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New Quinoline-2-one/thiazolium bromide Derivatives; Synthesis, Characterization and Mechanism of Formation

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ABSTRACT

We report on the formation of new quinoline-2-one derived by thiazolium bromides from the reaction of 3-thiosemicarbazides derived by 2-quinolones with 2-bromoacetophenones. The structure of products was elucidated by mass, IR and NMR spectra together with elemental analysis. The mechanism of products formation was discussed.

1. Introduction

Thiazole molecule is one of the interesting class present in many natural and synthetic products with a broad range of biological activities with wide spectrum pharmacological activities such as antioxidant, antibacterial, antifungal, antitubercular, diuretic, anti-inflammatory and anticancer activities [1]. Phosphoinositide 3 (PI 3) kinase modulators thiazolo[4,5-*g*]dihydroindazoles [2], HIV-integrase inhibitor thiazolo[5,4-*b*] pyrimidine-5(4*H*)-ones and a serine/threonine protein kinase-3 (GSK-3) inhibitors thiazole[5,4-*f*]quinazolin-9-ones [3] revealed their therapeutic potential in various diseases. Pramipexole possessing 2-amino-thiazole fused with cyclohexane ring, where aminothiazole moiety is an isostere to the catechol ring of dopamine, demonstrated dopamine D2 agonist activity [4]. Riluzole containing aminothiazole moiety is a new neuroprotective drug that was approved for the treatment of amyotrophic lateral sclerosis (ALS) [5]. Moreover, Hofmann Le Roche has developed a benzothiazole derivative ASN115 (tozadent) as a potent adenosine A2AR antagonist for treatment of Parkinson's disease which is in phase II clinical trials [6]. Tetrahydrobenzothiazoles [7], phenolic thiazoles [8] and benzothiazoles [9] are well also studied as neuroprotective agents. Furthermore, ethynyl thiazole [10] and pyrimidyl thiazole derivatives [11] displayed good glutamate receptors antagonist activity for the management of anxiety disorders. Derivatives of butylthiazole [12], imidazothiazole [13], 2-aminothiazole [14], and triazole linked thiazole [15] showed potent anti-Alzheimer activity. Riluzole analogues [16], thiazole-semicarbazides [17], thiazolepyridons [18], as well as thiazolo-carboxamide [19] derivatives exhibited promising anticonvulsant properties.

Researchers have reviewed that 2-quinolone (carbostyril) skeleton is an important structural moiety present in a large number of alkaloids [20,21] and in numerous biologically active compounds [2,20-27]. Some of them exhibited for example, antioxidative activity [21], nitric oxide production inhibitory activity [27], and cytotoxicity against human tumor cell lines [22]. Others revealed angiotensin II receptor antagonist [21], glycine NMDA receptor antagonists [23], endothelin receptor antagonist [24], antiplatelet agents [26], and antitumor agents [25]. Therefore, 2-quinolones are taken into consideration as valuable intermediates in organic synthesis [28-33].

Recently, Aly *et al.* prepared ethyl pyranoquinoline-4-carboxylates and dialkyl 2(4-oxo-1,4-dihydroquinolin-3-yl)fumarates [34] as well as 4-hydroxy-2-quinolones with 2-(2-

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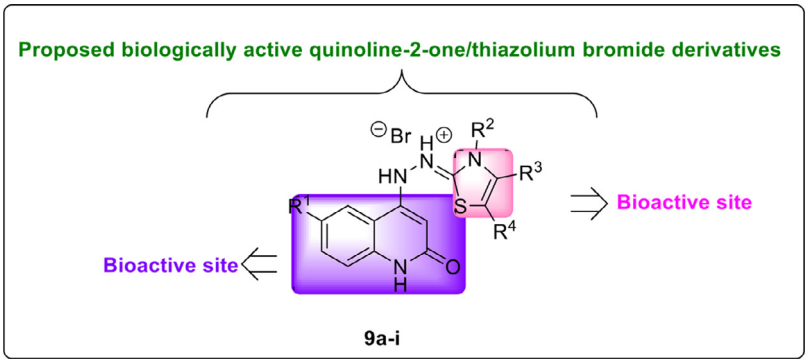


Fig. 1. Design of the target quinoline-2-one/thiazolium bromide derivatives **9a-i**

oxo-1,2-dihydroindol-3-ylidene)malononitrile and spiro(indoline-3,4'-pyranoquinoline)-3'-carbonitriles [35]. Moreover, Aly and his co-workers synthesized bis(1,2-dihydroquinolin-3-yl)succinic acid derivatives by one-pot reaction of one equivalent aromatic amines with two equivalents diethyl malonate [36]. Reaction of four equivalents of 4-hydroxyquinolin-2(1*H*)-ones with one equivalent acenaphthoquinone gave 1,2-dihydroacenaphthylene)-1,1,2,2-tetrayl-tetrakis(4-hydroxyquinolin-2(1*H*)-ones) in good to excellent yields [37]. In the view of the biological and pharmaceutical activities, we also reported the design and synthesis of a series of fused naphthofuroquinoline-6,7,12-triones and pyrano[3,2-*c*]quinoline-6,7,8,13-tetraones as potential ERK inhibitors [38]. The synthesized compounds were targeted as candidates to extracellular signal-regulated kinases ERK1/2 with considerable antineoplastic activity along with a molecular docking study using ATP-binding site of ERK2 [38]. Two series of diethyl 2-[2-(substituted-2-oxo-1,2-dihydroquinolin-4-yl)hydrazono]succinates and 1-(2-oxo-1,2-dihydro-quinolin-4-yl)-1*H*-pyrazoles have been designed and synthesized [39]. Seven compounds were further examined against the most sensitive cell lines, leukemia CCRF-CEM, and MOLT-4 [39]. Another two series of *N*-2,3-bis(6-substituted quinolin-3-yl)naphthalene-1,4-diones and bisquinolinone triethylammonium salts were successfully synthesized [40]. We have also recently reported review dealt with the interesting synthetic approaches and biological applications of quinolones [41].

Recently, it has been reported on the synthetic routes of different thiazolidinones from several thiosemicarbazides and thiocarbohydrazides by using different reagents, and their biological evaluation was also discussed [42,43]. Thiosemicarbazones were used as a starting material for the synthesis of different heterocyclic compounds, i.e., naphthothiazole and naphtho-thiadiazepines [44], 4-thiazolidinone derivatives [45,46], 1,3,4-thiadiazoles [47] which possessed potential biological activities such as anticancer [48], antioxidants [49], antifungal [50], and antibacterial [51]. Recently, Aly *et al*, synthesized also a series of 6-substituted quinolin-2-one thiosemicarbazides [52] whereas the designed final compounds were evaluated for their *in vitro* activity against the urease-producing *R. mucilaginosa* and *Proteus mirabilis* bacteria as fungal and bacterial pathogens, respectively [52]. Based on the previously mentioned aspects, we encouraged to design and synthesize new thiazolium derived by 2-quinolone derivatives *via* reaction of thiosemicarbazides with 2-bromoacetophenones. The designed target quinoline-2-one/thiazolium bromide derivatives of assumed biological activity is as illustrated in Fig. 1.

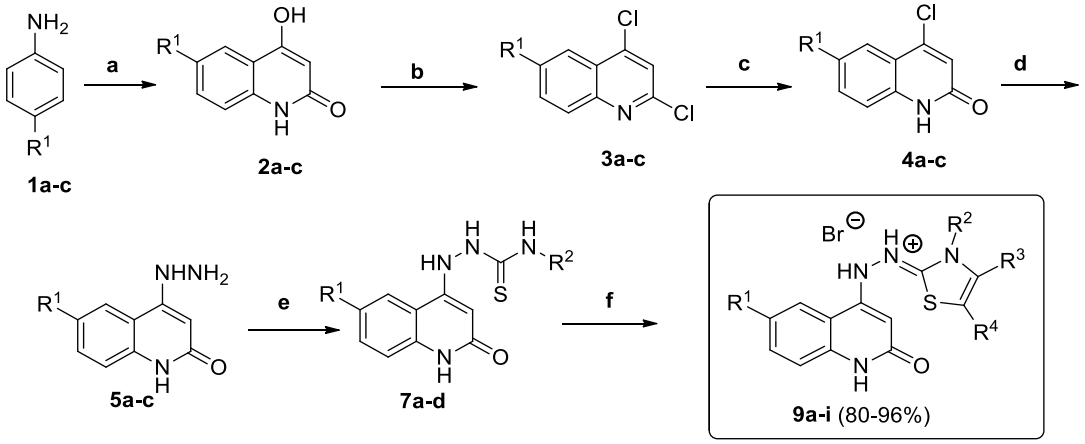
2. Results and Discussion

Compounds **2-5** were synthesized according to reported method and their structures were confirmed by matching their spectral data with the reported ones [53-55]. The key intermediates hydrazine quinolone **5a-c** were prepared by reacting compounds **4a-c** with hydrazine hydrate [39]. Whereas the corresponding quinoline-2-one/thiosemicarbazide derivatives **7a-d** were obtained during reaction of hydrazine quinolones **5a-c** with the appropriate isothiocyanates **6a-c** [47]. Thus, reaction of quinoline-2-one/ thiosemicarbazide derivatives **7a-d** with 2-bromoacetophenones **8a-c** gave the newly prepared quinoline-2-one/thiazolium bromide derivatives **9a-i** (Scheme 1). The structures of thiazol-2(3*H*)-ylidene)-2-oxo-quinolin-4-yl) hydrazinium bromide **9a-i** were elucidated by IR, NMR, mass spectra and elemental analyses.

As an example, quinoline-2-one/thiazolium bromide derivative **9a**, its molecular formula was proved from elemental analysis as $C_{26}H_{22}BrN_4OS$ (Experimental section). Since, mass spectroscopy unlikely showed the base peak of the salt to be assigned at $m/z = 439$. The IR spectrum of quinoline-2-one/thiazolium bromide derivative **9a** showed absorption band at ν = 3330-3320 cm^{-1} assigned for the NH group. No absorption was noted for free carbonyl of quinolone in the IR spectrum. The ^{1}H NMR spectrum of **9a** showed one broad singlet for one proton at δ = 12.20 ppm assigned to the quinolone NH-proton. The ^{1}H NMR spectrum of **9a** showed a broad singlet at δ = 10.25 ppm assigned to the deshielded exo-hydrazonium NH-proton. Three singlets were appeared at δ = 2.15, 2.30 and 6.00 ppm for thiazole-CH_3, quinolone-CH_3 and quinolone-CH-3, respectively. In ^{13}C NMR spectrum of **9a**, it was observed carbon signals at δ = 162.0 ppm (quinolone-C-2), and 156.4 ppm (C=N) (Experimental Section). The quinolone-CH_3 appears at δ = 20.8 ppm, whereas the thiazole-CH_3 appeared at δ = 22.0 ppm. Both of the thiazole-C-5 and quinolone-CH-3 resonated in the ^{13}C NMR spectrum at δ = 115.0 and 95.4 ppm, respectively (see the experimental section).

Another example was shown in case of the quinoline-2-one/thiazolium bromide derivative **9h**, whereas the mass spectrum showed the molecular peak at m/z = 468/466 (37/100). The ^{1}H NMR showed a multiplet integrated with two protons at δ = 5.25-5.15 ppm (allyl=CH_2) in addition to a multiplet at δ = 4.06-4.02 ppm (allyl-CH_2). The allyl=CH appeared as a multiplet at δ = 6.22-6.11 ppm. The remarkable proton signal of the CH-4-thiazole resonated at δ = 7.15 ppm. In ^{13}C NMR spectrum of **9h**, it was observed carbon signals at δ = 161.4 ppm (for C=O), and 154.9 ppm (for C=N) (Experimental Section). The allyl=CH, allyl=CH_2, quinolone-CH-3, and quinolone-CH_3 resonated at δ =134.0, 118.2, 95.8 and 21.0 ppm, respectively.

The mechanism described the formation of quinoline-2-one/thiazolium bromide derivatives **9a-i** can be based upon an initial proton abstract by triethylamine (Et_3N) led to increase the nucleophilicity of sulphur as shown in Scheme 2. Thereafter, sulphur anion would attack to the electrophilic-CH in **8** to form the intermediate **11** accompanied by elimination of a bromide anion to form **12**. Subsequently, cyclization process would then



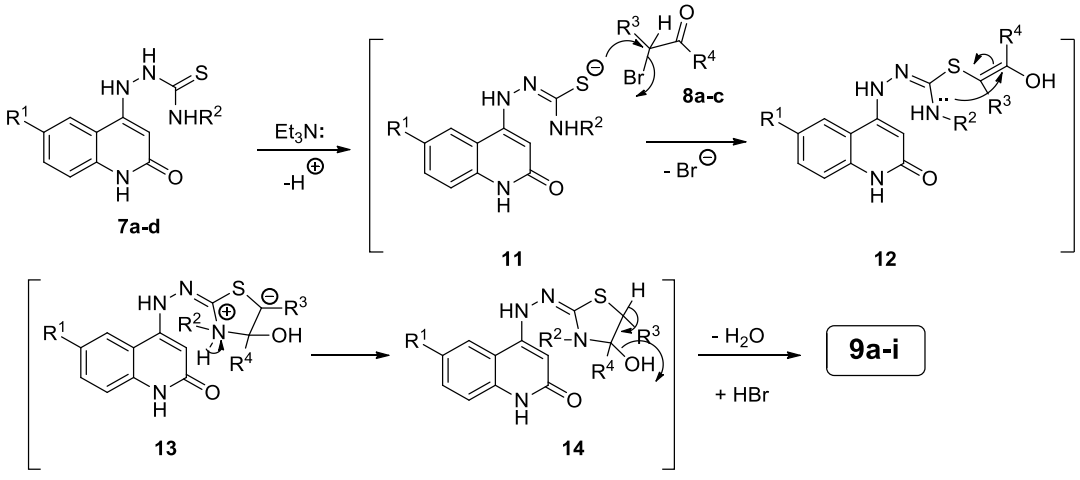
1a-c and **5a-c**
a; $R^1 = CH_3$
b; $R^1 = OCH_3$
c; $R^1 = Cl$

7a: $R^1 = CH_3$; $R^2 = Ph$
7b: $R^1 = OCH_3$; $R^2 = CH_2Ph$
7c: $R^1 = Cl$; $R^2 = Ph$
7d: $R^1 = CH_3$; $R^2 = allyl$

9a: $R^1 = R^4 = CH_3$; $R^2 = R^3 = Ph$ (80%)
9b: $R^1 = OCH_3$; $R^2 = CH_2Ph$, $R^3 = H$; $R^4 = p$-Br-Ph (84%
9c: $R^1 = OCH_3$; $R^2 = allyl$, $R^3 = H$, $R^4 = Ph$ (86%)
9d: $R^1 = Cl$; $R^2 = R^3 = H$, $R^4 = Ph$ (82%)
9e: $R^1 = Cl$; $R^2 = Ph$, $R^3 = H$, $R^4 = p$-Br-Ph (94%)
9f: $R^1 = Cl$; $R^2 = allyl$, $R^3 = H$, $R^4 = p$-Br-Ph (90%)
9g: $R^1 = Cl$; $R^2 = Ph$, $R^3 = p$-Br-Ph, $R^4 = H$ (96%)
9h: $R^1 = CH_3$; $R^2 = allyl$; $R^3 = H$; $R^4 = p$-Br-Ph (92%)
9i: $R^1 = CH_3$; $R^2 = H$, $R^3 = p$-Br-Ph; $R^4 = Ph$ (88%)

Reagent and reaction conditions: **a**) Diethyl malonate, PPA, reflux 3 h; **b**) $POCl_3$, reflux 2 h; **c**) AcOH, reflux 10 h; **d**) $NH_2NH_2{\cdot}H_2O$ (85%), EtOH, reflux 12 h; **e**) Isothiocyanate derivatives (PhNCS, $PhCH_2NCS$, CH_2=CH-CH_2-NCS, **6a-c**); dioxane, reflux 3-4 h, **f)** 2-bromoacetophenones **8a-c** (**a:** $BrCH_2CO$-*p*-BrPh, **b:** $BrCH_2COPh$, **c:** $BrCH(CH_3)COPh$); EtOH, reflux 12-16 h

Scheme 1. Synthesis of quinoline-2-one/thiazolium bromide derivatives **9a-i**



Scheme 2. Mechanism describes the formation of quinoline-2-one/thiazolium bromide derivatives **9a-i**

occurs by the attack of the lone pair of the hydrazinyl-NH to the β-electrophilic vinyl would give the salt **13**. Neutralization of **13** *via* proton transfer would give intermediate **14**. Finally, elimination of water molecule from **14** followed by addition of the extrusion hydrogen bromide would finally give compounds **9a-i** (Scheme 2).

3. Experimental

Melting points were determined using open glass capillaries on a Gallenkamp melting point apparatus (Weiss-Gallenkamp, Loughborough, UK), and are uncorrected. The IR spectra were recorded from potassium bromide disks with a FT device, Minia University NMR spectra were measured in DMSO-d_6 on a Bruker AV-400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C, and 40.55 MHz for ^{15}N); chemical shifts are expressed in δ (ppm), versus internal tetramethylsilane (TMS) = 0 ppm for ^{1}H and ^{13}C, and external liquid ammonia = 0 ppm for ^{15}N. Coupling constants are stated in Hz. Mass spectra were recorded on a Finnigan Fab 70 eV, Institute of Organic Chemistry, Karlsruhe University, Karlsruhe, Germany. TLC was performed on analytical Merck 9385 silica aluminum sheets (Kieselgel 60) with Pf_{254} indicator; TLC's were

viewed at λ_{max} = 254 nm. Elemental analyses were carried out at the Microanalytical Center, Cairo University, Egypt.

General preparation of quinoline-2-one/ thiosemicarbazide derivatives 7a-d

To a suspension of hydrazinoquinolones **5a-c** (1 mmol) in dioxan (25 mL), the appropriate isothiocyanate derivatives **6a-c** (1 mmol) were added and the mixture was heated at reflux on a boiling water-bath for 3-4 h. The mixture was then left to cool and the precipitate so formed was filtered off, washed with hot ethanol and recrystallized to give the target compounds [47].

General procedure for the synthesis of quinoline-2-one/thiazolium bromide derivatives 9a–i

To a suspension of quinoline-2-one/ thiosemicarbazide derivatives **7a-d** (1 mmol) in absolute EtOH (50 mL) containing 0.5 mL of Et_3N, the appropriate bromoacetophenones **8a-c** derivatives (1 mmol) were added and the mixture was heated at reflux on a boiling water bath for 12–16 h. The mixture was then left to cool, and the precipitate of quinoline-2-one/thiazolium bromide derivatives **9a-h** was collected by filtration, then washed by 100 mL cyclohexane and recrystallized from the stated solvents.

6-Methyl-4-(2-(5-methyl-3,4-diphenylthiazol-2(3*H*)-ylidene)-2-(2-oxo-quinolin-4-yl)hydrazinium bromide (9a). Yellow crystals (DMF/EtOH), yield: 0.415.2 g (80%), mp = 340-342 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.20 (s, 1H, quinolone-NH), 10.25 (s, 1H, hydrazine-NH), 8.00 (s, 1H, Ar-H), 7.51-7.39 (m, 4H, Ar-H, NH), 7.35-7.22 (m, 5H, Ar-H), 7.20-7.04 (m, 4H, Ar-H), 6.00 (s, 1H, quinolone-CH-3), 2.30 (s, 3H, quinolone-CH_3), 2.15 ppm (s, 3H, thiazole-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.0 (quinolone-C-2), 156.4 (C=N), 149.0 (thiazole-C-4), 139.5, 138.5, 135.0 (Ar-C), 130.4, 128.8, 128.4, 127.3, 126.9, 125.1 (Ar-CH), 124.6, 123.4, 122.0 (Ar-C), 121.8, 121.0, 120.1 (Ar-CH), 115.0 (thiazole-C-5), 95.4 (quinolone-CH-3), 22.0 (thiazole-CH_3), 20.8 (quinolone-CH_3) ppm; IR (KBr): $\acute{\upsilon}$ = 3330-3320 (NH·s), 3010 (Ar-CH), 2980-2860 (Aliph-CH), 1640 (C=O), 1613 cm^{-1} (C=N). MS (70 eV, %): *m/z* = 439 (100), 424 (27), 409 (32), 391 (5), 376 (17), 343 (3), 267 (7), 102 (50%). Anal. Calcd for $C_{26}H_{23}BrN_4OS$ (519.46): C, 60.12; H, 4.46; N, 10.79; S, 6.17. Found: C, 60.16, H, 4.33; N, 10.70; S, 6.25.

4-(2-(3-Benzyl-5(4-bromophenyl)thiazol-2(3*H*)-ylidene)-2-(6-methoxy-2-oxo-quinolin-4-yl) hydrazinium bromide (9b). Yellow crystals (DMF/EtOH), yield: 0.491 g (84%), mp = 320-322 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.25 (s, 1H, quinolone-NH), 10.20 (s, 1H, hydrazine-NH), 8.20 (s, 1H, Ar-H), 7.77-7.58 (m, 4H, Ar-H + NH), 7.57-7.44 (m, 4H, Ar-H), 7.25-7.19 (m, 4H, Ar-H), 6.95 (s, 1H, thiazole-CH-4), 5.94 (s, 1H, quinolone-CH-3), 4.00 (s, 2H, CH_2-benzyl), 3.95 ppm (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.4 (quinolone-C-2), 155.8 (C=N), 143.0, 140.0, (Ar-C), 138.1 (thiazole-C-5), 135.0, 129.8, 129.0, 127.6, 127.4 (Ar-CH), 127.0, 126.8, 126.7 (Ar-C), 122.0, 121.8, 121.0 (Ar-CH), 119.2 (Ar-C), 105.1 (thiazole-CH-4), 95.0 (quinolone-CH-3), 56.0 (OCH_3), 40.4 (CH_2-Ph) ppm; IR (KBr): $\acute{\upsilon}$ = 3340-3330 (NH·s), 3030 (Ar-CH), 2988-2810 (Aliph-CH), 1650 (C=O), 1611 cm^{-1} (C=N). MS (70 eV, %): *m/z* = 534/532 (22/100), 501/499 (8/12), 468/466 (89/39), 453 (30), 410/408 (24/44), 390 (41), 375 (11), 349 (30). Anal. Calcd for $C_{26}H_{22}Br_2N_4O_2S$ (614.35): C, 50.83; H, 3.61, N, 9.21; S, 5.22. Found: C, 50.99; H, 3.55; N, 9.33; S, 5.18.

4-(2(3-Allyl-4-phenylthiazol-2(3*H*)-ylidene))-2-(6-methoxy-2-oxo-quinolin-4-yl)hydrazinium bromide (9c). Yellow crystals (DMF/MeOH), yield: 0.418 (86%), mp = 270-272 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.33 (s, 1H, quinolone-NH), 10.22 (s, 1H, hydrazine-NH), 8.00 (s, 1H, Ar-H), 7.80-7.60 (m, 4H, Ar-H + NH), 7.5-7.29 (m, 4H, Ar-H), 6.97 (s, 1H, thiazole-CH4), 6.00 (m, 1H, allyl-CH=), 5.98 (s, 1H, quinolone-CH-3), 5.28 (m, 2H, allyl-CH_2=), 4.15 (m, 2H, CH_2-N), 3.95 ppm (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 161.0 (quinolone-C-2), 155.0 (C=N), 143.0, 140.0, 135.0 (Ar-C), 138.2(thiazole-C-5), 134.0 (allyl-CH=), 128.6, 127.6, 127.0 (Ar-CH), 126.8 (Ar-C), 122.0, 121.8, 121.0 (Ar-CH), 120.0 (Ar-C), 114.8 (allyl-CH_2=), 105.2 (thiazole-CH-4), 95.4 (quinolone-CH-3), 56.5 (OCH_3), 45.7 (allyl-CH_2-N) ppm; IR (KBr): $\acute{\upsilon}$ = 3320-3308 (NH·s), 3052 (Ar-CH), 2933-2820 (Aliph-CH), 1643 (C=O), 1612 cm^{-1} (C=N). MS (70 eV, %): *m/z* = 405 (54), 375 (98), 365 (63), 329 (72), 282 (17), 136 (67), 107 (19). Anal. Calcd for $C_{22}H_{21}BrN_4O_2S$ (485.40): C, 54.44; H, 4.36; N, 11.54; S, 6.61; Found: C, 54.60; H, 4.22; N, 11.60; S, 6.44.

6-Chloro-4(2-(3,5-diphenylthiazol-2(3*H*)-ylidene)-2-oxo-quinolin-4-yl)hydrazinium bromide (9d). Yellow crystals (DMF/H_2O), yield: 0.431 g (82%), mp = 314-316 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.30 (s, 1H, quinolone-NH), 10.00 (s, 1H, hydrazine-NH), 7.60-7.49 (m, 6H, Ar-H + NH), 7.40-7.32 (m, 8H, Ar-H), 6.85 (s, 1H, thiazole-CH-4), 6.10 ppm (s, 1H, quinolone-CH-3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.4 (quinolone-C-2), 156.0 (C=N), 139.4, 139.0 (Ar-C), 138.5 ppm (thiazole-C-5), 135.0 (Ar-C), 128.9, 127.8, 127.0, 126.6, 126.2 (Ar-CH), 125.4, 125.0, 124.6 (Ar-C), 122.0, 121.8, 121.0, 119.0 (Ar-CH), 105.3 ppm (thiazole-CH-4), 95.8 (quinolone-CH-3); IR (KBr): $\acute{\upsilon}$ = 3320-3310 (NH·s), 3016 (Ar-CH), 2982-2870 (Aliph-CH), 1654 (C=O), 1610 cm^{-1} (C=N). MS (70 eV, %): *m/z* = 446/445 (100/33), 411 (33), 368 (22), 291 (19), 270 (11), 175 (12), 124 (40), 110 (21). Anal. Calcd for $C_{24}H_{18}BrClN_4OS$ (525.85): C, 54.82; H, 3.45; N, 10.65; S, 6.10; Found: C, 55.90, H, 3.30; N, 10.80; S, 6.22.

4-(2-(2-5(4-Bromophenyl)-3-phenylthiazol-2(3*H*)-ylidene)-2-(6-chloro-2-oxo-quinolin-4-yl hydrazinium bromide (**9e**).

Yellow crystals (DMF/EtOH), yield: 0.568 g (94%), mp = 283-285 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.25 (s, 1H, quinolone-NH), 10.10 (s, 1H, hydrazine-NH), 8.40-8.25 (m, 4H, Ar-H +NH), 7.90-7.75 (m, 4H, Ar-H), 7.35-7.25 (m, 5H, Ar-H), 7.00 (s, 1H, thiazole-CH-4), 6.10 ppm (s, 1H, quinolone-CH-3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 161.8 (quinolone-C-2), 156.8 (C=N), 139.8, 139.4, 135.0 (Ar-C), 133.0 (thiazole-C-5), 129.5, 128.9, 128.0, 127.4, 125.4 (Ar-CH), 125.0, 124.6, 123.8, 122.7 (Ar-C), 122.0, 121.8, 121.0 (Ar-CH), 109.0 (thiazole-CH-4), 96.0 ppm (quinolone-CH-3); IR (KBr): $\acute{\upsilon}$ = 3342-3305 (NH·s), 3021 (Ar-CH), 2980-2848 (Aliph-CH), 1653 (C=O), 1605 cm^{-1} (C=N). MS (70 eV, %): *m/z* = 524/522 (36/66), 489 (25), 438 (17), 391 (47), 313 (4), 199 (13), 154 (61), 149 (100). Anal. Calcd for $C_{24}H_{17}Br_2ClN_4OS$ (604.74): C, 47.67; H, 2.83; N, 9.26; S, 5.30. Found: C, 47.52; H, 2.70; N, 9.37; S, 5.44.

4-(2-(3-Allyl-5(4-bromophenyl)thiazol-2(3*H*)-ylidene)-2-(6-chloro-2-oxoquinolin-4-yl) hydrazinium bromide (9f). Yellow crystals (DMF), yield: 0.523 g (90%), mp = 250-252 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.33 (s, 1H, quinolone-NH), 10.20 (s, 1H, hydrazine-NH), 7.70-7.52 (m, 5H, Ar-H +NH), 7.45-7.20 (m, 3H, Ar-H), 7.00 (s, 1H, Thiazole-CH-4), 6.00 (m, 1H, allyl-CH=), 5.98 (s, 1H, quinolone-CH-3), 5.28 (m, 2H, allyl-CH_2=), 4.15 (m, 2H, CH_2-N); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 161.1 (quinolone-C-2), 154.9 (C=N),); 139.0, (Ar-C), 138.2 (Thiazole-C-5), 136.5, 135.0 (Ar-C), 134.0 (allyl-CH=), 128.6, 127.6 (Ar-CH), 127.0, 126.8 (Ar-C), 122.0, 121.8, 121.0 (Ar-CH), 120.0 (Ar-C), 114.9 (allyl-CH_2=), 105.3 (thiazole-CH-4), 95.4 (quinolone-CH-3), 45.8 (allyl-CH_2-N) ppm; IR (KBr): ν = 3340-3322 (NH·s), 3025 (Ar-CH), 2980-2850 (Aliph-CH), 1608 (C=O), 1600 cm^{-1} (C=N). MS (70 eV, %): *m/z* = 488/486 (17/100), 414 (4), 398 (5), 307 (15), 289 (12), 183 (15), 136 (83), 91 (38). Anal. Calcd for $C_{21}H_{17}Br_2ClN_4OS$ (568.71): C, 44.35; H, 3.01; N, 9.85; S, 5.64; Found: C, 44.44; H, 2.90; N, 9.90; S, 5.70.

4-(2(4-(4-Bromophenyl)-3-phenylthiazol-2(3*H*)-ylidene)-6-chloro-2-oxoquinolin-4-yl)- hydrazinium bromide (9g). Yellow crystals (DMF/MeOH), yield: 0.581 g (96%), mp = 260-262 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.25 (s, 1H, quinolone-NH), 10.10 (s, 1H, hydrazine-NH), 8.40-8.25 (m, 4H, Ar-H + NH), 7.90-7.79 (m, 4H, Ar-H), 7.75 (s, 1H, thiazole-CH-5), 7.35-7.25 (m, 5H, Ar-H), 6.10 ppm (s, 1H, quinolone-CH-3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 161.8 (quinolone-C-2), 156.8 (C=N), 139.8, 139.4 (Ar-C), 137.0 (thiazole-C-4), 135.0 (Ar-C), 129.5, 128.9, 128.0, 127.4, 125.4 (Ar-CH), 125.0, 124.6, 123.8, 122.7 (Ar-C), 122.0, 121.8, 121.0

(Ar-CH), 105.3 (thiazole-CH-5), 96.0 ppm (quinolone-CH-3); IR (KBr): ν = 3340-3310 (NH·s), 3022 (Ar-CH), 2990-2890 (Aliph-CH), 1650 (C=O), 1606 cm^{-1} (C=N). MS (70 eV, %): *m/z* = 524/522 (50/100), 436 (54), 313 (4), 307 (48), 199 (75), 167 (23), 154 (61), 149 (73). Anal. Calcd for $C_{24}H_{17}Br_2ClN_4OS$ (604.74): C, 47.67; H, 2.83; N, 9.26; S, 5.30. Found: C, 47.52; H, 2.70; N, 9.37; S, 5.44.

4-(2(3-Allyl-5-(4-bromophenyl)thiazol-2(3*H*)-ylidene)-2-(6-methyl-2-oxoquinolin-4-yl)-hydrazinium bromide (**9h**). Yellow crystals (DMF/EtOH), yield: 0.504 g (92%), mp = 300-302 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.70 (s, 1H, quinolone-NH), 9.88 (s, 1H, hydrazine-NH), 7.70-7.52 (m, 5H, Ar-H + NH), 7.45-7.20 (m, 3H, Ar-H), 7.15 (s, 1H, thiazole-CH-4), 6.22-6.11 (m, 1H, allyl-CH), 5.97 (s, 1H, quinolone-CH-3), 5.25-5.15 (m, 2H, ally=CH_2), 4.06-4.02 (m, 2H, allyl-CH_2), 2.10 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 161.4 (quinolone-C-2), 154.9 (C=N), 139.0, (Ar-C), 138.2 (Thiazole-C-5), 136.5, 135.0 (Ar-C), 134.0 (allyl-CH=), 128.5, 127.5 (Ar-CH), 127.1, 126.6 (Ar-C), 122.1, 121.9, 121.1 (Ar-CH), 120.0 (Ar-C), 118.2 (allyl=CH), 105. 3 (thiazole-CH-4), 95.8 (quinolone-CH-3), 45.8 (allyl-CH_2-N), 21.0 ppm (CH_3); IR (KBr): $\acute{\upsilon}$ = 3332-3320 (NH·s), 3020 (Ar-CH), 2991-2888 (Aliph-CH), 1652 (C=O), 1602 cm^{-1} (C=N). MS (70 eV, %): *m/z* = 468/466 (37/100), 414/412 (15/50), 398 (26), 313 (9), 307 (38), 289 (11), 163 (11), 136 (65), 91 (39). Anal. Calcd for $C_{22}H_{20}Br_2N_4OS$ (548.29): C, 48.19; H, 3.68; N, 10.22; S, 5.85. Found: C, 48.30; H, 3.81; N, 10.40; S, 5.76.

1-(5(4-Bromophenyl)-3,4-diphenylthiazol-2(3*H*)-ylidene)-2-(6-methyl-2-oxo-1,2-dihydro-quinolin-4-yl)hydrazinium bromide (9i). Yellow crystals (DMF/H_2O), yield: 0.514 g (88%), mp = 290-292 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.90 (s, 1H, thiazole-NH), 12.20 (s, 1H, quinolone-NH), 10.25 (s, 1H, hydrazine-NH),), 7.70-7.56 (m, 4H, Ar-H + NH), 7.35-7.22 (m, 5H, Ar-H), 7.20-7.04 (m, 4H, Ar-H), 6.00 (s, 1H, quinolone-CH-3), 2.30 (s, 3H, quinolone-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.0 (quinolone-C-2), 156.4 (C=N), 149.0 (thiazole-C-4), 139.5, 138.5 (Ar-C), 137.4 (thiazole-C-5), 135.0 (Ar-C), 130.4, 128.8, 128.4, 127.3, 126.9, 125.1 (Ar-CH), 124.6, 123.4, 122.0 (Ar-C), 121.8, 121.0, 120.1 (Ar-CH), 95.4 (quinolone-CH-3), 20.8 (quinolone-CH_3) ppm; IR (KBr): $\acute{\upsilon}$ = 3350-3290 (NH·s), 3080 (Ar-CH), 2960-2810 (Aliph-CH), 1644 (C=O), 1603 cm^{-1} (C=N). MS (70 eV, %): *m/z* = 504/502 (32/53), 359/358 (30/97), 347 (69), 304/302 (36/7), 247 (6), 201 (10), 174 (15), 89 (9). Anal. Calcd for $C_{25}H_{20}Br_2N_4OS$ (584.33): C, 51.39; H, 3.45; N, 9.59; S, 5.49. Found: C, 51.22; H, 3.56; N, 9.70; S, 5.60.

4. Conclusion

The work in this paper describes the formation of new thiazolium bromides derived by quinoline-2-one through the reaction of 3-thiosemicarbazides derived by 2-quinolones with 2-bromoacetophenones. The obtained compounds are expected to possess potential biological activity that we recommend performing further biological study.

Declaration of Competing Interest

No financial or commercial conflicts of interest were declared by all authors

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.molstruc.2021.130501.

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