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Research Article

Synthesis and Cytotoxic Activity against K562 and MCF7 Cell Lines of Some *N*-(5-Arylidene-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazoline-2-yl)thio) acetamide Compounds

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Ethyl 2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetate (**3**) which was synthesized starting from anthranilic acid (**1**) via 2-thioxo-3-phenylquinazolin-4(3*H*)-one (**2**) reacted with hydrazine hydrate to afford 2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetohydrazide (**4**). Reaction of (**4**) with thiocarbonyl-*bis*-thioglycolic acid gave a new compound name *N*-(4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**5**). Knoevenagel condensation of (**5**) with appropriate aldehydes gave fourteen (*Z*)-*N*-(5-arylidene-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide compounds (**6a–o**) with moderate yield. The chemical structure of the compounds was elucidated on the basis of IR, ^{1}H-NMR, ^{13}C-NMR, and HR-MS spectral data. The 5-arylidene-2-thioxothiazolidinone compounds exhibited mild-to-moderate cytotoxic activity against both K562 (chronic myelogenous leukemia) cells and MCF7 (breast cancer) cells.

1. Introduction

Quinazolinones were considered to be a scaffold with potential biological activities. Besides possessing a variety of biological effects including antimicrobial [1–6], anticonvulsant [7, 8], and antihistamine [9, 10] activities, compounds containing quinazolin-4-one nucleus also showed promising anticancer potency [11–20]. Along with that, 5-arylidene-2-thioxothiazolidine-4-one compounds are an important class of compounds with a wide range of pharmaceutical properties. The 5-arylidene-2-thioxothiazolidine-4-one derivatives have been shown to inhibit aldose reductase [21–24], hepatitis C virus (HCV) [25, 26], human immunodeficiency virus (HIV) [27–29], JNK-stimulating phosphatase-1 (JSP-1) [30], glycogen synthase kinase-3 (GSK-3) [31, 32], 17β-hydroxysteroid dehydrogenase type 3 [33], and histone acetyltransferases (HATs) [34]. Specifically, the 5-arylidene-2-thioxothiazolidine-4-one moiety is reported to possess anticonvulsant [35], antimicrobial [36], antidiabetic [37], antitumor [38–40], and anticancer activities [41–44]. The aforementioned compounds have inspired the idea of synthesizing hybrid derivatives where moieties of quinazolin-4-one and 2-thioxothiazolidin-4-one could be incorporated with each other to be an organic molecule with more effective anticancer activity. Therefore, we report here the synthesis of *N*-(4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide and 5-arylidene derivatives of this compound as

well as evaluate their toxicity on some cell lines including K562 (chronic myelogenous leukemia) cells and MCF7 (breast cancer) cells.

2. Materials and Methods

All starting materials were purchased from Acros and used without purification. Melting points were measured in open capillary tubes on a Gallenkamp melting point apparatus.

The structure of all compounds was confirmed by their IR, ^{1}H-NMR, ^{13}C-NMR, and HR-MS spectral data. IR spectra (ν, cm^{-1}) were recorded on a FTIR-8400S-SHIMADZU spectrometer using KBr pellets. The NMR spectra were recorded on a Bruker Avance III spectrometer (500 MHz for ^{1}H-NMR and 125 MHz for ^{13}C-NMR) using residual solvent DMSO-d_6 signals (δ_H 2.50, δ_C 39.52) as internal references. The spin-spin coupling constants (J) are given in Hz. Peak multiplicity is reported as *s* (singlet), *d* (doublet), *dd* (doublet-doublet), *t* (triplet), *q* (quartet), and *m* (multiplet). The HR-ESI-MS spectra were recorded on a Bruker micrOTOF-Q 10187 spectrometer.

The cytotoxic activity of **6a–o** compounds was tested on K562 (chronic myelogenous leukemia) and MCF7 (breast cancer) cell lines using the MTT assay.

3. Experimental

The synthesis of the target compounds is carried out as outlined in Scheme 1.

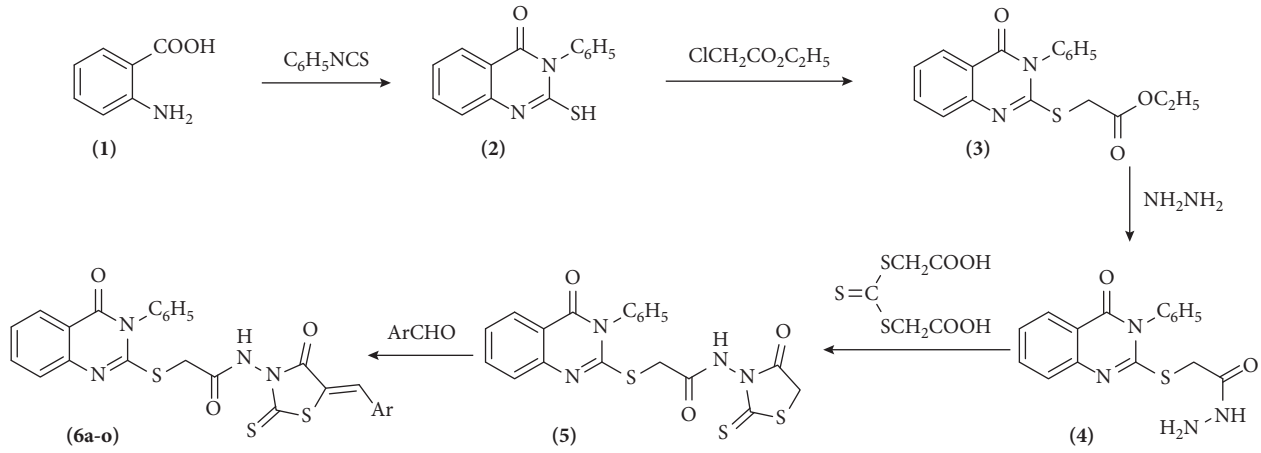
3.1. Synthesis of 2-Mercapto-3-phenylquinazolin-4-one (**2**). To the solution of anthranilic acid 1 (13.7 g, 0.1 mol) and phenyl isothiocyanate (13.5 g, 0.1 mol) in absolute ethanol (200 mL), triethylamine (3.0 mL) was added and the reaction mixture was refluxed for 4.0 h. After cooling to room temperature, the reaction mixture was poured into water and then filtered. The precipitate was recrystallized from a mixture of DMF and water and washed with cold ethanol to give crystals. Yield: 80.0%; mp: 295–297°C (lit. [2, 5] 296–298°C); IR (ν, cm^{-1}): 3217, 3134 (N-H, S-H), 3028 (C-H aromatic), 1659 (C=O), 1618, 1524, and 1485 (C=N, C=C aromatic); ^{1}H-NMR (δ, ppm): 13.05 (1H, *s*, SH), 7.96 (1H, *d*, ^3J = 8.0 Hz, Ar-H), 7.80 (1H, *dd*, $^3J_1 = {}^3J_2$ = 8.0 Hz, Ar-H), 7.50–7.40 (4H, *m*, Ar-H), 7.36 (1H, *dd*, $^3J_1 = {}^3J_2$ = 7.5 Hz, Ar-H), and 7.29 (2H, *d*, ^3J = 7.5 Hz, Ar-H) (see S1a and S1b from Supporting Information).

3.2. Synthesis of Ethyl 2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetate (**3**). An equimolar mixture of 2-mercapto-3-phenylquinazolin-4-one (**2**) (5.08 g, 20 mmol) and anhydrous potassium carbonate (2.76 g, 20 mmol) in dry DMF (30 mL) was stirred for 30 minutes, and then, ethyl chloroacetate (2.45 g, 20 mmol) was added. The reaction mixture was refluxed for 5 h then cooled to room temperature and poured into ice-cold water. The white precipitate was filtered off and purified by crystallization from ethanol to afford pure product 3. Yield: 65.0%; mp: 106–107°C (lit. [45]: 105–107°C); IR (ν, cm^{-1}): 3059 (C-H aromatic), 2976, 2906 (C-H aliphatic), 1732 (C=O ester), 1680 (C=O ketone), 1607, 1598, and 1468 (C=N, C=C aromatic); ^{1}H-NMR (δ, ppm): 8.09 (1H, *d*, ^3J = 8.0 Hz, Ar-H), 7.84 (1H, *d*, ^3J = 7.5 Hz, Ar-H), 7.61–7.48 (7H, *m*, Ar-H), 4.15 (2H, *q*, ^3J = 7.0 Hz, -$\underline{CH_2}CH_3$), 3.99 (2H, *s*, -SCH_2-), and 1.23 (3H, *t*, ^3J = 7.0 Hz, CH_3) (see S2a and S2b from Supporting Information).

3.3. Synthesis of 2-((4-Oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetohydrazide (**4**). To a solution of ester 3 (6.8 g, 20 mmol) in ethanol (50 mL), excess of hydrazine hydrate 80% (1.5 g, 30 mmol) was added. The reaction mixture was refluxed on a water bath for 10 h. After cooling, the solid separated was filtered and recrystallized from ethanol to give crystals of compound **4**. Yield: 68%; mp: 194–196°C (lit. [15]: 195–196°C); IR (ν, cm^{-1}): 3279 (N-H), 3059 (C-H aromatic), 2916 (C-H aliphatic), 1690, 1659 (C=O), 1605, 1547, and 1466 (C=N, C=C aromatic); ^{1}H-NMR (δ, ppm): 9.33 ppm (1H, *s*, NH), 8.09 (1H, *d*, ^3J = 8.0 Hz, Ar-H), 7.86 (1H, *dd*, $^3J_1 = {}^3J_2$ = 8.0 Hz, Ar-H), 7.63 (1H, *d*, ^3J = 8.0 Hz, Ar-H), 7.59–7.62 (3H, *m*, Ar-H), 7.48–7.51 (3H, *m*, Ar-H), 4.28 ppm (2H, *br*, -NH_2-), and 3.86 ppm (2H, *s*, -SCH_2-) (see S3a and S3b from Supporting Information).

*3.4. Synthesis of N-(4-Oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**5**).* A mixture of compound **4** (1.63 g, 5 mmol) and thiocarbonyl-*bis*-thioglycolic acid (1.13 g, 5 mmol) in absolute ethanol (15 mL) was refluxed for 8 h. After cooling, the resulting solid was filtered, dried, and recrystallized from AcOH to give yellowish powder compound **5**. Yield: 55.0%; mp: 237–238°C. IR (ν, cm^{-1}): 3202 (N-H), 3001 (C-H aromatic), 1759, 1690 (C=O), 1551, 1466 (C=C aromatic, C=N), and 1250 (-N-C=S); ^{1}H-NMR (δ, ppm): 11.31 (1H, *s*, NH), 8.09 (1H, *d*, ^3J = 8.0 Hz, Ar-H), 7.86 (1H, *dd*, $^3J_1 = {}^3J_2$ = 8.0 Hz, Ar-H), 7.76 (1H, *d*, ^3J = 8.0 Hz, Ar-H), 7.62–7.60 (3H, *m*, Ar-H), 7.51–7.48 (3H, *m*, Ar-H), 4.41 ppm (2H, *m*, -CH_2- thiazolidine ring), and 4.13 (2H, *m*, -S-CH_2-CONH); ^{13}C-NMR (δ, ppm): 200.1 (C=S), 170.5, 166.0, 161.2 (C=O), 156.5, 147.6, 136.2, 135.2, 130.5, 130.1, 129.9, 127.0, 126.9, 126.6, 120.0 (C_{Ar}), 34.5 (-SCH_2-), and 33.8 (-CH_2- thiazolidine ring); HR-ESI-MS *m/z* 443.0367 $(M + H)^+$ calcd. for ($C_{19}H_{15}N_4O_3S_3$) 443.0306 (see S4a–S4d from Supporting Information).

3.5. General Procedure for Synthesis of N-(5-Arylidene-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)sulfanyl) acetamides (**6a–o**). To a mixture of compound **5** (0.442 g, 1 mmol) and CH_3COONa (0.082 g, 1 mmol) in glacial acetic acid (15 mL), 1 mmol of appropriate aldehyde was added and the solution was refluxed for 5 h. After cooling to room temperature, the reaction mixture was poured into ice-cold water and filtered. The precipitate was recrystallized from an appropriate solvent to give **6a–o** compounds, respectively.



Ar = 4-$(CH_3)_2NC_6H_4$ (**6a**), 4-BrC_6H_4 (**6b**), 4-ClC_6H_4 (**6c**), 4-FC_6H_4 (**6d**), 2-FC_6H_4 (**6e**), 4-$CH_3OC_6H_4$ (**6f**), 4-HOC_6H_4 (**6g**), 3-HOC_6H_4 (**6h**), C_6H_5 (**6i**), 4-$O_2NC_6H_4$ (**6j**), 3-$O_2NC_6H_4$ (**6k**), 2-$O_2NC_6H_4$ (**6l**), 3,4-$(OCH_2O)C_6H_3$ (**6m**), 3-CH_3O-4-HOC_6H_3 (**6n**), $C_6H_5CH{=}CH$ (**6o**)

Scheme 1: Synthetic route for the preparation of the target compounds. Ar = 4-$(CH_3)_2NC_6H_4$ (**6a**), 4-BrC_6H_4 (**6b**), 4-ClC_6H_4 (**6c**), 4-FC_6H_4 (**6d**), 2-FC_6H_4 (**6e**), 4-$CH_3OC_6H_4$ (**6f**), 4-HOC_6H_4 (**6g**), 3-HOC_6H_4 (**6h**), C_6H_5 (**6i**), 4-$O_2NC_6H_4$ (**6j**), 3-$O_2NC_6H_4$(**6k**), 2-$O_2NC_6H_4$ (**6l**), 3, 4-$(OCH_2O)C_6H_3$ (**6m**), 3-CH_3O-4-HOC_6H_3 (**6n**), and $C_6H_5CH{=}CH$ (**6o**).

3.5.1. N-(5-(4-Dimethylamino)benzylidene)-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**6a**). Yield: 59.0%; mp: 268–269°C; IR (ν, cm^{-1}): 3237 (N-H), 2918 (Csp^3-H), 1734, 1686 (C=O), 1584, 1553, 1526 (C=N, C=C), and 1254 (-N-C=S); ^{1}H-NMR (δ, ppm): 11.44 (1H, *s*, NH), 8.10 (1H, *d*, $^3J = 8.0$ Hz, Ar-H), 7.88 (1H, *dd*, $^3J_1 = {}^3J_2 = 7.5$ Hz, Ar-H), 7.80 (1H, *d*, $^3J = 8.0$ Hz, Ar-H), 7.75 (1H, *s*, -CH =), 7.62–7.58 (3H, *m*, Ar-H), 7.53–7.49 (5H, *m*, Ar-H), 6.85 (2H, *d*, $^3J = 9.0$ Hz, Ar-H), and 4.17 (2H, *m*, $-CH_2-$); ^{13}C-NMR (δ, ppm): 190.1 (C=S), 166.1, 163.7, 161.2 (C=O), 156.5, 152.7, 147.7, 136.5, 136.2 135.3, 134.0, 130.5, 130.1, 129.9, 127.0, 126.9, 126.6, 120.1, 120.0, 112.8 and 110.9 (C_{Ar}), 34.6 ($-CH_2-$), and 39.4 ($-N(CH_3)_2$); HR-ESI-MS *m/z* 574.1050 $(M + H)^+$ calcd. for ($C_{28}H_{24}N_5O_3S_3$) 574.1041 (see S5a–S5d from Supporting Information).

3.5.2. N-(5-(4-Bromobenzylidene)-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**6b**). Yield: 56.0%; mp: 224–225°C; IR (ν, cm^{-1}): 3192 (N-H), 3009 (Csp^2-H), 2918 (Csp^3-H), 1736, 1688 (C=O), 1601, 1578, 1551 (C=N, C=C), and 1254 (-N-C=S); ^{1}H-NMR (δ, ppm): 11,47 (1H, *s*, NH), 8.01 (1H, *d*, $^3J = 7.5$ Hz, Ar-H), 7.98 (1H, *s*, –CH =), 7.78 (1H, *d*, $^3J = 7.5$ Hz, Ar-H), 7.71–7.67 (3H, *m*, Ar-H), 7.54–7.51 (5H, *m*, Ar-H), 7.43–7.39 (4H, *m*, Ar-H), and 4.17 (2H, *m*, $-CH_2-$); ^{13}C-NMR (δ, ppm): 190.3 (C=S), 166.2, 163.5, 161.2 (C=O), 156.5, 147.6, 136.5, 136.2, 135.3, 133.8, 133.0, 132.1, 130.6, 130.1, 130.07, 129.9, 127.0, 126.6, 120.5, and 120.0 (C_{Ar}), 34.5 ($-CH_2-$); HR-ESI-MS *m/z* 608.9667 $(M + H)^+$ calcd. for ($C_{26}H_{18}BrN_4O_3S_3$) 608.9724 (see S6a–S6d from Supporting Information).

3.5.3. N-(5-(4-Chlorobenzylidene)-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**6c**). Yield: 60.0%; mp: 226–228°C; IR (ν, cm^{-1}): 3190 (N-H), 3009 (Csp^2-H), 2920 (Csp^3-H), 1738, 1688 (C=O), 1600, 1580, 1551 (C=N, C=C), and 1254 (-N-C=S); ^{1}H-NMR (δ, ppm): 11.55 (1H, *s*, NH), 8.10 (1H, *d*, $^3J = 7.0$ Hz, Ar-H), 7.93 (1H, *s*, –CH =), 7.89 (1H, *dd*, $^3J_1 = {}^3J_2 = 8.0$ Hz, Ar-H), 7.79 (1H, *d*, $^3J = 8.0$ Hz, Ar-H), 7.72 (2H, *d*, $^3J = 8.5$ Hz, Ar-H), 7.64 (2H, *d*, $^3J = 9.0$ Hz, Ar-H), 7.63–7.60 (3H, *m*, Ar-H), 7.53–7.48 (3H, *m*, Ar-H), and 4.17 (2H, *m*, $-CH_2-$); ^{13}C-NMR (δ, ppm): 188.7 (C=S), 167.3, 163.2, 161.1, (C=O), 158.8, 146.7, 137.4, 135.3, 135.0, 133.4, 131.8, 131.5, 130.7, 130.1, 129.8, 129.1, 127.8, 126.9, 125.4, 120.6 and 119.9 (C_{Ar}), and 33.6 ($-CH_2-$); HR-ESI-MS *m/z* 565.0236 $(M + H)^+$ calcd. for ($C_{26}H_{18}ClN_4O_3S_3$) 565.0230 (see S7a–S7d from Supporting Information).

3.5.4. N-(5-(4-Fluorobenzylidene)-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio) acetamide (**6d**). Yield: 62.0%; mp: 262–263°C; IR (ν, cm^{-1}): 3204 (N-H), 2990 (Csp^3-H), 1736, 1686 (C=O), 1593, 1553, 1508 (C=N, C=C), and 1240 (-N-C=S); ^{1}H-NMR (δ, ppm): 11.48 (1H, *s*, NH), 8.10 (1H, *d*, $^3J = 8.0$ Hz, Ar-H), 7.94 (1H, *s*, –CH =), 7.89 (1H, *dd*, $^3J_1 = {}^3J_2 = 8.0$ Hz, Ar-H), 7.80–7.76 (3H, *m*, Ar-H), 7.63–7.61 (3H, *m*, Ar-H), 7.53–7.49 (3H, *m*, Ar-H), 7.43 (2H, *dd*, $^3J_1 = {}^3J_2 = 9.0$ Hz, Ar-H), and 4.18 (2H, *m*, $-CH_2-$); ^{13}C-NMR (δ, ppm): 190.4 (C=S), 166.2, 163.5, 161.2 (C=O), 163.9 ($^1J_{C\text{-}F} = 251.0$), 156.5, 147.6, 136.2, 135.3, 134.1, 134.0, 133.9, 130.6, 130.1, 129.9, 127.0, 126.9, 126.6, 120.0, 119.5, and 117.3 ($^2J_{C\text{-}F} = 22.0$) (C_{Ar}), 34.5 ($-CH_2-$); HR-ESI-MS *m/z* 549.0527 $(M + H)^+$ calcd. for ($C_{26}H_{18}FN_4O_3S_3$) 549.0520 (see S8a–S8c from Supporting Information).

3.5.5. N-(5-(2-Fluorobenzylidene)-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio) acetamide (**6e**). Yield: 61.0%; mp: 264–265°C; IR (ν, cm^{-1}): 3256 (N-H), 2978 (Csp^3-H), 1738, 1690 (C=O), 1605, 1551, 1487 (C=N, C=C), and 1258 (-N-C=S); ^{1}H-NMR (δ, ppm): 11.59 (1H, *s*, NH), 8.10 (1H, *d*, $^3J = 7.5$ Hz, Ar-H), 7.89 (1H, *dd*, $^3J_1 = {}^3J_2 = 8.0$ Hz, Ar-H), 7.86 (1H, *s*, –CH =), 7.79 (1H, *d*, $^3J = 8.5$ Hz, Ar-H), 7.66–7.61 (5H, *m*, Ar-H), 7.53–7.41 (5H, *m*, Ar-H), and 4.18 (2H, *m*, $-CH_2-$); ^{13}C-NMR (δ, ppm):

190.3 (C=S), 166.3, 163.4, 161.2 (C=O), 161.1 ($^1J_{C\text{-}F} = 251.6$), 156.5, 147.6, 136.2, 135.3, 134.2, 130.6, 130.5, 130.1, 129.9, 127.0, 126.6, 126.4 ($^2J_{C\text{-}F} = 21.6$), 126.3, 126.2, 122.5, 121.1, 121.0, 120.0 (C_{Ar}), and 116.9 ($^2J_{C\text{-}F} = 21.1$), 34.5 (-CH_2-); HR-ESI-MS *m/z* 549.0462 $(M + H)^+$ calcd. for ($C_{26}H_{18}FN_4O_3S_3$) 549.0520 (see S9a–S9c from Supporting Information).

3.5.6. N-(5-(4-Methoxybenzylidene)-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**6f**). Yield: 54.0%; mp: 218–219°C; IR (ν, cm^{-1}) 3208 (N-H), 3009 (C*sp*^{2}-H), 2920 (C*sp*^{3}-H), 1736, 1686 (C=O), 1578, 1551, 1506 (C=N, C=C), and 1248 (-N-C=S); ^{1}H-NMR (δ, ppm) 11.51 (1H, *s*, NH), 8.10 (1H, *d*, $^3J = 8.0$ Hz, Ar-H), 7.93 (1H, *s*, –CH =), 7.89 (1H, *dd*, $J_1 = J_2 = 8.0$, Ar-H), 7.79 (1H, *d*, $^3J = 8.0$ Hz, Ar-H), 7.72 (2H, *d*, $^3J = 9.0$ Hz, Ar-H), 7.64 (2H, *d*, $^3J = 8.5$ Hz, Ar-H), 7.63–7.61 (3H, *m*, Ar-H), 7.53–7.48 (3H, *m*, Ar-H), 4.18 (2H, *m*, -CH_2-), and 3.86 (3H, *s*, –OCH_3); ^{13}C-NMR (δ, ppm) 190.4 (C=S), 166.2, 163.6, 162.3, 161.2, 156.5, 147.7, 136.2, 135.3, 135.27, 133.7, 130.5, 129.9, 127.0, 126.9, 126.6, 125.8, 120.0, 116.3 and 115.7(C_{Ar}), 56.13 (-OCH_3), and 34.55 (-CH_2-); HR-ESI-MS *m/z* 561.0731 $(M + H)^+$ calcd. for ($C_{27}H_{21}N_4O_4S_3$) 561.0647 (see S10a–S10c from Supporting Information).

3.5.7. N-(5-(4-Hydroxybenzylidene)-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**6g**). Yield: 57.0%; mp: 215–216°C; IR (ν, cm^{-1}): 3196 (*br*) (O-H, N-H), 3013 (C*sp*^{2}-H), 2918 (C*sp*^{3}-H), 1728, 1711, 1651 (C=O), 1572, 1551, 1468 (C=N, C=C), and 1246 (-N-C=S); ^{1}H-NMR (δ, ppm): 11.48 (1H, *s*, NH), 10.57 (1H, *s*, OH), 8.10 (1H, *d*, $^3J = 7.5$ Hz, Ar-H), 7.89 (1H, *dd*, $^3J_1 = {}^3J_2 = 8.0$ Hz, Ar-H), 7.82 (1H, *s*, –CH =), 7.79 (1H, *d*, $^3J = 8.0$ Hz, Ar-H), 7.63–7.60 (3H, *m*, Ar-H), 7.56 (2H, *d*, $^3J = 8.5$ Hz, Ar-H), 7.52–7.48 (3H, *m*, Ar-H), 6.96 (2H, *d*, $^3J = 8.5$ Hz, Ar-H), and 4.17 (2H, *m*, -CH_2-); ^{13}C-NMR (δ, ppm): 190.5 (C=S), 166.2, 163.7, 162.8, 161.5, 161.2, 156.5, 147.6, 136.2, 135.8, 135.3, 134.2, 130.5, 130.1, 129.9, 127.0, 126.9, 126.6, 124.3, 120.0, 117.2, and 115.0 (C_{Ar}), 34.5 (-CH_2-); HR-ESI-MS *m/z* 547.0598 $(M + H)^+$ calcd. for ($C_{26}H_{19}N_4O_4S_3$) 547.0568 (see S11a–S11c from Supporting Information).

3.5.8. N-(5-(3-Hydroxybenzylidene)-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**6h**). Yield: 54.0%; mp: 233–234°C; IR (ν, cm^{-1}): 3447 (*br*, O-H, N-H), 1734, 1654 (C=O), 1607, 1576, 1554, and 1253 (-N-C=S); ^{1}H-NMR (δ, ppm): 11.53 (1H, *s*, NH), 10.48 (1H, *s*, OH), 8.10 (1H, *d*, $^3J = 7.0$ Hz, Ar-H), 7.89 (1H, *dd*, $^3J_1 = {}^3J_2 = 8.0$ Hz, Ar-H), 7.82 (1H, *s*, –CH =), 7.79 (1H, *d*, $^3J = 8.0$ Hz, Ar-H), 7.63–7.61 (3H, *m*, Ar-H), 7.53–7.48 (3H, *m*, Ar-H), 7.38 (1H, *dd*, $^3J_1 = {}^3J_2 = 8.0$ Hz, Ar-H), 7.13 (1H, *d*, $^3J = 7.5$ Hz, Ar-H), 7.05 (1H, *s*, Ar-H), 6.95 (1H, *dd*, $^3J = 8.0$ Hz, $^4J = 2.0$ Hz, Ar-H), and 4.18 (2H, *m*, -CH_2-); ^{13}C-NMR (δ, ppm): 190.08 (C=S), 165.7, 163.0, 160.6 (C=O), 158.0, 156.0, 147.1, 135.6, 134.9, 134.7, 133.8, 130.6, 130.0, 129.5, 129.4, 126.5, 126.4, 126.1, 122.2, 119.5, 119.0, 118.7, and 116.5 (C_{Ar}), 34.0 (-CH_2-); HR-ESI-MS *m/z* 547.0570 $(M + H)^+$ calcd. for ($C_{26}H_{19}N_4O_4S_3$) 547.0563 (see S12a–S12c from Supporting Information).

3.5.9. N-(5-Benzylidene-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**6i**). Yield: 56.0%; mp: 272–273°C; IR (ν, cm^{-1}): 3253 (N-H), 2918 (C*sp*^{3}-H), 1728, 1694 (C=O), 1605, 1577, 1553 (C=N, C=C), and 1261 (-N-C=S); ^{1}H-NMR (δ, ppm): 11.54 (1H, *s*, NH), 8.10 (1H, *d*, $^3J = 7.5$ Hz, Ar-H), 7.92 (1H, *s*, –CH =), 7.89 (1H, *dd*, $^3J_1 = {}^3J_2 = 8.0$ Hz, Ar-H), 7.79 (1H, *d*, $^3J = 8.0$ Hz, Ar-H), 7.69 (2H, *d*, $J = 7.5$ Hz, Ar-H), 7.64–7.48 (9H, *m*, Ar-H), and 4.17 (2H, *m*, -CH_2-); ^{13}C-NMR (δ, ppm): 190.5 (C=S), 166.2, 163.5, 161.2, 156.5, 147.6, 136.2, 135.3, 135.2, 133.2, 131.8, 131.3, 130.6, 130.1, 130.0, 129.9, 127.0, 126.6, 120.0, and 119.8 (C_{Ar}), 34.53 (-CH_2-); HR-ESI-MS *m/z* 554.0449 $(M + Na)^+$ calcd. for ($C_{26}H_{18}N_4O_3S_3Na$) 553.0433 (see S13a–S13c from Supporting Information).

3.5.10. N-(5-(4-Nitrobenzylidene)-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**6j**). Yield: 53.0%; mp: 233–234°C; IR (ν, cm^{-1}): 3265 (N-H), 3067 (C*sp*^{2}-H), 2972, 2918 (C*sp*^{3}-H), 1734, 1682 (C=O), 1602, 1551, 1524, 1468 (C=N, C=C), and 1260 (-N-C=S); ^{1}H-NMR (δ, ppm): 11.61 (1H, *s*, NH), 8.37 (2H, *d*, $J = 8.5$ Hz, Ar-H), 8.10 (1H, *d*, $^3J = 7.5$ Hz, Ar-H), 8.04 (1H, *s*, –CH =), 7.95 (2H, *d*, $J = 8.5$, Ar-H), 7.89 (1H, *dd*, $J_1 = J_2 = 8.0$, Ar-H), 7.79 (1H, *d*, $J = 8.0$ Hz, Ar-H), 7.63–7.61 (3H, *m*, Ar-H), 7.53–7.49 (3H, *m*, Ar-H), and 4.19 ppm (2H, *m*, -CH_2-); ^{13}C-NMR (δ, ppm): 187.8 (C=S), 167.3, 162.9, 161.0, 158.8, 148.3, 146.7, 138.8, 135.3, 135.0, 131.2, 131.0, 130.7, 130.1, 129.1, 127.8, 127.0, 125.3, 124.7, 124.5, and 119.9 (C_{Ar}), 34.5 (-CH_2-); HR-ESI-MS *m/z* 576.0445 $(M + H)^+$ calcd. for ($C_{26}H_{18}N_5O_5S_3$) 576.0464 (see S14a–S14a from Supporting Information).

3.5.11. N-(5-(3-Nitrobenzylidene)-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio) acetamide (**6k**). Yield: 51.0%; mp: 200–201°C; IR (ν, cm^{-1}): 3557, 3418, 3179 (N-H), 3011 (C*sp*^{2}-H), 2924 (C*sp*^{3}-H), 1736, 1682 (C=O), 1543, 1466 (C=N, C=C), and 1250 (-N-C=S); ^{1}H-NMR (δ, ppm): 11.60 (1H, *s*, NH), 8.55 (1H, *s*, Ar-H), 8.35 (1H, *dd*, $^3J = 8.0$, $^4J = 2.0$ Hz, Ar-H), 8.10 (1H, *s*, –CH =), 8.09 (2H, *m*, Ar-H), 7.91–7.84 (2H, *m*, Ar-H), 7.80 (1H, *d*, $^3J = 8.0$ Hz, Ar-H), 7.63–7.61 (3H, *m*, Ar-H), 7.53–7.49 (3H, *m*, Ar-H), and 4.19 (2H, *m*, -CH_2-); ^{13}C-NMR (δ, ppm): 190.3 (C=S), 166.3, 163.3, 161.2, 156.5, 148.8, 147.6, 136.4, 136.2, 135.3, 134.8, 132.7, 131.6, 130.6, 130.1, 129.9, 127.0, 126.6, 125.9, 125.7, 122.8, and 120.0, (C_{Ar}), 34.51 (-CH_2-); HR-ESI-MS *m/z* 576.0468 $(M + H)^+$ calcd. for ($C_{26}H_{18}N_5O_5S_3$) 576.0470 (see S15a–S15c from Supporting Information).

3.5.12. N-(5-(2-Nitrobenzylidene)-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio) acetamide (**6l**). Yield: 63.0%; mp: 230–231°C; IR (ν, cm^{-1}): 3252 (N-H), 2974 (C*sp*^{3}-H), 1740, 1686 (C=O), 1603, 1551, 1524, 1468 (C=N, C=C), and 1250 (-N-C=S); ^{1}H-NMR (δ, ppm) 11.59 (1H, *s*, NH), 8.26 (1H, *d*, $^3J = 8.0$, Ar-H), 8.17 (1H,

s, –CH =), 8.10 (1H, *d*, $^3J = 8.0$, Ar-H), 7.96–7.87 (2H, *m*, Ar-H), 7.80–7.77 (3H, *m*, Ar-H), 7.64–7.58 (3H, *m*, Ar-H), 7.52–7.49 (3H, *m*, Ar-H), and 4.18 (2H, *m*, -CH_2-); ^{13}C-NMR (δ, ppm) 190.7 (C=S), 166.3, 162.8, 161.2 (C=O), 156.5, 148.3, 147.6, 136.2, 135.3, 132.4, 132.2, 130.6, 130.1, 130.0, 129.9, 128.9, 127.0, 126.95, 126.6, 126.2, 124.1, and 120.0 (C_{Ar}), 34.5 (-CH_2-); HR-ESI-MS *m/z* 576.0427 $(M + H)^+$ calcd. for ($C_{26}H_{18}N_5O_5S_3$) 576.0470 (see S16a–S16c from Supporting Information).

3.5.13. N-(5-(Benzo[d][1,3]dioxol-5-yl-methylene)-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**6m**). Yield: 62.0%; mp: 231–232°C; IR (ν, cm^{-1}) 3429, 3103, 3051 (Csp^2-H), 2974 (Csp^3-H), 2778, 2457, 1776, 1713, 1632 (C=O), 1607, 1573, 1492 (C=N, C=C), and 1244 (-N-C=S); ^{1}H-NMR (δ, ppm) 11.51 (1H, *s*, NH), 8.10 (1H, *d*, $^3J = 7.5$, Ar-H), 7.88 (1H, *dd*, $^3J_1 = {}^3J_2 = 7.5$, Ar-H), 7.84 (1H, *s*, –CH =), 7.79 (1H, *d*, $^3J = 8.0$, Ar-H), 7.64–7.61 (3H, *m*, Ar-H), 7.53–7.49 (3H, *m*, Ar-H), 7.27 (1H, *d*, $^3J = 8.0$, Ar-H), 7.22 (1H, *s*, Ar-H), 7.14 (1H, *d*,$^3J = 8.5$, Ar-H), 6.17 (2H, *s*,-OCH_2-), and 4.18 (2H, *m*, -CH_2-); ^{13}C-NMR (δ, ppm) 190.3 (C=S), 166.2, 163.6, 161.2 (C=O), 156.5, 150.7, 148.9, 147.6, 136.2, 135.4, 135.3, 130.5, 130.1, 129.9, 127.9, 127.4, 127.0, 126.9, 126.6, 120.0, 117.0, 110.3 and 109.9 (C_{Ar}), 102.8 (-OCH_2O-), and 34.5 (-CH_2-); HR-ESI-MS *m/z* 597.0361 $(M + Na)^+$ calcd. for ($C_{27}H_{18}N_4O_5S_3Na$) 597.0337 (see S17a–S17c from Supporting Information).

3.5.14. N-(5-(4-Hydroxy-3-methoxybenzylidene)-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**6n**). Yield: 58.0%; mp: 234–235°C; IR (ν, cm^{-1}) 3358, 3290, 3063 (Csp^2-H), 2978, 2932 (Csp^3-H), 2851, 1728, 1682 (C=O), 1572, 1549, 1497 (C=N, C=C), and 1249 (-N-C=S); ^{1}H-NMR (δ, ppm) 11.48 (1H, *s*, NH), 10.24 (1H, *s*, OH), 8.10 (1H, *d*, $^3J = 7.5$, Ar-H), 7.89 (1H, *dd*, $^3J_1 = {}^3J_2 = 7.5$, Ar-H), 7.83 (1H, *s*, –CH =), 7.80 (1H, *d*, $J = 8.0$, Ar-H), 7.63–7.61 (3H, *m*, Ar-H), 7.53–7.49 (3H, *m*, Ar-H), 7.25 (1H, *d*, $^4J = 1{,}5$ Hz, Ar-H), 7.18 (1H, *dd*, $^3J = 8.5$ Hz, $^4J = 2.0$ Hz, Ar-H), 6.97 (1H, *d*, $^3J = 8.0$ Hz, Ar-H), 4.17 (2H, *m*, -CH_2-), and 3.85 (3H, *s*, –OCH_3); ^{13}C-NMR (δ, ppm) 190.4 (C=S), 166.2, 163.7, 161.2 (C=O), 156.5, 151.1, 148.7, 147.7, 136.2, 136.1, 135.3, 130.6, 130.1, 129.9, 127.0, 126.9, 126.6, 126.1, 124.7, 120.0, 117.0, 115.4, and 115.1 (C_{Ar}), 56.2 (-OCH_3), 34.5 (-CH_2-); HR-ESI-MS *m/z* 577.0659 $(M + H)^+$ calcd. for ($C_{27}H_{21}N_4O_5S_3$) 577.0668 (see S18a–S18c from Supporting Information).

3.5.15. 2-((4-Oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)-N-(4-oxo-5-(phenylallylidene)-2-thioxothiazolidin-3-yl)acetamide (**6o**). Yield: 60.0%; mp: 246–247°C; IR (ν, cm^{-1}) 3233 (N-H), 2920 (Csp^3-H), 2851, 1740, 1690 (C=O), 1607, 1578, 1551, 1470 (C=N, C=C), and 1246 (-N-C=S); ^{1}H-NMR (δ, ppm) 11.48 (1H, *s*, NH), 8.10 (1H, *d*, $^3J = 8.0$, Ar-H), 7.89 (1H, *dd*, $^3J_1 = {}^3J_2 = 8.5$, Ar-H), 7.79 (1H, *d*, $^3J = 8.0$, Ar-H), 7.73 (2H, *d*, $^3J = 7.0$, Ar-H), 7.65 (1H, *d*, $^3J = 12.0$ Hz, –CH=CH-), 7.61–7.58 (3H, *m*, Ar-H), 7.53–7.49 (4H, *m*, Ar-H), 7.46–7.31 (3H, *m*, Ar-H), 7.16 (1H, *dd*, $^3J_1 = {}^3J_2 = 12.0$, Ar-H), and 4.16 (2H, *m*, -CH_2-); ^{13}C-NMR (δ, ppm) 190.4 (C=S), 166.2, 163.0, 161.2 (C=O), 156.5, 147.6, 146.9, 136.2, 135.9, 135.7, 135.3, 130.8, 130.5, 130.1, 129.9, 129.5, 128.8, 127.0, 126.9, 126.6, 123.5, 120.7, and 120.0 (C_{Ar} and C_{ankene}), 34.5 (-CH_2-); HR-ESI-MS *m/z* 557.0791 $(M + H)^+$ calcd. for ($C_{28}H_{21}N_4O_3S_3$) 557.0770 (see S19a–S19c from Supporting Information).

3.6. Cell Viability Assay. The experimental procedure was followed by the steps presented in the literature [46, 47]. In brief, K562 cells and MCF7 cells were cultured in the DMEM medium supplemented with 10% fetal bovine serum (FBS), 100 IU/mL penicillin, and 100 μg/mL streptomycin and maintained at 37°C and 5% CO_2 with 95% humidity. Viable cells were counted and inoculated in 96-well plate with a density of 10^5 cells/100 μL/well for K562 and 5×10^4 cells/100 μL/well for MCF7. After 24 hours, the cells were treated with the compounds and doxorubicin (positive control) diluted in culture media at 100, 50, 25, 12.5, 6.25, 3.125, and 0 μg/mL concentration containing 1, 0.5, 0.25, 0.125, 0.0625, 0.03125, and 0% dimethyl sulfoxide (DMSO), respectively. DMSO in culture media was used as negative control. In addition, the culture medium without cells was used as blank. All experiments were done in triplicate. The plates were incubated in 5% CO_2 and 95% humidity at 37°C for 72 hours. 10 μL of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) was added into each well and incubated in 37°C in 5% CO_2 for 3.5 hours. 70 μL of detergent reagent (10% SDS) was added into each well, and the plate was maintained in 37°C for 16 hours. The optical density of each well was read by using a scanning multiwall spectrophotometer (Sunrise) at a wavelength of 595 nm. Cell survival was measured as the percentage absorbance compared to the negative control (DMSO-treated cells). Cell death (% inhibition) was estimated by the following formula:

$$\%\ \text{inhibition} = 100 - \frac{\left(A_{\text{Sample}} - A_{\text{Blank}}\right)}{\left(A_{\text{DMSO}} - A_{\text{Blank}}\right)} 100, \quad (1)$$

where A_{Sample} is the absorbance of sample at 595 nm, A_{DMSO} is the absorbance of negative control at 595 nm, and A_{Blank} is the absorbance of blank at 595 nm.

Statistical analyses were performed using GraphPad Prism version 5.0 software.

4. Results and Discussion

2-Mercapto-3-phenylquinazolin-4-one (2), ethyl 2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetate (3), and 2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetohydrazide (4) were prepared according to reported methods [1, 3, 7, 14, 15, 18]. The similarity in both melting points and spectral characteristics of these compounds with the ones of the corresponding compounds in literature confirmed their formation.

The reaction of a hydrazide compound with thiocarbonyl-*bis*-thioglycolic acid to form a 2-thioxothiazolidine-4-one compound was mentioned by some authors [36,38–43]. Therefore, the hydrazide 4 was used in the reaction with thiocarbonyl-*bis*-thioglycolic acid in ethanol to obtain *N*-(4-oxo-2-thioxothiazolidin-3-yl)-2-

((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (5). In the IR spectrum of compound **5**, beside the absorption peak of the –NH– group at 3202 cm^{-1} and the absorption peak of lactam and amide carbonyl groups at 1690 cm^{-1}, the appearance of a new band at 1759 cm^{-1} indicated the presence of the C=O group in the 2-thioxothiazolidin-4-one ring. The mass spectrum of the product showed the $[M+H]^+$ ion peak at *m/z* 443.0367 in agreement with the molecular formula of $C_{19}H_{15}N_4O_3S_3$ ((M + H) = 443.0306). In the ^{1}H-NMR spectrum of the compound, besides the signal of the methylene group bonding with the quinazoline ring via the sulfur atom at δ 4.13, there was an appearance of a new signal at δ 4.41, which was imputed to the methylene group on the thiazolidinone ring. Similar to the 3-(4-methylcoumarin-7-yloxyacetylamino)-2-thioxo-1,3-thiozolidin-4-one compound [36], the signals of the methylene groups in the molecule of compound **5** were not also *singlets* as expected. They were split by a non-first-order splitting effect. 17 signals appeared in the ^{13}C-NMR spectrum of 5 including 2 signals at δ 34.5 and 33.8 (2 methylene carbon), a signal at δ 200.1 (carbon in the thioxo group), 3 signals at δ 170.5, 166.0, and 161.2 (3 carbon carbonyl), and 14 signals at δ 120.0–156.5 (unsaturated and aromatic carbon) are good accordant to the structure of compound **5**.

Compound **5** with the 2-thioxothiazolidin-4-one ring containing the active methylene group was then further reacted with appropriate aldehydes to give the raw of *N*-(5-arylidene-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)sulfanyl)acetamide compounds (**6a–o**) in the conditions of the Knoevenagel condensation reaction. In the IR spectra, the signal of the C=O group in the thioxothiazolidin-4-one ring of the 6a–o compounds in a comparison with that one of the compound 5 appeared at a lower frequency because of the conjugation of the carbonyl group with the benzylidene moiety. Mass spectra of the synthesized **6a–o** compounds showed the molecular peaks in agreement with their molecular formula. In the ^{1}H-NMR spectra of **6a–o** compounds, the signals of the methylene group outside the thiazolidinone ring (-SCH_2CONH-) still appeared as *multiplet* peaks at around δ 4.16–4.19, but the signal of the methylene group on the ring was disappearance. Along with the additional signals of the aromatic protons in accordance with those ones of the initial aldehyde, a signal of the methylidene proton as a *singlet* at δ 7.79–7.93 also appeared in the spectrum of each compound. These were evidence for the conversion of compound **5** to compounds **6a–h** by Knoevenagel condensation. According to the previous reports [21, 22, 24, 25, 43, 48], because of the interaction with the carbonyl group at the 4 position, the methylidene proton of the *Z*-isomer of 5-arylidene-2-thioxo-thiazolidin-4-one compounds was more downfield (δ 7.9) than that of the *E*-isomer (δ 7.4). Comparing the vinylic proton shift in ^{1}H-NMR spectra of **6a–o** with these chemical shifts indicated that the exocyclic double bond of the thiazolidinone **6a–o** compounds exists in the *Z*-configuration. The formation of the *Z*-isomers may be explained by the high degree of thermodynamic stability of these isomers [21, 22, 24].

All compounds were evaluated for their potential cytotoxicity against K562 and MCF7 tumor cell lines using doxorubicin as a positive control. The results were expressed in terms of the percentage growth inhibition (Table 1) and the IC_{50} value of the compounds (Table 2). The results showed that compounds **5**, **6f**, and **6l** exert moderate cytotoxicity against MCF7 cells with a % inhibition of cell growth of 64.4 ± 6.5 μg/mL, 82.5 ± 5.2 μg/mL, and 64.4 ± 2.1 μg/mL, respectively. Other compounds showed mild proliferative inhibition on both tested tumor cell lines.

Table 1: The selective cytotoxicity of compounds **5** and **6a–o** against K562 and MCF7 cell lines

No	Compounds	Inhibition of cell growth (%)	
		K562	MCF7
1	Doxorubicin	99.1 ± 0.3	96.5 ± 1.3
2	**5**	7.6 ± 0.6	64.4 ± 6.5
3	**6a**	23.4 ± 0.6	51.3 ± 0.4
4	**6b**	13.5 ± 0.7	14.8 ± 3.3
5	**6c**	4.6 ± 0.1	38.2 ± 1.3
6	**6d**	34.4 ± 2.7	22.2 ± 0.9
7	**6e**	36.6 ± 2.0	33.6 ± 2.3
8	**6f**	22.9 ± 0.6	82.5 ± 5.2
9	**6g**	8.4 ± 1.1	23.8 ± 0.4
10	**6h**	33.0 ± 0.7	7.7 ± 0.1
11	**6i**	15.7 ± 2.3	27.1 ± 0.6
12	**6j**	52.7 ± 1.0	11.7 ± 0.5
13	**6k**	38.0 ± 2.1	37.1 ± 2.8
14	**6l**	22.2 ± 1.3	64.4 ± 2.1
15	**6m**	18.1 ± 1.2	9.8 ± 0.4
16	**6n**	23.4 ± 2.0	21.0 ± 1.0
17	**6o**	3.0 ± 0.1	15.5 ± 0.4

Table 2: IC_{50} (μg/mL) on two cancer cell lines of the compounds.

No	Compounds	IC_{50} (μg/mL)	
		K562	MCF7
1	Doxorubicin	1.8 ± 0.1	2.4 ± 0.1
2	**5**	>100	58.1 ± 3.8
3	**6a**	>100	98.0 ± 0.4
4	**6b**	>100	>100
5	**6c**	>100	>100
6	**6d**	>100	>100
7	**6e**	>100	>100
8	**6f**	>100	65.4 ± 7.6
9	**6g**	>100	>100
10	**6h**	>100	>100
11	**6i**	>100	>100
12	**6j**	93.8 ± 0.7	>100
13	**6k**	>100	>100
14	**6l**	>100	87.4 ± 2.2
15	**6m**	>100	>100
16	**6n**	>100	>100
17	**6o**	>100	>100

The experiments were done in triplicate. The presented data show mean ± SD. The values were calculated by using GraphPad Prism 5 software.

5. Conclusions

In the present paper, a new compound named *N*-(4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (5) and fourteen new 5-arylidene derivatives of this compound were successfully

synthesized and then the structure was determined by IR, ^{1}H-NMR, ^{13}C-NMR, and HR-MS spectral data. The investigation also indicated that the *Z*-isomer of the *N*-(5-arylidene-4-oxo-2-thioxothiazolidin-3-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide compounds was formed in the Knoevenagel reaction of (5) and appropriate aldehydes. All of the 5 arylidene derivatives exhibited mild-to-moderate cytotoxic activity against K562 and MCF7 cell lines.

Data Availability

The IR, NMR, and HR-MS spectral data used to support the findings of this study are included within the supplementary information file.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Supplementary Materials

Supplementary data associated with this article can be found in the attached file. These data include IR, ^{1}H-NMR, ^{13}C-NMR, and HR-MS spectra of the synthesized compounds (**2**, **3**, **4**, **5,** and **6a–o**). (*Supplementary Materials*)

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