

Synthesis, characterization, crystal structures, and antibacterial activity of some new 1-(3,4,5-trimethoxybenzoyl)-3-aryl thioureas

Aamer SAEED^{1,*}, Rasheed Ahmad KHERA¹, Naeem ABBAS¹, Muhammad LATIF¹,
Imran SAJID² and Ulrich FLÖRKE³

¹*Department of Chemistry, Quaid-I-Azam University, Islamabad 45320, PAKISTAN*
e-mail: aamersaeed@yahoo.com

²*Department of Microbiology, Punjab University, Lahore-PAKISTAN*

³*Department Chemie, Fakultät für Naturwissenschaften, Universität Paderborn,*
Warburgerstrasse 100, D-33098 Paderborn-GERMANY

Received 28.10.2009

Synthesis of some novel 1-(3,4,5-trimethoxy)benzoyl-3-arylthiourea derivatives (**1a-o**) was accomplished in 2 steps. The synthetic route involves the reaction of 1-(3,4,5-trimethoxy)benzoyl chloride with potassium thiocyanate in 1:1 molar ratio in acetone to afford the corresponding isothiocyanate followed by treatment with suitably substituted anilines. The structures of the products were established by elemental analyses, IR, ¹H- and ¹³C-NMR, and mass spectroscopy and for **1b** and **1m** from single crystal X-ray diffraction data. All of the synthesized compounds (**1a-o**) were screened for antibacterial activity against gram positive and gram negative bacterial strains and were found to exhibit low activity towards the tested microorganisms, compared to chloramphenicol, the standard drug.

Key Words: 1-(3,4,5-trimethoxy)benzoyl-3-arylthioureas, antibacterial, crystal structure.

Introduction

There has been considerable interest in recent years in the synthesis of various 1,3-disubstituted thioureas.¹ Thiourea derivatives are exceptionally versatile building blocks for the synthesis of a variety of heterocyclic compounds and exhibit a wide spectrum of bioactivities.² N,N-Dialkyl-N-aryl thioureas are efficient ligands for the separation of platinum group metals.³ 1,3-Dialkyl or diaryl thioureas exhibit significant antifungal activity against the plant pathogens *Pyricularia oryzae* and *Drechslera oryzae*.⁴ N-aryl N-phenyl

*Corresponding author

thioureas have been developed as anion-binding sites in a hydrogen-bonding receptor,⁵ thiocalix[4]arenes containing thioureas as neutral receptors towards α,α -dicarboxylate anions,⁶ and N-4-substituted-benzyl-N-*tert*-butylbenzyl thioureas as vanilloid receptors ligands and antagonists in rat DRG neurons.⁷ 1-Benzoyl-3-(4,6-disubstituted-pyrimidinyl)thioureas have shown excellent herbicidal activity.⁸ Acyl thioureas are well known for their superior pesticidal, fungicidal, antiviral, and regulating activity for plant growth.⁹ Thioureas have been widely used in enantioselective synthesis, such as in nitro-Mannich reactions, Aza-Henry reactions, and the Michael addition.^{10–12} Symmetrical and asymmetrical phenethyl thioureas, 5-halo-substituted thiophene pyridyl thioureas, and heterocyclic thioureas are non-nucleoside inhibitors of HIV-1 reverse transcriptase.^{13–15} Synthesis and anion recognition of molecular tweezers receptors based on acyl thioureas¹⁶ and efficient colorimetric anion sensors have recently been reported.¹⁷ Moreover, thiourea analogues are potent influenza virus neuraminidase inhibitors.¹⁸

Condensation of thiourea derivatives with carbonyl compounds has been used in the synthesis of N-alkyl-1,3-thiazol-2-amines and 3-alkyl-1,3-thiazolines,¹⁹ 1-aryl-3-aryl-4-substituted imidazole-2-thiones,²⁰ and 2-(aroylimino)-3-aryl-4-methyl/phenyl-1,3-thiazolines.²¹ Cyclocondensation of unsymmetrical perfluoroalkyl substituted beta-diketones with urea, thiourea, and guanidine leads to various heterocycles.²² Regioselective synthesis of 2H-[1,2,4]thiadiazolo pyrimidine derivatives²³ and 2-(9H-fluoren-9-ylmethoxy-carbonylamino)-thiazole-4-carboxylic acids via N-Fmoc thioureas²⁴ has recently been described.

Taking into consideration the aforementioned biological and synthetic significance of thioureas, the synthesis of some new 1-(3,4,5-trimethoxy)benzoyl-3-arylthiourea derivatives was undertaken as precursors towards novel heterocycles and for the systematic study of their bioactivity and complexation behavior.

Experimental

Melting points were recorded using a digital Gallenkamp (SANYO) model MPD.BM 3.5 apparatus and are uncorrected. ¹H- and ¹³C-NMR spectra were determined in CDCl₃ at 300 MHz and 75 MHz, respectively, using a Bruker spectrophotometer. FTIR spectra were recorded on an FTS 3000 MX spectrophotometer. Mass spectra (EI, 70 eV) were recorded on a GC-MS instrument (Agilent Technologies), and elemental analyses were conducted using a LECO-183 CHNS analyzer. Bioactivities were investigated at the Department of Microbiology, Punjab University, Lahore, Pakistan. Thin layer chromatography (TLC) was conducted on 0.25 mm silica gel plates (60 F254, Merck). Visualization was performed with ultraviolet light. Reagents were obtained commercially and used as received.

X-ray data collection and structure refinement

1b: C₁₈H₂₀N₂O₄S, Mr = 360.4, monoclinic, space group P2₁/c, a = 11.5786(11), b = 7.1613(7), c = 21.831(2) Å, β = 104.117(2)°, V = 1755.5(3) Å³, Z = 4, D_x = 1.364 g/cm³, F(000) = 760, T = 120(2) K. Bruker-AXS SMART APEX CCD²⁷ graphite monochromator, λ (MoK α) = 0.71073 Å, μ = 0.21 mm⁻¹, colorless crystal, size 0.23 × 0.20 × 0.19 mm³, 15,183 intensities collected 1.8 < θ < 27.9°, -15 < h < 15, -9 < k < 9, -28 < l < 28. Structure solved by direct methods,²⁵ full-matrix least-squares refinement²⁵ with 4198 independent reflections based on F² and 243 parameters, all but H atoms and C182 refined anisotropically. Hydrogen atoms

were located from difference Fourier maps and refined at idealized positions riding on the carbon atoms with isotropic displacement parameters U_{iso} (H) = $1.2U_{eq}$ (C) or $1.5U_{eq}$ (methyl-C). H(N) atom parameters were refined freely. The methyl group is disordered over 2 sites with site occupation factors 0.719(3) for C181 at C17 and 0.281(3) for C182 at C13. Hydrogen atoms at C13 and C17 were treated accordingly. Refinement converged at $R1(I > 2\sigma(I)) = 0.050$, $wR2(\text{all data}) = 0.087$, $S = 0.85$, $\max(\delta v\sigma) < 0.001$, min/max height in final ΔF map $-0.34/0.35 \text{ e}/\text{\AA}^3$. The molecular structure of **1b** and selected bond lengths and angles are depicted in Figure 1.

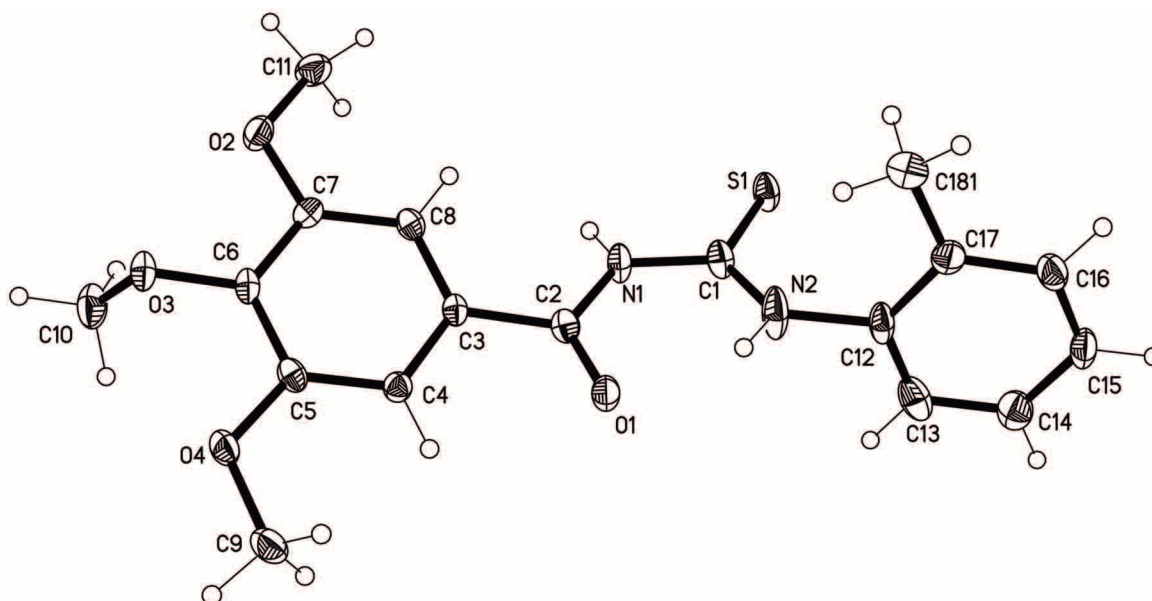


Figure 1. Molecular structure of **1b** with displacement ellipsoids plotted at 50% probability level. Only major part (C181) of disordered CH_3 group shown. Selected bond lengths (\AA) and angles ($^\circ$): C2-O1 1.222(2), C2-C3 1.492(3), C2-N1 1.388(2), N1-C1 1.395(2), C1-S1 1.669(2), C1-N2 1.325(3); C3-C2-N1 117.15(18), C2-N1-C1 126.45(18), N1-C1-N2 116.76(18), C1-N2-C12 123.82(18).

1m: $\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}_4\text{S}$, $M_r = 352.4$, monoclinic, space group $P2_1/c$, $a = 12.852(3)$, $b = 16.725(3)$, $c = 8.3899(17) \text{ \AA}$, $\beta = 107.255(5)^\circ$, $V = 1722.2(6) \text{ \AA}^3$, $Z = 4$, $D_x = 1.359 \text{ g/cm}^3$, $F(000) = 752$, $T = 120(2) \text{ K}$. Bruker-AXS SMART APEX CCD,²⁷ graphite monochromator, $\lambda(\text{MoK}\alpha) = 0.71073 \text{ \AA}$, $\mu = 0.21 \text{ mm}^{-1}$, colorless crystal, size $0.40 \times 0.11 \times 0.10 \text{ mm}^3$, 15,025 intensities collected $1.7 < \theta < 27.9^\circ$, $-16 < h < 16$, $-21 < k < 22$, $-11 < l < 10$. Structure solved by direct methods,²⁵ full-matrix least-squares refinement²⁵ with 4103 independent reflections based on F^2 and 227 parameters, all but H atoms refined anisotropically. Hydrogen atoms were located from difference Fourier maps and refined at idealized positions riding on the carbon atoms with isotropic displacement parameters U_{iso} (H) = $1.2U_{eq}$ (C) or $1.5U_{eq}$ (methyl-C). H(N) atom parameters were refined freely. Refinement converged at $R1(I > 2\sigma(I)) = 0.042$, $wR2(\text{all data}) = 0.107$, $S = 1.02$, $\max(\delta v\sigma) < 0.001$, min/max height in final ΔF map $-0.21/0.39 \text{ e}/\text{\AA}^3$. The molecular structure of **1m** and selected bond lengths and angles are depicted in Figure 3.

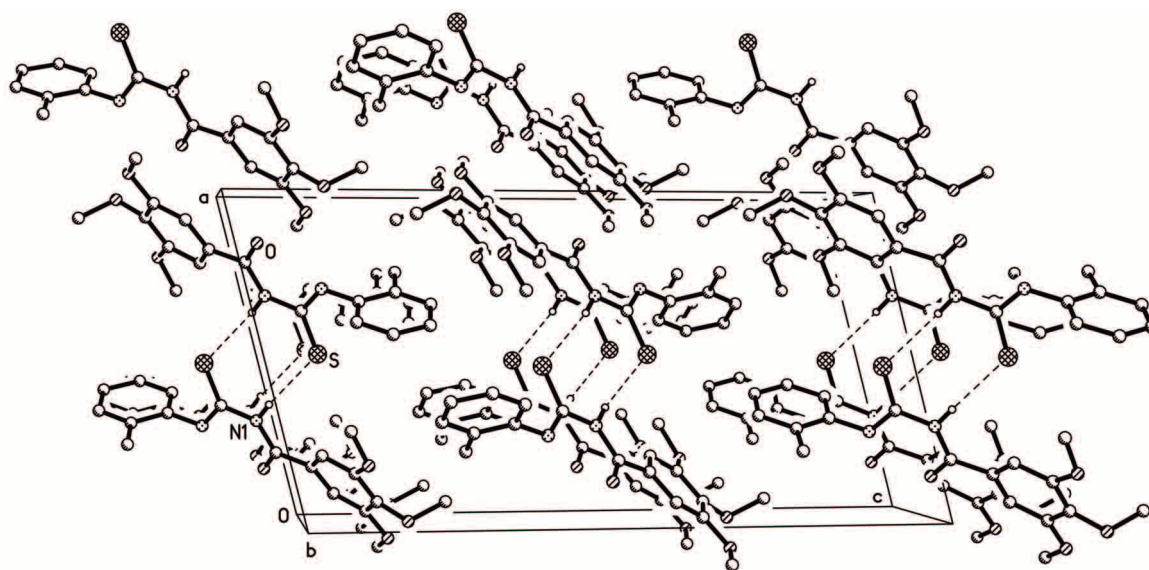


Figure 2. Crystal packing of **1b** viewed along [010] with intermolecular hydrogen bonding pattern indicated as dashed lines (N1-H...S1(-x+1, -y+1, -z)) H-atoms not involved in hydrogen bonding are omitted. The dimers are stacked along [001].

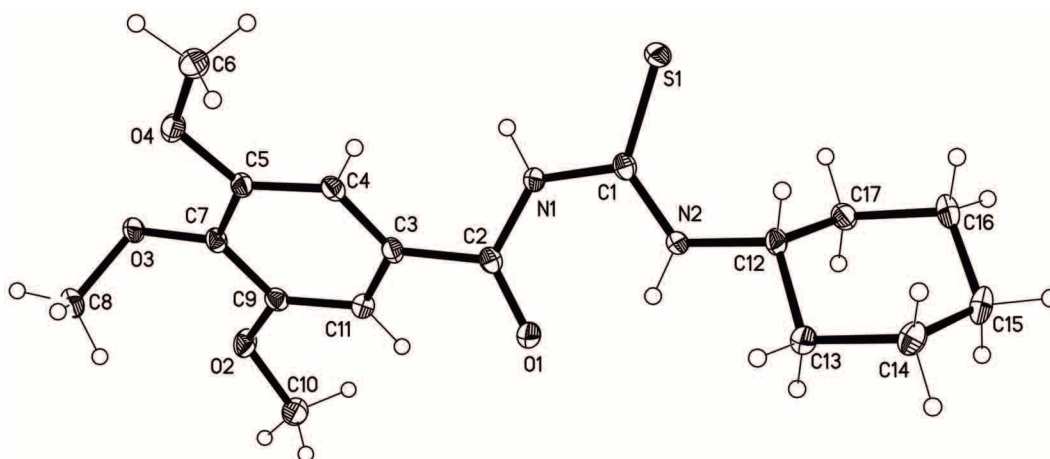


Figure 3. Molecular structure of **1m** with displacement ellipsoids plotted at 50% probability level. Selected bond lengths (Å) and angles (°): C2-O1 1.2268(19), C2-C3 1.498(2), C2-N1 1.368(2), N1-C1 1.403(2), C1-S1 1.6739(16), C1-N2 1.325(2); C3-C2-N1 114.97(13), C2-N1-C1 128.47(13), N1-C1-N2 116.93(14), C1-N2-C12 123.13(13).

Synthesis of 1-(3,4,5-trimethoxybenzoyl)-3-aryl thioureas, general procedure

A solution of 1-(3,4,5-trimethoxy)benzoyl chloride (10 mmol) in acetone (50 mL) was added dropwise to a suspension of potassium thiocyanate (10 mmol) in acetone (30 mL) and the reaction mixture was refluxed for 30 min. After cooling to room temperature, a solution of the substituted aniline (10 mmol) in acetone (10 mL)

was added and the resulting mixture refluxed for 2-3 h. The reaction mixture was poured into cold water and the precipitated thioureas were recrystallized from aqueous ethanol.

The physicochemical and spectral data are given in Tables 1 and 2, respectively. All compounds gave satisfactory elemental analyses.

Table 1. Physicochemical data of thioureas (**1a-o**).

Compd	Yield (%)	R_f^a	Mp (°C)	Molecular formula (MW)	EIMS [M ⁺]
1a	70	0.47	134-135	C ₁₇ H ₁₈ N ₂ O ₄ S (346.09)	346.0
1b	65	0.45	142-143	C ₁₈ H ₁₈ N ₂ O ₄ S (360.11)	360.0
1c	68	0.46	138-139	C ₁₈ H ₁₈ N ₂ O ₄ S (360.11)	360.0
1d	72	0.27	166-167	C ₁₈ H ₂₀ N ₂ O ₅ S (376.10)	376.0
1e	69	0.25	145-146	C ₁₈ H ₂₀ N ₂ O ₅ S (376.10)	376.0
1f	72	0.48	136-137	C ₁₇ H ₁₇ ClN ₂ O ₄ S (380.00)	380.0
1g	63	0.47	111-112	C ₁₇ H ₁₇ ClN ₂ O ₄ S (380.00)	380.0
1h	71	0.49	127-128	C ₁₇ H ₁₇ ClN ₂ O ₄ S (380.00)	380.0
1i	69	0.51	124-125	C ₁₇ H ₁₇ BrN ₂ O ₄ S (424.00)	424.0
1j	68	0.53	136-137	C ₁₈ H ₁₉ ClN ₂ O ₄ S (394.07)	394.0
1k	62	0.28	103-107	C ₁₇ H ₁₇ N ₃ O ₆ S (391.08)	391.0
1l	72	0.26	145-146	C ₁₇ H ₁₇ N ₃ O ₆ S (391.08)	391.0
1m	75	0.54	152-153	C ₁₇ H ₂₄ N ₂ O ₄ S (352.14)	352.1
1n	64	0.56	124-125	C ₁₃ H ₁₈ N ₂ O ₄ S (298.09)	298.0
1o	56	0.58	129-130	C ₁₅ H ₂₂ N ₂ O ₄ S (326.13)	326.1

a Solvent system: Pet. ether: Ethyl acetate (1:0.25); Recrystallization solvent: ethanol (aq)

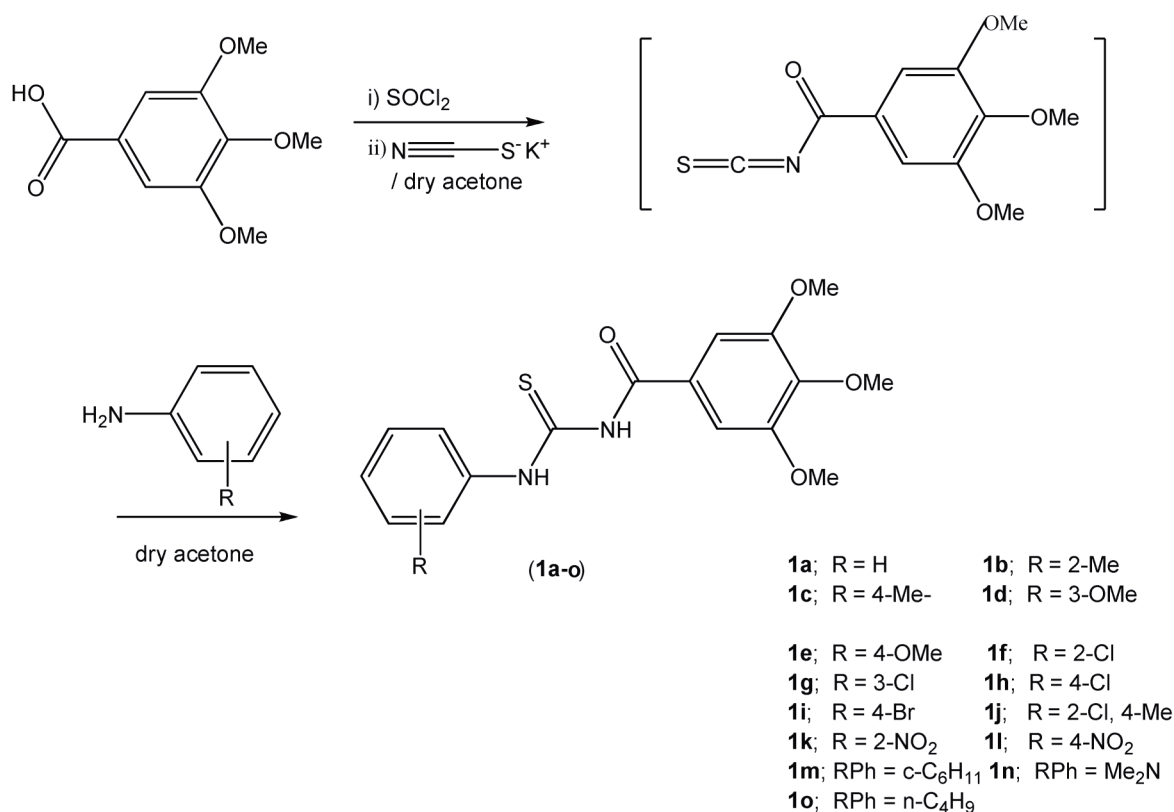
Results and discussion

The reaction sequence leading to the formation of thioureas is outlined in the Scheme. Commercial 1-(3,4,5-trimethoxy)benzoic acid was converted into corresponding acid chloride by treatment with thionyl chloride according to the standard procedure. The latter was treated with an equimolar quantity of potassium thiocyanate in acetone to afford the corresponding isothiocyanate intermediate, which was not separated. Addition of an equimolar quantity of substituted anilines in acetone furnished the title thiourea derivatives (**1a-o**).²⁶

Typically, thioureas are characterized by IR absorptions at 3350 and 3200 for free and associated NH respectively, at 1660-1670 for carbonyl, and at 1230-1250 cm⁻¹ for thiocarbonyl groups. The characteristic broad singlets at ca. δ 9.0 and 12 ppm for HN(1) and HN(2) and peaks at ca. 170 and 179 for carbonyl and thiocarbonyl were also observed in the ¹H- and ¹³C-NMR spectra, respectively. The physicochemical properties and the spectroscopic data of thioureas **1a-o** are given in Tables 1 and 2, respectively. Mass spectra of all of the compounds showed the molecular ion peaks. The major fragments correspond to the N-McLafferty rearrangement and the base peak is derived from the trimethoxybenzoyl cation.

Table 2. Spectral data (IR, ^1H -, ^{13}C -NMR) of thioureas (**1a-o**).

Compd	IR (ν , cm^{-1})	^1H -NMR (δ , ppm, $J(\text{Hz})$)	^{13}C -NMR (δ , ppm)
1a	3250 (NH), 1660 (C=O), 1579 (C=C), 1236 (C=S), 1132 (C-N)	12.63 (NH), 9.15 (NH), 7.72-7.09 (m, 7H, Ar'), 3.94 (s, 9H, OCH_3).	56.50, 61.07, 104.94, 124.15, 126.57, 126.99, 128.95, 137.57, 142.90, 153.52, 166.77 (C=S), 178.38 (C=O).
1b	3259 (NH), 1663 (C=O), 1579 (C=C), 1254 (C=S), 1143 (C-N)	12.29 (NH), 9.22 (NH), 7.12-7.77 (m, 6H, Ar'), 3.95 (s, 9H, OCH_3), 2.34 (s, 3H, CH_3).	18.04 (CH_3), 56.52, 61.07, 105.02, 124.19, 126.17, 126.49, 127.73, 130.82, 133.27, 136.36, 142.92, 153.54, 166.79 (C=S), 179.39 (C=O).
1c	3265 (N-H), 1666 (C=O), 1586 (C=C), 1259 (C=S), 1144 (C-N).	12.53 (NH), 9.18 (NH), 7.05-7.59 (m, 6H, Ar'), 3.94 (s, 9H, OCH_3), 2.38 (s, 3H, CH_3).	21.12 (CH_3), 56.511, 61.04, 105.25, 122.10, 124.19, 126.63, 136.95, 142.91, 153.37, 166.74, 178.48 (C=S), 189.65 (C=O).
1d	3223 (N-H), 1669 (C=O), 1587 (C=C), 1261 (C=S), 1153 (C-N).	12.46 (NH), 9.13 (NH), 6.92-7.56 (m, 6H, Ar'), 3.94 (s, 9H, OCH_3), 3.85 (s, 3H, OCH_3).	55.47 (OCH_3), 56.50, 61.02, 104.92, 114.0, 125.73, 126.61, 127.5, 128.7, 130.5, 142.93, 153.21, 158.23, 165.63 (C=S), 178.65 (C=O).
1e	3221 (N-H), 1670 (C=O), 1590 (C=C), 1256 (C=S), 1153 (C-N)	12.44 (NH), 9.10 (NH), 7.60-6.95 (m, 6H, Ar'), 3.95 (s, 9H, OCH_3), 3.85 (s, 3H, CH_3).	55.49, 56.52, 61.05, 104.96, 114.14, 125.84, 126.63, 127.32, 128.4, 130.53, 142.95, 153.56, 158.33, 166.66 (C=S), 178.66 (C=O).
1f	3219 (N-H), 1668 (C=O), 1593 (C=C), 1233 (C=S), 1155 (C-N)	12.77 (br s, 1H, NH), 9.16 (br s, 1H, NH), 7.04 -7.51 (Ar-Hx6), 3.96 (s, 9H, OCH_3)	56.54, 61.07, 105.07, 126.19, 126.43, 126.92, 127.75, 127.96, 130.3, 135.01, 143.01, 153.55, 166.48 (C=S), 178.68 (C=O).
1g	3229 (N-H), 1689 (C=O), 1603 (C=C), 1246 (C=S), 1151 (C-N)	12.39 (br s, 1H, NH), 9.41 (br s, 1H, NH), 7.28 -7.76 (Ar-Hx6), 3.92 (s, 9H, OCH_3).	56.43 (OCH_3), 121.41, 125.40, 126.65, 127.58, 129.84, 130.61, 133.18, 133.43, 134.82, 136.13, 153.1, 166.30 (C=S), 177.92 (C=O).
1h	3296 (N-H), 1660 (C=O), 1586 (C=C), 1238 (C=S), 1173 (C-N)	12.64 (br s, 1H, NH), 9.07 (br s, 1H, NH), 7.04 -7.65 (Ar-Hx6), 3.92 (s, 9H, OCH_3).	56.52, 104.98, 121.52, 125.31, 126.38, 128.2, 129.06, 130.4, 136.50, 143.09, 153.34, 165.7 (C=S), 178.41 (C=O)
1i	3243 (N-H), 1663 (C=O), 1587 (C=C), 1241 (C=S), 1153 (C-N)	12.65 (br s, 1H, NH), 9.13 (br s, 1H, NH), 7.28 -7.76 (Ar-Hx5), 3.92 (s, 9H, OCH_3).	56.45, 61.07, 105.19, 120.08, 126.36, 132.03, 136.6, 143.09, 153.57, 162.19, 166.80, 178.39 (C=S), 189.62 (C=O).
1j	3285 (N-H), 1672 (C=O), 1586 (C=C), 1239 (C=S), 1128 (C-N)	12.65 (br s, 1H, NH), 9.15 (br s, 1H, NH), 6.67-8.19 (Ar-Hx6), 3.93 (s, 9H, OCH_3), 2.38 (s, 3H, CH_3).	20.39 (CH_3), 56.54, 61.07, 105.06, 126.17, 126.49, 127.88, 128.5, 130.07, 138.32, 143.00, 153.56, 166.45 (C=S), 178.79 (C=O).
1k	3297 (N-H), 1667 (C=O), 1581 (C=C), 1239 (C=S), 1134 (C-N)	12.93 (br s, 1H, NH), 10.5 (br s, 1H, NH), 7.12 -8.03 (Ar-Hx6), 3.96 (s, 9H, OCH_3).	56.24, 60.98, 107.36, 116.92, 118.74, 124.13, 126.21, 128.3, 130.4, 135.64, 142.92, 152.96, 166.56 (C=S), 178.17 (C=O).
1l	3310 (N-H), 1659 (C=O), 1574 (C=C), 1237 (C=S), 1137 (C-N)	12.94 (br s, 1H, NH), 10.7 (br s, 1H, NH), 7.05 -8.08 (Ar-Hx6), 3.97 (s, 9H, OCH_3).	56.29, 61.06, 107.39, 116.95, 118.76, 124.15, 126.24, 135.66, 142.95, 152.98, 166.58 (C=S), 178.18 (C=O)
1m	3411 (N-H), 1657 (C=O), 1572 (C=C), 1239 (C=S), 1134 (C-N)	10.76 (br s, 1H, NH), 8.89 (br s, 1H, NH), 7.26 (s, Ar-Hx2), 4.25 (m, 1H), 3.92 (s, 9H, OCH_3), 1.22-2.11 (m, 10H).	24.32, 24.96, 25.44, 56.46, 60.91, 104.79, 126.87, 130.66, 142.71, 153.40, 166.56 (C=S), 178.17 (C=O).
1n	34310 (N-H), 1657 (C=O), 1572 (C=C), 1239 (C=S), 1134 (C-N)	11.51 (br s, 1H, NH), 8.6 (br s, 1H, NH), 7.07 (s, Ar-Hx2), 3.91 (s, 9H, OCH_3), 3.26 (s, 6H, CH_3).	43.16, 43.30, 56.41, 61.00, 105.23, 127.41, 142.24, 153.29, 163.04 (C=S), 180.14 (C=O).
1o	3415 (N-H), 1657 (C=O), 1572 (C=C), 1239 (C=S), 1134 (C-N)	11.69 (br s, 1H, NH), 8.90 (br s, 1H, NH), 7.03 (s, Ar-Hx2), 3.91 (s, 9H, OCH_3), 3.40 (t, 2H), 1.60 (m, 2H, Hx2), 1.36 (m, 2H), 1.06 (t, 3H, Hx3).	14.6, 21.03, 32.05, 25.44, 56.41, 60.91, 47.0, 130.66, 142.06, 152.04, 168.53 (C=S), 185.01 (C=O)



Scheme. Synthesis of some new 1 (3,4,5-trimethoxybenzoyl)-3-aryl thioureas.

Antibacterial activity

The synthesized compounds were screened for their antibacterial activities against pathogenic bacteria such as avian pathogenic *E. coli* (APEC), *Staphylococcus aureus*, *Pseudomonas* sp., *Klebsella* sp., *Bacillus subtilis*, and *Salmonella paratyphae* using disk diffusion method (Kirby-Bauer method). The test compounds were dissolved in methanol at a concentration of 1 $\mu\text{g}/\mu\text{L}$ using chloramphenicol was used as a standard drug.²⁷ The tests were repeated 3 times and the results are reported as means of at least 3 determinations. The results are summarized in Table 3. The figures represent the zone of inhibition in millimeters. As is evident from the table all compounds (**1a-j**) exhibited in general low inhibitory activity against the 6 strains compared to the standard drug at the tested concentration. Most of them are active against *B. subtilis* and *Klebsella* spp., while for the rest of the strains only 1 or 2 compounds showed activity.

Geometric parameters for **1b** (Figure 1) and **1m** (Figure 3) display C=S and C=O double bonds as well as shortened C-N bonds (range 1.325(2) to 1.403(2) Å), which is typical for these thiourea units. The substitution of benzene (**1b**) with the cyclohexyl ring (**1m**) leads to slight elongation of the N2-C12 bond from 1.441(3) to 1.469(2) Å.

The torsion angles C1-N1-C2-O1 of $-5.2(3)^\circ$ and C2-N1-C1-N2 of $-7.6(3)^\circ$ for **1b** and of $-8.0(3)^\circ$ and of $3.7(2)^\circ$ for **1m**, respectively, reflect the almost planar conformations with respect to the carbonyl and

thiocarbonyl parts. The trimethoxybenzene ring planes and the C2-O1-N1 planes form dihedral angles of $25.1(2)^\circ$ for **1b** and $37.1(2)^\circ$ for **1m**. For both structures the 2 methoxy groups O2 and O4 lie almost in plane with the aromatic ring, whereas the O3 groups are oriented perpendicular with C5-C6-O3-C10 of $92.4(2)^\circ$ (**1b**) and C5-C7-O3-C8 of $110.6(2)^\circ$ (**1m**).

Table 3. Antibacterial bioassay screening of thioureas (**1a-o**).

Compound	APEC	Staphylococcus aureus	Pseudomonas sp.	Klebsella sp.	Bacillus subtilis	Salmonella paratyphae
1a	-	-	-	-	-	-
1b	-	-	-	-	10	-
1c	-	-	-	-	11	7
1d	\pm	-	-	-	+	-
1e	11	-	-	7	-	-
1f	+	-	-	-	10	-
1g	-	-	-	\pm	12	-
1h	-	12	\pm	-	11	-
1i	10	-	-	9	-	-
1j	-	-	-	11	-	-
1k	+	7	+	10	10	-
1l	-	-	-	\pm	10	-
1m	-	-	-	-	10	-
1n	+	-	-	-	10	-
1o	\pm	-	-	-	+	-
Chloremphenicol	30	20	20	28	30	24

Diameter of inhibition (5 mm)

APEC = Avian pathogenic *E. coli*

Concentration used: 1 $\mu\text{g}/\mu\text{L}$

Volume loaded in each well = 50 μL

(weight of the sample in each well is 50 μg)

(-) = no activity

(+) = significant activity around the well

(\pm) = minor zone of inhibition

In the crystal structure of **1b**, intermolecular N1-H...S($-x+1$, $-y+1$, $-z$) hydrogen bonds with H...S 2.52 Å, N-H...S 161.1° link molecules into centrosymmetric dimers, which are stacked along [010] (Figure 2). Similarly in **1m** intermolecular N1-H...O3($-x$, $-y$, $-z+2$) hydrogen bonds with H...O 2.16 Å, N-H...O 152.8° link molecules into centrosymmetric dimers as well (Figure 4). The intramolecular N2-H...O1 interactions for both structures are common features.

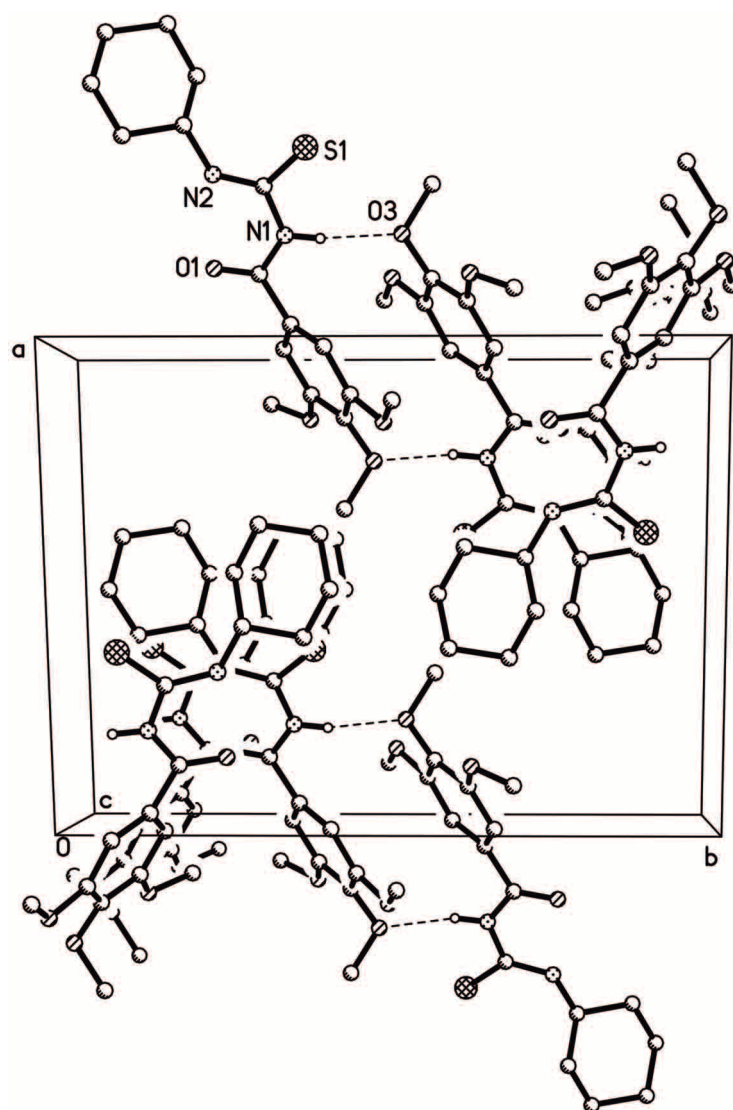


Figure 4. Crystal packing of **1m** viewed along [001] with intermolecular hydrogen bonding pattern indicated as dashed lines (N1-H...O3(-x, -y, -z+2)). H-atoms not involved in hydrogen bonding are omitted. The dimers are stacked along [010].

Supplementary material

Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data CCDC-703773 (**1b**) and 703774 (**1m**) can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [e-mail: deposit@ccdc.cam.ac.uk].

Acknowledgement

N.A. gratefully acknowledges a research scholarship from HEC Islamabad under HEC Indigenous PhD Scholarship 5000 Scheme.

References

1. Bowman, W. R.; Heaney, H.; Smith, P. H. G. *ARKIVOC* **2003** (x) 434-442.
2. Boboshko, L. G.; Zubritskii, M. Yu.; Kovalenko, V. V.; Mikhailov, V. A.; Popov, A. F.; Rybakov, V. B.; Savelova, V. A.; Taran, N. A. *Zhurnal Organ. Farma. Khim.* **2007**, *5*, 61-70.
3. Koch, K. R. *Coord. Chem. Rev.* **2001**, 473-488,
4. Krishnamurthy, R.; Govindaraghavan, S.; Narayanasamy, J. *Pesticide Science* **1999**, *52*, 145-151.
5. Nie, L.; Li, Z.; Han, J.; Zhang, X.; Yang, R.; Liu, W. X.; Wu, F. Y.; Xie, J. W.; Zhao, Y. F.; Jiang, Y. B. *J. Org. Chem.* **2004**, *69*, 6449-6454.
6. Zlatuskova, P.; Stibor, I.; Tkadlecova, M.; Lhotaka, P. *Tetrahedron* **2004**, *60*, 11383-11390.
7. Park, H.; Choi, J.; Choi, S.; Park, M.; Lee, J.; Suh, Y.; Cho, H.; Oh, U.; Lee, J.; Kang, S. U.; Lee, J.; Kim, H.; D.; Park, Y. H.; Jeong, Y. S.; Choi, J. K.; Jew, S. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 787-791.
8. Sijia, X.; Liping, D.; Shaoyong, K.; Liangbin, J. *Chemical Journal on Internet* **2003**, *5*, 67-70.
9. Namgun, L.; Mi-Hyun, C.; Taek, H. K. *J. Korean Chem. Soc.* **2001**, *45*, 96-99.
10. Kea, S.-Y.; Xueb, S.-J. *ARKIVOC* (x) **2006**, 63-68.
11. Huangand, E. H.; Jacobsen, N. *J. Am. Chem. Soc.* **2006**, *128*, 7170-1715.
12. Okino, T.; Nakamura, S.; Furukawa, T.; Takemoto, Y. *Org. Lett.* **2004**, *6*, 625-629.
13. Jahn, U.; Andersch, J.; Schroth, W. *Synthesis* **1997**, 573-575.
14. Gopalsamy, A.; Yang, H. *J. Comb. Chem.* **2000**, *2*, 378-381.
15. Venkatachalam, T. K.; Uckun, F. M. *Syn. Commun.* **2005**, *35*, 2039-2056
16. Venkatachalam, T. K.; Uckun, F. M. *Synthetic Commun.* **2004**, *34*, 2451-2461; **2006**, *36*, 2103-2112
17. Yang, R.-Y.; Kapalan, A. P. *Tetrahedron Lett.* **2001**, *42*, 4433-4436.
18. Upadlgaya, J. S.; Srivastava, P. K. *J. Ind. Chem. Soc.* **1982**, *59*, 767-769.
19. Boga, C.; Forlani, L.; Silvestroni, C.; Corradi, A. B.; Sgarabotto, P. *J. Chem. Soc. Perkin Trans. 1.* **1999**, 1363-1368.
20. Nair, P. C.; Sobhia, M. E. *Euro. J. Med. Chem.* **2008**, *43*, 293-299.
21. Boga, C.; Forlani, L.; Silvestroni, C.; Corradi, A. B.; Sgarabotto, P. *J. Chem. Soc. Perkin Trans. 1.* **1999**, 1363-1368.
22. Zeng, R. S.; Zou, J. P.; Zhi, S. J.; Chen, J.; Shen, Q. *Org. Lett.* **2003**, *61*, 1657-1659. b) Wang, X-C.; Wang, F.; Quan, Z-J.; Wang, M-G.; Li, Z. *J. Chem. Res.* **2005**, *61*, 689-690.
23. Saeed, A.; Zaman, S.; Bolte, M. *Synthetic Commun.* **2008**, *38*, 2185-2199.
24. Popova, L. M.; Ginak, A. I. *Russian J. Org. Chem.* **2008**, *44*, 489-494.

25. Kidwai, M.; Mishra, A. *J. Serb. Chem. Soc.* **2004**, *69*(4), 247-254.
26. Kang, Le.; Robert, A.; Goodnow, Jr. *Syn. Commun.* **2004**, *34*, 1891-1895.
27. Bruker (2002). SMART (Ver. 5.62), SAINT (Ver. 6.02), SHELXTL (Ver. 6.10). Bruker AXS Inc., Madison, Wisconsin, USA.
28. Cappuccino, J. G.; Sherman, N. *In Microbiology: a Laboratory Manual*, **1995**, pp 247-251, *The Benjamin/Cummings publishing Co. California (USA)*.
29. Xiao, M. L.; Chen, F. H.; Chen, Z. J.; Guo, B. S.; Lv, X. H.; Tang, W. M. *Chin. Chem. Lett.* **2007**, *8*, 258-260.

Copyright of Turkish Journal of Chemistry is the property of Scientific and Technical Research Council of Turkey and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.