Synthesis and Antimicrobial Evaluation of Certain Novel Thiazoles

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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 1H-NMR 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 CO2H 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 effort10 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-1.1H-NMR spectra were recorded on JEOL MODEL GSX 270 FT NMR Spectrometer and NMR 200 MHz Supercon machine, using CDCl3 and DMSO – d6 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-phenylyazo-imidazol-1-yl)-acetic acid 3

Phenyl aryl bromides and 3-(4'-substituted phenyl)-4-bromo acetyl sydnone were synthesized by the procedures reported in the literature.7-10 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 yield 2-methyl5-nitro-4-phenyl azo-imidazole-1-yl)-acetie thiosemicarbazone 2. The structure of 2 was confirmed by IR and 1H-NMR spectral data.

Elemental analysis (Compound: Molecular Formula; Yield %; m.p (°C); found (cald) %)
2: C14H14N4O6S; 68; 230 °C; C 43.58(43.09), H 3.67(3.89), N 31.24(30.92), O 13.46(13.25), S 68; 8.34(8.85).

IR spectral details

The IR (KBr) spectrum of 2 showed absorption bands around 3220 cm-1 (asymmetric stretching, Nitro group), 1329 cm-1 (symmetric stretching, Nitro group).

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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 1H NMR 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-toly (pt), p-anisyl (pa), p-hydroxy phenyl (php), p-nitro phenyl (pnp), p-chloro phenyl (pcp), p-bromo phenyl (p-bp), p-phenyl sydnonyl (p-ps), N-p-toly sydnonyl (p-ts), N-p-anisyl sydnonyl (p-as)]

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

phe: phenyl; C_{21}H_{16}N_{10}O_{5}; 66; 258; C 54.54(54.44), H 3.92(3.72), N 24.23(23.73), O 10.60(10.39), S 6.67(6.93).
p-tp: p-toly; C_{22}H_{20}N_{10}O_{5}; 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_{10}O_{5}; 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).

hp: p-hydroxyphenyl; C_{21}H_{19}N_{10}O_{5}; 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).

np: p-nitro phenyl; C_{21}H_{17}N_{10}O_{5}; 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).

cp: p-chloro phenyl; C_{21}H_{15}N_{10}O_{5}; 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(6.82), Cl 7.99(7.55).

bp: p-bromo phenyl; C_{21}H_{13}BrN_{10}O_{5}; 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).

ps: p-phenyl sydnonyl; C_{23}H_{23}N_{10}O_{5}; 52; 197; C 50.36(49.84), H 3.66(3.43), N 25.53(25.06), O 0.00(0.00), S 0.00(5.84).

ps: N-p-toly sydnonyl; C_{23}H_{22}N_{10}O_{5}; 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).

as: N-p-anisyl sydnonyl; C_{23}H_{22}N_{10}O_{5}; 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 data (ν in cm\(^{-1}\)):

phe: NH 3210, CH 2942, C=O 1672, C=N 1526, N=N 1612, N=O str.

1H NMR spectral details

The 1H NMR (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-imidazol-1-yl)-acetyl thiosemicarbazone 2 (0.01 mole) in DMF (10 mL) and various bromoacetyl

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\(^{-1}\)):
Among the compounds tested, 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 fumigatus 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

<table>
<thead>
<tr>
<th>Compound</th>
<th>Escherichia coli (diameter of zone inhabitation in mm)</th>
<th>Pseudomonas aeruginosa</th>
<th>Klebsiella pneumonia</th>
<th>Staphylococcus aureus</th>
<th>Candida albicans</th>
<th>Aspergillus flavus</th>
<th>Aspergillus fumigatus</th>
<th>Trichophyton rubrum</th>
</tr>
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<tbody>
<tr>
<td>p-t</td>
<td>23</td>
<td>25</td>
<td>25</td>
<td>26</td>
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<td>p-np</td>
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<td>p-cp</td>
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<td>12</td>
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<tr>
<td>p-ts</td>
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<tr>
<td>p-as</td>
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<td>16</td>
<td>15</td>
<td>14</td>
<td>13</td>
<td>08</td>
<td>11</td>
<td>11</td>
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<tr>
<td>Ciprofloxacin (Std)</td>
<td>20</td>
<td>22</td>
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<td>20</td>
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<tr>
<td>Ciclopiroxolamine (Std)</td>
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<tr>
<td>Solvent control (DMF)</td>
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</tr>
</tbody>
</table>

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

### References


3. Bharti SK, Nath G, Tilak R, Singh SK. Synthesis, anti-bacterial and anti-fungal activities of some...