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Potassium carbonate mediated one-pot synthesis and antimicrobial activities of 2-alkoxy-4-(aryl)-5*H*-indeno[1,2-*b*]pyridine-3-carbonitriles

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Abstract. 2-Alkoxy-4-(aryl)-5*H*-indeno[1,2-*b*]pyridine-3-carbonitriles (**3a-e** and **4a-e**) were synthesized *via* multicomponent reaction from 2-aryl-methylidineindan-1-ones (**1a-e**), malononitrile and K_2CO_3 in ethanol and/or methanol. The structures of obtained compounds (**3a-e** and **4a-e**) were characterized using the spectroscopic methods (NMR, IR) and elemental analysis. Addition, the *in vitro* antimicrobial activities of compounds (**3a-e**) were tested against the five human pathogenic bacteria. Penicillin G and Ceftriaxone antibiotics were used as positive control. The results were given as MIC values (minimum inhibition concentration), and compounds **3b-d** showed very high activity against *Escherichia coli* 111.

Keywords: 1-Indanone; malononitrile; pyridine-3-carbonitrile; antimicrobial activity.

1. Introduction

Carbocyclic compounds containing an aromatic moiety, such as indanones, are an important component of compounds exhibiting pharmacological properties. Indanone derivatives are used as drugs in the treatment of diseases such as cancer and Alzheimer's disorders.[1] The indanones are also used as drug intermediates, as ligands of olefinic polymerization catalysts and as discotic liquid crystals.[1,2] On the other hand, pyridine and its derivatives are the most popular N-heteroaromatics used in the chemical industry for the production of stain, pesticide and pharmaceutical products,[3] and many different derivatives are known to exhibit biological activity.[4] Cyanopyridines containing different aryl and alkyl groups have also been found to possess properties such as antimicrobial,[5] antihypertensive,[6] cardiovascular,[7] antipyretic,[8] analgesic,[8] antitumor[9] and IKK-β inhibitors.[10] For the synthesis of these type compounds, several methods have been developed.[11-14] One of these methods is multicomponent reactions which are very usefulness for the synthesis of heterocyclic compounds.[15-18] Tyndall *et al*.[19]

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have applied this method to 1,3-diphenylpropenone for the synthesis of 1,4-diphenyl-2-methoxypyridine-3-carbonitriles. Furthermore, they have synthesized the 2-Methoxy-4-phenyl-5*H*-indeno[1,2-*b*]pyridine-3-carbonitrile (**4e**) from the one-pot reaction of 2-benzylidene-2,3-dihydro-1H-inden-1-one, malonitrile and NaOH in CH_3OH in yield of 50%. Then, Mishriky *et al*.[20] have synthesized some 5*H*-indeno[1,2-*b*]pyridine derivatives (**3a, c, e** and **4a, c, e**) with the same method using the KOH instead of NaOH.

Our previous work,[21] the 2-(1,3-dihetaryl)-3-oxopropyl)malononitrile derivatives were submitted to K_2CO_3 prompted cyclization reaction for the synthesis of 4,6-dihetaryl-2-alkoxypyridine-3-carbonitriles. The reactions were performed in methanol and/or ethanol at reflux temperature and desired compounds were obtained in high yields.

Encouraged by the above-mentioned findings and in the continuation of our ongoing research in the field of synthesis and biological screening of nitrogen containing heterocycles we reported the synthesis of two series of 2-alkoxy-4-(aryl-5*H*-indeno[1,2-*b*]pyridine-3-carbonitriles (**3a-e** and **4a-e**) from the one-pot reaction of 2-benzylidene-2,3-dihydro-1H-inden-1-one (**1a-e**), malonitrile and K_2CO_3 in CH_3OH and/or C_2H_5OH at reflux temperature and evaluated their antimicrobial activities against some human pathogenic microorganisms.

2. Experimental

IR spectra (KCl disc) were recorded on a Jasco FT/IR-430 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DPX-400 instrument. As internal standards served TMS (δ 0.00) for ^{1}H NMR and $CDCl_3$ (δ 77.0) for ^{13}C NMR spectroscopy J values are given in Hz. Melting points were measured on Electrothermal 9100 apparatus. Elemental analyses were obtained from a LECO CHNS 932 Elemental Analyzer. The major chemicals were purchased from Sigma-Aldrich and Fluka.

2.1. Chemistry

*General Procedure for the Synthesis of 2-Alkoxy-4-aryl-5H-indeno[1,2-b]piridin-3-Carbonitrile Derivatives (**3a-e** and **4a-e**):* 2-Aryl-methylidineindan-1-ones (**1a-e**) (0.80 mmol) were dissolved in ethanol and/or methanol. Malononitrile (**2**) (0.95 mmol) and K_2CO_3 (3.2 mmol) was added to the mixture and stirred at reflux temperature for 16 hours followed by acidification with 5% HCl. The reaction mixture was extracted with $CHCl_3$ and/or CH_2Cl_2 (20 mL), dried over Na_2SO_4, the solvent removed under reduced pressure. The solid crude product was purified on a short silica gel column eluting with chloroform-hexane (3:1), and the obtained solid was recrystallized from chloroform-hexane (2:1) and/or ethanol-diethylether (2:1).

*2-Ethoxy-4-(4-methoxyphenyl)-5H-indeno[1,2-b]pyridine-3-carbonitrile (**3a**):* Yellowish crystals, Yield, 82%, M.P. 170- 173°C, (lit.[20] 170-172°C). IR (KCl, cm^{-1}): 2979, 2937, 2904, 2834, 2215, 1698, 1608, 1583, 1558, 1517, 1484, 1438, 1375, 1336, 1294, 1253, 1186, 1155, 1033, 929, 838, 767, 730, 649, 590, 559, 518, 420. ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 8.08-8.06 (m, 1H), 7.57-7.52 (m, 3H), 7.51-7.46 (m, 2H), 7.09 (d, *J* = 8.4 Hz, 2H), 4.70 (q, *J* = 7.2 Hz, 2H), 3.91 (s, 3H), 3.78 (s, 2H), 1.55 (t, *J* = 7.0 Hz, 3H). ^{1}H-NMR data is agreement with data given in the literature.[20]
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ 166.0, 161.5, 160.0, 151.7, 145.5, 140.0, 130.1 (2C), 129.8, 127.6, 127.4, 127.3, 125.1, 121.9, 116.5, 114.3 (2C), 92.5, 63.3, 55.5, 34.0, 14.6. Anal. calc. for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.08; H, 5.12; N, 8.11.

*2-Ethoxy-4-(p-tolyl)-5H-indeno[1,2-b]pyridine-3-carbonitrile (**3b**):* Yellowish crystals, Yield, 73%, M.P. 160- 163°C. IR (KCl, cm^{-1}): 2983, 2906, 2360, 2217, 1716, 1654, 1616, 1556, 1515, 1376, 1340, 1193, 1149, 1031, 923, 825, 763, 651, 503, 418. ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 8.09-8.07 (m, 1H), 7.56-7.54 (m, 1H), 7.51-7.46 (m, 4H), 7.37 (d, *J* = 8.0 Hz, 2H), 4.70 (q, *J* = 7.2 Hz, 2H), 3.78 (s, 2H), 2.49 (s, 3H), 1.55 (t, *J* = 7.0 Hz 3H). ^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ 165.9, 161.5, 152.0, 145.5, 139.9, 139.6, 132.2, 129.8, 129.5 (2C), 128.4 (2C), 128.3, 127.6, 127.4, 125.1, 121.9, 92.6,

63.3, 33.9, 21.5, 14.6. Anal. calc. for $C_{22}H_{18}N_2O$: C, 80.96; H, 5.56; N, 8.58. Found: C, 80.88; H, 5.48; N, 8.49.

*2-Ethoxy-4-(4-chlorophenyl)-5H-indeno[1,2-b]pyridine-3-carbonitrile (**3c**):* Colorless crystals, Yield, 78%, M.P. 213-216°C, (lit.[20] 213-214°C). IR (KCl, cm^{-1}): 2983, 2904, 2358, 2217, 1556, 1484, 1440, 1334, 1197, 1153, 1091, 1033, 927, 831, 765, 728, 644, 499, 420. ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 8.11-8.08 (m, 1H), 7.59-7.53 (m, 3H), 7.52-7.48 (m, 4H), 4.71 (q, J = 7.2 Hz, 2H), 3.76 (s, 2H), 1.55 (t, J = 7.0 Hz, 3H). ^{1}H-NMR data is agreement with data given in the literature.[20]
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ 165.9, 161.8, 150.6, 145.4, 139.8, 135.8, 133.5, 130.1, 129.8 (2C), 129.2 (2C), 127.6, 127.4, 125.2, 122.1, 115.9, 92.4, 63.4, 33.7, 14.5. Anal. calc. for $C_{21}H_{15}ClN_2O$: C, 72.73; H, 4.36; N, 8.08. Found: C, 72.69; H, 4.28; N, 8.00.

*2-Ethoxy-4-(3-bromophenyl)-5H-indeno[1,2-b]pyridine-3-carbonitrile (**3d**):* Yellowish crystals, Yield, 76%, M.P. 188-191°C. IR (KCl, cm^{-1}): 2987, 2215, 1698, 1558, 1475, 1419, 1373, 1332, 1274, 1236, 1155, 1033, 892, 763, 732, 620, 543, 491, 420. ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 8.11-8.08 (m, 1H), 7.71-7.65 (m, 2H), 7.58-7.56 (m, 1H), 7.52-7.48 (m, 3H), 7.47 (br d, *J* = 7.6 Hz, 1H), 4.72 (q, *J* = 7.0 Hz 2H), 3.76 (s, 2H), 1.55 (t, *J* = 7.0 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ 165.9, 161.8, 150.0, 145.5, 139.7, 137.1 132.6, 131.3, 130.5 (2C), 127.5, 127.2 (2C), 125.2, 122.8, 122.0, 115.7, 92.4, 63.5, 33.6, 14.6. Anal. calc. for $C_{21}H_{15}BrN_2O$: C, 64.46; H, 3.86; N, 7.16. Found: C, 64.37; H, 3.75; N, 7.09.

*2-Ethoxy-4-(phenyl)-5H-indeno[1,2-b]pyridine-3-carbonitrile (**3e**):* Yellowish crystals, Yield, 81%, M.P. 186-189°C, (lit.[20] 187-189°C). IR (KCl, cm^{-1}): 3056, 2983, 2362, 2219, 1868, 1558, 1506, 1436, 1375, 1334, 1240, 1155, 1024, 763, 721, 698, 620, 482, 420. ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 8.11-8.06 (m, 1H), 7.57-7.54 (m, 6H), 7.51-7.47 (m, 2H), 4.72 (q, *J* = 7.0 Hz, 2H), 3.78 (s, 2H), 1.56 (t, *J* = 7.0 Hz, 3H). ^{1}H-NMR data is agreement with data given in the literature.[20]
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ 165.9, 161.6, 151.9, 145.6, 139.8, 135.1 129.9, 129.5, 128.9 (2C), 128.4 (2C), 127.6, 127.4, 125.1, 122.0, 116.1, 92.6, 63.4, 54.7, 33.8. Anal. calc. for $C_{21}H_{16}N_2O$: C, 80.75; H, 5.16; N, 8.97. Found: C, 80.69; H, 5.05; N, 8.88.

*2-Methoxy-4-(4-methoxyphenyl)-5H-indeno[1,2-b]pyridine-3-carbonitrile (**4a**)[20]:* Yellowish crystals, Yield, 80%, M.P. 181-184°C, (lit.[20] 195-197°C). IR (KCl, cm^{-1}): 3052, 2994, 2950, 2221, 1924, 1606, 1552, 1482, 1455, 1355, 1290, 1241, 1186, 1025, 952, 842, 763, 728, 646, 590, 516, 489, 422. ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 8.10 (dd, *J*= 6.2, 2.2 Hz, 1H), 7.57-7.52 (m, 3H), 7.50-7.47 (m, 2H), 7.08 (d, *J*= 8.8 Hz, 2H), 4.23 (s, 3H), 3.91 (s 3H), 3.80 (s, 2H). ^{1}H-NMR data is agreement with data given in the literature.[20]
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ 166.3, 161.5, 160.6, 151.7, 145.5, 139.9, 130.1 (2C), 129.8, 127.8, 127.4, 127.2, 125.1, 122.0, 116.4, 114.3 (2C), 92.3, 55.4, 54.6, 34.0. Anal. calc. for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91; N, 8.53. Found: C, 76.73; H, 4.86; N, 8.48.

*2-Methoxy-4-(p-tolyl)-5H-indeno[1,2-b]pyridine-3-carbonitrile (**4b**):* Yellowish crystals, Yield, 70%, M.P. 171-1874°C. IR (KCl, cm^{-1}): 2954, 2356, 2219, 1691, 1625, 1558, 1484, 1361, 1272, 1207, 1149, 1010, 956, 823, 767, 730, 646, 520, 484, 418. ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 8.10 (br d, *J* = 7.4 Hz, 1H), 7.55 (br d, *J* = 7.2 Hz, 1H), 7.51-7.43 (m, 4H), 3.37 (d, *J* = 8.0 Hz, 2H), 4.24 (s, 3H), 3.79 (s, 2H), 2.48 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ 166.2, 161.5, 152.0, 145.6, 139.9, 139.7, 132.1, 130.8, 129.8, 129.5, 128.4, 127.9, 127.4, 125.1, 122.0, 92.5, 54.6, 33.9, 21.5. Anal. calc. for $C_{21}H_{16}N_2O$: C, 80.75; H, 5.16; N, 8.97. Found: C, 80.68; H, 5.09; N, 8.87.

*4-(4-Chlorophenyl)-2-methoxy-5H-indeno[1,2-b]pyridine-3-carbonitrile (**4c**)[20]:* Yellowish crystals, Yield, 81%, M.P. 236-239°C, (lit.[20] 237-239°C). IR (KCl, cm^{-1}): 2983, 2946, 2360, 2225, 1868, 1579,

1556, 1484, 1457, 1361, 1280, 1149, 1091, 1008, 954, 831, 761, 725, 638, 482, 420. ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 8.12-8.07 (m, 1H), 7.58-7.53 (m, 3H), 7.52-7.47 (m, 4H), 4.23 (s, 3H), 3.74 (s, 2H). ^{1}H-NMR data is agreement with data given in the literature.[20]
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ 166.2, 161.9, 150.6, 145.5, 139.7, 135.9, 133.4, 130.2, 129.9 (2C), 129.3 (2C), 127.7, 127.6, 125.2, 122.1, 115.9, 92.3, 54.7, 33.7. Anal. calc. for $C_{20}H_{13}ClN_2O$: C, 72.18; H, 3.94; N, 8.42. Found: C, 72.14; H, 3.86; N, 8.34.

*4-(3-Bromophenyl)-2-methoxy-5H-indeno[1,2-b]pyridine-3-carbonitrile (**4d**):* Yellowish crystals, Yield, 84%, M.P. 183-185°C. IR (KCl, cm^{-1}): 3058, 2952, 2360, 2223, 1637, 1556, 1475, 1405, 1359, 1276, 1240, 1211, 1153, 1074, 869, 798, 765, 619, 485, 420. ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 8.13-8.09 (m, 1H), 7.71-7.66 (m, 2H), 7.58-7.56 (m, 1H), 7.52-7.48 (m, 3H), 7.45 (t, *J* = 8.0 Hz, 1H), 4.25 (s, 3H), 3.77 (s, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ 166.2, 161.9, 150.1, 145.5, 139.7, 137.0, 132.6, 131.2, 130.5, 130.2, 127.7, 127.6, 127.2, 125.2, 122.9, 122.1, 115.7, 92.4, 54.7, 33.7. Anal. calc. for $C_{20}H_{13}BrN_2O$: C, 63.68; H, 3.47; N, 7.43. Found: C, 63.54; H, 3.43; N, 7.39.

*2-Methoxy-4-phenyl-5H-indeno[1,2-b]pyridine-3-carbonitrile (**4e**)*[19,20]*:* Yellowish crystals, Yield, 74%, M.P. 172-175°C, (lit.[20] 143-144°C). IR (KCl, cm^{-1}): 3058, 2948, 2223, 1965, 1635, 1558, 1484, 1359, 1278, 1211, 1174, 1020, 860, 765, 727, 696, 663, 617, 522, 470, 420. ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 8.11-8.09 (m, 1H), 7.61-7.53 (m, 6H), 7.52-7.44 (m, 2H), 4.24 (s, 3H), 3.77 (s, 2H). ^{1}H-NMR data is agreement with data given in the literature.[20]
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ 166.2, 161.5, 152.0, 145.5, 139.8, 135.0, 130.0, 129.6, 128.9 (2C), 128.5 (2C), 127.9, 127.5, 125.1, 122.1, 116.1, 92.4, 55.4, 34.3. Anal. calc. for $C_{20}H_{14}N_2O$: C, 80.52; H, 4.73; N, 9.39. Found: C, 80.46; H, 4.66; N, 9.24.

2.2 Biological Activity Assay

All newly synthesized compounds **3a-e** were screened for their *in vitro* antimicrobial activities by disc-diffusion method using Mueller-Hilton agar medium against *Staphylococcus aureus* ATCC 29213 and *β-Hemolitic Streptococcus* ATCC 2957, *Escherichia coli* 111, *Salmonella Enteritidis* ATCC 13076 and *Klebsiella pneumoniae* ATCC 13883. The results were given as MIC values (minimum inhibition concentration) compared with positive control (Penicillin G and Ceftriaxone antibiotics).[22-24]

3. Results and discussion

3.1. Chemistry

In this work, the synthesis of (2-alkoxy-4-aryl-5*H*-indeno [1,2-*b*] pyridine-3-carbonitrile) derivatives (**3a-e** and **4a-e**) containing both the indane and the pyridine ring in a single structure was targeted. For this, firstly known 2-aryl-methylidineindan-1-ones (**1a-e**) were synthesized according to published methods.[25-28] The multicomponent (one-pot) rection of 2-aryl-methylidineindan-1-ones (**1a-e)** malononitrile and K_2CO_3 in EtOH and/or MeOH at reflux temperature for 16 hours gave the (2-alkoxy-4-aryl-5*H*-indeno [1,2-*b*] pyridine-3-carbonitrile) derivatives (**3a-e** and **4a-e**) in good yields (74%-84%) (Figure 1, Table 1).

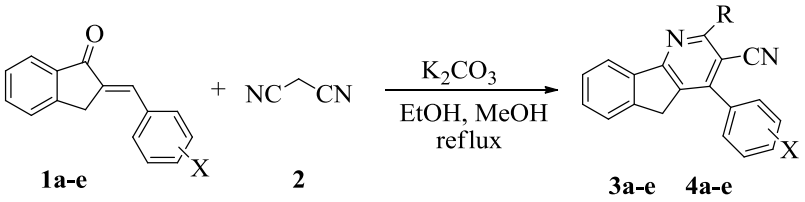
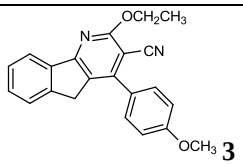
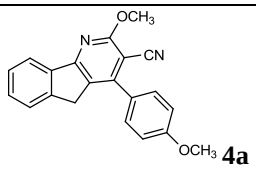
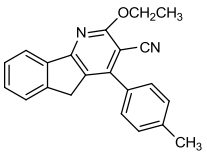
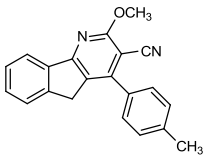
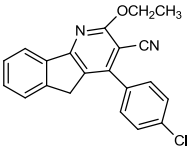
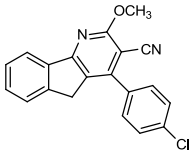
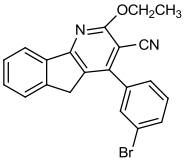
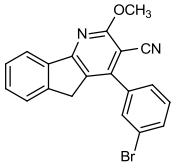
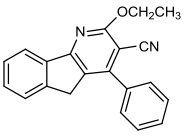
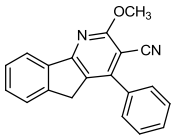


Figure 1. Synthetic path way for compounds **3a-e** and **4a-e**

Table 1. Synthesized (2-alkoxy-4-aryl-5*H*-indeno [1,2-*b*] pyridine-3-carbonitrile) derivatives (**3a-e** and **4a-e**)

Entry	Products	Yield (%)	Entry	Products	Yield (%)
1	 **3a**	82	6	 **4a**	80
2	 **3b**	73	**7**	 **4b**	70
3	 **3c**	78	8	 **4c**	81
4	 **3d**	55	9	 **4d**	84
5	 **3e**	81	10	 **4e**	74

Among the synthesized compounds, six compounds (**3a, c, e** and **4a, c, e**) were previously synthesized by Mishriky *et al*.[20] from the one-pot reaction of 2-aryl-methylidineindan-1-ones, malononitrile and KOH in EtOH and/or MeOH at room temperature for 24 hours, They reported that the compounds (**3a, c, e** and **4a, c, e**) were obtained in modarate yields (40%-54%) with the formation of 2-(2-aryl-2,3-dihydro-1H-inden-1-ylidene)malononitriles, as side products. In our present procedure, the desired compounds were obtained higher yields (74%-84%) without formation of by-products. The structures of all synthesized compounds were determined on the basis of spectral data (NMR and IR) and comparison with their authentic samples.[19,20] The ^{1}H-NMR data of compounds are in good agreement

with data of reported by Mishriky *et al*.[20] Furthermore, the most decisive signal ^{13}C-MR spectra of **3a-3e** and **4a-e** is the presence of a signal in the region at δ 116-114 ascribable to CN. Another noteworthy feature is the appearance of a signal in the region at δ 93-92 which was assigned to C3 as evidenced by literature in similar structures.[29,30] Addition, all physical and spectral data were in good agreement with proposed structures.

3.2. Antimicrobial activity

The synthesized compounds (**3a-e**) were tested for their antibacterial activity against five different types of human pathogenic bacterial strains. Used microorganisms were: *Staphylococcus aureus* ATCC 29213 and *β-Hemolitic Streptococcus* ATCC 2957 which are Gram-positive bacteria and *Escherichia coli* 111, *Salmonella Enteritidis* ATCC 13076 *and Klebsiella pneumoniae* ATCC 13883 which are Gram-negative bacteria. In these tests, P (Penicillin) and CEF (Ceftriaxone) were used as standard and DMSO was used as negative control. The results were given as MIC values (minimum inhibition concentration) compared with positive control (Penicillin G and Ceftriaxone antibiotics) (Table 2).

Table 2. Minimum-inhibitory concentrations (MIC, μg/mL) of synthesized compounds **3a-e**

Compounds	**Microorganisms**				
	Staphylococcus aureus ATCC 29213	*β-Hemolytic Streptococcus* ATCC 2957	*Escherichia coli* 111	*Salmonella Enteritidis* ATCC 13076	*Klebsiella pneumoniae* ATCC 13883
3a	250	250	125	62.25	125
3b	125	250	7.81	125	125
3c	250	250	3.91	125	250
3d	125	250	7.81	125	250
3e	250	250	62.25	250	125
PEN	32.25	⟩500	1.95	0.98	⟩500
CEF	31.25	15.63	31.25	62.25	⟩500
DMSO	250	250	250	250	250

PEN: Penicillin G; CEF: Ceftriaxone antibiotics

As seen Table 2, all compounds (**3a-e**) showed low activity against *Staphylococcus aureus* with 125-250 μg/mL MIC values compared to standards (MIC = PEN = CEF = 31.25 μg/mL). While compounds (**3a-e**) showed very lower activity than the standard CEF (MIC = 15.63 μg/mL) with 250 μg/mL MIC values, they exhibited higher activity than standard PEN (MIC = 500 μg/mL) against *β-Hemolytic Streptococcus*. Almost all compounds (**3a-e**) displayed very good activity against *Escherichia coli* 111. The MIC values of compounds (**3a-e**) were 125 μg/mL for **3a**, 7.81 μg/mL for **3b**, 3.91 μg/mL for **3c**, 7.81 μg/mL for **3d** and 62.25 μg/mL for **3e**, whereas MIC values standard PEN and CEF were 1.95 μg/mL and 31.25 μg/mL, respectively. While compound **3a** demonstrated the same activity with CEF against *Salmonella Enteritidis* (MIC = 62.25 μg/mL), it showed lower activity than the PEN (MIC = 0.98 μg/mL). The other compounds displayed low activity than standards. All compounds **3a-e** exhibited higher activity than standards (MIC = PEN = CEF = 500 μg/mL) against *Klebsiella pneumoniae* with MIC values (125 μg/mL for **3a**, **3b** and **3e**, and 250 μg/mL for **3c** and **3d**). According to these results, further researches can be performed for compounds **3a-d** as potential antibacterial agents against *Escherichia coli* 111. The structure activity relationship (SAR), the most active compounds were **3c** (MIC = 3.91 μg/mL) containing chlorine atom against *Escherichia coli* 111 and **3a** (MIC = 62.25 μg/mL) containing methyl group against *Salmonella Enteritidis*.

4. Conclusion

The 2-Alkoxy-4-(aryl)-5*H*-indeno[1,2-*b*]pyridine-3-carbonitriles (**3a-e** and **4a-e**) were synthesized via K_2CO_3 mediated one-pot reaction from 2-aryl-methylidineindan-1-ones (**1a-e**), malononitrile and K_2CO_3 in ethanol and/or methanol in high yields. Addition, the *in vitro* antimicrobial activities of compounds (**3a-e**) were tested against the five human pathogenic bacteria. Compounds **3b-d** showed very high activity against *Escherichia coli* 111 with MIC 7.81 μg/mL for **3b**, 3.91 μg/mL for **3c**, 7.81 μg/mL for **3d** and 62.25 μg/mL for **3e**, compared to standards PEN and CEF (MIC = 1.95 μg/mL and 31.25 μg/mL, respectively). From these results, further researches can be performed for compounds **3a-d** as potential antibacterial agents against *Escherichia coli* 111.

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