HETEROCYCLES, Vol. 83, No. 8, 2011, pp. 1831 - 1841. © The Japan Institute of Heterocyclic Chemistry
Received, 6th March, 2011, Accepted, 30th May, 2011, Published online, 7th June, 2011
DOI: 10.3987/COM-11-12201

SYNTHESIS OF NOVEL TETRAHYDRO[4,5]IMIDAZO[2,1-*b*]-CHROMENO[4,3,2-*de*]QUINAZOLINE AND BENZOTHIAZOL-2-YLAMINOXANTHENONE DERIVATIVES

Mina Saeedi,* Yahya S. Beheshtiha, Majid M. Heravi,* and Hossein A. Oskooie

Department of Chemistry, School of Sciences, Alzahra University, PO Box 1993891176, Vanak, Tehran, Iran (e-mail: saeedi.mina@gmail.com and mmh1331@yahoo.com)

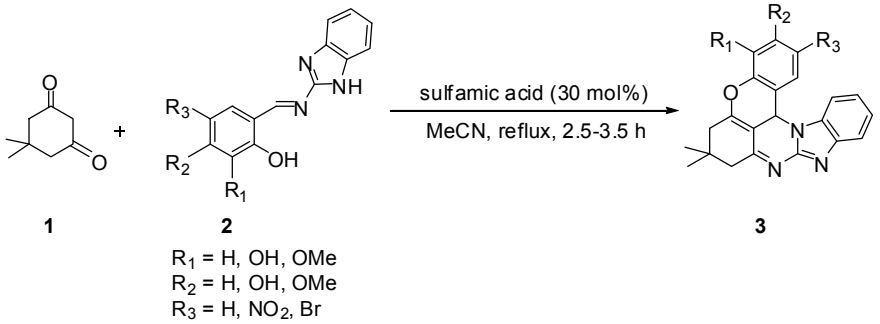
Abstract – Some novel tetrahydroquinazoline and xanthenone derivatives were synthesized from the reaction of dimedone and Schiff base in the presence of sulfamic acid in good yields.

Heterocycles containing nitrogen and oxygen are important targets in medicinal chemistry. The quinazoline ring system along with many alkaloids is a widely recognized moiety in organic syntheses and medicinal application.[1-3] It has been reported that quinazoline derivatives possess interesting biological activities, such as anticonvulsant, antibacterial, antidiabetic and anticancer properties.[4] Many quinazolines have been found to inhibit kinases by competing with ATP for the kinase active site.[5] Large numbers of quinazolinones have been synthesized or isolated from plants, animals and microorganisms[6] and also in several areas as materials in electronics, in electrochemistry as anticorrosive agents, as polymers or optical materials and fluorescent tags in DNA sequencing.[7,8] It was reported that benzimidazo-quinazoline derivatives show various therapeutic activities, such as anticancer,[9] antiviral,[10] antimicrobial,[11] anti-inflammatory[12] and anticonvulsants.[13]

Xanthenone derivatives have been reported to possess interesting cytotoxic activities.[14,15] They are reported to possess antileukemic, antitumor, antiulcer, antimicrobial, antihepatotoxic and CNS-depressant activities.[16,17] Therefore, development of efficient preparation of novel quinazoline and xanthenone derivatives is an interesting challenge.

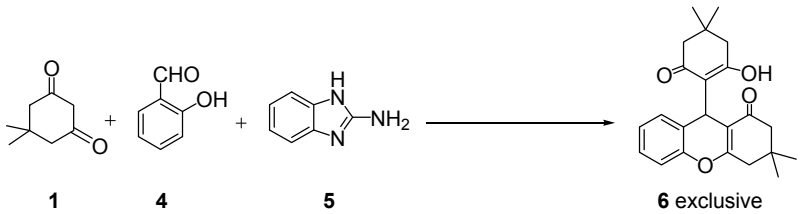
Recently we have developed synthesis of new heterocyclic compounds in the presence of sulfamic acid (SA) as an efficient and useful catalyst.[18-20] Sulfamic acid is a common sulfur-containing amino acid with mild acidity. It is green, inexpensive, easy to handle, non toxic, available and efficient catalyst for various organic chemistry transformations and its use has been growing rapidly.[21]

In the context of our interest in designing new ways for synthesis of heterocyclic compounds,[18-20,22] herein, we have developed a novel and convenient approach to synthesize new tetrahydrobenzo[4,5]imidazo[2,1-*b*]chromeno[4,3,2-*de*]quinazoline and benzothiazol-2-ylamino-xanthenone derivatives *via* reaction of dimedone **1** and Schiff bases **2** and **7** catalyzed by sulfamic acid (Schemes 1 and 3).



Scheme 1. Synthesis of tetrahydrobenzo[4,5]imidazo[2,1-*b*]chromeno[4,3,2-*de*]quinazoline derivatives **3**

We initially used the most direct approach, a Biginelli-type condensation and subjected dimedone **1**, salicylaldehyde **4** and 2-aminobenzimidazole **5** to a one-pot three-component reaction as a model reaction (Scheme 2). Then the model reaction was carried out under different conditions. Some conditions and results are summarized in Table 1.



Scheme 2. Investigation of one-pot three-component reaction of dimedone **1**, salicylaldehyde **4** and 2-aminobenzimidazole **5**, under different conditions as can be seen in Table 1

At first we studied the reaction in solvent-free conditions (Table 1, entries 1 and 3). Any products were not obtained at ambient condition or evaluated temperatures (100 °C). When the model reaction performed under solvent-free condition at 100 °C in the presence of sulfamic acid (30 mol%), product **6**

was exclusively isolated as proved by physical and spectral characterization.[23] The results show that 2-aminobenzimidazole has not participated in the reaction. It is worthy to mention that when the model reaction was carried out in different solvents in the presence of a variety of catalysts as can be seen in Table 1, same product was detected and there was no evidence for formation of desired product. We also applied microwave irradiation to the model reaction and **6** was isolated as the only product (Table 1).

Table 1. Investigation of various conditions for a one-pot three-component reaction of dimedone **1**, salicylaldehyde **4** and 2-aminobenimidazole **5**

Entry	Conditions	Catalyst	Time	Yield of **6** (%)[a]
1	solvent free (100 °C)	-	12 h	0
2	MW irradiation (500 W)	-	6 min	5
3	solvent free (100 °C)	sulfamic acid (30 mol%)	12 h	45
4	MW irradiation (400 W)	sulfamic acid (30 mol%)	7 min	30
5	MeCN (reflux)	K_2CO_3 (36 mol%)	8 h	45
6	MeCN (reflux)	PTSA (17 mol%)	10 h	25
7	EtOH (reflux)	I_2 (40 mol%)	5 h	55
8	MeCN (reflux)	I_2 (40 mol%)	5 h	50
9	toluene (reflux)	K_2CO_3 (36 mol%)	8 h	30
10	CH_2Cl_2 (reflux)	sulfamic acid (30 mol%)	8 h	35

[a] Isolated yields.

To overcome this apparent failure, another alternative synthetic route was designed. For this purpose, various Schiff bases **2** were prepared by reaction of salicylaldehyde **4** and its derivatives with 2-aminobenzimidazole **5**. We tried to prepare the corresponding Schiff bases **2** *via* reported procedures,[24,25] we could not prepare them however in high yields. We found that under microwave conditions, condensation reaction could proceed very fast and efficiently. A mixture of salicylaldehyde derivative (1 mmol) and 2-aminobenzimidazole (1 mmol) in methanol (5 mL) was irradiated in microwave oven (700 W/ 7 min). After cooling to room temperature, the precipitate was collected, washed three times with cold methanol. In most cases, Schiff bases were analytically pure without recrystallization however they can be crystallized from methanol.

Next the reaction of dimedone and Schiff base was investigated. As can be seen in Table 2, to optimize the reaction conditions, the Schiff base of salicylaldehyde and 2-aminobenzimidazole was treated with dimedone **1** under different reaction conditions to form the corresponding product **3a** (Scheme 1). The best result was obtained in the presence of 30 mol% sulfamic acid in MeCN under reflux condition. It is also to be noted that any undesired products were not observed.

Table 2. Investigation of various conditions on synthesis of **3a** by the reaction of **1** and **2**

Entry	Conditions	Catalyst	Time	Yield of **3a** (%)[a]
1	solvent free (100 °C)	-	24 h	0
2	MW irradiation[b]	-	10 min	0
3	solvent free (100 °C)	sulfamic acid (30 mol%)	9 h	45
4	MW irradiation[b]	sulfamic acid (30 mol%)	10 min	0
5	MeCN (reflux)	sulfamic acid (30 mol%)	3.5 h	70
6	MeCN (room temperature)	sulfamic acid (30 mol%)	12 h	30
7	EtOH (reflux)	sulfamic acid (30 mol%)	9 h	55
8	MeCN (reflux)	K_2CO_3 (36 mol%)	12 h	55
9	MeCN (reflux)	$ZnCl_2$ (37 mol%)	12 h	35
10	MeCN (reflux)	I_2 (40 mol%)	12 h	55
11	MeCN (reflux)	KF-Al_2O_3 (0.1 g)	10 h	50

[a]Isolated yields.
[b] Different powers, 200 W, 300 W, 400 W and 500 W were examined.

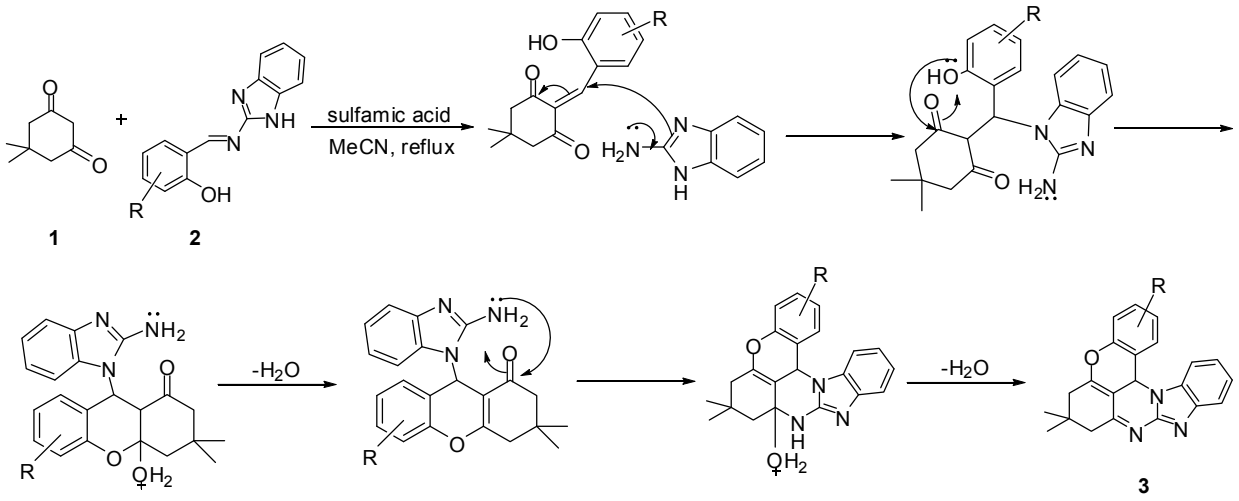
The model reaction was achieved under microwave irradiation and different power inputs were examined. It was found that no product was obtained even in the presence of sulfamic acid. We also investigated the effect of other catalysts such as I_2, $ZnCl_2$ and KF/Al_2O_3 and in all case the desired product was not obtained. In order to expand the scope of the present work, various Schiff bases **2** were examined and desired products were obtained in good yields. The results are summarized in Table 3.

Proposed mechanism for the synthesis of tetrahydrobenzo[4,5]imidazo[2,1-*b*]chromeno-[4,3,2-*de*]quinazoline derivatives **3** can be explained in Scheme 3, based on reference[26] that discussed reaction of imines and dimedone.

Table 3. Synthesis of **3** by the reaction of **1** and **2**

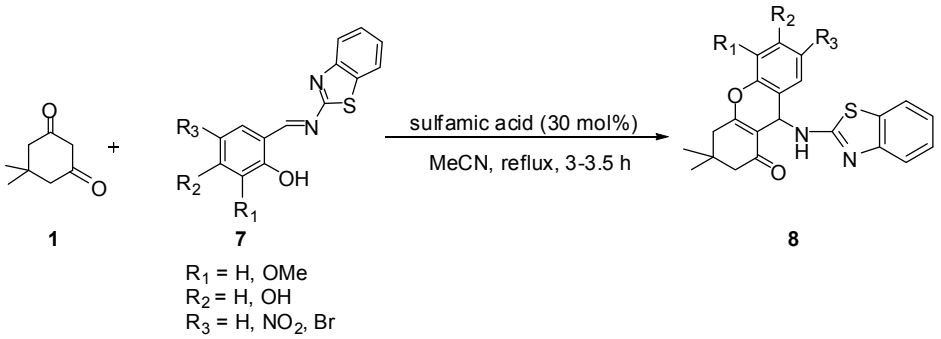
Entry	R_1	R_2	R_3	Product	Time (h)	Yield (%)[a]
1	H	H	H	**3a**	3.5	70
2	OMe	H	H	**3b**	3	75
3	H	OMe	H	**3c**	3.5	70
4	OH	H	H	**3d**	3.5	70
5	H	OH	H	**3e**	3.5	65
6	H	H	NO_2	**3f**	2.5	85
7	H	H	Br	**3g**	3	80

[a]Isolated yields



Scheme 3. Proposed mechanism for the synthesis of tetrahydrobenzo[4,5]imidazo[2,1-*b*]chromeno-[4,3,2-*de*]quinazoline derivatives **3**

We next prepared Schiff bases derived from 2-aminothiazole and salicylaldehyde derivatives. General procedure is the same as described for compounds **2**. Under optimized conditions, reaction of dimedone **1** and mentioned Schiff bases **7** were examined. In this case, interestingly corresponding tetrahydro-1*H*-1-xanthenone derivatives were formed (Scheme 4). In order to show the generality and scope of this new protocol, reaction of dimedone **1** and Schiff bases **7** were conducted in the presence of 30 mol% sulfamic acid under reflux condition and related tetrahydro-1*H*-1-xanthenone derivatives were obtained in good yields. Corresponding data are shown in Table 4.



Scheme 4. Synthesis of benzothiazol-2-ylaminoxanthenone derivatives

Table 4. Synthesis of **8** by the reaction of **1** and **7**

Entry	R_1	R_2	R_3	Product	Time (h)	Yield (%)[a]
1	H	H	H	**8a**	3	75
2	OMe	H	H	**8b**	3.5	70
3	H	OH	H	**8c**	3.5	70
4	H	H	NO_2	**8d**	3	85
5	H	H	Br	**8e**	3	80

[a]Isolated yields

In conclusion, we have described a new and efficient procedure for the preparation of novel tetrahydrobenzo[4,5]imidazo[2,1-*b*]chromeno[4,3,2-*de*]quinazoline and tetrahydro-1*H*-1-xanthenone derivatives *via* reaction of dimedone and Schiff base in the presence catalytic amount of sulfamic acid in MeCN under reflux condition. The procedure was simple and products were obtained in good yields.

EXPERIMENTAL

Melting points were measured, using a capillary tube method with a Bamstead Electrothermal 9200 apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AQS-AVANCE spectrometer at 500 and 125 MHz, using TMS as an internal standard. FTIR spectra were recorded using, KBr disks on FT-IR Bruker Tensor 27 instrument. Mass spectra were documented on an Agilent Technology (HP) mass spectrometer operating at an ionization potential of 70 eV. The elemental analysis was performed with an Elemetar Analysensystem GmbH VarioEL CHNS mode.

General procedure for the synthesis of compounds 3a-g and 8a-e

A mixture of dimedone (1.2 mmol), Schiff base (1 mmol), sulfamic acid (30 mol%) and MeCN (5 mL) was heated at reflux for indicated time as required to complete the reaction (Table 3). Upon completion of the reaction, monitored by TLC, the mixture was cooled to room temperature. The precipitated product was separated by filtration, washed with water and acetone. Corresponding products were analytically pure without recrystallization.

7,7-Dimethyl-6,7,8,15a-tetrahydrobenzo[4,5]imidazo[2,1-b]chromeno[4,3,2-de]quinazoline (3a)

Compound **3a** was obtained as white powder. Mp 185-186 °C. FTIR (KBr, cm^{-1}) ν_{max}: 3067, 2957, 1682, 1615. ^1H NMR (500 MHz, DMSO-d_6) δ_H: 1.02 (s, 6H, CH_3), 2.21 (m, 4H, CH_2), 6.12 (s, 1H, CH), 6.78-8.35 (m, 8H, Ar). ^{13}C NMR (125 MHz DMSO-d_6) δ_C: 29.4, 32.1, 38.9, 49.8, 50.9, 53.0, 109.2, 110.2, 111.0, 118.1, 118.9, 123.1, 123.9, 125.9, 126.2, 127.4, 132.3, 140.1, 152.2, 154.0, 155.2, 165.0. MS *m/z*: 341 $[M]^+$. Anal. Calcd for $C_{22}H_{19}N_3O$: C, 77.40; H, 5.61; N, 12.31. Found: C, 77.65; H, 5.95; N, 12.11.

4-Methoxy-7,7-dimethyl-6,7,8,15a-tetrahydrobenzo[4,5]imidazo[2,1-b]chromeno[4,3,2-de]quinozaline (3b)

Compound **3b** was obtained as white powder. Mp 274-275 °C. FTIR (KBr, cm^{-1}) ν_{max}: 3113, 2884, 1691, 1634 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ_H: 1.02 (s, 6H, CH_3), 2.20 (m, 4H, CH_2), 3.78 (s, 3H, CH_3), 6.06 (s, 1H, CH), 6.69-8.35 (m, 7H, Ar). ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 28.9, 32.3, 38.7, 50.5, 51.1, 53.2, 57.2, 109.9, 110.3, 113.0, 118.1, 120.9, 124.9, 125.9, 126.3, 127.0, 132.9, 140.1, 144.8, 152.3, 154.2, 156.3, 165.3. MS *m/z*: 371 $[M]^+$. Anal. Calcd for $C_{23}H_{21}N_3O_2$: C, 74.37; H, 5.70; N, 11.31. Found: C, 74.66; H, 5.95; N, 11.57.

3-Methoxy-7,7-dimethyl-6,7,8,15a-tetrahydrobenzo[4,5]imidazo[2,1-b]chromeno[4,3,2-de]quinozaline (3c)

Compound **3c** was obtained as white powder. Mp 277-278 °C. FTIR (KBr, cm^{-1}) ν_{max}: 3115, 1688, 1630 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ_H: 1.02 (s, 6H, CH_3), 2.21 (m, 4H, CH_2), 3.84 (s, 3H, CH_3), 6.15 (s, 1H, CH), 6.61-8.33 (m, 7H, Ar). ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 28.3, 32.4, 38.7, 50.4, 51.1, 53.4, 57.1, 110.0, 110.2, 112.7, 118.2, 120.9, 124.8, 125.7, 126.3, 127.1, 133.2, 140.1, 144.4, 152.3, 154.2, 156.4, 166.3. MS *m/z*: 371 $[M]^+$. Anal. Calcd for $C_{23}H_{21}N_3O_2$: C, 74.37; H, 5.70; N, 11.31. Found: C, 74.01; H, 6.05; N, 10.97.

7,7-Dimethyl-6,7,8,15a-tetrahydrobenzo[4,5]imidazo[2,1-b]chromeno[4,3,2-de]quinazolin-4-ol (3d)

Compound **3d** was obtained as light brown powder. Mp 282-283 °C. FTIR (KBr, cm^{-1}) ν_{max}: 3440, 2950, 1680, 1625 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ_H: 1.02 (s, 6H, CH_3), 2.21 (m, 4H, CH_2), 6.05 (s, 1H,

CH), 6.90-8.32 (m, 7H, Ar), 10.45 (s, 1H, OH). ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 29.1, 32.4, 38.7, 49.5, 50.1, 51.3, 109.2, 110.3, 117.1, 119.1, 119.9, 122.0, 122.3, 123.4, 124.1, 128.2, 133.8, 145.0, 146.2, 151.5, 155.5, 165.5. MS *m/z*: 357 $[M]^+$. Anal. Calcd for $C_{22}H_{19}N_3O_2$: C, 73.93; H, 5.36; N, 11.76. Found: C, 73.65; H, 5.25; N, 11.91.

7,7-Dimethyl-6,7,8,15a-tetrahydrobenzo[4,5]imidazo[2,1-b]chromeno[4,3,2-de]quinazolin-3-ol (3e)

Compound **3e** was obtained as orange powder. Mp 280-282 °C. FTIR (KBr, cm^{-1}) ν_{max}: 3437, 2957, 1698, 1620 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 1.02 (s, 6H, CH_3), 2.20 (m, 4H, CH_2), 6.05 (s, 1H, CH), 6.71-8.33 (m, 7H, Ar), 10.26 (s, 1H, OH). ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 29.1, 32.5, 38.5, 49.7, 50.3, 51.4, 109.1, 110.1, 117.3, 119.2, 120.0, 122.3, 122.5, 123.2, 124.2, 128.1, 133.6, 145.2, 146.1, 151.5, 155.5, 166.5. MS *m/z*: 357 $[M]^+$. Anal. Calcd for $C_{22}H_{19}N_3O_2$: C, 73.93; H, 5.36; N, 11.76. Found: C, 74.21; H, 5.41; N, 11.38.

2-Nitro-7,7-dimethyl-6,7,8,15a-tetrahydrobenzo[4,5]imidazo[2,1-b]chromeno[4,3,2-de]quinazoline (3f)

Compound **3f** was obtained as white powder. Mp 284 °C. FTIR (KBr, cm^{-1}) ν_{max}: 3188, 2958, 1672, 1615, 1581, 1378 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 1.02 (s, 6H, CH_3), 2.20 (m, 4H, CH_2), 6.25 (s, 1H, CH), 6.83-8.32 (m, 7H, Ar). ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 29.1, 32.4, 38.6, 49.5, 50.1, 53.2, 109.9, 112.2, 112.3, 118.1, 123.0, 123.3, 123.6, 124.9, 129.2, 132.7, 138.9, 140.0, 151.6, 154.1, 155.3, 164.8. MS *m/z*: 386 $[M]^+$. Anal. Calcd for $C_{22}H_{18}N_4O_3$: C, 68.38; H, 4.70; N, 14.50. Found: C, 68.62; H, 4.43; N, 14.30.

2-Bromo-7,7-dimethyl-6,7,8,15a-tetrahydrobenzo[4,5]imidazo[2,1-b]chromeno[4,3,2-de]quinazoline (3g)

Compound **3g** was obtained as white powder. Mp 206-207 °C. FTIR (KBr, cm^{-1}) ν_{max}: 3188, 2960, 1675, 1616 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 1.02 (s, 6H, CH_3), 2.21 (m, 4H, CH_2), 6.05 (s, 1H, CH), 6.70-8.38 (m, 7H, Ar). ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 29.1, 33.0, 38.5, 49.2, 50.6, 52.4, 109.8, 112.1, 112.2, 118.1, 122.9, 123.4, 124.1, 124.9, 129.5, 133.0, 139.0, 140.0, 151.2, 152.1, 153.1, 164.8. MS *m/z*: 419 $[M]^+$. Anal. Calcd for $C_{22}H_{18}BrN_3O$: C, 62.87; H, 4.32; N, 10.00. Found: C, 63.16, H, 3.98; N, 10.28.

9-(1,3-Benzothiazol-2-ylamino)-3,3-dimethyl-2,3.4.9-tetrahydro-1H-1-xanthenone (8a)

Compound **8a** was obtained as pale yellow powder. Mp 277 °C. FTIR (KBr, cm^{-1}) ν_{max}: 3439, 2960, 1621, 1574 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 0.96 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.11 (d, J = 15.75 Hz, 1H, CH_2), 2.27 (d, J = 15.10 Hz, 1H, CH_2), 2.45 (d, J = 16.38 Hz, 1H, CH_2), 2.56 (d, J = 15.10 Hz,

1H, CH_2), 6.50 (s, 1H, CH), 6.90-8.45 (m, 8H, Ar), 11.70 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 27.3, 29.4, 33.5, 46.3, 52.1, 54.0, 112.1, 119.3, 123.6, 124.4, 124.9, 126.9, 127.3, 128.1, 128.3, 139.0, 139.8, 144.3, 159.8, 161.0, 165.5, 194.0. MS *m/z*: 376 $[M]^+$. Anal. Calcd for $C_{22}H_{20}N_2O_2S$: C, 70.19; H, 5.35; N, 7.44. Found: C, 69.95; H, 5.50; N, 7.78.

9-(1,3-Benzothiazol-2-ylamino)-5-methoxy-3,3-dimethyl-2,3,4,9,-tetrahydro-1H-1-xanthenone (8b)

Compound **8b** was obtained as pale pink powder. Mp 226-227 °C. FTIR (KBr, cm^{-1}) ν_{max}: 3409, 2954, 1642, 1585 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 0.96 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.11 (d, J = 15.70 Hz, 1H, CH_2), 2.30 (d, J = 15.11 Hz, 1H, CH_2), 2.48 (d, J = 16.30 Hz, 1H, CH_2), 2.53 (d, J = 15.08 Hz, 1H, CH_2), 3.84 (s, 3H, CH_3), 6.48 (s, 1H, CH), 6.80-8.42 (m, 7H, Ar), 11.75 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 27.1, 29.3, 33.5, 45.6, 51.3, 53.5, 57.8, 111.5, 116.3, 121.2, 121.6, 125.4, 126.1, 127.3, 128.0, 128.1, 137.1 140.0, 140.3, 161.3, 163.0, 166.7, 194.5. MS *m/z*: 406 $[M]^+$. Anal. Calcd for $C_{23}H_{22}N_2O_3S$: C, 67.96, H, 5.46; N. 6.89. Found: C, 68.25; H, 5.15; N, 7.11.

9-(1,3-Benzothiazol-2-ylamino)-6-hydroxy-3,3-dimethyl-2,3,4,9,-tetrahydro-1H-1-xanthenone (8c)

Compound **8c** was obtained as pale yellow powder. Mp 240-242 °C. FTIR (KBr, cm^{-1}) ν_{max}: 3415, 2960, 1640, 1570 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 0.96 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.10 (d, J = 15.71 Hz, 1H, CH_2), 2.28 (d, J = 15.09 Hz, 1H, CH_2), 2.45 (d, J = 16.39 Hz, 1H, CH_2), 2.60 (d, J = 15.07 Hz, 1H, CH_2), 6.52 (s, 1H, CH), 6.72-8.41 (m, 7H, Ar), 11.65 (s, 2H, NH, OH). ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 27.1, 29.5, 33.3, 44.9, 51.8, 53.8, 115.0, 119.1, 123.6, 124.7, 124.9, 126.9, 127.1, 127.9, 128.1, 136.6, 139.1, 141.2, 158.3, 164.2, 166.6, 194.8. MS *m/z*: 392 $[M]^+$. Anal. Calcd for $C_{22}H_{20}N_2O_3S$: C, 67.33; H, 5.14; N, 7.14. Found: C, 67.65; H, 4.86; N, 6.86.

9-(1,3-Benzothiazol-2-ylamino)-3,3-dimethyl-7-nitro-2,3,4,9,-tetrahydro-1H-1-xanthenone (8d)

Compound **8d** was obtained as yellow powder. Mp 286-287 °C. IR (KBr, cm^{-1}) ν_{max}: 3443, 3063, 1625, 1588, 1387 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 0.96 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.10 (d, J = 15.73 Hz, 1H, CH_2), 2.29 (d, J = 15.06 Hz, 1H, CH_2), 2.44 (d, J = 16.36 Hz, 1H, CH_2), 2.58 (d, J = 15.05 Hz, 1H, CH_2), 6.81 (s, 1H, CH), 6.92-8.48 (m, 7H, Ar), 11.71 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 27.4, 29.8, 33.1, 45.5, 51.2, 53.3, 113.1, 117.0, 123.4, 123.7, 125.0, 126.4, 127.4, 127.5, 127.8, 138.9, 139.2, 140.1, 160.0, 162.2, 165.9, 194.9. MS *m/z*: 421 $[M]^+$. Anal. Calcd for $C_{22}H_{19}N_3O_4S$: C, 62.69; H, 4.54; N, 9.97. Found: C, 62.40; H, 4.77; N, 10.25.

9-(1,3-Benzothiazol-2-ylamino)-7-bromo-3,3-dimethyl-2,3,4,9,-tetrahydro-1H-1-xanthenone (8e)

Compound **8e** was obtained as pale yellow powder. Mp 242-243 °C. FTIR (KBr, cm^{-1}) ν_{max}: 3440, 3103,

2962, 1617, 1570 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ_H: 0.96 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.12 (d, J = 15.81 Hz, 1H, CH_2), 2.27 (d, J = 15.10 Hz, 1H, CH_2), 2.45 (d, J = 16.21 Hz, 1H, CH_2), 2.56 (d, J = 15.10 Hz, 1H, CH_2), 6.40 (s, 1H, CH), 6.60-8.45 (m, 7H, Ar), 11.70 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: = 27.2, 29.4, 33.1, 45.2, 51.2, 53.3, 113.1, 117.0, 123.4, 123.7, 125.0, 126.8, 127.0, 127.8, 127.9, 139.0, 139.3, 140.7, 160.4, 162.2, 165.7, 194.7. MS *m/z*: 454 $[M]^+$. Anal. Calcd for $C_{22}H_{19}BrN_2O_2S$: C, 58.03; H, 4.21; N, 6.15. Found: C, 58.33; H, 4.51; N, 5.90.

ACKNOWLEDGEMENTS

We gratefully acknowledge the partial financial support from Alzahra University Research Council.

REFERENCES

1. G. G. Spence, E. C. Taylor, and O. Buchardt, *Chem. Rev*., 1970, **70**, 231.
2. P. Zhichkin, E. Kesicki, J. Treiberg, L. Bourdon, M. Ronsheim, H. C. Ooi, S. T. White, A. Judkins, and D. Fairfax, *Org. Lett*., 2007, **9**, 1415.
3. M. A. H. Ismail, S. Barker, D. A. Abou El Ella, K. A. M. Abouzid, R. A. Toubar, and M. H. Todd, *J. Med. Chem*., 2006, **49**, 1526.
4. N. Touroutoglou and R. Pazdur, *Clin. Cancer Res*., 1996, **2**, 227; A. L. Jackman, F. T. Boyle, and K. R. Harrap, *New Drug*, 1996, **14**, 305; T. M. Sielecki, T. L. Johnson, J. Liu, J. K. Muckelbauer, R. H. Grafstrom, S. Cox, J. Boylan, C. R. Burton, H. Chen, A. Smallwood, C. H. Chang, M. Boisclair, P. A. Benfield, G. L. Trainora, and S. P. Seitza, *Bioorg. Med. Chem. Lett*., 2001, **11**, 1157; K. Matsuno, M. Ichimura, T. Nakajima, K. Tahara, S. Fujiwara, H. Kase, J. Ushiki, N. A. Giese, A. Pandey, R. M. Scarborough, N. A. Lokker, J.-C. Yu, J. Irie, E. Tsukuda, S.-I. Ide, S. Oda, and Y. Nomoto, *J. Med. Chem*., 2002, **45**, 3057.
5. V. Kumar, C. Mohan, M. Gupta, and M. P. Mahajan, *Tetrahedron*, 2005, **61**, 3533.
6. S. B. Mhaske and N. P. Argade, *J. Org. Chem.*, 2001, **66**, 9038.
7. K. P. Chan, H. Yang, and A. S. Hay, *J. Polym. Sci*., 1996, **34**, 1923.
8. C. J. Daly, C. M. Milligan, G. Milligan, J. F. Mackenzie, and J. C. Mcgrath, *J. Pharmacol. Exp. Ther*., 1998, **286**, 984.
9. L. D. Via, O. Gia, S. M. Mango, A. D. Settimo, A. M. Marini, G. Primofiore, F. D. A. Settimo, and S. Salerno, *Farmaco*, 2001, **56**, 159.
10. A. A. Spasov, I. N. Yozhitsa, L. I. Bugaeva, and V. A. Anisimova, *Pharma. Chem. J.*, 1999, **33**, 232.
11. B. A. Insuasty, H. Torres, J. Quiroga, R. Abonia, R. Rodriguez, M. Nogueras, A. Sanchez, C. Saitz, S. L. Alvarez, and S. A. Zacchino, *J. Chil. Chem. Soc*., 2006, **51**, 927.
12. G. D. Galarcei, R. E. Foncea, A. M. Edwards, H. Pessoamahana, C. D. P. Mahana, and R. A.

Ebenspergeri, *Biol. Res*., 2008, **41**, 43.

13. L. N. Vostrova, T. A. Voronina, T. L. Karaseva, S. A. Gernega, E. I. Ivanov, A. M. Kirichenko, and M. Yu. Totrova, *Pharma. Chem. J*., 1986, **20**, 404.
14. A. Banerji, A. D. Deshpande, B. R. Prabhu, and P. Pradhan, *J. Nat. Prod.,* 1994*,* **57**, 396.
15. J. P. Horwitz, I. Massova, T. E. Wiese, B. H. Besler, and T. H. Corbett, *J. Med. Chem*., 1994, **37**, 781.
16. R. T. Scannell and R. Stevenson, *J. Heterocycl. Chem*., 1986, **23**, 857.
17. C. Gopalakrishnan, D. Shankaranarayanan, S. K. Nazimudeen, and L. Kameswaran, *Ind. J. Pharmacol.*, 1980, 12, 181.
18. M. M. Heravi, M. Saeedi, Y. S. Beheshtiha, and H. A. Oskooie, *Mol. Divers.*, 2010, in press.
19. M. M. Heravi, H. Alinejhad, K. Bakhtiari, and H. A. Oskooie, *Mol. Divers.*, 2010, **14**, 621.
20. M. M. Heravi, M. Saeedi, Y. S. Beheshtiha, and H. A. Oskooie, *Heterocycles*, 2011, **83**, 535.
21. M. M. Heravi, B. Baghernejad, and H. A. Oskooie, *Curr. Org. Chem*., 2009, **13**, 1002.
22. M. Saeedi, M. M. Heravi, Y. S. Beheshtiha, and H. A. Oskooie, *Tetrahedron*, 2010, **66**, 5345.
23. X.-S. Wang, D.-Q. Shi, Y.-L. Li, H. Chen, X.-Y. Wei, and Z. M. Zong, *Synth. Commun*., 2005, **35**, 97; P. Zhang, Y.-D. Yu, and Z.-H. Zhang, *Synth. Commun*., 2008, **38**, 4474.
24. M. M. Sprung, *Chem. Rev*., 1940, **26**, 297.
25. P. S. Chittilapilly and K. K. M. Yusuff, *Indian J. Chem*., 2008, **47A**, 848.
26. X.-S. Wang, M.-M. Zhang, Z.-S. Zeng, D.-Q. Shi, S.-J. Tu, X.-Y. Wei, and Z.-M. Zong, *Tetrahedron Lett.*, 2005, **46**, 7169.