Turkish Journal of Chemistry

http://journals.tubitak.gov.tr/chem/

Research Article

Turk J Chem
(2015) 39: 235 – 243

doi:10.3906/kim-1408-26

Synthesis of new oxindole derivatives containing benzothiazole and thiazolidinone moieties using nano silica-bonded 5-n-propyl-octahydro-pyrimido[1,2-a]azepinium chloride (NSB-DBU) as catalyst

Robabeh BAHARFAR*, Narges SHARIATI
Faculty of Chemistry, University of Mazandaran, Babolsar, Iran

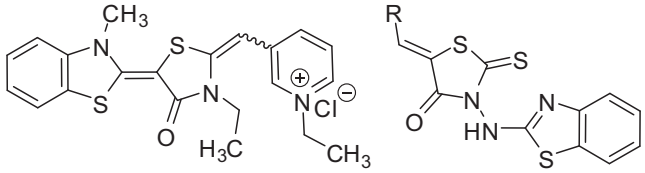
Received: 10.08.2014 • **Accepted/Published Online:** 17.10.2014 • **Printed:** 30.04.2015

Abstract: A facile one-pot synthesis of novel oxindole derivatives bearing benzothiazolylmethyl-2-thioxothiazolidin-4-one was accomplished via one-pot reaction of 5-oxoindolinylidene rhodanine-3-acetic acid derivatives, 2-aminothiophenol, and triphenyl phosphite in the presence of tetrabutylammonium bromide (TBAB) and nano silica-bonded 5-n-propyl-octahydro-pyrimido[1,2-a]azepinium chloride (NSB-DBU) as heterogeneous reusable nanocatalyst. The target compounds were obtained in excellent yields (85%–92%) and short reaction times under fairly mild reaction conditions.

Key words: Oxindole derivatives, benzothiazoles, 4-thiazolidinones, nano silica-bonded 5-n-propyl-octahydro-pyrimido [1,2-a]azepinium chloride, nano silica-supported catalyst

1. Introduction

The chemistry and pharmacology of thiazolidinone derivatives have generated considerable interest because of their outstanding biological activities.[1,2] They are reported to have antitumor,[3,4] anticonvulsant,[5] antibacterial,[6] antiviral,[7] cardiotonic,[8,9] and antidiabetic[10,11] properties. In particular, thiazolidinone-linked benzothiazole analogs have recently proven to be attractive compounds considering that benzothiazole derivatives have a wide spectrum of pharmacological activities.[12–14] Some examples of mentioned structures with anticancer activity are shown in Figure 1.[15,16]



R= 2-(4-OMe-C_6H_4NHCOCH_2O)-5-ClC_6H_5

Figure 1. The structures of some thiazolidinone–benzothiazole hybrid molecules with anticancer activity.

The oxindole framework is a versatile structural motif found in a variety of biologically and pharmaceutically active natural products and as a useful synthon in organic synthesis.[17–20] Oxindole derivatives possess various biological activities such as anesthetic,[21] antirheumatic,[22] and anti-inflammatory[23] properties. It has

*Correspondence: baharfar@umz.ac.ir

been found that combination of two or more heterocyclic scaffolds in one hybrid molecule can give access to a series of compounds with a broad spectrum of biological activity. Therefore, it is a great challenge to develop an efficient and convenient strategy to access the new compounds containing thiazolidinone, benzothiazole, and oxindole rings.

Recently, the use of nano silica-based materials as heterogeneous catalysts has attracted considerable attention in organic synthesis.[24−27] They have different physical and chemical properties when compared to bulk material due to the higher surface area of silica nanoparticles.[28] They offer several advantages, including great catalytic activity, good thermal stability, low cost and toxicity, easy work-up, high catalyst loading capacity, and good dispersion of active reagent sites.[29,30] Many homogeneous catalysts can be converted to heterogeneous ones by immobilizing on silica nanoparticles. Diazabicyclo[5.4.0]undec-7-ene (DBU) is a strong homogeneous base catalyst that has been extensively used in various organic reactions.[31−34] Recently, we have prepared nano silica-bonded 5-n-propyl-octahydro-pyrimido[1,2-a]azepinium chloride (NSB-DBU) by the reaction of nano silica-n-propyl chloride and DBU, which was used for the synthesis of novel benzothiazole substituted 4-thiazolidinones.[35] In continuation of our ongoing program aiming at yielding novel heterocyclic compounds,[35−38] herein we report a facile process for one-pot synthesis of new oxindole derivatives bearing a benzothiazolylmethyl-2-thioxothiazolidin-4-one fragment using nano silica-bonded 5-n-propyl-octahydro-pyrimido[1,2-a]azepinium chloride (NSB-DBU) as heterogeneous nanocatalyst.

2. Results and discussion

NSB-DBU was prepared from the reaction of nano silica-n-propyl chloride and DBU as shown in Figure 2.[35] In an effort to optimize the process, the one-pot reaction of 2-(4-oxo-5-(2-oxoindolin-3-ylidene)-2-thioxothiazolidin-3-yl)acetic acid **1a** (1 mmol), 2-aminothiophenol **2** (1 mmol), and triphenyl phosphite **3** (TPP) (1 mmol) was carried out in various conditions as a simple model reaction (Figure 3). Initially, we focused on systematic evaluation of different catalysts for the model reaction (Table 1). As shown in Table 1, the reaction did not take place without any catalyst (Table 1, entry 1). The most interesting result was obtained with NSB-DBU as the catalyst. Then the reaction was examined in the presence of different molar ratios of NSB-DBU and TBAB. The best result was obtained with 10 mol% of NSB-DBU and 25 mol% TBAB at 100 °C (Table 1, entry 9).

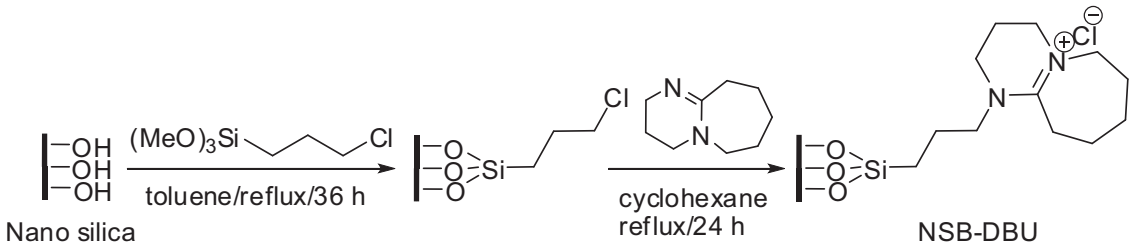


Figure 2. Preparation of NSB-DBU.

After optimization of the model reaction, the scope and generality of these conditions with other reactants were examined by using 5-oxoindolinylidene rhodanine-3-acetic acid derivatives **1a**–**i** (1 mmol), triphenyl phosphite (TPP) (1 mmol), and 2-aminothiophenol (1 mmol) in the presence of NSB-DBU (10 mol%, 0.09 g) and TBAB (25 mol%) according to Figure 3. As shown in Table 2, the compounds **4a**–**i** were produced in excellent yields (85%–92%). The structures of the products were established by IR, ^{1}H and ^{13}C NMR spectroscopy, mass spectrometry, and elemental analysis.

Table 1. Optimization of the reaction conditions.[a]

Entry	Catalyst (mol %)	TBAB (mol %)	Temperature (°C)	Time (h)	Yield (%)
1	-	-	100	10	5
2	-	25	100	4	20
3	Et_3N (20)	25	100	3	25
4	DABCO (20)	25	100	3	25
5	SiO_2-NPs (20)	25	100	5	20
6	DBU (20)	25	100	3	30
7	SB-DBU[b] (20)	25	100	2.5	65
8	NSB-DBU (5)	25	100	3	70
9	NSB-DBU (10)	25	100	2	92
10	NSB-DBU (20)	25	100	2	92
11	NSB-DBU (30)	25	100	3	85
12	NSB-DBU (10)	-	100	4	42
13	NSB-DBU (10)	50	100	2	92
14	NSB-DBU (10)	25	120	2	92
15	NSB-DBU (10)	25	70	5	52

[a] Reaction and conditions: 2-(4-oxo-5-(2-oxoindolin-3-ylidene)-2-thioxothiazolidin-3-yl)acetic acid **1a** (1 mmol), 2-aminothiophenol (1 mmol), TPP (1 mmol), different conditions, stirring. [b] Silica-Bonded 5-n-Propyl-Octahydro-Pyrimido[1,2-a]Azepinium Chloride[40]

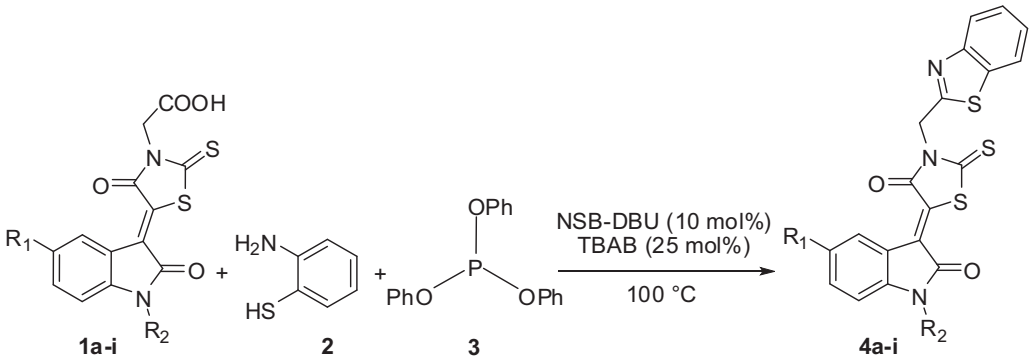


Figure 3. Preparation of new oxindole derivatives.

Table 2. The synthesis of the compounds **4a**–**i**[a].

Entry	R^1	R^2	Product	Melting point (°C)	Time (min)	Yield[b] (%)
1	H	H	**4a**	330–332	100	92
2	Cl	H	**4b**	336–338	115	90
3	Br	H	**4c**	319–321	100	85
4	NO_2	H	**4d**	290–292	90	89
5	H	Et	**4e**	171–173	120	91
6	H	CH_2Ph	**4f**	264–266	110	90
7	Cl	CH_2Ph	**4g**	170–172	105	88
8	H	CH_2CO_2Et	**4h**	288–290	110	92
9	Cl	CH_2CO_2Et	**4i**	279–281	120	87

[a] Reaction and conditions: 5-oxoindolinylidene rhodanine-3-acetic acid derivatives **1a**–**i** (1 mmol), TPP (1 mmol), 2-aminothiophenol (1 mmol), NSB-DBU (10 mol%), TBAB (25 mol%), 100 °C, stirring. [b] Isolated yield.

The mass spectrum of **4a** displayed the molecular ion ($M^{+\bullet}$) peak at m/z 409.0, which was consistent with the product structure. The ^{1}H NMR spectrum of **4a** in DMSO exhibited two sharp signals at 5.73 and 11.34 ppm for the methylene group and NH of oxindole, respectively. The four aromatic protons of the benzothiazole ring appeared as one multiplet at 7.43–7.52 ppm and two doublets at 7.96 and 8.10 ppm ($^{3}J_{HH}$ = 7.6 Hz). The protons of oxindole moiety were observed as two doublets at 6.98 and 8.87 ppm ($^{3}J_{HH}$ = 7.6 Hz), one triplet at 7.08 ppm ($^{3}J_{HH}$ = 7.6 Hz), and one multiplet at 7.43–7.52. The ^{13}C NMR spectrum of **4a** exhibited 19 signals in agreement with the proposed structure.

In order to investigate the recyclability of the NSB-DBU, the synthesis of **4a** was examined as a model reaction. The recovered dried catalyst was reused for the next run of reaction. The results showed that the catalyst could be reused 9 times and no significant loss in the product yield was apparent (Table 3).

Table 3. Recyclability study of NSB-DBU[a].

Run	1	2	3	4	5	6	7	8	9
Time (min)	100	100	105	105	110	110	110	120	120
Yield[b] (%)	92	92	92	90	90	90	90	89	88

[a] Model reaction: **1a** (1 mmol), TPP (1 mmol), 2-aminothiophenol (1 mmol), NSB-DBU (10 mol%), TBAB (25 mol%), 100 °C, stirring. [b] Isolated yield.

The probable mechanism for the formation of products is depicted in Figure 4. First, the reaction of carboxylic acid **1** with triphenylphosphite in the presence of basic catalyst gives intermediate **5**, which is attacked by the anion of 2-aminothiophenol leading to adduct **6**. Finally, the target product, **4**, is formed by intramolecular cyclization and dehydration of intermediates under the reaction conditions.

In summary, a series of unreported compounds containing thiazolidinone, benzothiazole, and oxindole rings were synthesized using NSB-DBU as a heterogeneous reusable catalyst. The major advantages of the present synthetic protocol are excellent yields, short reaction times, ecofriendly and reusable catalyst, and easy reaction work-up procedure.

3. Experimental

All chemicals and reagents were purchased from Fluka and Merck and used without further purification. Nano silica-n-propyl chloride was prepared according to the reported procedure.[39] Melting points were measured on an Electrothermal 9100 apparatus. NMR spectra were recorded with a Bruker DRX-400 AVANCE instrument (400.1 MHz for ^{1}H, 100.6 MHz for ^{13}C) with DMSO as solvent. Chemical shifts (δ) are given in parts per million (ppm) relative to TMS, and coupling constants (J) are reported in hertz (Hz). IR spectra were recorded on an FT-IR Bruker vector 22 spectrometer. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. Elemental analyses were carried out with a PerkinElmer 2400II CHNS/O Elemental Analyzer.

3.1. Preparation of nano silica-bonded 5-n-propyl-octahydro-pyrimido[1,2-a]azepinium chloride (NSB-DBU)

NSB-DBU was prepared according to our previously reported procedure.[35] A mixture of nano silica-n-propyl chloride (1.0 g) and DBU (0.76 g, 5.0 mmol) in cyclohexane (30 mL) was added to a 50-mL round-bottomed flask connected to a reflux condenser. The mixture was stirred under reflux conditions for 36 h. The resulting

mixture was then filtered, extracted with toluene in a Soxhlet extractor for 24 h, and dried at 60 °C in vacuo to give NSB-DBU as a white powder (1.3 g). The amount of DBU grafted on nano silica was evaluated as 1.15 mmol g^{-1}, on the basis of elemental analysis and thermogravimetric (TG) analysis (see supplementary information).

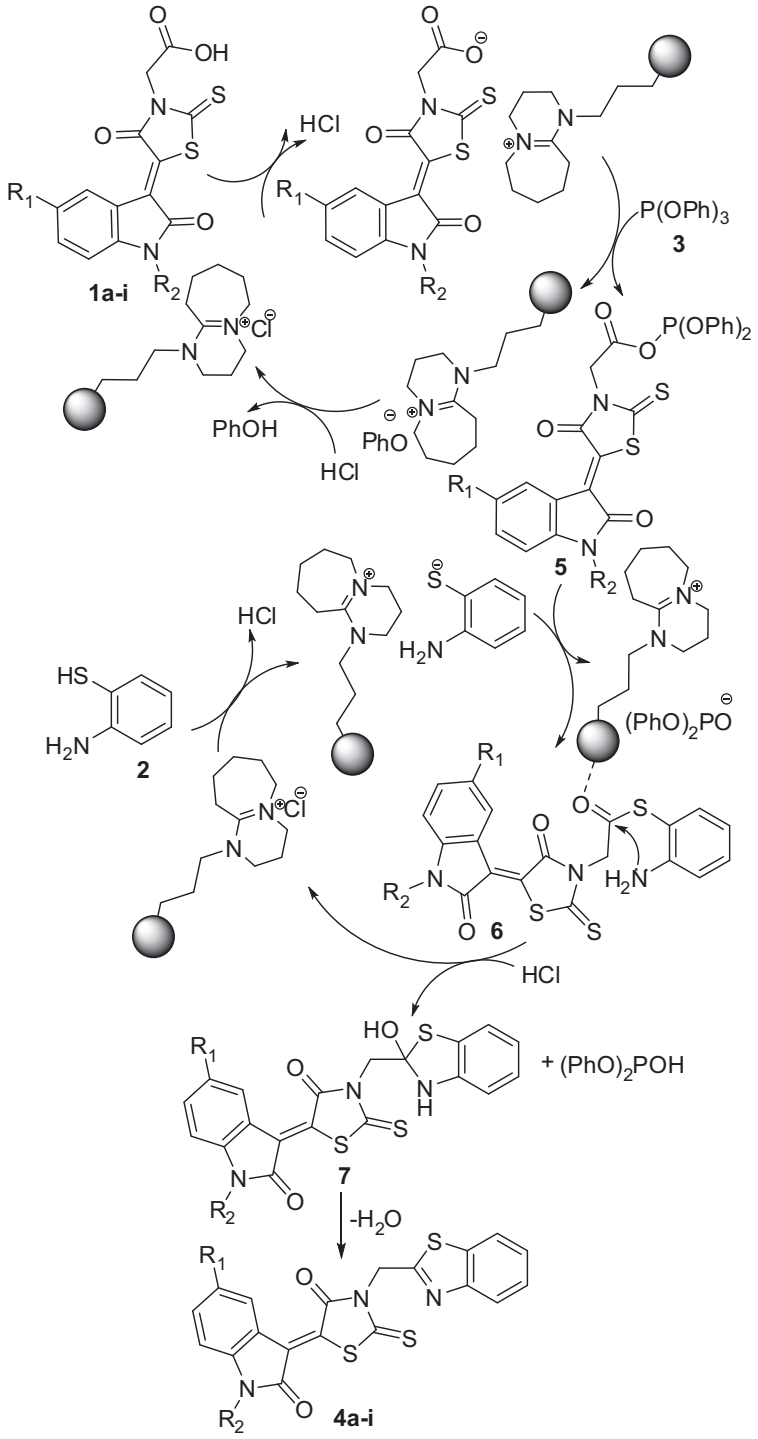


Figure 4. Plausible mechanism for the formation of products **4a**–**i**.

3.2. General procedure for the synthesis of compounds 4a–i

5-Oxoindolinylidene rhodanine-3-acetic acid derivatives **1a**–**i** were obtained by the reaction of rhodanine-3-acetic acid with isatin derivatives in ethanol medium.[40] A mixture of 5-oxoindolinylidene rhodanine-3-acetic acid derivatives **1a**–**i** (1 mmol), triphenyl phosphite (TPP) (1 mmol), 2-aminothiophenol (1 mmol), TBAB (0.25 mmol), and NSB-DBU (10 mol%, 0.09 g) as catalyst in a 10-mL round-bottomed flask was placed in an oil bath. The solution was stirred at 100 °C for the specified time period. After completion of the reaction, the mixture was diluted by the addition of 3 mL of hot methanol and filtered to separate the products as filtrate from the catalyst. The recovered catalyst was washed with methanol–acetone (1:1), dried for about 60 min at 60 °C, and reused for the next run of reaction. The product was obtained by evaporating the filtrate and then recrystallizing from methanol.

3.2.1. 3-(Benzo[d]thiazol-2-ylmethyl)-5-(2-oxoindolin-3-ylidene)-2-thioxothiazolidin-4-one (4a)

Orange red powder, mp: 330–332 °C; yield (0.38 g, 92%); IR (KBr) ν_{max}: 3154, 1691, 1660, 1616, 1579, 1344, 1320, 1153 cm^{-1}; ^{1}H NMR (400.1 MHz, DMSO-d$_6$)δ: 5.73 (s, 2H, CH_2), 6.98 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 7.08 (t, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 7.43–7.52 (m, 3H, 3CH_{Ar}), 7.96 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 8.10 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 8.78 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 11.34 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d$_6$)δ: 45.7, 111.4, 120.2, 122.8, 122.9, 123.2, 126.0, 126.8, 126.9, 128.4, 129.8, 134.0, 135.3, 145.5, 152.4, 164.5, 166.8, 168.4, 197.7; MS, m/z: 409.0 ($M^{+\cdot}$); Anal. Calcd for $C_{19}H_{11}N_3O_2S_3$ (409.50): C, 55.73; H, 2.71; N, 10.26; S, 23.49%. Found: C, 55.81; H, 2.72; N, 10.20; S, 23.53%.

3.2.2. 3-(Benzo[d]thiazol-2-ylmethyl)-5-(5-chloro-2-oxoindolin-3-ylidene)-2-thioxothiazolidin-4-one (4b)

Dark red powder, mp: 336–338 °C; yield (0.40 g, 90%); IR (KBr) ν_{max}: 3424, 1701, 1614, 1564, 1543, 1347, 1323, 1156 cm^{-1}; ^{1}H NMR (400.1 MHz, DMSO-d$_6$)δ: 5.74 (s, 2H, CH_2), 7.00 (d, $^3J_{HH}$ = 8.4, 1H, CH_{Ar}), 7.45 (td, $^3J_{HH}$ = 8.0, $^4J_{HH}$ = 1.2, 1H, CH_{Ar}), 7.49–7.53 (m, 2H, 2CH_{Ar}), 7.97 (d, $^3J_{HH}$ = 8.0, 1H, CH_{Ar}), 8.11 (dd, $^3J_{HH}$ = 8.0, $^4J_{HH}$ = 1.2, 1H, CH_{Ar}), 8.81 (s, 1H, CH_{Ar}), 11.48 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d$_6$)δ: 49.7, 114.9, 122.9, 123.2, 126.1, 126.5, 126.9, 128.9, 130.5, 132.3, 133.1, 135.4, 139.7, 144.3, 152.4, 160.2, 168.0, 172.1, 197.4; MS, m/z: 445.0 ($M^{+\cdot}$+2), 443.0 ($M^{+\cdot}$); Anal. Calcd for $C_{19}H_{10}ClN_3O_2S_3$ (443.95): C, 51.40; H, 2.27; N, 9.47; S, 21.67%. Found: C, 51.56; H, 2.27; N, 9.45; S, 21.58%.

3.2.3. 3-(Benzo[d]thiazol-2-ylmethyl)-5-(5-bromo-2-oxoindolin-3-ylidene)-2-thioxothiazolidin-4-one (4c)

Dark red powder, mp: 319–321 °C; yield (0.41 g, 85%); IR (KBr) ν_{max}: 3424, 1701, 1655, 1613, 1563, 1543, 1504, 1347, 1322, 1156 cm^{-1}; ^{1}H NMR (400.1 MHz, DMSO-d$_6$)δ: 5.74 (s, 2H, CH_2), 6.96 (d, $^3J_{HH}$ = 8.4, 1H, CH_{Ar}), 7.45 (td, $^3J_{HH}$ = 7.2, $^4J_{HH}$ = 1.6, 1H, CH_{Ar}), 7.51 (td, $^3J_{HH}$ = 7.2, $^4J_{HH}$ = 1.6, 1H, CH_{Ar}), 7.63 (dd, $^3J_{HH}$ = 8.4, $^4J_{HH}$ = 1.6, 1H, CH_{Ar}), 7.97 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 8.11 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 8.94 (d, $^4J_{HH}$ = 1.6, 1H, CH_{Ar}), 11.49 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d$_6$)δ: 45.7, 114.2, 122.0, 122.9, 123.2, 125.3, 126.0, 126.9, 130.3, 132.2, 135.4, 135.9, 144.5, 152.3, 157.9, 162.8, 164.4, 167.0, 197.7; MS, m/z: 488.9 ($M^{+\cdot}$+2), 486.9 ($M^{+\cdot}$); Anal. Calcd for $C_{19}H_{10}BrN_3O_2S_3$ (488.40): C, 46.72; H, 2.06; N, 8.60; S, 19.70%. Found: C, 46.70; H, 2.03; N, 8.66; S, 19.68%.

3.2.4. 3-(Benzo[d]thiazol-2-ylmethyl)-5-(5-nitro-2-oxoindolin-3-ylidene)-2-thioxothiazolidin-4-one (4d)

Dark red powder, mp: 290–292 °C; yield (0.40 g, 89%); IR (KBr) ν_{max}: 3391, 1705, 1620, 1521, 1450, 1339, 1224, 1157 cm^{-1}; ^{1}H NMR (400.1 MHz, DMSO-d_6)δ: 5.78 (s, 2H, CH_2), 7.20 (d, $^3J_{HH}$ = 8.0, 1H, CH_{Ar}), 7.45 (td, $^3J_{HH}$ = 7.6, $^4J_{HH}$ = 1.6, 1H, CH_{Ar}), 7.50 (td, $^3J_{HH}$ = 7.6, $^4J_{HH}$ = 1.6, 1H, CH_{Ar}), 7.97 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 8.11 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 8.36 (d, $^3J_{HH}$ = 8.0, 1H, CH_{Ar}), 9.69 (s, 1H, CH_{Ar}), 12.02 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 46.0, 112.7, 123.0, 123.1, 123.2, 126.0, 126.9, 132.2, 132.2, 132.9, 133.2, 135.2, 136.4, 148.9, 152.4, 161.2, 164.6, 166.8, 197.3; MS, m/z: 454.0 ($M^{+\cdot}$); Anal. Calcd for $C_{19}H_{10}N_4O_4S_3$ (454.50): C, 50.21; H, 2.22; N, 12.33; S, 21.16%. Found: C, 50.33; H, 2.20; N, 12.37; S, 21.17%.

3.2.5. 3-(Benzo[d]thiazol-2-ylmethyl)-5-(1-ethyl-2-oxoindolin-3-ylidene)-2-thioxothiazolidin-4-one (4e)

Red powder, mp: 171–173 °C; yield (0.40 g, 91%); IR (KBr) ν_{max}: 3402, 1731, 1707, 1611, 1563, 1525, 1339, 1207 cm^{-1}; ^{1}H NMR (400.1 MHz, DMSO-d_6)δ: 1.21 (t, $^3J_{HH}$ = 7, 3H, CH_3), 3.83 (q, $^3J_{HH}$ = 7, 2H, CH_2), 5.74 (s, 2H, CH_2), 7.24 (d, $^3J_{HH}$ = 8.0, 1H, CH_{Ar}), 7.43–7.56 (m, 4H, 4CH_{Ar}), 7.96 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 8.10 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 8.83 (d, $^3J_{HH}$ = 8.0, 1H, CH_{Ar}); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 13.0, 35.2, 45.8, 110.3, 115.0, 119.7, 122.9, 123.2, 123.2, 126.0, 126.9, 128.4, 133.9, 135.4, 138.6, 145.4, 152.4, 164.5, 166.9, 167.9, 197.7; MS, m/z: 437.0 ($M^{+\cdot}$); Anal. Calcd for $C_{21}H_{15}N_3O_2S_3$ (437.56): C, 57.64; H, 3.46; N, 9.60; S, 21.98%. Found: C, 57.59; H, 3.48; N, 9.64; S, 21.90%.

3.2.6. 3-(Benzo[d]thiazol-2-ylmethyl)-5-(1-benzyl-2-oxoindolin-3-ylidene)-2-thioxothiazolidin-4-one (4f)

Orange red powder, mp: 264–266 °C; yield (0.45 g, 90%); IR (KBr) ν_{max}: 1716, 1690, 1608, 1507, 1462, 1352, 1321, 1221, 1147 cm^{-1}; ^{1}H NMR (400.1 MHz, DMSO-d_6)δ: 5.05 (s, 2H, CH_2), 5.75 (s, 2H, CH_2), 7.10 (d, $^3J_{HH}$ = 8.0, 1H, CH_{Ar}), 7.14 (t, $^3J_{HH}$ = 8.0, 1H, CH_{Ar}), 7.26–7.37 (m, 5H, 5CH_{Ar}), 7.43–7.52 (m, 3H, 3CH_{Ar}), 7.96 (d, $^3J_{HH}$= 7.6, 1H, CH_{Ar}), 8.10 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 8.85 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}); ^{13}C NMR (100 MHz, DMSO-d_6)δ: 43.6, 45.8, 110.7, 119.8, 122.9, 123.2, 123.5, 125.5, 126.0, 126.9, 127.7, 128.1, 128.4, 129.2, 131.6, 133.8, 135.3, 136.2, 145.3, 152.3, 164.5, 166.7, 167.1, 197.3; MS, m/z: 499.0 ($M^{+\cdot}$); Anal. Calcd for $C_{26}H_{17}N_3O_2S_3$ (499.63): C, 62.50; H, 3.43; N, 8.41; S, 19.25%. Found: C, 62.54; H, 3.39; N, 8.40; S, 19.36%.

3.2.7. 3-(Benzo[d]thiazol-2-ylmethyl)-5-(1-benzyl-5-chloro-2-oxoindolin-3-ylidene)-2-thioxothiazolidin-4-one (4g)

Yellow powder, mp: 170–172 °C; yield (0.47 g, 88%); IR (KBr) ν_{max}: 1750, 1708, 1633, 1520, 1456, 1326, 1198 cm^{-1}; ^{1}H NMR (400.1 MHz, DMSO-d_6)δ: 5.00 (s, 2H, CH_2), 5.79 (s, 2H, CH_2), 6.89 (d, $^3J_{HH}$ = 8.4, 1H, CH_{Ar}), 7.23–7.36 (m, 6H, 6CH_{Ar}), 7.45 (td, $^3J_{HH}$ = 7.6, $^4J_{HH}$ = 1.2, 1H, CH_{Ar}), 7.51 (td, $^3J_{HH}$ = 7.6, $^4J_{HH}$ = 1.2, 1H, CH_{Ar}), 7.6 (s, 1H, CH_{Ar}), 7.96 (d, $^3J_{HH}$ = 8.0, 1H, CH_{Ar}), 8.04 (d, $^3J_{HH}$ = 8.0, 1H, CH_{Ar}); ^{13}C NMR (100 MHz, DMSO-d_6)δ: 46.3, 47.2, 111.4, 122.7, 123.2, 125.1, 126.0, 126.8, 127.2, 127.2,

127.7, 127.8, 128.0, 129.0, 129.1, 129.4, 135.4, 136.1, 143.0, 152.4, 164.4, 173.5, 174.2, 200.5; MS, m/z: 535.0 ($M^{+\cdot}+2$), 533.0 ($M^{+\cdot}$); Anal. Calcd for $C_{26}H_{16}ClN_3O_2S_3$ (534.07): C, 58.47; H, 3.02; N, 7.87; S, 18.01%. Found: 58.59; H, 3.00; N, 7.91; S, 17.94%.

3.2.8. Ethyl 2-(3-(3-(benzo[d]thiazol-2-ylmethyl)-4-oxo-2-thioxothiazolidin-5-ylidene)-2-oxoindolin-1-yl)acetate (4h)

Orange red powder, mp: 288–290 °C; yield (0.46 g, 92%); IR (KBr) ν_{max}: 1743, 1718, 1694, 1472, 1347, 1317, 1227, 1146 cm^{-1}; ^1H NMR (400.1 MHz, DMSO-d_6)δ: 1.22 (t, $^3J_{HH}$ = 7.2, 3H, CH_3), 4.17 (q, $^3J_{HH}$ = 7.2, 2H, CH_2), 4.75 (s, 2H, CH_2), 5.74 (s, 2H, CH_2), 7.17–7.22 (m, 2H, $2CH_{Ar}$), 7.43–7.55 (m, 3H, $3CH_{Ar}$), 7.97 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 8.10 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 8.87 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}); ^{13}C NMR (100 MHz, DMSO-d_6)δ: 14.5, 41.9, 45.8, 61.9, 110.5, 119.5, 122.9, 123.2, 123.7, 124.9, 126.0, 126.9, 128.3, 131.9, 133.9, 135.4, 145.2, 152.3, 154.7, 164.4, 166.6, 168.0, 197.0; MS, m/z: 495.0 ($M^{+\cdot}$); Anal. Calcd for $C_{23}H_{17}N_3O_4S_3$ (495.59): C, 55.74; H, 3.46; N, 8.48; S, 19.41%. Found: C, 55.87; H, 3.43; N, 8.48; S, 19.40%.

3.2.9. Ethyl 2-(3-(3-(benzo[d]thiazol-2-ylmethyl)-4-oxo-2-thioxothiazolidin-5-ylidene)-5-chloro-2-oxoindolin-1-yl)acetate (4i)

Dark red powder, mp: 279–281 °C; yield (0.46 g, 87%); IR (KBr) ν_{max}: 1738, 1694, 1543, 1414, 1348, 1222, cm^{-1}; ^1H NMR (400.1 MHz, DMSO-d_6)δ: 1.22 (t, $^3J_{HH}$ = 7.2, 3H, CH_3), 4.17 (q, $^3J_{HH}$ = 7.2, 2H, CH_2), 4.76 (s, 2H, CH_2), 5.75 (s, 2H, CH_2), 7.28 (d, $^3J_{HH}$ = 8.4, 1H, CH_{Ar}), 7.45 (td, $^3J_{HH}$ = 7.6, $^4J_{HH}$ = 1.2, 1H, CH_{Ar}), 7.50 (td, $^3J_{HH}$ = 7.6, $^4J_{HH}$ = 1.2, 1H, CH_{Ar}), 7.61 (d, $^3J_{HH}$ = 8.4, 1H, CH_{Ar}), 7.97 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}), 8.10 (d, $^3J_{HH}$ = 7.6, 1H, CH_{Ar}); 8.89 (s, 1H, CH_{Ar}); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 14.5, 42.1, 45.8, 61.9, 112.1, 117.4, 121.6, 122.9, 123.2, 126.1, 126.2, 126.9, 127.5, 131.7, 133.0, 135.5, 147.8, 152.4, 155.1, 157.7, 162.4, 168.9, 197.3; MS, m/z: 531.0 ($M^{+\cdot}+2$), 529.0 ($M^{+\cdot}$); Anal. Calcd for $C_{23}H_{16}ClN_3O_4S_3$ (530.04): C, 52.12; H, 3.04; N, 7.93; S, 18.15%. Found: C, 52.26; H, 3.07; N, 7.88; S, 18.14%.

Acknowledgment

This research was supported by the Research Council of the University of Mazandaran, Iran.

References

1. Lesyk, R. B.; Zimenkovsky, B. S. *Curr. Org. Chem.* **2004**, *8*, 1547–1577.
2. Tomasic, T.; Masic, L. P. *Curr. Med. Chem.* **2009**, *16*, 1596–1629.
3. Lesyk, R.; Zimenkovsky, B.; Atamanyuk, D.; Jensen, F.; Kieć-Kononowicz, K.; Gzella, A. *Bioorg. Med. Chem.* **2006**, *14*, 5230–5240.
4. Havrylyuk, D.; Zimenkovsky, B.; Vasylenko, O.; Zaprutko, L.; Gzella, A.; Lesyk, R. *Eur. J. Med. Chem.* **2009**, *44*, 1396–1404.
5. Rydzik, E.; Szadowska, A.; Kaminska, A. *Acta Pol. Pharm.* **1984**, *41*, 459–464.
6. Samir, B.; Wesam, K.; Fadda, A. A. *Eur. J. Med. Chem.* **2007**, *42*, 948–954.
7. Elbarbary, A. A.; Khodair, A. I.; Pedersen, E. B.; Nielsen, C. *Monatsh. Chem.* **1994**, *125*, 593–598.
8. Andreani, A.; Rambaldi, M.; Leoni, A.; Locatelli, A.; Bossa, R.; Chiericozzi, M.; Galatulas, I.; Salvatore, G. *Eur. J. Med. Chem.* **1996**, *31*, 383–387.

9. Andreani, A.; Rambaldi, M.; Locatelli, A.; Leoni, A.; Bossa, R.; Chiericozzi, M.; Galatulas, I.; Salvatore, G. *Eur. J. Med. Chem.* **1993**, *28*, 825–829.
10. Ohishi, Y.; Mukai, T.; Nagahara, M.; Yajima, M.; Kajikawa, N.; Miyahara, K.; Takano, T. *Chem. Pharm. Bull.* **1990**, *38*, 1911–1919.
11. Momose, Y.; Meguro, K.; Ikeda, H.; Hatanaka, C.; Oi, S.; Sohda, T. *Chem. Pharm. Bull.* **1991**, *39*, 1440–1445.
12. Patel, N. B.; Shaikh, F. M. *Sci. Pharm.* **2010**, *78*, 753–765.
13. Pattan, S. R.; Suresh, C. H.; Pujar, V. D.; Reddy, V. V. K.; Rasal, V. P.; Koti, B. C. *Indian J. Chem. B*, **2005**, *44*, 2404–2408.
14. Patel, N. B.; Shaikh, F. M. *Saudi Farm. J.* **2010**, *18*, 129–136.
15. Havrylyuk, D.; Mosula, L.; Zimenkovsky, B.; Vasylenko, O.; Gzella, A.; Lesyk, R. *Eur. J. Med. Chem.* **2010**, *45*, 5012–5021.
16. Kawakami, M.; Koya, K.; Ukai, T.; Tatsuta, N.; Ikegawa, A.; Ogawa, K.; Shishido, T.; Chen, L. B. *J. Med. Chem.* **2002**, *37*, 197–206.
17. Rudrangi, S. R. S.; Bontha, V. K.; Manda, V. R.; Bethi, S. *Asian J. Res. Chem.* **2011**, *4*, 335–338.
18. Millemaggi, A.; Taylor, R. J. K. *Eur. J. Org. Chem.* **2010**, *2010*, 4527–4547.
19. Trost, B. M.; Brennan, M. K. *Synthesis* **2009**, *2009*, 3003–3025.
20. Galliford, C. V.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 8748–8758.
21. Kornet, M. J.; Thio, A. P. *J. Med. Chem.* **1976**, *19*, 892–898.
22. Robinson, R. P.; Reiter, L. A.; Barth, W. E.; Campeta, A. M.; Cooper, K.; Cronin, B. J.; Destito, R.; Donahue, K. M.; Falker, F. C.; Fiese, E. F. et al. J. Med. Chem. **1996**, *39*, 10–18.
23. Conklyn, M. J.; Kadin, S. B.; Showell, H. J. *Int. Arch. Allergy Appl. Immunol.* **1990**, *91*, 369–373.
24. Schiestel, T.; Brunner, H.; Tovar, G. E. *J. Nanosci. Nanotechnol.* **2004**, *4*, 504–511.
25. Rahman, I. A.; Jafarzadeh, M.; Sipaut, C. S. *Ceram. Int.* **2009**, *35*, 1883–1888.
26. Safaei, S.; Mohammadpoor-Baltork, I.; Khosropour, A. R.; Moghadam, M.; Tangestaninejad, S.; Mirkhani, V. *Catal. Sci. Technol.* **2013**, *3*, 2717–2722.
27. Taki, B. S. G.; Mirkhani, V.; Mohammadpoor-Baltork, I.; Moghadam, M.; Tangestaninejad, S.; Rostami, M.; Khosropour, A. R. *J. Inorg. Organomet. Polym. Mat.* **2013**, *23*, 758–765.
28. Lewis, L. N. *Chem. Rev.* **1993**, *93*, 2693–2730.
29. Ray, S.; Das, P.; Bhaumik, A.; Dutta, A.; Mukhopadhyay, C. *Appl. Cat. A*, **2013**, *458*, 183–195.
30. Rafiee, E.; Khodayari, M.; Kahrizi, M.; Tayebee, R. *J. Mol. Cat. A*, **2012**, *358*, 121–128.
31. Reed, R.; Réau, R.; Dahan, F.; Bertrand, G. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 399–401.
32. Ghosh, N. *Synlett* **2004**, *2004*, 574–575.
33. Baidya, M.; Mayr, H. *Chem. Commun.* **2008**, *2008*, 1792–1794.
34. Ying, A. G.; Liu, L.; Wu, G. F.; Chen, G.; Chen, X. Z.; Ye, W. D. *Tetrahedron Lett.* **2009**, *50*, 1653–1657.
35. Baharfar, R.; Shariati, N. *Aust. J. Chem.* **2014**, DOI 10.1071/CH13712.
36. Baharfar, R.; Shariati, N. *C. R. Chimie* **2014**, *17*, 413–419.
37. Shariati, N.; Baharfar, R. *J. Chin. Chem. Soc.* **2014**, *61*, 337–340.
38. Baharfar, R.; Baghbanian, S. M.; Vahdat, S. M. *Tetrahedron Lett.* **2011**, *52*, 6018–6020.
39. Qiu, H.; Jiang, Q.; Wei, Z.; Wang, X.; Liu, X.; Jiang, S. *J. Chromatogr. A* **2007**, *1163*, 63–69.
40. Pardasani, R. T.; Pardasani, P.; Jain, A.; Kohli, S. *Phosphorus, Sulfur Silicon Relat. Elem.* **2004**, *179*, 1569–1575.