Scientific Research Publishing

Open Journal of Medicinal Chemistry, 2016, 6, 59-69
http://www.scirp.org/journal/ojmc
ISSN Online: 2164-313X
ISSN Print: 2164-3121

Synthesis and Evaluation of Antituberculosis Activity of Substituted 2,7-Dimethylimidazo [1,2-a]Pyridine-3-Carboxamide Derivatives

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How to cite this paper: Jadhav, B., Kenny, R., Nivid, Y., Mandewale, M. and Yamgar, R. (2016) Synthesis and Evaluation of Antituberculosis Activity of Substituted 2,7-Dimethylimidazo[1,2-a]Pyridine-3-Carboxamide Derivatives. *Open Journal of Medicinal Chemistry*, **6**, 59-69.
http://dx.doi.org/10.4236/ojmc.2016.64006

Received: October 15, 2016
Accepted: December 26, 2016
Published: December 29, 2016

Abstract

A series of substituted 2,7-dimethylimidazo[1,2-a]pyridine-3-carboxamides derivatives **5a-5m** were synthesized through multi-step reactions. To achieve the synthesis of the desired compounds monobromo and dibromo substituted 2-amino-*γ*-picoline was reacted with ethyl 2-chloroacetoacetate. The crude ethyl ester subjected to hydrolysis in presence of lithium hydroxide to get **2a** and **2b**, with imidazo[1,2-a]pyridine-3-carboxylic acid to get **3a-3b**, on treatment with substituted amines **4a-4g** to get desired product **5a-5m** in presence of EDCI and HOBt. The substituted imidazo[1,2-a]pyridine-3-carboxamides are characterized by FTIR, ^{1}H-NMR, ^{13}C-NMR and mass spectra. These newly synthesized compounds were tested *in vitro* for their antimycobacterial activity. The preliminary results of antituberculosis study showed that most of the synthesized compounds **5a-5m** demonstrated moderate to good antituberculosis activity. Among the tested compounds **5b**, **5d** and **5e** were found to be the most active with minimum inhibitory concentration (MIC) of 12.5 μg/mL against *Mycobacterium tuberculosis* (H37 RV strain) ATCC No-27294.

Keywords

Carboxamides, Imidazo[1,2-a]Pyridine, Tuberculosis

1. Introduction

The imidazo[1,2-a]pyridines are found to possess various potential biological activities. A large number of substituted imidazo[1,2-a]pyridines have been synthesized and

tested for various biological activities such as antiulcer [1], antibacterial [2], antimicrobial [3], antifungal [4], and antiviral [5] [6] agents. Various imidazo fused heterocycles with aryloxy alkylamines side chain including imidazo[1,2-a]pyridines act as calcium channel blockers or as local anaesthetics [7]. Byth and co-workers [8] have synthesized various pyrimidine sulfonamide substituted imidazo[1,2-a]pyridine as cyclin-dependent kinase (CDK) inhibitors which led to the identification of potent and selective inhibitors of CDK2 and CDK1. Several 8-arylimidazo[1,2-a]pyridines have been synthesized and evaluated as cardiotonic agents [9]. Some highly substituted imidazo[1,2-a]pyridines have been substituted as gastric antisecretory agents useful as gastric antiulcer agents [10]. Zhonghui Lu, Gregory R. Ott. and co-worker [11] [12] have synthesized a series of 2,3-substituted imidazo[1,2-a]pyridine derivatives which resemble (3*S*, 4*S*)pyrrolidine-*N*-hydroxy-3-carboxamide and (3*R*, 4*R*)pyran-*N*-hydroxy-3-carboxamide has been reported to have potent selectivity against tumor necrosis factor converting enzyme (TACE). The synthesis and tuberculosis activity of various substituted imidazo[1,2-a]pyridine-3-carboxamides have been reported [13]. Katherine A. Abrahams *et al.* [14] described the synthesis and biological activity of imidazo[1,2-a] pyridine-3-carboxamides against *Mycobacterium tuberculosis*. Garrett C. Moraski *et al.* synthesized a series of nine 2,7-dimethylimidazo[1,2-a]pyridine-3-car- boxamides and one 2,6-dime-thylimidazo[1,2-a]pyrimidine-3-carboxamide and evaluated for their *in vitro* antituberculosis activity against replicating, nonreplicating, multi- and extensive drug resistant Mtb strains [15]. Linhu Li *et al.* [16] have developed the synthesis and antituberculosis activity of various imidazo[1,2-a]pyridine-3-car- boxamide hybrids with extended amine functionality. Recently Samala G. *et al.* [17] synthesized 2-methylimidazo[1,2-a]-pyridine-3-carboxamides as *Mycobacterium tuberculosis* Pantothenate synthetase inhibitors.

In continuation of our research for new antimicrobial agents [18] [19] [20] [21] [22], we have undertaken research studies on synthesis and biological screening of some new imidazo[1,2-a]pyridine derivatives.

2. Materials and Methods

Melting points of compounds were determined in open capillary tubes in silicon oil bath using a Veego melting point apparatus and are uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were acquired on Bruker (400 MHz), chemical shifts were given on the delta scale as parts per million (ppm) with tetramethylsilane (TMS) as the internal standard. Electron impact ionization mass spectra were recorded on Agilent Technologies 5975C MSD detector at 70 eV. Infrared spectra were measured with KBr pellet on a FTIR-7600 Lambda Scientific Pvt. Ltd. in the range 4000 - 400 cm^{-1}. Thin layer chromatography (TLC) was performed on silica F254 coated aluminum plates (Merck) as adsorbent and the spots were visualized using ultraviolet light or iodine chamber.

3. Chemistry

We synthesized imidazo[1,2-a]pyridine-3-carboxamide derivatives and evaluated them

for Antituberculosis Activity. Figure 1 envisages the schematic representation for the synthesis of (un)substituted 2,7-dimethylimidazo[1,2-a]pyridine-3-carboxamides (**5a-5m**). For the synthesis of the desired molecules, mono bromo and dibromo substituted 2-amino-γ-picoline (**1a-1b**) were reacted with ethyl 2-chloroacetoacetate in presence of base to give ethyl imidazo[1,2-a]pyridine-3-carboxylates (**2a-2b**). These esters were then hydrolized to give imidazo[1,2-a]pyridine-3-carboxylic acids (**3a-3b**). These acid derivatives were treated with (un)substituted anilines (**4a-4f**) using hydroxybenzotriazole (HOBt) and EDCI as coupling agent to afford (un)substituted 2,7-di-methylimidazo[1,2-a]pyridine-3-carboxamides (**5a-5m**).

The FT-IR spectrum of hydrazone **5a**, as a representative example, showed strong absorption bands at 1654 and 1595 cm^{-1} due to amide, C=O stretching and N-H bending respectively. The broad peak at 3138 cm^{-1} is attributed to amide N-H stretching. Its ^{1}H-NMR spectrum revealed, in addition to expected aromatic signals, three singlets at δ 2.69, 2.87, 9.67 ppm are assignable to the two methyl groups and amide proton (-NH-C=O), respectively. In addition, the ^{13}C-NMR spectrum of **5a** displayed characteristic peak at δ 158.5 ppm assignable to carbonyl carbon of amide. Moreover the EIMS spectrum of 5a revealed molecular ion peak at m/z 423.9 (M+) corresponding to molecular formula [$C_{16}H_{13}Br_2N_3O$]. In a similar manner, compounds **5b-5m** were prepared and characterized as shown in Table 1 and Table 2.

4. Experiment

4.1. Preparation of Ethyl 6-Bromo-2,7-Dimethylimidazo[1,2-a] Pyridine-3-Carboxylate (2a)

A mixture of 5-bromo-4-methylpyridin-2-amine (10.0 g, 53.5 mmol) and ethyl 2-chloroacetoacetate (8.13 ml, 58.8 mmol) were taken in 1,2-dimethoxyethane (107 mL) and heated to reflux for 16 hours. The reaction mixture was concentrated under reduced pressure to get crude compound.

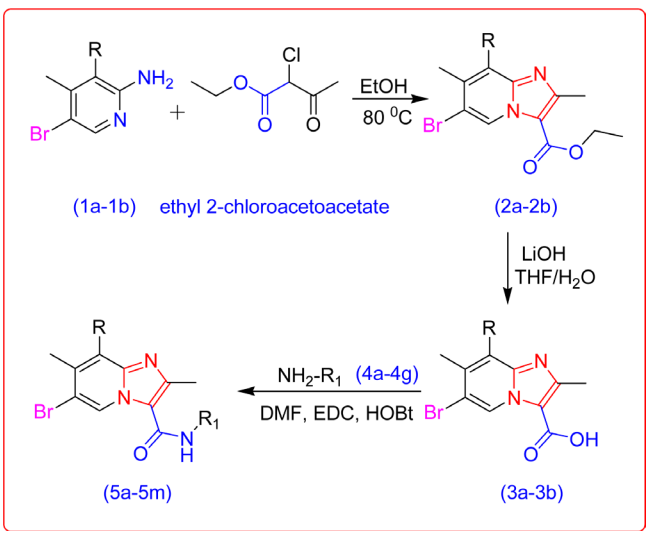


Figure 1. Reaction scheme for preparation of compounds 5a-5m.

Table 1. Structures of compounds 5a-5g.

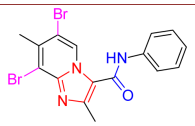
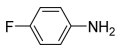
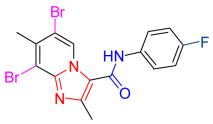
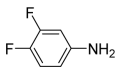
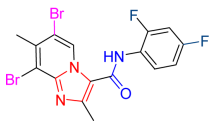
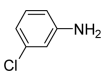
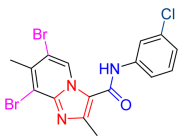
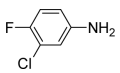
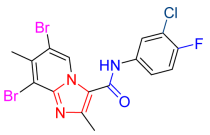
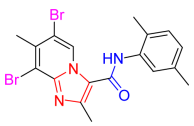
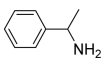
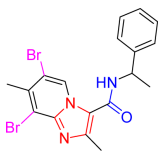
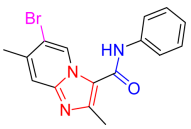
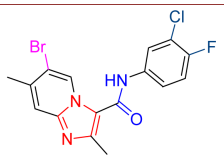
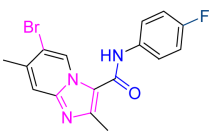
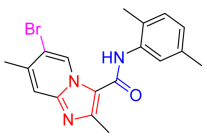
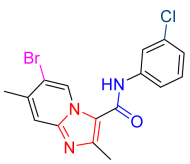
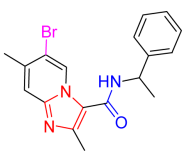
Entry	Amine [4]	Product [5]
a		
b		
c		
d		
e		
f		
g		

Table 2. Structures of compounds 5h-5m.

Entry	Product [5]	Entry	Product [5]
h		k	
i		l	
j		m	

The crude compound was then purified by column chromatography using 15% ethylacetate (EtOAc) in hexane as eluent to get ethyl 6-bromo-2,7-dimethylimidazo-

[1,2-a]pyridine-3-carboxylate (**2a**) (9.50 g, 66%) as an Off-white solid; ESIMS *m*/*z*: 299 [M + 2].

4.2. Preparation of Ethyl 6,8-Dibromo-2,7-Dimethylimidazo[1,2-a] Pyridine-3-Carboxylate (2b)

Compound (**2b**) prepared by similar process 4.1. (11.47 g, 57%) as an off-white solid.

4.3. Preparation of 6-Bromo-2,7-Dimethylimidazo[1,2-a] Pyridine-3-Carboxylic Acid (3a)

A mixture of 6-bromo-2,7-dimethylimidazo[1,2-a]pyridine-3-carboxylate (9.000 g, 30.3 mmol) and Lithium hydroxide (1.088 g, 45.4 mmol) were taken in THF/Water (1:1) (60 mL) and stirred at room temperature for 14 h. The reaction mixture extracted three times with 25 ml of ethyl acetate, further organic layers were discarded. Aqueous layer acidified with 2 NHCl at 5˚C - 10˚C till the reaction mixture turned to pH ~5, the precipitate formed was filtered and dried to get 6-bromo-2,7-dimethylimidazo [1,2-a]pyridine-3-carboxylic acid (**3a**) (7.34 g, 92%) as an off-white solid. EIMS *m*/*z*: 271 [M + 2].

4.4. Preparation of 6,8-Dibromo-2,7-Dimethylimidazo[1,2-a] Pyridine-3-Carboxylic Acid (3b)

Compound (**3b**) is prepared by process 4.3. (8.35 g, 82%) as an off-white solid. EIMS *m*/*z*: 348 [M + 1].

4.5. General Procedure for the Preparation of 6,8-Dibromo-2, 7-Dimethyl-N-Phenylimidazo[1,2-a]Pyridine-3-Carboxamides (5a-5m)

To the stirred solution of carboxylic acid (3a-3b) (1.0 equiv), EDCI (1.2 equiv), HOBt (1.2 equiv) and Et_3N (2.5 equiv) in DMF at 0˚C, was added compound (4a-4g) (1.05 equiv) and allowed to stir at room temperature for 22 h. The reaction mixture was diluted with dichloromethane, washed with water and the separated organic layer was concentrated under reduced pressure. The crude compound was further purified by column chromatography using 30% EtOAc/Hexanes as the eluent.

4.5.1. Preparation of 6,8-Dibromo-2,7-Dimethyl-N-Phenylimidazo[1,2-a] Pyridine-3-Carboxamide (5a)

The stirred solution of 6,8-dibromo-2,7-dimethylimidazo[1,2-a]pyridine-3-carboxylic acid (0.5 g, 1.437 mmol) in DMF (14.37 ml) at 0˚C was mixed with EDCI (0.331 g, 1.724 mmol), HOBt (0.233 g, 1.724 mmol) and Triethylamine (0.505 ml, 3.59 mmol). The reaction mixture was stirred for 30 min and then aniline 4a (0.138 ml, 1.509 mmol) was added. The reaction mixture was allowed to stir further at room temperature for 22 h. The reaction mixture was then diluted with dichloromethane and washed with water and the separated organic layer was concentrated under reduced pressure, purified by column chromatography using 30% EtOAc/Hexanes as eluent to get title compound in 70% yield (0.42 g) White solid; m.p. = 134˚C - 137˚C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.69 (s, 3H), 2.87 (s, 3H), 7.22 - 7.18 (m, 1H), 7.43 - 7.39 (t, 2H), 7.61 - 7.59 (d, J = 8.0

Hz, 1H), 7.69 - 7.78 (m, 2H), 9.67 (s, 1H); ^{13}C-NMR (400 MHz,$CDCl_3$): δ 16.1, 22.7, 110.3, 110.9, 116.5, 120.0, 122.4, 123.1, 124.2, 124.5, 126.5, 128.8, 136.8, 137.3, 145.5, 158.5; IR (cm^{-1}): 3448 (Aromatic C-H Stretch), 3138 (Amide N-H Stretch), 1654 (Amide C=O Stretch), 1595 (Amide N-H bending); EIMS *m*/*z*: 423.9 [M^+].

4.5.2. Preparation of 6,8-Dibromo-2,7-Dimethyl-N-(4-Fluorophenyl) Imidazo[1,2-a]Pyridine-3-Carboxamide (5b)

73% yield (0.46 g), White solid; m.p. = 142˚C - 143˚C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.69 (s, 3H), 2.86 (s, 3H), 7.13 - 7.09 (m, 2H), 7.48 - 7.50 (m, 1H), 7.57 - 7.54 (dd, 2H), 9.63 (s, 1H); ^{13}C-NMR (400 MHz, $CDCl_3$): δ 16.3, 22.7, 110.7, 111.1, 115.4, 115.7, 116.2, 122.0, 122.1, 123.4, 124.1, 126.2, 126.6, 145.6, 158.2, 158.6; IR (cm^{-1}): 3443 (Aromatic C-H Stretch), 3141 (Amide N-H Stretch), 1653 (Amide C=O Stretch), 1607 (Amide N-H bending); EIMS *m*/*z*: 441.8 [M^+].

4.5.3. Preparation of 6,8-Dibromo-N-(2,4-Difluorophenyl)-2, 7-Dimethylimidazo[1,2-a]Pyridine-3-Carboxamide (5c)

68% yield (0.44 g), White solid; m.p. = 151˚C - 154˚C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.70 (s, 3H), 2.88 (s, 3H), 6.99 - 6.93 (m, 2H), 8.40 - 8.34 (m, 2H), 9.69 (s, 1H); IR (cm^{-1}): 3292 (Aromatic C-H Stretch), 3122 (Amide N-H Stretch), 1664 (Amide C=O Stretch), 1611 (Amide N-H bending); EIMS *m*/*z*: 459.8 [M^+].

4.5.4. Preparation of 6,8-Dibromo-N-(3-Chlorophenyl)-2, 7-Dimethylimidazo[1,2-a]Pyridine-3-Carboxamide (5d)

69% yield (0.45 g), White solid; M.P = 161˚C - 163˚C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.70 (s, 3H), 2.87 (s, 3H), 7.19 - 7.16 (m, 2H), 7.44 - 7.42 (m, 2H), 7.76 - 7.75 (t, 1H), 9.66 (s, 1H); IR (cm^{-1}): 3413 (Aromatic C-H Stretch), 3129 (Amide N-H Stretch), 1651 (Amide C=O Stretch), 1587 (Amide N-H bending); EIMS *m*/*z*: 457.8 [M^+].

4.5.5. Preparation of 6,8-Dibromo-N-(3-Chloro-4-Fluorophenyl)-2, 7-Dimethylimidazo[1,2-a]Pyridine-3-Carboxamide (5e)

61% yield (0.41 g) White solid; m.p. = 146˚C - 148˚C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.70 (s, 3H), 2.86 (s, 3H), 7.20 - 7.15 (t, 1H), 7.42 - 7.38 (m, 2H), 7.82 - 7.80 (dd, 1H), 9.63 (s, 1H); IR (cm^{-1}): 3426 (Aromatic C-H Stretch), 3129 (Amide N-H Stretch), 1650 (Amide C=O Stretch), 1500 (Amide N-H bending); EIMS *m*/*z*: 475.8 [M^+].

4.5.6. Preparation of 6,8-Dibromo-N-(2,5-Dimethylphenyl)-2, 7-Dimethylimidazo[1,2-a]Pyridine-3-Carboxamide (5f)

70% yield (0.45 g) White solid; m.p. = 159˚C - 163˚C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 3H), 2.38 (s, 3H), 2.69 (s, 3H), 2.88 (s, 3H), 6.97 - 6.95 (d, 1H), 7.15 - 7.13 (m, 2H), 7.83 (s, 1H), 9.72 (s, 1H); IR (cm^{-1}): 3452 (Aromatic C-H Stretch), 3127 (Amide N-H Stretch), 1651 (Amide C=O Stretch), 1580 (Amide N-H bending); EIMS *m*/*z*: 451.9 [M^+].

4.5.7. Preparation of 6,8-Dibromo-2,7-Dimethyl-N-(1-Phenylethyl)Imidazo [1,2-a]Pyridine-3-Carboxamide (5g)

68% yield (0.44 g) White solid; m.p. = 132˚C - 134˚C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ

1.65 - 1.64 (t, 3H), 2.66 (s, 3H), 2.73 (s, 3H), 5.36 - 5.29 (q, 2H), 7.41 - 7.28 (m, 5H), 9.64 (s, 1H); IR (cm^{-1}): 3451 (Aromatic C-H Stretch), 3125 (Amide N-H Stretch), 1655 (Amide C=O Stretch); EIMS *m*/*z*: 451.9 [M^+].

4.5.8. Preparation of 6-Bromo-2,7-Dimethyl-N-Phenylimidazo[1,2-a] Pyridine-3-Carboxamide (5h)

54% yield (0.34 g) as white solid; m.p. = 121˚C - 123˚C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.48 (s, 3H), 2.81 (s, 3H), 7.20 - 7.16 (t, 1H), 7.44 - 7.37 (m, 3H), 7.48 (brs, 1H), 7.61 - 7.58 (d, 2H), 9.64 (s, 1H); IR (cm^{-1}): 3305 (Aromatic C-H Stretch), 3044 (Amide N-H Stretch), 1625 (Amide C=O Stretch), 1597 (Amide N-H bending); EIMS *m*/*z*: 346.20 [M + 2].

4.5.9. Preparation of 6-Bromo-N-(4-Fluorophenyl)-2,7-Dimethyl Imidazo[1,2-a]Pyridine-3-Carboxamide (5i)

64% yield (0.43 g), White solid; m.p. = 144˚C - 146˚C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.50 (s, 3H), 2.82 (s, 3H), 7.12 - 7.08 (m, 2H), 7.51 (s, 1H), 7.60 - 7.56 (m, 2H), 7.70 (brs, 1H), 9.60 (s, 1H); ^{13}C-NMR (400 MHz, $CDCl_3$): δ 16.3, 22.5, 112.3, 115.1, 115.4, 121.6, 122.0, 127.8, 138.5, 158.1, 158.8, 160.5; IR (cm^{-1}): 3292 (Aromatic C-H Stretch), 3043 (Amide N-H Stretch), 1625 (Amide C=O Stretch); EIMS *m*/*z*: 364.0 [M + 2].

4.5.10. Preparation of 6-Bromo-N-(3-Chlorophenyl)-2,7-Dimethyl Imidazo[1,2-a]Pyridine-3-Carboxamide (5j)

62% yield (0.45 g), as white solid; m.p. = 144˚C - 146˚C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.50 (s, 3H), 2.82 (s, 3H), 7.17 - 7.15 (d, 1H), 7.34 - 7.30 (t, 1H), 7.49 - 7.43 (m, 3H), 7.76 - 7.76 (m, 1H), 9.65 (s, 1H); IR (cm^{-1}): 3326 (Aromatic C-H Stretch), 3025 (Amide N-H Stretch), 1632 (Amide C=O Stretch), 1589 (Amide N-H bending); EIMS *m*/*z*: 379.9 [M + 2].

4.5.11. Preparation of 6-Bromo-N-(3-Chloro-4-Fluorophenyl)-2, 7-Dimethylimidazo[1,2-a]Pyridine-3-Carboxamide (5k)

62% yield (0.45 g), White solid; m.p. = 136˚C - 138˚C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.50 (s, 3H), 2.82 (s, 3H), 7.19 - 7.15 (t, 1H), 7.42 - 7.38 (m, 2H), 7.47 (t, 1H), 7.82 - 7.79 (dd, 1H), 9.64 (s, 1H); IR (cm^{-1}): 3336 (Aromatic C-H Stretch), 3027 (Amide N-H Stretch), 1630 (Amide C=O Stretch), 1599 (Amide N-H bending); EIMS *m*/*z*: 397.9 [M + 2].

4.5.12. Preparation of 6-Bromo-N-(2,5-Dimethylphenyl)-2, 7-Dimethylimidazo[1,2-a]Pyridine-3-Carboxamide (5l)

66% yield (0.45 g) White solid; m.p. = 151˚C - 154˚C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 3H), 2.41 (s, 3H), 2.50 (s, 3H), 2.82 (s, 3H), 7.19 - 7.15 (t, 1H), 7.42 - 7.38 (m, 2H), 7.47 (t, 1H), 7.82 - 7.79 (dd, 1H), 9.64 (s, 1H); IR (cm^{-1}): 3453 (Aromatic C-H Stretch), 3135 (Amide N-H Stretch), 1644 (Amide C=O Stretch), 1582 (Amide N-H bending); EIMS *m*/*z*: 374.0 [M + 2].

4.5.13. Preparation of 6-Bromo-2,7-Dimethyl-N-(1-Phenylethyl)Imidazo [1,2-a]Pyridine-3-Carboxamide (5m)

64% yield (0.44 g), White solid; m.p. = 181˚C - 186˚C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ

1.65 - 1.63 (d, 3H), 2.48 (s, 3H), 2.69 (s, 3H), 5.37 - 5.30 (q, 1H), 6.01 - 5.99 (d, 1H), 7.42 - 7.28 (m, 6H), 9.64 (s, 1H); IR (cm^{-1}): 3317 (Aromatic C-H Stretch), 3027 (Amide N-H Stretch), 1615 (Amide C=O Stretch); EIMS *m*/*z*: 374.0 [M + 2].

5. Results and Discussion

Antimycobacterial activity

The anti-tubercular activity of the synthesized compounds (**5a-5m**) against *Mycobacterium tuberculosis* (H37 RV strain) ATCC No-27294, were assessed at the Department of Microbiology, Maratha Mandal's NGH Institute of Dental Sciences and Research Centre, Belgaum-590010, India. The method applied is similar to that reported by Maria and Lourenco [23].

The *M. Tuberculosis* stain H37Rv (ATCC 27294) was cultured at 37˚C in Lowestein-Jensenn medium until log phase growth. Then a cell suspension was prepared at a concentration of about 2×10^6 UFC Ml-CM and further diluted 1:20 in Middlebrook 7H9 medium. The later was supplemented with 10% OADC (oleic acid-albumin-dextrose-catalase) and 0.001% Tween 80. One mL bactarial suspention was added to each tube (Capped, glass) to gather with the sample solutions of various concentrations. The final concentrations of the compounds under test ranged from 0.8 to 100 μg per mL and adjusted to a final 2 mL volume. After a 7 day incubation 100 μl of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) (5 mg/mL) with 20% Tween 80 was added to the glass tubes. A violet colour indicated bacterial growth. The tubes were evaluated for colour change on day 8. For standard tests MIC value of Pyrazinamide-3.125 μg/mL, Streptomycin-6.25 μg/mL and Ciprofloxacin-3.125 μg/mL, were determined each time. The MIC of each sample corresponded to the lowest concentration at which the bacteria tested did not show growth. Susceptibility testing was performed three times. The results were expressed as the mean of three tests.

However, compounds **5a-5m** showed moderate to good anti-tubercular activity as represented in **Figure 2**. This is due to the presence of active structural moieties like imidazo[1,2-a]pyridine and carboxamide group, which might interfere in the mechanism of cell mitosis and hence stop further growth of *Mycobacterium tuberculosis*. All the studied samples are showing dissimilar potency due to the effective barrier of cell wall membrane of *Mycobacterium tuberculosis* for entrance of external substances like test compounds under this study. In addition, these compounds disturb the respiration process of the cell and thereby restrict the biosynthesis of proteins. If the biosynthesis of proteins is blocked then formation of bacterial cell wall is not possible which ultimately results in cell death and therefore restricts further growth and infection due to bacteria [24].

6. Conclusion

In conclusion, new derivatives of imidazo[1,2-a]pyridine have been synthesized successfully with good yield. The experimental data for the evaluation of anti-tuberculosis activity revealed that most of the synthesized compounds 5a-5m demonstrated

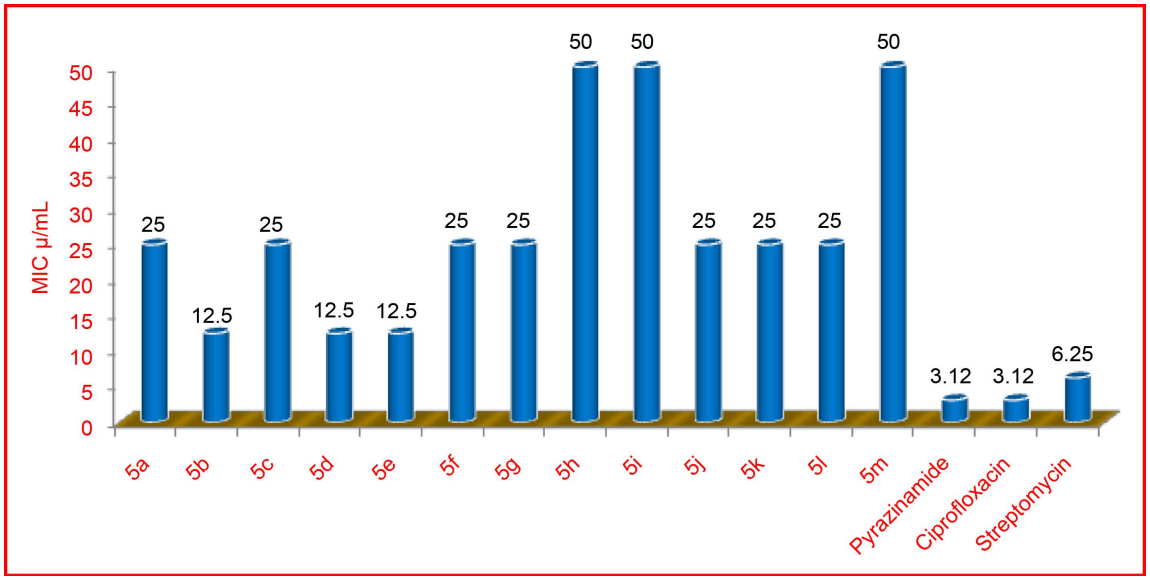


Figure 2. MIC in µg/mL for test samples 5a-5m.

moderate to good antituberculosis activity. Among the tested compounds 5b, 5d and 5e were found to be the most active with minimum inhibitory concentration (MIC) of 12.5 µg/mL against *Mycobacterium tuberculosis* (H37 RV strain) ATCC No-27294 with minimum inhibitory concentration of 12.5 µg/ml. This study would pave the way for future development of more effective imidazo[1,2-a]pyridine analogs for applications in biological science.

Acknowledgements

The authors thank Principal and Head Department of Chemistry, Government of Maharashtra, Ismail Yusuf Arts, Science and Commerce College for providing research and library facilities. The authors also thank Management and Principal of C. S.'s Patkar-Varde College, Goregaon (W), Mumbai for their constant encouragement and support. The authors also acknowledge the help of Dr. Kishore Bhat of Governmental Dental College, Belgaum, for facilitating anti-TB assays and providing the procedure for the same.

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