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Synthesis of novel products from the reaction of benzaldehyde and benzoic acid derivatives with aromatics carrying two hydroxyl groups under microwave irradiation

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Original Research

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Abstract:

The bond-forming of Carbon-heteroatom and carbon-carbon are the spinal columns for synthetic organic chemistry. Today, scientists constantly attempt to establish novel approaches for such bond-forming reactions based on green chemistry since they are valuable instruments for synthesizing molecular entities with diverse structures. An effective one-pot four-component method was studied for the synthesis of (5-hydroxy-2,4-dipheny-2H-benzo[e][1,3]oxazin-3(4H)-yl)(phenyl)methanone derivatives by the condensation reaction of Resorcinol with various aromatic aldehydes, carboxylic acids, and ammonia. The reaction was carried out in an aqueous medium under reflux/ microwave irradiation conditions with short reaction times, resulting in high yields. The chemical structures of all synthesized compounds were determined using elemental analysis, FT-IR, ^{1}HNMR, and ^{13}CNMR spectroscopies.

Keywords: Heterocyclic compounds; 1,3-oxazines; synthesis

1. Introduction

The FDA databases indicate the structural significance of nitrogen-driven heterocyclic in pharmaceutical engineering and drug design. Almost one nitrogen heterocyclic is included in 75% of unique small-molecule drugs [1]. Among heterocycles, oxazines have appealed significant interest as a result of their biological and pharmacological activities compared with cephalexin and ciprofloxacin as they are biodegradable agrochemicals [2], antimicrobial [3, 4], antifungal [5], antitumor [6], anti-HIV [7], anticancer [8], anti-inflammatory [9, 10], analgesic [11], antimalarial [12], antiulcer agents, anticonvulsant drug, anesthetic agent and herbicides [13] and anti-inflammatory properties potential inhibitors of human Chk1 kinase [14]. The compound Sustiva (Efavirenz), also known as (S)-6-chloro-4-cyclopropylethynyl-1,4-dihydro-4-trifluoromethyl-2H-[3,1]-benzoxazin-2-one, features the 1,3-oxazine nucleus (Figure. 1). Efavirenz is a non-nucleoside reverse transcriptase inhibitor (NNRTI) that gained approval from the US FDA in 1998 and is currently in clinical use [15] (Figure 1). DNA-PK inhibitors such as chromone 2 (NU7441), 3 (KU0060648), and quinolinone 3 also contain the 1,3-oxazine nucleus (Fig. 1) and have significant therapeutic potential as agents for enhancing the effects of chemotherapy and radiotherapy in cancer treatment by blocking DNA double-strand break repair [16].
The rise of microbial resistance to existing antimicrobial drugs has become a significant cause for concern in treating microbial infections [17]. This current scenario underscores the pressing need to explore the development of new chemical compounds that offer improved effectiveness and lowest side effects [18, 19]. Consequently, discovering novel molecules capable of providing enhanced reliability and effi-

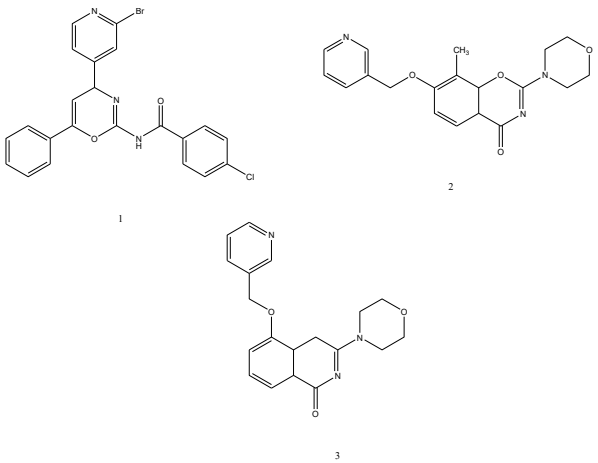


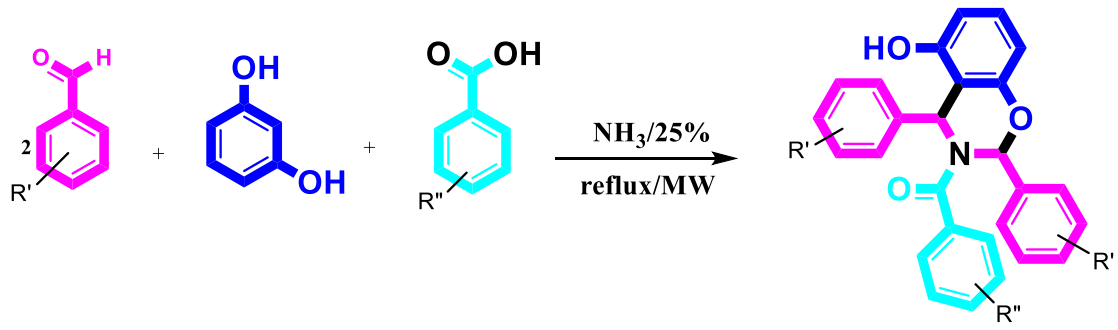
Figure 1. Several newly synthesized structures are reported.

cacy presents an ongoing challenge for medicinal chemists. Therefore, chemists continually seek methods to synthesize new antibacterial compounds with reduced side effects and increased effectiveness. These methods include molecular docking, rational design, and the production of new homopiperazine-linked imidazol[1,2-a] pyrimidine products, as demonstrated by Mantipally et al [20]. Another approach is the synthesis of novel 1,3-oxazine derivatives with antibacterial activity, as explored by Zinad et al [21]. In this study, we aimed to produce efficient heterocyclic compounds. To achieve this, we synthesized derivatives of (5-hydroxy-2,4-diphenyl-2H-benzo[e][1,3]oxazin-3(4H)-yl)(phenyl)methanone through a one-pot, four-component reaction involving benzaldehyde, benzoic acid derivatives, resorcinol, and ammonia (as illustrated in Scheme 1). These (5-hydroxy-2,4-diphenyl-2H-benzo[e][1,3]oxazin-3(4H)-yl)(phenyl)methanone derivatives were successfully synthesized under solvent-free conditions and also using reflux/microwave methods, offering shorter reaction times. Furthermore, microwave irradiation was employed to expedite various organic syntheses, leveraging its ability to enhance thermal conductivity.

2. Results and discussion

The benzaldehyde derivatives with substitutions in the aromatic ring (i.e., H, 3-NO_2, 4-dimethylamine,4-OMe, and 4-OH groups) were reacted with benzoic acid derivatives with substitution in the aromatic ring (i.e.4-OH and H) in the presence of resorcinol and ammonia under reflux and solvent-free conditions. As listed in Table 1, ten bioactive (5-hydroxy-2, 4-diphenyl-2H-benzo[e] [1,3] oxazin-3(4H)-yl)(phenyl) methanone derivatives were synthesized, and their characteristics have been studied. According to Table 1, N_9 and N_3 products achieved the highest yield of 96%, 91% respectively, under solvent-free and reflux conditions. The synthesis time of N_9 product was 27 min, while N_3 reached its highest yield in 55 min. N_{19} exhibited the lowest yield among the synthesized products, with a moderate yield of 43% in 60 min. The rest of the products achieved exceptionally high yields, 68% to 84%, in less than 70 min.

As can be observed in N_5 and N_9 reaction pathways,



1. R′= H, 4-dimethylamino, 3-OH, 4-OMe, 4-Me, 4-OH, 3-NO2.
2. R″= H , 4-OH.

Scheme 1. One-pot Synthesis (5-hydroxy-2,4-diphenyl-2H-benzo[e][1,3]oxazin-3(4H)-yl) (phenyl)methanone derivatives.

Table 1. synthesized bioactive (5-hydroxy-2,4-diphenyl-2H-benzo[e][1,3]oxazin-3(4H)-yl)(phenyl)methanone derivatives and their characteristics.

No	Product	R'	R"	Reaction time (min)	Yield (%)*	Melting point (°C)
1	N_1	H	H	50	75	157-159
2	N_{11}	4-OH	H	43	79	201-203
3	N_5	4-$N(CH_3)_2$	H	25	83	232-234
4	N_7	3-OH	H	65	73	215-217
5	N_8	4-OMe	H	65	77	204-206
6	N_9	4-Me	H	27	96	195-197
7	N_3	H	4-OH	55	91	186-188
8	N_{14}	4-OH	4-OH	70	84	189-192
9	N_{17}	3-NO_2	4-OH	23	68	218-220
10	N_{19}	4-Me	4-OH	60	43	198-200

*Isolated yield of the pure product.

electron-donating groups (EDG) on aldehyde functional groups significantly decreased reaction time while achieving a very high yield. On the other hand, in the reactions including 4-OH substitute on acid groups (N_3, N_{14}, and N_{19} products), EDGs on aldehyde functional groups caused a substantial rise in reaction time. In contrast, electron-withdrawing groups (EWG) on aldehyde significantly increase the reaction time (N_{17} product).

Next, novel (4-hydroxy-1,3-diphenylisoindolin-2yl) (phenyl) methanone derivatives were synthesized under the microwave irradiation condition (Table 2). Table 2 presents the short times and high yields obtained under microwave with a power of 385 W in return conventional method.

The IR spectra of the bioactive (5-hydroxy-2,4-diphenyl-2H-benzo[e][1,3]oxazin-3(4H)-yl)(phenyl)methanone derivatives was investigated. The IR spectrum of all the synthesized compounds revealed the absorption band at 500 to 850 cm^{-1} for aromatic groups (asymmetric bending vibration). It also showed the adsorption band at 1000 to 1350 cm^{-1} for C-N groups (stretching vibration). The adsorption band for C=O groups (stretching vibration) was observed at 1600 to 1620 cm^{-1}. Lastly, The IR spectrum revealed the absorption band at 3000 to 3500 cm^{-1} for O-H groups (stretching vibration).

The ^{1}H NMR spectra analysis was carried out to analyze the synthesized products′ characteristics further. In ^{1}HNMR spectra, a singlet peak was displayed by all the products at about δ 6.24-7.28 ppm for aliphatic hydrogen, which shifted to the left due to its proximity to the nitrogen and benzene ring. The chemical shift of Alcohol protons of all products was observed at δ 10.10-11.18 ppm. The aromatic protons were also detected at the expected areas (δ 6.05 – 8.24 ppm) (4).^{1}HNMR spectrum of the N_5 product exhibited signals at δ 3.59 ppm, characteristic of the protons of methyl amino groups. ^{1}HNMR spectrum of the N_8 product revealed signals at δ 3.97 and 4.09 ppm for the protons of methoxy groups shifted to the left due to their connection with oxygen. ^{1}HNMR spectrum of the N_9 compound displayed singlet signals at δ 2.11 and 2.30 ppm, showing characteristics of the protons of methyl groups. ^{1}HNMR spectrum of the N_{19} product revealed singlet signals at δ 2.18 and 2.38 ppm for the protons of methyl groups connected to a benzene ring.

The ^{13}CNMR spectra analysis was investigated to analyze the synthesized products′ characteristics further. In ^{13}CNMR spectra, a signal was observed by all the compounds at about 164.6-179.1 ppm for N-C=O as well as a signal at about 42.3-53.4 ppm for -CH_3 group and 49.1-54.8 ppm for R_2N-CH. The aromatic group carbons were also detected at 108.8-164.6 ppm for all the products, which was to be expected. The ^{13}CNMR spectra analysis also displayed signals around 150 ppm, corresponding

Table 2. Comparison of yield and reaction time under microwave and reflux conditions.

			Conventional method		Microwave method	
No	R2	R1	Time(min)	Yield (%)*	Time(min)	Yield (%)*
1	H	H	50	75	7	81
2	4-OH	H	43	79	4	80
3	4-$N(CH_3)_2$	H	25	83	2	89
4	3-OH	H	65	73	7	81
5	4-OMe	H	65	77	5	79
6	4-Me	H	27	96	2	98
7	H	4-OH	55	91	3	97
8	4-OH	4-OH	70	84	7	85
9	3-NO_2	4-OH	23	68	2	78
10	4-Me	4-OH	60	43	6	51

*Isolated yield of the pure product.

to the carbons attached to the alcohol group for all the compounds. The ^{13}CNMR spectrum of the N_5 product revealed a signal at 44.6 and 46.1 ppm for the carbons of methyl amino groups. The ^{13}CNMR spectrum of the N8 product exhibited signals at 65.1 and 66.2 ppm, which are characteristic of the carbons of the methoxy groups. Lastly, the ^{13}CNMR spectrum of N_9 and N_{19} compounds showed signals for the protons of methyl groups at 43.2 and 43.7 ppm, respectively.

3. Experimental sections

Melting points were defined and uncorrected with a thermal digital apparatus. Thin-layer chromatography (TLC) of Polygram's SIL/UV 245 and 366 were utilized to control the progress of the reaction. An elemental analysis experiment for all the synthesized compounds (C, H, N, and O) was carried out by an elemental analysis system GmbH-Vario EL V.3 micro-analyzer. The Elemental analysis data of (5-hydroxy-2,4-diphenyl-2H-benzo[e][1,3]oxazin-3(4H)-yl)(phenyl)methanone derivatives was listed in Table 3. Fourier Transform Infrared (FT-IR) spectra were obtained by a Bruker instrument Series FT-IR 5000 spectrophotometer in KBr. A Bruker 300 spectrometer recorded the NMR (Nuclear magnetic resonance) spectra, and utilizing TMS as an internal standard, chemical shifts were provided in ppm in DMSO-d_6. Microwave reactions were carried out in a multi-synth series microwave system (Milestone). Materials, reagents, and solvents were purchased and used at the highest laboratory-grade quality by Sigma-Aldrich and Merck without further purification unless otherwise stated in the procedure.

3.1 General Synthesis Procedure of (5-hydroxy-2, 4-diphenyl-2H-benzo[e] [1,3] oxazin-3(4H)-yl)(phenyl)methanone derivatives

A combination of benzoic acid derivatives (1 mmol), aromatic aldehyde derivatives (2 mmol), resorcinol (1 mmol), and a quantity of ammonia %25 (5ml) were heated under reflux/microwave irradiation (385w) for a proper time (Scheme 2). Thin-Layer Chromatography (TLC) controlled the reaction progress by utilizing n-hexane-ethyl acetate (1:1) as an eluent, and cooling the reaction mixture was performed at room temperature after the competition. The rest of the solid was filtered, then dried, and recrystallized using chloroform or ethanol. The proposed reaction mechanism is shown in Scheme 3.

3.2 The spectral data of selected products

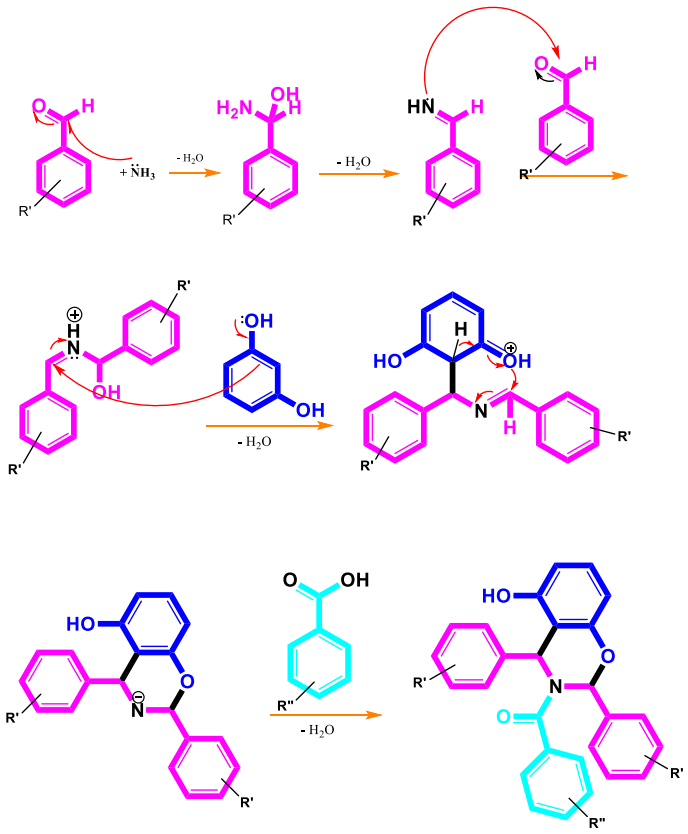
(5-hydroxy-2,4-diphenyl-2H-benzo[e][1,3]oxazin-3(4H)-yl)(phenyl)methanone (N_1). MP: 157–159 °C; IR (KBr) υ: 3777, 3706, 3004, 2921, 2774, 2670, 2351, 1611, 1497, 1448, 1301, 1227, 1104, 842, 750, 701 cm^{-1}; ^{1}HNMR (DMSO-d_6, 300 MHz, TMS) σ: 7.23 (s, 1H, CH), 7.25 (s, 1H, CH), 6.10-7.94 (m , 18H, Ar-H), 10.79 (s, 1H, OH) ppm; ^{13}CNMR (75 MHz, DMSO-d_6, TMS) σ: 53.6(C_4), 54.1(C_3), 121.8 (C_2), 123.2 (C_{20}), 123.9 (C_{21}), 124.3 (C_8), 125.8 (C_{17}), 126.2 ($C_{11,11'}$) ,126.7 (C_{19}), 128.3 ($C_{6,6'}$), 129.8 ($C_{15,15'}$), 130.5 ($C_{12,12'}$), 132.4 ($C_{7,7'}$), 135.4 ($C_{16,16'}$), 135.8 (C_{13}), 140.1 (C_{10}), 143.4 (C_5), 145.3 (C_{14}), 147.1 (C_1), 149.3 (C_{18}), 164.6 (C=O) ppm. Anal. Calcd for $C_{27}H_{21}NO_3$: C, 79.59; H, 5.19; N, 3.44. Found: C, 79.84; H, 5.41; N, 3.58.

(5-hydroxy-2,4-diphenyl-2H-benzo[e][1,3]oxazin-3(4H)-yl)(4-hydroxyphenyl)methanone (N_3). MP: 186–188 °C; IR (KBr) υ: 3433, 2859, 2374, 1610, 1507, 1446, 1289, 1215, 1095, 845, 753, 703, 568 cm^{-1}; ^{1}HNMR (DMSO-d_6, 300 MHz, TMS) σ: 7.29 (s, 1H, CH), 7.32 (s, 1H, CH), 6.31-7.81 (m , 18H, Ar-H), 10.27 (s, 1H, OH) ppm; ^{13}CNMR (75 MHz, DMSO-d_6, TMS) σ:49.1 (C_4), 50.7 (C_3), 111.2 (C_2), 114.5 (C_{20}), 117.0 (C_{21}), 117.6 (C_8), 118.2 (C_{17}), 120.6 ($C_{11,11'}$), 123.6 (C_{19}), 129.5 ($C_{6,6'}$), 130.0 ($C_{15,15'}$), 133.7 ($C_{12,12'}$), 134.5 ($C_{7,7'}$), 136.8 ($C_{16,16'}$), 138.7 (C_{13}), 140.1 (C_{10}), 140.6 (C_5), 143.4 (C_{14}), 150.7 (C_1), 152.3 (C_{18}), 165.7 (C=O) ppm. Anal. Calcd for $C_{27}H_{21}NO_4$: C, 76.58; H, 5.00; N, 3.31. Found: C, 76.59; H, 5.19; N, 3.44.

(2,4-bis(4-(dimethylamino)phenyl)-5-hydroxy-2H-benzo[e][1,3]oxazin-3(4H)-yl)(phenyl) methanone (N_5). MP: 232–234 °C; IR (KBr) υ: 3743, 3438, 2378, 2313, 1600, 1516, 1448, 1355, 1168, 941, 814, 725, 641cm^{-1}; ^{1}HNMR (DMSO-d_6, 300 MHz, TMS) σ: 7.24 (s, 1H, CH), 7.26 (s, 1H, CH), 3.59 (s, 12H, CH_3), 6.46-7.93 (m , 16H, Ar-H), 10.10 (s, 1H, OH) ppm; ^{13}CNMR (75 MHz, DMSO-d_6, TMS) σ: 44.6 (CH_3),46.1 (CH_3), 54.6 (C_4), 54.8 (C_3), 120.1 (C_2), 121.1 (C_{20}), 121.3 ($C_{7,7'}$), 123.7 ($C_{16,16'}$), 123.9 (Ctextsubscript21), 125.5 ($C_{11,11'}$), 128.2 (C_{19}), 130.3 ($C_{12,12'}$), 131.0 ($C_{6,6'}$), 136.6 ($C_{15,15'}$), 136.8 (C_{13}), 137.8 (C_5), 138.0 (C_{14}), 139.2 (C_{10}), 140.4 (C_1),

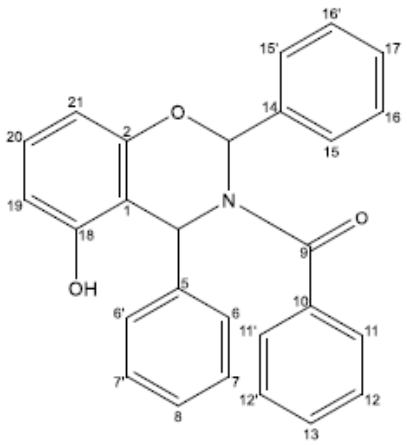
Table 3. Elemental analysis calculated (found) of (5-hydroxy-2,4-diphenyl-2H-benzo[e][1,3] oxazin-3(4H)-yl) (phenyl) methanone derivatives 1-10.

No.	Product	C	H	N
1	N_1	79.59(79.84)	5.19(5.41)	3.44(3.58)
2	N_{11}	73.79(73.58)	4.82(5.00)	3.19(3.31)
3	N_5	75.43(75.96)	6.33(6.54)	8.51(8.80)
4	N_7	73.79(73.58)	4.82(5.00)	3.19(3.31)
5	N_8	74.50(74.14)	5.39(5.58)	3.00(3.10)
6	N_9	79.98(79.03)	5.79(6.01)	3.22(3.34)
7	N_3	76.58(76.59)	5.00(5.19)	3.31(3.44)
8	N_{14}	71.20(71.79)	4.65(4.82)	3.08(3.19)
9	N_{17}	63.16(63.19)	3.73(3.85)	8.18(8.45)
10	N_{19}	77.14(77.98)	5.58(5.79)	3.10(3.22)



R′ = H, 4-OH, 4-N(CH$_3$)$_2$, 3-OH, 4-OMe, 4-Me, 3-NO$_2$
R″= H, 4-OH

Scheme 2. Proposed mechanism [29].



Scheme 3. Show carbon number for ^{13}CNMR spectral data.

147.9 (C_8), 149.6 (C_{17}), 153.1 (C_{18}), 177.6 (C=O) ppm. Anal. Calcd for $_{31}H_{31}N_3O_3$: C, 75.43; H, 6.33 ; N, 8.51. Found: C, 75.96; H, 6.54; N, 8.80.

(5-hydroxy-2,4-bis(3-hydroxyphenyl)-2H-benzo[e][1,3]oxazin-3(4H)-yl)(phenyl)methanone (N_7). MP: 215–217 °C; IR (KBr) υ: 3233, 2178, 1908, 1762, 1649, 1448, 1194, 984, 856, 781, 573 cm^{-1}; ^{1}HNMR (DMSO-d_6, 300 MHz, TMS) σ: 7.11 (s, 1H, CH), 7.12 (s, 1H, CH), 6.10-7.81 (m , 15H, Ar-H), 10.83, (s, 1H, OH) ppm; 11.19 (s, 1H, OH) ppm; ^{13}CNMR (75 MHz, DMSO-d_6, TMS) σ: 50.3 (C_4), 51.2 (C_3), 108.8 (C_2), 111.2 (C_8), 112.4 (C_{17}), 114.5 (C_6), 115.9 ($C_{15'}$), 117.0 (C_{20}), 117.8 ($C_{6'}$), 120.8 (C_{15}), 123.2 (C_{16}), 123.7 (C_{21}), 126.2 ($C_{11,11'}$), 127.0 (C_{19}), 128.6 ($C_{12,12'}$), 129.8 (C_{13}), 131.4 ($C_{7'}$), 132.8 (C_{10}), 134.9 (C_5), 136.8 (C_{14}), 137.3 (C_1), 148.1 (C_{18}), 151.4 (C_7), 152.8 ($C_{16'}$), 165.3 (C=O) ppm. Anal. Calcd for $C_{27}H_{21}NO_5$: C, 73.79; H, 4.82 ; N, 3.19. Found: C, 73.58; H, 5.00 ; N, 3.31.

(5-hydroxy-2,4-bis(4-methoxyphenyl)-2H-benzo[e][1,3]oxazin-3(4H)-yl)(phenyl)methanone (N_8). MP: 204–206 °C; IR (KBr) υ: 3431, 3001, 2929, 2838, 1607, 1510, 1458, 1305, 1252, 1173, 1107, 1032, 832, 559, 530 cm^{-1}; ^{1}HNMR (DMSO-d_6, 300 MHz, TMS) σ:3.97 (s, 3H, CH_3), 4.09 (s, 3H, CH_3), 7.29 (s, 1H, CH), 7.32 (s, 1H, CH), 6.05-7.79 (m , 15H, Ar-H), 10.54 (s, 1H, OH) ppm; ^{13}CNMR (75 MHz, DMSO-d_6, TMS) σ: 52.8 (C_4), 53.4 (C_3), 65.1 (CH_3), 66.2 (CH_3), 108.8 (C_2), 110.9 (C_{20}), 111.2 ($C_{7,7'}$), 112.4 ($C_{16,16'}$), 114.9 (C_{13}),117.0 (C_{21}), 118.0 ($C_{11,11'}$), 118.5 (C_{19}), 124.1 ($C_{12,12'}$), 127.0($C_{6,6'}$), 129.3 ($C_{15,15'}$), 131.2 (C_5), 135.2 (C_{14}), 136.6 (C_{10}), 141.5 (C_1), 144.6 (C_{18}), 149.5 (C_8), 154.4 (C_{17}), 167.2 (C=O) ppm. Anal. Calcd for $C_{29}H_{25}NO_5$: C, 74.50; H, 5.39; N, 3.00. Found: C, 74.14; H, 5.58 ; N, 3.10.

(5-hydroxy-2,4-dip-tolyl-2H-benzo[e][1,3]oxazin-3(4H)-yl)(phenyl)methanone (N_9). MP: 195–197 °C; IR (KBr) υ: 3735, 3463, 3020, 2922, 2314, 1606, 1509, 1454, 1375, 1293, 1181, 1099, 811, 725, 641 cm^{-1}; ^{1}HNMR (DMSO-d_6, 300 MHz, TMS) σ: 2.11 (s, 3H, CH_3), 2.30 (s, 3H, CH3), 7.18 (s, 1H, CH), 7.23 (s, 1H, CH), 6.09-7.76 (m , 16H, Ar-H), 10.40 (s, 1H, OH) ppm; ^{13}CNMR (75 MHz, DMSO-d_6, TMS) σ: 42.3 (CH_3), 43.2 (CH3), 51.7 (C_4),52.2 (C_3), 111.2 (C_2), 112.4 (C_{20}), 112.8 (C_{21}), 119.2 ($C_{11,11'}$), 122.7 (C_{19}), 123.7 ($C_{6,6'}$), 124.6 ($C_{15,15'}$),128.3 ($C_{12,12'}$), 132.4 ($C_{7,7'}$), 133.7 ($C_{16,16'}$), 138.9 (C_{13}), 139.9 (C_{10}), 142.0 (C_8), 143.7 (C_{17}), 144.3 (C_5), 150.0 (C_{14}), 152.8 (C_1), 155.6 (C_{18}), 171.4 (C=O) ppm. Anal. Calcd for $C_{29}H_{25}NO_3$: C, 79.98; H, 5.79; N, 3.22. Found: C, 79.03 ; H, 6.01; N, 3.34.

(5-hydroxy-2,4-bis(4-hydroxyphenyl)2H-benzo[e][1,3]oxazin-3(4H)-yl)(phenyl)methanone (N_{11}). MP: 201–203 °C; IR (KBr) υ: 3188, 1677, 1600, 1510, 1440, 1387, 1230, 1079, 932, 834, 718, 554 cm^{-1}; ^{1}HNMR (DMSO-d_6, 300 MHz, TMS) σ: 7.26 (s, 1H, CH), 7.28 (s, 1H, CH), 6.18-7.89 (m , 15H, Ar-H), 10.60 (s, 1H, OH), 10.88 (s, 2H, OH), ppm; ^{13}CNMR (75 MHz, DMSO-d_6, TMS) σ: 53.8 (C_4), 54.5 (C_3), 112.4 (C_2), 114.0 (C_{20}), 114.7 ($C_{7,7'}$), 118.0 ($C_{16,16'}$), 122.7 (C_{21}), 123.7 ($C_{11,11'}$), 124.6 (C_{19}), 129.8 ($C_{12,12'}$), 131.0 ($C_{6,6'}$), 131.6 ($C_{15,15'}$), 134.0 (C_{13}), 134.7 (C_{10}), 139.4 (C_5), 139.9 (C_{14}), 141.3 (C_1), 148.1 (C_{18}), 149.5 (C_8), 153.3 (C_{17}), 167.8 (C=O) ppm. Anal. Calcd for $C_{27}H_{21}NO_5$: C, 73.79; H, 4.82; N, 3.19. Found: C, 73.58; H, 5.00; N, 3.31.

(5-hydroxy-2,4-bis(4-hydroxyphenyl)2H-benzo[e][1,3]oxazin-3(4H)-yl)(4-hydroxyphenyl) methanone (N_{14}). MP: 189–192 °C; IR (KBr) υ: 3487, 2446, 2009, 1986, 1785, 1652, 1670, 1421, 1108, 864, 725, 558 cm^{-1}; ^{1}HNMR (DMSO-d_6, 300 MHz, TMS) σ: 6.24 (s, 1H, CH), 7.08 (s, 1H, CH), 6.46-7.87 (m , 15H, Ar-H), 10.83 (s, 2H, OH), 11.16 (s, 2H, OH) ppm; ^{13}CNMR (75 MHz, DMSO-d_6, TMS) σ: 52.2 (C_4),52.4 (C_3),111.2 (C_2), 111.7 (C_{20}), 112.4 ($C_{12,12'}$), 114.2 ($C_{7,7'}$), 116.4 ($C_{16,16'}$), 117.8 (C_{21}), 125.3 (C_{10}), 126.2 (C_{19}), 130.0 ($C_{11,11'}$), 131.2 ($C_{6,6'}$), 132.1 ($C_{15,15'}$), 139.1 (C_5), 141.5 (C_{14}), 142.5 (C_1), 150.0 (C_{18}), 151.2 (C_{13}), 151.7 (C_8), 152.8 (C_{17}), 171.9 (C=O) ppm. Anal. Calcd for $C_{27}H_{21}NO_6$: C, 71.20; H, 4.65; N, 3.08. Found: C, 71.79; H, 4.82; N, 3.19.

(5-hydroxy-2,4-bis(3-nitrophenyl)-2H-benzo[e][1,3]oxazin-3(4H)-yl)(4-hydroxyphenyl) methanone (N_{17}). MP: 218–220 °C; IR (KBr) υ: 3874, 3733, 3199, 2888, 2313, 1604, 1508, 1442, 1374, 1225, 1173, 1081, 833, 723, 683,644 cm^{-1}; ^{1}HNMR (DMSO-d_6, 300 MHz, TMS) σ: 7.25 (s, 1H, CH), 7.27 (s, 1H, CH), 6.12-8.24 (m , 15H, Ar-H), 11.16 (s, 2H, OH) ppm; ^{13}CNMR (75 MHz, DMSO-d_6, TMS) σ: 53.4 (C_4), 53.8 (C_3), 114.2 (C_2), 114.7 (C_{20}), 117.0 ($C_{12,12'}$), 118.9 (C_8), 120.8 (C_{17}), 121.3 (C_{18}), 123.6 ($C_{6'}$), 127.4 ($C_{15'}$), 128.8 (C_{10}), 130.2 (C_{19}), 131.0 ($C_{11,11'}$), 136.2 (C_7), 138.3 (C_{16}), 139.6 (C_6), 139.9 (C_{15}), 140.1 (C_5), 144.1 (C_{14}), 146.7 (C_1), 148.3 ($C_{7'}$), 153.8 ($C_{16'}$), 154.7 (C_{18}), 156.8 (C_{13}), 171.6 (C=O) ppm. Anal. Calcd for $C_{27}H_{19}N_3O_8$: C, 63.16; H, 3.73; N, 8.18. Found: C, 63.19; H, 3.85; N, 8.45.

(5-hydroxy-2,4-dip-tolyl-2H-benzo[e][1,3]oxazin-3(4H)-yl)(4-hydroxyphenyl) methanone (N_{19}). MP: 198–200 °C; IR (KBr) υ: 3425, 2832, 1993, 1849, 1646, 1598, 1570, 1274, 1005, 845, 736, 586 cm^{-1}; ^{1}HNMR (DMSO-d_6, 300 MHz, TMS) σ: 2.18 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 7.24 (s, 1H, CH), 7.27 (s, 1H, CH), 6.10-7.78 (m , 15H, Ar-H), 10.04 (s, 1H, OH), 10.26 (s, 1H, OH) ppm; ^{13}CNMR (300 MHz, DMSO-d_6, TMS) σ: 43.2 (CH_3), 43.7 (CH_3), 53.1 (C_4), 53.4 (C_3), 116.1 (C_2), 117.4 (C_{20}), 119.6 ($C_{12,12'}$), 121.2 (C_{21}), 122.4 (C_{10}), 123.7 (C_{19}), 126.5 ($C_{6,6'}$), 128.0 ($C_{15,15'}$), 128.7 ($C_{11,11'}$), 131.2 ($C_{7,7'}$), 132.5 ($C_{16,16'}$), 135.2 (C_8), 138.7 (C_{17}), 140.0 (C_5), 140.6 (C_{14}), 154.4 (C_1), 159.2 (C_{13}), 156.8 (C_{18}), 179.1 (C=O) ppm. Anal. Calcd for $C_{29}H_{25}NO_4$: C, 77.14; H, 5.58; N, 3.10. Found: C, 77.98; H, 5.79; N, 3.22.

4. Conclusion

In this study, (5-hydroxy-2,4-diphenyl-2H-benzo[e] [1,3] oxazin-3(4H)-yl) (phenyl) methanone derivatives were synthesized through one-pot four components reaction between benzaldehyde and benzoic acid derivatives, resorcinol, and ammonia. The synthesized compounds showed excellent green and simple work-up procedure, rational yield and fast reaction time. ^{1}HNMR, ^{13}CNMR, and IR spectroscopies were used to characterize the novel synthesized compounds. The synthesis of new 1,3-oxazines derivatives has been done

by two methods, reflux and microwave. The microwave irradiation conditions has shown that the reactions are carried out with more speed and efficiency than the reflux method. Therefore, it can be concluded that the microwave irradiation will be much more effective and economical in these reactions. Also, because the reaction time is shorter, less reaction by-products will be synthesized. Derivatives 1,3-oxazines have medicinal properties, so it is suggested to investigate the biological activity of the compounds synthesized in this study. It is also suggested to perform these reactions with aldehydes and other aromatic acids and aromatic cyclic compounds with two hydroxyl functional groups.

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Authors Contributions
All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Narges Samoori, Naser foroughi Far and Alireza Khaje Amiri. The first draft of the manuscript was written by Narges Samoori and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Availability of Data and Materials
The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests
The authors have no relevant financial or non-financial interests to disclose.

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