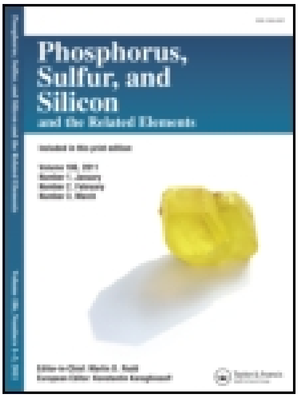

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Synthesis and Characterization of Novel Quinazoline-Substituted 1,3,4-Thiadiazolium-5-thiolates

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SYNTHESIS AND CHARACTERIZATION OF NOVEL QUINAZOLINE-SUBSTITUTED 1,3,4-THIADIAZOLIUM-5-THIOLATES

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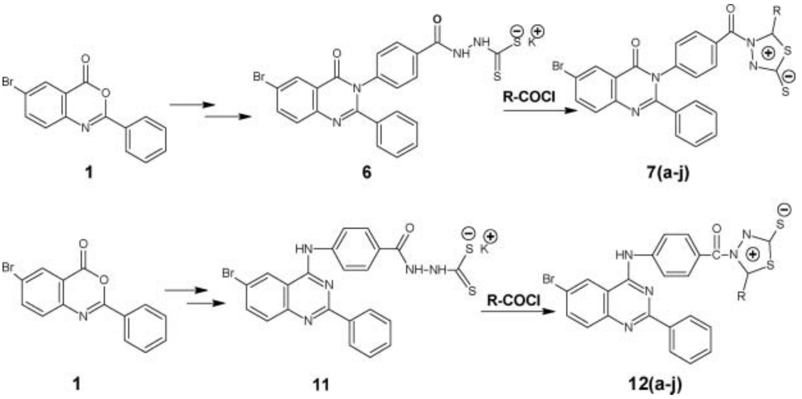
GRAPHICAL ABSTRACT



Abstract *Novel 3-[4-(6-bromo-4-oxo-2-phenylquinazolin-3(4H)-yl)benzoyl]-2-substituted-1,3,4-thiazolium-5-thiolate **7(a–j)** and 3-{4-[(6-bromo-2-phenylquinazolin-4-yl)amino] benzoyl}-2-substituted-1,3,4-thiadiazolium-5-thiolate **12(a–j)** were synthesized from 6-bromo-2-phenyl-4H-3,1-benzoxazin-4-one (**1**). The structures of the newly synthesized compounds were confirmed by spectral data and elemental analysis.*

Supplemental materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.*

Keywords Carbodithioic acid; mesoionic; quinazoline; 1,3,4-thiadiazolium-5-thiolate

INTRODUCTION

A literature survey revealed that mesoionic compounds are one of the most important classes of heterocyclic compounds.[1–3] The compounds containing a bisheterocyclic system

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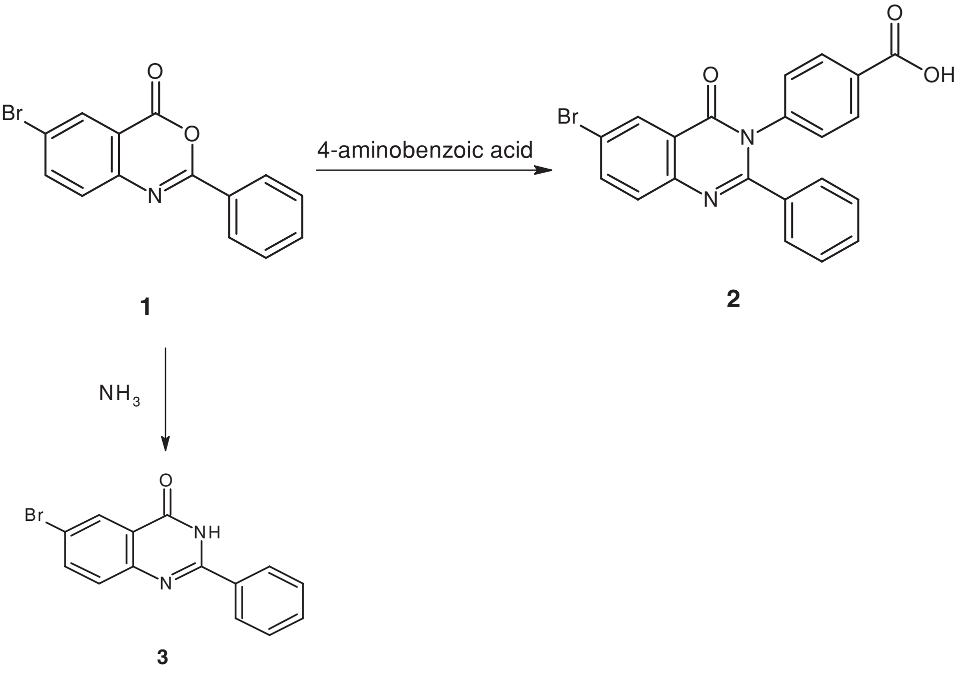
displayed much better antibacterial activity than monoheterocyclic compounds.[4] Recently there have been broad developments in investigations of both the synthesis and study of the chemical and biological properties of mesoionic compounds, and attention has been increasingly paid to the synthesis of bisheterocyclic compounds.[5–7] Thiadiazolium derivatives were found to possess a vast array of synthetic as well as biological importance.[8–10] Quinazoline derivatives are interesting because of their diverse range of biological activities and synthetic applications.[11–13]

In a search for novel compounds with pharmaceutical value and to expand the applications of quinazoline and thiadiazole in organic synthesis, we report herein the synthesis of novel quinazoline-substituted 1,3,4-thiadiazolium-5-thiolate derivatives.

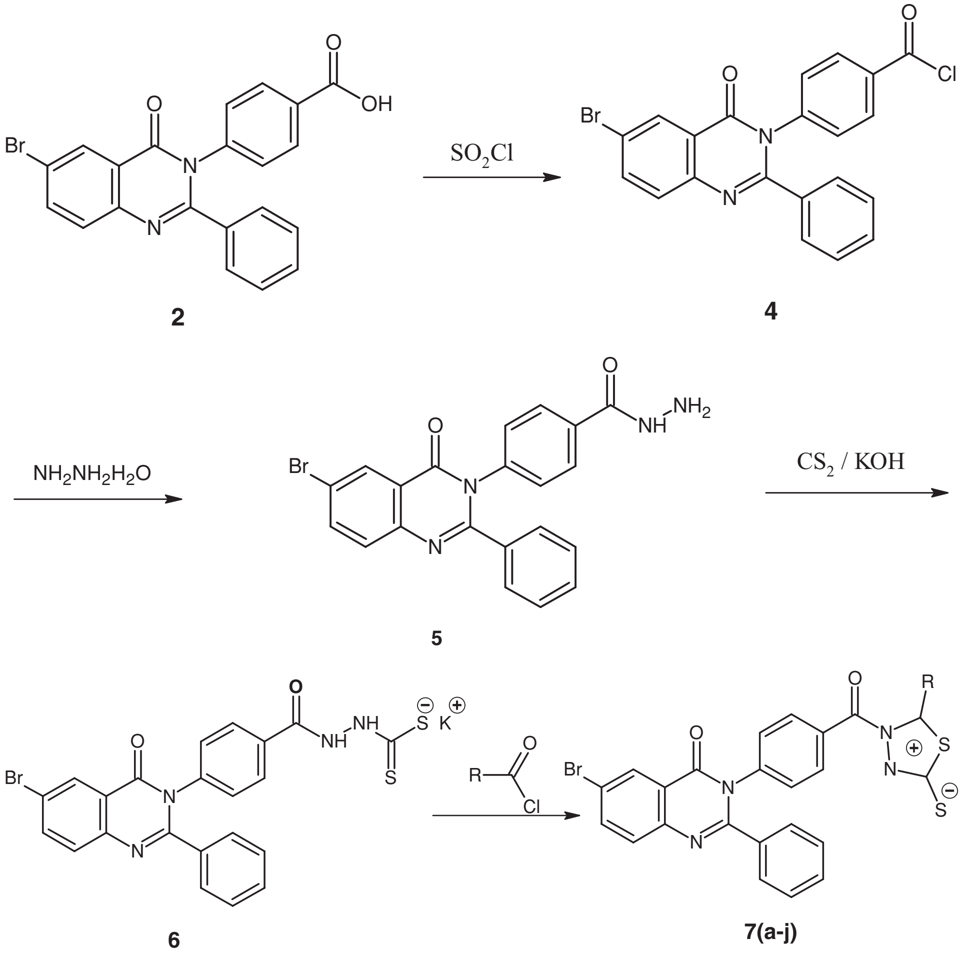
RESULTS AND DISCUSSION

In the present investigation, 3-[4-(6-bromo-4-oxo-2-phenylquinazolin-3(*4H*)-yl)benzoyl]-2-substituted-1,3,4-thiadiazolium-5-thiolate **7**(**a–j**) and 3-{4-[(6-bromo-2-phenylquinazolin-4-yl)amino]benzoyl}-2-substituted-1,3,4-thiadiazolium-5-thiolate **12**(**a–j**) were synthesized from 4-(6-bromo-4-oxo-2-phenylquinazolin-3-(4*H*)-yl) benzoic acid (**2**) and 6-bromo-2-phenylquinazolin-4(*3H*)-one (**3**), respectively. Scheme 1 shows synthesis of compounds 2 and 3. 4-(6-Bromo-2-phenyl-4-oxoquinazoline-3(4*H*)-yl) benzohydrazide (**5**) was synthesized from compound (**2**) according to a literature method.[14]

The hydrazino group of compounds (**5**) and (**10**) was reacted with carbon disulfide and potassium hydroxide to give the corresponding hydrazino carbodithioic acid



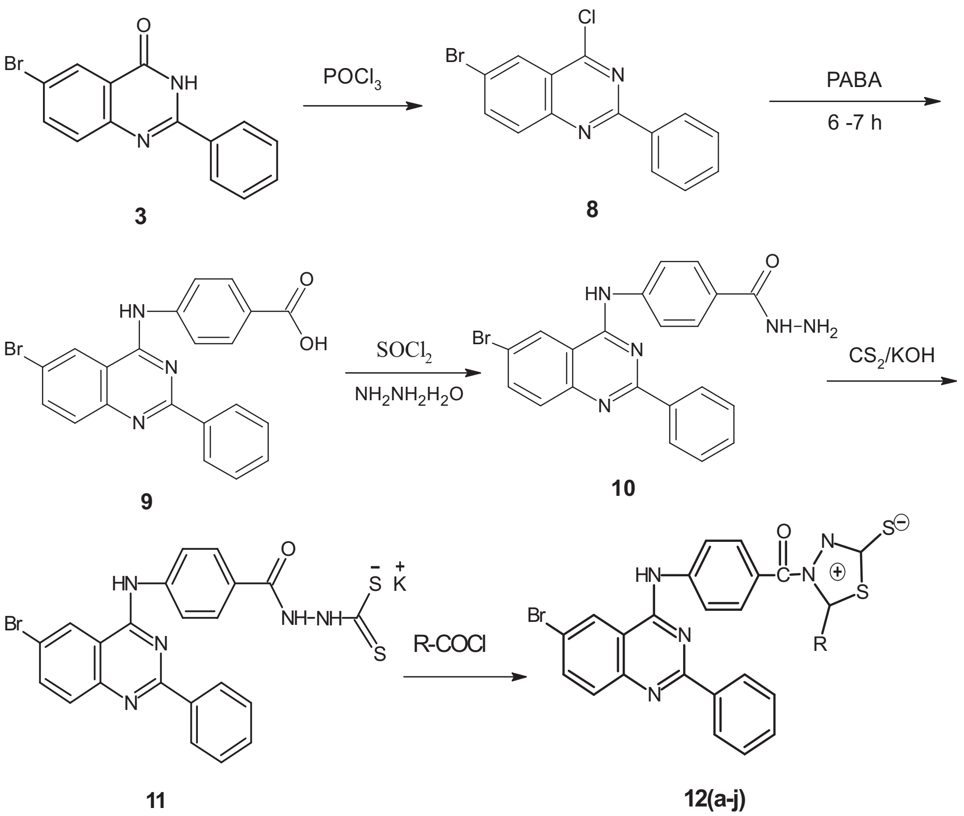
Scheme 1 Synthesis of 4-(6-bromo-4-oxo-2-phenylquinazolin-3-(4*H*)-yl) benzoic acid (**2**) and 6-bromo-2-phenylquinazolin-4(*3H*)-one (**3**).



(a) R = C_6H_5 (b) R = $ClCH_2$ (c) R = CH_3 (d) R = 2-NO_2-C_6H_4 (e) R = 3-NO_2-C_6H_4
(f) R = 4-NO_2-C_6H_4 (g) R = 2-Cl-5-NO_2-C_6H_3 (h) R = 4-OCH_3-3-NO_2-C_6H_3
(i) R = 4-Cl-C_6H_4 (j) R = 3-Cl-5-NO_2-C_6H_3

Scheme 2 Synthesis of 3-[4-(6-bromo-4-oxo-2-phenylquinazolin-3(*4H*)-yl)benzoyl]-2-substituted-1,3,4-thia diazolium-5-thiolate **7**(**a–j**).

derivatives, which, on cyclization with different acid chloride derivatives, gave substituted-1,3,4-thiadiazolium-5-thiolate **7**(**a–j**) and **12**(**a–j**). The hydrazine group of compounds (**5**) and (**10**) was used to build the 1,3,4-thiadiazolium-5-thiolate ring. Both aliphatic and aromatic acid chloride derivatives were used for the cyclization process. The rate of cyclization was not affected by the nature of the acid chloride derivatives. It is noteworthy that potassium dithioformates ($H{-}C{=}S\ S^{-}K^{+}$) can also be used as cyclizing agents in the process.[15] The structures of the compounds **7**(**a–j**) and 12(**a–j**) were determined by elemental analysis, infrared (IR), and nuclear magnetic resonance (NMR) spectra. Examination of the elemental data revealed that the elemental contents were consistent with the predicted formulas shown in Schemes 2 and 3.



(a) R = C_6H_5 (b) R = $ClCH_2$ (c) R = CH_3 (d) R = 2-NO_2-C_6H_4 (e) R = 3-NO_2-C_6H_4
(f) R = 4-NO_2-C_6H_4 (g) R = 2-Cl-5-NO_2-C_6H_3 (h) R = 4-OCH_3-3-NO_2-C_6H_3
(i) R = 4-Cl-C_6H_4 (j) R = 3-Cl-5-NO_2-C_6H_3

Scheme 3 Synthesis of 3-{4-[(6-bromo-2-phenylquinazolin-4-yl)amino]benzoyl}-2-substituted-1,3,4-thiadiazolium-5-thiolate.

The IR spectra showed bands at 550–646 cm^{-1} (C—Br), 1655–1690 cm^{-1} (C=O amide), 1313–1385 cm^{-1} (C=S thiadiazole), and 1583–1617 cm^{-1} (CN quinazoline). In addition, compounds **7**(**a–j**) showed absorption bands at 1678–1690 cm^{-1} (C=O quinazoline) and compound **12**(**a–j**) showed absorption bands at 1296–1324 cm^{-1} due to C—N stretching of the NH group. Furthermore, compounds **7**(**a–j**) and **12**(**a–j**) contain different substitutions at C-2 of the thiadiazole ring. IR spectral characteristics of all of the synthesized compounds were consistent with their proposed structures. The ^{1}H-NMR spectra of compounds **12**(**a–j**) showed signals in the range of δ 9.80–9.85 ppm for N—H protons. The aromatic protons of compounds **7**(**a–j**) and **12**(**a–j**) appeared as multiplets in the range of δ 7.10–8.79 ppm. Other signals were consistent with the predicted structures. Further, the ^{13}C—NMR spectra exhibited confirmatory signals for the carbon of C=S of the thiadiazole ring of around δ 164.0 ppm, and the carbon at C-2 of the thiadiazole ring appeared between δ 136.5–137.7 ppm. The signals for the carbonyl carbon directly attached to the thiadiazole ring appeared between δ 176.0–178.0 ppm. The carbonyl group (C=O) directly attached at

N-3 of the thiadiazole ring is electron withdrawing in character; therefore, the $^{13}C{-}NMR$ values of C-2 and C-5 of the thiadiazole ring varied from literature values.[16] For compounds **7**(**a-j**), the signals for the carbonyl carbon of quinazoline and C=S of the thiadiazole ring were found in close proximity to each other.

EXPERIMENTAL

Melting points were determined by an open capillary method and were uncorrected. The IR spectra were recorded on a Shimadzu Fourier transform infrared (FTIR) instrument (Shimadzu, Japan) using KBr pellets. NMR spectra were recorded on a Bruker Avance II NMR at 400 MHz at SAIF, Chandigarh, using tetramethylsilane (TMS) as the internal standard and DMSO-d_6 as a solvent. Thin-layer chromatography (TLC) was performed on E-Merck precoated 60 F_{254} plates and the spots were rendered visible by exposure to ultraviolet (UV) light. Some selected NMR spectra for **7a** and **12a** are shown in Figures S1–S4 (Supplemental Materials). Physical characterization data are summarized in Table 1 and IR and NMR spectra for **7a–j** and **12a–j** are presented in Table 2.

General Procedure for 7(a–j) as Exemplified for 7a

4-(6-Bromo-2-phenyl-4-oxoquinazoline-3(4*H*)-yl)benzohydrazide (**5**) was synthesized from anthranilic acid by the reported procedure.[14,17]

Potassium 2-{[4-(6-bromo-2-phenyl-4-oxoquinazoline-3(4*H*)-yl) phenyl] carbonyl} hydrazine carbodithioic acid (6). Carbon disulfide (0.60 mL, 0.01 mol) was added dropwise to the solution of 4-(6-bromo-2-phenyl-4-oxoquinazolin-3(4*H*)-yl)benzohydrazide (2.17 g, 0.005 mol) and potassium hydroxide (0.28 g, 0.005 mol) in ethanol (25 mL) and the mixture was stirred for 1 h at room temperature. The precipitates were treated with ether (30 mL). The solid that separated was filtered, washed with ether, and dried.

Yield: 65%; m.p. 210–213 °C. IR (KBr): 1687, 1635, 1605, 1338, 632; $^1H{-}NMR$ (400 MHz, DMSO-d_6): δ 7.42–8.00 (m, 12H, Ar—H), 9.82 (s, 1H, CONH), 9.94 (s, 1H, CSNH). $^{13}C{-}NMR$ (100 MHz, DMSO-d_6): δ 120.6, 121.9, 122.3, 125.5, 128.5, 128.7, 129.4, 130.0, 131.2, 131.7, 132.8, 135.7, 136.4, 149.2, 151.8, 162.7, 165.7, 196.8. Anal. Calcd. (%) for $C_{22}H_{14}O_2N_4S_2BrK$: C, 48.09; H, 2.57; N, 10.20; S, 11.67. Found: C, 48.13; H, 2.45; N, 10.29; S, 11.76.

3-[4-(6-Bromo-4-oxo-2-phenylquinazolin-3(*4H*)-yl)benzoyl]-2-phenyl-1,3, 4-thiazolium-5-thiolate (7a). To a stirred solution of 2-{[4-(6-bromo-2-phenyl-4-oxoquinazoline-3(4*H*)-yl) phenyl] carbonyl} hydrazine carbodithioic acid (1.24 g, 0.005 mol) in water was added benzoyl chloride (0.58 mL, 0.005 mol). The reaction mixture was stirred for 2 h at room temperature. The yellowish solid that separated was filtered, washed repeatedly with cold water, and recrystallized from ethanol.

Following the above procedure, compounds **7**(**b–j**) were prepared by using chloroacetyl chloride, acetyl chloride, 2-nitrobenzoyl chloride, 3-nitrobenzoyl chloride, 4-nitrobenzoyl chloride, 2-chloro-5-nitrobenzoyl chloride, 4-methoxy-3-nitrobenzoyl chloride, 4-chlorobenzoyl chloride, and 3-chloro-5-nitrobenzoyl chloride as acid chlorides and the products were purified by crystallization from ethanol.

Table 1 M.p. yield and elemental analysis of the synthesized compounds **7(a–j)** and **12(a–j)**

No.	M.P. (°C)	Yield (%)	Mol. Formula	Analysis% Found (Calcd.)			
				C	H	N	S
7a	170	69	$C_{29}H_{17}O_2S_2N_4Br$	58.18 (58.29)	2.96(2.87)	9.29 (9.38)	10.68 (10.73)
7b	158–160	72	$C_{24}H_{14}O_2S_2N_4BrCl$	50.64 (50.58)	2.43 (2.48)	9.77 (9.83)	11.34 (11.25)
7c	121–124	65	$C_{24}H_{15}O_2S_2N_4Br$	53.78 (53.84)	2.89 (2.82)	10.52 (10.46)	12.10 (11.98)
7d	136–138	64	$C_{29}H_{16}O_4N_5S_2Br$	54.13 (54.21)	2.59 (2.51)	10.82 (10.90)	10.12 (9.98)
7e	145–147	70	$C_{29}H_{16}O_4N_5S_2Br$	54.16 (54.21)	2.45 (2.51)	10.97 (10.90)	9.87 (9.98)
7f	152–154	69	$C_{29}H_{16}O_4N_5S_2Br$	54.15 (54.21)	2.58; (2.51)	10.96; (10.90)	9.86 (9.98)
7g	168–171	75	$C_{29}H_{15}O_4N_5S_2ClBr$	51.52 (51.45)	2.29; (2.23)	10.28; (10.35)	9.53 (9.47)
7h	147–149	76	$C_{30}H_{18}O_5N_5S_2Br$	53.49 (53.58)	2.63 (2.70)	10.49 (10.41)	9.59 (9.54)
7i	163–165	71	$C_{29}H_{16}O_2N_4S_2ClBr$	55.22 (55.12)	2.62 (2.55)	8.78 (8.87)	10.04 (10.15)
7j	170–173	66	$C_{29}H_{15}O_4N_5S_2ClBr$	51.36 (51.45)	2.30 (2.23)	10.42 (10.35)	9.53 (9.47)
12a	152–154	74	$C_{29}H_{18}ON_5S_2Br$	58.30 (58.39)	3.11 (3.04)	11.69 (11.74)	10.68 (10.75)
12b	168–171	69	$C_{24}H_{15}ON_5S_2ClBr$	50.60 (50.67)	2.71 (2.66)	12.22 (12.31)	11.34 (11.27)
12c	139–141	71	$C_{24}H_{16}ON_5S_2Br$	53.85 (53.94)	3.11 (3.02)	13.20 (13.10)	12.07 (12.00)
12d	148–151	68	$C_{29}H_{17}O_3N_6S_2Br$	54.37 (54.29)	2.58 (2.67)	13.18 (13.10)	10.14 (10.00)
12e	157–159	65	$C_{29}H_{17}O_3N_6S_2Br$	54.21 (54.29)	2.73 (2.67)	13.18 (13.10)	10.11 (10.00)
12f	146–149	64	$C_{29}H_{17}BrN_6O_3S_2$	54.36; (54.29)	2.61; (2.67)	13.19; (13.10)	9.88 (10.00)
12g	118–121	72	$C_{29}H_{16}O_3N_6S_2ClBr$	51.61 (51.53)	2.46 (2.39)	12.51 (12.43)	9.56 (9.49)
12h	130–133	62	$C_{30}H_{19}O_4N_6S_2Br$	53.73 (53.66)	2.77 (2.85)	12.44 (12.51)	9.43 (9.55)
12i	155–157	69	$C_{29}H_{17}ON_5S_2ClBr$	55.12 (55.20)	2.64 (2.72)	11.19 (11.10)	10.07 (10.16)
12j	129–131	66	$C_{29}H_{16}BrClN_6O_3S_2$	51.45 (51.53)	2.31 (2.39)	12.39 (12.43)	9.60 (9.49)

Table 2 IR and NMR data of the synthesized compounds **7**(**a–j**) and **12**(**a–j**)

No.	IR	^{1}H-NMR	^{13}C-NMR
7a	1688, 1660, 1605, 1313, 550	7.24–8.36 (m, 17H, Ar-H)	123.4, 123.5, 124.2, 126.2, 126.9, 127.2, 129.0, 129.1, 129.4, 129.5, 129.9, 130.2, 130.7, 130.8, 135.1, 135.7, 136.5, 140.1, 148.1, 156.3, 163.8, 164.1, 178.5
7b	2910, 1678, 1665, 1596, 1343, 1093, 598	4.14 (s, 2H, CH_2Cl), 7.21–8.13 (m, 12H, Ar-H)	44.8, 123.2, 123.3, 124.4, 125.6, 127.3, 128.6, 128.9, 129.8, 129.9, 131.5, 134.1, 135.5, 137.1, 139.8, 147.3, 156.3, 163.9, 164.1, 178.1
7c	2970, 1690, 1667, 1597, 1347, 592	2.31 (s, 3H, CH_3), 6.87–8.06 (m, 12H, Ar-H)	15.9, 123.2, 123.9, 124.2, 125.6, 127.5, 128.4, 129.0, 130.2, 130.9, 131.1, 135.2, 135.9, 136.7, 140.0, 148.6, 156.8, 164.3, 164.7, 178.3
7d	1683, 1659, 1584, 1542, 1368, 1333, 567	7.15–8.10 (m, 16H, Ar-H)	123.4, 123.5, 123.7, 124.0, 125.8, 126.7, 126.9, 128.7, 128.9, 129.8, 130.1, 130.7, 130.9, 131.5, 134.1, 135.5, 136.3, 137.3, 140.0, 148.3, 151.2, 156.0, 164.1, 164.5, 177.3
7e	1687, 1656, 1583, 1537, 1361, 1329, 565	7.12–8.17 (m, 16H, Ar-H)	123.7, 123.8, 123.9, 125.3, 125.7, 125.8, 126.9, 128.5, 128.9, 129.1, 129.8, 130.1, 131.1, 132.0, 135.0, 135.1, 135.9, 136.6, 140.1, 148.4, 150.4, 156.4, 163.8, 164.7, 178.5
7f	1683, 1667, 1586, 1546, 1366, 1336, 582	7.10–8.17 (m, 16H, Ar-H)	123.5, 123.9, 124.2, 125.8, 126.4, 127.9, 129.0, 129.1, 129.8, 130.3, 131.1, 131.2, 132.9, 135.0, 136.0, 136.7, 140.4, 148.2, 148.4, 156.5, 163.8, 164.1, 178.4
7g	1680, 1658, 1585, 1530, 1359, 1347, 1080, 590	7.40–8.90 (m, 15H, Ar-H)	123.3, 123.8, 124.0, 125.5, 126.3, 126.9, 127.4, 127.5, 128.7, 129.3, 129.6, 130.6, 130.9, 132.7, 135.7, 135.9, 136.9, 139.5, 140.0, 148.3, 149.6, 156.8, 164.3, 164.4, 178.2
7h	2963, 1684, 1655, 1586, 1349, 1052, 581	4.07 (s, 3H, OCH_3), 7.28–8.35 (m, 15H, Ar-H)	57.9, 114.6, 122.5, 122.8, 123.5, 123.7, 125.8, 126.8, 127.3, 128.3, 128.9, 129.8, 130.4, 131.2, 135.3, 135.7, 135.8, 136.5, 139.6, 141.3, 148.5, 154.6, 156.4, 163.8, 164.7, 178.5
7i	1684, 1656, 1599, 1335, 1087, 564	7.56–8.74 (m, 16H, Ar-H)	123.5, 123.8, 124.0, 125.8, 125.9, 127.1, 129.0, 129.2, 129.7, 130.5, 130.9, 131.1, 131.7, 135.1, 136.2, 136.4, 136.8, 140.3, 148.0, 156.6, 163.3, 164.3, 178.3
7j	1679, 1657, 1614, 1546, 1373, 1340, 1083, 589	7.68–8.50 (m, 15H, Ar-H)	123.4, 123.5, 123.7, 124.6, 125.6, 125.7, 127.7, 128.4, 128.8, 129.4, 129.7, 130.4, 131.0, 131.5, 135.6, 135.8, 135.9, 137.4, 140.3, 145.6, 147.8, 156.8, 163.6, 163.9, 178.5
12a	1665, 1596, 1349, 1324, 581	7.45–8.73 (m, 17H, Ar-H), 9.83 (s, 1H, NH)	114.4, 115.7, 116.4, 116.6, 119.9, 127.1, 127.7, 128.5, 130.3, 130.5, 130.6, 130.8, 130.9, 131.5, 133.4, 135.7, 137.7, 141.7, 150.6, 151.6, 163.9, 167.0, 177.4
12b	2912, 1663, 1601, 1351, 1310, 1080, 610	4.28 (s, 2H, CH_2), 7.60–8.64 (m, 12H, Ar-H), 9.84 (s, 1H, NH)	44.0, 114.3, 115.6, 116.6, 116.9, 119.7, 126.8, 128.2, 130.3, 130.5, 131.5, 133.6, 134.8, 137.0, 141.6, 150.4, 151.7, 163.7, 167.4, 176.4
12c	2942, 1677, 1598, 1344, 1318, 624	2.54 (s, 3H, CH_3), 7.50–8.60 (m, 12H, Ar-H), 9.82 (s, 1H, NH)	15.5, 114.6, 115.8, 115.9, 116.9, 118.1, 126.8, 128.6, 130.4, 130.6, 131.6, 133.6, 134.8, 136.5, 141.7, 150.2, 151.4, 163.7, 167.8, 177.4
12d	1680, 1596, 1518, 1368, 1363, 1296, 578	7.58–8.32 (m, 16H, Ar-H), 9.80 (s, 1H, NH)	114.5, 114.7, 116.3, 116.4, 120.0, 123.7, 126.9, 127.1, 128.5, 130.3, 130.6, 130.8, 131.0, 131.7, 133.1, 134.5, 134.9, 137.4, 141.4, 150.4, 151.5, 151.9, 163.2, 167.3, 176.1
12e	1687, 1608, 1524,1369, 1346, 1311, 615	7.63–8.26 (m, 16H, Ar-H), 9.82 (s, 1H, NH)	114.7, 115.7, 115.8, 116.3, 120.1, 125.8, 125.9, 126.9, 127.7, 128.2, 130.3, 130.6, 131.5, 131.6, 133.7, 134.6, 135.7, 136.8, 141.7, 150.1, 150.3, 151.9, 163.7, 167.0, 178.3
12f	1674, 1584, 1537, 1372, 1369, 1317, 568	7.60–8.34 (m, 16H, Ar-H), 9.85 (s, 1H, NH)	113.8, 115.8, 116.6, 116.8, 120.1, 126.6, 126.8, 128.5, 130.3, 130.5, 130.6, 130.7, 132.6, 133.7, 135.2, 136.3, 141.7, 148.0, 150.2, 151.9, 163.5, 167.4, 177.4
12g	1690, 1590, 1552, 1367, 1357, 1312, 1087, 646	7.81–8.79 (m, 15H, Ar-H), 9.83 (s, 1H, NH)	114.4, 115.9, 116.2, 116.4, 121.1, 126.4, 127.1, 127.3, 128.3, 128.4, 130.2, 130.5, 131.7, 132.8, 133.7, 134.8, 136.5, 140.0, 142.8, 149.2, 150.2, 151.6, 163.6, 167.9, 175.3
12h	2975, 1684, 1589, 1570, 1373, 1366, 1296, 1284, 1063, 610	4.13 (s, 3H, OCH_3), 7.64–8.75 (m, 15H, Ar-H), 9.80 (s, 1H, NH)	58.0, 114.1, 114.7, 115.8, 115.9, 116.5, 120.3, 122.1, 127.3, 127.5, 128.5, 130.5, 130.7, 131.5, 133.7, 135.7, 136.2, 137.7, 141.2, 141.5, 150.0, 151.7, 154.7, 163.4, 167.1, 178.6
12i	1674, 1617, 1385, 1313, 1093, 643	7.47–8.61 (m, 16H, Ar-H), 9.81 (s, 1H, NH)	113.7, 116.0, 116.4, 116.7, 120.7, 126.7, 126.9, 128.4, 130.6, 130.7, 131.1, 131.7, 132.6, 133.2, 135.3, 136.3, 137.7, 141.9, 150.4, 152.4, 163.4, 166.5, 177.4
12j	1675, 1591, 1533, 1380, 1370, 1307, 1086, 638	7.53–8.68 (m, 15H, Ar-H), 9.85 (s, 1H, NH)	113.6, 115.8, 116.7, 116.8, 120.6, 126.7, 126.8, 127.3, 127.5, 128.2, 130.5, 130.7, 131.9, 132.8, 133.7, 134.9, 137.6, 140.7, 141.8, 149.7, 150.4, 151.8, 163.7, 167.5, 176.7

General Procedure for 12(a–j) as Exemplified for 12a

6-Bromo-4-chloro-2-phenyl quinazoline (**8**) was synthesized according to the previously reported procedure.[18]

4-[(6-Bromo-2-phenylquinazoline-4-yl)amino]benzoic acid (9). A mixture of 6-bromo-4-chloro-2-phenylquinazoline (3.19 g, 0.01 mol), 4-aminobenzoic acid (1.37 g, 0.01 mol), and potassium carbonate (1.38 g, 0.01 mol) in isopropyl alcohol (15.0 mL) was heated to 90–95 °C for 6 h. After completion of the reaction, the mixture was cooled to room temperature and poured into cold water. The solid product obtained was filtered and dried and recrystallized from methanol. Yield: 83%; m.p. 230–233 °C. IR (KBr): 2950 (br), 1705, 1610, 1310, 625; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.42–7.95 (m, 12H, Ar-H), 9.79 (s, 1H, NH), 10.98 (s, 1H, COOH). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 110.3, 112.9, 118.0, 118.3, 125.3, 125.8, 128.1, 129.6, 131.2, 131.4, 133.4, 137.0, 139.3, 150.2, 151.5, 166.4, 167.5; Anal. Calcd. (%) for $C_{21}H_{14}O_2N_3Br$: C, 60.02; H, 3.36; N, 10.00; Found: C, 59.91; H, 3.27; N, 9.93.

4-[(6-Bromo-2-phenylquinazoline-4-yl)amino] benzo hydrazine (10). 4-[(6-Bromo-2-phenylquinazoline-4-yl)amino]benzoic acid (4.20 g, 0.01 mol) and thionyl chloride (1.10 mL, 0.015 mol) were refluxed for 2 h. The excess thionyl chloride was distilled off. The resultant mixture was cooled and dissolved in ethanol (40 mL). The excess of the hydrazine hydrate (5.0 mL) was added slowly with constant stirring. The reaction mixture was kept under reflux conditions for 6 h. The solution was poured into ice. The solid product obtained was filtered off and recrystallized from ethanol. Yield: 67%; m.p. 190–193 °C. IR (KBr): 3346, 3272, 1645, 1593, 1310, 580; ^{1}H—NMR (400 MHz, DMSO-d_6): δ 4.80 (s, 2H, $\text{NH}\underline{\text{NH}_2}$), 7.53–8.15 (m, 12H, Ar—H), 9.87 (s, 1H, NH), 10.14 (s, 1H, $\underline{\text{NH}}\text{NH}_2$); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 110.4, 113.8, 114.6, 118.3, 126.1, 128.8, 129.7, 130.7, 131.1, 131.8, 133.5, 137.8, 139.4, 149.9, 150.8, 165.7, 166.3. Anal. Calcd. (%) for $C_{21}H_{16}ON_5Br$: C, 58.08; H, 3.71; N, 16.13. Found: C, 58.13; H, 3.82; N, 16.21.

Potassium 2-({4-[(6-bromo-2-phenylquinazoline-4-yl)amino]phenyl}carbonyl)hydr azine carbodithioic acid (11). To a stirred solution of 4-[(6-bromo-2-phenylquinazoline-4-yl)amino]benzo hydrazine (2.17 g, 0.005 mol) and potassium hydroxide (0.28 g, 0.005 mol) in absolute alcohol (25 mL), carbon disulfide (0.60 mL, 0.01 mol) was added dropwise and the mixture was stirred for 1 h at room temperature. The yellowish-colored precipitate was treated with ether. The solid that separated was filtered, washed with ether, and dried.

Yield: 73%; m.p. 227–230 °C. IR (KBr): 3262, 1640, 1597, 1342, 1318, 586; ^{1}H—NMR (400 MHz, DMSO-d_6): δ 7.68–8.12 (m, 12H, Ar-H), 9.80 (s, 1H, NH), 9.97 (s, 1H, CONH), 10.18 (s, 1H, CSNH); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 110.7, 114.2, 114.7, 117.8, 126.0, 129.0, 129.6, 130.3, 131.4, 131.8, 132.6, 136.9, 140.4, 150.2, 151.6, 165.5, 165.8, 193.6. Anal. Calcd. (%) for $C_{22}H_{15}ON_5S_2BrK$: C, 48.17; H, 2.76; N, 12.77; S, 11.69. Found: C, 48.29; H, 2.69; N, 12.85; S, 11.76.

3-{4-[(6-Bromo-2-phenylquinazolin-4-yl)amino]benzoyl}-2-phenyl-1,3,4-thiadiazolium-5-thiolate (12a). To a stirred solution of potassium salt of 2-({4-[(6-bromo-2-phenylquinazoline-4yl) amino]phenyl}carbonyl)hydrazine carbodithioic acid (0.005 mol) in water (50 mL) was added benzoyl chloride (0.005 mol). The reaction mixture was stirred for 2 h at room temperature. The yellowish solid that separated was filtered, washed repeatedly with cold water, and recrystallized from ethanol.

Following the above procedure, compounds **12**(**b-j**) were synthesized by using chloroacetyl chloride, acetyl chloride, 2-nitrobenzoyl chloride, 3-nitrobenzoyl chloride, 4-nitrobenzoyl chloride, 2-chloro-5-nitrobenzoyl chloride, 4-methoxy-3-nitrobenzoyl chloride, 4-chlorobenzoyl chloride, and 3-chloro-5-nitrobenzoyl chloride as acid chloride derivatives and the products were purified by crystallization from ethanol.

REFERENCES

1. Cardoso, J. C.; Cadena, S. M. S. C.; Zampronio, A.; Arruda, A. M. S.; Carnieri, E. G. S.; Echevarria, A.; Constantin, J.; Bracht, A.; Oliveira, M. B. M. *Drug Dev. Res.* **2004,** *61*, 207–217.
2. Badami, B. V. *Resonance* **2006,** *11*, 40–48.
3. Rodrigues, R. F.; da Silva, E. F.; Echevarria, Á.; Fajardo-Bonin, R.; Amaral, V. F.; Leon, L. L.; Canto-Cavalheiro, M. M. *Eur. J. Med. Chem.* **2007,** *42*, 1039–1043.
4. Zhang, Z. Y.; Chen, X. L.; Wei, L.; Ma, Z. L. *Chem. Res. Chin. Univ.* **1991,** *7*, 129.
5. Desai, N. C. *Indian J. Chem.* **1993,** *32B*, 343.
6. Ghorab, M. M.; El-Sharief, A. M. S.; Ammar, Y. A.; Mohamed, S. I. *Farmaco* **2000,** *55*, 354–361.
7. Mohan, J.; Anjaneyula, G. S. R.; Sudhir, S.; Arora, D. R. *J. Indian Chem. Soc.* **1989,** *66*, 330.
8. Stewart, T. G.; Kier, L. B. *J. Pharm. Sci.* **1965,** *54*, 731–734.
9. Kier, L. B.; Dodda, M. C.; Sapko, P. T.; Stewart, G. *Nature* **1964,** *204*, 697–697.
10. Maffii, G.; Soncin, E. *Br. J. Pharmacol. Chemother.* **1958,** *13*, 357–363.
11. Bedi, P. M. S.; Kumar, V.; Mahajan, M. P. *Bioorg. Med. Chem. Lett.* **2004,** *14*, 5211–5213.
12. Schleiss, M.; Eickhoff, J.; Auerochs, S.; Leis, M.; Abele, S.; Rechter, S.; Choi, Y.; Anderson, J.; Scott, G.; Rawlinson, W.; Michel, D.; Ensminger, S.; Klebl, B.; Stamminger, T.; Marschall, M. *Antiviral Res.* **2008,** *79*, 49–61.
13. Ibrahim, S. S.; Abdel-Halim, A. M.; Gabr, Y.; El-Edfawy, S.; Abdel-Rahman, R. M. *J. Chem. Res.* **1997,** 154–155.
14. Desai, A. R.; Desai, K. R. *Arkivoc*. **2005,** *13*, 98–108.
15. Jogul, J. J.; Badami, B. V. *J. Serb. Chem. Soc*. **2006,** *71*, 851–860.
16. Katritzky, A. R.; Pozharskii, A. F. *Handbook of Heterocyclic Chemistry*, 2nd ed.; Pergamon: Kidlington, 2000.
17. Wheeler, A. S. *J. Am. Chem. Soc.* **1909,** *31*, 565–569.
18. Chandrika, P. M.; Yakaiah, T.; Rao, A. R. R.; Narsaiah, B.; Reddy, N. C.; Sridhar, V.; Rao, J. V. *Eur. J. Med. Chem.* **2008,** *43*, 846–852.