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MICROWAVE-ASSISTED SYNTHESIS AND EVALUATION OF ANTIBACTERIAL ACTIVITY OF 2,2'-(NAPHTHALENE-2,7-DIYLBIS(OXY))BIS(N'-SUBSTITUTED ACETOHYDRAZIDE) DERIVATIVES

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ABSTRACT. A series of Schiff base of 2,2'-(naphthalene-2,7-diylbis(oxy))bis(N'-substituted acetohydrazide) (**4a-m**) derivatives has been synthesized by the acid catalyzed condensation of aryl/hetero aromatic aldehydes with 2,2'-(naphthalene-2,7-diylbis(oxy))diacetohydrazide (**3**) under microwave irradiation and conventional method for comparison. The structures of all the newly synthesized compounds have been characterized by IR, ^{1}H NMR, ^{13}C NMR and Mass spectra. All the synthesized compounds have been screened for their in vitro antibacterial activity.

KEY WORDS: 2,2'-(Naphthalene-2,7-diylbis(oxy))diacetohydrazide, Schiff base, Microwave irradiation, Spectral characterization, Antibacterial activity

INTRODUCTION

The chemistry of the carbon-nitrogen double bond plays a vital role in the advancement of synthetic organic chemistry. Schiff bases are usually synthesized by the condensation of primary amines with compounds containing active carbonyl groups. Schiff bases are an important class of compounds in medicine and pharmaceutics. They show biological applications including antibacterial [1-6], antifungal [3-6], antitumor [7, 8], antioxidant [9, 10], anti-inflammatory [11], antihypertensive [12], anti-HIV [13], antifilarial [14], anticonvulsant [15], herbicidal, insecticidal, schistosomicidal and anthelmintic activities [16]. Schiff bases are used as protective agents in natural rubber [17]. Recently there has been a considerable interest in the chemistry of hydrazine and hydrazone compounds because of their potential pharmacological applications [18]. The remarkable reactivity of acid hydrazides R–CONHNH$_2$ [19] and the biological activity associated with their corresponding hydrazones attributed to the presence of the active pharmacophore (-CONH-N=CH-). Hence many hydrazone compounds containing this active moiety are known to exhibit good anticancer bioactivities according to the literature [20]. Some of the Schiff bases complex combinations with metals are used as insecticides, fungicides, herbicides [21].

Microwave-assisted organic synthesis (MAOS) has been known since 1986 [22]. This "non-conventional" synthetic method has shown broad applications as a very efficient way to accelerate the course of many organic reactions, producing high yields and higher selectivity, lower quantities of side products and consequently, easier work-up procedures and purification of the products. MAOS is considered as "green" technology, principally since many organic reactions can be carried out in solvent-free conditions [23]. In recent years, researchers have applied microwave as a tool in order to reduce reaction time, avoid side products, increase yield and simplify the course of reaction for combinatorial chemistry [24]. Solvent-free reactions are of interest not only from an ecological point of view but in many cases they also offer considerable advantages in terms of yield, selectivity and simplicity.

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In many cases reactions that normally require many hours at reflux temperature under normal synthetic conditions can be completed within several minutes or even seconds in a microwave oven. Recent simplification of microwave organic reaction enhancement (MORE) technique has increased safety and practical utility of the microwave oven for their use in organic laboratories without any modification.

Hence, in this paper, we are reporting eco-friendly synthesis of some new Schiff bases by condensing 2,2'-(naphthalene-2,7-diylbis(oxy))diacetohydrazide with aryl/hetero aromatic aldehydes using microwave irradiation technique and the yields are compared with traditional method and their characterization carried out using IR, ^{1}H NMR,^{13}CNMR and Mass spectra. All the synthesized compounds have been screened for their antibacterial activity.

EXPERIMENTAL

Screening of antibacterial activity

The newly synthesized Schiff base compounds **(4a-m)** were screened for their antibacterial activity against *Escherichia coli* (ATTC-25922) (*E. coli*), *Staphylococcus aureus* (ATTC-25923) (*S. aureus*) and *Pseudomonas aeruginosa* (ATCC-27853) (*P. aeruginosa*) bacterial strains by agar well diffusion method in Muller Hinton agar medium. Twenty milliliters of agar media was poured into each Petri dish and plates were dried by placing in an incubator at 37 °C for an hour. Using a punch, wells were made on these seeded agar plates and concentrations of the test compounds in dimethylsulfoxide (DMSO) were added into each labelled well. A control was also prepared for the plates in the same way using solvent DMSO. All the plates were incubated at 37 °C for 24 hrs for incubation. The degree of effectiveness was measured by determining the diameters of the zone of inhibition caused by the compounds. Activity of each compound was compared with standard drug tetracycline which is available in the market.

General

All reagents were purchased from Aldrich, SD Fine Chemicals and Qualigens and used without further purification. For the microwave irradiation experiments described below a conventional (unmodified) household microwave oven equipped with a turntable was used (LG, MG-395 WA, 760 W) and operating at 2450 MHz. The melting points were determined by open capillaries and are uncorrected. Infrared (IR) spectra were recorded at room temperature from 4000 cm^{-1} to 400 cm^{-1} with KBr pellets at a resolution of 4 cm^{-1}, using Avatar 330 equipped with DTGS detector. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AV-500 MHz, spectrometer in DMSO-d_6, $CDCl_3$ using TMS as internal standard and the values are expressed in ppm. Mass spectra were obtained by using HRMS.

*Procedure for the preparation of compound diethyl 2,2'-[naphthalene-2,7-diylbis(oxy)]di acetate (**2**)*

To a solution of 2,7-dihyroxy naphthalene (**1**) (1.0 molar equiv.) in dry DMF, anhydrous potassium carbonate (2.0 molar equiv.) and ethyl chloroacetate (2.0 molar equiv.) were added. The resultant mixture was stirred at 80 °C for 16 h, cooled and then it was poured into a large amount of water. The solid separated was filtered and washed with excess of water. The crude product was recrystallized from ethanol. Yield of the product was 81-82% [lit. yield 40%] [25]. M.p. 92-94 ºC; IR (KBr) ν_{max}: 3258, 2917, 1760, 1654, 1628, 1518, 1384, 1204, 1173, 1076, 1024 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, ppm), δ_H = 7.71 (d, 2H, *J* = 9.0 Hz , C-4,5 ArH of naphthalene ring), 7.12 (dd, 2H, *J* = 2.5 and 9.0 Hz, C-3,6 ArH of naphthalene ring), 6.99 (d,

2H, *J* = 2.5 Hz, C-1,8 ArH of naphthalene ring), 4.73 (s, 4H, OCH_2), 4.31 (q, 4H, *J* = 7.25 Hz, $COOCH_2$), 1.33 (t, 6H, *J* = 7.25 Hz, CH_3); ^{13}C NMR (125.757 MHz, $CDCl_3$, ppm), δ_C = 168.84, 156.51, 135.36, 129.47, 125.26, 116.48, 106.74, 65.51, 61.43, 14.17; HRMS (EI): *m/z* [M^+] calcd. for $C_{18}H_{20}O_6$: 332.1260; found: 332.1254.

*Procedure for the preparation of compound 2,2'-[naphthalene-2,7-diylbis(oxy)]diaceto hydrazide (**3**)*

Compound **2** (0.01 mole) in ethanol (20 mL) were stirred at room temperature for 20 min. To this mixture hydrazine hydrate (0.03 mol) was added and stirring continued for 15 more min. The resultant mixture was refluxed for 6 h and the separated solid was filtered using a sintered glass funnel. The residue was dried and then desiccated to afford a crystalline powder. The powder was recrystallized from chloroform/methanol and gave half white solid. Yield of the product was 88-90%. M.p. 232-234 ºC; IR (KBr) ν_{max}: 3311, 3206, 3029, 2923, 1699, 1622, 1471, 1385, 1212, 1174, 1060 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, ppm), δ_H = 9.41 (s, 2H, NH), 7.76 (d, 2H, *J* = 9.0 Hz, C-4,5 ArH of naphthalene ring), 7.04-7.16 (m, 4H, C-1,3,6,8 ArH of naphthalene ring), 4.86 and 4.96 (2s, 4H, OCH_2), 4.58 (s, 4H, NH_2); ^{13}CNMR (125.757 MHz, DMSO-d_6, ppm), δ_C = 169.15, 167.03, 156.76, 156.54, 135.72, 129.68, 129.54, 124.81, 116.84, 116.76, 107.13, 107.01, 66.72, 65.17; HRMS (EI): *m/z* [M^+] calcd. for $C_{14}H_{16}N_4O_4$: 304.1172; found: 304.1169.

General procedure for the preparation of compound 2,2'-[Naphthalene-2,7-diylbis(oxy)]bis [N'-substituted acetohydrazide] (4a-m)

Method A. A mixture of compound 2,2'-(naphthalene-2,7-diylbis(oxy))diacetohydrazide **3** (0.01 mol) in chloroform/methanol (1:1) mixture (30 mL), aryl/hetero aromatic aldehyde (0.02 mole) and 1mL of glacial acetic acid was refluxed for 4-5 h. The mixture was allowed to cool; the solid separated was filtered, washed with excess of methanol and then dried at room temperature.

Method B. A mixture of 2,2'-(naphthalene-2,7-diylbis(oxy))diacetohydrazide **3** (0.01 mol), aryl/hetero aromatic aldehyde (0.02 mol) and catalytic amount of glacial acetic acid were taken in DMSO (2 mL) in a beaker and then the reaction mixture was subjected to microwave irradiation at an interval of 1 min at 180 W for about 1-2 min; progress of the reaction was monitored by TLC. After the completion of the reaction, the obtained product was poured into ice cold water stirred well and the solid separated was filtered, washed with excess of methanol and then dried at room temperature.

*2,2'-[Naphthalene-2,7-diylbis(oxy)]bis[N'-benzylideneacetohydrazide] (**4a**)*. M.p. 199-201 ºC; IR (KBr) ν_{max}: 3432, 3091, 2925, 1691, 1629, 1399, 1259, 1070 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-*d6*, ppm), δ_H = 11.61 (t, 2H, *J* = 8.25 Hz, NH), 8.34 (d, 1H, *J* = 22.0 Hz, N=CH), 8.03 (d, 1H, *J* = 10.5 Hz, N=CH), 7.69-7.83 (m, 6H, *o*-ArH of bezylidene ring and C-4,5 ArH of naphthalene ring), 7.41-7.53 (m, 6H, *m*,*p*- ArH of bezylidene ring), 7.05-7.26 (m, 4H, C-1,8 and C-3,6 ArH of naphthalene ring), 5.25 (d, 2H, *J* = 11.0 Hz, OCH2), 4.77 (d, 2H, *J* = 13.0 Hz, OCH_2); ^{13}C NMR (125.757 MHz, DMSO-d_6, ppm), δ_C = 169.36, 164.64, 157.24, 157.15, 156.81, 156.70, 148.47, 144.34, 144.26, 135.94, 135.85, 134.46, 130.64, 130.38, 129.57, 129.51, 129.41, 129.39, 129.29, 129.24, 128.83, 127.60, 127.42, 124.74, 124.55, 116.79, 116.55, 107.17, 106.99, 106.91, 67.07, 65.25; HRMS (EI): *m/z* [M+] calcd. for $C_{28}H_{24}N_4O_4$: 480.1798; found: 480.1784.

2,2'-[Naphthalene-2,7-diylbis(oxy)]bis[N'-(4-chlorobenzylidene)acetohydrazide] ***(4b)***. M.p. 236-238 ºC; IR (KBr) ν_{max}: 3428, 3091, 2979, 1689, 1630, 1514, 1402, 1308, 1206, 1178, 1088 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, ppm), δ_H = 11.67 (d, 2H, *J* = 12.0 Hz, NH), 8.33 (d, 1H, *J* = 14.0 Hz, N=CH), 8.02 (d, 1H, *J* = 9.5 Hz, N=CH), 7.70-7.71 (m, 6H, *o*-ArH of bezylidene ring and C-4,5 ArH of naphthalene ring), 7.47-7.60 (m, 4H, *m*-ArH of bezylidene ring), 7.04-7.24 (m, 4H, C-1,8 and C-3,6 ArH of naphthalene ring), 5.24 (d, 2H, *J* = 11.5 Hz, OCH_2), 4.77 (d, 2H, *J* = 12.0 Hz, OCH_2); HRMS (EI): *m/z* [M+] calcd. for $C_{28}H_{22}Cl_2N_4O_4$: 548.1018; found: 548.1015.

2,2'-[Naphthalene-2,7-diylbis(oxy)]bis[N'-(4-methoxybenzylidene)acetohydrazide] ***(4c)***. M.p. 189-191 ºC; IR (KBr) ν_{max} 3424, 3059, 2913, 1678, 1605, 1540, 1509, 1445, 1384, 1253, 1170, 1084 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, ppm), δ_H = 11.46 (t, 2H, *J* = 12.75 Hz, NH), 8.29 (s, 1H, N=CH), 7.97 (d, 1H, *J* = 10.5 Hz, N=CH), 7.74-7.82 (m, 2H, C-4,5 ArH of naphthalene ring), 7.62-7.68 (m, 4H, *o*-ArH of bezylidene ring), 7.04-7.25 (m, 4H, C-1,8 and C-3,6 ArH of naphthalene ring), 6.97-7.01 (m, 4H, *m*-ArH of bezylidene ring), 5.21 (d, 2H, *J* = 12.0 Hz, OCH_2), 4.74 (d, 2H, *J* = 13.5 Hz, OCH_2); 3.79 (d, 6H, *J* = 8.5Hz, OCH3); HRMS (EI): *m/z* [M+] calcd. For $C_{30}H_{28}N_4O_6$: 540.2009; found: 540.2004.

2,2'-[Naphthalene-2,7-diylbis(oxy)]bis[N'-(2,4-dichlorobenzylidene)acetohydrazide] ***(4d)***. M.p. 230-232 ºC; IR (KBr) ν_{max}: 3432, 3091, 2925, 1691, 1629, 1399, 1259, 1070 cm-1; ^{1}H NMR (500 MHz, DMSO-d_6, ppm), δ_H = 11.83 and 11.92 (2d, 2H, *J* = 9.0 and 9.5 Hz, NH), 8.36 & 8.71 (d and s, 1H, *J* = 10.0 Hz, N=CH), 7.96 and 8.05 (d & t, 1H, *J* = 8.5 and 9.0 Hz, N=CH), 7.70-7.83 (m, 4H, *o*-ArH of bezylidene ring and C-4,5 ArH of naphthalene ring), 7.44-7.52 (m, 2H, *m*-ArH of bezylidene ring), 7.05-7.26 (m, 6H, C-1,8 and C-3,6 ArH of naphthalene ring and *m*-ArH of bezylidene ring), 5.26 (d, 2H, *J* = 12.0 Hz, OCH_2), 4.79 (d, 2H, *J* = 12.0 Hz, OCH_2); HRMS (EI): *m/z* [M+] calcd. for $C_{28}H_{20}Cl_4N_4O_4$: 618.0209; found: 618.0209.

2,2'-[Naphthalene-2,7-diylbis(oxy)]bis[N'-(4-(dimethylamino)benzylidene)acetohydrazide] ***(4e)***. M.p. 220-222 ºC; IR (KBr) ν_{max}: 3443, 2926, 1664, 1604, 1520, 1368, 1213, 1169, 1068 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, ppm), δ_H = 11.30 (split peak, 2H, NH), 8.19 (s, 1H, N=CH), 7.90 (d, 1H, *J* = 11.5 Hz, N=CH), 7.64-7.81 (m, 2H, C-4,5 ArH of naphthalene ring), 7.49-7.54 (m, 4H, *o*-ArH of bezylidene ring), 7.03-7.25 (m, 4H, C-1,8 and C-3,6 ArH of naphthalene ring), 6.70-6.77 (m, 4H, *m*-ArH of bezylidene ring), 5.19 (d, 2H, *J* = 12.0 Hz, OCH2), 4.71 (d, 2H, *J* = 14.5 Hz, OCH2), 2.98 (q, 12H, *J* = 19.0 Hz, CH3); ^{13}C NMR (125.757 MHz, DMSO-d_6, ppm), δ_C = 168.74, 168.72, 163.91, 160.26, 157.29, 157.21, 156.86, 156.74, 152.05, 151.89, 151.84, 149.31, 145.18, 145.08, 135.97, 135.86, 129.95, 129.64, 129.53, 129.48, 129.37, 128.94, 128.68, 124.69, 124.50, 121.82, 116.76, 116.48, 112.24, 112.16, 107.15, 106.94, 67.13, 65.27; HRMS (EI): *m/z* [M+] calcd. for $C_{32}H_{34}N_6O_4$: 566.2642; found: 566.2640.

2,2'-[Naphthalene-2,7-diylbis(oxy)]bis[N'-(4-ethoxy-3-methoxybenzylidene)acetohydrazide] ***(4f)***. M.p. 169-171 ºC; IR (KBr) ν_{max}: 3442, 3061, 2927, 1679, 1634, 1513, 1466, 1391, 1266, 1139, 1080 cm-1; ^{1}H NMR (500 MHz, DMSO-d_6, ppm), δ_H = 11.48 (q, 2H, *J* = 16.0 Hz, NH), 8.26 (s, 1H, N=CH), 7.94 (d, 1H, *J* = 12.0 Hz, N=CH), 7.74-7.82 (m, 2H, C-4,5 ArH of naphthalene ring), 7.29-7.34 (m, 2H, *o*'-ArH of bezylidene ring), 7.04-7.23 (m, 6H, C-1,3,6,8 ArH of naphthalene ring and *o*-ArH of bezylidene ring), 6.95-7.00 (m, 2H, *m*-ArH of bezylidene ring), 5.24 (d, 2H, *J* = 14.0 Hz, OCH_2), 4.74 (d, 2H, *J* = 15.0 Hz, OCH_2), 4.01-4.07 (m, 4H, OCH_2 of ethoxy group), 3.78 (t, 6H, *J* = 5.0 and 10.5 Hz, OCH_3), 1.33 (q, 6H, *J* = 6.75 Hz, CH_3); HRMS (EI): *m/z* [M+] calcd. For $C_{34}H_{36}N_4O_8$: 628.2533; found: 628.0453.

2,2'-[Naphthalene-2,7-diylbis(oxy)]bis[N'-(3-nitrobenzylidene)acetohydrazide] (***4g***). M.p. 251-253 ºC; IR (KBr) ν_{max}: 3429, 3190, 3043, 2920, 1676, 1628, 1385, 1255, 1169, 1067 cm-1; ^{1}H NMR (500 MHz,DMSO-d_6, ppm), δ_H = 11.85 (t, 2H, *J* = 16.0 Hz, NH), 8.46-8.51 (split peak, 2H, N=CH), 8.12-8.24 (m, 6H, *o*- and *p*-ArH of bezylidene ring), 7.67-7.82 (m, 4H, *m*-ArH of bezylidene ring and C-4,5 ArH of naphthalene ring), 7.06-7.23 (m, 4H, C-1,8 and C-3,6 ArH of naphthalene ring), 5.30 (d, 2H, *J* = 12.5 Hz, OCH_2), 4.80 (d, 2H, *J* = 12.5 Hz, OCH_2); HRMS (EI): *m/z* [M+] calcd. for $C_{28}H_{22}N_6O_8$: 570.1499; found: 570.1495.

2,2'-[Naphthalene-2,7-diylbis(oxy)]bis[N'-(3-ethoxy-4-ydroxybenzylidene)acetohydrazide] (***4h***). M.p. 210-212 ºC; IR (KBr) ν_{max}: 3369, 3070, 2989, 1668, 1598, 1511, 1438, 1394, 1284, 1167, 1070 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, ppm), δ_H = 11.42 (t, 2H, *J* = 16.5 Hz, NH), 9.48 (d, 1H, *J*= 3.0 Hz, OH), 9.41 (d, 1H, *J* = 11.0 Hz, OH), 8.21 (s, 1H, N=CH), 7.89 (d, 2H, *J* = 11.0 Hz, N=CH), 7.74-7.80 (m, 2H, C-4,5 ArH of naphthalene ring), 7.05-7.28 (m, 8H, *o*-ArH of bezylidene ring and C-1,8 and C-3,6 ArH of naphthalene ring), 6.81-6.85 (q, 2H, *J* = 8.25 Hz, *m*-ArH of bezylidene ring), 5.21 (d, 2H, *J* = 13.0 Hz, OCH_2), 4.73 (d, 2H, *J* = 13.5 Hz, OCH_2), 4.00-4.05 (m, 4H, OCH_2 of ethoxy), 1.28-1.36 (m, 6H, CH_3); HRMS (EI): *m/z* [M+] calcd. for $C_{32}H_{32}N_4O_8$: 600.2220;found: 600.2219.

2,2'-[Naphthalene-2,7-diylbis(oxy)]bis[N'-(4-hydroxy-3-methoxybenzylidene) acetohydrazide] (***4i***). M.p. 216-218 ºC; IR (KBr) ν_{max}: 3445, 3048, 2993, 2432, 1661, 1606, 1513, 1437, 1291, 1163, 1077, 1027 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, ppm), δ_H = 11.42 (t, 2H, *J* = 17.5 Hz, NH), 9.51 (split peak, 2H, OH), 8.23 (s, 1H, N=CH), 7.91 (d, 1H, *J* = 9.5 Hz, N=CH), 7.74-7.80 (m, 2H, C-4,5 ArH of naphthalene ring), 7.04-7.23 (m, 8H, *o,o*'-ArH of bezylidene ring and C-1,8 and C-3,6 ArH of naphthalene ring), 6.82 (t, 2H, *J* = 8.5 and 8.5 Hz, *m*-ArH of bezylidene ring), 5.23 (d, 2H, *J* = 13.0 Hz, OCH_2), 4.74 (d, 2H, *J* = 13.5 Hz, OCH_2), 3.79 (split peak, 6H, OCH_3); HRMS (EI): *m/z* [M+] calcd. for $C_{30}H_{28}N_4O_8$: 572.1907; found: 572.1905.

2,2'-[Naphthalene-2,7-diylbis(oxy)]bis[N'-(3-methylbenzylidene)acetohydrazide] (***4j***). M.p. 227-229 ºC; IR (KBr) ν_{max}: 3417, 3262, 3070, 2989, 1668, 1598, 1438, 1394, 1284, 1167, 1080 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, ppm), δ_H = 11.58 (d, 2H, *J* =15.0 Hz, NH), 8.30 (s, 1H, N=CH), 7.99 (d, 1H, *J* = 12.5 Hz, N=CH), 7.75-7.82 (m, 2H, C-4,5 ArH of naphthalene ring), 7.46-7.55 (m, 4H, *o*-ArH of bezylidene ring), 7.04-7.34 (m, 8H, *m,p*-ArH of benzylidene ring and C-1,8 and C-3,6 ArH of naphthalene ring), 5.24 (d, 2H, *J* = 12.5 Hz, OCH_2), 4.76 (d, 2H, *J* = 14.0 Hz, OCH_2), 2.33 (t, 6H, *J* =7.75 Hz, CH_3); HRMS (EI): *m/z* [M+] calcd. for $C_{30}H_{28}N_4O_4$: 508.2111; found: 508.2108.

2,2'-[Naphthalene-2,7-diylbis(oxy)]bis[N'-(4-ethoxybenzylidene)acetohydrazide] (***4k***). M.p. 218-220 ºC; IR (KBr) ν_{max}: 3421, 3069, 2927, 1676, 1606, 1511, 1392, 1253, 1170, 1070 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, ppm), δ_H = 11.47 (q, 2H, *J* = 11.25 Hz, NH), 8.28 (s, 1H, N=CH), 7.96 (d, 1H, *J* = 10.5 Hz, N=CH), 7.74-7.82 (m, 2H, C-4,5 ArH of naphthalene ring), 7.61-7.67 (m, 4H, *o*-ArH of bezylidene ring), 7.04-7.25 (m, 4H, C-1,8 and C-3,6 ArH of naphthalene ring), 6.94-6.99 (m, 4H, *m*-ArH of bezylidene ring), 5.21 (d, 2H, *J* = 12.0 Hz, OCH_2), 4.74 (d, 2H, *J* = 13.5 Hz, OCH2), 4.02-4.079 (m, 4H, OCH_2 of ethoxy group), 1.32-1.35 (m, 6H, CH3); HRMS (EI): *m/z* [M+] calcd. for $C_{32}H_{32}N_4O_6$: 568.2322; found: 568.2320.

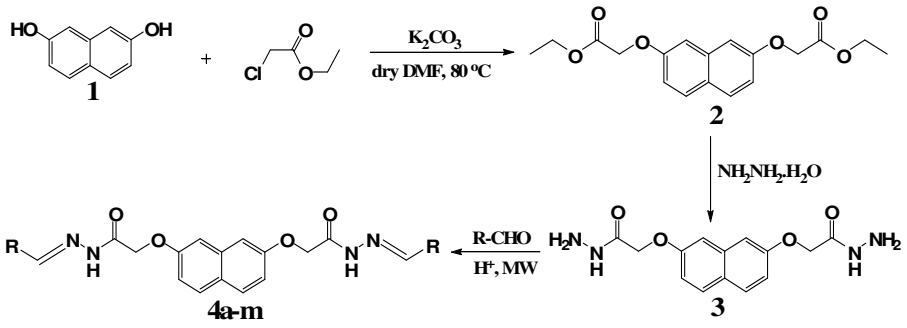
2,2'-[Naphthalene-2,7-diylbis(oxy)]bis[N'-(3-phenylallylidene)acetohydrazide] (***4l***). M.p. 221-223 ºC; IR (KBr) ν_{max}: 3450, 3053, 2922, 1701, 1623, 1526, 1374, 1206, 1060 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, ppm), δ_H = 11.51 (t, 2H, *J* = 11.0 Hz, NH), 8.13 (d, 1H, *J* = 4.0 Hz, N=CH), 7.75-7.87 (m, 3H, C-4,5 ArH of naphthalene ring and N=CH), 7.59-7.62 (m, 4H, *o*-ArH of bezylidene ring), 7.28-7.41 (m, 6H, *m,p*-ArH of bezylidene ring), 7.05-7.24 (m, 8H, C-

1,8 and C-3,6 ArH of naphthalene ring and CH=CH), 5.14 (d, 2H, *J* = 9.0 Hz, OCH2), 4.75 (d, 2H, *J* = 10.0 Hz, OCH_2); 13C NMR (125.757 MHz, DMSO-d_6, ppm), δ_C = 168.99, 164.48, 157.17, 157.11, 150.36, 146.87, 146.79, 139.80, 139.48, 139.41, 136.30, 129.56, 129.41, 129.30, 127.58, 127.52, 125.91, 125.46, 116.74, 116.54, 107.12, 106.87, 106.81,67.02, 65.13; HRMS (EI): *m/z* [M+] calcd. for $C_{32}H_{28}N_4O_4$: 532.2111; found: 532.2109.

*2,2'-[Naphthalene-2,7-diylbis(oxy)]bis[N'-(thiophen-2-ylmethylene)acetohydrazide] (**4m**)*. M.p. 162-164 ºC; IR (KBr) ν_{max}: 3431, 3105, 2928, 1686, 1631, 1425, 1266, 1170, 1073 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, ppm), δ_H = 11.57 (q, 2H, *J* = 14.5 Hz, NH), 8.57 (s, 1H, N=CH), 8.21 (d, 1H, *J* = 11.0 Hz, N=CH), 7.74-7.82 (m, 2H, C-4,5 ArH of naphthalene ring), 7.61-7.67 (m, 2H, C-5 ArH of thiophene ring), 7.44-7.46 (m, 2H, C-3 ArH of thiophene ring), 7.03-7.25 (m, 6H, C-1,8 and C-3,6 ArH of naphthalene ring and C-4 ArH of thiophene ring), 5.14 (d, 2H, *J* = 10.5 Hz, OCH_2), 4.75 (d, 2H, *J* = 12.5 Hz, OCH_2); ^{13}C NMR (125.757 MHz, DMSOd_6, ppm), δ_C = 168.98, 164.47, 157.20, 156.77, 156.66, 143.63, 139.48, 139.42, 139.29, 139.10, 135.81, 131.60, 131.01, 130.95, 129.66, 129.56, 129.42, 129.05, 129.00, 128.33, 124.75, 116.74, 116.56, 107.24, 107.18, 106.92, 106.86, 67.08, 65.02; HRMS (EI): *m/z* [M+] calcd. For $C_{24}H_{20}N_4O_4S_2$: 492.0926; found: 492.1065.

RESULTS AND DISCUSSION

In the present study, diethyl 2,2'-(naphthalene-2,7-diylbis(oxy))diacetate (**2**) was synthesized from 2,7-dihydroxy naphthalene **1** on reacting with ethyl chloroacetate in anhydrous potassium carbonate and dry DMF at 80ºC for 16 hours resulting in 82% yield (Scheme 1) [25]. The IR spectrum of compound **2** exhibited absorption frequency at 1760 cm^{-1} for carbonyl group. In ^1H NMR of compound **2** the characteristic signals of an ester moiety confirm the presence of ester group in the structure by resonating as quartet and triplet for -CH_2 and -CH_3 at δ 4.31 ppm and δ 1.32 ppm respectively, which indicates acetate formation. Treatment of compound **2** with hydrazine hydrate in ethanol and refluxing for 6 hours resulted in the formation of 2,2'-(naphthalene-2,7-diylbis(oxy))diacetohydrazide **3**. The structure of compound **3** was confirmed by IR, ^1H NMR and Mass spectra. IR spectrum showed the absence of ester stretching frequency, instead it gave band at 1699 cm^{-1} for carbonyl group and showed two sharp bands in the region of 3311 and 3206cm^{-1} due to -NH and –NH_2 groups.



Scheme 1. Synthetic pathway for the preparation of compounds **4a**-**m**.

Table 1. Data of synthesized Schiff base compounds **4a-m**.

Entry	R	Reaction time (min)		Yield[a] (%)		M.p. (ºC)
		MW	Conventional	MW	Conventional	
4a	Phenyl	1.0	180	90	83	199-201
4b	4-ClPh	1.5	210	88	80	236-238
4c	4-CH_3OPh	1.0	210	87	80	189-191
4d	2,4-ClPh	1.5	240	85	76	230-232
4e	4-$N(CH_3)_2$Ph	1.5	240	86	77	220-222
4f	4-OEt,3-CH_3OPh	1.5	240	83	75	169-171
4g	3-NO_2Ph	2.0	240	85	77	251-253
4h	3-OEt,4-OHPh	1.5	210	84	76	210-212
4i	4-OH,3-CH_3OPh	1.5	210	83	75	216-218
4j	3-CH_3Ph	1.5	240	86	79	227-229
4k	4-EtOPh	1.0	210	87	80	218-220
4l	Cinnamyl	2.0	240	82	73	221-223
4m	2-Thiophenyl	1.5	210	84	78	162-164

[a] = Isolated yield; MW = Microwave.

^{1}H NMR spectrum of compound **3** exhibited no peak corresponding to ester, instead it showed signals at δ 9.41 ppm and δ 4.58 ppm for -NH and -NH_2 of hydrazide.

Compound **3** was treated with substituted aromatic aldehyde in presence of catalytic amount of acetic acid in (1:1) methanol/chloroform mixture and DMSO under reflux temperature and microwave irradiation to synthesise 2,2'-(naphthalene-2,7-diylbis(oxy))bis(N'-substituted acetohydrazides **4a-m**. The IR spectra of the compound **4a** revealed two strong absorption bands at 1629 cm^{-1} and 1691 cm^{-1} for C=O and C=N group respectively. The ^{1}H NMR spectra of compound (**4a**) displayed two doublets due to methylene protons at δ 5.25 & 4.77 ppm and the NH group was resonated as triplet at δ 11.61 ppm. The peaks of naphthalene aromatic and phenyl group protons appeared between 7.05-7.83 ppm. The signals belonging to -N=CH protons were observed as doublets at δ 8.03 & 8.34 ppm, the disappearance of NH_2 signal of compound **3** in compound **4a** indicates the functionalization of hydrazide to hydrazone. The structures of all the new Schiff base derivatives (**4a-m**) were confirmed by the spectral characterization using FT-IR, ^{1}H NMR, ^{13}C NMR and mass spectra. Shorter reaction times were observed for the formation of compounds **4a-m** under microwave irradiation rather than the reflux temperature. Reaction time for the formation of compound **4a** is one minute under microwave irradiation and 180 minutes under reflux temperature with slightly improved yields, respectively. Comparative yields of all the synthesized products with respect to reaction time and reflux temperature as well as microwave irradiation and are given in Table 1.

The newly synthesized Schiff base compounds **(4a-m)** were screened for their antibacterial activity against *E. coli*, *S. aureus* and *P. aeruginosa* bacterial strains by agar well diffusion method in Muller Hinton agar medium. Zone of inhibition was determined for all the newly synthesized compounds and the results are summarized in Table 2. The synthesized compounds **4h** and **4i**, having 3-ethoxy-4-hydroxybenzylidene and 3-methoxy-4-hydroxybenzylidene ring as substitute **R** showed potent activity against *S.aureus*, *E.coli* and *P.aeruginosa*, whereas the compounds **4d** and **4l**, having 3-nitro benzylidene and cinnamyl ring as substitute R showed least activity against *S.aureus*, *E.coli* and *P.aeruginosa*. The compounds **4a**, **4b, 4c, 4f** and **4m** showed good activity against *E.coli*, *S.aureus* and *P.aeruginosa*. The compound **4e** also showed good activity against *E.coli* and moderate activity against *S.aureus* and *P.aeruginosa*. The above results indicate that the compounds containing electron donating groups show good activity than the compounds containing electron withdrawing groups and the results were depicted in Table 2.

Table 2. Antibacterial activities of the Schiff base compounds **4a-m**.

Compound	Antibacterial activity[a] (MIC, mg/mL)		
	S. aureus	*E. coli*	*Ps. aeruginosa*
4[a]	8 (250)	8 (250)	9 (500)
4b	11 (500)	8 (250)	8 (250)
4c	8 (250)	9 (250)	9 (250)
4d	10 (750)	11 (500)	9 (500)
4e	9 (500)	12 (500)	9 (500)
4f	9 (250)	9 (250)	10 (250)
4g	10 (500)	8 (500)	8 (500)
4h	12 (250)	11 (250)	8 (250)
4i	19 (250)	15 (250)	9 (250)
4j	9 (500)	10 (750)	8 (500)
4k	10 (500)	8 (500)	9 (500)
4l	11 (750)	8 (500)	10 (500)
4m	9 (250)	9 (250)	9 (500)
Tetracycline[b]	14 (250)	16 (250)	12 (250)

[a]zone of inhibition in mm; [b]Standard antibacterial drug.

CONCLUSIONS

In this work, the synthesis of naphthalene substituted Schiff base derivatives **4a-m** derived from 2,2'-(naphthalene-2,7-diylbis(oxy))diacetohydrazide **3** with aromatic/hetero aldehyde in presence of acid catalyst under conventional heating and by the use of microwave irradiation, is reported. The advantages of the method employed include simple reaction set-up, high product yield, short reaction times and use of small amount of solvents or no solvents. The structures of the synthesized compounds have been confirmed through spectral characterization such as IR, ^{1}H NMR, ^{13}C NMR and mass spectra. From the antibacterial screening carried out, it is observed that compounds **4a-m** exhibited activity which is comparable with activity of standard drug.

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