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NOTE

A New Dihydronaphthoquinone from the Flowers of *Rosa rugosa* and Its Cytotoxicities

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A new dihydronaphthoquinone, rugosaquinone A (**1**) was isolated from the flowers of *Rosa rugosa.* Its structure was elucidated by spectroscopic methods, including extensive 1D NMR and 2D NMR experiments. Compound **1** was tested for its cytotoxicity against five human tumor cell lines, NB4, A549, SHSY5Y, PC3 and MCF7 and it showed potential cytotoxicity against NB4 and SHSY5Y cell lines with IC_{50} values of 4.2 and 2.8 μM, respectively.

Keywords: *Rosa rugosa*, Dihydronaphthoquinone, Rugosaquinone A, Cytotoxicity.

Rosa rugosa Thunb. (Rosaceae) is a common ornamental flower distributed in the temperate regions of eastern Asia and widely cultivated in the Yunnan Province of China[1,2]. The petals and buds of *R. rugosa* are often used as food, incense and as Chinese medicinal materials for the treatment of stomach ache, diarrhea and gynecological problems[3]. Previous studies have shown the presence of tannins[4], terpenoids[5-7], flavonoids[8,9] and chromones[10,11] in this genus. Continuing the effort to search for novel and bioactive metabolites from medicinal plants, we now report the isolation and characterization of a new dihydronaphthoquinone (**1**) (Fig. 1).

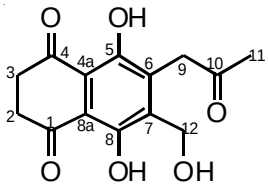

Fig. 1. Structure of compound **1**

UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. IR spectra were obtained in KBr disc on a Bio-Rad Wininfmred spectrophotometer. ESI-MS were measured on a VG Auto Spec-3000 MS spectrometer. ^{1}H NMR, ^{13}C NMR and 2D NMR spectra were recorded on Bruker DRX-500 instrument with TMS as internal standard. Column chromatography was performed on silica gel (200-300 mesh), or on silica gel H (10~40 μm, Qingdao Marine Chemical Inc., China). Second separation was performed by an Agilent 1100 HPLC equipped with ZORBAX-C_{18} (21.2 mm × 250 mm, 7.0 μm) column and DAD detector.

The flowers of *Rosa rugosa* were collected in Hanzhoung county, Shaanxi Province, in September 2012. The plant was identified by Prof. Y.-J. Chen (Yunnan Nationalities University). A voucher specimen (YNNI 12-09-68) has been deposited in our laboratory.

Extraction and isolation. The air-dried and powdered flowers of *R. damascena* (2.5 kg) were extracted three times with 95 % EtOH (3 × 4 L) at room temperature. The combined residue, after removal of solvent, was partitioned between ethyl acetate and water. The ethyl acetate crude extract (81.4 g) was applied to silica gel (200-300 mesh) column chromatography, eluting with CH_2Cl_2-$(CH_3)_2CO$ gradient system (50:1, 20:1, 9:1, 8:2, 7:3, 6:4, 5:5), to give seven fractions A-G. The further separation of fraction D (7:3, 9.27 g) by silica gel column chromatography, eluted with $CHCl_3$-MeOH (9:1, 8:2, 7:3, 6:4, 1:1), yielded mixtures D1–D6. Fraction D2 (8:2, 1.53 g) was subjected to Sephadex LH-20, Chromatorex RP-18 gel and then prepa-rative HPLC (43 % MeOH, 3 mL/min) to give **1** (18.4 mg).

Rugosaquinone A (1): Obtained as a red gum; UV (MeOH), λ_{max} (log ε) 210 (4.22), 243 (3.76), 272 (3.59), 395 (3.63) nm; IR (KBr, ν_{max}, cm^{-1}): 3452, 2952, 2928, 2869, 1713, 1631, 1455, 1408, 1360, 1327, 1261, 1189, 857, 764; ^{1}H NMR and ^{13}C NMR data (Table-1); ESI-MS (positive ion mode) *m/z* 277 $[M-H]^-$; HR-ESI-MS (negative ion mode) *m/z* 277.0718 $[M-H]^-$ (calcd. 277.0712 for $C_{14}H_{13}O_6$).

The ethyl acetate-soluble fraction from a 95 % EtOH extract of *R. rugosa* were purified by repeated column chromatography on silica gel, Sephadex LH-20, RP-18, as well as preparative HPLC, to yield a new dihydronaphthoquinone (**1**). Its structure was shown in Fig. 1 and its ^{1}H NMR and ^{13}C NMR spectroscopic data were listed in Table-1.

TABLE-1
^{1}H NMR AND ^{13}C NMR DATA OF COMPOUND **1**
(500 and 125 MHz, in C_5D_5N)

No.	δ_C (mult)	δ_H (mult, *J*)	No.	δ_C (mult)	δ_H (mult, *J*)
1	201.2 (s)		4a	114.1 (s)	
2	36.3 (t)	3.06 (s)	8a	115.4 (s)	
3	36.4 (t)	3.06 (s)	9	41.8 (t)	3.96 (s)
4	201.0 (s)		10	205.2 (s)	
5	152.8 (s)		11	30.2 (q)	2.25 (s)
6	130.2 (s)		12	58.2 (t)	4.68 (s)
7	135.5 (s)		5-OH		12.53 (s)
8	151.6 (s)		8-OH		12.58 (s)

The molecular formula of $C_{14}H_{14}O_6$ for compound **1** was determined by HRESIMS. The IR spectrum showed absorption bands at 1713 and 1631 cm^{-1} corresponding to carbonyl groups. ^{1}H NMR signals at δ_H 12.53 (1H, s) and δ_H 12.58 (1H, s) indicated the presence of two hydrogen-bonded hydroxy groups, as shown in Table-1. The ^{13}C NMR spectrum revealed all 14 carbon atoms, comprising three carbonyl carbons, six aromatic carbons, four methylene carbons and one methyl carbons. It was noteworthy that each chemical shift value of C-3, C-4, C-4a, C-5 and C-6 was almost the same as those of C-2, C-1, C-8a, C-8 and C-7, respectively. A singlet signal at δ_H 3.06, implying four protons in the ^{1}H NMR spectrum, was assigned to four methylene protons on the basis of HMQC correlations from these protons to two methylene carbons, C-2 (δ_C 36.3) and C-3 (δ_C 36.4). Moreover, the δ_H 3.06 signal correlated with C-1 (δ_C 201.2), C-4 (δ_C 201.0), C-4a (δ_C 114.1) and C-8a (δ_C 115.4) in the HMBC spectrum (Fig. 2). These data revealed the presence of a symmetrical 5,8-dihydroxy-2,3-dihydro-1,4-naphthoquinone moiety[12]. HMBC correlations from H-11 (δ_H 2.25) to C-9 (δ_C 41.8) and C-10 (δ_C 205.2) suggested the presence of an acetonyl group[13], which was connected at C-6 of the naphthoquinone moiety on the basis of HMBC correlations from H-9 (δ_H 3.96) to C-5 (δ_C 152.8), C-6 (δ_C 130.2) and C-7 (δ_C 135.5). A hydroxymethyl group was found to be located at C-7 of the naphthoquinone by the HMBC correlations from H-12 (δ_H 4.68) to C-6 (δ_C 130.2), C-7 (δ_C 135.5) and C-8 (δ_C 151.6) (Fig. 2). Thus, the structure of compound **1** was determined and named rugosaquinone A (Fig. 2).

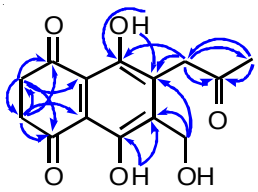

Fig. 2. Key HMBC (↷) correlations of compound **1**

Since some phenolic compounds are known to exhibit potential cytotoxicity[14-16], Compounds **1** was tests for its cytotoxicities against five human tumor cell lines, NB4, A549, SHSY5Y, PC3 and MCF7, using a previously reported procedure with taxol as the positive control[17]. Compound **1** showed potential cytotoxicity against NB4 and SHSY5Y cell lines with IC_{50} values of 4.2 and 2.8 μM, respectively.

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