Synthesis and antibacterial evaluation of novel xanthone sulfonamides

Mina Malekpoor[a], Sajjad Gharaghani[b], Ali Sharifzadeh[a,c], Syied Nezamoddin Mirsattari[a] and Ahmad Reza Massah[a]*

[a]*Department of Chemistry, Shahreza Branch, Islamic Azad University, Shahreza, Isfahan, 86145-311, Iran*
[b]*Laboratory of Chemoinformatics & Drug Design, Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran*
[c]*Department of Biochemistry, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran*

Twenty novel 4-(*N*-substituted-sulfonamide) derivatives of xanthone have been prepared from the 4-sulfonyl chloride of 1-hydroxy-3-methoxyxanthone and a variety of alkylamines and arylamines under mild conditions and their *in vitro* anti-bacterial activities against *Staphylococcus aureus* and *Escherichia coli* have been determined

Keywords: xanthone sulfonamide, synthesis of 4-(*N*-substituted-sulfonamide) derivatives, antibacterial activity

Despite significant progress in antimicrobial therapy with several classes of antibacterial agents presently available, infectious diseases caused by bacteria remain a major worldwide health problem due to rapid development of resistance to the existing antibacterial drugs.[1] Sulfonamide derivatives belong to one of the most important structural classes of drug molecules and constitute the largest class of antibacterial agents. Such agents *e.g.* sulfadiazine, have been used therapeutically for many decades.[2] Indeed, approved drugs with a sulfonamide structure have found widespread utility in a number of pharmacological and medicinal applications.[3]

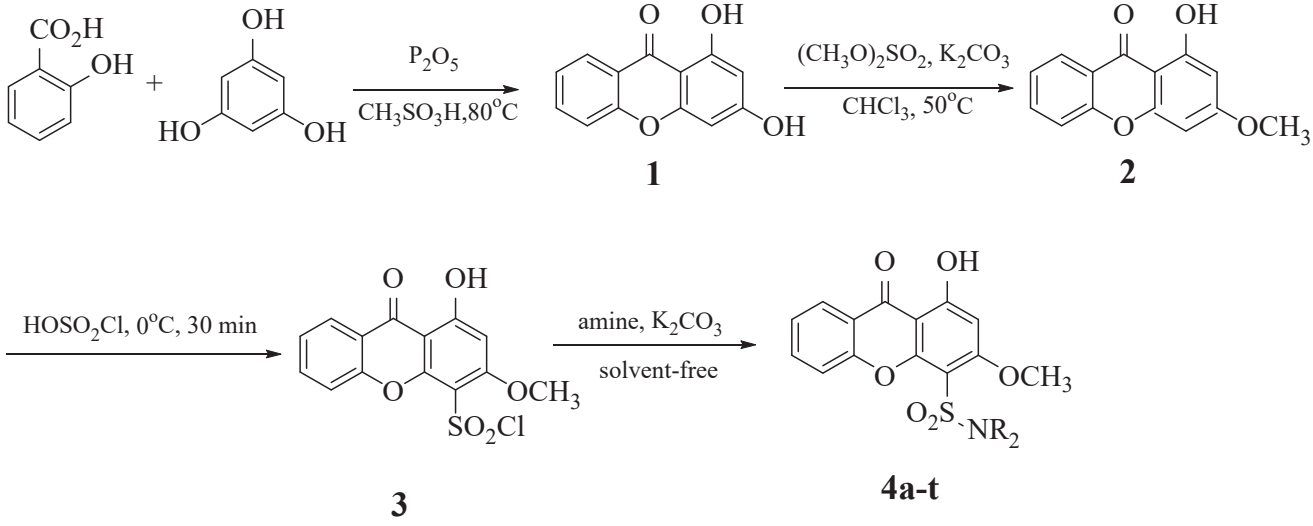
The xanthone skeleton makes up the core structure of numerous important natural and biologically active families of compounds present in higher plants, fungi and microorganisms.[4,5] These compounds have demonstrated wide-ranging pharmacological properties including use as antioxidant,[6] anticancer,[7] and anti-infective agents.[8] Among the xanthones reported to date, oxygenated xanthones inhibit the proliferation of several cancer cell lines[9] and some of them are useful antibacterial and antifungal agents.[10]

The antibacterial activity of sulfonamides and xanthones has pointed to xanthone sulfonamides being attractive as a versatile platform for the development of a new class of antibacterial agents and, to our knowledge, there has been no report on the synthesis and antibacterial study of xanthone sulfonamide derivatives. In continuation of our research on the synthesis and biological study of sulfonamide derivatives,[11-13] we now report the synthesis of a series of novel xanthone sulfonamides and test their biological activity.

Results and discussion

The synthetic route used to synthesise xanthone sulfonamide derivatives **4a–t** is shown in Scheme 1. The dihydroxylated xanthone scaffold **1** was prepared from phloroglucinol and salicylic acid by a literature method in 95% yield[14] and its 3-hydroxyl group was methylated with dimethyl sulfate in the presence of potassium carbonate to yield 1-hydroxy-3-methoxy-9H-xanthon-9-one **2**. The ^{1}H NMR spectrum of **2** showed one singlet peak at δ 3.91 corresponding to the methyl protons of the methoxy group, confirming that monomethylation had occurred. Also, due to hydrogen bonding between the hydrogen of the 1-hydroxy group with the C=O group, this hydrogen appeared at δ 12.90. Furthermore, in support of the structure of the monomethylated product **2**, in the ^{13}C NMR spectrum only one peak was observed at δ 55.3, corresponding to the carbon of the methoxy group.

The chlorosulfonation of 1-hydroxy-3-methoxy-9H-xanthon-9-one **2** was conducted using chlorosulfonic acid at 0 °C for 30 min. 1-Hydroxy-3-methoxy-9-oxo-9H-xanthone-4-sulfonyl chloride **3** was obtained in 79% yield with high purity and this was used in the next step without any purification. The regioselectivity of the chlorosulfonation of 1-hydroxy-3-



Scheme 1

* Correspondent. E-mail: Massah@iaush.ac.ir

methoxy-9H-xanthon-9-one **2** is likely to be directed by higher electron density at positions 2 and 4, compared to that of other positions. Between positons C-2 and C-4, it appears that position 4 was chlorosulfonated selectively. The selective reaction on C-4 was confirmed by NMR and density functional theory (DFT) calculations[15] that were performed using the Gaussian 98 program.[16] The geometry of the compound was optimised using DFT/B3LYP theory and a 6-31G(d,p) basis set. Vibrational frequency calculations were used to characterise all stationary points as minima (the number of imaginary frequencies: Nimag = 0). Atomic charges of 1-hydroxy-3-methoxy-9H-xanthen-9-one **2**, which were calculated by the Mulliken method at the B3LYP/6-31G(d,p) level of theory, are given in Fig. 1. The charge distribution of compound **2** shows that the C-4 atom has the highest negative charge, which explains chlorosulfonation in that position.

Comparison between the ^{1}H NMR of compounds **2** and **3** is useful. In the ^{1}H NMR spectrum, 1-hydroxy-3-methoxy-9H-xanthon-9-one **2** showed two doublet peaks at δ 6.39 and δ 6.47 with a coupling constant of 1.5 Hz corresponding to the protons connected to C-2 and C-4 respectively. After chlorosulfonation, the doublet at δ 6.39 was absent and the doublet at δ 6.47 was converted to a singlet peak, confirming that the chlorosulfonyl group must have been introduced at the 4-position.

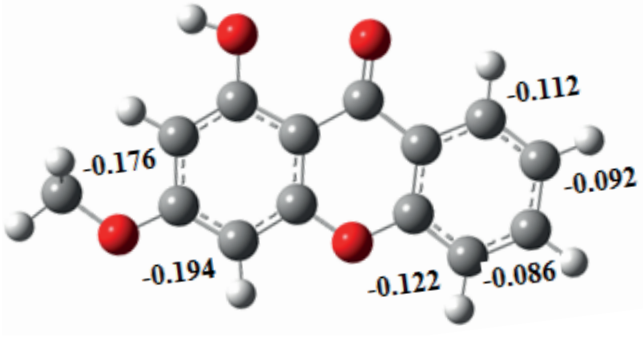


Fig. 1 The NBO charges calculated for compound **2** optimised at the B3LYP/6-31G(d,p) level.

As was shown in Scheme 1, the last step in the synthesis of xanthone sulfonamides **4a–t** is simple mixing of xanthone sulfonyl chloride **3** with an amine in the presence of K_2CO_3 at room temperature.[17-19] After completion of the reaction, the product was separated from the reaction mixture just by adding water and simple filtration. Interestingly, most of the xanthone sulfonamides were obtained in high purity without any purification.

A wide range of structurally and electronically varied amines were subjected to the reaction with xanthone sulfonyl chloride **3** (Table 1). The results showed that the aromatic as well as aliphatic amines reacted with xanthone sulfonyl chloride **3** within 15 min–4 h to produce the corresponding sulfonamides in moderate to high yield. It is interesting to note that aromatic amines were sulfonated in a shorter reaction time in comparison with aliphatic amines. Also, primary aromatic amines reacted faster than secondary aromatic amines and the products were obtained in higher yield. Furthermore, aromatic amines with electron–donating groups such as alkyl or alkoxy in the *para*-position were converted to the corresponding sulfonamides in higher yields and in a shorter reaction time than those with electron-withdrawing groups (entries 9–19). Finally, a heterocyclic amine reacted to give the corresponding sulfonamide in high yield (entry 20).

All of the synthesised xanthone sulfonamides **4a–t** were screened for their antibacterial activity against *Escherichia coli* (ATCC25922) as Gram-negative and *Staphylococcus aureus*

Table 1 Yields/reaction times for the preparation of xanthone sulfonamides **4a–t** from a variety of amines 1 (Scheme 1) and their antibacterial activities[a]

Entry	Amine	Product number	Time/min	Yield/%[b]	*E. coli* (ATCC25922)	*S. aureus* (ATCC29213)
1	Cyclohexylamine	**4a**	180	35	500	>1000
2	Piperazine	**4b**[c]	40	56	500	500
3	1,4-Diaminobutane	**4c**[c]	240	30	>1000	>1000
4	$PhCH_2NH_2$	**4d**	65	39	>1000	>1000
5	$PhNH_2$	**4e**	60	45	>1000	>1000
6	$PhNHCH_2CH_3$	**4f**	80	33	>1000	>1000
7	Ph_2NH	**4g**	60	30	500	500
8	HO-4-$C_6H_4NH_2$	**4h**	60	55	500	500
9	MeO-4-$C_6H_4NH_2$	**4i**	15	85	>1000	>1000
10	MeO-2-$C_6H_4NH_2$	**4j**	20	75	>1000	>1000
11	Me-4-$C_6H_4NH_2$	**4k**	15	80	>1000	>1000
12	Me-2-$C_6H_4NH_2$	**4l**	20	70	>1000	500
13	2,4-Me_2-$C_6H_4NH_2$	**4m**	25	60	>1000	>1000
14	Br-4-$C_6H_4NH_2$	**4n**	35	63	500	500
15	Cl-4-$C_6H_4NH_2$	**4o**	40	60	250	500
16	Cl-3-$C_6H_4NH_2$	**4p**	35	61	250	500
17	Cl-2-$C_6H_4NH_2$	**4q**	45	60	250	250
18	2,4-Cl_2-$C_6H_4NH_2$	**4r**	50	55	250	250
19	O_2N-3-$C_6H_4NH_2$	**4s**	120	50	500	500
20	2-Aminothiazole	**4t**	20	90	125	125
21		Kanamycin			3	5

[a]MICs, μg mL^{-1}.
[b]Isolated yield.
[c]Bis-substituted derivatives.

(ATCC29213) as Gram-positive bacteria using conventional agar–dilution methods. The MICs (minimum inhibitory concentrations) of the compounds against these bacteria are presented in Table 1. Also kanamycin, as a standard antibacterial agent, was screened under identical conditions for comparison. Structure–activity relationships in these xanthone sulfonamide derivatives showed that compounds with electron-withdrawing halogen groups on the 2- and 4-positions of an arylamine in the sulfonamide moiety were conducive to antibacterial activity (compounds **4m–r**). Meanwhile, the derivatives which have electron-donating substituents (such as CH_3, OCH_3) on the 2- and 4-positions of the same ring exhibited less potent activity(compounds **4i–m**). Of the new synthetic xanthone sulfonamide derivatives, 1-hydroxy-3-methoxy-9-oxo-*N*-(thiazol-2-yl)-9H-xanthone-4-sulfonamide **4t**, exhibited the most potent antibacterial activity with an MIC of 125 μg mL^{-1} against *E. coli* and *S. aureus*.

In conclusion, we have described a facile and efficient approach for the preparation of several structurally varied novel xanthone sulfonamides in four steps, starting from salicylic acid and phloroglucinol. The reactions are characterised by simple reaction procedures, ease of separation, high yields and chemoselectivity. The final step of the synthesis of xanthone sulfonamides was carried out under solvent–free conditions and the products were separated by simple filtration giving it good agreement with 'green chemistry' credentials. Furthermore, the microbiological activity of the synthesised xanthone sulfonamides was evaluated against one Gram-positive and one Gram-negative microorganism.

Experimental

All chemicals were purchased from the Merck or Fluka chemical companies. IR spectra were recorded on a PerkinElmer VIR spectrophotometer. NMR spectra were obtained on a Bruker 400 FT spectrometer (^{1}H NMR at 400 Hz and ^{13}C NMR at 100 Hz) in $CDCl_3$ or DMSO-d_6 using TMS as internal standard. Chemical shifts (δ) are given in ppm and coupling constants (*J*) in Hz. Column chromatography was performed using silicagel 60 (230–400 mesh). All reactions were conducted open to the atmosphere and the yields refer to the isolated products.

1,3-Dihydroxy-9H-xanthone-9-one (**1**): Eaton's reagent (100 mL) (P_2O_5/CH_3SO_3H, Aldrich) was added slowly to a mixture containing salicylic acid (9.13 g, 60 mmol) and phloroglucinol (7.56 g, 60 mmol). The mixture was heated at 80 °C for 20 min. under stirring. After cooling to room temperature, the reaction mixture was poured into ice (300 g) and stirred for 2 h. The resulting solid was collected by filtration, washed with water until pH 6, and dried at 60 °C. The product was obtained as a reddish brown solid in 95% yield and was used in the next step without further purification; m.p. 249–251 °C (lit.[20] 254–256 °C); R_f = 0.59 (20% ethyl acetate 80% *n*-hexane); IR: (KBr, cm^{-1}) 3331 (O–H), 1656 (CO); ^{1}H NMR: (DMSO-d_6) δ (ppm) 4.20 ($2H_{OH}$, br), 6.19 ($1H_{arom}$, d, *J* = 2.0 Hz), 6.36 ($1H_{arom}$, d, *J* = 2.0 Hz), 7.42 ($1H_{arom}$, t, *J* = 7.6 Hz), 7.53 ($1H_{arom}$, d, *J* = 8.0 Hz), 7.78–7.83 ($1H_{arom}$, m), 8.06–8.09 ($1H_{arom}$, m).

1-Hydroxy-3-methoxy-9H-xanthone-9-one (**2**): Dimethyl sulfate (10 mL) was added to a stirred mixture of dihydroxyxanthone **1** (10 mmol, 2.28 g) and K_2CO_3 (36 mmol, 3.6 g) in $CHCl_3$ (50 mL). The mixture was heated to 50 °C and the progress of the reaction was monitored by TLC. After completion of the reaction (25 min), the mixture was cooled and washed with 5% HCl (10 mL), water (20 mL) and dried over $NaSO_4$. After evaporation of the solvent, the product was obtained as a yellow solid in 79% yield and used in the next step without further purification; m.p. 149–152 °C; R_f = 0.59 (20% ethyl acetate 80% hexane); IR: (KBr, cm^{-1}) 3488 (O–H), 1660 (CO); ^{1}H NMR: ($CDCl_3$) δ (ppm) 3.93 ($3H_{OMe}$, s), 6.39 ($1H_{arom}$, d, *J* = 1.6Hz), 6.47 ($1H_{arom}$, d, *J* = 2.0 Hz), 7.39–7.47 ($1H_{arom}$, m), 7.75 ($2H_{arom}$, t, *J* = 8.4 Hz), 8.28 ($1H_{arom}$, d, *J* = 7.6 Hz), 12.90 ($1H_{OH}$, s); ^{13}C NMR ($CDCl_3$): δ (ppm) 55.3, 92.8, 97.0, 103.9, 117.6, 120.6, 124.0, 125.9, 135.0, 156.0, 157.7, 163.6, 166.7, 180.8. Anal. calcd for $C_{14}H_{10}O_4$: C, 69.42; H, 4.16; found: C, 69.28; H, 4.12%.

1-Hydroxy-3-methoxy-9-oxo-9H-xanthone-4-sulfonyl chloride (**3**): Chlorosulfonic acid (20 mmol) was added slowly at 0 °C to a stirred solution of 1-hydroxy-3-methoxy-9H-xanthone-9-one **2** (10 mmol, 2.42 g) in $CHCl_3$ (10 mL),. The mixture was stirred at 0 °C for 30 min. to 60 min at room temperature. After completion of the reaction (as shown by TLC) the mixture was poured onto ice. The mixture was extracted with chloroform (25 mL) and washed with water (20 mL), saturated $NaHCO_3$ (2×20 mL) and dried over Na_2SO_4. After evaporation of solvent, the product was obtained as an orange solid with high purity and used in the next step without any purification; m.p. 173–176 °C; R_f = 0.31 (50% ethyl acetate 50% hexane); IR: (KBr, cm^{-1}) 3394 (O–H), 1647 (CO), 1388, 1170 (SO_2); ^{1}H NMR: ($CDCl_3$) δ (ppm) 4.13 ($3H_{OMe}$, s), 6.46 ($1H_{arom}$, s), 7.05–7.54 ($1H_{aroma}$, m), 7.68–7.71 ($1H_{arom}$, m), 7.83–7.87 ($1H_{arom}$, m), 8.27–8.29 ($1H_{arom}$, m), 14.12 ($1H_{OH}$, s); ^{13}C NMR: ($CDCl_3$) δ (ppm) 57.6, 95.1, 102.9, 112.1, 118.6, 119.9, 124.0, 125.7, 136.3, 155.5, 155.6, 165.1, 169.4, 180.8.

Synthesis of xanthone sulfonamides; general procedure

An amine (1 mmol) was added to a vigorously stirred mixture of xanthone sulfonyl chloride **3** (1 mmol) and K_2CO_3 (1 g). The progress of the reaction was monitored by TLC. After completion of the reaction, water (10 mL) was added and the sulfonamide was easily isolated by simple filtration and washing with additional water (3×10 mL). The products were obtained in high purity, which was confirmed by spectroscopic data. In the case of xanthone sulfonamides **4a**–**c** column chromatography was used for purification using ethyl acetate: hexane as eluent.

N-Cyclohexyl-1-hydroxy-3-methoxy-9-oxo-9-H-xanthene-4-sulfonamide (**4a**): Cream needles; m.p. 134–137 °C ; R_f= 0.59 (100% ethyl acetate); IR: (KBr, cm^{-1}) 3429 (O–H), 3241 (N–H), 1660 (CO), 1379, 1179 (SO_2); ^{1}H NMR: (DMSO) δ (ppm) 0.89–0.92 ($2H_{CH2-}$, m), 1.15–1.28 ($8H_{CH2-}$, m), 3.74–3.83 (1H, m), 4.13 ($3H_{OMe}$, s), 6.45 ($1H_{arom}$, s), 7.49–7.53 ($1H_{arom}$, m), 7.68 ($1H_{arom}$, dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz), 7.83–7.87 ($1H_{arom}$, m), 8.27 ($1H_{arom}$, dd, J_1 = 6.0 Hz, J_2 = 1.6 Hz), 9.50 ($1H_{NH}$, s), 13.74 ($1H_{OH}$, s); ^{13}C NMR: ($CDCl_3$) δ (ppm) 24.5, 26.7, 37.4, 42.4, 55.8, 92.9, 97.1, 103.9, 117.6, 120.7, 124.0, 125.9, 135.0, 156.1, 157.8, 163.6, 166.8, 180.9. Anal. calcd for $C_{20}H_{21}NO_6S$: C, 59.54; H, 5.25; N, 3.47; found: C, 59.28; H, 5.12; N, 3.55%.

bis(1-Hydroxy-3-methoxy-9-oxo-9-H-xanthene-4-sulfonamide) piperazine (**4b**): Light brown needles; m.p. 256–260 °C; R_f = 0.19 (80% ethyl acetate 20% *n*-hexane); IR: (KBr, cm^{-1}) 3483 (O–H), 1660 (CO), 1395, 1119 (SO_2); ^{1}H NMR: (DMSO) δ (ppm) 2.88 ($8H_{CH2-CH2}$, t, *J* = 5.6 Hz), 4.13 ($6H_{OMe}$, s), 6.46 ($2H_{arom}$,s), 7.50–7.54 ($2H_{arom}$, m), 7.68–7.71 ($2H_{arom}$, m), 7.83–7.88 ($2H_{arom}$, m), 8.27–8.29 ($2H_{arom}$, m), 14.12 ($2H_{OH}$, s); ^{13}C NMR: ($CDCl_3$) δ (ppm) 49.9, 56.8, 96.0, 111.6, 111.7, 113.0, 118.8, 129.1, 129.4, 129.5, 148.5, 148.5, 158.2, 162.3, 185.0. Anal. calcd for $C_{32}H_{26}N_2O_{12}S_2$: C, 55.33; H, 3.77; N, 4.03; found: C, 55.17; H, 3.85; N, 4.02%.

N,N'-(Butane-1,4-diyl)bis(1-hydroxy-3-methoxy-9-oxo-9H-xanthene-4-sulfonamide) (**4c**): Light brown solid; m.p. 149–153 °C; R_f = 0.36 (90% ethyl acetate 10% *n*-hexane); IR: (KBr, cm^{-1}) = 3599 (O–H), 3239 (N–H), 1636 (CO), 1397, 1153 (SO_2); ^{1}H NMR: ($CDCl_3$) δ (ppm) 1.25–1.28 (4H, m), 3.79–3.82 (4H, m), 3.98 ($6H_{OMe}$, s), 6.37 ($2H_{arom}$, s), 7.28–7.45 ($4H_{arom,NH}$ m), 7.71–8.25 ($4H_{arom}$,m), 8.27 ($2H_{arom}$, dd, J_1 = 1.2 Hz, J_2 = 0.8 Hz), 12.88 ($2H_{OH}$, s); Anal. calcd for $C_{32}H_{28}N_2O_{12}S_2$: C, 55.17; H, 4.05; N, 4.02; found: C, 55.35; H, 3.95; N, 3.93%.

N-Benzyl-1-hydroxy-3-methoxy-9-oxo-9H-xanthene-4-sulfonamide (**4d**): Light brown solid (EtOH); m.p. 156–160 °C; R_f = 0.53 (80% ethyl acetate 20% *n*-hexane); IR: (KBr, cm^{-1}) 3499 (O–H), 3299 (N–H), 1653 (CO), 1395, 1122 (SO_2); ^{1}H NMR: ($CDCl_3$) δ (ppm) 3.75 ($2H_{-CH2-Ph}$, d, *J* = 12.8 Hz), 4.16 ($3H_{OMe}$, s), 6.29 ($1H_{arom}$, s), 7.17–7.29 ($5H_{arom}$, m), 7.35 ($1H_{N-H}$, s), 7.47 ($1H_{arom}$, t, *J* = 7.6 Hz), 7.57 ($1H_{arom}$, d, *J* = 8.4 Hz), 7.72 ($1H_{arom}$, t, *J* = 8.4 Hz), 8.29 ($1H_{arom}$, d, *J* = 7.6 Hz),

13.95 ($1H_{OH}$, s); ^{13}C NMR: ($CDCl_3$) δ (ppm) 45.5, 55.8, 92.9, 104.0, 117.7, 119.9, 120.7, 123.41, 124.0, 125.9, 129.7, 131.5, 135.5, 145.5, 156.1, 157.8, 163.6, 166.8, 180.9. Anal. calcd for $C_{21}H_{17}NO_6S$: C, 61.30; H, 4.16; N, 3.40; found: C, 59.95; H, 3.98; N, 3.53%.

1-Hydroxy-3-methoxy-9-oxo-N-phenyl-9H-xanthene-4-sulfonamide (**4e**): Brown solid (EtOH); m.p. 140–145 °C; R_f = 0.53 (80% ethyl acetate 20% *n*-hexane); IR: (KBr, cm^{-1}) 3419 (O–H), 3260 (N–H), 1661 (CO), 1390, 1122 (SO_2); ^{1}H NMR: ($CDCl_3$) δ (ppm) 4.13 ($3H_{OMe}$, s), 6.42 ($1H_{arom}$, s), 7.01–7.05 ($5H_{arom}$, m), 7.28 ($1H_{N-H}$, s), 7.45 ($1H_{arom}$, t, *J* = 7.2 Hz), 7.66 ($1H_{arom}$, d, *J* = 8.0 Hz), 7.79 ($1H_{arom}$, t, *J* = 7.2 Hz), 8.23 ($1H_{arom}$, d, *J* = 6.8 Hz), 13.89 ($1H_{OH}$, s); ^{13}C NMR: ($CDCl_3$) δ (ppm) 55.8, 92.9, 97.1, 104.0, 117.7, 119.9, 120.7, 123.41, 124.0, 125.9, 129.7, 131.5, 135.5, 156.1, 157.8, 163.6, 166.8, 180.9. Anal. calcd for $C_{20}H_{15}NO_6S$: C, 60.45; H, 3.80; N, 3.52; found: C, 60.23; H, 3.91; N, 3.63%.

N-Ethyl-1-hydroxy-3-methoxy-9-oxo-N-phenyl-9H-xanthene-4-sulfonamide (**4f**): Light brown solid (EtOH); m.p. 123–127 °C; R_f = 0.433 (80% ethyl acetate 20% *n*-hexane); IR: (KBr, cm^{-1}) 3453 (O–H), 1662 (CO), 1397, 1176 (SO_2); ^{1}H NMR: ($CDCl_3$) δ (ppm) 1.27 ($3H_{Me}$, t, *J* = 6.0 Hz), 3.23 ($2H_{-CH2}$, q, *J* = 7.2 Hz), 4.13 ($3H_{OMe}$, s), 6.13 ($1H_{arom}$, s), 6.98–7.03 ($5H_{arom}$, m), 7.45 ($1H_{arom}$, t, *J* = 7.2 Hz), 7.67 ($1H_{arom}$, d, *J* = 8.0 Hz), 7.79 ($1H_{arom}$, t, *J* = 7.2 Hz), 8.22 ($1H_{arom}$, d, *J* = 6.8 Hz), 13.89 ($1H_{OH}$, s); ^{13}C NMR: ($CDCl_3$) δ (ppm) 11.5, 40.6, 55.8, 92.9, 97.1, 104.0, 117.7, 119.9, 120.7, 123.41, 124.0, 125.9, 129.7, 131.5, 135.5, 156.1, 157.8, 163.6, 166.8, 180.9. Anal. calcd for $C_{22}H_{19}NO_6S$: C, 62.11; H, 4.50; N, 3.29; found: C, 62.23; H, 4.37; N, 3.43%.

1-Hydroxy-3-methoxy-9-oxo-N,N–diphenyl-9H-xanthene-4-sulfonamide (**4g**): Brown solid (EtOH); m.p. 156–160 °C; R_f =0.23 (80% ethyl acetate 20% *n*-hexane); IR: (KBr, cm^{-1}) 3393 (O–H), 1661 (CO), 1403, 1178 (SO_2); ^{1}H NMR: ($CDCl_3$) δ (ppm) 4.02 ($3H_{OMe}$, s), 6.46 ($1H_{arom}$, s), 6.99–7.05 ($10H_{arom}$, m), 7.44–7.47 ($1H_{arom}$, m), 7.66–7.68 ($1H_{arom}$, m), 7.79–8.01 ($1H_{arom}$, m), 8.29–8.33 ($1H_{arom}$, m), 13.99 ($1H_{OH}$, s); ^{13}C NMR: ($CDCl_3$) δ (ppm) 55.8, 95.1, 102.5, 106.0, 117.2, 119.1, 120.9, 123.4, 124.3, 125.9, 129.6, 131.2, 143.2, 156.6, 157.1, 162.5, 166.1, 179.9. Anal. calcd for $C_{26}H_{19}NO_6S$: C, 65.95; H, 4.04; N, 2.96; O, 20.27; S, 6.775; found: C, 65.63; H, 4.17; N, 3.03%.

1-Hydroxy-N-(4-hydroxyphenyl)-3-methoxy-9-oxo-9H-xanthene-4-sulfonamide (**4h**): Cream solid (EtOH); m.p. 151–155 °C; R_f = 0.25 (80% ethyl acetate 20% *n*-hexane); IR: (KBr, cm^{-1}) 3474 (O–H), 3289 (N–H), 1656 (CO), 1400, 1148 (SO_2); ^{1}H NMR: ($CDCl_3$) δ (ppm) 4.13 ($3H_{OMe}$, s), 4.90 ($1H_{OH}$, s, br), 6.42 ($1H_{arom}$, s), 6.63 ($2H_{arom}$, d, *J* = 8.4 Hz), 6.97–7.05 ($3H_{arom,NH}$ m), 7.45 ($1H_{arom}$, t, *J* = 7.6 Hz), 7.67 ($1H_{arom}$, d, *J* = 8.4 Hz), 7.81 ($1H_{arom}$, t, *J* = 7.2 Hz), 8.23 ($1H_{arom}$, d, *J* = 8.0 Hz), 13.89 ($1H_{OH}$, s); ^{13}C NMR: ($CDCl_3$) δ (ppm) 56.9, 99.2, 107.0, 117.6, 120.7, 121.3, 124.0, 125.9, 126.9, 127.8, 129.9, 131.4, 135.1, 136.0, 145.5, 156.1, 157.8, 163.7, 164.3, 167.0, 180.9. Anal. calcd for $C_{20}H_{15}NO_7S$: C, 58.11; H, 3.66; N, 3.39; found: C, 58.23; H, 3.47; N, 3.43%.

1-Hydroxy-3-methoxy-N-(4-methoxyphenyl)-9-oxo-9H-xanthene-4-sulfonamide (**4i**): Cream solid (EtOH); m.p. 193–195 °C; R_f = 0.45 (70% ethyl acetate 30% *n*-hexane); IR: (KBr, cm^{-1}) 3419 (O–H), 3311 (N–H), 1643 (CO), 1399, 1155 (SO_2); ^{1}H NMR: ($CDCl_3$) δ (ppm) 3.71 ($3H_{OMe}$, s), 4.15 ($3H_{OMe}$, s), 6.45 ($1H_{arom}$, s), 6.79 ($2H_{arom}$, d, *J* = 8.0 Hz), 7.08 ($2H_{arom}$, d, *J* = 8.0 Hz), 7.07 ($1H_{N-H}$, s), 7.45 ($1H_{arom}$, d, *J* = 7.6 Hz), 7.64 ($1H_{arom}$, d, *J* = 8.4 Hz), 7.80 ($1H_{arom}$, t, *J* = 7.6 Hz), 8.24 ($1H_{arom}$, t, *J* = 8.0 Hz), 13.92 ($1H_{OH}$, s); ^{13}C NMR: ($CDCl_3$) δ (ppm) 48.4, 50.5, 88.0, 107.5, 107.6, 107.7, 111.1, 112.9, 117.2, 118.6, 122.1, 129,1, 148.7, 149.3, 150.8, 160.6, 174.2. Anal. calcd for $C_{21}H_{17}NO_7S$: C, 59.01; H, 4.01; N, 3.28; found: C, 59.18; H, 4.13; N, 3.36%.

1-Hydroxy-3-methoxy-N-(2-methoxyphenyl)-9-oxo-9H-xanthene-4-sulfonamide (**4j**): Light brown solid (EtOH); m.p. 227–230 °C; R_f = 0.36 (70% ethyl acetate 30% *n*-hexane); IR: (KBr, cm^{-1}) 3443 (O–H), 3353 (N–H), 1650 (CO), 1402, 1161(SO_2); ^{1}H NMR: (DMSO-d_6) δ (ppm) 3.57 ($3H_{OMe}$, s), 3.91 ($3H_{OMe}$, s), 6.65 ($1H_{arom}$, s), 6.81 ($1H_{aroma}$, t, *J* = 8.0 Hz), 6.88 ($1H_{aroma}$, d, *J* = 7.2 Hz), 7.00 ($1H_{arom}$, t, *J* = 7.6 Hz), 7.36 ($1H_{arom}$, d, *J* = 6.4 Hz), 7.55 ($1H_{arom}$, t, *J* = 7.6 Hz), 7.76 ($1H_{arom}$, d, *J* = 8.4 Hz), 7.93–7.98 ($1H_{arom}$, m), 8.15 ($1H_{arom}$, d, *J* = 8.0 Hz), 9.00 ($1H_{N-H}$, s), 13.89 ($1H_{OH}$, s); ^{13}C NMR: (DMSO-d_6) δ (ppm) 66.3, 66.9, 94.7, 103.2, 110.5, 118.5, 119.2, 119.9, 121.3, 124.5, 125.0, 125.6, 126.5, 135.9, 140.7, 141.7, 164.6, 167.4, 170.4, 170.5, 185.7. Anal. calcd for $C_{21}H_{17}NO_7S$: C, 59.01; H, 4.01; N, 3.28; found: C, 59.23; H, 4.16; N, 3.39%.

*1-Hydroxy-3-methoxy-9-oxo-N-*p*-tolyl-9H-xanthene-4-sulfonamide* (**4k**): Cream solid (EtOH); m.p. 194–197 °C; R_f = 0.33 (70% ethyl acetate 30% *n*-hexane); IR: (KBr, cm^{-1}) 3456 (O–H), 3261 (N–H), 1663 (CO), 1399, 1155(SO_2); ^{1}H NMR: ($CDCl_3$) δ (ppm) 2.27 ($3H_{Me}$, s), 4.14 ($3H_{OMe}$, s), 6.42 ($1H_{arom}$, s), 6.64 ($1H_{aroma}$, d, *J* = 7.6Hz), 7.01–7.05 ($3H_{arom}$, m), 7.26 ($1H_{N-H}$, s), 7.46 ($1H_{arom}$, t, *J* = 7.64 Hz), 7.67 ($1H_{arom}$, d, *J* = 8.4 Hz), 7.81 ($1H_{arom}$, t, *J* = 7.64 Hz), 8.24 ($1H_{arom}$, d, *J* = 8.0 Hz), 13.90 ($1H_{OH}$, s); ^{13}C NMR: ($CDCl_3$) δ (ppm) 20.7, 57.40, 94.9, 103.5, 106.1, 115.3, 118.6, 119.8, 121.0, 125.0, 125.5, 129.8, 129.9, 134.2, 135.2, 135.9, 155.8, 156.3, 164.0, 167.5, 181.1. Anal. calcd for $C_{21}H_{17}NO_6S$: C, 61.30; H, 4.16; N, 3.40; found: C, 60.18; H, 4.13; N, 3.36%.

*1-Hydroxy-3-methoxy-9-oxo-N-*o*-tolyl-9H-xanthene-4-sulfonamide* (**4l**): Cream solid (EtOH); m.p. 186–190 °C R_f = 0.36 (70% ethyl acetate 30% n-hexane); IR: (KBr, cm^{-1}) 3450 (O–H), 3300 (N–H), 1650 (CO), 1379, 1175(SO_2); ^{1}H NMR: (DMSO-d_6) δ (ppm) 2.21 ($3H_{Me}$, s), 3.99 ($3H_{OMe}$, s), 6.99 ($1H_{arom}$, s), 7.00–7.15 ($4H_{arom}$, m), 7.52–7.56 ($2H_{arom}$, m), 7.88–7.93 ($1H_{arom}$, m), 8.15 ($1H_{arom}$, dd, J_1 = 9.6 Hz, J_1 = 4.0 Hz), 9.00 ($1H_{N-H}$, s), 13.90 ($1H_{OH}$, s); ^{13}C NMR: (DMSO-d_6) δ (ppm) 23.0, 57.4, 100.7, 107.7, 113.5, 123.4, 124.5, 130.1, 130.3, 130.5, 131.0, 131.6, 135.9, 138.4, 138.8, 140.7, 141.7, 160.2, 169.8, 171.3, 185.7. Anal. calcd for $C_{21}H_{17}NO_6S$: C, 61.30; H, 4.16; N, 3.40; found: C, 60.41; H, 4.19; N, 3.50%.

N-(2,4-Dimethylphenyl)-1-hydroxy-3-methoxy-9-oxo-9H-xanthene-4-sulfonamide (**4m**): Light brown solid (EtOH); m.p. 150–154 °C, R_f = 0.42 (70% ethyl acetate 30% n-hexane); IR: (KBr, cm^{-1}) 3470 (O–H), 3266(N–H), 1666 (CO), 1380, 1170 (SO_2); ^{1}H NMR: ($CDCl_3$) δ (ppm) 3.70 ($6H_{CH3}$, s), 4.15 ($3H_{OMe}$, s), 6.44 ($1H_{arom}$, s), 6.73 ($1H_{arom}$, d, *J* = 9.2 Hz), 7.07 ($2H_{arom}$, d, *J* = 8.8 Hz), 7.18 ($1H_{NH}$, s), 7.44 ($1H_{arom}$, t, *J* = 7.6 Hz), 7.64 ($1H_{arom}$, d, *J* = 8.4 Hz), 7.73 ($1H_{arom}$, d, *J* = 6.8 Hz), 8.22 ($1H_{arom}$, dd, J_1 = 6.4 Hz, J_2 = 1.2 Hz), 13.91 ($1H_{OH}$, s). Anal. calcd for $C_{22}H_{19}NO_6S$: C, 62.11; H, 4.50; N, 3.29; found: C, 62.41; H, 4.29; N, 3.20%.

N-(4-Bromophenyl)-1-hydroxy-3-methoxy-9-oxo-9H-xanthene-4-sulfonamide (**4n**): Brown solid (EtOH); m.p. 211–215 °C; R_f = 0.45 (70% ethyl acetate 30% *n*-hexane); IR (KBr, cm^{-1}) 3439 (O–H), 3272 (N–H), 1649 (CO), 1392, 1139 (SO_2); ^{1}H NMR: ($CDCl_3$) δ (ppm) 4.11 ($3H_{OMe}$, s), 6.50 ($1H_{arom}$, s), 7.29–7.475 ($4H_{arom}$, m), 7.44 ($1H_{N-H}$, s), 7.51 ($1H_{arom}$, t, *J* = 8.0 Hz), 7.79 ($1H_{arom}$, t, *J* = 8.4 Hz), 7.80 ($1H_{arom}$, d, *J* = 8.4 Hz), 8.30 ($1H_{arom}$, t, *J* = 8.4 Hz), 13.07 ($1H_{OH}$, s); ^{13}C NMR: ($CDCl_3$) δ (ppm) 55.9, 95.1, 106.1,116.1, 117.6,1199, 120.7, 124.0, 125.9, 131.5, 135.7,136.6, 156.1, 157,8, 163.6, 164.3, 166.8, 180.9. Anal. calcd for $C_{20}H_{14}BrNO_6S$: C, 50.43; H, 2.96; N, 2.94; found: C, 50.51; H, 3.09; N, 3.03%.

N-(4-Chlorophenyl)-1-hydroxy-3-methoxy-9-oxo-9H-xanthene-4-sulfonamide (**4o**): Cream solid (EtOH); m.p. 237–241 °C; R_f = 0.34 (70% ethyl acetate 30% *n*-hexane); IR: (KBr, cm^{-1}) 3440 (O–H), 3209 (N–H), 1659 (CO), 1399, 1175 (SO_2); ^{1}H NMR: ($CDCl_3$) δ (ppm) 4.14 ($3H_{OMe}$, s), 6.43 ($1H_{arom}$, s), 7.10 ($2H_{arom}$, d, *J* = 8.8 Hz), 7.26 ($1H_{N-H}$, s), 7.18–7.21 ($2H_{arom}$, m), 7.48 ($1H_{arom}$, t, *J* = 7.2 Hz), 7.67 ($1H_{arom}$, d, *J* = 8.0 Hz), 7.83 ($1H_{arom}$, t, *J* = 7.2 Hz), 8.26 ($1H_{arom}$, d, *J* = 8.0 Hz), 13.95 ($1H_{OH}$, s); ^{13}C NMR: (DMSO-d_6) δ (ppm) 55.9, 95.1, 106.1, 117.6, 120.7, 121.3, 124.0, 125.9, 127.9, 129.8, 135.2, 135.7, 156.1, 157,8, 163.6, 164.3, 166.8, 180.9. Anal. calcd for $C_{20}H_{14}ClNO_6S$: C, 55.62; H, 3.27; N, 3.24; found: C, 55.41; H, 3.39; N, 3.20%.

N-(3-Chlorophenyl)-1-hydroxy-3-methoxy-9-oxo-9H-xanthene-4-sulfonamide (**4p**): Cream solid (EtOH); m.p. 231–235 °C; R_f = 0.38 (70% ethyl acetate 30% *n*-hexane); IR: (KBr, cm^{-1}) 3457 (O–H), 3271 (N–H), 1647 (CO), 1388, 1148(SO_2); ^{1}H NMR: ($CDCl_3$) δ (ppm) 4.13($3H_{OMe}$, s), 6.47($1H_{arom}$, s), 7.03 ($1H_{arom}$, t, *J* = 6.0 Hz), 7.15 ($1H_{arom}$, t, *J* = 8.0 Hz), 7.21 ($2H_{arom}$, d, *J* = 9.2 Hz), 7.38 ($1H_{N-H}$, s), 7.48 ($1H_{arom}$, t, *J* = 7.6 Hz), 7.70 ($1H_{arom}$, d, *J* = 8.4 Hz), 7.84 ($1H_{arom}$, t, *J* = 8.8 Hz), 8.26 ($1H_{arom}$, d, *J* = 8.0 Hz), 13.71 ($1H_{OH}$, s); ^{13}C NMR: ($CDCl_3$) δ (ppm) 57.6, 95.13, 102.9, 112.0, 117.6, 118.6, 119.9, 120.7, 123.4, 125.7, 130.3, 131.4, 135.2, 136.3, 138.8, 155.5, 155.6, 164.0, 165.1, 169.4, 180.8. Anal. calcd

for $C_{20}H_{14}ClNO_6S$: C, 55.62; H, 3.27; N, 3.24; found: C, 55.72; H, 3.41; N, 3.22%.

N-(2-Chlorophenyl)-1-hydroxy-3-methoxy-9-oxo-9H-xanthene-4-sulfonamide (**4q**): Cream solid (EtOH); m.p. 134–138 °C; R_f = 0.33 (70% ethyl acetate 30% *n*-hexane); IR: (KBr, cm^{-1}) 3474 (O–H), 3226 (N–H), 1664 (CO), 1374, 1178 (SO_2); ^1H NMR: ($CDCl_3$) δ (ppm) 4.09 ($3H_{OMe}$, s), 6.44 ($1H_{arom}$, s), 6.95-7.10 ($3H_{arom,NH}$ m), 7.13–7.29 ($1H_{arom}$, m), 7.37 ($1H_{arom}$, d, *J* = 8.0 Hz), 7.47 ($1H_{arom}$, t, *J* = 8.0 Hz), 7.65 ($1H_{arom}$, d, *J* = 8.0 Hz), 7.82 ($1H_{arom}$, t, *J* = 8.0 Hz), 8.26 ($1H_{arom}$, d, *J* = 8.0 Hz), 13.91 ($1H_{OH}$, s). Anal. calcd for $C_{20}H_{14}ClNO_6S$: C, 55.62; H, 3.27; N, 3.24; found: C, 55.70; H, 3.31; N, 3.18%.

N-(2,4-Dichlorophenyl)-1-hydroxy-3-methoxy-9-oxo-9H-xanthene-4-sulfonamide (**4r**): Brown solid (EtOH); m.p. 144–148 °C; R_f = 0.50 (70% ethyl acetate 30% *n*-hexane); IR: (KBr, cm^{-1}) 3474 (O–H), 3303 (N–H), 1657 (CO), 1396, 1156 (SO_2); ^1H NMR: ($CDCl_3$) δ (ppm) 4.13 ($3H_{OMe}$, s), 6.41 ($1H_{arom}$, s), 6.63 ($1H_{arom}$, d, *J* = 8.0 Hz), 6.98–7.05 ($2H_{arom}$, m), 7.25 ($1H_{NH}$, s), 7.45 ($1H_{arom}$, t, *J* = 7.2 Hz), 7.67 ($1H_{arom}$, d, *J* = 8.4 Hz), 7.80 ($1H_{arom}$, d, *J* = 7.2 Hz), 8.22 ($1H_{arom}$, d, *J* = 6.8 Hz), 13.90 ($1H_{OH}$, s). Anal. calcd for $C_{20}H_{13}Cl_2NO_6S$: C, 51.52; H, 2.81; N, 3.00; found: C, 51.70; H, 3.01; N, 3.11%.

1-Hydroxy-3-methoxy-N-(3-nitrophenyl)-9-oxo-9H-xanthene-4-sulfonamide (**4s**): Brown solid (EtOH); m.p. 172–176 °C; R_f =0.48 (50% ethyl acetate 50% *n*-hexane); IR: (KBr, cm^{-1}) 3430 (O–H), 3267 (N–H), 1650 (CO), 1380, 1163 (SO_2); ^1H NMR: ($CDCl_3$) δ (ppm) 4.15 ($3H_{OMe}$, s), 6.50 ($1H_{arom}$, s), 6.54 ($1H_{arom}$, s), 6.83–7.03 ($1H_{arom}$, m), 7.29–7.39 ($2H_{arom}$, m), 7.50 ($1H_{NH}$, s) 7.65–7.69 ($1H_{arom}$, m), 7.92–7.93 ($1H_{arom}$, m), 8.09–8.10 ($1H_{arom}$, m), 8.25–8.33 ($1H_{arom}$, m), 13.95 ($1H_{OH}$, s); ^{13}C NMR: ($CDCl_3$) δ (ppm) 55.8, 94.7, 102.5, 107.7, 113.1, 113.9, 117.2, 123.4, 124.3, 125.1, 125.5, 130.4, 135.4, 138.6, 148.7, 155.6, 157.1, 162.6, 166.1, 179.9. Anal. calcd for $C_{20}H_{14}N_2O_8S$: C, 54.30; H, 3.19; N, 6.33; found: C, 54.50; H, 3.31; N, 6.18%.

1-Hydroxy-3-methoxy-9-oxo-N-(thiazol-2-yl)-9H-xanthene-4-sulfonamide (**4t**): Light brown solid (EtOH); m.p. 172–176 °C; R_f = 0.25 (ethyl acetate); IR: (KBr, cm^{-1}) 3428 (O–H), 3130 (N–H), 1660 (CO), 1403, 1187 (SO_2); ^1H NMR: ($CDCl_3$) δ (ppm) 4.14 ($3H_{OMe}$, s), 6.42 ($1H_{arom}$, s), 6.64 ($1H_{arom}$, d, *J* = 7.6 Hz), 7.27 ($1H_{arom}$, d, *J* = 9.0 Hz), 7.26 ($1H_{N\text{-}H}$, s), 7.46 ($1H_{arom}$, t, *J* = 7.6 Hz), 7.67 ($1H_{arom}$, d, *J* = 8.4 Hz), 7.81 ($1H_{arom}$, t, *J* = 7.6 Hz), 8.24 ($1H_{arom}$, t, *J* = 8.0 Hz), 13.90 ($1H_{OH}$, s). Anal. calcd for $C_{17}H_{12}N_2O_6S_2$: C, 50.49; H, 2.99; N, 6.93; found: C, 50.70; H, 3.07; N, 6.78%.

Antibacterial activity

The antibacterial activities of the synthetic compounds were tested against a Gram-negative: *E. coli* (ATCC25922) and a Gram-positive bacterial strain: *S. aureus* (ATCC 25213). *In vitro* activities of the xanthone sulfonamides were tested in nutrient broth for bacteria by the two-fold serial dilution method. The turbidity of all the bacterial cultures was adjusted to 0.5 McFarland standards in order to achieve a concentration of $1.5\acute{}10^8$ bacterial colony-forming units (CFU) mL^{-1}. Each test compound (50 mg) was dissolved in DMSO (0.5 mL) and the solution was diluted with water (4.5 mL) to give a stock solution of 10,000 μg mL^{-1} of each compound. Further progressive double dilution with Muller–Hinton broth was performed to obtain the required concentrations of 1000, 500, 250, 125 and 62.5 μg mL^{-1}. To ensure that the solvent had no effect on the bacterial growth, a control test was performed with a test medium supplemented with DMSO at the same dilutions as used in the experiment.

We appreciate financial support of Shahreza Branch, Islamic Azad University (IAUSH) Research Council.

Received 4 June 2015 ; accepted 7 July 2015
Paper 1503398 doi: 10.3184/174751915X14373971129805
Published online: 7 August 2015

References

1 M. Leeb, *Nature*, 2004, **431**, 892.
2 D.J. Abraham and E. Burger, Burger's *Medicinal chemistry and drug discovery*. John Wiley and Sons, Hoboken, 2003.
3 M. Lopez, L.F. Bornaghi, A. Innocenti, D.S. Vullo, S.A. Charman, C.T. Supuran and S.A. Poulsen, *J. Med. Chem.,* 2010, **53**, 2913.
4 K. Matsumoto, Y. Akao, E. Kobayashi, K. Ohguchi, T. Ito, T. Tanaka, M. Iinuma, Y. and J. Nozawa*, Nat. Prod*., 2003, **66**, 1124.
5 M. M. M. Pinto, M. E. Sousa and M. S. J. Nascimento, *Curr. Med. Chem.,* 2005, **12**, 2517.
6 B. W. Lee, J. H. Lee, S. T. Lee, H.S. Lee, W. S. Lee, T.S. Jeong and K.H. Park, *Bioorg. Med. Chem. Lett*., 2005, **15**, 5548.
7 R. Giri, J.R. Goodell, C. Xing, A. Benoit, H. Kaur, H. Hiasa and D.M. Ferguson, *Bioorg. Med. Chem*., 2010, **18**, 1456.
8 S. Woo, D. Kang, J. M. Nam, C.S. Lee, E.S. Lee, Y. Kwon and Y. Na, *Eur. J. Med. Chem*., 2010, **45**, 4221.
9 Y.S. Zhou, A.J. Hou, G.F. Zhu, Y.F. Chen, H.D. Sun and Q.S. Zhao, *Bioorg. Med. Chem.,* 2004, **12**, 1947.
10 H.R. Seedi, M.A. El-Barbary, D.M.H. El-Ghorab, L. Bohlin, A.K. Borg-Karlson, U. Goransson and R. Verpoorte, *Curr. Med. Chem.,* 2010, **17**, 854.
11 A.R. Massah, H. Adibi, R. Khodarahmi, R. Abiri, M.B. Majnooni, S. Shahidi, B. Asadi, M. Mehrabi and M.A. Zolfigol, *Bioorg. Med. Chem*., 2008, **16**, 54.
12 A.R. Massah, M. Dabagh, S. Shahidi, H. Javaherian Naghash, A.R. Momeni and H. Aliyan, *J. Iran. Chem. Soc*., 2009, **6**, 405.
13 N.K. Maghsoodi, T. Khazaeli and A.R. Massah, *J. Chem. Res*., 2015, **39**, 141.
14 S. Woo, J. Jung, C. Lee, Y. Kwonb, and Y. Na, *Bioorg. Med. Chem. Lett*., 2007, **17**, 1163.
15 A.D. Becke, *Phys. Rev. A*., 1988, **38**, 3098.
16 M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, V.G. Zakrzewski, J.A. Montgomery, Jr., R.E. Stratmann, J.C. Burant, S. Dapprich, J.M. Millam, A.D. Daniels, K.N. Kudin, M.C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G.A. Petersson, P.Y. Ayala, Q. Cui, K. Morokuma, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J. Cioslowski, J.V. Ortiz, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P.M.W. Gill, B. G. Johnson, W. Chen, M.W. Wong, J.L. Andres, C. Gonzalez, M. Head-Gordon, E.S. Replogle and J.A. Pople, *Gaussian 98*, Revision A.7; Gaussian, Inc.: Pittsburgh PA, 1998.
17 A.R. Massah, R.J. Kalbasi and N. Samah, *Bull. Korean Chem. Soc.,* 2011, **32**, 1703.
18 A.R. Massah, D. Azadi, H. Aliyan, A.R. Momeni, H. Javaherian Naghash and F. Kazemi, *Monatsh. Chem*., 2008, **139**, 233.
19 A.R. Massah, M. Dabagh, S. Shahidi, H. Javaherian Naghash, A.R. Momeni and H. Aliyan, *J. Iran Chem. Soc*., 2009, **6**, 405.
20 N.N. Pogodaeia, *Chem. Nat. Compd*., 2011, **47**, 38.