Microwave-Mediated Synthesis and Antibacterial Activity of Some Novel 2-(Substituted Biphenyl) Benzimidazoles *via* Suzuki-Miyaura Cross Coupling Reaction and Their *N*-Substituted Derivatives

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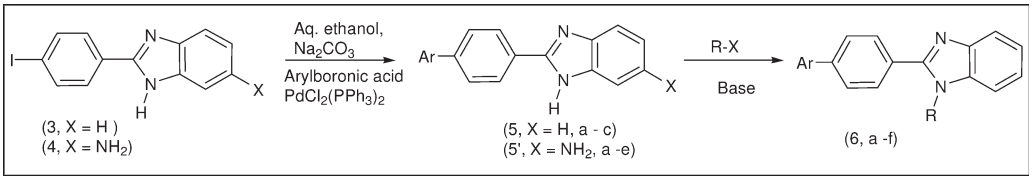

A series of some novel 2-(substituted biphenyl) benzimidazoles and their *N*-substituted derivatives were synthesized *via* microwave-mediated Suzuki-Miyaura coupling of 2-(4-iodophenyl)-1*H*-benzimidazole or 2-(4-iodophenyl)-6-amino-1*H*-benzimidazole and arylboronic acids. The method reported herein offers advantageous shorter reaction times, higher yields and is applicable to a large set of substrates. All the synthesized compounds were screened for their antibacterial activity against *Staphylococcus aureus* and *Salmonella typhimurium* bacterial species.

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INTRODUCTION

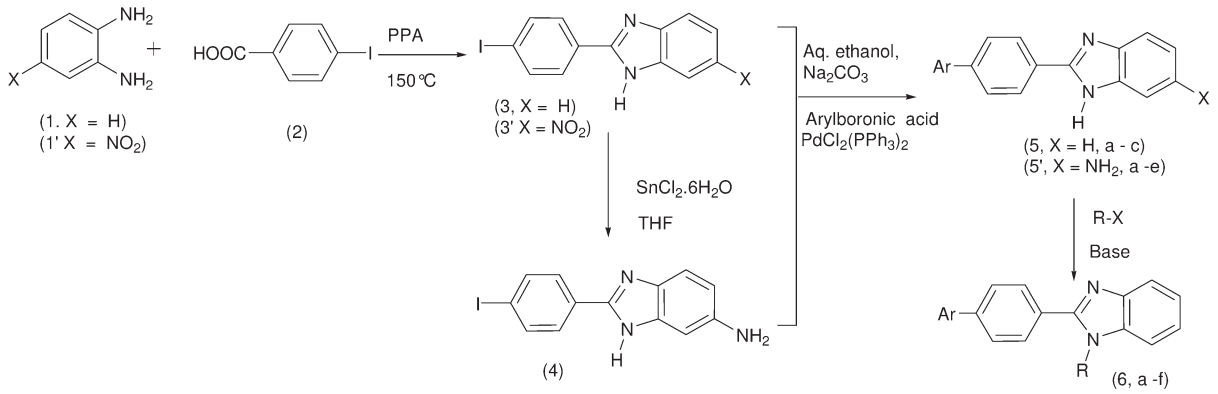
Various substituted benzimidazoles are important compounds because of their varied biological activities [1–10]. These classes of compounds, which act as angiotensin II AT1 receptor blockers and used in the treatment of hypertension, are Sartans [11] that possess biphenyl moiety as an integral part. Losartan potassium is commercially known as Covance, Lorzaar and Losaprex; Telmisartan as Kinzalmono, Micardis and Pritor; Candesartan cilexetil as Amias, Atacand and Blopress; Olmesartan medoxomil as Benevas, Benicar and Olmetec and Irbesartan as Aprovel, Avapro and Karvea. Bifonazol having biphenyl as an integral part exhibits antifungal and antimycotic activity [12]. Fluoro substituted biphenyls like Diflunisal and Flurbiprofen sodium exhibit anti-inflammatory activity and Diflunisal [13] is commercially known as Dolobid and Flurbiprofen sodium as Ocufen [14].

The Suzuki-Miyaura cross coupling reaction has emerged as one of the most powerful platform for carbon–carbon bond formation because of its mild reaction conditions and its compatibility with a broad range of functional groups [15]. Suzuki-Miyaura cross coupling reactions on the multifunctional molecules requires protection and deprotection, which unnecessarily increases the number of steps in organic synthesis, thereby decreasing the yields and increases pollution level and time wastage [16–18]. Therefore organic chemists are engaged in efforts to find new reagents with increased selectivity.

Green chemistry is destined to be a global goal in the near future. In the course of studies on green chemistry one of our goals has been to design microwave-mediated synthetic methods in aqueous medium and make them more ecofriendly and consistent with higher atom economy. Microwave (MW) irradiation is widely used to promote chemical reactions and a number of reviews have advocated the use of MW technology in organic synthesis [19,20]. Microwave activation as a nonconventional energy source is becoming a very popular and useful technique in organic chemistry. The combination of solvent-free reaction conditions and microwave irradiation leads to significantly reduced reaction times, enhanced conversions and sometimes higher selectivity with several advantages for the ecofriendly approach, termed green chemistry [21].

Looking the importance of microwave irradiation in organic synthesis, we nicely demonstrated the use of microwave conditions for Suzuki-Miyaura cross coupling of unprotected halogen-substituted benzimidazoles. The synthesized compounds were tested for their antibacterial action against two different bacterial species namely, *Staphylococcus aureus* and *Salmonella*

Scheme 1



Compd. No.	Arylboronic acid
5a	2-Methoxyphenylboronic acid
5b	4-Trifluoromethanephenylboronic acid
5c	2-[2,3-dihydro-1-methyl-2-triphenylmethyl-1*H*-5-isoindolyl]-1,3,6,2-dioxazaborocane
5'a	Phenylboronic acid
5'b	4-Chlorophenylboronic acid
5'c	2-Methoxyphenylboronic acid
5'd	4-Trifluoromethanephenylboronic acid
5'e	2-[2,3-dihydro-1-methyl-2-triphenylmethyl-1*H*-5-isoindolyl]-1,3,6,2-dioxazaborocane

Compd. No.	R-X
6a	Ethyl chloroformate
6b	Methanesulfonyl chloride
6c	Benzyl bromide
6d	4-Fluorobenzyl bromide
6e	3,5-Difluorobenzyl bromide
6f	4-Chlorobenzyl bromide

typhimurium in comparison with Cephalexin as a reference standard.

RESULT AND DISCUSSION

All the reactions were carried out under both microwave irradiation and conventional methods.

The condensation *o*-phenylenediamine (OPDA) (**1**) or 4-nitrobenzene 1,2-diamine (**1′**) with 4-iodobenzoic acid (**2**) in presence of polyphosphoric acid (PPA) was carried out in microwave oven at 100 W for 5–10 minutes at 150°C to obtain the 2-(4-iodophenyl)-1*H*-benzimidazole **(3)** or 2-(4-iodophenyl)-6-nitro-1*H*-benzimidazole **(3′)**. The reduction of (**3′**) using $SnCl_2.6H_2O$ in ethyl acetate and tetrahydrofuran yielded 2-(4-iodophenyl)-6-amino-1*H*-benzimidazole **(4)**.

Suzuki-Miyaura coupling of compounds **3**, **4** ideally, the approach should allow access to the free NH and NH_2 benzimidazoles utilizing readily available components and catalysts directly without the need for subsequent deprotection to obtain a series of novel 2-(substituted biphenyl)-1*H*-benzimidazoles **(5**, **a-c)**, or 2-(substituted biphenyl)-6-amino-1*H*-benzimidazoles **(5′**, **a-e)**.

The Suzuki-Miyaura coupling product **5b** was then alkylated or acylated at the benzimidazole -NH with different electrophilic reagents leading to functionalized derivatives (**6**, **a-f)** (Scheme 1). The structure of synthesized compounds was confirmed by IR, ^{1}H-NMR, Mass, and ^{13}C-NMR.

EXPERIMENTAL

Melting points were recorded on a MRVIS series, Lab India Instrument and are uncorrected. The monitoring of reaction and checking of purity of the product were done using precoated silica gel plates and visualization using iodine chamber/UV lamp. IR spectra were recorded on a Perkin-Elmer Spectrum One FTIR spectrometer. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on a (Varian Mercury Vx) SWBB 300 MHz spectrometer. Chemical shifts (δ) are reported in ppm from internal TMS standard. The solvents for NMR spectra were CD_3OD. Mass spectra were recorded from

an HP 1100 LC/MSD mass spectral instrument (positive and negative APCI ion source, 50–200 V, nitrogen). Elemental analysis was carried out on a Perkin-Elmer Series-II CHNS/O Analyzer 2400. All microwave reactions were carried out in Biotage (Initiator^{TM} Eight) microwave synthesizer. Arylboronic acid, *o*-phenylenediamine, 4-nitrobenzene-1,2-diamine, and 4-iodobenzoic acid were obtained from S. D. Fine Chem, Mumbai, India. Palladium catalyst was obtained from Aldrich, India.

Synthesis of compounds 3 and 3′ *via* microwave irradiation method. A mixture of *o*-phenylenediamine (**1**) (1.29 g, 12 mmole) or 4-nitrobenzene-1,2-diamine (**1′**) (1.83 g, 12 mmole), 4-iodobenzoic acid (**2**) (2.47 g, 10 mmole) and polyphosphoric acid (PPA) (20 g) were stirred and irradiated in microwave oven at 100 W for 10 min at 150°C in sealed vessel (monitored by TLC, Hexane: Ethyl acetate, 7:3). The reaction mixture was then cooled to room temperature and neutralized with aqueous ammonia solution. The product was extracted with ethyl acetate (10 mL × 2). The combined organic layer was washed with 5*N* HCl (10 mL) and sodium bicarbonate solution (5%, 10 mL), water (10 mL) and then organic layer was dried over anhydrous sodium sulphate. The solvent was evaporated under reduced pressure to obtain crude product, which was recrystallized from ethyl acetate to afford an off-white solid 2-(4-iodophenyl)-1*H*-benzimidazole **(3)** or 2-(4-iodophenyl)-6-nitro-1*H*-benzimidazole **(3′)**.

General procedure for the synthesis of compounds 3 and 3′. A mixture of *o*-phenylenediamine (**1**) (1.29 g, 12 mmole) or 4-nitrobenzene-1, 2-diamine (**1′**) (1.83 g, 12 mmole), 4-iodobenzoic acid (**2**) (2.47g, 10 mmole), and PPA (20 g) was stirred at 150°C for 6 h (monitored by TLC, Hexane: Ethyl acetate, 7:3). The reaction mixture was then cooled to room temperature and neutralized with aqueous ammonia solution. The product was extracted with ethyl acetate (10 mL × 2). The combined organic layer was washed with 5*N* HCl (10 mL) and sodium bicarbonate solution (5%, 10 mL), water (10 mL) and then organic layer was dried over anhydrous sodium sulphate. The solvent was evaporated under reduced pressure to obtain crude product, which was recrystallized from ethyl acetate to afford an off-white solid 2-(4-iodophenyl)-1*H*-benzimidazole **(3)** or 2-(4-iodophenyl)-6-nitro-1*H*-benzimidazole **(3′)**.

Synthesis of 2-(4-iodophenyl)-6-amino-1*H*-benzimidazole (4). A solution of compound **3′** (3.65 g, 10 mmole) dissolved in tetrahydrofuran (15 ml) and water (15 mL). Stannous chloride hexahydrate (10 g, 36 mmole) was added in the reaction mass room temperature. After complete addition, the mixture was stirred at room temperature for 30 min. Thereafter, the solution was allowed to the 40–45°C and stirring continued for 2 h (monitored by TLC, Hexane: Ethyl acetate 1:1). The mixture was again cooled to room temperature and then ethyl acetate (50 mL), and aqueous ammonia solution (20 mL) was added at same temperature. The ethyl acetate layer was separated, dried over anhydrous sodium sulphate and the solvent was evaporated under reduced pressure to obtain the crude product, which was recrystallized from ethyl acetate to afford a white solid of 2-(4-iodophenyl)-6-amino-1*H*-benzimidazole **(4)**.

Synthesis of compound 4 by alternative method. A solution of compound **3′** (3.65 g, 10 mmole) dissolved in methanol (20 mL). Palladium carbon (5%, 0.5 g) was added under nitrogen atmosphere. The reaction was hydrogenated in an autoclave at 60 psig pressure for 3 h (monitored by TLC, Hexane: Ethyl acetate 1:1). After completion of reaction the mixture was filtered and solvent was evaporated under reduced pressure to obtain the crude product, which was recrystallized from ethyl acetate to afford a white solid **4**.

Synthesis of compounds (5, a-c) and (5′, a-e) *via* microwave irradiation method. To the solution of compound **3** (3.19 g, 10 mmole) or **4** (3.35 g, 10 mmole) in ethanol (20 mL), arylboronic acids (12 mmole), aqueous sodium carbonate solution 10% (20 mmole) and bis(triphenylphosphine)palladium(II)dichloride (0.87 g, 0.125 mmole) were irradiated in microwave oven at 100 W for 5–15 min at 80°C in sealed vessel (monitored by TLC, Hexane: Ethyl acetate, 7:3). After completion of reaction, the mixture was cooled to room temperature and filtered through celite. The filtrate was extracted with ethyl acetate (25 mL × 2), and the organic layer was washed with water (25 mL × 2) and dried over anhydrous sodium sulphate. Evaporation of the solvent yielded crude products which were subjected to column chromatography (silica gel) using hexane and ethyl acetate mixture (9:1) to isolate the pure products (**5**, **a-c**) or (**5′**, **a-e**), respectively.

Synthesis of compounds (5, a-c) and (5′, a-e) by conventional heating method. To the solution of compound **3** (3.19 g, 10 mmole) or **4** (3.35 g, 10 mmole) in ethanol (50 mL), arylboronic acids (12 mmole), 10% aqueous sodium carbonate solution (20 mmole) and bis(triphenylphosphine)palladium(II)-dichloride (0.87 g, 0.125 mmole) were added and the mass was refluxed for 8–10 h (monitored by TLC, Hexane: Ethyl acetate, 7:3). After completion of reaction, the mixture was cooled to room temperature and filtered through celite. The filtrate was extracted with ethyl acetate (50 mL × 2), and the organic layer was washed with water (25 mL × 2) and dried over anhydrous sodium sulphate. Evaporation of the solvent yielded crude products which were subjected to column chromatography (silica gel) using hexane and ethyl acetate mixture (9:1) to isolate the pure products **(5**, **a-c)** or **(5′**, **a-e)**.

Synthesis of compounds 6a and 6b *via* microwave irradiation method. To a solution of compound **5b** (3.38 g, 10 mmole) in pyridine (10 mL), ethyl chloroformate (1.62 g, 15 mmole)or methane sulfonyl chloride (1.7 g, 15 mmole) were irradiated in microwave oven at 100 W for 5–10 min at 45–50°C in sealed vessel (monitored by TLC, Hexane: Ethyl acetate, 1:1). After completion of reaction the mixture was cooled to room temperature, then a solution of 2*N* HCl was added to neutralize the reaction mixture. The solid was then extracted with ethyl acetate (50 mL), which was washed with aqueous sodium bicarbonate (5%, 25 mL), water (50 mL × 2), and dried over anhydrous sodium sulphate. Solvent was evaporated under reduced pressure to give the crude product, which was recrystallized from ethyl acetate to afford compound **6a** or **6b**.

Synthesis of compounds 6a and 6b by conventional method. To a solution of compound **5b** (3.38 g, 10 mmole) in pyridine (25 mL), ethyl chloroformate (1.62 g, 15 mmole) or methane sulfonyl chloride (1.7 g, 15 mmole) was added slowly at 0°C. After complete addition, the reaction mixture was allowed to attain room temperature and stirred for 6–8 h at same temperature (monitored by TLC, Hexane Ethyl acetate, 1:1). A solution of 2N HCl was then added to neutralize the reaction mixture. The solid was then extracted with ethyl acetate (50 mL), which was washed with aqueous sodium bicarbonate (5 %, 25 mL), water (50 mL × 2), and dried over anhydrous sodium sulphate. Solvent was evaporated under

Table 1

Physical and yield comparison data of synthesized compounds

Sr. No.	Compd. No.	Molecular formula	M.P. (°C)	Microwave irradiation		Conventional heating	
				Time (min)	Yield (%)	Time (h)	Yield (%)
1	**3**	$C_{13}H_9IN_2$	289–290	10	85	6	75
2	**3′**	$C_{13}H_8IN_3O_2$		10	87	6	80
3	**5a**	$C_{20}H_{16}N_2O$	215–216	10	90	8	82
4	**5b**	$C_{20}H_{13}F_3N_2$	203–205	10	91	10	85
5	**5c**	$C_{41}H_{33}N_3$	150–152	15	87	9	82
6	**5′a**	$C_{19}H_{15}N_3$	250–254	10	92	8	78
7	**5′b**	$C_{19}H_{14}ClN_3$	220–221	15	90	10	75
8	**5′c**	$C_{20}H_{17}N_3O$	280–281	10	90	9	87
9	**5′d**	$C_{20}H_{14}N_3F_3$	285–286	10	91	9	78
10	**5′e**	$C_{41}H_{34}N_4$	230–231	15	85	10	78
11	**6a**	$C_{23}H_{17}N_2O_2F_3$	80–81	10	90	6	75
12	**6b**	$C_{21}H_{15}N_2O_2SF_3$	240–245	15	90	10	85
13	**6c**	$C_{27}H_{19}N_2F_3$	185–186	10	92	8	90
14	**6d**	$C_{27}H_{18}N_2F_4$	85–86	15	90	10	87
15	**6e**	$C_{27}H_{17}N_2F_5$	105–108	10	89	8	83
16	**6f**	$C_{27}H_{18}ClN_2F_3$	78–80	10	93	9	87

reduced pressure to give the crude product, which was recrystallized from ethyl acetate to afford compound **6a** or **6b**.

Synthesis of compounds (6, c-f) *via* microwave irradiation method. To a solution of compound **5b** (3.38 g, 10 mmole) in acetonitrile (20 mL), aqueous sodium hydroxide solution (10%, 20 mmole) was added and the mixture was stirred for 15 min. Various benzyl bromides (15 mmole) were added and irradiated in microwave oven at 100 W for 5–10 min at 50–55°C in sealed vessel (monitored by TLC, Hexane: Ethyl acetate, 1:1). After the completion of the reaction, acetonitrile from the reaction mixture was evaporated under reduced pressure and water (50 mL) was added to residue to separate solid. The solid was then extracted with ethyl acetate (20 mL), the extract was washed with water (25 mL × 2), and dried over anhydrous sodium sulphate. Solvent was evaporated under reduced pressure to afford the crude products, which were recrystallized from ethanol to yield pure compounds **(6, c-f)**.

Synthesis of compounds (6, c-f) by conventional method. To a solution of compound **5b** (3.38 g, 10 mmole) in acetonitrile (50 mL), aqueous sodium hydroxide solution (5%, 25 mL) was added and the mixture was stirred for 15 min. Various benzyl bromides (15 mmole) were then added slowly with stirring to the reaction mixture at 0–10°C. After complete addition, the reaction mixture was allowed to attain room temperature and stirred for 8–10 h (monitored by TLC, Hexane: Ethyl acetate, 7:3). After the completion of the reaction, acetonitrile from the reaction mixture was evaporated under reduced pressure and water (50 mL) was added to residue to separate solid. The solid was then extracted with ethyl acetate (50 mL), the extract was washed with water (50 mL × 2), and dried over anhydrous sodium sulphate. Solvent was evaporated under reduced pressure to afford the crude products, which were recrystallized from ethanol to yield pure compounds **(6, c- f)**. (Table 1)

BIOLOGICAL ACTIVITY

All the compounds prepared herein were screened for their antibacterial activities against *Staphylococcus aureus* (Gram positive) and *Salmonella typhimurium* (Gram negative) bacteria strains in comparison with Cephalexin as reference standard and the results are summarized in Tables 2 and 3. Most of the compounds tested were found to have good antibacterial activity against *Staphylococcus aureus* NCIM 5021 and *Salmonella typhimurium* NCIM 2501 when compared to standard.

CONCLUSION

We report a simple, rapid, efficient, economic, and environment-friendly method for the synthesis of some novel 2-(substituted biphenyl-2-yl)-1*H*-benzimidazoles and their *N*-substituted derivatives using microwave-mediated Suzuki-Miyaura coupling reaction. The advantage of the microwave irradiation shorter reaction times with an excellent yield compared to conventional method and also tested their antibacterial activity. The compounds 5a, 5b, 5′b, 5′c, 5′c, 5′d, 6c, 6d, and 6e showed completely inhibited the growth of both test bacterial species, namely, *S. aureus* and *S. typhi,* however, 6c, 6d, and 6e showed better antibacterial activity against *S. typhi*.

2-(4-Iodophenyl-1*H*-benzimidazole (3). IR (KBr): 3300, 2970, 1458, 1410, 1326, 1074, 834, 816 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 7.22–7.26 (m, 2H, Ar—H), 7.62–7.63 (m, 2H, Ar—H), 7.78 (d, J = 8.4 Hz, 2H, Ar—H), 8.17 (d, J = 8.4 Hz, 2H, Ar—H), 13.08 (bs, 1H, —NH); *Anal*. Calcd. for $C_{13}H_9IN_2$: C, 48.77; H, 2.83; N, 8.75; Found: C, 48.64; H, 3.10; N, 8.57.

2-(2-Methoxybiphenyl-4-yl)-1*H*-benzimidazole (5a). IR (KBr): 3421, 2962, 1740, 1621, 1596, 1427, 1261, 1161, 1099, 799, 741 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 3.82 (s, 3H, OCH_3), 7.01–7.10 (m, 2H, Ar—H), 7.24–7.27 (m,

Table 2

Antibacterial activity of synthesized compounds against *staphylococcus aureus*.

Comp. No.	Concentrations (μg/mL) 1	10	100	200	500	Approx. MIC (μg/mL)
5a	++	++	+	−−	−−	200
5b	++	++	+	−−	−−	200
5c	++	++	++	+	−−	500
5′a	++	++	++	+	−−	500
5″b	++	++	P	−−	−−	200
5′c	++	++	−−	−−	−−	100
5′d	++	+	−−	−−	−−	100
5′e	++	++	++	+	−−	500
6a	++	++	+	−−	−−	200
6b	++	++	++	+	−−	500
6c	++	++	+	−−	−−	200
6d	++	+	−−	−−	−−	100
6e	++	P	−−	−−	−−	100
6f	++	++	P	−−	−−	200
Cephalexin	++	−−	−−	−−	−−	10

−−, Total inhibition, no growth of organism; P, poor growth compared to controls; +, medium growth compared to controls; ++, confluent growth, no inhibition.

2H, Ar—H), 7.32–7.59 (m, 3H, Ar—H), 7.60–7.68 (m, 3H, Ar—H), 8.08–8.11 (m, 2H, Ar—H); ms: m/z 301.28 (M^++1); *Anal*. Calcd. for $C_{20}H_{16}N_2O$: C, 79.98; H, 5.37; N, 9.33; Found: C, 80.12; H, 5.15; N, 9.48.

2-(4-Ttrifluoromethylbiphenyl-4-yl)-1*H*-benzimidazole (5b). IR (KBr): 2924, 1618, 1449, 1428, 1333, 1262, 1159, 1079, 799 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 7.21–7.24 (m, 2H, Ar—H), 7.49–7.64 (m, 4H, Ar—H), 7.78–7.92 (m, 4H, Ar—H), 8.14–8.16; (m, 2H, Ar—H); ms: m/z 339.30 (M^++1); *Anal*. Calcd. for $C_{20}H_{13}F_3N_2$: C, 71.00; H, 3.87; F, 16.85; N, 8.28; Found: C, 71.14; H, 4.02; N, 8.06.

2-(1-Methyl-2-tritylisoindolin-4-yl)phenyl-1*H*-benzimidazole (5c). IR (KBr): 2924, 2854, 1747, 1594, 1463, 1377, 1314, 1276, 1156, 1032, 901, 848, 825, 768, 749, 708, 638.cm^{-1}; ^{1}H-NMR (CD_3OD): δ 1.44 (d, J = 6.6 Hz, 3H, —CH), 4.08–4.13, 4.53–4.54 (2H, —CH_2), 4.38–4.43 (m, 1H, —CH), 6.85 (d, J = 7.8 Hz, 2H, Ar—H), 6.94 (s, 1H, Ar—H), 7.02 (d, J = 6.9Hz, 2H, Ar—H), 7.06–7.16 (m, 4H, Ar—H), 7.25 (d, J = 3Hz,

Table 3

Antibacterial activity of synthesized compounds against *Salmonella typhimurium*.

Comp. No.	Concentrations (μg/mL) 1	10	100	200	500	Approx. MIC (μg/mL)
5a	++	++	+	P	−−	500
5b	++	++	+	−−	−−	200
5c	++	++	++	++	p	500
5′a	++	++	++	++	−−	500
5′b	++	++	+	P	−−	500
5′c	++	++	+	−−	−−	200
5′d	++	++	+	−−	−−	200
5′e	++	++	++	+	−−	500
6a	++	++	++	P	−−	500
6f	++	++	++	+	−−	500
6b	++	++	++	+	−−	500
6c	++	++	P	−−	−−	200
6d	++	++	+	−−	−−	200
6e	++	++	P	−−	−−	500
Cephalexin	++	++	P	−−	−−	200

−−, Total inhibition, no growth of organism; P, poor growth compared to controls; +, medium growth compared to controls; ++, confluent growth, no inhibition.

2H, Ar—H), 7.44–7.55 (m, 8H, Ar—H), 7.58–7.70 (m, 2H, Ar—H), 7.81 (s, 2H, Ar—H), 7.97 (s, 1H, Ar—H), 8.07 (d, 8.4Hz, 2H, Ar—H); ms: m/z Fragments 326.33 2-(1R)-2,3-dihydro-1-methyl-1*H*-5-isoindol, 243.25- triphenylmethyl; *Anal*. Calcd. for $C_{41}H_{33}N_3$: C, 86.74; H, 5.86; N, 7.40; Found: C, 86.64; H, 5.98; N, 7.52.

2-(Biphenyl-4-yl)-6-amino-1*H*-benzimidazole (5′a). IR (KBr): 3421, 3320, 3205, 1635, 1476, 1476, 1419, 1363, 1123, 813, 770, 728 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 6.76 (d, J = 8.1 Hz, 1 H, Ar—H), 6.93 (s, 1H, Ar—H), 7.35–7.47 (m, 4H, Ar—H), 7.66 (d, J = 7.8Hz, 2H, Ar—H), 7.75 (d, J = 7.8 Hz, 2H, Ar—H), 8.08 (d, J = 8.1Hz, 2H, Ar—H); *Anal*. Calcd. for $C_{19}H_{15}N_3$: C, 79.98; H, 5.30; N, 14.73; Found: C, 79.86; H, 5.38; N, 14.62.

2-(4-Chlorobiphenyl-4-yl)-6-amino-1*H*-benzimidazole (5′b). IR (KBr): 3396, 1902, 1635, 1475, 1436, 1403, 1261, 1180, 1091 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 6.61–6.68 (m, 1H, Ar—H), 7.30–7.35 (m, 3H, Ar—H), 7.45–7.65 (m, 5H, Ar—H), 7.98 (d, J = 9 Hz, 2H, Ar—H); ^{13}C-NMR (CD_3OD): δ 114.80, 117.65, 127.89, 127.89, 128.37, 128.37, 129.36, 129.36, 129.40, 129.40, 129.45, 129.89, 129.95, 130.03, 134.90, 139.72, 141.10, 145.18, 151.46, 157.46 (aromatic carbons); ms: m/z 320.37 (M^++1); *Anal*. Calcd. for $C_{19}H_{14}ClN_3$: C, 71.36; H, 4.41; N, 13.14; Found: C, 71.28; H, 4.54; N, 13.31.

2-(2-Methoxybiphenyl-4-yl)-6-amino-1*H*-benzimidazole (5′c). IR (KBr): 3391, 2036, 1612, 1509, 1471, 1392, 1259, 1239, 1181, 1124, 1057, 1025, 835, 762 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 3.83 (s, 3H, OCH_3), 7.06–7.16 (m, 2H, Ar—H), 7.4 (d, J = 7.8Hz, 2H, Ar—H), 7.58 (d, J = 8.7Hz, 1H, Ar—H), 7.85–7.98 (m, 4H, Ar—H), 8.18 (d, J = 8.4 Hz, 2H, Ar—H); ^{13}C-NMR (CD_3OD): δ 56.10 (OCH_3), 109.56, 112.8, 116.69, 121.67, 122.21, 122.47, 128.83, 128.83, 129.57, 131.40, 131.57, 131.57, 132.17, 132.68, 133.60, 133.63, 145.51, 146.45, 157.98 (aromatic carbons); ms: m/z 316.22 (M^++1); *Anal*. Calcd. for $C_{20}H_{17}N_3O$: C, 76.17; H, 5.43; N, 13.32; Found: 76.32; H, 5.30; N, 13.44.

2-(4-Trifluoromethylbiphenyl-4-yl)-6-amino-1*H*-benzimidazole (5′d). IR (KBr): 3399, 2712, 1634, 1571, 1473, 1367, 1337, 1261, 1122, 807, 826, 699 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 7.51 (d, J = 8.1Hz, 1H, Ar—H), 7.62–7.67 (m, 2H, Ar—H), 7.79 (s, 1H, Ar—H), 7.88–8.01 (m, 5H, Ar—H), 8.2 (d, J = 8.1Hz, 2H, Ar—H); ^{13}C-NMR (CD_3OD): δ 109.70, 116.81, 122.60, 122.68, 123.25, 124.87, 126.55, 129.79, 129.79, 131.40, 130.05, 130.05, 131.27, 132.11, 132.79, 133.75, 133.80, 145.56, 146.39, 157.42 (aromatic carbons); ms: m/z 354.34 (M^++1); *Anal*. Calcd. for $C_{20}H_{14}N_3F_3$: C, 67.98; H, 3.99; 13; N, 11.89; Found: C, 68.04; H, 4.18; 13; N, 11.74.

2-(1-Methyl-2-tritylisoindolin-4-yl)phenyl-6-amino-1*H*-benzimidazole (5′e). IR (KBr): 2925, 2854, 2727,. 1747, 1594, 1463, 1377, 1156, 1023, 722, 540 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 1.39 (d, J = 6.8 Hz, 3H, —CH), 3.99–4.05, 4.35–4.45 (2H, —CH_2), 4.50–4.56 (m, 1H, —CH), 4.99 (s, 1H, —NH), 6.51(d, J = 8.7Hz, 1H, Ar—H), 6.57(d, J = 7.8Hz, 1H, Ar—H), 6.71 (m, 1H, Ar—H), 6.91 (d, J = 7.8Hz, 2H, Ar—H), 7.07–7.20 (m, 2H, Ar—H), 7.29 (d, J = 8.7Hz, 2H, Ar—H), 7.43–7.47 (m, 6H, Ar—H), 7.50–7.56 (m, 6H, Ar—H), 7.62–7.79 (m, 2H, Ar—H), 8.04 (d, J = 8.1Hz, 2H, Ar—H); ms: m/z 583.25 (M^++1); *Anal*. Calcd. for $C_{41}H_{34}N_4$: C, 84.50; H, 5.88; N, 9.61; Found: C, 84.61; H, 5.76; N, 9.74.

2-(4-Ttrifluoromethylbiphenyl-4-yl)-1-(ethylcarboxylate)-1*H*-benzimidazole (6a). IR (KBr): 2936, 1739, 1476,1 452, 1398, 1377,1338, 1283, 1214, 1065, 1007, 854 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 1.15–1.26 (m, 3H, —CH_3), 4.35–4.42 (m, 2H, CH_2), 7.39–7.47 (m, 2H, Ar—H), 7.64–7.69 (m, 3H, Ar—H), 7.71–7.74 (m, 4H, Ar—H), 7.96–8.08 (m, 2H, Ar—H), 8.1 (d, J = 2.1Hz, 1H, Ar—H); ms: m/z 411.04 (M^++1); *Anal*. Calcd. for $C_{23}H_{17}N_2O_2F_3$: C, 67.31; H, 4.18; F, 13.89; N, 6.83; Found: C, 67.22; H, 4.11; F, 13.97; N, 6.72.

2-(4-Trifluoromethylbiphenyl-4-yl)-1-(methylsulfonyl)-1*H*-benzimidazloe (6b). IR (KBr): 3420, 2627, 1633, 1518, 1458, 1436, 1334, 1264, 1239, 1149, 1037, 796, 751 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 2.7 (s, 3H, —CH_3), 7.63–7.66 (m, 2H, Ar—H), 7.71–7.76 (m, 2H, Ar—H), 7.84–7.87 (m, 2H, Ar—H), 7.88–8.09 (m, 4H, Ar—H), 8.26 (d, J = 8.4 Hz, 2 H, Ar—H); ms: m/z Fragment 339.2 (fragment of without methane sulfonyl group); *Anal*. Calcd. for $C_{21}H_{15}N_2O_2SF_3$: C, 60.57; H, 3.63; N, 6.73; Found: C, 60.66; H, 3.72; N, 6.64.

2-(4-Trifluoromethylbiphenyl-4-yl)-1-benzyl-1*H*-benzimidazole (6c). IR (KBr): 2958, 1600, 1509, 1470, 1452, 1389, 1271, 1222, 1190, 1168, 1006, 836 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 5.68 (s, 2H, CH_2), 7.04–7.09 (m, 2H, Ar—H), 7.18–7.22 (m, 2H, Ar—H), 7.72–7.80 (m, 7H, Ar—H), 7.93–8.03 (m, 6H, Ar—H); ms: m/z 429.25 (M^++1); *Anal*. Calcd. for $C_{27}H_{19}N_2F_3$: C, 75.69; H, 4.47; N, 6.54; Found: C, 75.71; H, 4.36; N, 6.65.

2-(4-Trifluoromethylbiphenyl-4-yl)-1-(4-fluorobenzyl)-1*H*-benzimidazole (6d). IR (KBr): 2922, 2853, 1747, 1610, 1494, 1460, 1406, 1377, 1337, 1264, 1162, 1122, 1097, 1075, 1035, 978, 900, 851, 805, 764 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 5.69 (s, 2H, CH_2), 7.05 (d, J = 6.9 Hz, 2H, Ar—H), 7.16–7.21(m, 3H, Ar—H), 7.27–7.39 (m, 3H, Ar—H), 7.62–7.67 (m, 3H, Ar—H), 7.73–7.79 (m, 3H, Ar—H), 7.94 (d, J = 8.7 Hz, 2H, Ar—H); ms: m/z 447.28 (M^++1); *Anal*. Calcd. for $C_{27}H_{18}N_2F_4$: C, 72.64; H, 4.06; N, 6.27; Found: C, 72.76; H, 4.18; N, 6.20.

2-(4-Trifluoromethylbiphenyl-4-yl)-1-(3,5-difluorobenzyl)-1*H*-benzimidazole (6e). IR (KBr): 2924, 2854, 1731, 1611, 1520, 1458, 1438, 1332, 1161, 1126, 804, 751 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 5.58 (s, 2H, —CH_2), 6.83 (d, J = 8.1Hz, 1H, Ar—H), 6.96–7.01 (m, 1H, Ar—H), 7.14–7.23 (m, 1H, Ar—H), 7.29–7.37 (m, 2H, Ar—H), 7.41–7.44 (m, 1H, Ar—H), 7.64–7.69 (m, 2H, Ar—H), 7.75–

7.86 (m, 5H, Ar—H), 7.96 (s, 2H, Ar—H); ms: m/z 465.35 (M^++1); *Anal*. Calcd. for $C_{27}H_{17}N_2F_5$: C, 69.83; H, 3.69; N, 6.03; Found: C, 69.72; H, 3.58; N, 6.13.

2-(4-Trifluoromethylbiphenyl-4-yl)-1-(4-chlorobenzyl)-1*H*-benzimidzloe (6f). IR (KBr): 2926, 1898, 1611, 1406, 1334, 1263, 1164, 1097, 1014, 801 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 5.63, (s, 2H, —CH_2), 7.04 (d, J = 7.8 Hz, 1H, Ar—H), 7.16 (d, J = 7.8 Hz, 1H, Ar—H), 7.30–7.39 (m, 7H, Ar—H), 7.68–7.85 (m, 5H, Ar—H), 7.96–8.0 (m, 2H, Ar—H); ms: m/z 463.12 (M^++1); *Anal*. Calcd. for $C_{27}H_{18}ClN_2F_3$: C, 70.06; H, 3.92; N, 6.05 Found: C, 70.14; H, 3.81; N, 5.82.

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