



Synthesis of Novel Benzohydrazides Bearing 4-[3-Methyl-4-(methylsulfonyl)pyridin-2-yl] Moiety as Potential Antibacterial Agents

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This work reports the synthesis and antibacterial activity of novel hydrazone derivatives **8a-k** bearing 4-[3-methyl-4-(methylsulfonyl)pyridin-2-yl] moiety. Spectroscopic techniques like ¹H NMR, mass and IR tools was utilized for the characterization of these hydrazone derivatives. The synthesized hydrazone derivatives were tested against a set of bacterial strains, namely, *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus pyogenes* by paper disc diffusion method. Compounds **8b**, **8d**, **8e**, **8f**, **8h**, **8i** showed good antibacterial activity against the test organisms.

Keywords: Antibacterial activity, Hydrazone, 4-Hydroxy benzaldehyde, Synthesis.

INTRODUCTION

Hydrazones, belong to a class of organic compounds with the structure, R₁R₂C=NNH₂ [1]. Hydrazones have been found to exhibit antitubercular, antibacterial, antileishmanial, antiinflammatory, antiplatelet, anticonvulsant and analgesic, antitumoral activities [2-4]. These compounds possess diverse biological and pharmacological properties such as antitubercular (isoniazid) and antibiotic (nifuroxazide) [5,6].

Infectious diseases still remains an important and challenging problem; therefore the treatment of the disease is necessary. Because of an increasing number of multi-drug resistant microbial pathogens, there is a need for the discovery of new compounds capable of antimicrobial activities, which are distinctive from the well-known classes of antimicrobial agents to which many clinically relevant pathogens are now resistant [7-9].

Dexlansoprazole (INN, trade names Kapidex, Dexilant) is a proton pump inhibitor that is marketed by Takeda Pharmaceuticals for the treatment of erosive esophagitis and gastro-oesophageal reflux disease. Dexlansoprazole is used to heal and maintain healing of erosive esophagitis and to treat heartburn associated with gastroesophageal reflux disease (GERD). It lasts longer than lansoprazole, to which it is chemically related and needs to be taken less often, making it possible to better control gastric acid [10]. Dexlansoprazole is prepared by condensing the key intermediates 2-chloromethyl-

4-methanesulfonyl-3-methylpyridine (A) [11] with 2-mercaptoimidazole.

The present paper aims to synthesis novel hydrazone derivatives **8a-k** utilizing starting materials 2-chloromethyl-4-methanesulfonyl-3-methylpyridine (A) and 4-hydroxy benzaldehyde. The newly synthesized hydrazone derivatives were screened for antibacterial activity against Gram-positive and Gram-negative bacteria.

EXPERIMENTAL

Chemical and solvents used were purchased either from Fluka or Merck. All the reagents were of analytical grade. Thin-layer chromatography (TLC) was performed on E.Merck AL silica gel 60 F254 plates and visualized under UV light. IR spectra were recorded as KBr pellet with a Perkin-Elmer spectrum gx FTIR instrument and only diagnostic and/or intense peaks are reported. ¹H NMR spectra were recorded in DMSO-*d*₆ with a Varian Mercury plus 400 MHz instrument. ¹³C NMR spectra were recorded in DMSO-*d*₆ with a Varian Gemini 100 MHz instrument. Signals due to the solvent (¹³C NMR) or residual protonated solvent (¹H NMR) served as the internal standard. All the chemical shifts were reported in δ (ppm) using TMS as an internal standard. The ¹H NMR chemical shifts and coupling constants were determined assuming first-order behaviour. The list of coupling constants (*J*) corresponds to the order of multiplicity assignment. Mass

spectra were recorded with a PE Sciex model API 3000 instrument. All the reactions were carried out under argon atmosphere.

Synthesis of ethyl 4-hydroxybenzoate (2): To a solution of compound **2** (2 g, 14.48 mmol) in ethanol (20 mL) was added sulphuric acid (0.1 mL) and refluxed for 12 h. Ethanol was evaporated under reduced pressure and the obtained residue was taken in ethyl acetate (30 mL), washed with 10 % aq. NaHCO₃ solution (3 × 15 mL) followed by water and brine solution. The organic layer was separated, dried over Na₂SO₄, filtered and evaporated to afford compound **3**. Pale yellow solid, Yield: 1.7 g, 75 %; m.p.: 114–117 °C.

Synthesis of 4-(hydroxymethyl)phenol (3): To a stirred mixture of zinc borohydride (3 mmol of BH₄) and THF (20 mL) was added to ethyl 4-hydroxybenzoate (**2**) (6 mmol) and refluxed under nitrogen for 4 h. The excess borohydride was quenched by adding 2 mL of aqueous methanol (50 % v/v). The solution was saturated with potassium carbonate and the THF layer was separated. The residue was extracted with THF and the combined extracts were dried over anhydrous K₂CO₃. The solvent was removed under reduced pressure to obtain alcohol **3**. Yield: 0.52 g, 70 %; m.p.: 110–112 °C.

Synthesis of 4-hydroxybenzaldehyde (4): A mixture of 4-(hydroxymethyl)phenol (**3**) (7.94 mmol), Cu(OAc)₂ (0.08 mmol) and TEMPO (0.08 mmol) in acetonitrile:water was stirred at room temperature for 3 h. After the completion of the reaction (monitored by TLC), the reaction mixture was diluted with dichloromethane. The organic layer was separated and the aqueous layer was further extracted with dichloromethane (2 × 10 mL). The combined organic layer was dried over sodium sulphate and concentrated to give a residue which was purified by column chromatography (eluents: petroleum ether:ethyl acetate = 10:1) to afford aldehyde **4**. Yield: 84 %. m.p.: 114–118 °C.

Synthesis of 4-[(3-methyl-4-(methylsulfonyl)pyridin-2-yl)methoxy]benzaldehyde (6): To a stirred solution of aldehyde **4** (1 g, 8.2 mmol) in DMF (7 mL) was added potassium carbonate (1.36 g, 9.84 mmol) followed by compound **5** (1.8 g, 8.2 mmol) and heated to 80 °C for 3 h. The reaction mixture was cooled to room temperature and then poured into cold water to obtain pale yellow solid, which was filtered and dried at the pump to afford compound **6**. Yield: 88 %. m.p.: 106–107 °C. White solid; Yield: 84 %; m.p.: 100–101 °C; IR (KBr, ν_{\max} , cm⁻¹): 3445, 3086, 3063, 3007, 2954, 2927, 2839, 2754, 1682, 1598, 1509, 1470, 1416, 1404, 1367, 1304, 1260, 1238, 1219, 1164, 1133, 1119, 1025, 999, 963, 888, 857, 836, 798, 765, 748, 671, 616, 588, 562, 534, 519, 511, 466; ¹H MR (400 MHz, DMSO-*d*₆): δ 9.90 (s, 1H), 8.72 (d, *J* = 6.4 Hz, 1H), 7.88 (t, *J* = 12.0 Hz, 3H), 7.22 (d, *J* = 11.2 Hz, 2H), 5.50 (s, 2H), 3.88 (s, 3H), 2.74 (s, 3H); ESI-MS: *m/z*, 306.35 (M + H)⁺.

General procedure for the synthesis of benzohydrazides 7a-k [12,13]: A mixture of benzoic acid (6.42 mmol), catalytic quantity of conc. H₂SO₄ in ethanol was heated to reflux for 10 h. The reaction mixture was diluted with ethyl acetate followed by water. The organic layer was washed with saturated NaHCO₃ followed by water and brine solution. The organic layer was dried over sodium sulphate, filtered and evaporated to obtain respective ethyl benzoates.

To a stirred solution of ethyl benzoates (5 mmol) in ethanol was added hydrazine-hydrate (12.5 mmol) and refluxed for 8 h. The reaction mixture was diluted with ethyl acetate followed by water. The organic layer was dried over sodium sulphate, filtered and evaporated to obtain respective benzohydrazides **7a-k**.

General procedure for the synthesis of hydrazone derivatives 8a-k: To a stirred solution of compound **6** (100 mg, 3.2 mmol) in ethanol was added corresponding benzohydrazides **7a-k** (3.2 mmol) and refluxed for 1 h. After cooling to room temperature the precipitated solids were filtered and washed with minimum quantity of ethanol and dried to obtain hydrazone derivatives **8a-k** in quantitative yields

(E)-N'-[4-((3-Methyl-4-(methylsulfonyl)pyridin-2-yl)methoxy)benzylidene]benzohydrazide (8a): White solid; Yield: 80 %; m.p.: 118–119 °C; ¹H NMR (400 MHz, DMSO-*d*₆): δ 11.76 (s, 1H), 8.72 (d, *J* = 5.2 Hz, 1H), 8.40 (s, 1H), 7.89 (t, *J* = 8.8 Hz, 3H), 7.68 (d, *J* = 10.4 Hz, 2H), 7.59–7.52 (m, 3H), 7.14 (d, *J* = 10.4 Hz, 2H), 5.42 (s, 2H), 3.34 (s, 3H), 2.71 (s, 3H); ESI-MS: *m/z*, 424 (M+H)⁺.

(E)-N'-[4-((3-Methyl-4-(methylsulfonyl)pyridin-2-yl)methoxy)benzylidene]-3-chlorobenzohydrazide (8b): White solid; Yield: 80 %; m.p.: 82–83 °C; ¹H NMR (400 MHz, DMSO-*d*₆): δ 11.84 (s, 1H), 8.72 (d, *J* = 6.8 Hz, 1H), 8.40 (s, 1H), 7.95 (s, 1H), 7.87 (t, *J* = 6.0 Hz, 2H), 7.68 (t, *J* = 11.2 Hz, 2H), 7.54 (t, *J* = 10.0 Hz, 2H), 7.14 (d, *J* = 11.6 Hz, 2H), 5.42 (s, 2H), 3.39 (s, 3H), 2.71 (s, 3H); ESI-MS: *m/z*, 458 (M+H)⁺.

(E)-N'-[4-((3-methyl-4-(methylsulfonyl)pyridin-2-yl)methoxy)benzylidene]-3-nitrobenzohydrazide (8c): White solid; Yield: 84 %; m.p.: 128–129 °C; IR (KBr, ν_{\max} , cm⁻¹): 3445, 3317, 3083, 3034, 2989, 2926, 2909, 1668, 1605, 1568, 1557, 1530, 1509, 1479, 1421, 1349, 1301, 1238, 1170, 1131, 1063, 1027, 1009, 960, 891, 834, 817, 807, 766, 724, 713, 670, 588, 567, 533, 465; ¹H NMR (400 MHz, DMSO-*d*₆): δ 12.08 (s, 1H), 8.75 (t, *J* = 3.6 Hz, 2H), 8.44 (s, 1H), 8.35 (d, *J* = 10.4 Hz, 2H), 7.85 (t, *J* = 6.0 Hz, 2H), 7.71 (d, *J* = 11.2 Hz, 2H), 7.16 (d, *J* = 11.2 Hz, 2H), 5.43 (s, 2H), 3.40 (s, 3H), 2.71 (s, 3H); ESI-MS: *m/z*, 469 (M+H)⁺.

(E)-N'-[4-((3-Methyl-4-(methylsulfonyl)pyridin-2-yl)methoxy)benzylidene]-4-methoxybenzohydrazide (8d): White solid; Yield: 86 %; m.p.: 91–92 °C; IR (KBr, ν_{\max} , cm⁻¹): 3444, 3251, 3074, 3039, 3021, 3004, 2962, 2924, 2836, 1654, 1607, 1575, 1548, 1507, 1464, 1419, 1410, 1370, 1315, 1293, 1252, 1235, 1211, 1170, 1138, 1108, 1061, 1028, 1010, 970, 960, 917, 889, 843, 827, 815, 802, 760, 671, 647, 621, 587, 566, 535, 465; ¹H NMR (400 MHz, DMSO-*d*₆): δ 11.64 (s, 1H), 8.74 (s, 1H), 8.40 (s, 1H), 7.89 (d, *J* = 10.0 Hz, 4H), 7.67 (d, *J* = 7.2 Hz, 1H), 7.14 (d, *J* = 8.8 Hz, 2H), 7.05 (d, *J* = 9.2 Hz, 2H), 5.41 (s, 2H), 3.83 (s, 3H), 3.40 (s, 3H), 2.71 (s, 3H); ESI-MS: *m/z*, 454 (M+H)⁺.

(E)-N'-[4-((3-Methyl-4-(methylsulfonyl)pyridin-2-yl)methoxy)benzylidene]-3,4,5-trimethoxybenzohydrazide (8e): Pale yellow solid; Yield: 86 %; m.p.: 128–129 °C; IR (KBr, ν_{\max} , cm⁻¹): 3444, 3251, 3074, 3039, 3021, 3004, 2962, 2924, 2836, 1654, 1607, 1575, 1548, 1507, 1464, 1419, 1410, 1370, 1315, 1293, 1252, 1235, 1211, 1170, 1138, 1108, 1061, 1028, 1010, 970, 960, 917, 889, 843, 827, 815, 802, 760, 671, 647, 621, 587, 566, 535, 465; ¹H NMR (400 MHz, DMSO-

d_6): δ 11.61 (s, 1H), 8.72 (d, $J = 7.2$ Hz, 1H), 8.42 (s, 1H), 7.85 (d, $J = 6.8$ Hz, 1H), 7.68 (d, $J = 11.2$ Hz, 2H), 7.23 (s, 2H), 7.15 (d, $J = 11.6$ Hz, 2H), 5.42 (s, 2H), 3.86 (s, 6H), 3.72 (s, 3H), 3.38 (s, 3H), 2.71 (s, 3H); ESI-MS: m/z , 514 (M+H)⁺.

(E)-N'-[4-((3-Methyl-4-(methylsulfonyl)pyridin-2-yl)methoxy)benzylidene]-4-chlorobenzohydrazide (8f): White solid; Yield: 82 %; m.p.: 111-112 °C; IR (KBr, ν_{\max} , cm^{-1}): 3444, 3261, 3098, 3077, 3022, 3006, 2952, 2925, 1920, 1661, 1603, 1552, 1510, 1487, 1408, 1374, 1316, 1302, 1266, 1252, 1241, 1210, 1169, 1141, 1091, 1058, 1014, 1007, 968, 959, 918, 891, 851, 842, 836, 818, 802, 758, 671, 646, 621, 587, 567, 537, 480, 466; ¹H NMR (400 MHz, DMSO- d_6): δ 11.82 (s, 1H), 8.72 (d, $J = 6.4$ Hz, 1H), 8.40 (s, 1H), 7.92 (d, $J = 11.2$ Hz, 2H), 7.85 (d, $J = 6.8$ Hz, 1H), 7.68 (d, $J = 11.2$ Hz, 2H), 7.60 (d, $J = 10.8$ Hz, 2H), 7.14 (d, $J = 11.2$ Hz, 2H), 5.42 (s, 2H), 3.35 (s, 3H), 2.71 (s, 3H); ESI-MS: m/z , 458 (M+H)⁺.

(E)-N'-[4-((3-Methyl-4-(methylsulfonyl)pyridin-2-yl)methoxy)benzylidene]-4-(methylsulfonyl)benzohydrazide (8g): White solid; Yield: 80 %; m.p.: 130-132 °C; ¹H NMR (400 MHz, DMSO- d_6): δ 11.98 (s, 1H), 8.72 (brs, 1H), 8.41 (s, 1H), 8.15-8.12 (m, 4H), 7.82 (d, $J = 6.8$ Hz, 2H), 7.70 (d, $J = 11.2$ Hz, 2H), 7.15 (d, $J = 10.8$ Hz, 2H), 5.42 (s, 2H), 3.38 (s, 3H), 3.30 (s, 3H), 2.71 (s, 3H); ESI-MS: m/z , 502 (M+H)⁺.

(E)-N'-[4-((3-Methyl-4-(methylsulfonyl)pyridin-2-yl)methoxy)benzylidene]-4-fluorobenzohydrazide (8h): White solid; Yield: 82 %; m.p.: 124-126 °C; ¹H NMR (400 MHz, DMSO- d_6): δ 11.78 (s, 1H), 8.72 (s, 1H), 8.40 (s, 1H), 7.98 (brs, 2H), 7.87 (brs, 1H), 7.68 (d, $J = 10.0$ Hz, 2H), 7.37 (brs, 2H), 7.14 (d, $J = 10.8$ Hz, 2H), 5.42 (s, 2H), 3.38 (s, 3H), 2.71 (s, 3H); ESI-MS: m/z , 442 (M+H)⁺.

(E)-N'-[4-((3-Methyl-4-(methylsulfonyl)pyridin-2-yl)methoxy)benzylidene]-3,5-dichlorobenzohydrazide (8i): White solid; Yield: 82 %; m.p.: 130-131 °C; IR (KBr, ν_{\max} , cm^{-1}): 3445, 3211, 3077, 3054, 3011, 2925, 1645, 1607, 1566, 1552, 1511, 1465, 1418, 1365, 1307, 1253, 1237, 1213, 1169, 1127, 1064, 1025, 1009, 968, 954, 866, 834, 805, 764, 594, 569, 533, 468; ¹H NMR (400 MHz, DMSO- d_6): δ 11.88 (s, 1H), 8.74 (d, $J = 6.4$ Hz, 1H), 8.40 (s, 1H), 7.94 (s, 1H), 7.86 (d, $J = 6.8$ Hz, 2H), 7.69 (d, $J = 11.2$ Hz, 2H), 7.16 (d, $J = 11.2$ Hz, 2H), 5.43 (s, 2H), 3.39 (s, 3H), 2.72 (s, 3H); ESI-MS: m/z , 492 (M+H)⁺.

(E)-N'-[4-((3-Methyl-4-(methylsulfonyl)pyridin-2-yl)methoxy)benzylidene]-2,5-difluorobenzohydrazide (8j): White solid; Yield: 80 %; m.p.: 98-99 °C; ¹H NMR (400 MHz, DMSO- d_6): δ 11.97 (* 11.80, s, 1H), 9.89 (* 8.28, s, 1H), 8.73 (t, $J = 6.4$ Hz, 1H), 8.28 (* 8.03, s, 1H), 7.90-7.84 (m, 2H), 7.69 (d, $J = 11.2$ Hz, 1H), 7.54-7.37 (m, 3H), 7.18 (td, $J = 11.6$ Hz, 2H), 5.50 (* 5.43, s, 2H), 3.38 (* 3.37, s, 3H), 2.72 (* 2.69, s, 3H); ESI-MS: m/z , 460 (M+H)⁺.

(E)-N'-[4-((3-Methyl-4-(methylsulfonyl)pyridin-2-yl)methoxy)benzylidene]-4-cyanobenzohydrazide (8k): White solid; Yield: 78 %; m.p.: 96-98 °C; ¹H NMR (400 MHz, DMSO- d_6): δ 11.96 (s, 1H), 8.74 (s, 1H), 8.43 (s, 1H), 8.19-8.10 (m, 4H), 7.86 (d, $J = 6.8$ Hz, 2H), 7.70 (d, $J = 11.2$ Hz, 2H), 7.15 (d, $J = 10.8$ Hz, 2H), 5.42 (s, 2H), 3.40 (s, 3H), 2.71 (s, 3H); ESI-MS: m/z , 449 (M+H)⁺.

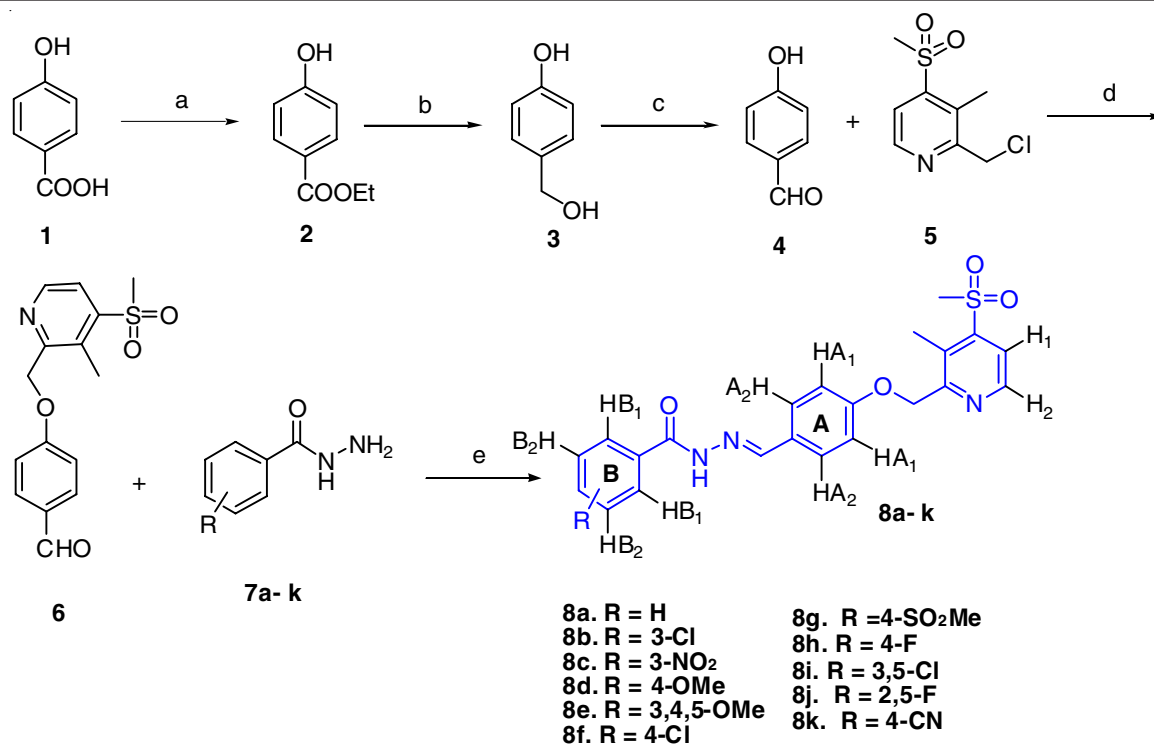
Antibacterial assay: All the synthesized hydrazones were tested for their anti-bacterial activity against a set of bacterial

strains, namely, *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus pyogenes* by paper disc diffusion method with concentration of the solutions (250 $\mu\text{g/mL}$) prepared in dimethyl sulfoxide. The reason of choosing DMSO for antibacterial studies was that it has no effect on the above mentioned bacterial strains. Nutrient agar was used as the culture medium for the growth of bacterial colony that was prepared by using peptone (3 g), NaCl (3 g), Yeast (1.5 g), Agar (6 g) in 300 mL of distilled water with pH at 7. The prepared medium is auto-claved at 15 pa for 20 min and kept at 85 °C for 30 min to sterilize the media. This media was then poured into petri dishes slowly in laminar flow environment, allowed to solidify and kept at 30 °C for 24 h. The bacterial strains were inoculated by spreading in peptidases and its temperature is maintained at 30 °C for 24 h. Using paper disc (8 mm) in nutrient agar culture medium, the newly synthesized hydrazones (**8a-k**) of concentration 250 $\mu\text{g/mL}$ were loaded through bacteria free micro pipettes. The antibacterial activity was determined by measuring the zone of inhibition in millimeters and compared with standard drug chloramphenicol.

RESULTS AND DISCUSSION

The newly synthesized hydrazone derivatives (**8a-k**) was prepared by the condensation of the key intermediate 4-[(3-methyl-4-(methylsulfonyl)pyridin-2-yl)methoxy]benzaldehyde (**6**) with various benzohydrazides (**7a-k**) in quantitative yields. The intermediate **6** was prepared by coupling 2-(chloromethyl)-3-methyl-4-(methylsulfonyl)pyridine (**5**) with 4-hydroxy benzaldehyde (**4**) in presence of potassium carbonate in DMF at 80 °C for 2 h in 88 % yield. The intermediate **5** was prepared according to the literature procedure [11]. The oxidation of alcohol **3** was carried out in presence of Cu(OAc)₂, TEMPO in acetonitrile: water at room temperature for 3 h to obtain aldehyde **4** [14]. The alcohol **3** was obtained by the reduction of ethyl 4-hydroxybenzoate **2** in presence zinc borohydride following the protocol of Narasimhan *et al.* [15]. Ethyl 4-hydroxybenzoate **2** was obtained by the esterification of 4-hydroxy benzoic acid **1** in presence of catalytic quantity of conc; H₂SO₄ in ethanol at reflux temperature. The overall synthetic scheme for the preparation of hydrazone derivatives **8a-k** is presented in Scheme-I.

The structures of the compounds (**8a-k**) were confirmed by IR, ¹H NMR and mass spectral data analyses. The mass spectra of all compounds (**8a-k**) showed (M+1) peaks, in agreement with their molecular formula. In the ¹H NMR spectra of compound **8c**, the hydrazone proton (-C=O-**NH**-, singlet) appeared at 11.64 ppm, imine proton (-N=**CH**-) proton appeared at 8.40 ppm (singlet), thus confirming the presence of the hydrazide-hydrazone group. The aliphatic protons were observed in the expected region such as, -O-**CH**₂- (singlet, 2H), -O**CH**₃- (singlet, 3H), -**CH**₃-SO₂- (singlet, 3H) and -**CH**₃- (singlet, 3 H) group appeared at 5.41 ppm, 3.83 ppm, 3.40 ppm and 2.71 ppm respectively. The aromatic protons appeared in the region 7.05-7.89 ppm. The protons resonating at 8.74 ppm as a broad singlet and at 7.67 ppm as a doublet are assigned to the aromatic pyridine ring protons. The aromatic protons HA₁ and HB₂ resonated at 7.05 ppm (doublet, 2H), 7.14 ppm (doublet, 2H) while the protons HA₂ and HB₁



Experimental conditions: a) conc; H₂SO₄, EtOH, 12 h; b) ZnBH₄, cyclohexene, reflux, 4 h; c) Cu(OAc)₂, TEMPO, acetonitrile:water, r.t, 3 h; d) **5**, K₂CO₃, DMF, 80 °C, 3 h; e) Benzohydrazide **7a-k**, ethanol, reflux, 1 h

Scheme-I: Synthesis of novel hydrazone derivatives **8a-k**

resonated at 7.89 ppm (doublets, 4H). In the IR spectra, all the hydrazone derivatives (**8a-k**) had a strong, characteristic band in the region 1646-1668 cm⁻¹ due to the C=O stretching vibration. The N-H stretching vibration of the compounds (**8a-k**) gave rise to a band at 3317-3460 cm⁻¹. The stretching bands for C=C and C=N groups were observed at 1608-1503 cm⁻¹. The spectroscopic data of the remaining hydrazone derivative comply with the above description.

in vitro Antibacterial activity: The antibacterial results showed that most of the synthesized hydrazone derivatives were active against both Gram-positive and Gram-negative bacteria. Among the tested hydrazones **8a-k**, the compounds **8b**, **8d**, **8e**, **8f**, **8h**, **8i** showed good antibacterial activity against the test organisms while compounds **8a** and **8c** had moderate

activity and compound **8j** showed weak activity where as compounds **8g**, **8k** had no antibacterial activity against the test organisms. It was observed that maximum antibacterial activity was shown by compounds containing the 4-methoxy, 3,4,5-trimethoxy, 3-chloro, 4-chloro, 3,5-dichloro and 4-fluoro group with highly reactive azomethine (-NH=N=CH-) group. On the other hand, compared to the standard antibacterial drug namely, chloramphenicol the synthesized hydrazones was having moderate antibacterial activity against test organisms. The result of antibacterial activity is tabulated in Table-1.

Conclusion

In summary, the present paper describes the synthesis of novel hydrazone derivatives **8a-8k** from commercially available

TABLE-1
ANTIMICROBIAL ACTIVITY OF HYDRAZONE DERIVATIVES **8a-k**

Compound	Gram-positive bacteria		Gram-negative bacteria	
	<i>S. aureus</i> MTCC 96	<i>S. pyogenes</i> MTCC 442	<i>E. coli</i> MTCC 443	<i>P. aeruginosa</i> MTCC 424
8a	++	++	++	++
8b	+++	+++	+++	+++
8c	++	++	++	++
8d	+++	+++	+++	+++
8e	+++	+++	+++	+++
8f	+++	+++	+++	+++
8g	-	-	-	-
8h	+++	+++	+++	+++
8i	+++	+++	+++	+++
8j	+	+	+	+
8k	-	-	-	-
DMSO	-	-	-	-
*Chloramphenicol	21	20	23	21

*Concentration: 250 µg/mL; -: nil activity; +: weak activity; ++: moderate activity; +++: good activity

2-chloromethyl-4-methanesulfonyl-3-methylpyridine (**A**) and 4-hydroxy benzoic acid. The structures of the synthesized hydrazones **8a-k** were confirmed by ^1H NMR, mass and IR spectral data. Among the tested hydrazones **8a-k**, the compounds **8b**, **8d**, **8e**, **8f**, **8h**, **8i** showed good antibacterial activity against *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus pyogenes*.

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