SÍNTESE DE NOVOS DERIVADOS DE BIOCIDAS N-ALQUILADOS DE QUINAZOLINA-4(3H)-ONA USANDO ATIVAÇÃO DE MICROONDAS

CONSTRUCTION OF SOME NOVEL BIOCIDAL N-ALKYLATED QUINAZOLINE-4(3H)-ONE DERIVATIVES USING MICROWAVE ACTIVATION

تشييد بعض مشتقات الكينازولينون الحيوية الجديدة المستبدلة فى الوضع-ن بإستخدام التنشيط بأشعة الميكروويف

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RESUMO

Foi realizada a síntese assistida por micro-ondas de 2-propilquinazolinona **1**, seguida por suas utilidades subsequentes na sintese de uma atraente série de quinazolinonas funcionais 2,3-dissubstituídas **2-10**. O uso da irradiação de microondas na realização da N-alquilação para a quinazolinona 1 foi aplicado como uma técnica simples, eficiente e ecologicamente correta. Além disso, o rastreio antimicrobiano *in vitro* dos compostosobtidos **3-10** foi investigado contra quatro estirpes bacterianas e duas estirpes fúngicas. A estrutura das moléculas sintetizadas foi afirmada utilizando ferramentas analíticas e espectrais.

Palavras-chave: *Irradiação por microondas, quinazolinonas funcionais, atividade antibacteriana, atividade antifúngica*.

ABSTRACT

Microwave-assisted construction of 2-propylquinazolinone**1** has been achieved, followed by its subsequent utilities in constructing an attractive series of 2,3-disubstituted functional quinazolinones **2-10**. The use of microwave irradiation in performing *N*-alkylation for the titled quinazolinone 1 was applied as a simple, efficient and eco-friendly green technique. Furthermore, the *in vitro* antimicrobial screening of the obtained compounds **3-10** has been investigated against four bacterial strains and two fungal strains. The structure of the synthesized molecules was affirmed using analytical and spectral tools.

Keywords: *Microwave irradiation, Functional quinazolinones, Antibacterial activity, antifungal activity*

الملخص

تم تشييد 2-بروبيل الكينازولينون رقم **(1)** باستخدام أشعة الميكروويف، ومن ثم استغلالها في تشييد سلسلة من الكينازولينونات الوظيفية**(2-10)**المستبدلة في الوضع 2،3. وقد تم تطبيق أشعة الميكروويف في عمل الألكلة للكينازولينون رقم واحد كأحد تطبيقات التقنيات الخضراء صديقة البيئة وكوسيلة سهلة وكفء. وبالإضافة إلي ذلك تم تقدير النشاط الميكروبي للمركبات **(3-10)**التي تم تحضيرها ضد أربع سلالات من البكتريا وسلالاتين من الطحالب. وقد تم اثبات التراكيب الدقيقة للمركبات التي تم تحضيرها باستخدام الطرق الفيزيقية والطيفية.

الكلمات المفتاحية:*أشعةالميكروويف،كينازولياتوظيفية،مضاداتالبكتريا،مضاداتالفطريات*

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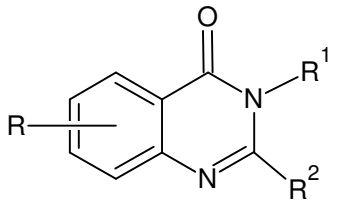
INTRODUCTION

Quinazolin-4(3*H*)-ones are frequently encountered unit in natural products such as L-Vasicinone (I)[1] and Diproqualone (II)[2]. It was revealed that the quinazolinone moiety associated with various aromatic as well as heterocyclic compounds have a wide range of pharmaceutical and biological activities[3-10]. Recently, there is focusing on developments of the synthetic methodology of 2,3-disubstituted quinazolin-4(3*H*)-ones in order to enhance their subsidiary medicinal counterparts. Accordingly, uses of microwaves are modern attractive approaches; which successfully applied for heterocyclic synthesis and the quinazolin-4(3*H*)-ones in particular[11-13].

Furthermore, microbial resistance expresses a challenge for the scientific district to improve new bioactive molecules. The improvement of promising therapeutic agents for the controlling microorganisms has undergone continual domination to the evolution of more adequate classes of drugs. In continuation of our program[14-18], the present work will explore a novel series of quinazolinones. Derivatives of attractive quinazolinoneswill be synthesized and characterized with the aim obtaining a source of functionalized molecules. Moreover, getting quinazoline derivatives possess some interesting pharmaceutical and biological applications. Thereafter, the synthesized derivatives will be screened for their antimicrobial activities.



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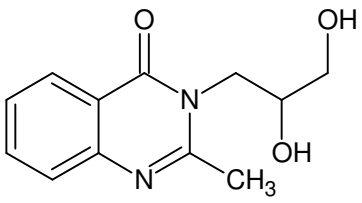

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MATERIALS AND METHODS

Reagents and instruments

Reagents and solvents were dried and purified before use by the usual procedures. M.p.: Büchi® melting point apparatus; uncorrected. TLC: Merck TLC aluminum sheets, silica gel $60F_{254}$ with detection by UV quenching at 254 nm. IR spectra: FT-IR Nicolet Impact 400D; KBr pellets; v in cm^{-1}. ^{1}H-NMR spectra were recorded on a Varian at 300 MHz; in $CDCl_3$ or DMSO-d_6; δ in ppm relative to Me_4Si as an internal standard, *J* in Hz. EIMS were recorded on a gas chromatographic GCMS–HP model MS5988. Elemental analyses were carried out at the Micro Analytical Center, Cairo University, Giza, Egypt. Antimicrobial analyses were carried out at Regional Center for Mycology and Biotechnology (RCMB), Al-Azhar University, Cairo, Egypt.

2-Propylquinazolin-4(3*H*)-one (1)

A solution of 2-propyl-4*H*-3,1-benzoxazinone (10 mmol) in 10 mL of formamide was irradiated in an open Erlenmeyer flask in a domestic microwave oven at 100W and 120 °C for 3-5 min. The resulting crude was filtered off, washed with cold water and recrystallized from pet. Ether to give **1.**Yield 93%, mp. 200–202 °C. IR (KBr, cm^{-1}): 3215 (NH), 1675 (C=O), 1597 (C=N). ^{1}H-NMR ($CDCl_3$, δ ppm): 1.10 (t, *J* = 7.0 Hz, 3H, CH_3), 1.92 (h, *J* = 7.0 Hz, 2H, CH_2), 2.78 (t, *J* = 7.0 Hz, 2H, CH_2), 7.49 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.72-7.93 (m, 3H, Ar-H), 12.27 (brs, 1H, D_2O-exchangeable, NH). MS *m/z*: 188 [M^+]. Anal. Calcd. for $C_{11}H_{12}N_2O$ (188.23): C, 70.19; H, 6.43, Found: C, 70.28; H, 3.37.

General procedure for formation of compounds 2 and 3a,b

To a solution of quinazolinone**1** (10 mmol) in DCM (20 mL) was added K_2CO_3 (12 mmol). The reproduced mixture was irradiated in domestic microwave at 600W and 100 °C for 3 min. then KI (5 mmol) was provided and the formed blend was stirred further for 15 min, 0.5 mL a solution of respective alkylating agents (namely, chloroacetyl chloride, benzyl bromide and/or methyl 4-(bromomethyl)benzoate) in DCM was dropped slowly into the blend. Then the

formed blend was irradiated in microwave at 600W and 100 °C for 6min, it was allowed to cool down and then was poured into ice-cold water. The solid that formed was scrubbed with water, filtered and crystallized using the suitable solvent to give the respective compounds **2** and **3a,b**.

***(4-Oxo-2-propylquinazolin-3(4H)-yl)acetyl chloride* (2)**

Yield 92%, mp. 285–287 °C (EtOH). IR (KBr, cm^{-1}): 1710, 1668 (C=O), 1607 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 1.10 (t, *J* = 7.0 Hz, 3H, CH_3), 1.92 (h, *J* = 7.0 Hz, 2H, CH_2), 2.73 (t, *J* = 7.0 Hz, 2H, CH_2), 4.75 (s, 2H, CH_2), 7.44 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.75-7.84 (m, 2H, Ar-H), 8.16 (d, *J* = 8.0 Hz, 1H, Ar-H). MS *m/z*: 265 [M^+]. Anal. Calcd. for $C_{13}H_{13}N_2O_2$ (264.71): C, 58.99; H, 4.95, Found: C, 58.78; H, 4.87.

3-Benzyl-2-propylquinazolin-4(3*H*)-one (3a)

Yield 87%, mp. 248–250 °C (EtOH). IR (KBr, cm^{-1}): 1671 (C=O), 1605 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 1.10 (t, *J* = 7.0 Hz, 3H, CH_3), 1.92 (h, *J* = 7.0 Hz, 2H, CH_2), 2.73 (t, *J* = 7.0 Hz, 2H, CH_2), 4.13 (s, 2H, CH_2), 7.27-7.84 (m, 9H, Ar-H). MS *m/z*: 278 [M^+]. Anal. Calcd. For $C_{18}H_{18}N_2O$ (278.35): C, 77.67; H, 6.52, Found: C, 77.98; H, 6.67.

Methyl 4-[(4-oxo-2-propylquinazolin-3(4*H*)-yl)methyl]benzoate (3b)

Yield 84%, mp. 263–264 °C (AcOH). IR (KBr, cm^{-1}): 1738, 1671 (C=O), 1606 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 1.10 (t, *J* = 7.0 Hz, 3H, CH_3), 1.92 (h, *J* = 7.0 Hz, 2H, CH_2), 2.43 (s, 3H, CH_3), 2.72 (t, *J* = 7.0 Hz, 2H, CH_2), 4.19 (s, 2H, CH_2), 7.33-7.87 (m, 9H, Ar-H). MS *m/z*: 336 [M^+]. Anal. Calcd. For $C_{20}H_{20}N_2O_3$ (336.38): C, 71.41; H, 5.99, Found: C, 71.65; H, 6.07.

1,4-Di(4-oxo-2-propylquinazolin-3(4*H*)-yl)-1,4-diphenylbutane-2,3-dione (4)

A mixture of compound **3a** (1.4 mmol), oxalyl chloride (0.7 mmol) and triethylamine (1.4 mmol) in 10 mL tetrahydrofuran was stirred at r.t for 12h. The reaction mixture was poured into ice-cold water and the solid that formed was scrubbed with water, filtered, and crystallized from MeOH to give butane-dione**4**.

Yield 77%, mp. >300 °C. IR (KBr, cm^{-1}): 1714, 1670 (C=O), 1604 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 1.08 (t, *J* = 7.0 Hz, 6H, $2CH_3$), 1.90 (h, *J* = 7.0 Hz, 4H, $2CH_2$), 2.68 (t, *J* = 7.0 Hz, 4H, $2CH_2$), 6.24 (s, 2H, 2CH), 7.26-7.93 (m, 18H, Ar-H). MS *m/z*: 610 [M^+]. Anal. Calcd. For $C_{38}H_{34}N_4O_4$ (610.70): C, 74.73; H, 5.61, Found: C, 75.11; H, 5.43.

***N*-Hydroxy-4-[(4-oxo-2-propylquinazolin-3(4*H*)-yl)methyl]benzamide (5)**

A solution of quinazolinone**3b** (10 mmol) and hydroxylamine hydrochloride in 15 mL of dry pyridine was heated under reflux for 4h. The reaction mixture after cooling was poured onto crushed ice/HCl. The solid that separated was washed with water and crystallized from AcOH to give the benzamide analogous **5**.

Yield 81%; mp. 177-178 °C. IR (KBr, cm^{-1}): 3374 (OH), 1678, 1671 (C=O), 1601 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 1.10 (t, *J* = 7.0 Hz, 3H, CH_3), 1.92 (h, *J* = 7.0 Hz, 2H, CH_2), 2.43 (s, 3H, CH_3), 2.72 (t, *J* = 7.0 Hz, 2H, CH_2), 4.36 (s, 2H, CH_2), 6.41 (brs, 1H, D_2O-exchangeable, NH), 7.26-7.84 (m, 8H, Ar-H), 13.42 (brs, 1H, D_2O-exchangeable, OH). MS *m/z*: 276 [M^+- CH_3NO]. Anal. Calcd. For $C_{19}H_{19}N_3O_3$ (337.37): C, 67.64; H, 5.68, Found: C, 67.87; H, 5.80.

***General procedure for formation of compounds* 6a,b**

A solution of compound **3b** (10 mmol) in 10 mL of piperidine and/or morpholine has been refluxed for 8h. The produced mixture was cooled, evaporated under reduced pressure and cold water was added. The solid that formed was filtered off and recrystallized toluene to give **6a** and/or **6b** respectively.

3-{[4-(Piperidine-1-carbonyl)phenyl]methyl}-2-Propylquinazolin-4(3*H*)-one (6a)

Yield 73%; mp. 127-129 °C. IR (KBr, cm^{-1}): 1670, 1664 (C=O), 1597 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 1.10 (t, *J* = 7.0 Hz, 3H, CH_3), 1.46-1.52 (m, 6H, piperidine), 1.92 (h, *J* = 7.0 Hz, 2H, CH_2), 2.72 (t, *J* = 7.0 Hz, 2H, CH_2), 3.22-3.28 (m, 4H, piperidine), 4.34 (s, 2H, CH_2), 7.29-8.11 (m, 8H, Ar-H). MS *m/z*: 389 [M^+]. Anal. Calcd. For $C_{24}H_{27}N_3O_2$ (389.49): C, 74.01; H, 6.99, Found: C, 74.33; H, 6.75.

3-{[4-(Morpholine-4-carbonyl)phenyl]methyl}-2-propylquinazolin-4(3*H*)-one(6b)

Yield 76%; mp. 140-142 °C. IR (KBr, cm^{-1}): 1670, 1665 (C=O), 1600 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 1.10 (t, *J* = 7.0 Hz, 3H, CH_3), 1.92 (h, *J* = 7.0 Hz, 2H, CH_2), 2.72 (t, *J* = 7.0 Hz, 2H, CH_2), 3.20-3.31 (m, 4H, morpholine), 3.74-3.86 (m, 4H, morpholine), 4.31 (s, 2H, CH_2), 7.30-8.09 (m, 8H, Ar-H). MS *m/z*: 391 [M^+]. Anal. Calcd. For $C_{23}H_{25}N_3O_3$ (391.46): C, 70.57; H, 6.44, Found: C, 70.82; H, 6.60.

2-Propyl-3-{[(1,3-thiazol-2-yl)amino]acetyl}quinazolin-4(3*H*)-one (7)

A mixture of quinazolinone**2** (10 mmol) and 2-aminothiazole (10 mmol) in 15 mL of DMF was heated under reflux for 6h. The reaction mixture was concentrated under reduced pressure and the solid that formed was filtered off and crystallized from AcOH to give **7**.

Yield 69%; mp. 214-216 °C. IR (KBr, cm^{-1}): 3217 (NH), 1677, 1668 (C=O), 1607 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 1.10 (t, *J* = 7.0 Hz, 3H, CH_3), 1.92 (h, *J* = 7.0 Hz, 2H, CH_2), 2.72 (t, *J* = 7.0 Hz, 2H, CH_2), 4.93 (s, 2H, CH_2), 6.52 (d, *J* = 6.8 Hz, 1H, =CH), 6.94 (d, *J* = 6.8 Hz, 1H, =CH), 7.41-7.86 (m, 4H, Ar-H), 12.36 (brs, 1H, D_2O-exchangeable, NH). MS *m/z*: 284 [M^+- C_3H_8]. Anal. Calcd. For $C_{16}H_{16}N_4O_2S$ (328.39): C, 58.52; H, 4.91, Found: C, 58.26; H, 4.77.

***General procedure for formation of compounds* 8-10**

An equimolar mixture of quinazolinone**2** and selective diamine (namely, hydrazine hydrate, ethane-1,2-diamine and/or piperazine) (10 mmol) in 15 mL of 1,4-dioxane was heated under reflux for 8h. The reaction mixture was left overnight and the solid that formed was washed with water, filtered off and crystallized from EtOH/H_2O to give the respective bis-compound **8-10**.

3,3'-[hydrazine-1,2-diylbis(1-oxoethane-2,1-diyl)]bis(2-propylquinazolin-4(3*H*)-one) (8)

Yield 73%; mp. 204-205 °C. IR (KBr, cm^{-1}): 3221 (NH), 1675, 1668 (C=O), 1605 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 1.12 (t, *J* = 7.0 Hz, 6H, $2CH_3$), 1.89 (h, *J* = 7.0 Hz, 4H, $2CH_2$), 2.74 (t, *J* = 7.0 Hz, 4H, $2CH_2$), 4.48 (s, 4H, $2CH_2$), 7.35-7.81 (m, 8H, Ar-H), 12.29 (brs, 2H, D_2O-exchangeable, 2NH). MS *m/z*: 488 [M^+]. Anal. Calcd. For $C_{26}H_{28}N_6O_4$ (488.54): C, 63.92; H, 5.78, Found: C, 64.15; H, 5.95.

3,3'-{ethane-1,2-diylbis[azanediyl(1-oxoethane-2,1-diyl)]}bis(2-propylquinazolin-4(3*H*)-one) (9)

Yield 64%; mp. 211-213 °C. IR (KBr, cm^{-1}): 3219 (NH), 1678, 1667 (C=O), 1599 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 1.11 (t, *J* = 7.0 Hz, 6H, $2CH_3$), 1.89 (h, *J* = 7.0 Hz, 4H, $2CH_2$), 2.58 (d, *J* = 6.5 Hz, 4H, $2CH_2$), 2.74 (t, *J* = 7.0 Hz, 4H, $2CH_2$), 4.43 (s, 4H, $2CH_2$), 7.33-7.79 (m, 8H, Ar-H), 12.33 (brs, 2H, D_2O-exchangeable, 2NH). MS *m/z*: 328 [M^+-$C_{11}H_{11}N_2O$]. Anal. Calcd. For $C_{28}H_{32}N_6O_4$ (516.59): C, 65.10; H, 6.24, Found: C, 64.95; H, 6.10.

3,3'-[piperazine-1,4-diylbis(1-oxoethane-2,1-diyl)]bis(2-propyquinazolin -4(3*H*)-one) (10)

Yield 72%; mp. 211-213 °C. IR (KBr, cm^{-1}): 1672, 1668 (C=O), 1604 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 1.12 (t, *J* = 7.0 Hz, 6H, $2CH_3$), 1.90 (h, *J* = 7.0 Hz, 4H, $2CH_2$), 2.74 (t, *J* = 7.0 Hz, 4H, $2CH_2$), 3.22-3.35 (m, 8H, piperazine), 4.28 (s, 4H, $2CH_2$), 7.30-7.77 (m, 8H, Ar-H). MS *m/z*: 542 [M^+]. Anal. Calcd. For $C_{30}H_{34}N_6O_4$ (542.63): C, 66.40; H, 6.32, Found: C, 66.75; H, 6.20.

Antimicrobial Activity

The antimicrobial activity of compounds **3-10**was determined by agar well diffusion method[19]; the microbial inocula were uniformly spread using a sterile L-Shaped rod on sterile Petri dishes loaded with nutrient agar and potato dextrose agar for antibacterial and antifungal tests respectively. Solvation of the screened compounds in DMSO was performed in order to prepare a solution of (5 mg/mL) concentration. Reference substances were amphotericin B for fungi, ampicillin, and gentamicin for G-positive and G-negative bacteria respectively, all with (1mg/mL) concentration.

A Hundred micrograms of solution were added to 5 wells (6 mm diameter holes scooped out with sterile cork borer); the system was then incubated under aerobic conditions (24h at 37ºC for bacteria and 48h at 28ºC for fungi). Inhibition zones were determined; the diameter was

expressed in millimeter.

RESULTS AND DISCUSSION:

A multitude of efficient procedures for the construction of quinazolinone derivatives is using classical methods of heating[20,21]. Recently, uses of microwave activation for performing chemical reactions was accomplished as a non-conventional heating source; particularly for the 4(3*H*)-quinazolinones[22,23].

In this circumstance, construction of 2-propylquinazolin-4(3*H*)-one **1** in 93% yield was achieved via the irradiation of a solution of 3,1-benzoxazin-4-one in formamide using a domestic microwave for 3-5min. It was observed that the reaction has been completed in few minutes and it gives excellent yield. The structure of quinazolinone**1**was inferred from its correct analytical data and spectral analysis, which in full agreement with the proposed structure (cf. Scheme 1 and Experimental section).

In order to gain enriched quinazolinone derivatives in their functionality; the *N*-alkylation was chosen as a model tool to achieve our target. The *N*-alkylation of the titled quinazolinone**1** was pronounced using the different interesting alkylating agents namely, chloroacetyl chloride, benzyl bromide and/or methyl 4-(bromomethyl)benzoate in dichloromethane (DCM) through a microwave-assisted reaction and the *N*-alkylated quinazolinone derivatives **2** and **3 a, b** were afforded in excellent yields (cf. Scheme 1 and Experimental section).

In case of formation of quinazolinone **2**, the reaction was proposed possibly to take place via a nucleophilic substitution at the acyl moiety in priority to alkyl moiety. Which is obviously emphasize the fact that tetrahedral mechanism is more facile than S_N2 mechanism. Reversely, in case of benzyl bromides, it does not apply and the reaction involves a nucleophilic attack on the alkyl halide moiety according to the S_N2 mechanism.

Furthermore, the 3-benzylquinazolinone **3 a** was endowed to react with oxalyl chloride (ethanedioyl dichloride) in presence of a catalytic amount of triethyl amine in tetrahydrofuran furnishing (2,3-dioxo-1,4-diphenylbutane-1,4-diyl)di{-3-(2-propyl)quinazolin-4-one} **(4)**. The *N*-hydroxybenzamide incorporated quinazolinonewas explored in the present study in order to get biologically active quinazolinones. Therefore, the interaction of quinazolinone derivative **3b** with hydroxyl amine hydrochloride in dry pyridine afforded the corresponding *N*-hydroxy-4-[(4-oxo-2-propylquinazolin-3(4*H*)-yl)methyl]benzamide**(5)**. Also, quinazolinone **3b** was reacted as an ester with 2ry amines like piperidine and morpholine and afforded the quinazolinone derivatives **6 a, b** respectively (cf. Scheme 1 and Experimental section).

The structure of the quinazolinone **2** was confirmed chemically as well as was exploited via its reaction with 2-aminothiazole encouraging us for the generating a second interesting chromophore at *N*-3. In this respects, the titled quinazolinone **2** has been reacted with 2-aminothiazole in *N,N*-dimethylformamide and the 2-propyl-3-{[(1,3-thiazol-2-yl)amino]acetyl}quina_ zolin-4(3*H*)-one **(7)** was furnished. Additionally, the titled quinazolinone **2** was invested in the attaining an attractive bis-compounds. The reaction of quinazolinone **2** with distinctive diamines like hydrazine hydrate, ethane-1,2-diamine and/or piperazine in presence of 1,4-dioxane afforded the bis-compounds **8-10**. The analytical and spectral data of bis-compounds **8-10** were in full agreement with the proposed structures (cf. Scheme 2 and Experimental section).

Antimicrobial activity

In the present work, all the obtained compounds were investigated for their in vitro antimicrobial activities. The screening was performed at (5 mg/mL) concentration against four bacterial strains, two Gram-positive bacteria (*Bacillus subtilis"B. subtilis"*, *Streptococcus aureus"S. pneumonia"*), two Gram-negative bacteria (*Escherichia coli"E. coli"*, *Pseudomonas aeroginosa "P. aeroginosa"*), and two yeasts (*Aspergillus niger* "*A. niger*", *Candida albicans* "*C. albicans*"). Ampicillin, gentamicin, and amphotericin B were used as control drug standards for G-positive bacteria, G-negative bacteria, and fungi references respectively. The zone of inhibition (mm) of the mentioned compounds was accounted in table 1.

Table 1 revealed that compounds **4**, **5** and **10** displayed potent activity against *B. subtilis*. Compounds **5**, **6 a** and **10** revealed strong potent activity against *S. pneumonia*. Compound **6 b** showed powerful potency and its effect exceeded the control drug against the two G-negative bacterial strains (*E. coli* and *P. aeroginosa*).

Against *A. niger* compounds **4**, **5** and **7** displayed strong potent activity and their bacteriostatic effect were closed to the control drug. Quinazolinones **6 b** and **7** exhibited powerful potent activity against *C. albicans*. Moreover, compounds **5**, **6 b** and **10** recorded potent activities, while **3 a**, **3 b** and **8** were the less active against all strains.

CONCLUSIONS:

The authors successfully endeavor to modify the synthetic methodology for the 2-propylquinazolin-4(3*H*)-one in excellent yield using microwave-assisted reaction conditions. The powerful and selective microwaves action on producing the *N*-alkylated quinazolinoneshas been successfully achieved. Which in turn were used to produce some interesting functionalized heterocycles containing the important 4(3*H*)-quinazolinone core.We hereby highlighted the potential of such new heterocycles for their bactericidal and fungicidal activities.

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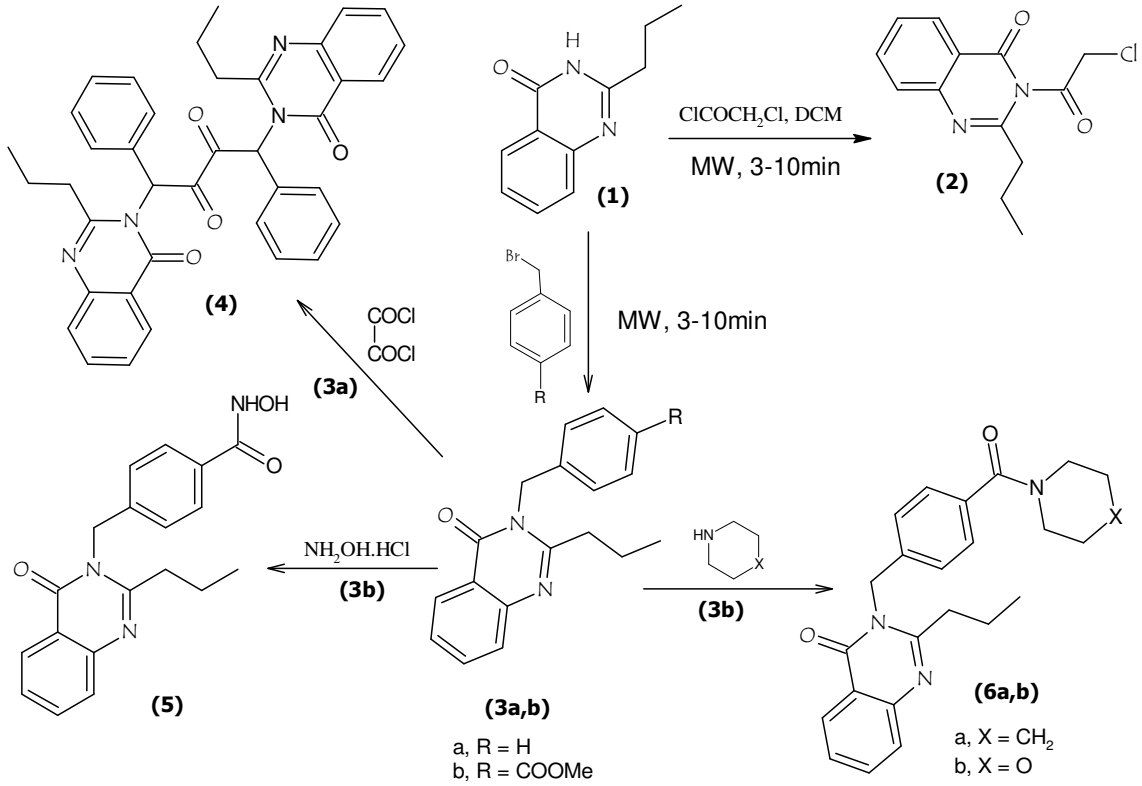
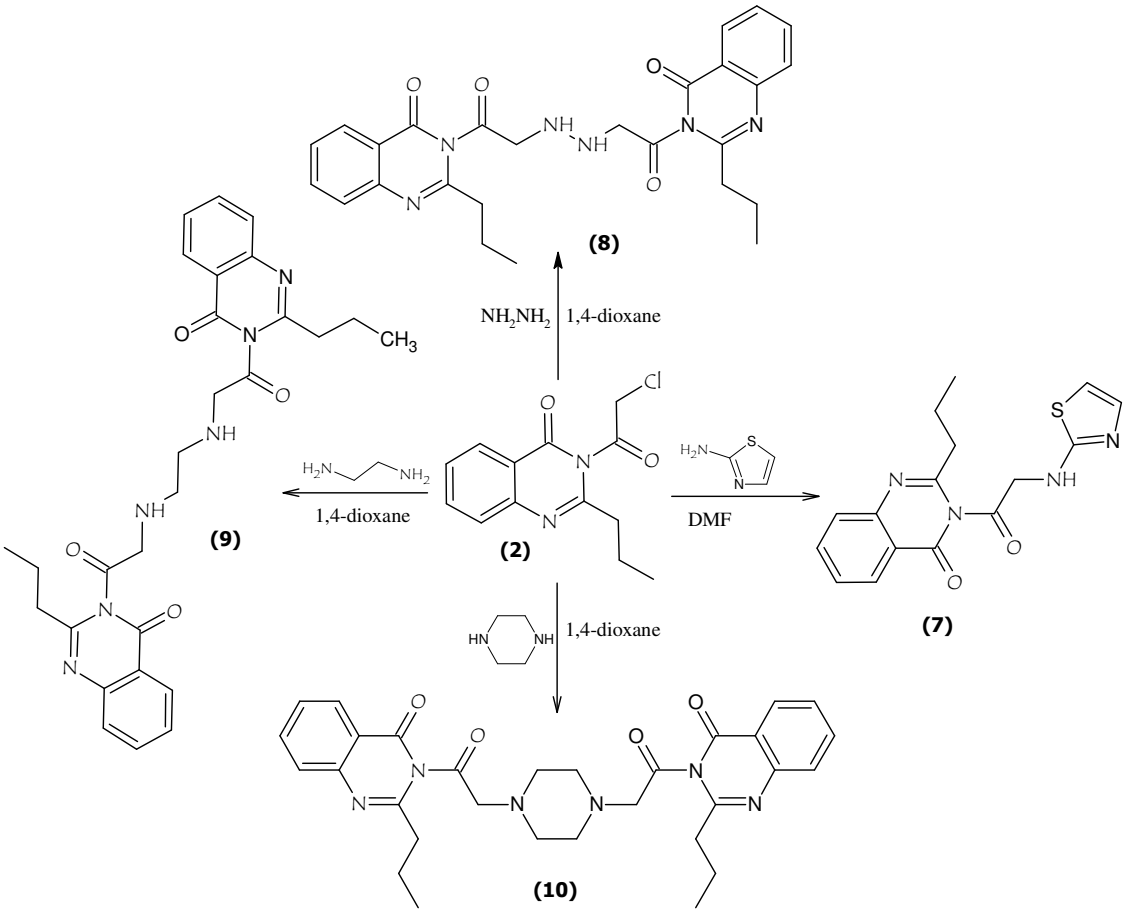


Scheme 1.*Formation N-alkylation of quinazolinone derivatives.*



Scheme 2.*Reactions with quinazolinone****2****.*

Table 1. *Antimicrobial activity of the synthesized compounds* ***3-10*** *using agar well diffusion method (5 mg/mL).*

Comp. No.	Zone of inhibition					
	Gram-positive		Gram-negative		Antifungal activity	
	B. subtilis	***S. aureus***	***E. coli***	***P. aeroginosa***	***A. niger***	***C. albicans***
3a	15	12	18	16	18	15
3b	9	15	16	NA	NA	12
4	21	18	17	15	19	17
5	29	27	19	16	18	16
6a	15	13	16	14	NA	15
6b	18	23	22	19	17	20
7	19	18	25	27	19	23
8	17	14	16	NA	13	8
9	19	16	14	NA	14	NA
10	23	24	23	NA	18	NA
Ampicillin[a]	**30**	**31**	**-**	**-**	**-**	**-**
Gentamicin[a]	**-**	**-**	**23**	**25**	**-**	**-**
amphotericin B[a]	**-**	**-**	**-**	**-**	**20**	**25**

NA no activity
[a] Control drug concentrations (1 mg/mL), 6.00 mm, (100 µL was tested)