acetyl carbonyl stretching in addition to that at 1718 cm^{-1} for non chelated lactonic carbonyl in the IR spectra. In ^{1}H-NMR spectra the characteristic doublet at δ 4.90 for the anomeric proton (with a coupling constant of 7.2 Hz) of β-D-glucopyranosyl moiety and singlets for the acetate protons at δ 2.03 − 2.08 were observed. The diastereotopic methylenic protons at C-6″ (due to the chiral center at C-5″) showed two double doublet at δ 4.19 (J = 12.0, 2.2) and at δ 4.29 (J = 12.0, 5.5) and the multiplet (ddd) for C-5″ proton appeared at δ 3.92. The anomeric carbon appeared at δ 103.5 and C-5″ & C-6″ at δ 71.4 and δ 61.5, respectively. Finally, the deacetylation of the 6-methoxy-8-*O*-glucoside tetraacetate (**7**) was accomplished using sodium methoxide to afford 1:1 diastereomeric mixture of R and S 6-*O*-methylscorzocreticin 8-*O*-glucoside (**8**) [20–22]. The mixture was separated by carefully repeated thick layer chromatography using chloroform-methanol-water system to afford the 'natural' 6-*O*-methyl scorzocreticoside I (**1b**) identified by its sign of rotation alongwith the unnatural isomer.

Regioselective cleavage of the 6-methoxy ether in (**8**) leaving 4′methoxyl intact was attempted under a variety of conditions but was not successful. However, the 4′-methoxyl could be cleaved selectively without affecting 6-methoxyl but the reverse was not possible. The results indicate that the relative ease of cleavage of methoxy ethers in dihydroisocoumarins observes the following order: 8-MeO > 4′-MeO > 6-MeO.

3. Experimental

3.1 General experimental procedure

^{1}H and ^{13}C NMR spectra were determined as $CDCl_3$ or acetone-d_6 solutions at 400 MHz (Bruker AM-400) and 100 MHz (Bruker AM-100) machines, respectively. FT IR spectra were recorded on an FTS 3000 MX spectrophotometer; Mass Spectra (EI, 70 eV) on a MAT 312 instrument and elemental analyses were conducted using the CHN-Rapid Heräus. Optical rotations were measured on a PE-241 MC polarimeter. All compounds were purified by thick layer chromatography using silica gel 60HF from Merck.

3.2 6,8-Dimethoxy-3-(4-methoxyphenyl)isocoumarin (3)

A stirred mixture of 3,5-dimethoxyhomophthalic acid (**2**) (0.5 g, 2.0 mmol) and 4-methoxybenzoyl chloride (1.42 g, 8.33 mmol) was heated in an oil bath at 200° C for 4 h. Thick layer chromatography of the residue using petroleum ether: ethyl acetate (8:2) followed by recrystallization from MeOH gave the isocoumarin (**3**) (0.49 g, 1.58 mmol, 76%) as orange yellow needles. IR (KBr): 1721, 1640, 1598, 1565, 1516, 1254, 1209, 1151, 991 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$): 3.89 (3H, s, OMe), 3.92 (3H, s, OMe), 3.95 (3H, s, OMe), 6.39 (1H, d, $J = 2.2$ Hz, H-7), 6.46 (1H, d, $J = 2.2$ Hz, H-5), 6.64 (1H, s, H-4), 6.88 (2H, d, $J = 8.4$ Hz, H-3′, 5′), 7.31 (2H, d, $J = 8.6$ Hz, H-2′, 6′); ^{13}C NMR (100 MHz, $CDCl_3$): 165.3 (C1, C = O), 164.5 (C8), 161.0 (C4′), 159.8 (C6), 154.1 (C3), 137.7 (C4a), 135.0 (C1′), 126.8 (C2′, C6′), 119.5 (C3′, C5′), 100.9 (C8a), 100.1 (C5), 100.6 (C4), 99.7 (C7), 56.4 (MeO-6), 55.7 (MeO-8), 55.4 (MeO-4′); EIMS *m/z* (%): 312 [M^+] (31.5), 282 (37.0), 256 (11.6), 178 (100); elemental analysis found (%): C 69.0, H 5.26 calcd. for $C_{18}H_{16}O_5$: C 69.22, H 5.16.

3.3 4,6-Dimethoxy-2-(4′-methoxybenzoylmethyl)benzoic acid (4)

A solution of isocoumarin (**3**) (0.4 g, 1.28 mmol) in ethanol (40 mL) and potassium hydroxide (5% 40 mL) was refluxed for 4 h. The solvent was rotary evaporated, cold water (10 mL) was added and the reaction mixture acidified using conc. hydrochloric acid. The aqueous phase extracted with ethyl acetate (3 × 50 mL), the organic phase separated, dried ($MgSO_4$) and concentrated to yield a crude solid which was recrystallized from MeOH to give 4,6-dimethoxy-2-(4′methoxybenzoyl-methyl)benzoic acid (**4**) (0.35 g, 1.08 mmol, 85%). IR (film, ν, cm^{-1}): 3065, 1716, 1695, 1601, 1202, 1162; ^{1}H NMR (400 MHz, acetone-d_6, δ, ppm) 3.82 (s,3H, MeO-4), 3.88 (s,3H, MeO-2), 3.95 (3H, s, OMe-4′), 4.02 (s, 2H, Ar-CH_2), 6.30 (d, $J = 2.0$, 1H, H3), 6.41 (d, $J = 2.2$, 1H, H5), 6.88 (2H, d, $J = 8.4$ Hz, H-3′, 5′), 7.31 (2H, d, $J = 8.4$ Hz, H-2′, 6′) 11.2 (1H, br s COOH); ^{13}C NMR (100 MHz acetone-d_6, δ, ppm): 170.8 (COOH), 195.5 (C3), 45.3 ($ArCH_2$), 139.2 (C6), 99.8 (C5), 165.5 (C4), 98.3 (C3), 164.5 (C2), 109.4 (C8a), 135.2 (C1′), 129.3 (C2′, C6′), 129.9 (C3′, C5′), 128.0 (C4′), 56.4 (MeO-4), 55.7 (MeO-2) 55.4 (MeO-4′). EIMS *m/z* (%): 330

[M^+] (11.5), 312 (54.7) 282 (37.09), 256 (11.6), 177 (100); elemental analysis found (%): C 65.27, H 5.10 calcd for $C_{18}H_{18}O_6$: C 65.45, H 5.07.

3.4 (±)-6,8-Dimethoxy-3-(4-methoxyphenyl)-3,4-dihydroisocoumarin (5)

Sodium borohydride (0.96 g, 20 mmol) was added portionwise to a stirred solution of (**4**) (0.3 g, 0.91 mmol) in ethanol (30 ml) and water (75 ml). The reaction mixture was stirred for 2 h at room temperature, diluted with water (150 ml), acidified with conc. HCl and stirred for further 2 h. It was then saturated with ammonium sulfate, and extracted with EtOAc (3 × 100 ml). The layers were separated and the organic layer dried ($MgSO_4$) and concentrated. Preparative TLC (Petroleum ether: ethyl acetate 7:2) afforded (**5**) as yellow prisms (0.23 g, 0.73 mmol, 80%). EIMS *m/z* (%): 314 (M^+, 56), 312 (14), 178 (100), 147 (14), 118 (42), 90 (59), 89 (15); IR (film), 2850, 1720, 1710, 1604, 1583, 1572, 1464, 1198, 832 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.08 (dd, 1H, J_{gem} 16.3 Hz, J_{cis} 3.2 Hz, H-4), 3.16 (dd, 1H, J_{gem} 16.5, J_{trans}12.6, H-4), 3.80 (s, 3H, MeO-4′), 3.85 (s, 3H, MeO-6), 3.94 (s, 3H, MeO-8), 5.52 (dd, J = 12.0, 3.6 H-3), 6.37 (d, J = 2.1, 1H, H-7), 6.45 (d, J = 2.2, 1H, H-5), 6.89 (d, J = 7.5, 2H, H-3′, H-5′), 7.40 (d, J = 7.5, 2H, H-2′, H-6′) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.8 (C1), 163.8 (C6), 163.2 (C8), 162.1 (C4′), 142.0 (C4a), 131.2 (C1′), 126.7 (C2′, C6′), 117.3 (C3′, C5′), 107.2 (C5), 103.9 (C8a), 102.8 (C7), 81.6 (C3), 55.7 (MeO-6). 55.6 (MeO-4′), 56.4 (MeO-8), 36.0 (C4); elemental analysis found (%): C 68.64, H 5.76 calcd for $C_{18}H_{18}O_5$: C 68.78, H 5.79.

3.5 (±)-8-Hydroxy-6-methoxy-3-(4-methoxyphenyl)-3,4-dihydroisocoumarin {(±)-6-O-methylscorzocreticin (6)}

A 1 M solution of BBr_3 in CH_2Cl_2 (1.26 ml, 1.26 mmol) was injected to a stirred solution of (**5**) (0.2 g, 0.63 mmol) in dry CH_2Cl_2 (8 ml) at −78°C, under Ar. After stirring for 15 min at this temperature the reaction mixture was warmed to room temperature and stirred further for 20 mins. The reaction mixture was poured into ice-water (20 ml) and stirred for 10 min. The layers were separated and the aqueous layer extracted with CH_2Cl_2 (3 × 30 ml). The combined organic phase were dried ($MgSO_4$) and concentrated. Preparative TLC using (petroleum ether: ethyl acetate 7:3) afforded 6 (132 mg, 0.44 mmol, 70% yield) as a pale yellow solid. EIMS *m/z* (%): 300 (M^+, 56), 178 (100), 147 (14), 118 (42), 90 (59), 89 (15); IR (film), 2850, 1685, 1604, 1583, 1572, 1464, 1198, 832 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.08 (dd, 1H, J_{gem} 16.3 Hz, J_{cis} 3.2 Hz, H-4), 3.16 (dd, 1H, J_{gem} 16.5, J_{trans}12.6, H-4), 3.79 (s, 3H, MeO-4′), 3.85 (s, 3H, MeO-6), 5.40 (dd, J 12.0, 3.5 H-3), 6.33 (d, J 2.1, 1H, H-7), 6.45 (d, J 2.2, 1H, H-5), 6.89 (d, J = 7.5, 2H, H-3′, H-5′), 7.40 (d, J = 7.5, 2H, H-2′, H-6′) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.8 (C1), 163.8 (C6), 163.2 (C8), 162.1 (C4′), 142.0 (C4a), 107.2 (C5), 103.9 (C8a), 102.8 (C7), 81.6 (C3), 35.7 (C4), 131.2 (C1′), 126.7 (C2′, C6′), 117.3 (C3′, C5′), 56.4 (MeO), 55.7 (MeO); Anal. Calcd. for $C_{17}H_{16}O_5$: C, 67.99 H, 5.37 found: 67.85 H, 5.23; elemental analysis found (%): C 67.85, H 5.23 calcd for $C_{17}H_{16}O_5$: C 67.99, H 5.37.

3.6 8-O-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-6-O-methylscorzocreticin (7)

A solution of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (250 mg, 0.6 mmol), Ag_2CO_3 (110 mg, 0.4 mmol) and 8-hydroxy compound (**6**) (120 mg, 0.4 mmol) in

quinoline (6 ml) was stirred for 3 h at room temperature. The reaction mixture was poured into methanol; the solution was filtered through a short pad of silica gel and rotary evaporated. The residue was dissolved into ethyl acetate and washed successively with 1 N HCl and brine, and dried over anhydrous $MgSO_4$. After evaporation, the resulting crude product was purified by thick layer chromatography (petroleum ether-AcOEt 1:1) to afford (**7**) (190 mg, 0.3 mmol, 75%) as a white foam. The product was an inseparable diastereomers mixture (1:1) of R and S of 6-*O*-methylscorzocreticosides. IR (KBr) 3421, 1756, 1718, 1644, 1374, 1227 cm^{-1}; MS (70 eV): *m/z* (%) = 631(M^+,4.9), 571 (32), 300 (4.3), 271 (18), 206 (20), 191 (28), 177 (41), 163 (21),135 (19); ^1H NMR (400 MHz, $CDCl_3$): δ = 1.99 (6H, s, Ac-3″,4″), 2.01 (3H, s, Ac-6″), 2.06 (3H, s. Ac-2″), 3.0 (dd, 1H, J_{gem} 16.3 Hz, J_{cis} 3.2 Hz, H-4), 3.16 (dd, 1H, J_{gem} 16.5, J_{trans}12.6, H-4), 3.80 (s, 3H, MeO-4′), 3.85 (s, 3H, MeO-6), 3.92 (1H, ddd, *J* = 10.0, 5.4, 2.5 Hz, H-5″), 4.90 (1H, d, *J* = 7. 2 Hz, H-1″), 4.27 (IH, dd, *J* = 12.0, 5.5 Hz, H-6″b), 4.21 (1H, dd, *J* = 12.0, 2.1 Hz, H-6″a), 5.25 (3H, m, H-2″,3″,4″), 5.42 (dd, *J* 12.0, 3.65 H-3), 6.33 (d, *J* 2.1, 1H, H-7), 6.45 (d, *J* 2.2, 1H, H-5), 6.87 (d, *J* = 7.5, 2H, H-3′, H-5′), 7.41 (d, *J* = 7.5, 2H, H-2′, H-6′) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 170.5, 171.2 (Ac), 167.3 (C6), 165.4 (Ac), 163.7 (C8), 162.3 (C = O, lactonic), 155.7 (C3), 141.8 (C9), 132.0 (C1′), 129.3 (C6′), 13.9 (C-4a), 104.1 (C4), 103.5 (Cl″), 102.9 (C5), 102.6 (C7), 101.9 (C8a), 98.3 (C-4), 72.6 (C-2″), 71.3 (C-3″), 71.4 (C-5″), 61.5 (C-4″), 68.6 (C-6″), 56.6 (MeO), 29.7, 29.8 (2 CH_3, acetyl), 21.2 (C1′) 20.5, 20.6 (2 CH_3, acetyl); elemental analysis found (%): C 59.05, H 5.43 calcd for $C_{31}H_{34}O_{14}$: C 58.85, H 5.47.

3.7 3(R)-8-O-β-D-glucopyranosyl)-6-O-methylscorzocreticin (3(R)-6-O-methyl scorzocreticoside I) (8)

To a solution of tetra acetate (**7**) (150 mg, 0.24 mmol) in a mixture of CH_3OH (4 ml) and $CHCl_3$ (2 ml) was added $NaOCH_3$ (60 mg) at room temperature. After stirring for 2 h, the reaction mixture was neutralized with Dowex 50W-8X (H^+), filtered, and rotary evaporated. The residue was recrystallized from EtOH to afford (**8**) as 1:1 diastereomeric mixture of R and S 6-*O*-methylscorzocreticin 8-*O*-glucoside (**8**) in 85% yield. The mixture was separated by carefully repeated thick layer chromatography using $CHCl_3$-MeOH-H_2O (10:3:1) system to afford the natural 3(R)-6-*O*-methyl scorzocreticoside I (**1b**) as a white solid (44 mg, 0.096 mmol, 40% $[\alpha]_D^{25}$ −12.57° (c 0.3, MeOH); IR ν_{max} (KBr): = 2956, 1718, 1680, 1271, 741 cm^{-1}; MS (70 eV): *m/z* (%) = 462 (6.4), 300 (32), 206 (42), 191 (36), 177 (41), 163 (21),137 (12); ^1H NMR (400 MHz, $CDCl_3$): 3.80 (s, 3H, MeO), 3.87 (s, 3H, MeO), 3.93 (1H, ddd, *J* = 10.2, 5.5, 2.3 Hz, H-5″), 4.20 (1H, dd, *J* = 12.2, 2.4 Hz, H-6″a), 4.26 (1H, dd, *J* = 12.3, 5.4 Hz, H-6″b), 5.17-5.32 (3H, m, H-2″,3″,4″), 5.2 (d, 1H, *J* = 7.3, H1″), 6.47 (d, *J* = 2.2, 1H, H7), 6.54 (d, *J* = 2.2, 1H, H5) 6.53 (1H, d, *J* = 7.4 Hz, H-l″) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.3 (C1), 166.1 (C6), 163.7 (C8), 161.8 (C4′), 143.8 (C4a), 132.0 (C1′), 129.7 (C2′, C6′), 110.7 (C5), 108.2 (C8a), 106.2 (C7), 104.6 (C-l″), 115.6 (C3′,C5′), 81.4 (C3), 76.7 (C3″), 79.1.4 (C-5″), 73.9 (C2″), 71.5 (C4″), 63.4 (C6″), 56.5 (MeO), 56.1 (MeO), 37.9 (C4); elemental analysis found (%): C 59.72, H 5.69 calcd for $C_{23}H_{26}O_{10}$: C 59.74, H 5.67.

3(S)-6-O-methyl scorzocreticoside I (1b′) white solid (33 mg, 0.072 mmol, 35%) $[\alpha]_D^{25}$ + 8.94° (c 0.3, MeOH).

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