Microwave-assisted synthesis of 4,7-diaryl substituted indole derivatives with various boronic acid

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Abstract— The synthesis of 4,7–dibromo indole with various functionalized aryl boronic acids were investigated. We first optimized the combination of 4,7–diaryl indole derivatives with Suzuki–Miyaura reaction. We have also demonstrated that Heck and Sonogashira reactions of 4,7–dibromo indole did not occurs at conventional and microwave irradiation condition. Second, the Suzuki–Miyaura reactions procedure proceeds in excellent overall yield were found to increase yields of the desired products in microwave irradiation.

Keywords: Suzuki-Miyaura coupling; 4,7-diaryl substituted indole; microwave irradiation

I. INTRODUCTION

Indoles and their derivatives are common heterocyclic compounds in nature. The indole ring system it is well recognised that integral part in many drugs.[1-2] Indoles are very important compounds in many aspects. Consequently, the research and development of synthetic methods for indoles continues to be one of the most active areas in synthetic chemistry.[3] Moreover, a large number of indole core compounds show potential as therapeutic agents.[2] The palladium catalyzed Suzuki-miyaura cross coupling is a powerful method for the construction of carbon-carbon bond formation in organic synthesis.[4] The Suzuki cross-coupling reactions of arylboronic acids and aryl halides provide an effective synthetic route to biaryls, since the biaryls unit is represented in natural products, advanced materials, pharmaceuticals, polymers and liquid crystals etc.[5] There are various biaryl coupling methods, in which the applications of these methods have been reviewed comprehensively in the literature.[6] Microwave-assisted heating under controlled conditions has been proven as an invaluable technology for organic synthesis[7] and their application in several cases has lead to acceleration of reactions, improvement of yields and selectivities.[8] The heating effect, that is, utilized in microwave-assisted organic transformations is due to the dielectric constant of the solvent. It is particularly convenient that, qualitatively, the larger the dielectric constant of the reaction medium, the greater the coupling with microwaves.[9] However, the C–C coupling reaction requires longer reaction time and is performed in the presence of ligands, usually at high temperature. So, there is a need to decrease the reaction time as well as to simplify the purification procedure. Thus, high-density microwave heating has become an effective procedure because it allows rapid and convenient superheating to high temperatures in combination with excellent reaction control and low energy consumption. It has been proven recently that microwave heating improves the preparative efficiency and reduces the reaction time for several different types of organic transformations.[10-12] Herein, we wish to report the observation of difference in conventional heating and microwave irradiation in the synthesis of indole core. The development of a fast microwave-enhanced C–C coupling reaction for preparing 4,7-diaryl indole derivatives by palladium-catalyzed coupling of boronic acids with various substituted aryl compounds. In comparison with the current methods of the C–C bond formation, our approach displays specific advantages: (i) it proceeds faster and gives moderate to good yields; (ii) it requires only the inexpensive palladium and (iii) it is applicable to a broader substrate scope (various boronic acids and electron-rich and electron-deficient aryl groups).

II. EXPERIMENTAL

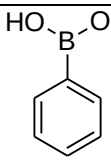
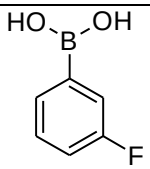
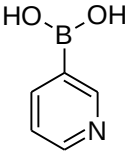
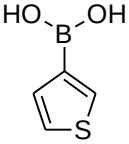
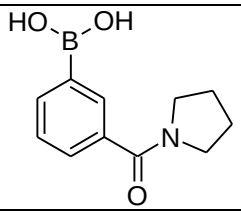
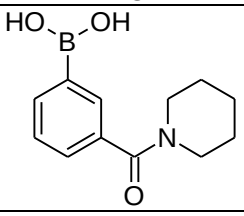
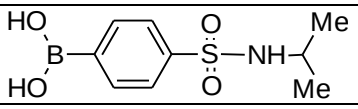
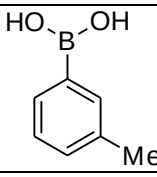
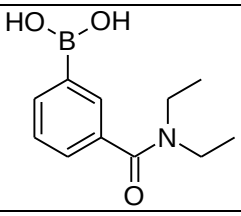
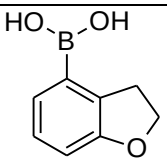
All reagents were purchased from Aldrich, Fluka and/or Merck and were used without further purification unless otherwise stated. All reactions were carried out with dry, freshly distilled solvents under anhydrous conditions or in an inert atmosphere. THF was purified by distillation from sodium in the presence of benzophenone under nitrogen atmosphere. The NMR spectra were collected on a Bruker ACF 400 spectrometer with $CDCl_3$ and

DMSO–d_6 as solvent. Elemental analyses were done in VarioMicro analyzer.

General procedure for the preparation of 4,7-Di-aryl-3-yl-1*H*-indoles (1a-10j)

A mixture of 4,7-dibromoindole (1 mmol), 3-pyridine boronic acid (1 mmol), Bis(triphenylphosphine) palladium (II) chloride (10 mol %), K_2CO_3 (1.5 mmol), 1,4-Dioxane and H_2O (3:1 mL) was heated for 20 min in a 10 mL vessel. The vessel was sealed with a septum and placed inside the microwave cavity in the Biotage microwave reactor and subjected to microwave irradiation. The temperature was fixed at 110 ^{0}C. Initial microwave irradiation of 150W was used; with the temperature being ramped from room temperature to the desired temperature of 110 ^{0}C (measured using the built-in IR temperature device). Once this was reached, the reaction mixture was held at this temperature until a total time of 15 min had elapsed. During this time, the power was modulated automatically to hold the reaction mixture at 110 ^{0}C. The mixture was not stirred during the reaction. In order to cool the reaction mixture vessel, nitrogen gas was passed to the surroundings of the vessel in microwave cavity, and after being cooled to room temperature the reaction mixture was diluted with 10 mL of ethyl acetate and 10 mL of water. The organic layer was separated, washed with brine (20 mL), dried (Na_2SO_4) and the solvent evaporated in vacuo. Purification of the crude product by combiflash chromatography (20% ethyl acetate:hexane) to afford the desired pure coupling product.

Table 1- Palladium–catalyzed coupling reaction of 4,7–dibromo indole and aromatic boronic acids [a]

Entry	Ar–B(OH)$_2$	Time (min)	Yield (%) [b]
1a		18	93
2b		20	98
3c		20	88
4d		19	90
5e		20	95
6f		20	95
7g		20	92
8h		19	88
9i		20	90
10j		20	91

[a]Reaction conditions: 10 mol % palladium (II) chloride, 1.5 mmol K_2CO_3, 1 mmol Ar-B(OH)$_2$, 1 mmol 4,7-dibromo indole, 1,4-Dioxane/water (3:1 mL), under microwave irradiation (110 ^{0}C). [b] Isolated yield.

4,7-Di phenyl-1*H*-indole (1a)

Pale yellow solid; yield 93%; mp 120–121°C. δ_H (400 MHz, MeOD) 6.68 (d, J 2.52, 1H, Indole CH), 7.16–7.23 (m, 2H, Ph CH), 7.25 (s, 1H, Indole CH), 7.30–7.42 (m, 3H, Ph CH), 7.48–7.54 (m, 4H, Ind & Ph CH), 7.67–7.72 (m, 4H, Ph CH). δ_C (100 MHz, MeOD) 100.7, 119.1, 121.4, 124.8, 125.1, 126.3, 126.8, 128.0, 128.1, 128.2, 128.3, 128.5, 133.1, 133.9, 139.3, 141.5. m/z 269.1 (M). Anal. Calcd. for $C_{20}H_{15}N$: C, 89.19; H, 5.61; N, 5.20. Found: C, 89.11; H, 5.57, N, 5.25%.

4,7-Bis-(3-fluoro-phenyl)-1*H*-indole (2b)

Yellow solid; yield 98%; mp 149–150°C. δ_H NMR (400 MHz, $CDCl_3$) 6.82 (d, J 2.2, 1H, Indole CH), 6.83–7.09 (m, 2H, Ph CH), 7.30 (q, J 7.6, 4H, Ind & Ph CH), 7.38–7.43 (m, 5H, Ind & Ph CH), 8.56 (s, 1H, Indole NH). δ_C (100 MHz, $CDCl_3$) 102.6, 113.9, 114.6, 115.7, 120.3, 122.3, 123.9, 124.0, 124.4, 125.1, 126.5, 129.9, 130.7,

130.9, 132.9, 133.9, 141.2, 143.2, 161.8, 164.6. m/z 305.01 (M). Anal. Calc. for $C_{20}H_{13}F_2N$: C, 78.68; H, 4.29; N, 4.59. Found: C, 78.59; H, 4.25; N, 4.48%.

4,7-Diphenyl pyridin-3-yl-1*H*-indole (3c)

White solid; yield 88%; mp 187–190°C. δ_H (400 MHz, MeOD) 6.67 (d, J 4.0, 1H, Indole CH), 7.19 (t, J 4.0, 2H, Indole CH), 7.30–7.33 (m, 3H, Pyridine CH), 7.41–7.45 (m, 3H, Pyridine CH), 7.69 (q, J 8.0, 4H, Pyridine CH). δ_C (100 MHz, MeOD) 100.7, 119.1, 121.4, 124.8, 125.1, 126.3, 126.8, 128.0, 128.1, 128.2, 128.3, 128.5, 133.1, 133.9, 139.3, 141.5. m/z 271.12 (M). Anal. Calcd. for $C_{18}H_{13}N_3$: C, 79.68; H, 4.83; N, 15.49. Found: C, 79.51; H, 4.80; N, 15.61%.

4,7-Di-thiophen-3-yl-1*H*-indole (4d)

Brown solid; yield 90%; mp 128–129ºC. δ_H (400 MHz, DMSO–d_6) 6.78 (s, 1H, Indole CH), 7.29 (q, J 7.6, 2H, Indole CH), 7.42 (s, 1H, Thiophene CH), 7.55 (t, J 4.6, 2H, Indole CH), 7.68 (d, J 3.6, 1H, Thiophene CH), 7.74 (d, J 3.6, 1H, Thiophene CH), 7.83 (dd, J 1.4, 11.6, 2H, Thiophene CH), 11.10 (s, 1H, Indole NH). δ_C (100 MHz, DMSO-d_6) 101.2, 118.7, 119.3, 121.0, 121.6, 121.9, 122.1, 126.2, 126.5, 126.9, 127.0, 127.6, 127.8, 133.2, 138.9, 141.4. m/z 281.3 (M). Anal. Calcd. for $C_{16}H_{11}NS_2$: C, 68.29; H, 3.94; N, 4.98; S, 22.79. Found: C, 68.37; H, 3.90; N, 4.81; S, 22.72%.

(3-{7-[3-(Pyrrolidine-1-carbonyl)-phenyl]-1*H*-indol-4-yl}-phenyl)-pyrrolidin-1-yl-methanone (5e)

Yellow solid; yield 95%; mp 196–198ºC. δ_H (400 MHz, $CDCl_3$) 1.90 (m, 4H, pyrolidine CH_2), 1.92 (m, 4H, pyrolidine CH_2), 3.53 (q, J 7.1, 2H, pyrolidine CH_2), 3.69 (d, J 3.4, 4H, pyrolidine CH_2), 6.71 (s, 1H, Indole CH), 6.78 (t, J 1.2, 3H, Indole CH), 7.27–7.31 (m, 4H, Ph CH), 7.50–7.53 (m, 1H, Indole CH), 7.71–7.73 (m, 1H, Ph), 7.88 (s, 2H, Ph CH), 9.13 (s, 1H, Indole NH). δ_C (100 MHz, $CDCl_3$) 23.4. 25.3, 28.7, 29.9, 30.9, 45.7, 48.7, 64.8, 101.0, 119.1, 121.1, 123.3, 124.6, 124.7, 124.9, 125.1, 125.7, 125.8, 126.2, 127.5, 127.8, 128.1, 128.6, 129.1, 132.1, 132.9, 136.7, 140.1, 168.6, 168.8. m/z 464.1 (M). Anal. Calcd. for $C_{30}H_{29}N_3O_2$: C, 77.73; H, 6.31; N, 9.06. Found: C, 77.81; H, 6.22; N, 9.13%.

(3-{7-[3-(Piperidine-1-carbonyl)-phenyl]-1*H*-indol-4-yl}-phenyl)-piperidin-1-yl-methanone (6f)

White solid; yield 89%; mp 194–196ºC. δ_H (400 MHz, $CDCl_3$) 1.22 (s, 6H, piperidine CH_2), 1.24 (t, J 3.8, 6H, piperidine CH_2), 3.34–3.41 (m, 4H, piperidine N[CH_2]$_2$), 3.59–3.64 (m, 4H, piperidine N[CH_2]$_2$), 6.75 (s, 1H, Indole CH), 7.30 (q, J 3.0, 3H, Indole CH), 7.41–7.46 (m, 4H, Ph CH), 7.72 (d, J 1.8, 4H, Ph CH), 9.13 (s, 1H, Indole NH). δ_C (100 MHz, $CDCl_3$) 24.6, 25.3, 26.5, 30.8, 36.2, 39.5, 39.7, 40.2, 42.0, 48.2, 101.2, 119.9, 122.2, 124.8, 126.9, 127.5, 127.6, 127.7, 127.9, 128.6, 128.7, 132.4, 133.9, 135.4, 135.8, 136.7, 139.8, 142.0, 169.1, 169.2. m/z 491.3 (M). Anal. Calc. for $C_{32}H_{33}N_3O_2$: C, 78.18; H, 6.77; N, 8.55. Found: C, 78.24; H, 6.72; N, 8.63%.

4,7-Di-sulfonyl-3-yl-1*H*-indole (7g)

Yellow solid; yield 92%; mp 101–103ºC. δ_H (400 MHz, MeOD) 1.10–1.12 (m, 12H), 3.32–3.45 (m, 2H), 6.72–6.73 (s, 2H), 7.32–7.39 (m, 3H), 7.91 (d, J 8.6, 4H), 8.03 (d, J 7.4, 4H). δ_C (100 MHz, MeOD) 23.8, 23.9, 102.0, 121.1, 123.3, 125.5, 127.6, 128.2, 128.3, 128.6, 130.0, 130.2, 133.6, 135.2, 141.3, 141.8, 144.6, 146.8. m/z 510.16 (M). Anal. Calc. for $C_{26}H_{29}N_3O_4S_2$: C, 61.3; H, 5.51; N, 7.82. Found: C, 61.03; H, 5.71; N, 8.21%.

4,7-Dim-tolyl-1*H*-indole (8h)

Yellow solid; yield 88%; mp 110–112ºC. δ_H (400 MHz, MeOD) 2.35 (s, 6H, CH_3), 6.66 (d, J 4.0, 1H, Indole CH), 7.14–7.15 (m, 4H, Ph CH), 7.29 (s, 1H, Indole CH), 7.33–7.35 (m, 2H), 7.48 (d, J 8.0, 4H). δ_C (100 MHz, MeOD) 21.6, 102.2, 120.4, 122.7, 126.3, 126.4, 126.5, 126.8, 128.1, 128.4, 128.8, 129.3, 129.8, 130.1, 130.3, 134.6, 135.3, 139.1, 139.6, 140.7, 142.8. m/z 297.15 (M). Anal. Calc. for $C_{22}H_{19}N$: C, 88.77; H, 5.96; N, 3.71. Found: C, 88.73; H, 5.89; N, 3.80%.

4,7-Bis-(3-N,N-diethylbenz- amide)-1*H*-indole (9i)

Brown solid; yield 90%; mp 224ºC. δ_H (400 MHz, DMSO–d_6) 1.64–1.67 (m, 12H, CH_2CH_3), 3.36–3.42 (m, 4H, CH_2CH_3), 3.61 (s, 4H, NCH_2), 6.65 (s, 1H, Indole CH), 6.67 (q, J 1.7, 2H, Ph CH), 7.25 (t, J 7.6, 1H, Indole CH), 7.42–7.51 (m, 4H, Ind & Ph CH), 7.74 (q, J 8.3, 4H, Ph CH), 11.26 (s, 1H, Indole NH). δ_C (100 MHz, DMSO–d_6) 12.9, 14.2, 21.0, 29.2, 39.4, 43.4, 53.4, 60.4, 120.2, 122.1, 124.3, 124.9, 125.4, 126.0, 126.6, 127.8, 128.4, 128.9, 129.2, 129.5, 132.1, 133.3, 133.9, 137.6, 137.9, 139.4, 140.7, 141.3, 171.1, 171.3. m/z 467.1 (M). Anal. Calc. for $C_{30}H_{33}N_3O_2$: C, 77.06; H, 7.11; N, 8.99. Found: C, 77.13; H, 7.03; N, 8.91%.

4,7-Bis-(2,3-dihydro-benzofuran-4-yl)-1*H*-indole (10j)

Brown solid; yield 91%; mp 210ºC. δ_H (400 MHz, DMSO–d_6) 3.28–3.35 (m, 4H, CH_2), 4.59 (q, J 8.4, 4H, OCH_2), 5.75 (s, 1H, Indole CH), 6.59 (q, J 1.8, 2H, Indole CH), 6.89 (q, J 8.2, 2H, Ph CH), 7.05–7.07 (m, 3H, Ind & Ph CH), 7.52 (d, J 3.5, 2H, Ph CH), 10.99 (s, 1H, Indole NH). δ_C (100 MHz, DMSO–d_6) 29.2, 29.3, 71.0, 71.1, 100.9, 108.9, 109.2, 118.8, 121.2, 124.2, 124.9, 125.0, 126.1, 126.3, 127.7, 127.8, 127.9, 129.7, 130.9, 132.0, 133.3, 133.5, 158.9, 159.1. m/z 353.1 (M). Anal. Calc. for $C_{24}H_{19}NO_2$: C, 81.56; H, 5.42; N, 3.96. Found: C, 81.50; H, 5.51; N, 3.99 %.

III. RESULTS AND DISCUSSION

Heating in oil bath and in microwave shows different temperature gradients.[12] In the case of heating with external heat sources as hot oil, for example, the heat comes from the outer environment and becomes less in the inner reaction solution. Otherwise, microwaves directly heat up the reactive centres of the reagents and the solvent, if a dipole moment exists. The reaction vessels used are, in general, transparent to microwaves. In this way the most effective energy transfer can be provided. We first designed a set of commonly used catalysts was selected to screen the coupling reaction between 4,7−dibromo indole 1 and aryl boronic acid, trimethylsilyl acetylene and tributyl vinyltin chloride under oil bath and microwave irradiation. But with indole the Sonogahasira and Heck coupling procedure was unsuccessful. Several bases and conditions were tested for the 4,7−dibromo indole the results were summarized in table 1 and 2. Then finally we have found the alternate route to synthesis of target compounds using Suzuki coupling. We established that the 4,7−dibromo indole can be converted into the corresponding indole derivatives by Suzuki coupling.

Our earlier investigation in the synthesis of 4,7 diaryl indole core by heating in an oil bath at higher reaction temperature were found in poor yield of the desired product and complete consumption of starting materials.[13] Microwave irradiation with heating to 110 ^{0}C for 20 min promoted the formation of the desired indole core **3** in higher yield. It is interesting to note that both microwave irradiation with heating at a low temperature and the reaction flask in an oil bath at high temperature optimal result. The 4,7-disubstituted heterocyclic molecules a-j was obtained in moderate to high yields and the results were summarized in Table 3.

Table 1. Reaction conditions on the Sonogashira coupling by oil bath and microwave.

Entry	Ar	Vinyl	Reaction condition	Results
1	3	TMS	$PdCl_2(PPh_3)_2$, CuI, PPh_3, Et_3N, DMF	a
2	3	TMS	$PdCl_2(PPh_3)_2$, CuI, PPh_3, Et_3N, Toluene	a
3	3	TMS	$PdCl_2(PPh_3)_2$, CuI, PPh_3, Et_3N, THF	a
4	3	TMS	$PdCl_2(PPh_3)_2$, CuI, PPh_3, Et_3N, Dioxane	a
5	3	TMS	$PdCl_2(PPh_3)_2$,CuI, PPh_3, DIPA, Acetonitrile	a
6	3	TMS	$Pd(PPh_3)_4$, CuI, PPh_3, Et_3N, Dioxane	a

[a] no reaction

Table 2. Reaction conditions on the Heck coupling by oil bath and microwave.

Entry	Ar	Vinyl	Reaction condition	Results
1	3	Tributyl vinyl tin	$Pd(PPh_3)_4$, Toluene	a
2	3	Tributyl vinyl tin	$Pd(PPh_3)_4$, Toluene	a
3	3	Tributyl vinyl tin	$Pd_2(dba)_3$, CS_2CO_3, Toluene	a
4	3	Tributyl vinyl tin	$Pd_2(PPh_3)_4$, Dioxane	a
5	3	Trimethyl vinylsilane	$Pd(OAc)_2$, Et_3N, CH_3CN	a
6	3	Trimethyl vinylsilane	$Pd(OAc)_2$, L-proline, Dioxane	a

[a] no reaction

Scheme 1. C–C coupling reaction of 4,7-dibromo indole with boronic acids.

Initially, the coupling reaction of 3 (1 mmol) with 2 (1 mmol) was tried by using bis(triphenylphosphine) palladium(II)chloride (10 mol%) and Cs_2CO_3 (1 mmol) in DMF (3 mL) which gave only 45% maximum yield of the C–C coupled product. After that we increased the loading of Cs_2CO_3 from 1 mmol to 1.5 mmol, which yielded 56% of the product. Further increasing to 2 mmol did not result in any improvement of yield. All the reactions were done under conventional heating in an oil bath at 120°C in 16 h. In this paper, we report the reaction of 4,7−dibromo indole 3 with various heterocyclic boronic acids 2, in 1,4 dioxane/water and in the presence of 15% of bis(triphenylphosphine) palladium(II)chloride, sodium carbonate at 110 ^{0}C for 20 min in microwave conditions.

Table 3. Effect of base on coupling of compound, **1** with boronic acid, **2.**

Entry	Base	Time		Yield %	
		Oil bath (h)	MW (min)	Oil bath	MW
1	Cs_2CO_3	12h	30	33	82
2	CsF	8h	20	12	45
3	Na_2CO_3	10h	20	Trace	25
4	K_3PO_4	12h	30	Trace	Trace
5	K_2CO_3	12h	30	43	91

There was a clear improvement in using microwave heating over conventional heating in all of our studied substrates. The reaction time for microwave-assisted reactions was up to twenty times shorter than for comparable reactions under conventional heating. When the reaction time was shortened, thermal decomposition was also minimized, resulting in higher isolated yields and more simplified product purification. This was also the case for microwave-assisted reactions.

IV. CONCLUSION

In conclusion it can be stated that microwave-assisted preparation of 4,7-diaryl indole derivatives from various boronic acid is superior to currently existing preparation methods. The isolated yields are generally higher and the required Reaction time is significantly (up to 20 times) shorter in comparison with Conventional heating.

V. REFERENCES

[1] (a) Higuchi, K.; Kawasaki, T. Simple indole alkaloids and those with a nonrearranged monoterpenoid unit. Nat. Prod. Rep. 2007, 24, 843-868; (b) Sundberg, R.; Indoles, J. Academic Press; London, 1996.

[2] (a) Alex, K.; Schwarz, N.; Khedkar, V.; Ali, S. I.; Tillack, A.; Michalik, D.; Holenz. J.; Diaz, J. L.; Beller, M. Synthesis of 3-(2-N,N-diethylaminoethoxy) indoles as potential 5-HT6 receptor ligands. Org. Biomol. Chem. 2008, 6, 1802-1807; (b) Suzen, S. Antioxidant activities of synthetic indole derivatives and possible activity mechanisms. Top. Heterocycl. Chem. 2007, 11, 145-178; (c) Brancale, A.; Silvestri, R. Indole, a core nucleus for potent inhibitors of tubulin polymerization. Med. Res. Rev. 2007, 27, 209-238; (d) Lambert, G. A. Preclinical neuropharmacology of naratriptan. CNS Drug Rev. 2005, 11, 289-316; (e) Muller, G. Medicinal chemistry of target family-direct masterkeys. Drug Discovery Today 2003, 8, 681-691.

[3] (a) Humphrey, G. R.; Kuethe, J. T. Practical methodologies for synthesis of indoles. Chem. Rev. 2006, 106, 2875-2911; (b) Cacchi, S.; Fabrizi, G. Synthesis and functionalization of indoles through palladium-catalyzed reactions. Chem. Rev. 2005, 105, 2873-2920.

[4] (a) Miyaura, N. Organoboron compounds. Top. Curr. Chem. 2002, 219, 11-59; (b) Kotha, S.; Lahiri, K.; Kashinath, D. Recent applications of the Suzuki Miyaura cross coupling reaction in organic synthesis. Tetrahedron 2002, 58, 9633-9695.

[5] Miyaura, N.; Suzuki, A. Palladium-catalyzed cross-coupling reactions of organoboron compounds. Chem. Rev. 1995, 95, 2457-2483.

[6] (a) Sainsbury, M. Modern methods of aryl-aryl bond formation. Tetrahedron 1980, 36, 3327-3359; (b) Lioyd-Williams, P.; Giralt, E. Atropisomerism, biphenyls and the Suzuki coupling: peptide antibiotics. Chem. Soc. Rev. 2001, 30, 145-157; (c) Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. Aryl-aryl bond formation one century after the discovery of the Ullmann reaction. Chem. Rev. 2002, 102, 1359-1470.

[7] Kappe, C. O. Angew. Chem., Int. Ed. 2004, 43, 6250-6284.

[8] Nilson, P.; Olofsson, K.; Larhed, M. Microwave-assisted and metal-catalyzed coupling reactions. Top. Curr. Chem. 2006, 266, 103-144.

[9] (a) Lidstrom, P.; Tierney, J.; Wathey, B.; Westman, J. Microwave assisted organic synthesis-a review. Tetrahedron 2001, 57, 9225-9283; (b) Varma, R. S. Solvent-free organic syntheses using supported reagents and microwave irradiation. Green Chem. 1999, 1, 43-55; (c) Varma, R, S.; Naciker, K. P. Synthesis of allylbenzenes by cross-coupling of allyl bromide with arylboronic acids using a palladium chloride and tetraphenylphosphonium bromide intercalated clay catalyst. Green Chem. 1999, 1, 247-249; (d) Gabriel, C.; Garbriel, S.; Grant, E. H.; Halstead, B. S. J.; Mingos, D. M. P. Dielectic parameters relevant to microwave dielectric heating. Chem. Soc. Rev. 1998, 27, 213-224; (e) Caddick, S. Microwave assisted organic reactions. Tetrahedron 1995, 51, 10403-10432.

[10] Cherng, Y. I. Efficient nucleophilic substitution reaction of aryl halides with amino acids under focused microwave irradiation. Tetrahedron 2000, 56, 8287-8289.

[11] Appukkutan, P.; Eycken, E. V. Recent developments in microwave-assisted, transition-metal-catalyzed C-C and C-N bond forming reactions. Eur. J. Org. Chem. 2008, 1133-1155.

[12] Kappe, C. O. Controlled Microwave Heating in Modern Organic Synthesis. Angew. Chem., Int. Ed. 2004, 43, 6250-6284.

[13] Rathikrishnan, K. R.; Indirapriyadharshini, V.K.; Ramakrishna, S.; Murugan, R. 4,7-Diaryl indole-based fluorescent chemosensor for iodide ions Tetrahedron 2011, 67, 4025-4030.