# Microwave-assisted Synthesis of Some New N, N`-Bis-[(2-hydroxy-napthalene-1-yl) Substituted Phenyl-methyl] 4,4`-diaminodiphenyl-Sulphone

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**Abstract: An efficient and easy approach to N,N`-Bis-[(2-hydroxy-napthalene-1-yl) substituted phenylmethyl] 4,4`-diamine diphenyl sulphone derivatives is presented in this study. The products can be obtained both through the traditional method and via the microwave assisted protocol from the condensation of 4,4`-diamine diphenyl sulphone, benzaldehydes derivatives and β-naphthol. The characterization of the newly provided compounds elucidated by spectral methods: FT-IR, $^{1}$H-NMR, $^{13}$C-NMR, and Mass spectral data. Finally, the bis-Bestti bases have been screened for antimicrobial and antifungal activities.**

**Keyword: Bis-Betti Base, 2-Naphthol, Microwave, One-Pot Reaction, Aromatic Aldehydes.**

## 1. Introduction

Mario Betti was discovered a quick and exciting method for the synthesis of aminobenzylnaphthols which is so called Betti-base form the condensation of beta naphthol, benzaldehyde and ammonia (Betti, 1900; Betti, 1941). These kind of bases and their analogues have attracted considerable interest due to their potent, application (Heydenreich *et al.*, 2006) and biological activity (Shen *et al.*, 1999; Salamone *et al.*, 2014), because they are one of the most widely used synthetic aromatic chemicals. Furthermore, their synthetic applications, as well as the preparation of their derivatives have become an interesting and an important field in organic chemistry (Cardellicciho *et al.*, 2010; Szatmari *et al*, 2013). Several routes have been reported for their preparation (Gao *et al.*, 2014; Mou *et al.*, 2017).

The syntheses of a wide-ranging library of racemic and nonracemic Betti base derivatives were recently reviewed, with a special attention to the possibilities of their application as building blocks. These compounds can be transformed into derivatives having antibacterial, hypotensive, and brady cardiac activities. There are very few reports available using Brønsted acid surfactant (Kumar *et al.*, 2010), neutral and efficient non-ionic surfactant (Jha *et al.*, 2006), nano crystalline MgO (Karmakar & Banerhi, 2011) and Cu (OTf)2·SiO2 catalyst (Dindulkar *et al.*, 2012). However, some of these methods suffer from at least one of the following disadvantages: high cost and toxicity of the reagent and solvent, the synthesized and characterized one compound from each type of the compounds aminoalkyl and amidoalkyl naphthols through different methods such as oil bath, microwave irradiation, hot plate with magnetic stirrer and Grindstone chemistry method. Also the reactants used

are aromatic aldehyde (vanillin), 2- naphthol and aromatic amine (4-nitro aniline) or aromatic amide (benzamide) for getting aminoalkyl and amidoalkylnaphthols respectively has been reported (Deepam & Viswanadhan, 2017).

Today there is a string demand for the development of new, efficient, simple, selective, green and ecofriendly method for preparation of the mentioned-compounds and the new studies in this area is growing dramatically. Recently, microwave assisted technique have emerged as viable alternative to the conventional methods in the synthesis of different kinds of organic compounds (Kappe, 2006; Gawande *et al.*, 2014). In this project, a series of new bis-bases diaminobenzylnaphthol-derivatives was produced by using both traditional and microwave-routes, with and without solvent. The interest in this study is systematic comparison of the yield and reaction times. These products exhibit moderate biological-activities.

## 2. Materials and Methods

### 2.1 Experimental Notes

Thin Layer Chromatography (TLC) was carried out by using pre-coated aluminum sheets silica gel. IR-Spectra were recorded on FT-IR spectrophotometer, 1000 (USA) Perkin Elmer (KBr disc). $^{1}$H-NMR and $^{13}$C-NMR spectra were obtained using Ultrashield-500 plus instrument (BRUKER, Germany – 600MHz) spectrometers using DMSO &CDCl3 as a solvent. Mass-Spectra instrument used in this work is ISQ Single Quadrupole MS, Germany. Gas chromatography – mass spectroscopy was recorded on QP 2010 GC instrument (Shimadzu, Japan) for Elemental analysis Euro EA Elemental Analyzer type Euro EA 3000/Italy was used. Melting Point were determined using Automate Melting point System Digital Image Processing Technology Stanford Research Systems.7- The Sonication was performed by Elmasonic type E 30H.The Microwave Irradiation was carried out by domestic microwave oven 900 w,2500MHZ.

### 2.2 General procedure for the synthesis of N,N`-Bis-[(2-hydroxy-napthalene-1-yl) substituted (phenyl)methyl]4,4`diaminodiphenyl sulphone Ia-l:

Method [A] Traditional method:

A mixture of 4,4`diaminodiphenylsulphone (0.6g, 2.5mmol) and substituted aromatic aldehydes (5.0mmol) was dissolved in 10 ml of ethanol , after an appropriate time the formed precipitate was dissolved in THF with 2-naphthol (0.4g, 5.0mmol). The mixture was heated under reflux with stirring for an appropriate time (see Table 1). After completion of the reaction as monitored by TLC (disappearance of reactants), analytical thin layer chromatography was performed using plastic backed TLC extra-hard layer precoated with silica gel (60 $A^{o}$ pore-size, 0.25 mm) and visualized by exposure to iodine vapor. The solvent was removed at reduced pressure by rotatory evaporator. The crude solid residue was recrystallized from ethanol to afford pure crystalline product bis Betti bases (I a-l). The new products were characterized by FTIR, $^{1}$HNMR, $^{13}$CNMR, and CH analysis.

Method [B] Microwave:

Similar mole ratio of the reactants as in method [A] was triturated using mortar and pestle. The mixture was transferred to a (50ml) beaker, then placed vertically in the center of domestic microwave oven, and irradiated for (2-6) minute at high power (900) W the products were sonicated in cold ethanol. The product was filtered through a Buchner-funnel and dried in vacuum desiccator

as described in former method. The obtained products were identified by using spectroscopic techniques as in the previous methods.

The following new compounds were produced using both methods:

(1) N,N`-Bis-[(2-hydroxy-napthalene-1-yl)(pheny)methyl] 4,4`diamino diphenyl sulphone Ia:
Orange solid; yield (0.1g, 5.61%); m.p:230-232 $^{o}$C, recrystallized in ethanol, $R_f$=0.71 (n- hexane: ethyl acetate) (1:4), FT IR (cm-1):3600 (-OH), 3200 (-NH), 3060 (Ar-H), 2970 (-CH), 1630 (C=C), 1105 (CN).$^{1}$H-NMR (δ ppm): 4.0 (s), broad, 2H, NH); 5.0 (s, 2H, OH); 5.3 (s, 2H, CH); 6.6-7.7 ( m, 30 H, Ar-H). $^{13}$C-NMR (δ ppm): 51.3 (C-N); 113.3, 115.4, 118.5, 122.2, 122.8, 125.8, 126.0, 126.9, 127.3, 128.0, 128.3, 128.4, 128.8, 129.0, 133.4, 141.0, 148.0 (C- aromatic); 153.7 (C-OH). Anal.calc.for $C_{46}H_{36}O_4N_2S$: C, 77.52; H, 5.05; N, 3.93; S, 4.49%, found: C, 77.50; H, 5.0; N, 3.8; S, 4.40%

(2) N,N`-Bis-[(2-hydroxy-napthalene-1-yl)2-hydroxy(phenyl)-methyl] 4,4`diaminodiphenylsulphone Ib:
Orange solid; yield (0.5g, 26.88%); m.p:255-257 $^{o}$C, recrystallized in ethanol, $R_f$=0.50 (n-hexane: ethyl acetate) (1:4), IR (cm-1): 3500 (-OH), 3200 (-NH), 3051 (Ar-H), 2970 (-CH), 1617 (C=C), 1150 (C-N). $^{1}$H-NMR (δ ppm): 4.0 (s, broad, 2H, NH); 5.0 (s, 4H, OH); 5.3 (s, 2H, CH); 6.6-7.7 ( m,28H,Ar-H).$^{13}$C-NMR (δ ppm): 41.3 (C-N); 113.3, 115.4, 116.2, 118.2, 121.6, 122.2, 122.8, 125.9, 126.9, 127.3, 127.4, 128.0, 129.8, 130.2, 133.4, 148.5 (C- aromatic); 153.7, 157.2 (C-OH). Anal.calc.for$C_{46}H_{36}O_6N_2S$: C, 74.19; H, 4.83; N, 3.76; S, 4.30%, found: C, 74.02; H, 4.80; N, 3.74; S, 4.27%

(3) N,N`-Bis-[(2-hydroxy-napthalene-1-yl)4-hydroxy(phenyl)-methyl] 4,4`diaminodiphenylsulphone Ic:
Yellow solid; yield (0.2g, 21%); m.p:270-272 $^{o}$C, recrystallized in ethanol, $R_f$=0.22 (n-hexane: ethyl acetate) (1:4), FT-IR (cm-1):3400 (-OH), 3200 (-NH), 3064 (Ar-H), 2912 (-CH), 1595 (C=C) , 1105 (C-N). $^{1}$H-NMR (δ ppm): 2.5 (s, broad, 2H, NH); 5.3 (s, 2H, CH); 6.5-7.8 (m, 28 H, Ar-H); 9.5 (s, 4H, OH). $^{13}$C-NMR (δ ppm): 51.3 (C-N); 113.3, 116.2, 117.6, 118.5, 122.2, 122.4, 122.8, 125.8, 126.9, 127.3, 128.0, 128.7, 129.9, 133.3, 137.0, 148.5 (C- aromatic); 153.7, 154.8 (C-OH). Anal.calc.for$C_{46}H_{36}N_2O_6S$: C, 74.19; H, 4.83; N, 3.76; S, 4.30%, found: C, 74.39; H, 4.18 ; N, 3.20; S, 4.30%

(4) N,N`-Bis - [(2-hydroxy – naphthalene – 1 - yl) 3,4 – dihydroxyl (phenyl) - methyl] 4,4`diamine diphenyl sulphone Id:
Yellow solid; yield (0.1g, 11%); m.p:230-232 $^{o}$C, recrystallized in ethanol, $R_f$=0.56 (n-hexane: ethyl acetate) (1:4), FT - IR (cm-1): 3400 (-OH), 3200 (-NH), 3058 (Ar-H), 2910 (-CH), 1626 (C=C), 1140 (C-N). $^{1}$H-NMR (δ ppm): 4.6 (s, broad, 2H, NH); 5.0 (s, 2H, CH); 6.3-7.8 (m, 26 H, Ar-H); 10.5 (s, 6H, OH). $^{13}$C-NMR (δ ppm): 51.3 (C-N); 113.3, 117.0, 117.6, 118.5, 122.2, 122.4, 122.8, 125.8, 126.9, 127.3, 128.0, 128.7, 133.3, 137.0 (C- aromatic); 142.0. 145.0, 153.7 (C-OH). Anal. calc. for $C_{46}H_{36}O_8N_2S$: C, 71.13; H, 4.63; N, 3.6;S, 4.2%, found: C, 71.01; H, 4.6; N, 3.6;S, 4.2%

(5) N,N`-Bis-[(2-hydroxy-napthalene-1-yl)2-chloro(phenyl)-methyl] 4,4`diaminodiphenylsulphone Ie:
White solid; yield (0.1g, 10.2%); m.p:200-202 $^{o}$C, recrystallized in ethanol, $R_f$=0.33 (n-hexane:ethyl acetate) (1:4), i.r (cm-1): 3600 (-OH), 3200 (-NH), 3060 (Ar-H), 2910 (-CH), 1600 (C=C), 1145 (C-N). $^{1}$H-NMR (δ ppm): 4.0 (s, broad, 2H, NH); 5.0 (s, 2H, OH);5.3 (s, 2H, CH); 6.6-7.7 (m, 28 H, Ar-H). $^{13}$C-NMR (δ ppm): 42.3 (C-N); 113.3, 115.4, 118.2, 122.2, 122.7, 125.9, 126.9, 127.1, 127.3, 127.4, 128.0, 128.7, 129.4, 129.8, 133.3, 133.7, 143.0, 148.0 (C- aromatic); 153.7 (C-OH). Anal.

calc. for $C_{46}H_{34}O_4N_2SCl_2$: C, 70.67; H, 4.35; N, 3.58; S, 4.09%, found: C, 70.44; H, 4.34; N, 3.50; S, 4.0%

(6) N,N`-Bis-[(2-hydroxy-napthalene-1-yl)4-chloro(phenyl)-methyl]4,4`diamino diphenylsulphone If:
Yellow solid; yield (0.1g, 11%); m.p:153-155 $^oC$, recrystallized in ethanol, $R_f$=0.55 (n-hexane: ethyl acetate) (1:4), i.r. (cm-1): 3500 (-OH), 3200 (-NH), 3058 (Ar-H), 2974 (-CH), 1600 (C=C), 1103 (C-N). $^1$H-NMR (δ ppm): 4.0 (s, broad, 2H, NH); 5.0 (s, 2H, OH); 5.2 (s, 2H, CH); 6.6-7.7 (m, 28 H, Ar-H). $^{13}$C-NMR (δ ppm): 51.3 (C-N); 113, 115, 118.5,122.2, 122.8, 125.8, 126.9, 127.3, 128.0, 128.3, 128.8, 129.2, 129.4, 129.8, 131.3, 133.4, 141.0, 148.0 (C- aromatic ); 153.7 (C-OH). Anal. calc. for $C_{46}H_{34}O_4N_2SCl_2$: C, 70.67; H, 4.35; N, 3.58; S, 4.09%, found: C, 70.66; H, 4.35; N, 3.57; S, 4.09%

(7) N,N`-Bis-[(2-hydroxy-napthalene-1-yl)2-fluoro(phenyl)methyl]4,4`diaminodiphenylsulphone Ig: Yellow solid; yield (0.1g,10.7%); m.p:213-215 $^oC$, recrystallized in ethanol, $R_f$=0.85 (n-hexane: ethyl acetate) (1:4), IR (cm-1): 3600 (-OH), 3200 (-NH), 3063 (Ar-H), 2972 (-CH), 1600 (C=C),1145 (C-N). $^1$H-NMR (δ ppm): 4.0 (s, broad, 2H, NH); 5.0 (s, 2H, OH); 5.2 (s, 2H, CH); 6.6-7.7(m,28H,Ar-H). $^{13}$C-NMR (δ ppm): 40.5 (C-N); 113.3, 115.4, 116.5, 118.2, 122.2.122.8, 124.5, 125.9, 126.9, 127.3, 127.6, 128.0, 128.8, 129.2, 129.4, 129.8, 130.3, 133.4, 148.0 (C- aromatic); 153.7 (C-OH); 162.0 (C-F). Anal. calc. for $C_{46}H_{34}O_4N_2SF_2$: C, 73.79; H, 4.54; N, 3.74; S, 4.27%, found: C, 73.70; H, 4.50; N, 3.72; S, 4.20%

(8) N,N`-Bis-[(2-hydroxy-napthalene-1-yl)4-nitro(phenyl)-methyl] 4,4`diaminodiphenylsulphone Ih: Orange solid; yield (0.2g, 20%); m.p:240-242 $^oC$, recrystallized in ethanol, $R_f$=0.57 (n-hexane: ethyl acetate) (1:4), FT IR (cm-1): 3600 (-OH), 3200 (-NH), 3070 (Ar-H), 2910 (-CH), 1600, (C=C) , 1143 (C-N). $^1$H-NMR (δ ppm): 4.0 (s, broad, 2H, NH); 5.0 (s, 2H, OH); 5.3 (s, 2H, CH); 6.5-8.0 (m, 28 H, Ar-H). $^{13}$C-NMR (δ ppm): 51.3 (C-N); 113.0, 115.4, 118.5, 122.2, 122.8, 124.1, 125.9, 127.3, 128.0, 128.8, 129.2, 129.8, 133.4, 148.0, 149.0 (C- aromatic); 145.9 (C-NO2); 153.7 (C-OH). Anal. calc. for $C_{46}H_{34}O_6N_4S$: C, 71.88; H, 4.41; N, 7.27; S, 4.15%, found: C, 71.60; H, 4.20; N, 6.90; S, 4.01%

(9) N,N – Bis - [(2-hydroxy – naphthalene – 1 - yl) – 4 – dimethyl amino (phenyl) methyl] 4,4`diamine diphenyl sulphone Ii:
Yellow solid; yield (0.5g, 50%); m.p:263-265 $^oC$, recrystallized in ethanol, $R_f$=0.285 (n-hexane: ethyl acetate) (1:4), FT IR (cm-1):3467 (-OH), 3200 (-NH), 3086 (Ar-H), 2891 (-CH), 1624 (C=C), 1102 (C-N). $^1$H-NMR (δ ppm):2.9 (s, 12H, $CH_3$); 4.1 (s, broad, 2H, NH); 5.3 (s, 2H, CH); 6.6-7.7 (m, 28 H, Ar-H); 9.7 (s, 2H, OH). $^{13}$C-NMR (δ ppm): 40.16, ($CH_3N$); 52.0 (C-N); 109.0, 111.0, 114.0, 114.4, 121.4, 121.6, 123.6, 126.3, 126.4, 128.4, 128.8, 129.7, 129.8, 130.3, 131.0, 137.6.0, 152.5 (C- aromatic); 156.5 (C-OH). Anal. calc. for $C_{50}H_{44}N_4O_4S$: C, 75.37; H, 5.52; N, 7.03; S, 4.02%, found: C, 75.76; H, 5.25; N, 7.0; S, 4.0%

(10) N,N`-Bis-[(2-hydroxy-napthalene-1-yl)4-methyl(phenyl)-methyl] 4,4`diaminodiphenylsulphone Ij:
Light yellow solid; yield (0.5g, 54%); m.p:257-259 $^oC$, recrystallized in ethanol, $R_f$=0.628 (n-hexane: ethyl acetate) (1:4), FT IR (cm-1):3467 (-OH), 3200 (-NH), 3027 (Ar-H), 2975 (-CH), 1629 (C=C), 1104 (C-N). $^1$H-NMR (δ ppm): 2.3 (s, 6H, $CH_3$); 4.0 (s, broad, 2H, NH); 5.1 (s, 2H, CH); 6.7-7.8 (m, 28 H, Ar-H); 9.3 (s, 2H, OH). $^{13}$C-NMR (δ ppm): 20.9 (CH3); 51.3 (C-N); 113.3, 115.2, 118.5, 122.2, 122.8, 125.8, 126.9, 127.3, 128.0, 128.3, 128.8, 129.8, 133.3, 135.4, 141.0, 148.0 (C-

aromatic); 153.7 (C-OH). Anal. calc. for $C_{48}H_{40}N_2O_4S$: C, 77.83; H, 5.40; N, 3.78; S ,4.33%, found: C, 77.59; H, 4.87; N, 3.6; S ,4.0%

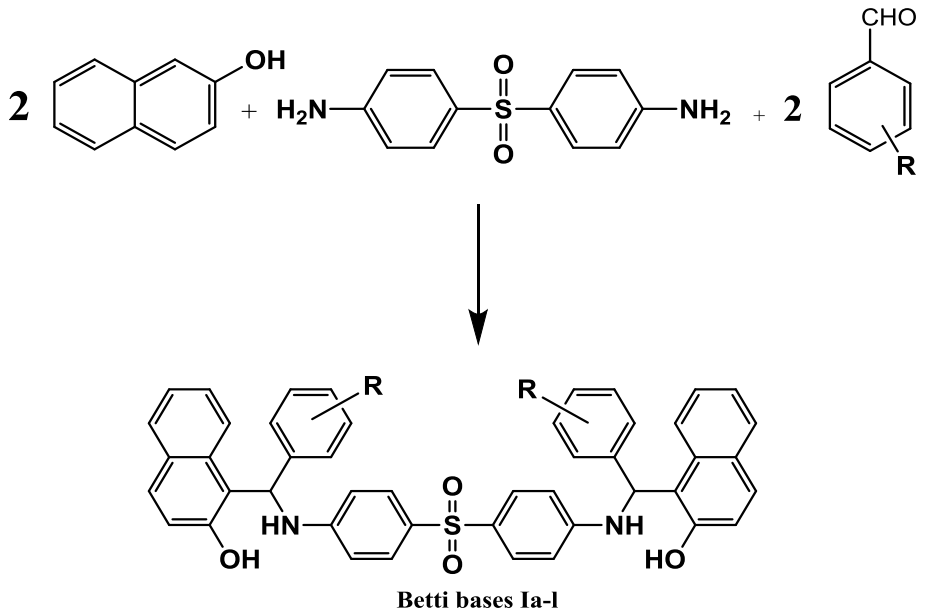
(11) N,N`-Bis-[(2-hydroxy-napthalene-1-yl)4-methoxy(phenyl)-methyl] 4,4`diaminodiphenyl sulphone Ik:
Light yellow solid; yield (0.8g, 82.9%); m.p:220-222 $^oC$, recrystallized in ethanol, $R_f$=0.714 (n-hexane: ethyl acetate) (1:4), FT IR (cm-1):3475 (-OH), 3248 (-NH), 3090 (Ar-H), 2970 (-CH), (C=C), 1631, 1105 (C-N). $^1$H-NMR (δ ppm): 3.9 (s, 6H, $CH_3$); 4.0 (s, broad, 2H, NH); 4.5 (s, 2H, CH); 6.7-8.0 (m, 28 H, Ar-H); 8.3 (s, 2H, OH). $^{13}$C-NMR (δ ppm): 51.3 (C-N); 55.5 (CH3O) 114.2, 114.3, 115.2, 118.5, 121.2, 121.3, 121.5, 128.0, 128.2, 128.3, 128.4, 128.5, 129.8, 131.0, 138.1, 141.0, 148.0 (C- aromatic); 156.8 (C-OH); 161.6 (C-O). Anal. calc. for $C_{48}H_{40}N_2O_6S$: C.74, 61; H, 5.18; N, 3.62; S, 4.14%, found: C,74.60; H, 5.0; N, 3.60; S, 4.03%

(12)N,N`-Bis-[(2-hydroxy-napthalene-1-yl)3-benzyloxy(phenyl)-methyl]4,4` diaminodiphenyl sulphone Il:
Pink solid; yield (0.7g, 36%); m.p:158-160 $^oC$, recrystallized in ethanol, $R_f$=0.11 (n-hexane: ethyl acetate) (1:4), FT IR(cm-1):3600 (-OH), 3200 (-NH), 3062 (Ar-H), 2985 (-CH), 1623 (C=C), 1104 (C-N). $^1$H-NMR (δ ppm): 2.2 (s, broad, 2H, NH); 5.1 (s, 2H, CH); 5.16 ( s, 4H, $CH_2$); 6.5-8.0 (m, 38 H, Ar-H); 8.3 (s, 2H, OH). $^{13}$C-NMR (δ ppm): 60.63 (C-N); 77.3 (CH2-O) 113.2, 113.6, 113.7, 115.5, 120.7, 122.2, 122.8, 125.9, 126.9, 127.3, 127.4, 127.8, 128.0, 128.8, 129.2, 129.4, 129.8, 131.3, 133.4, 141.0, 148.0 (C- aromatic); 153.7 (C-OH); 162.2 (C-O). Anal. calc. for $C_{60}H_{48}O_6N_2S$: C, 77.92; H, 5.19; N, 3.03; S, 3.46%, found: C, 77.72; H, 5.05; N, 3.0; S, 3.45%

## 3. Results and Discussion

Betti base compounds are very important in pharmaceutical and medicinal chemistry, synthesis of bis Betti bases is of great importance as this bi-functional unit is one of the main structural components in biologically essential compounds. Consequently, on the basis of this significant roles, here in after it was thought proper to investigate preparation of different new bis Betti bases Ia-l from the reaction 4,4`diaminodiphenylsulphone, substituted aldehydes and β-naphthol (scheme 1). This kind of reaction might proceed through the imine formation of aldehyde and amine, followed by the attack of beta naphthol. The dehydrative produced-imine is characteristic feature of colloidal dispersions manner. To hit the target, different ways and techniques were followed such as traditional method, microwave-irradiation technique to obtain the products in convenient yields and short reaction time and in order for qualitative and quantitative comparison between the applied methods. The results showed that green methods are fast, clean and efficient, but relatively low yields were achieved in very short reaction times.

Under the framework of green-chemistry it has been described an environmentally benign green synthesis of bis-Betti bases by utilizing microwave and ultrasound. This method incorporates more than one principle of twelve-principles of green – chemistry, less hazardous, safer and energy efficiency (Capello *et al.*, 2007; Byrne *et al.*, 2014). On pursing the studies on the synthesis of betti bases, three elements were the focus of our subsequent investigations. The first one regards the synthesis of is betti bases which expect to be biologically more reactive than mono-product. Second, apply micro-wave technique which is green easy and economical way. Third, introducing of different active substituents and functional groups could be of remarkable interest for their potential biological-activities. Here, our designed strategy was proposed by using sulphone-diamine and benzaldehyde bearing a variety of substituents on different positions (ortho, meta and para positions).




**Betti bases Ia-l**

**R /a=H, b=2-OH, c=4-OH, d=3,4-OH, e=2-Cl, f=4-Cl, g=2-F, h=4-$NO_2$, i=4-$N(CH_3)_2$, j=4-$CH_3$, k=4-$OCH_3$, l=3-$OCH_2$ph**

**Scheme (1)**

Considerable interest has been focused on comparison efficient of two methods together, in traditional method obtained compounds Ia-l by refluxing and stirring between (20-96) hours, while in shorter reaction times: (2-5) minutes with microwave irradiation but yield was low. In classical method the condensation is carried out generally by refluxing the mixture in solvent to produce the target substances.

As mentioned earlier, it was shown that the organic-reactions could be quickly achieved using microwave and ultrasonic-irradiation. Therefore, the desired bis-compounds have been prepared by employing microwave technique without solvents. However, reactions under free-solvent conditions were more conventional technique than classical. Solvents which offer several advantages (Strauss e*t al.*, 1995) are often expensive, toxic, environment polluting agents and difficult to remove in the case of aprotic dipolar solvents which have high boiling points. The structure of synthesized new-compounds was fully characterized by virtue of spectroscopic investigations (ir, $^{1}$H-nmr, $^{13}$C-nmr) and analysis of elements.

Table 1: Percentage of yield and retention time for both methods

| Comp. I | R | Molecular formula | Method[A] | | Method[B] | |
|---|---|---|---|---|---|---|
| | | | Time hr. | Yield % | Time min. | Yield % |
| a | H | $C_{46}H_{36}O_4N_2S$ | 20 | 5.6 | 2 | 5.6 |
| b | 2-OH | $C_{46}H_{36}O_6N_2S$ | 42 | 26.88 | 4 | 20 |
| c | 4-OH | $C_{46}H_{36}N_2O_6S$ | 96 | 21 | 5 | 10 |
| d | 3,4-OH | $C_{46}H_{36}O_8N_2S$ | 72 | 11 | ------ | ----- |
| e | 2-Cl | $C_{46}H_{34}O_4N_2SCl_2$ | 40 | 10.2 | 4 | 10 |
| f | 4-Cl | $C_{46}H_{34}O_4N_2SCl_2$ | 72 | 11 | ------- | ----- |
| g | 2-F | $C_{46}H_{34}O_4N_2SF_2$ | 30 | 10.7 | 3 | 10 |
| h | 4-$NO_2$ | $C_{46}H_{34}O_6N_4S$ | 96 | 20 | 4 | 10 |
| i | 4-$N(CH_3)_2$ | $C_{50}H_{44}N_4O_4S$ | 24 | 50 | 4 | 20 |
| j | 4-$CH_3$ | $C_{48}H_{40}N_2O_4S$ | 24 | 54 | 3 | 54 |
| k | 4-$OCH_3$ | $C_{48}H_{40}N_2O_6S$ | 24 | 82.9 | 3 | 51.8 |
| l | 3-$OCH_2$ph | $C_{60}H_{48}O_6N_2S$ | 92 | 11 | ------ | ------ |

The Infrared spectra show the disappearance of coupled absorption bands at 2750-2850 $cm^{1-}$ which attributed to C-H stretching and overtone of aldehyde hydrogen and appearance of single peak at 3300 $cm^{1-}$ for secondary amine instead of two peaks for primary amine, which indicates that $1^o$ amine is converted to $2^o$ amine. The bands appeared at near 3500 $cm^{1-}$ was assigned to O-H str. Two other bands were observed at about 1600-1630 $cm^{1-}$ and 1102-1150 $cm^{1-}$ for C=C and C-N stretching-vibration respectively; these are good evidence for the formation of expected products. The $^1$H-NMR spectra show the disappearance of singlet signal at 9-10 ppm for proton of aldehyde and more evidence the appearance of a singlet at 2.2 ppm for two symmetrically protons of NH, singlet for four protons of $CH_2$, multiplet at 6.5-8.0 ppm for protons of aromatic rings and a singlet at 8.3 ppm for two protons of OH. On the other hand, the $^{13}$C-NMR spectra are also strong evidence on the composition of the formed compounds.

**4. Evaluation of Antifungal and Antimicrobial Activities**

We have demonstrated that these compounds have different biological activity. The anti-fungal and anti-microbial activities were studied. As it's shown in Table 2 the compounds (1d, 1g, and 1l) showed anti fungal activity against Candida albicaus and Candida parasilopis; in addition the three former active compounds (1a, 1f and 1j) exhibit moderate-activity.

Table 2: Antifungal Activity of synthesized Betti bases 1a-l

| Compounds | Candida albicaus | Candida parasilopis | Compounds | Candida albicaus | Candida parasilopis |
|---|---|---|---|---|---|
| 1a | - | + | 1g | + | + |
| 1b | - | - | 1h | - | - |
| 1c | - | - | 1i | - | - |
| 1d | + | + | 1j | - | + |
| 1e | - | - | 1k | - | - |
| 1f | - | + | 1l | + | + |

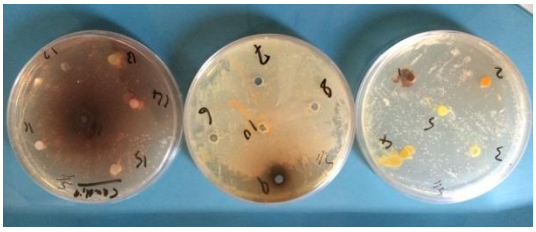


Figure 1: Candida it is fungi

The antibacterial activity results are shown in Table 3. The sensitivity of four kinds of bacteria to different prepared Betti-base-derivatives was carried out using compound disks. The effect of these compounds on described micro-organism are represented in Table 3, there is a significant effect against various bacteria. The most effective compound was 1g against all types of bacteria, the compounds (1a, 1c, 1f, 1j, and 1k) showed the lower sensitivity to the used microorganisms, while in the case of (1b, 1d, 1e, 1h and 1i) showed negative effect (no zone of inhabitation).

Table 3: Antimicrobial activities of synthesized Betti bases against test organism Gram positive and Gram negative

| Compounds | Bactria | | | |
|---|---|---|---|---|
| | Staphylococcus aureus | Bacillus subtilis | Pseudomonas aeruginosa | E-coli |
| 1a | + | - | + | - |
| 1b | - | - | - | - |
| 1c | + | - | + | + |
| 1d | - | - | - | - |
| 1e | - | - | - | - |
| 1f | + | + | + | ++ |
| 1g | +++ | ++ | ++ | +++ |
| 1h | - | - | - | - |
| 1i | - | - | - | - |
| 1j | + | | + | + |
| 1k | - | + | - | + |
| 1l | +++ | - | ++ | - |

Key to symbols (Jarrahpour *et al*, 2004): Highly active++++ (inhibition zone >24 mm); Active +++ (inhibition zone 20-24 mm); Moderately active ++ (inhibition zone 16-20 mm); Slightly active + (inhibition zone 12-16 mm); Inactive - (inhibition zone <12mm);

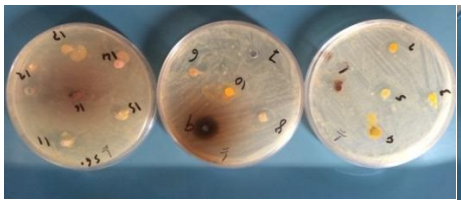


Figure 2: Staphylococcus aureus

Figure 3: Bacillus subtilis

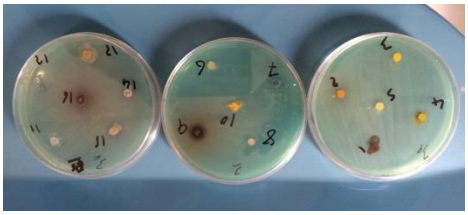


Figure 4: Pseudomonas aeruginosa

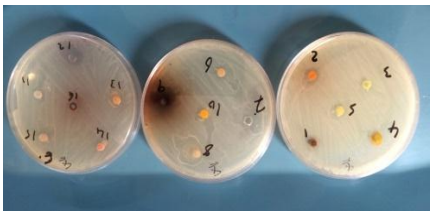


Figure 5: Escherichia coli

## 4. Conclusion

Twelve Bis Betti bases of 2-naphthol were successfully synthesized and purified. Although reflux conditions provided products with higher purity, the use of microwave-assisted conditions was shown to be the most efficient method of synthesizing compounds of this type in terms of atom economy, energy consumption and time required. In general, it has been noted that the Bis-compounds are biologically more sensitive than mono-compounds due to existence of two moiety of active-side.

## 5. Acknowledgement

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## References

Betti, M. (1900). On the addition of benzyl amine to naphthol. *Gazz. Chim. Ital*, *30*, 301-309.

Betti, M. (1941). β-Naphthol phenylaminomethane. *Org Synth Coll*, *1*, 381-3.

Cardellicchio, C., Capozzi, M. A. M., & Naso, F. (2010). The Betti base: The awakening of a sleeping beauty. *Tetrahedron: Asymmetry*, *21*(5), 507-517.

Deepam, A., & Viswanadhan, J. (2017). Green protocols for the one-pot synthesis of vanillin based aminoalkyl and Amidoalkyl Naphthols and their antibacterial activity. *Oriental Journal of Chemistry*, *33*(3), 1354-1365.

Dindulkar, S. D., Puranik, V. G., & Jeong, Y. T. (2012). Supported copper triflate as an efficient catalytic system for the synthesis of highly functionalized 2-naphthol Mannich bases under solvent free condition. *Tetrahedron Letters*, *53*(33), 4376-4380.

Gao, H., Sun, J., & Yan, C. G. (2015). Synthesis of new type of Betti bases via three-component reaction of β-naphthol, cyclic amines and isatins. *Chinese Chemical Letters*, *26*(3), 353-356.

Gawande, M. B., Shelke, S. N., Zboril, R., & Varma, R. S. (2014). Microwave-assisted chemistry: synthetic applications for rapid assembly of nanomaterials and organics. *Accounts of Chemical Research*, *47*(4), 1338-1348.

Heydenreich, M., Koch, A., Klod, S., Szatmári, I., Fülöp, F., & Kleinpeter, E. (2006). Synthesis and conformational analysis of naphth [1′, 2′: 5, 6][1, 3] oxazino [3, 2-c][1, 3] benzoxazine and naphth [1′, 2′: 5, 6][1, 3] oxazino [3, 4-c][1, 3] benzoxazine derivatives. *Tetrahedron*, *62*(48), 11081-11089.

Jha, A., Paul, N. K., Trikha, S., & Cameron, T. S. (2006). Novel synthesis of 2-naphthol Mannich bases and their NMR behaviour. *Canadian Journal of Chemistry*, *84*(6), 843-853.

Kappe, C. O. (2006). The use of microwave irradiation in organic synthesis. From laboratory curiosity to standard practice in twenty years. *CHIMIA International Journal for Chemistry*, *60*(6), 308-312.

Karmakar, B., & Banerji, J. (2011). A competent pot and atom-efficient synthesis of Betti bases over nanocrystalline MgO involving a modified Mannich type reaction. *Tetrahedron Letters*, *52*(38), 4957-4960.

Kumar, A., Gupta, M. K., & Kumar, M. (2010). Non-ionic surfactant catalyzed synthesis of Betti base in water. *Tetrahedron Letters*, *51*(12), 1582-1584.

Mou, J., Gao, G., Chen, C., Liu, J., Gao, J., Liu, Y., & Pei, D. (2017). Highly efficient one-pot three-component Betti reaction in water using reverse zinc oxide micelles as a recoverable and reusable catalyst. *RSC Advances*, *7*(23), 13868-13875.

Salamone, M., Amorati, R., Menichetti, S., Viglianisi, C., & Bietti, M. (2014). Structural and medium effects on the reactions of the cumyloxyl radical with intramolecular hydrogen bonded phenols. The interplay between hydrogen-bonding and acid-base interactions on the hydrogen atom transfer reactivity and selectivity. *The Journal of Organic Chemistry*, *79*(13), 6196-6205.

Shen, A. Y., Tsai, C. T., & Chen, C. L. (1999). Synthesis and cardiovascular evaluation of N-substituted 1-aminomethyl-2-naphthols. *European Journal of Medicinal Chemistry*, *34*(10), 877-882.

Szatmári, I., & Fülöp, F. (2013). Syntheses, transformations and applications of aminonaphthol derivatives prepared via modified Mannich reactions. *Tetrahedron*, *69*, 1255-1278.