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Studies on Quinazolines, Part IV: Fused Mesoionic Heterocycles from 3-Amino-2-aryl-4(3*H*)-quinazolinethiones

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ABSTRACT: *The 3-amino-4(3*H*)-quinazolinethiones* **2a–c** *react with phenyl isothiocyanate in DMF, giving N,N-disubstituted thioureas* **3a–c**. *When* **2a–c** *are treated with phenyl isothiocyanate in dry acetonitrile in the presence of triethylamine, the mesoionic compounds* **4a–c** *are isolated. The methiodide* **5a** *reacts with carbon nucleophiles such as malononitrile and/or ethyl cyanoacetate in the presence of triethylamine to give the corresponding 1,2,4-triazoles* **6a,b**. *On the other hand, compounds* **2a–c** *react with* CS_2–K_2CO_3 *combination to furnish 1,3,4-thiadiazolo[3,2-c]-4-quinazolinium-2-mercaptides* **7a–c**. *Treatment of the methiodide* **8a** *with malononitrile in the presence of potassium t-butoxide provides a mixture of 2-[2-(2-nitrophenyl)-3*H*-quinazolin-4-ylidene]malononitrile* **9** *(24%) and 2-amino-5-(2-nirophenyl)pyrazolo[1,5-c]quinazoline-1-carbonitrile* **10** *(40%). The reaction between Schiff bases* **11** *derived from* **2a** *and phenacyl bromide yields 2-benzoyl-1,3,4-thiadiazino[3,2-c]quinazolin-5-ium bromide derivatives* **12a,b**. © 2003 Wiley Periodicals, Inc. Heteroatom Chem 14:581–586, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10172

INTRODUCTION

The preparative use of 3-amino-4(3*H*)-quinazolinone derivatives as useful precursors for the synthesis of five- and six-membered heterocycles annelated to quinazolines was reported [1] from this laboratory. Aryl-substituted and heteroaryl-fused five-membered ring mesoionic heterocycles possess anti-inflammatory activity [2,3]. In addition, the chemistry of fused ring mesoionic systems has not been studied as extensively as monocyclic mesoionic systems [4–6]. In continuation of our studies on quinazolines [7,8], we thought it worthwhile to exploit the potential of 3-amino-4(3*H*)-quinazolinethione as starting material for the synthesis of some highly functionalized fused five-membered mesoionic heterocycles hitherto unreported.

The general strategy for the synthesis of 3-amino-4(3*H*)-quinazolinethione derivatives [9] **2** was hydrazinolysis of appropriately substituted 4*H*-3,1-benzothiazinethiones [10] **1**, readily available from direct thiation of the corresponding 3,1-benzoxazin-4-one derivatives [11]. Now we report in this paper a facile synthesis of [1,2,4]triazolo[1,5-*c*]quinazoline derivatives. It is based on the reaction of anhydro-5-methyl-2-mercapto[1,3,4]thiadiazolo-[3,2-*c*]quinazolin-4-ium hydroxide or its methiodide with *n*-butylamine or aniline [12]. The formation of these compounds seems to be strongly dependent on the nature of the substituent on the quinazoline ring.

Thus, the 3-amino-2-(2-nitrophenyl)-, 2-(4-tolyl)- or 2-(2-naphthyl)-4(3*H*)-quinazolinethiones (**2a–c**) react with phenyl isothiocyanate at reflux temperature in dimethylformamide for 5 h,

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giving 1-phenyl-3-(2-aryl-4-thioxo-4*H*-quinazolin-3-yl)thioureas (**3a–c**). However, when **2a–c** are treated with phenyl isothiocyanate in dry acetonitrile in the presence of triethylamine at reflux temperature for 24 h, the mesoionic compounds **4a–c** are isolated as crystalline solids in moderate yields. Compounds **4a–c** react with methyl iodide to form 2-methylthio-5-aryl-1-phenyl[1,2,4]triazolo[1,5-*c*]quinazolinium iodides (**5a–c**) that are obtained as stable crystalline solids in excellent yields. When compounds **5a–c** are heated at slightly above their melting points, they are transformed into the mesoionic compounds **4a–c** in near quantitative yields. Compound **5a** reacts with carbon nucleophiles such as malononitrile and ethyl cyanoacetate in the presence of base to furnish 2-carboethoxy-3-[2-(5-methylthio-4-phenyl-4*H*-[1,2,4]triazol-3-yl)phenylamino]-3-(2-nitrophenyl)acrylonitrile (**6a**) and 2-{[2-(5-methylthio-4-phenyl-4*H*-[1,2,4]triazol-3-yl)-phenylamino]-2-(4-tolyl)methylene}malononitrile (**6b**) as crystalline solids in good yields.

It was anticipated that treatment of **2a–c** with carbon disulfide in the presence of a base will lead to highly reactive isothiocyanate intermediates via dithiocarbamates, and these would in turn immediately cyclize to 5-aryl-2-mercapto-1,3,4-thiadiazolo[3,2-*c*]quinazolin-4-ium (**7a–c**). Upon reaction with methyl iodide in acetone at room temperature, compounds **7a–c** undergo S-methylation to give the corresponding 5-aryl-2-methylthio-1,3,4-thiadiazolo[3,2-*c*]quinazolin-4-ium iodide (**8a–c**). To be certain that the structural assignments are the same as that of the methiodides **5a–c** prepared from 3-amino-2-aryl-4(3*H*)-quinazolinethiones (**2a–c**), phenyl isothiocyanate, and methyl iodide, the same compounds were obtained by unequivocal synthesis involving amination of **8a–c** with aniline [12]. This reaction is similar to that reported for the conversion of monocyclic 2-methylthio-1,3,4-thiadiazolium into 2-methylthio-1,3,4-triazolium [13].

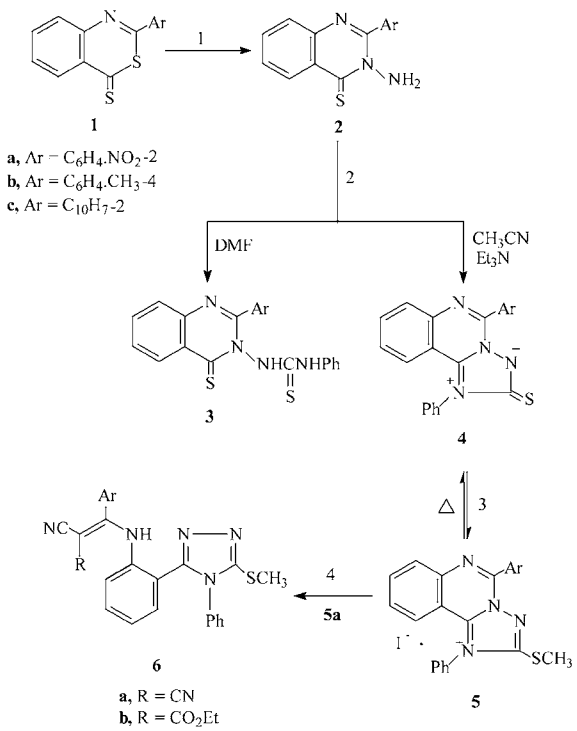
On the other hand, compound **8a** reacts with malononitrile in the presence of potassium *t*-butoxide to furnish a mixture of 2-[2-(2-nitrophenyl)-3*H*-quinazolin-4-ylidene]malononitrile (**9**) and 2-amino-5-(2-nitrophenyl)pyrazolo[1,5-*c*]quinazoline-1-carbonitrile (**10**, 40%). This latter compound can be obtained as the only reaction product in good yield (55%) from **8a**, malononitrile, and triethylamine as base.

Schiff bases have been shown to be highly useful as synthetic intermediates in preparative heterocyclic chemistry. Condensations of homophthalic anhydrides with Schiff bases have been the key steps for synthesizing isoquinolines and indole alkaloids [14]. Moreover, we previously reported [1] the preparative use of Schiff bases as open-chain precursors of functionalized 1,3-thiazolidine-4-one derivatives. We have now utilized the potential of this type of starting materials for the synthesis of some new annelated 1,3,4-thiadiazine derivatives of mesoionic character. Thus, the *N*-aminoheterocycle **2a** reacts with aromatic aldehydes, namely benzaldehyde or *p*-chlorobenzaldehyde, in the presence of hydrochloric acid to give 3-(arylideneamino)-2-(2-nitrophenyl)-3*H*-quinazoline-4-thiones (**11a,b**) in good yields. Aldimines **11a,b** reacted with phenacyl bromide in methanol or ethanol at reflux temperature for 24 h to afford the corresponding 2-benzoyl-3-phenyl- or 3-(4-chlorophenyl)-6-(2-nitrophenyl)-2*H*,3*H*,4*H*-1,3,4-thiadiazino[3,2-*c*]quinazolin-5-ium bromides (**12a,b**) as crystalline solids in moderate to good yields.

The structural assignments of all the compounds (Schemes 1 and 2) were based on elemental analyses and characteristic IR, ^{1}H NMR, and mass spectral data.

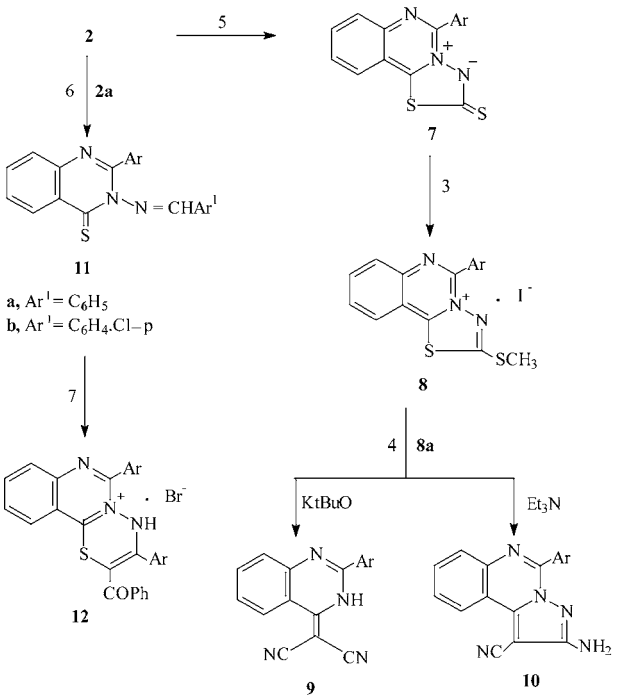
EXPERIMENTAL

Melting points were measured in open capillary tubes and are uncorrected. IR spectra in KBr were



1, N_2H_4; 2, PhNCS; 3, CH_3I; 4, $CH_2(CN)_2$ or $NCCH_2CO_2Et$

SCHEME 1



5, CS_2; 6, ArCHO; 7, $PhCOCH_2Br$

SCHEME 2

recorded on a Shimadzu 470 spectrophotometer and ^{1}H NMR spectra were recorded on a JOEL Fx 90 Q9 MHz (Fourier transform NMR spectrometer) using TMS as internal reference (chemical shifts δ, ppm). Mass spectra were recorded on an HP model MS 5988 spectrometer.

*2-(2-Nitrophenyl)-, 2-(4-Tolyl)-, or 2-(2-Naphthyl)-4H-3,1-benzothiazine-4-thiones (**1a–c**)*

These were prepared from appropriately substituted 3,1-benzoxazin-4-ones (0.07 mol) and phosphorus pentasulphide (0.14 mol) according to literature [10]. Recrystallization from ethanol furnished **1a–c**.

1a: Yield 10.5 g (50%), mp 146–148°C (lit. [10] mp 147°C); IR (cm^{-1}): 1618 (C=N), 1329 (C=S). Found: C, 55.77; H, 2.60; N, 9.52%. Calcd for $C_{14}H_8N_2O_2S_2$: C, 55.98; H, 2.68; N, 9.33%.

1b: Yield 6.6 g (35%), mp 158–160°C (lit. [10] mp 160°C); IR (cm^{-1}): 1613 (C=N), 1320 (C=S). Found: C, 66.98; H, 4.32; N, 5.28%. Calcd for $C_{15}H_{11}NS_2$: C, 66.88; H, 4.12; N, 5.20%.

1c: Yield 10.6 g (50%), mp 156–158°C (lit. [10] mp 157°C); IR (cm^{-1}): 1595 (C=N), 1335 (C=S). Found: C, 70.84; H, 3.82; N, 4.62%. Calcd for $C_{18}H_{11}NS_2$: C, 70.79; H, 3.63; N, 4.59%.

*3-Amino-2-(2-nitrophenyl)-, 2-(4-Tolyl)-, or 2-(2-Naphthyl)-4-(3H)-quinazolinethiones (**2a–c**)*

A solution of thiones **1a–c** (0.065 mol) and hydrazine hydrate (6.3 ml, 0.13 mol) in ethanol (180 ml) was refluxed for 5 h. The solid product separated on cooling was recrystallized from ethanol to give **2a–c**.

2a: Yield 14.1 g (73%), mp 169–171°C (lit. [9] mp 171°C); IR (cm^{-1}): 3295 and 3182 (NH_2), 1620 (C=N), 1325 (C=S). Found: C, 56.44; H, 3.41; N, 18.62%. Calcd for $C_{14}H_{10}N_4O_2S$: C, 56.37; H, 3.38; N, 18.78%.

2b: Yield 12.4 g (71%), mp 174–176°C (lit. [9] mp 175°C); IR (cm^{-1}): 3340 and 3300 (NH_2), 1615 (C=N), 1340 (C=S). Found: C, 67.42; H, 4.88; N, 15.66%. Calcd for $C_{15}H_{13}N_3S$: C, 67.39; H, 4.90; N, 15.72%.

2c: Yield 14.2 g (72%), mp 170–172°C (lit. [9] mp 172°C); IR (cm^{-1}): 3325 and 3280 (NH_2), 1610 (C=N), 1318 (C=S). Found: C, 72.41; H, 4.21; N, 13.75%. Calcd for $C_{18}H_{13}N_3S$: C, 71.26; H, 4.32; N, 13.85%.

*1-Phenyl-3-[2-(2-nitrophenyl)-, 2-(4-Tolyl)-, or 2-(2-Naphthyl)-4-thioxo-4H-quinazolin-3-yl]thioureas (**3a–c**)*

To a solution of **2a–c** (0.004 mol) in dry dimethylformamide (25 ml), phenyl isothiocyanate (0.96 ml, 0.008 mol) was added. The deep red solution was refluxed for 4 h. After cooling at room temperature, the mixture was poured into ice/water (25 ml) and the precipitated solid crude recrystallized from ethanol to yield products **3a–c** as crystalline solids.

3a: Yield 0.93 g (54%), mp 193–195°C, yellow plates; IR (cm^{-1}): 3340–3210 (NH), 1600 (C=C), 1550 (C=N), 1325 (C=S); ^{1}H NMR (Me_2SO-d_6): δ = 7.41–8.52 (m, 13H, Ar–H), 9.20–10.22 (br s, 2H, 2 × NH). Found: C, 58.40; H, 3.30; N, 16.28%. Calcd for $C_{21}H_{15}N_5O_2S_2$: C, 58.18; H, 3.49; N, 16.16%.

3b: Yield 0.84 g (52%), mp 198–200°C, yellow plates; IR (cm^{-1}): 3320–3195 (NH), 1600 (C=C), 1570 (C=N), 1365 (C=S); ^{1}H NMR (Me_2SO-d_6): δ = 2.36 (s, 3H, $ArCH_3$), 7.32–8.61 (m, 13H, Ar–H), 9.42–10.38 (br s, 2H, 2 × NH). Found: C, 65.72; H, 4.70; N, 13.75%. Calcd for $C_{22}H_{18}N_4S_2$: C, 65.64; H, 4.51; N, 13.92%.

3c: Yield 0.96 g (55%), mp 188–190°C, yellow plates; IR (cm^{-1}): 3350–3240 (NH), 1610 (C=C), 1570 (C=N), 1375 (C=S); ^{1}H NMR (Me_2SO-d_6): δ = 7.28–8.42 (m, 16H, Ar–H), 9.55–10.38 (br s, 2H, 2 × NH). Found: C, 68.22; H, 4.32; N, 12.91%. Calcd for $C_{25}H_{18}N_4S_2$: C, 68.47; H, 4.10; N, 12.77%.

*2,3-Dihydro-5-(2-nitrophenyl)-, 5-(4-Tolyl)-, or 5-(2-Naphthyl)-1-phenyl-2-thioxo-[1,2,4]triazolo[1,5-c]quinazolinium (**4a–c**)*

To a solution of *N*-aminoheterocycles **2a–c** (0.015 mol) in dry acetonitrile (50 ml), phenyl isothiocyanate (3.6 ml, 0.03 mol) and triethylamine (4.2 ml, 0.03 mol) were added. The mixture was heated at reflux for 25 h. After cooling at room temperature, the crude product was separated and recrystallized from chloroform to afford products **4a–c**.

4a: Yield 3.7 g (63%), mp 283–285°C, yellow needles; IR (cm^{-1}): 1620 (C=N), 1355 (polarized C–S); ^1H NMR (Me_2SO-d_6): $\delta = 7.25–8.81$ (m, 13H, Ar–H); MS (70 eV): *m/z* (%) = 399 (M^+, 76), 398 (50), 367 (15), 250 (100). Found: C, 63.28; H, 3.33; N, 17.62%. Calcd for $C_{21}H_{13}N_5O_2S$: C, 63.15; H, 3.28; N, 17.53%.

4b: Yield 3.3 g (61%), mp 290–292°C, pale yellow needles; IR (cm^{-1}): 2940 (alkyl-H), 1615 (C=N), 1362 (polarized C–S); ^1H NMR (Me_2SO-d_6): $\delta = 2.55$ (s, 3H, $ArCH_3$), 7.33–8.74 (m, 13H, Ar–H); MS (70 eV): *m/z* (%) = 368 (M^+, 33), 367 (31), 366 (12), 336 (13), 219 (100). Found: C, 71.62; H, 4.21; N, 15.10%. Calcd for $C_{22}H_{16}N_4S$: C, 71.72; H, 4.38; N, 15.21%.

4c: Yield 3.5 g (59%), mp 275–277°C, yellow needles; IR (cm^{-1}): 1621 (C=N), 1358 (polarized C–S); ^1H NMR (Me_2SO-d_6): $\delta = 7.28–8.76$ (m, 16H, Ar–H); MS (70 eV): *m/z* (%) = 406 ($M^+ + 2$, 8), 405 (10), 404 (M^+, 22), 403 (24), 372 (17), 255 (100). Found: C, 74.18; H, 3.72; N, 13.99%. Calcd for $C_{25}H_{16}N_4S$: C, 74.23; H, 3.99; N, 13.85%.

*2-Methylthio-5-(2-nitrophenyl)-, 5-(4-Tolyl)-, or 5-(2-Naphthyl)-1-phenyl-[1,2,4]triazolo-[1,5-c]quinazolinium Iodides (**5a–c**)*

To a solution of **4a–c** (0.008 mol) in dichloromethane (50 ml), methyl iodide (1 ml, 0.016 mol) was added. After 20 min, a yellow precipitated solid separates. The mixture was refluxed for an additional 20 min. After cooling, the precipitate was collected by filtration and recrystallized from chloroform to furnish methiodides **5a–c** as crystalline solids.

5a: Yield 3.9 g (91%), mp 290–292°C, yellow prisms; IR (cm^{-1}): 1624 (C=C), 1590 (C=N); ^1H NMR ($CDCl_3 + CF_3CO_2H$): $\delta = 2.95$ (s, 3H, SCH_3), 7.14–8.34 (m, 13H, Ar–H); MS (70 eV): *m/z* (%) = 399 (M^+-ICH_3, 28), 398 (24), 367 (12), 250 (65), 142 (100). Found: C, 48.60; H, 2.72; N, 12.75%. Calcd for $C_{22}H_{16}IN_5O_2S$: C, 48.81; H, 2.98; N, 12.94%.

5b: Yield 3.5 g (88%), mp 310–312°C, yellow prisms; IR (cm^{-1}): 2920 (alkyl-H), 1620 (C=C), 1600 (C=N); ^1H NMR ($CDCl_3 + CF_3CO_2H$): $\delta = 2.52$ (s, 3H, $ArCH_3$), 2.94 (s, 3H, SCH_3), 7.28–8.72 (m, 13H, Ar–H); MS (70 eV): *m/z* (%) = 368 (M^+-ICH_3, 30), 367 (25), 336 (14), 310 (6), 219 (68), 142 (100). Found: C, 54.22; H, 3.82; N, 10.77%. Calcd for $C_{23}H_{19}IN_4S$: C, 54.12; H, 3.75; N, 10.98%.

5c: Yield 3.8 g (87%), mp 285–287°C, yellow prisms; IR (cm^{-1}): 1628 (C=C), 1598 (C=N); ^1H NMR ($CDCl_3 + CF_3CO_2H$): $\delta = 2.98$ (s, 3H, SCH_3), 7.35–8.60 (m, 16H, Ar–H); MS (70 eV): *m/z* (%) = 406 ($M^+ + 2$-ICH_3, 10), 405 (12), 404 (M^+-ICH_3, 18), 403 (15), 372 (6), 346 (17), 255 (48), 142 (100). Found: C, 57.32; H, 3.61; N, 10.18%. Calcd for $C_{26}H_{19}IN_4S$: C, 57.15; H, 3.50; N, 10.25%.

*Thermolysis of Methiodides **5a–c**; Alternative Preparation of **4a–c***

The dry iodides **5a–c** (0.002 mol) were heated at a temperature slightly above their melting points under reduced pressure for 40 min. After cooling, the residues were recrystallized from chloroform to yield compounds identified to be **4a–c** by melting point and mixed melting point determinations.

*2-Carboethoxy-3-[2-(5-methylthio-4-phenyl-4H-[1,2,4]-triazol-3-yl)phenylamino]-3-(2-nitrophenyl)acrylonitrile (**6a**) and 2-{[2-(5-Methylthio-4-phenyl-4H-[1,2,4]triazol-3-yl)phenylamino]-2-(4-tolyl)-methylene}malononitrile (**6b**)*

To a well stirred solution of compound **5a** (1.1 g, 0.002 mol) in dry acetonitrile (25 ml), the nitriles (0.0022 mol), namely, malononitrile (0.15 g) and/or ethyl cyanoacetate (0.23 ml) and triethylamine (0.6 ml, 0.004 mol) were added. The reaction mixture was refluxed for 24 h. After cooling to room temperature, the precipitated solid was separated by filtration and recrystallized from chloroform–ethanol to furnish **6a,b**.

6a: Yield 0.63 g (66%), mp 254–256°C, yellow prisms; IR (cm^{-1}): 3345 (NH), 2215 (C≡N), 1618 (C=C), 1588 (C=N); ^1H NMR ($CDCl_3 + CF_3CO_2H$): $\delta = 2.88$ (s, 3H, SCH_3), 7.12–8.24 (m, 13H, Ar–H), 9.66 (br s, 1H, NH); MS (70 eV): *m/z* (%) = 479 (M^+, 55), 452 (10), 414 (100). Found: C, 62.71; H, 3.62; N, 20.32%. Calcd for $C_{25}H_{17}N_7O_2S$: C, 62.62; H, 3.57; N, 20.45%.

6b: Yield 0.61 g (58%), mp 262–264°C, yellow needles; IR (cm^{-1}): 3310 (NH), 2210 (C≡N), 1718 (CO ester), 1616 (C=C), 1588 (C=N); ^1H NMR ($CDCl_3 + CF_3CO_2H$): $\delta = 1.26$ (t, 3H, CH_3), 2.96 (s, 3H, SCH_3), 4.45 (q, 2H, CH_2), 7.17–8.42 (m, 13H, Ar–H), 9.87 (br s, 1H, NH); MS (70 eV): *m/z* (%) = 526 (M^+, 30), 453 (25), 414 (100). Found: C, 61.71; H, 4.30; N, 15.84%. Calcd for $C_{27}H_{22}N_6O_4S$: C, 61.59; H, 4.21; N, 15.96%.

*5-(2-Nitrophenyl)-, 5-(4-Tolyl)-, or 5-(2-Naphthyl)-2-mercapto-1,3,4-thiadiazolo[3,2-c]quinazolin-4-ium (**7a–c**)*

3-Amino-4-thioquinazolones **2a–c** (0.018 mol) were first suspended in DMF (10 ml). Carbon disulfide was added when most of the materials had dissolved after stirring for few minutes at room temperature. Anhydrous potassium carbonate (4.1 g, 0.03 mol) was then added to each with continuous stirring for 30 min at room temperature, after which yellow solids separated from the reaction mixture. After 4 h, the mixture was poured onto crushed ice and acidified with acetic acid. The yellow solids were collected, washed with water and then with alcohol, and then dried. The crude product was finally crystallized from chloroform–ethanol to furnish **7a–c**.

7a: Yield 4.8 g (79%), mp 208–210°C, yellow needles; IR (cm^{-1}): 1620 (C=C), 1604 (C=N), 1340 (polarized C–S); ^1H NMR (Me_2SO-d_6): $\delta = 7.12–8.42$ (m, 8H, Ar–H); MS (70 eV): *m/z* (%) = 340 (M^+, 28), 339 (18), 308 (16), 250 (100). Found: C, 52.82; H, 2.22; N, 16.24%. Calcd for $C_{15}H_8N_4O_2S_2$: C, 52.93; H, 2.37; N, 16.46%.

7b: Yield 4.1 g (75%), mp 214–216°C, yellow needles; IR (cm^{-1}): 2910 (alkyl-H), 1609 (C=N), 1355 (polarized C–S); ^1H NMR (Me_2SO-d_6): $\delta = 2.46$ (s, 3H, $ArCH_3$), 7.26–8.45 (m, 8H, Ar–H); MS (70 eV): *m/z* (%) = 309 (M^+, 30), 308 (26), 277 (16), 219 (100). Found: C, 62.40; H, 3.41; N, 13.22%. Calcd for $C_{16}H_{11}N_3S_2$: C, 62.11; H, 3.58; N, 13.58%.

7c: Yield 4.7 g (77%), mp 222–224°C, yellow needles; IR (cm^{-1}): 1626 (C=C), 1600 (C=N), 1336 (polarized C–S); ^1H NMR (Me_2SO-d_6): $\delta = 7.33–8.51$ (m, 11H, Ar–H); MS (70 eV): *m/z* (%) = 347 ($M^+ + 2$, 12), 346 (8), 345 (M^+, 24), 344 (20), 313 (19), 255 (100). Found: C, 66.18; H, 3.32; N, 12.26%. Calcd for $C_{19}H_{11}N_3S_2$: C, 66.06; H, 3.21; N, 12.16%.

*2-Methylthio-5-(2-nitrophenyl)-, 5-(4-Tolyl)-, or 5-(2-Naphthyl)-1,3,4-thiadiazolo-[3,2-c]quinazolin-4-ium Iodide (**8a–c**)*

A suspension of the mesoionic compounds **7a–c** (0.012 mol) in acetone (50 ml) containing iodomethane (1.5 ml, 0.024 mol) was left overnight at room temperature with occasional swirling. Mild reflux for 30 min followed by evaporation under water pump gave a crude methiodide that recrystallized from chloroform–ethanol to afford **8a–c**.

8a: Yield 4.6 g (80%), mp 191–193°C, orange–yellow needles; IR (cm^{-1}): 1625 (C=C), 1604 (C=N); ^1H NMR ($CDCl_3$+ CF_3CO_2H): $\delta = 2.98$ (s, 3H, SCH_3), 7.21–8.44 (m, 8H, Ar–H); MS (70 eV): *m/z* (%) = 340 (M^+-ICH_3, 24), 339 (19), 308 (14), 250 (100). Found: C, 39.92; H, 2.45; N, 11.71%. Calcd for $C_{16}H_{11}IN_4O_2S_2$: C, 39.84; H, 2.30; N, 11.63%.

8b: Yield 4.1 g (77%), mp 202–204°C, yellow needles; IR (cm^{-1}): 2936 (alkyl-H), 1618 (C=C), 1602 (C=N); ^1H NMR ($CDCl_3$ + CF_3CO_2H): $\delta = 2.42$ (s, 3H, $ArCH_3$), 2.97 (s, 3H, SCH_3), 7.16–8.61 (m, 8H, Ar–H); MS (70 eV): *m/z* (%) = 311 ($M^+ + 2$-ICH_3, 16), 310 (11), 309 (M^+-ICH_3, 19), 308 (14), 277 (22), 219 (64), 142 (100). Found: C, 45.27; H, 3.08; N, 9.22%. Calcd for $C_{17}H_{14}IN_3S_2$: C, 45.24; H, 3.13; N, 9.31%.

8c: Yield 4.5 g (78%), mp 210–212°C, orange–yellow needles; IR (cm^{-1}): 1628 (C=C), 1610 (C=N); ^1H NMR ($CDCl_3$+ CF_3CO_2H): $\delta = 2.99$ (s, 3H, SCH_3), 7.21–8.42 (m, 11H, Ar–H); MS (70 eV): *m/z* (%) = 347 ($M^+ + 2$-ICH_3, 12), 346 (14), 345 (M^+-ICH_3, 20), 344 (14), 313 (18), 287 (8), 255 (54), 142 (100). Found: C, 49.48; H, 2.71; N, 8.45%. Calcd for $C_{20}H_{14}IN_3S_2$: C, 49.29; H, 2.90; N, 8.62%.

Independent Synthesis of **5a–c**

To a solution of **8a–c** (0.002 mol) in toluene (20 ml), aniline (0.23 ml, 0.0025 mol) was added. The reaction mixture was refluxed for 24 h. After cooling to room temperature, the mixture was kept at 0°C overnight. The precipitated solid was collected by filtration and recrystallized from chloroform to yield a product identified as **5a–c** by melting point and mixed melting point determinations.

Reaction of **8a** *with Malononitrile*

Procedure A. To a stirred solution of malononitrile (0.53 g, 0.008 mol) in dry acetonitrile (20 ml), potassium *t*-butoxide (0.9 g, 0.008 mol) was added under nitrogen. The resultant solution was stirred for 20 min at room temperature and a solution of **8a** (1.93 g, 0.004 mol) in dry acetonitrile (20 ml) was added. The reaction mixture was refluxed for 3 h. After cooling to room temperature, the precipitated solid was collected by filtration, washed with cooled ethanol (15 ml), and treated with hot chloroform–benzene [1:1 (w:w)] (30 ml). The insoluble material was separated by filtration and recrystallized from ethanol to give **9**. The filtrate was kept at 0°C overnight and the precipitated solid was found to be the 2-amino-5-(2-nitrophenyl)-pyrazolo[1,5-*c*]quinazoline-1-carbonitrile (**10**).

9: Yield 0.3 g (24%), mp 220–222°C, yellow prisms; IR (cm^{-1}): 3260–3140 (NH), 2215–2190 (C≡N), 1623 (C=C), 1600 (C=N); ^1H NMR ($CDCl_3$): $\delta = 7.34–8.62$ (m, 8H, Ar–H), 10.81 (br s, 1H, NH); MS (70 eV): *m/z* (%) = 316 ($M^+ + 1$, 11), 315 (M^+, 65), 314 (22), 289 (32), 288 (4), 251 (100). Found: C, 64.92; H, 2.91; N, 22.42%. Calcd for $C_{17}H_9N_5O_2$: C, 64.76; H, 2.88; N, 22.21%.

10: Yield 0.5 g (40%), mp 241–243°C, yellow needles; IR (cm^{-1}): 3325 and 3222 (NH_2), 2218 (C≡N), 1630 (C=C), 1588 (C=N); MS (70 eV): *m/z* (%) = 330 (M^+, 19), 316 (21), 315 (62), 289 (14), 250 (100). Found: C, 61.64; H, 3.28; N, 25.31%. Calcd for $C_{17}H_{10}N_6O_2$: C, 61.82; H, 3.05; N, 25.44%.

Procedure B. To a well stirred solution of malononitrile (0.15 g, 0.0023 mol) in dry acetonitrile (15 ml), triethylamine (0.32 ml, 0.0023 mol) and **8a** (0.97 g, 0.002 mol) were added. The reaction mixture was refluxed for 24 h. After cooling to room temperature, the precipitated solid was collected by filtration and recrystallized from chloroform–benzene [1:1 (w:w)] to give yellow needles as product in 55% yield (identified as **10**) by melting point and mixed melting point determinations.

*3-(Arylideneamino)-2-(2-nitrophenyl)-3H-quinazoline-4-thiones (***11a,b***)*

Aromatic aldehydes (0.0041 mol), namely, benzaldehyde (0.41 ml) and/or *p*-chlorobenzaldehyde (0.58 g) and a catalylic amount of hydrochloric acid were added to a solution of the *N*-aminothioquinazolone **2a** (1.2 g, 0.004 mol) in methanol (30 ml). The resultant solution was heated at reflux temperature for 45 min after which it was cooled. The precipitated solid was filtered off, washed with cold methanol, dried, and crystallized from methanol to furnish **11a,b**.

11a: Yield 1.4 g (91%), mp 203–205°C, yellow plates; IR (cm^{-1}): 1625 (C=C), 1598 (C=N), 1410 (C=S); ^{1}H NMR ($CDCl_3$): $\delta = 7.48$–8.33 (m, 13H, Ar–H), 10.84 (s, 1H, ylidene H); MS (70 eV): *m/z* (%) = 386 (M^+, 42), 283 (100), 282 (20), 103 (10), 25. Found: C, 65.38; H, 3.81; N, 14.32%. Calcd for $C_{21}H_{14}N_4O_2S$: C, 65.27; H, 3.65; N, 14.50%.

11b: Yield 1.4 g (86%), mp 187–189°C, yellow plates; IR (cm^{-1}): 1629 (C=C), 1608 (C=N), 1420 (C=S); ^{1}H NMR ($CDCl_3$): $\delta = 7.35$–8.41 (m, 12H, Ar–H), 10.92 (s, 1H, ylidene H); MS (70 eV): *m/z* (%) = 422 ($M^+ + 2$, 10), 420 (M^+, 28), 283 (100), 282 (38), 250 (36), 102 (42). Found: C, 59.82; H, 3.22; N, 13.54%. Calcd for $C_{21}H_{13}N_4O_2S$: C, 59.93; H, 3.11; N, 13.31%.

*2-Benzoyl-3-phenyl- or 3-(4-Chlorophenyl)-6-(2-nitrophenyl)-2H,3H,4H-1,3,4-thiadiazino-[3,2-c]quinazolin-5-ium Bromides (***12a,b***)*

Phenacyl bromide (0.4 g, 0.002 mol) was added to a solution of the aldimine **11a,b** (0.002 mol) in hot methanol (25 ml) and the reaction mixture refluxed for 24 h. The solution was cooled to room temperature, diethyl ether (20 ml) was added, and the mixture was left at 0°C overnight. The precipitated solid was filtered off, dried, and recrystallized from methanol to furnish **12a,b**.

12a: Yield 0.7 g (60%), mp 193–195°C, pale yellow; IR (cm^{-1}): 3345 (NH), 1685 (CO), 1600 (C=N); ^{1}H NMR ($CDCl_3$): $\delta = 4.53$ (q, 1H, H-3), 6.85 (d, 1H, $J = 6.7$, H-2), 7.42–8.40 (m, 18H, Ar–H), 9.60 (d, 1H, $J = 5.6$, H-4); MS (70 eV): *m/z* (%) = 506 (M^+–Br, 20), 505 (10), 298 (38), 250 (60), 208 (28), 105 (55), 103 (100). Found: C, 59.32; H, 3.45; N, 9.48%. Calcd for $C_{29}H_{21}BrN_4O_3S$: C, 59.49; H, 3.62; N, 9.57%.

12b: Yield 0.68 g (55%), mp 175–177°C, pale yellow; IR (cm^{-1}): 3362 (NH), 1680 (CO), 1605 (C=N); ^{1}H NMR ($CDCl_3$): $\delta = 4.58$ (q, 1H, H-3), 6.77 (d, 1H, $J = 6.7$, H-2), 7.33–8.52 (m, 17H, Ar–H), 9.64 (d, 1H, $J = 5.6$, H-4); MS (70 eV): *m/z* (%) = 540 (M^+–Br, 22), 539 (14), 298 (31), 250 (43), 242 (10), 137 (14), 105 (100). Found: C, 56.28; H, 3.48; N, 9.22%. Calcd for $C_{29}H_{20}BrClN_4O_3S$: C, 56.19; H, 3.25; N, 9.04%.

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