A new 4-oxazolidinone from *Sorghum halepense* (L.) Pers.

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Abstract: *Sorghum halepense* (L.) Pers. is known as invasive weed in the world. In this paper we report three rare natural products from this weed. The compounds include a new rare natural product 2,2-dimethyl-5-(4-hydroxyphenyl)-4-oxazolidinone (**1**), and two other known mandelic acid derivatives, ethyl 4-hydroxymandelate (**2**) and 4-hydroxymandelamide (**3**). The structures of these compounds were elucidated by extensive spectroscopic analysis (MS, IR, ^{1}H, ^{13}C NMR and 2D NMR).

1. Plant Source

Sorghum halepense (L.) Pers. (Johnson grass), a globally distributed allelopathic invasive grass of Mediterranean origin [1, 2], is listed as one of the ten worst weeds in the world [3] and among the 16 most troublesome exotic species in China. The *S. halepense* was studied first by us is aiming at isolation of allelochemicals that responsible for the successful invasion in China. Three rare natural products were isolated including a new oxazolidinone (**1**) and two known derivatives of mandelic acid (**2**, **3**) from the rhizomes of *S. halepense*. All of the three compounds were obtained from genus *Sorghum* for the first time.

The rhizomes of *S. helepense* were collected from the experimental fields of Institute of Plant Protection of Chinese Academy of Agricultural Sciences, in August 2007, and identified by Dr. Shouhui Wei (Voucher number WL070801).

2. Previous Studies

Previous studies of *S. halepense* led to isolation of dhurrin, taxiphyllin, prunasin, sorgoleone, chlorogenic acid, *p*-coumaric acid, *p*-hydroxybenzaldehyde, *p*-hydroxybenzyl alcohol, *p*-hydroxybenzoic acid, phloroglucinol, aliphatic acids from the rhizome of *S. halepense* [4, 5]. Also, we had isolated flavonoids and flavonolignans including salcolins A and B, tricin, luteolin and apigenin from the aerial parts of the Johnson grass [6]. Some of the compounds have allelopathic actives [4, 5, 7].

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3. Present Study

Air-dried rhizomes of *S. halepense* (3.0 kg) were ground and extracted with 90% EtOH. The extract was concentrated to a crude brown gum. The gummy substance was dissolved in water and sequentially partitioned by hexane, chloroform, ethyl acetate and *n*-butanol. Each organic solvent fraction was evaporated to dryness below 45°C.

The ethyl acetate fraction was subjected to column chromatography (CC) on silica gel (silica gel G60, 100-200 mesh; Qingdao, China) and eluted stepwise with chloroform-methanol mixtures of increasing polarity. The CC fractions were detected on thin layer chromatography [TLC; Qingdao, 0.25mm thickness, fluorescent indicator (F)-254, using $CHCl_3$: MeOH (95:5 to 60:40) as the solvent system], and combined into three main fractions (FI-FIII) based on their TLC behavior. Fraction I was separated by silica gel CC eluted with $CHCl_3$-MeOH (100:0-80:20) followed by Sephadex LH-20 CC to afford **1** (8.5 mg) and **2** (15.4 mg). Fraction III was separated by silica gel CC eluted with $CHCl_3$-MeOH (95:5-60:40) followed by reversed-phase C-18 silica gel CC eluted with MeOH-H_2O (2:3) to afford four subfractions (SF-I to SF-IV). The SF-IV was further separated by Sephadex LH-20 CC to afford **3** (46.3 mg).

The structures of these compounds were elucidated by extensive spectroscopic analysis (MS, IR, ^{1}H, ^{13}C NMR and 2D NMR). The compounds include a new rare natural product 2,2-dimethyl-5-(4-hydroxyphenyl)-4-oxazolidinone (**1**), and two other known mandelic acid derivatives, ethyl 4-hydroxymandelate (**2**) and 4-hydroxymandelamide (**3**).

2,2-dimethyl-5-(4-hydroxyphenyl)-4-oxazolidinone (1), $C_{11}H_{13}O_3N$, colorless needles, $[\alpha]_D^{25}$ +60.88 (c 0.001, MeOH); positive HRESI-MS (*m/z*): 230.07899 $[M + Na]^+$ (calcd. for $C_{11}H_{13}O_3NNa$ 230.07931); IR (KBr) v_{max}, 3252 (NH), 1695 (amide band I), 1518 (amide band II), 1270 (amide band III), 2983, 1665, 1615, 1599, 1456, 1420, 1387, 1373, 1223, 1209, 1162, 1037, 834, 813, 706, 669, 639, 564 cm^{-1}. ^{1}H NMR (600 MHz, methanol-d_4): δ 7.18 (2H, d, *J* = 8.4 Hz, H-2′, 6′), 6.75 (2H, d, *J* = 8.4 Hz, H-3′, 5′), 5.17 (1H, s, H-5), 1.53 (3H, s, H-1″), 1.49 (3H, s, H-2″). ^{13}C NMR (150 MHz, methanol-d_4): δ 173.5 (C-4), 157.7 (C-4′), 128.5 (C-2′, 6′), 127.8 (C-1′), 114.9 (C-3′, 5′), 90.5 (C-2), 79.2 (C-5), 28.0 (C-1″), 27.0 (C-2″).

Ethyl 4-hydroxymandelate (2), $C_{10}H_{12}O_4$, colorless amorphous powder; positive ESI-MS (*m/z*): 219 $[M + Na]^+$. ^{1}H NMR (600 MHz, methanol-d_4): δ 7.22 (2H, d, *J* = 8.4 Hz, H-2, 6), 6.75 (2H, d, *J* = 8.4 Hz, H-3, 5), 5.04 (1H, s, H-α), 4.10 (1H, m, H-1′), 1.13 (1H, t, H-2′). The ^{13}C NMR (150 MHz, methanol-d_4): δ 173.6 (C=O), 157.4 (C-4), 130.0 (C-1), 129.9 (C-2, 6), 115.0 (C-3, 5), 72.8 (C-α), 61.0 (C-1′), 13.1 (C-2′).

4-Hydroxymandelamide (3), $C_8H_9NO_3$, colorless amorphous powder; positive ESI-MS (*m/z*): 190 $[M + Na]^+$, negative ESI-MS (*m/z*): 166 $[M − H]^-$; ^{1}H NMR (600 MHz, methanol-d_4): δ 7.23 (2H, d, *J* = 8.8 Hz, H-2, 6), 6.72 (2H, d, *J* = 8.8 Hz, H-3, 5), 4.87 (1H, s, H-α). ^{13}C NMR (150 MHz, methanol-d_4): δ 177.7 (C=O), 157.2 (C-4), 131.2 (C-1), 128.1 (C-2, 6), 114.8 (C-3, 5), 73.8 (C-α).
. int.): *m/z* 464.1 $[M]^+$ (30), 432 (70), 360 (65), 303 (33), 302 $[M-glucose]^+$ (55), 179 (50), 161 (30), 162 (44), 57 (40), 44 (22); HREIMS: *m/z* 464.1329 (calcd. 464.1318 for $C_{22}H_{24}O_{11}$).
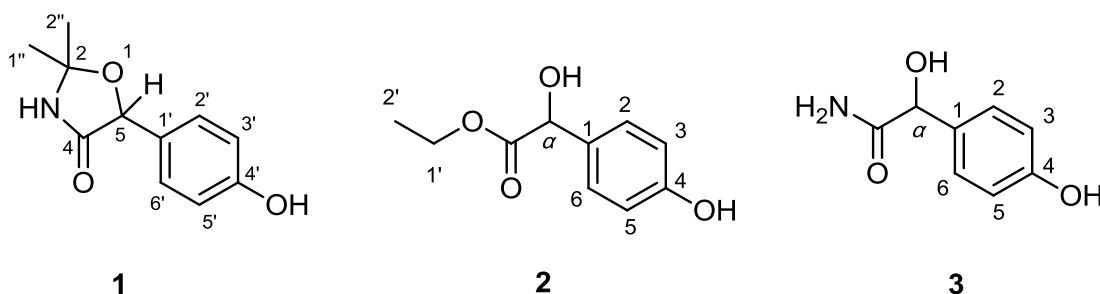

Figure 1. Structure of compounds (**1**-**3**) isolated from *S. halepense*

Compound **1** was isolated as a colorless amorphous powder. Its molecular formula was determined as $C_{11}H_{13}NO_3$ by the HRESIMS data of 230.07899 ($[M + Na]^+$, calc. 230.07876), with 6

degrees of unsaturation. The ^{1}H NMR data of δ 7.18 (2H, d, J = 8.4 Hz) and 6.75 (2H, d, J = 8.4 Hz), as well as the ^{13}C NMR data of δ 127.8, 157.7, 128.5 (× 2) and 114.9 (× 2) showed a *p*-hydroxyphenyl moiety, corresponding to 4 degrees of unsaturation. Furthermore, the occurrence of an amide moiety (1 degree of unsaturation) and a methine bearing an oxygen atom were indicated by combined analysis of the NMR signals of δ_C 173.5, 79.2 and δ_H 5.17 (1H, s), as well as the IR data of 3252 (secondary amino), 1695 (amide band I), 1518 (amide band II) and 1270 (amide band III) cm^{-1}, respectively. The above NMR data indicated a similar carbon skeleton for **1** and **3** (**Figure 1**). The main differences are the downfield shift of methine signal from δ 73.8 to 79.2, and the upfield shifts of carbonyl signal from δ 177.7 to 173.5, as well as phenyl carbon from δ 131.2 (C-1) to 127.8 (C-1′), respectively. By combined analysis of the HSQC spectrum, the remaining NMR data of **1** were assigned to one oxygenated quaternary carbon (δ_C 90.5, C-2), as well as two angular methyl groups [δ_H 1.53 (3H, s, H-1″), 1.49 (3H, s H-2″), and δ_C 28.0 (C-1″) and 27.0 (C-2″)], respectively. In the HMBC spectrum, the ^{1}H NMR data at δ_H 5.17 (H-5) showed cross peaks with the ^{13}C signals at δ 173.5 (C-4), 128.5 (C-2′, 6′) and 127.8 (C-1′), respectively. In addition, long range correlations were revealed between carbon signal at δ_C 90.5 (C-2) and the proton signals of two methyl groups (**Figure 2**). Though the cross peak between δ_C 90.5 (C-2) and δ_H 5.17 (H-5) was not observed in the HMBC spectrum, the epoxy between C-2 (δ 90.5) and C-5 (δ 79.2) was still confirmed, not only by the remaining one degree of unsaturation, but also by the chemical shifts of the C-2, 4, and 5. The above information showed structure of 4-oxazolidinone with gem-dimethyl at C-2 and *p*-hydroxyphenyl at C-5 positions. Therefore, **1** was identified as 2,2-dimethyl-5-(4-hydroxyphenyl)-4-oxazolidinone.
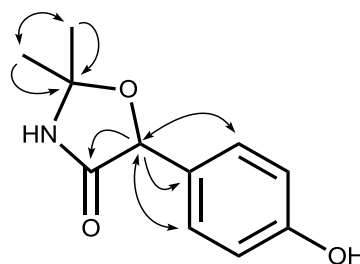

Figure 2. Key HMBC correlations of compound **1** (^{1}H to ^{13}C)

Compound **1** is a new natural product bearing a 4-oxazolidinone ring that is rare in the natural products. To our knowledge, natural 4-oxazolidinone derivatives have only been reported from marine organisms up to now [8, 9]. Compounds **2** and **3**, as derivatives of 4-hydroxymandelic acid, are also rarely described as natural products, although 4-hydroxymandelic acid was previously obtained from three natural sources [10-12].

We previously reported two rare diastereomeric flavonolignans salcolins A and B from aerial parts of *S. halepense* [6]. The present study reported occurrence of three rare natural products from the rhizomes of the species. These results agree with a hypothesis that the phytochemical features of invasive plants are generally unique, which may provide the plants with advantages in their new habitats [13]. According to the above results, the occurrence of three rare natural products in *S. halepense* indicates some different metabolic pathways from the other species.

Acknowledgements

References

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