*Advanced Pharmaceutical Bulletin*, **2013**, 3(1), 227-230
doi: http://dx.doi.org/10.5681/apb.2013.037
http://apb.tbzmed.ac.ir/

# Synthesis and Antimicrobial Evaluation of Certain Novel Thiazoles

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**ARTICLEINFO**

***Article Type:***
Research Article

***Article History:***
Received: 25 November 2012
Revised: 26 December 2012
Accepted: 27 December 2012
ePublished: 7 February 2013

***Keywords:***
Imidazole moiety
Thiazole moiety
Synthesis
Characterization
Antimicrobial activity

**ABSTRACT**

***Purpose:*** This article makes an attempt to synthesize certain compounds containing thiazole and imidazole moieties and screen for the antimicrobial properties. ***Methods***: The novel compounds synthesized were characterized by elemental analysis, IR and $^1$HNMR spectral data. The antimicrobial activity of novel compounds was evaluated by cup plate method. ***Results*:** The compound *p*-t showed more antibacterial activity than that of the standard. *p*-hp and *p*-as showed considerable antibacterial activity. *p*-t demonstrated higher antifungal activity than that of the standard while *p*-hp and *p*-as showed considerable antifungal activity. ***Conclusion*:** The antimicrobial activity studies were conducted on certain selected bacteria and fungi. In each case antimicrobial activity of the compounds was compared with that of standards. *p*-t, *p*-hp, *p*-np, *p*-cp, *p*-ts and *p*-as showed considerable antimicrobial activity.

## Introduction

The thiazole chemistry has been extensively developing because of their unique physiological properties. Thiazoles are stable, non-carcinogenic aromatic compounds with relatively small size. The reason being the susceptibility of reactive sites at 2-, 3- and 5-positions of the thiazole nucleus to biochemical attack during the metabolism involving reduction, hydrolysis, amination, decarboxylation of $CO_2H$ group etc. Their wide variety of applications in medicinal chemistry has been encouraging and is reflected by the extensive literature available.[1-5] The potent medicinal significance of imidazoles is also well known.[6-9] In continuation of our effort[10] to incorporate multiple pharmacologically important moieties in a single entity, we herewith propose to synthesize novel compounds containing both imidazole and thiazole moieties.

## Materials and Methods

The chemicals employed in the studies were of analytical reagent grade. Melting points were determined in open capillary tubes and were uncorrected. The infrared spectra were recorded on Perkin – Elmer KBr spectrometer. ν values were expressed in $cm^{-1}$. $^1$HNMR spectra were recorded on JEOL MODEL GSX 270 FT NMR Spectrometer and NMR 200 MHz Supercon machine, using $CDCl_3$ and DMSO – $d_6$ as solvents and TMS as an internal standard. Chemical shifts were expressed as δ values (ppm).

## Results and Discussion

### *Synthesis and characterization of (2-methyl-5-nitro-4-phenylazo–imidazol-1-yl)-aceticacid N-(4-phenyl-thiazol-2-yl)-hydrazides 3*

Phenyl aryl bromides and 3-(4|-substituted phenyl)-4-bromo acetyl sydnones were synthesized by the procedures reported in the literature.[10]

A mixture of (2-methyl-5-nitro -4-phenyl azo-imidazole-1-yl)-acetic acid hydrazide 1 (0.01 mole), potassium thiocyanate (0.02 mole), concentrated hydrochloric acid (1 mL), ethyl alcohol (10 mL) and water (20 mL) were refluxed for 3 hours. The cooled solution was filtered, the precipitate was washed with water, dried and recrystallized from ethanol-DMF mixture to yeild 2-methyl5-nitro-4-phenyl azo-imidazole-1-yl)-acete thiosemicarbazone 2. The structure of 2 was confirmed by IR and $^1$HNMR spectral data.

### *Elemental analysis (Compound: Molecular Formula; Yield %; m.p (°C); found (cald) %.)*

2: $C_{13}H_{14}N_8O_3S$; 68; 230 $^oC$; C 43.58(43.09), H 3.67(3.89), N 31.24(30.92), O 13.46(13.25), S 8.34(8.85).

### *IR spectral details*

The IR (KBr) spectrum of 2 showed absorption bands around 3220 $cm^{-1}$ (NH-str), 2950 $cm^{-1}$ (CH, str), 1679 $cm^{-1}$ (C=O, str), 1540 $cm^{-1}$ (C=N, str), 1610 $cm^{-1}$ (N=N, str), 1500 $cm^{-1}$ (asymmetric stretching, Nitro group), 1329 $cm^{-1}$ (symmetric stretching, Nitro group).

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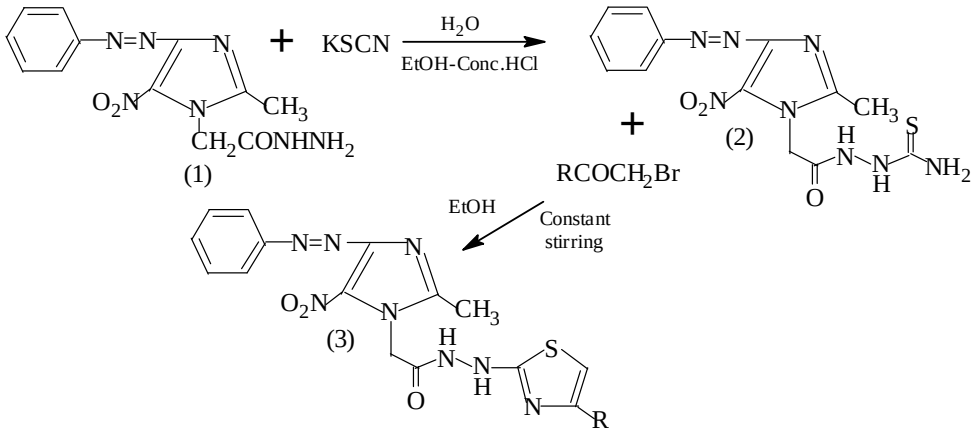
### *[1]HNMR spectral details*

The [1]HNMR (200MHz) spectrum of 2 was recorded in $CDCl_3$+DMSO-$d_6$. The signals were noticed at δ 2.29 (s, 3H, $CH_3$), δ 4.80 (s, 2H, N-$CH_2$-CO), δ 3.33 (s, 2H, $NH_2$), δ 9.40 (s, 2H, CO-NH-NH), δ 7.4 – 7.6 (m, 5H, Ar-H).

A mixture of (2-methyl 5-nitro-4-phenyl azo-imidazole-1-yl)-acetyl thiosemicarbazone 2 (0.01 mole) in DMF (10 mL) and various bromoacetyl derivatives (0.01 mol) in ethanol (10 mL) was stirred at room temperature for 2 hours. The solid separated was filtered, dried and recrystallized from ethanol-DMF mixture. The compounds synthesized 3 have been characterized by means of IR and [1]HNMR spectral data.

The reaction sequence leading to the formation of these compounds is outlined in Scheme 1.




**Scheme 1.** *Synthesis and characterization of (2-methyl-5-nitro-4-phenylazo–imidazol-1-yl)- aceticacid-N-(4-phenyl-thiazol-2-yl)-hydrazide 3.* [R = phenyl (phe), *p*-tolyl (*p*-t), *p*-anisyl (*p*-a), *p*-hydroxy phenyl (*p*-hp), *p*-nitro phenyl (*p*-np), *p*-chloro phenyl (*p*-cp), *p*-bromo phenyl (*p*-bp), *p*-phenyl sydnonyl (*p*-ps), N-*p*-tolyl sydnonyl (*p*-ts), *N*-*p*-anisyl sydnonyl (*p*-as)]

### *Elemental analysis (Compound: R; Molecular Formula; Yield %; m.p (°C); found (cald) %.)*

phe: phenyl; $C_{21}H_{18}N_8O_3S$; 66; 258; C 54.54(54.44), H 3.92(3.72), N 24.23(23.73), O 10.60 (10.39), S 6.47 (6.93).

*p*-t: *p*-tolyl; $C_{22}H_{20}N_8O_3S$; 45; 202; C 55.45(54.98), H 4.23(4.01), N 23.52(23.14), O 10.82 (10.08), S 6.57 (6.72).

*p*-a: *p*-anisyl; $C_{22}H_{20}N_8O_4S$; 54; 221; C 53.65(53.24), H 4.09(3.98), N 22.75(22.27), O 13.68 (13.01), S 6.89 (6.54).

*p*-hp: *p*-hydroxyphenyl; $C_{21}H_{18}N_8O_4S$; 50; 195; C 52.71(52.34), H 3.79(3.54), N 23.42(22.96), O 13.68 (13.39), S 6.49 (6.69).

*p*-np: *p*-nitro phenyl; $C_{21}H_{17}N_9O_5S$; 64; 232; C 49.70(49.27), H 3.38(3.16), N 24.84(24.40), O 16.47(15.78), S 6.21(6.31).

*p*-cp: *p*-chloro phenyl; $C_{21}H_{17}ClN_8O_3S$; 58; 193; C 50.76(50.31), H 3.45(3.23), N 22.55(22.10), O 10.65(10.22), S 6.21(82), Cl 7.99(7.55).

*p*-bp: *p*-bromo phenyl; $C_{21}H_{17}BrN_8O_3S$; 56; 204; C 46.59(46.13), H 3.17(2.95), N 20.70(20.31), O 9.24(8.87), S 6.31(5.92), Br 14.99(14.77).

*p*-ps: *p*-phenyl sydnonyl; $C_{23}H_{20}N_{10}O_5S$; 52; 197; C 50.36(49.84), H 3.68(3.43), N 25.53(25.06), O 00.00 (14.60), S 00.00 (5.84).

*p*-ts: *N*-*p*-tolyl sydnonyl; $C_{24}H_{22}N_{10}O_5S$; 57; 182; C 51.24(50.81), H 3.94(3.71), N 24.90(24.49), O 14.89(14.23), S 5.12(5.69).

*p*-as: N-*p*-anisyl sydnonyl; $C_{24}H_{22}N_{10}O_6S$; 43; 191; C 49.82 (49.45), H 3.83(3.69), N 24.21(23.78), O 17.21(16.61), S 5.12 (5.54).

### *IR spectral details*

The IR (KBr) spectrum of (2-methyl-5-nitro-4-phenylazo–imidazol-1-yl) - aceticacid N-(4-phenyl-thiazol-2-yl)-hydrazide (phe) exhibited absorption bands at 3210 $cm^{-1}$ (C = O str), 1526 $cm^{-1}$ (C = N str). The data is given below.

*IR spectral data (ν in $cm^{-1}$):*

phe: NH 3210, CH 2942, C=O 1672, C=N 1526, N=N 1612, N=O $\begin{bmatrix}1500\\1325\end{bmatrix}$.

*p*-hp: NH 3230, CH 2956, C=O 1687, C=N 1546, N=N 1612, N=O $\begin{bmatrix}1500\\1329\end{bmatrix}$.

*p*-np: NH 3240, CH 2960, C=O 1700, C=N 1540, N=N 1612, N=O $\begin{bmatrix}1500\\1325\end{bmatrix}$.

*p*-cp: NH 3202, CH 2940, C=O 1667, C=N 1528, N=N 1612, N=O $\begin{bmatrix}1500\\1327\end{bmatrix}$.

*p*-ps: NH 3256, CH 2921, C=O 1669, C=N 1539, N=N 1612, N=O $\begin{bmatrix}1500\\1325\end{bmatrix}$, sydnone C=O str 1719.

### *$^1$HNMR spectral details*

The $^1$HNMR (200MHz) spectrum of (2-methyl-5-nitro-4-phenylazo–imidazol-1-yl) – acetic acid N-(4-phenyl-thiazol-2-yl)-hydrazide (phe) in $CDCl_3$ + DMSO-$d_6$ showed signals at δ2.30 (S, 3H, $CH_3$), δ7.1 (S, 1H, ArNH), δ6.5 – 6.70 (m, 5H, Ar-H), δ 7.12 – 7.36 (m, 5H, Ar-H), δ 9.2 (S, 1H, N-NH). The data is given below.

*$^1$HNMR spectral data (δ ppm):* phe: 2.30 (s, 3H, $CH_3$), 4.65 (s, 2H, N-$CH_2$-CO), 10.40 (s, 1H, CO - NH), 9.70 (s, 2H, NH-N-NH), 7.23 (s, 1H, thiazole-4H), 6.9 – 7.1 (m, 5H, Ar-H), 7.2 – 7.3 (m, 5H, Ar-H).

*p*-hp: 2.25 (s, 3H, $CH_3$), 7.90 (s, 1H, imidazole – 4H), 4.66 (s, 2H, N-$CH_2$-CO), 10.45 (s, 1H, CO-NH), 8.9 (s, 2H, NH – NH), 7.3 (s, 1H, thiazole – 4H), 6.9 – 7.10 (m, 5H, Ar – H), 7.3 (d, 2H, Ar – H), 7.4 (d, 2H, Ar – H), 4.3 (S, 1H, OH).

*p*-np: 2.30 (s, 3H, $CH_3$), 4.70 (s, 2H, N – $CH_2$ – CO), 10.35 (s, 1H, CO – NH), 9.8 (s, 2H, N – NH), 7.23 (s, 1H, thiazole – 4H), 6.9 – 7.1 (m, 5H, Ar – H), 7.3 (d, 2H, Ar – H), 7.45 (d, 2H, Ar – H).

*p*-cp: 2.38 (s, 3H, $CH_3$), 4.95 (s, 2H, $NCH_2CO$), 7.49 (d, 2H, *o*-protons of *p*-chlorophenyl), 7.70 (d, 2H, m-protons of *p*-chlorophenyl), 7.27 ( s, 1H, thiazole – 4H), 9.69 (s, H, NH), 10.71 (s, H, CONH), 6.8-7.1 (m, 5H, Ar – H).

*p*-ps: 2.27 (s, 3H, $CH_3$), 4.66 (s, 2H, N-$CH_2$-CO), 7.61 – 7.81 (M, 5H, Ar – H), 7.26 (s, 1H, thiazole – 4H), 7.98 (s, 1H, imidazole – 4H), 9.85 (s, 1H, NH), 10.48 (s, 1H, CONH), 6.8 – 7.1 (m, 5H, Ar – H).

*p*-ts: 2.11 (s, 3H, $CH_3$), 2.25 (s, 3H, $CH_3$), 4.66 (s, 2H, N-$CH_2$-CO), 10.38 (s, 1H, CO-NH), 9.75 (s, 1H,N-NH) 7.25 (s, 1H, thiazole-4H), 6.8-7.1 (m, 5H, Ar-H), 7.2 (d, 2H, Ar-H), 7.4 (d, 2H, Ar-H), 7.94 (s, 1H, imidazole-4H).

### *Antibacterial Activity Studies*

The antibacterial activity of the newly synthesized compounds was assessed by cup-plate method.[11]

The newly synthesized thiazole derivatives 3 were screened for antibacterial activity against *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia and Staphylococcus aureus*. Among the compounds tested, the compound *p*-t showed more antibacterial activity than that of the standard. *p*-hp and *p*-as showed considerable antibacterial activity. The antifungal activity studies were carried out against *Candida albicans*, *Aspergillus flavus*, *Aspergillus fumigates and Trichophyton rubrum*. Among the compounds tested, *p*-t showed higher activity than that of the standard while *p*-hp and *p*-as showed considerable antifungal activity. The results are present in Table 1.

**Table 1.** *Details of antimicrobial studies of novel thiazoles 3.

| Compound | Antibacterial activity (diameter of zone inhabitation in mm) | | | | Antifungal activity (diameter of zone inhabitation in mm) | | | |
|---|---|---|---|---|---|---|---|---|
| | *Escherichia coli* | *Pseudomonas aeruginosa* | *Klebsiella pneumonia* | *Staphylococcus aureus* | *Candida albicans* | *Aspergillus flavus* | *Aspergillus fumigatus* | *Trichophyton rubrum* |
| ***p*-t** | 23 | 25 | 25 | 26 | 22 | 26 | 24 | 22 |
| ***p*-hp** | 14 | 17 | 19 | 16 | 15 | 16 | 20 | 18 |
| ***p*-np** | --- | --- | --- | --- | 10 | --- | --- | --- |
| ***p*-cp** | --- | 14 | --- | --- | --- | 12 | --- | 09 |
| ***p*-ts** | --- | 14 | --- | --- | --- | 14 | --- | --- |
| ***p*-as** | 12 | 16 | 15 | 14 | 13 | 08 | 11 | 11 |
| **Ciprofloxacin (Std)** | 20 | 22 | 22 | 20 | --- | --- | --- | --- |
| **Ciclopiroxola-mine (Std)** | --- | --- | --- | --- | 20 | 22 | 22 | 20 |
| **Solvent control (DMF)** | --- | --- | --- | --- | --- | --- | --- | --- |

*'---' indicates that the compound is inactive.

## Conclusion

The newly synthesized compounds containing thiazole and imidazole moieties 3 were characterized by elemental analysis and spectral analysis. The antimicrobial activity all compounds were evaluated and reported. Among the compounds tested, *p*-np, *p*-cp and *p*-ts showed antibacterial activity against certain microorganism only whereas *p*-t, *p*-hp and *p*-as showed considerable antibacterial activity against all the bacteria and fungi tested.

## Conflict of Interest

The authors report no conflicts of interest in this work.

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