



## Analysis of New Piperidine Substituted Benzothiazole Crystalline Derivatives

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### ABSTRACT

Recently, heterocyclic compounds play important role in drug industries. The benzothiazole (BTA) is a bicyclic compound in heterocyclic because of their biological properties. In this paper the synthesis and characterization of benzothiazole were reported. The chemical structures of synthesized compounds were established based on spectral data of <sup>1</sup>HNMR, <sup>13</sup>CNMR, and IR. The mass of the novel compounds was established with the help of the LCMS test. The formation of the crystal was confirmed by powder XRD and the sharp peaks show the purity and crystalline nature of the samples. The photoluminescence spectra explain the optical property of the compound. The biological studies of synthesized compounds show that compound 5c possesses good antibacterial activity and compound 5d has good antifungal activity.

**Keywords:** Piperidine derivatives, Benzothiazole, Biological property, Crystallization, Optical activity.

### INTRODUCTION

The benzothiazole derivatives possess superior biological and bio-physical properties such as antitumor and metabolic activities<sup>1</sup>, antimicrobial<sup>2-5</sup>, imaging agents for  $\beta$ -amyloid<sup>6</sup> anti-cancer<sup>7</sup>, anti-tuberculosis<sup>8</sup> anti-viral<sup>9</sup>, anti-oxidant<sup>10</sup> and hence driven the attention of the researchers for further development. Several substituted benzothiazoles have been identified as potent anthelmintic drugs<sup>11-14</sup>. Aminobenzothiazoles have manifested a large scale of biological activities such as antiparkinsonian, dopa-mine antagonist<sup>15-16</sup>, schistosomicidal agents<sup>17</sup>, anticonvulsant activity<sup>18</sup>, antileishmanial activity<sup>19</sup>, analgesic agents<sup>20</sup>, and

antiasthmatic drugs<sup>21</sup>. Moreover, compounds containing condensed pyrimidines have been used as herbicide antidotes<sup>22</sup>, and diuretics<sup>23</sup>. The BTA act as an effective catalyst<sup>24</sup> and the crystal nature shows fluorophore property<sup>25</sup>. Based on earlier studies, an attempt is made to prepare benzothiazole derivatives. The prepared samples were characterized for their potential applications.

### EXPERIMENTAL

#### Materials

The chemicals ethyl2-aminobenzo[d]thiazole-6-carboxylate, copper(II)bromide, t-nitrosobutane, piperidine, cesium carbonate,



sodiumhydroxide, acetonitrile, dimethylformamide, methanol, hydrochloric acid, ethylacetate, dichloromethane, triethyl amines, sodiumsulphate, propanephosphonic acid anhydride, substituted amines were of Sigma-Aldrich. These are used without purification. The dry ethyl acetate, hexane, and ethanol were obtained from Spectrochem for the crystallization process.

### Instruments and methods

The Perkin-Elmer spectrum 100 series spectrophotometer was used for FTIR studies of the sample. The information about the nature and number of protons was studied from the <sup>1</sup>HNMR spectrum. The <sup>1</sup>HNMR spectra were studied by using a 400 MHz Varian spectrometer. The information about carbon was obtained from the <sup>13</sup>CNMR spectrum of compound which was taken for the samples by subjected to 100MHz Bruker spectrometer with TMS as reference compound.

With the help of Shimadzu mass spectrometer, the mass spectra were obtained. All the reactions were monitored by TLC plates and their spots were visualized by exposing them to a UV lamp, iodine chamber, or KMnO<sub>4</sub>, and it was performed with silica gel 60-120mesh. The crystal formation and optical properties were ensured by powder XRD and photoluminescence studies respectively. The data were taken by XPERT-PRO-Gonio scan-2 m diffractometer and Cary Eclipse-EL08083851 photo spectrometer. The elemental analysis was done by the Varian instrument (VARIO EL-3 series analyzer).

### Synthesis and characterization

#### Synthesis of Ethyl 2-bromobenzo[d]thiazole-6-carboxylate (2)

In a round bottom flask, 5 g of ethyl2-aminobenzo[d]thiazole-6-carboxylate dissolved in 1eq of acetonitrile solvent then added 1eq of copper(II)bromide with t-nitrosobutane. The reaction mixture was mixed thoroughly using a magnetic stirrer up to 16 h maintaining in the room temperature. It was monitored by TLC complies. After that, the ethyl acetate was added with the reaction mixture to dilute it. The 1.5N HCl, water, and brine solution were used to wash the reaction mixture. Now the mixture was dried over sodium sulphate, and concentrated below 50°C. The crude has proceeded to the next step without purification.

It was obtained as yellow solid. The yield was 54%. (LCMS: 95% purity). B.pt.139-40°C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  1742(C=O), 1647(C=N), 1324(C-N), 684(C-S), 610(C-Br). <sup>1</sup>HNMR (400 MHz, DMSO-d<sub>6</sub>, ppm):  $\delta$  8.420 (s, 1H, ArH), 7.453-7.482 (d, 2H,  $J=11.6$ Hz ArH), 4.302 (m, 2H, -CH<sub>2</sub>), 1.289-1.301 (t, 3H,  $J=4.8$ Hz -CH<sub>3</sub>). <sup>13</sup>CNMR (100 MHz, DMSO-d<sub>6</sub>, ppm):  $\delta$  14.32, 60.50, 121.34, 123.52, 126.40, 128.63, 141.36, 155.77, 165.62. For C<sub>10</sub>H<sub>8</sub>BrNO<sub>2</sub>S, Calculated: C-41.97%, H-2.82%, Br-27.92%, N-4.89%, O-11.19%, S-11.21%. Found: C-42.04%, H-2.90%, Br-27.86%, N-4.92%, O-11.13%, S-11.15%. LCMS [M+1]<sup>+</sup>: m/z 287.1.

#### Synthesis of Ethyl 2-(piperidin-1-yl)benzo[d]thiazole-6-carboxylate (3)

The obtained compound (2) was dissolved in DMF and added to the N-alkylation base (CS<sub>2</sub>CO<sub>3</sub> 1.5 eq). Now piperidine (1.1 eq) was added and then subjected for thermal treatment to a temperature of 100°C for 3 hours. After complies, it was cooled and purified to get compound (III).

It was obtained as orange solid with 56% yield, (LCMS: 95.7% purity), m.pt.161-162°C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  1740(C=O), 1643(C=N), 1326(C-N), 681(C-S). <sup>1</sup>HNMR (400 MHz, DMSO-d<sub>6</sub>, ppm):  $\delta$  1.536-1.553 (m, 6H, -CH<sub>2</sub>), 3.691-3.724, (t, 4H,  $J=13.2$ Hz-CH<sub>2</sub>) 8.414 (s, 1H, ArH), 7.697-7.721 (d, 2H,  $J=9.2$ Hz ArH), 4.292 (m, 2H, -CH<sub>2</sub>), 1.292-1.313 (t, 3H,  $J=8.4$ Hz -CH<sub>3</sub>). <sup>13</sup>CNMR (100 MHz, DMSO-d<sub>6</sub>, ppm):  $\delta$  14.44, 24.21, 25.45, 54.2, 61.02 116.55, 123.26, 126.57, 130.61, 157.62, 165.87, 168.13. For C<sub>15</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>S, Calculated: C-62.04%, H-6.25%, N-9.65%, O-11.02%, S-11.04%. Found: C-61.98%, H-6.27%, N-9.69%, O-11.05%, S-11.01%. LCMS [M+1]<sup>+</sup>: m/z 291.3.

#### Synthesis of 2-(piperidin-1-yl)benzo[d]thiazole-6-carboxylic acid (4)

The 2 g measured compound (3) was dissolved in methanol. Now, 2 eq sodium hydroxide solution (NaOH dissolved in water) was added. Now it was stirred for a time duration of 1 h at room temperature. After TLC complies, acidified with 1.5 N HCl. Then it was extracted with ethyl acetate. The organic layer was washed with water, dried, and concentrated. With the help of column chromatography crude was purified and compound eluted with methanol (2.4%) and DCM to get the desired product.

It was obtained as yellow solid of 67% of yield, (LCMS: 95.3% purity), m.pt.169-70°C, IR (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  3242(O-H), 1761(C=O), 1645(C=N), 1321(C-N), 684(C-S).  $^1\text{H}$ NMR (400 MHz,  $\text{DMSO-d}_6$ , ppm):  $\delta$  1.546-1.5621 (m, 6H,  $-\text{CH}_2$ ), 3.716-3.734 (t, 4H,  $J=7.2\text{Hz}$   $-\text{CH}_2$ ), 8.618, (s, 1H, ArH), 7.882-7.894 (d, 2H,  $J=74.8\text{Hz}$  ArH), 11.121 (s, 1H, -OH).  $^{13}\text{C}$ NMR (100 MHz,  $\text{DMSO-d}_6$ , ppm):  $\delta$  24.14, 25.52, 54.36, 116.74, 123.62, 126.88, 130.73, 158.55, 166.72, 168.15. For  $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}_2\text{S}$ , Calculated: C-59.52%, H-5.38%, N-10.68%, O-12.20%, S-12.22%. Found: C-59.59%, H-5.41%, N-10.72%, O-12.12%, S-12.16%. LCMS  $[\text{M}+1]^+$ : m/z.263.3.

### Preparation of benzothiazole derivatives (5a-e)

In the solvent dichloromethane (1 mL), one

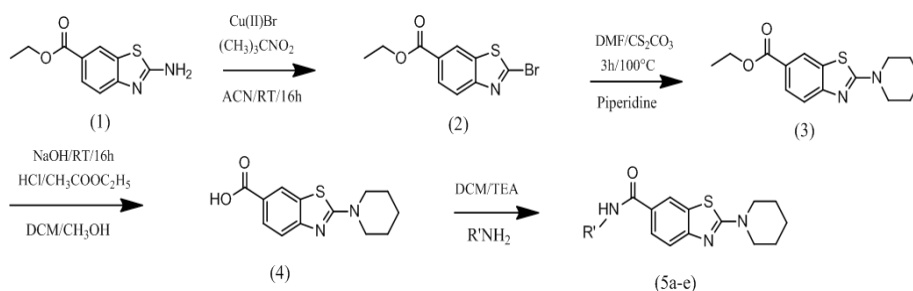


Fig. 1. The reaction scheme

Table 1: Results of reaction

Compound	Simple amine	Product	Yield %	m.pt $^\circ\text{C}$
5a	Aniline		68	230 - 31
5b	t-butyl amine		72	233 - 34
5c	3,4-difluoro aniline		63	218 - 19
5d	Morpholine		70	128 - 29
5e	Cyclo propyl amine		76	240 - 41

equivalent (100 mg) weighed compound (4) was dissolved. Now the solution was added to simple amine (1 eq), triethylamine (2 eq). The mixture was stirred for 2 hours. Then cooled to zero degrees Celsius. Now, propane phosphoric acid anhydride (T3P) (50% in ethyl acetate) (1.5 eq) was added and again stirred for 12 hours. At the end of the reaction, monitor by TLC, the addition of ice water was done and extracted with dichloromethane. Finally washed in water and brine solution, dried over sodium sulphate, then concentrated. The purification of crude was made by column chromatography (using silica gel) eluent (petroleum ether and 50 – 70% of ethyl acetate) to get desired product (5a-e). All the reaction schemes were shown in Fig. 1. The yield and melting point of these samples are presented in Table 1.

**Synthesis of N-phenyl-2-(piperidin-1-yl)benzo[d]thiazole-6-carboxamide(5a)**

The aniline was used to obtain the above compound (5a). The reactions results as white crystalline solid of 68% yield. (LCMS: 96.1% purity), m.pt. 230-31°C, IR (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  3230(N-H), 1629(C=O), 1629(C=N), 1322(C-N), 691(C-S).  $^1\text{H}$ NMR (400 MHz,  $\text{DMSO-d}_6$ , ppm):  $\delta$  1.542-1.562 (m, 6H,  $-\text{CH}_2$ ), 3.742-3.761 (t, 4H,  $J=7.6\text{Hz}$   $-\text{CH}_2$ ), 7.921-7.942 (d, 1H,  $J=8.4\text{Hz}$  ArH), 7.635-7.641 (d, 3H,  $J=2.4\text{Hz}$  ArH), 8.382 (s, 1H, ArH), 9.194 (s, 1H, -NH), 7.293-7.316 (t, 3H,  $J=9.2\text{Hz}$  ArH).  $^{13}\text{C}$ NMR (100 MHz,  $\text{DMSO-d}_6$ , ppm):  $\delta$  24.32, 25.26, 54.48, 121.17, 121.73, 123.85, 128.41, 131.07, 137.58, 156.53, 164.36, 167.92. For  $\text{C}_{19}\text{H}_{19}\text{N}_3\text{O}_2\text{S}$ . Calculated: C-67.63%, H-5.68%, N-12.45%, O-4.74%, S-9.50%. Found: C-67.57%, H-5.71%, N-12.41%, O-4.79%, S-9.52%. LCMS  $[\text{M}+1]^+$ : m/z.337.4.

**Synthesis of N-(tert-butyl)-2-(piperidin-1-yl)benzo[d]thiazole-6-carboxamide(5b)**

The t-butyl amine was added that reacts to give the compound 5(b). It was obtained as a white crystalline solid with a 72% yield. (LCMS: 95.3% purity), m.pt. 233-34°C, IR (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  3333(N-H), 1625(C=O), 1625(C=N), 1321(C-N), 694(C-S).  $^1\text{H}$ NMR (400 MHz,  $\text{DMSO-d}_6$ , ppm):  $\delta$  1.548-1.591 (m, 6H,  $-\text{CH}_2$ ), 3.695-3.702 (t, 4H,  $J=2.8\text{Hz}$   $-\text{CH}_2$ ), 7.878-7.895 (d, 1H,  $J=6.8\text{Hz}$  ArH), 7.672-7.685 (d, 1H,  $J=5.2\text{Hz}$  ArH), 8.402 (s, 1H, ArH), 8.108 (s, 1H, -NH), 1.402 (s, 9H,  $-\text{CH}_3$ ).  $^{13}\text{C}$ NMR (100 MHz,  $\text{DMSO-d}_6$ , ppm):  $\delta$  24.58, 25.32, 29.15, 54.62, 59.57, 121.13, 121.66, 123.72, 130.85, 156.42, 169.84, 168.12. For  $\text{C}_{17}\text{H}_{23}\text{N}_3\text{O}_2\text{S}$ , Calculated: C-64.32%, H-7.30%, N-13.24%, O-5.04%, S-10.10%. Found: C-64.38%, H-7.26%, N-13.21%, O-5.01%, S-10.14%. LCMS  $[\text{M}+1]^+$ : m/z.317.4.

**Synthesis of N-(3,4-difluorophenyl)-2-(piperidin-1-yl)benzo[d]thiazole-6-carboxamide (5c)**

The compound 5(c) was obtained by the addition of 3,4-difluoro aniline. It was obtained as a white crystalline solid with a 63% yield, (LCMS: 95.6% purity), m.pt. 218-19°C, IR (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  3262(N-H), 1638(C=O), 1638(C=N), 1324 (C-N), 1240(C-F), 687(C-S).  $^1\text{H}$ NMR (400 MHz,  $\text{DMSO-d}_6$ , ppm):  $\delta$  1.538-1.556 (m, 6H,  $-\text{CH}_2$ ), 3.707-3.719 (t,

4H,  $J=4.8\text{Hz}$   $-\text{CH}_2$ ), 7.796-7.812 (d, 1H,  $J=6.4\text{Hz}$  ArH), 7.578-7.601 (d, 3H,  $J=9.2\text{Hz}$  ArH), 8.412 (s, 1H, ArH), 9.562 (s, 1H, -NH), 7.742 (s, 1H, ArH).  $^{13}\text{C}$ NMR (100 MHz,  $\text{DMSO-d}_6$ , ppm):  $\delta$  24.58, 25.43, 54.56, 111.61, 114.95, 121.27, 121.73, 123.98, 130.92, 145.26, 147.22, 156.47, 164.57, 168.03. For  $\text{C}_{19}\text{H}_{17}\text{F}_2\text{N}_3\text{O}_2\text{S}$ , Calculated: C-61.11%, H-4.59%, F-10.18%, N-11.25%, O-4.28%, S-8.59%. Found: C-61.02%, H-4.52%, F-10.24%, N-11.30%, O-4.31%, S-8.61%. LCMS  $[\text{M}+1]^+$ : m/z.373.4.

**Synthesis of morpholine(2-(piperidin-1-yl)benzo[d]thiazol-6-yl)-methanone(5d)**

The addition of morpholine yields compound 5(d). It was obtained as pale yellow crystalline solid, with a 70% yield. (LCMS: 93% purity), m.pt. 128-29°C, IR (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  3332(N-H), 1625(C=O), 1625(C=N), 1330(C-N), 682(C-S).  $^1\text{H}$ NMR (400 MHz,  $\text{DMSO-d}_6$ , ppm):  $\delta$  1.526-1.549 (m, 6H,  $-\text{CH}_2$ ), 3.720-3.738 (t, 4H,  $J=7.2\text{Hz}$   $-\text{CH}_2$ ), 7.901-7.925 (d, 1H,  $J=9.6\text{Hz}$  ArH), 7.645-7.681 (d, 1H,  $J=14.4\text{Hz}$  ArH), 8.421 (s, 1H, ArH), 3.591-3.615 (t, 8H,  $J=11.2\text{Hz}$   $-\text{CH}_2$ ).  $^{13}\text{C}$ NMR (100 MHz,  $\text{DMSO-d}_6$ , ppm):  $\delta$  24.29, 25.63, 36.47, 46.33, 54.37, 66.18, 121.22, 121.67, 123.96, 131.10, 156.45, 168.17, 168.81. For  $\text{C}_{17}\text{H}_{21}\text{N}_3\text{O}_2\text{S}$ , Calculated: C-61.61%, H-6.39%, N-12.68%, O-9.65%, S-9.67%. Found: C-61.68%, H-6.35%, N-12.64%, O-9.69%, S-9.64%. LCMS  $[\text{M}+1]^+$ : m/z.331.4.

**Synthesis of N-cyclopropyl-2-(piperidin-1-yl)benzo[d]thiazole-6-carboxamide(5e)**

The reaction of cyclopropyl amine and the compound (5) results the compound 5(e) in the form of white crystalline solid. Its yield percentage is 76%. (LCMS: 95.4% purity), m.pt. 240-41°C, IR (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  3267(N-H), 1623(C=O), 1623(C=N), 1290(C-N), 672(C-S).  $^1\text{H}$ NMR (400 MHz,  $\text{DMSO-d}_6$ , ppm):  $\delta$  1.536-1.569 (m, 6H,  $-\text{CH}_2$ ), 3.701-3.718 (t, 4H,  $J=6.8\text{Hz}$   $-\text{CH}_2$ ), 7.902-7.916 (d, 1H,  $J=6.0\text{Hz}$  ArH), 7.625-7.646 (d, 1H,  $J=8.4\text{Hz}$  ArH), 8.368 (s, 1H, ArH), 8.102 (s, 1H, -NH), 2.765 (m, 1H, -CH), 0.612-0.850 (m, 4H,  $-\text{CH}_2$ ).  $^{13}\text{C}$ NMR (100 MHz,  $\text{DMSO-d}_6$ , ppm):  $\delta$  6.52, 24.45, 25.28, 26.62, 54.67, 121.08, 121.82, 123.74, 130.82, 156.55, 168.23, 167.14. For  $\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_2\text{S}$ , Calculated: C-63.76%, H-6.35%, N-13.94%, O-5.31%, S-10.64%. Found: C-63.68%,

H-6.41%, N-13.91%, O-5.39%, S-10.61%. LCMS [M+1]<sup>+</sup>: m/z 301.4.

## RESULT AND DISCUSSION

The functional groups present in all the compounds were identified by FTIR spectra of these compounds. The compound 5c shows an additional peak due to C-F functional group at 1240 cm<sup>-1</sup>. The result of FTIR confirms the formation of the synthesized compounds. In <sup>1</sup>HNMR, all the compounds display the almost same chemical shift values. However, in compound 5d singlet due to N-H is disappeared. It is because of the presence of two R-groups instead of one R-group and one H-atom which were present in all other groups. Similarly, when comparing the <sup>1</sup>HNMR spectrum of the compounds 5a and 5c, it is observed that the doublet at δ (7.635-7.641 ppm) is changed as a singlet at δ (7.742 ppm). It is due to the substitution of fluorine that replaces hydrogen at C-3 in aniline. The same result was also obtained in <sup>13</sup>CNMR the chemical shift value changes from 128.41 to 145.26 ppm. The structure of these compounds was confirmed from the <sup>1</sup>HNMR and <sup>13</sup>CNMR. From the Table 1, it is observed that the melting point of the synthesized compounds is almost the same except for compound 5d. The compound 5d shows a lower melting point value. The addition of heterocyclic compound (Morpholine) weakens the bond and hence reduces the melting point. The results of LCMS analysis establish the formation of the products. The percentage of the elements present in the products was obtained from elemental analysis. These values agree with theoretically calculated values. Hence the formation of the products is also confirmed from this analysis.

### Antibacterial and antifungal activity

#### Antibacterial activity

In earlier days, simple and easy method of screening the antibacterial activity of a sample by the

agar well diffusion method was used (Perez *et al.*, 1990, Perez *et al.*, 1999, Bagamboula *et al.*, 2004 and Erdemoglu *et al.*, 2003). In Brain Heart Infusion (BHI) (Difco, Detroit, MI) broth the microorganism was suspended. It was diluted to roughly 10<sup>6</sup> colony-forming units (cfu) per mL. On the surface of BHI agar and Sabouraud Dextrose Agar (SDA) (Difco, Detroit, MI), these diluted microorganisms were spread as "flood-inoculated". Then it was dried. The SDA was used for *C. albicans* and *C. tropicalis*. The wells of 5 mm size were cut from the agar using a sterile cork-borer. Now 25 μL of the sample solutions were poured in these wells. The plates were kept in an incubation chamber for 18 h at 35°C. The measurement of zone of inhibition gives the antimicrobial activity of the samples. Ciprofloxacin (10 μg/mL) was the standard drug for antibacterial activities. The tests were carried out in duplicates. The diameter of inhibition zone was measured and interpreted.

The Minimal Inhibitory Concentration (MIC) and Minimal Bactericidal Concentration (MBC) was measured by the broth dilution method (Van der Berghe and Vlietinck, 1991). About 1.0 to 0.25 mg/mL diluted plant extract was used. Test bacteria culture with concentration of 10<sup>5</sup> CFU/mL was used. After 24 h of incubation at 37°C the MIC values were taken as the lowest plant extracts concentration which restricts visible bacterial growth and MBC was the lowest concentration that completely inhibited bacterial growth. In this method the reference was Ciprofloxacin. The experimental procedure was done thrice.

The antibacterial activity of all the synthesized compounds was tested *In vitro* against pathogenic *Enterococcus faecalis*, *Staphylococcus aureus*, *Escherichia coli*, and *Salmonella typhi*. The results are presented in Table 2.

**Table 2: Antibacterial activity of the compounds**

Microorganisms	Control	5a	5b	5c	5d	5e	Ciprofloxacin
Zone of inhibition in mm							
<i>Enterococcus faecalis</i>	-	10.5±0.55	11.24±0.67	18.45±0.44	07.44±0.56	11.54±0.67	35.56±0.55
<i>Staphylococcus aureus</i>	-	08.42±0.10	07.12±0.10	10.56±0.66	12.34±0.30	07.55±0.10	40.54±0.48
<i>Escherichia coli</i>	-	07.55±0.00	08.15±0.00	11.87±0.54	13.44±0.45	08.45±0.00	38.54±0.60
<i>Salmonella typhi</i>	-	06.67±0.22	09.21±0.00	08.22±0.00	08.57±0.00	09.45±0.00	35.76±0.10

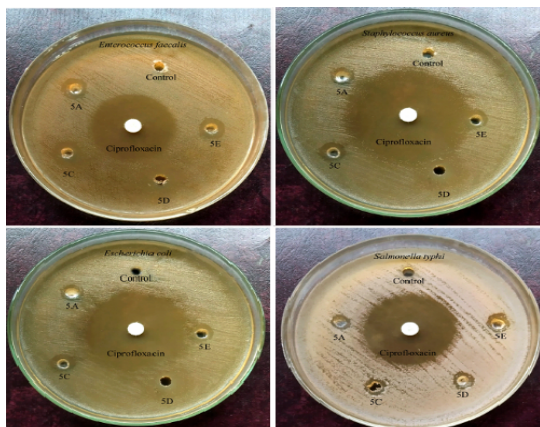


Fig. 2. Antibacterial activity

**Antifungal activity**

As reported earlier by Alves and Cury, 1992, the samples were examined for antifungal activity by dilution in agar technique. A 100 mg plant extracts were dissolved in 1 mL of dimethyl sulfoxide (DMSO) and then undergone two fold dilution in Yeast Nitrogen Base Phosphate (YNBP) agar (Merck,

Germany) to get a concentration range of 31.25-1000 µL/mL. The YNBP agar plates having only DMSO diluted in the same way, that didn't influence the fungal growth, were used as controls. These fungal strains were suspended in sterile physiological Tris buffer (pH 7.4, 0.05M), homogenized, and adjusted to an OD (530nm) of 0.05 (equivalent to 1 X 10<sup>6</sup> CFU/mL). This suspension was used as the inoculum for the test in the agar plates. Using an automatic micropipette, the fungal suspensions (3 µL) were inoculated. These plates (diameter: 25 cm) were kept for incubation at 37°C for 48 hours. The minimal inhibitory concentration (MIC) is defined as the minimum concentration of the plant extracts required to inhibit completely the visible growth of the fungus. Ketoconazole was used as a reference and appropriate controls with no plant extracts were used. Each experiment was carried out for three times.

The antifungal activity of all the synthesized compounds was tested *In vitro* against pathogenic *Aspergillus niger*, *Aspergillus flavus*, *Candida albicans*, and *Penicillium* sps. The results are given in Table 3.

Table 3: Antifungal activity of the compounds

Microorganisms	Control	5a	5b	5c	5d	5e	Ketoconazole
		Zone of inhibition in mm					
<i>Aspergillus niger</i>	-	07.32±0.10	08.13±0.00	10.55±0.20	10.67±0.10	08.34±0.00	12.54±0.50
<i>Aspergillus flavus</i>	-	06.35±0.00	06.64±0.10	08.22±0.01	09.56±0.30	07.10±0.10	09.30±0.30
<i>Candida albicans</i>	-	08.34±0.10	11.24±0.20	07.35±0.00	10.45±0.00	12.15±0.20	12.44±0.40
<i>Penicillium</i> sps	-	07.10±0.00	07.15±0.10	7.50±0.00	08.25±0.02	07.40±0.10	15.34±0.10

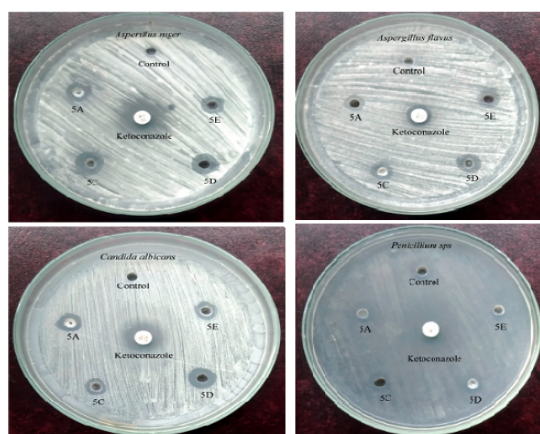


Fig. A. 3. Antifungal activity

**Powder XRD studies**

The powder XRD pattern is shown in Fig. 4. From the graph, it is observed that the peaks are sharp and intense. This shows that the sample is pure and crystalline in nature.

The crystalline size is calculated from the Debye-scherrer formula

$$D = \frac{k\lambda}{\beta \cos\theta} \text{ where } k = 0.9$$

$$D = \frac{0.9\lambda}{\beta \cos\theta}$$

λ → wavelength 1.546 Å°

β → Full width half (0.1476 deg = 0.002576 rad)

θ → Angle of diffraction (16.1967/2 = 8.09835 deg = 0.14134 rad)

$$D = 0.9 \times 1.546 / 0.002576 \times \cos(0.14134)$$

$$D = 54.3652 \text{ nm.}$$

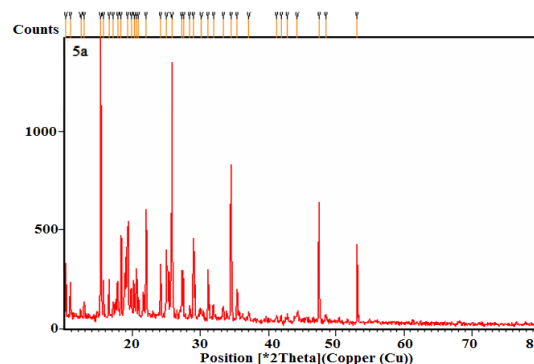


Fig. 4. Powder X-ray diffraction pattern of N-phenyl-2-(piperidin-1-yl)benzo[d]thiazole-6-carboxamide(5a)

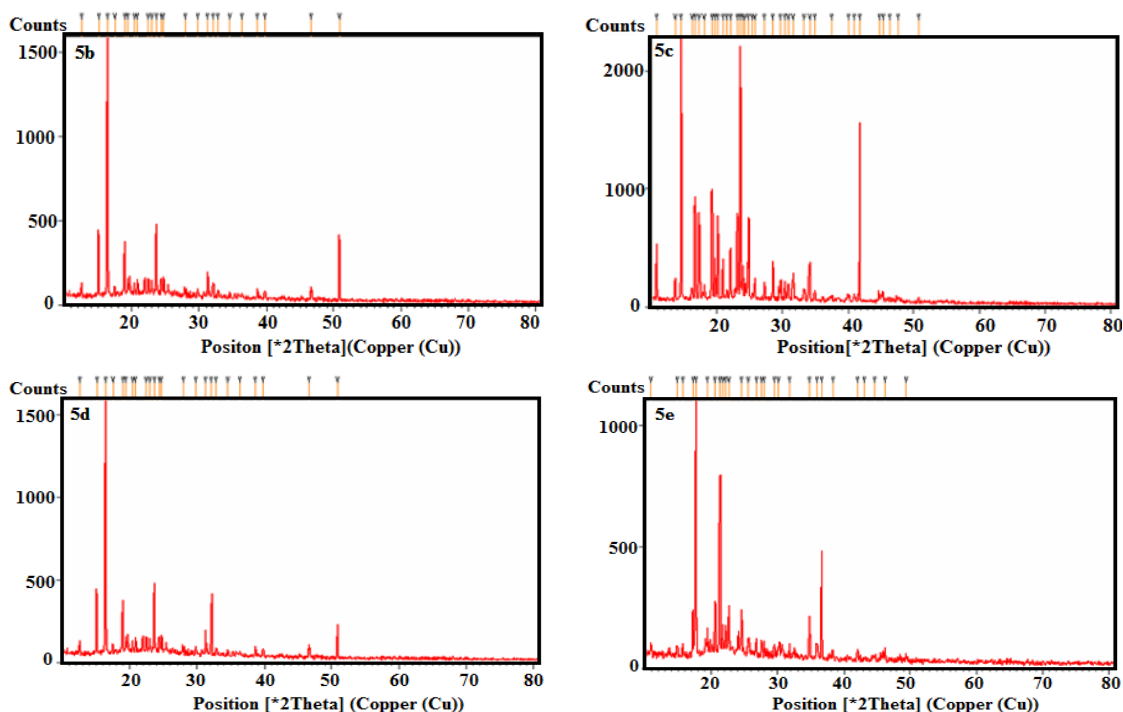


Fig. 5. Powder X-ray diffraction pattern of compounds 5b to 5e

The crystalline size of the samples are calculated and presented in Table 2.

Table 4: Crystalline size of the compounds

S. No	Compound name	Size (nm)
1	5a	54.3652
2	5b	54.4454
3	5c	54.2976
4	5d	54.4046
5	5e	54.6069

Generally, the crystalline size value will increase or decrease depending on the ordering inside the material. So when materials are added it will disturb the order of the parent compound also the additional compound produces strain inside the crystal. For example, the crystalline size of the compounds 5a and 5e are compared and presented in Table 4. It is observed that the crystalline size of compound 5a is less than that of compound 5e. It is because in compound 5a more carbon atoms are present when compared with compound 5e. The more carbon atoms produce more amount of strain that restricts the growth and size of the crystal.

### Photoluminescence

The photoluminescence (PL) spectrum

examines material for its wide applications in the field of medical, biochemical, and chemical research. In PL spectroscopy, generally, a beam of light excites the electrons in the molecule of given materials and causes them to emit light in a longer wavelength than the observed radiation. The figures Fig. 9 to Fig. 13 show the PL spectra of the samples. These spectra give the absorption wavelength at 362 to 381nm which means the emission of blue radiation. The absorption peak is due to the band-to-band electronic transition in a material. The result predicts the use of the materials as a color filter.

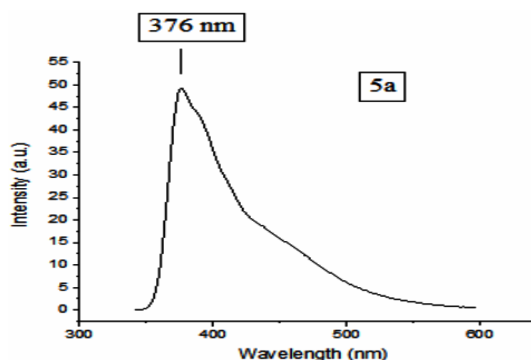


Fig. 6. Photoluminescence spectrum of N-phenyl-2-(piperidin-1-yl)benzo[d]thiazole-6-carboxamide(5a)

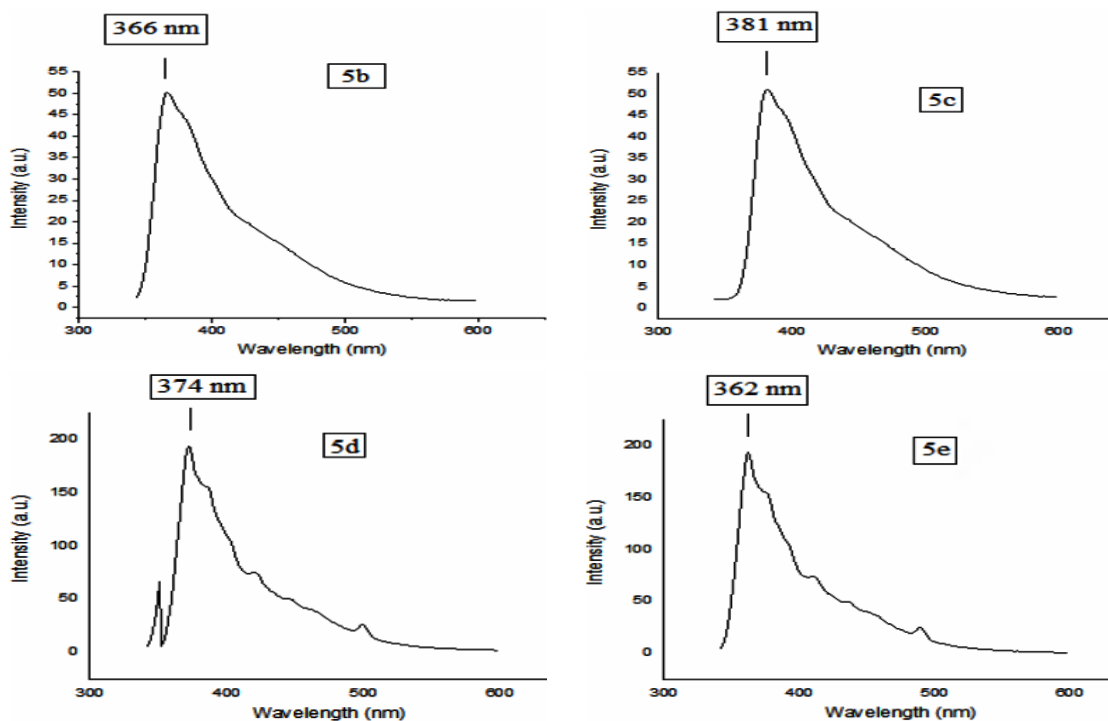


Fig. 7. Photoluminescence spectrum of compounds 5b to 5e

## CONCLUSION

The synthesis of derivatives of benzothiazole (5a-e) was carried out. The functional groups present in the samples were studied from the FTIR spectra and thus it confirms the synthesis of the compounds. The proton and carbon positions of these were obtained through  $^1\text{H}$ NMR and  $^{13}\text{C}$ NMR spectra respectively. The LCMS study indicates the good yield of all the compounds. The synthesized compounds exhibited antibacterial and antifungal activities. From the antibacterial test the compounds 5c, 5d, 5d, and 5e are show the highest activity of *Enterococcus faecalis*, *Staphylococcus aureus*, *Escherichia coli*, and *Salmonella typhi*, respectively. In the antifungal activity test the compounds 5c & 5d, 5d, 5b & 5e, and 5d show the higher activity of *Aspergillus niger*, *Aspergillus flavus*, *Candida albicans*, and *Penicillium* sps, respectively. The crystalline nature

of the samples was confirmed by the powder X-ray diffraction studies. These samples show good optical nature as studied from the PL study. Hence the synthesized compounds can be used as color filters and in pharmaceutical applications.

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## Conflict of interest

The authors declare no conflict of interest.

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