

# Domino Cyclization of 2-Isothiocyanatobenzonitrile with Carboxylic Hydrazides – One-Pot Synthesis of 1,2,4-Triazolo[1,5-*c*]quinazoline-5(6*H*)-thiones

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One-pot reactions between carboxylic hydrazides and 2-isothiocyanatobenzonitrile afforded pharmacologically relevant 1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thiones in good yields. These compounds were transformed into the corresponding

amino-substituted derivatives in good yields in one or two steps.

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## Introduction

The development of efficient syntheses of triazoloquinazolines is of considerable current interest. These compounds combine the pharmacologically relevant triazole and quinazoline moieties and exhibit a significant and broad activity spectrum. For example, 1,2,4-triazolo[5,1-*b*]quinazolines show antihypertonic activity.<sup>[1]</sup> Antirheumatic and antianaphylactic activity has been recognized for 3-heteroaryl-1,2,4-triazolo[5,1-*b*]quinazolines,<sup>[2]</sup> while 1,2,4-triazolo[1,5-*c*]quinazolines possess antiasthmatic, tranquilizing, and neuro-stimulating activity.<sup>[3]</sup> Aryl- and heteroaryl-substituted derivatives have been shown to possess benzodiazepine binding activity.<sup>[4]</sup> In addition, anti-inflammatory, antihypertonic, and antiviral activity has been reported.<sup>[5]</sup> Chlorinated 1,2,4-triazolo[1,5-*c*]quinazolines and the isomeric 1,2,4-triazolo[4,3-*c*]quinazolines exhibit anti-inflammatory and sedative activity.<sup>[6]</sup>

1,2,4-Triazolo[1,5-*c*]quinazolines have previously been prepared by treatment of 4-hydrazinoquinazolines with aliphatic carboxylic acids.<sup>[7]</sup> The use of orthoesters resulted in the formation of 1,2,4-triazolo[4,3-*c*]quinazolines, which could be transformed into the corresponding isomers by heating under reflux with aliphatic acids (by an azaanalogous Dimroth rearrangement).<sup>[8,9]</sup> Other syntheses rely on ring-transformation reactions of benzoxazine derivatives.<sup>[10]</sup> 1,2,4-Triazolo[1,5-*c*]quinazoline-5(6*H*)-ones have been prepared by cyclization of 2-(1,2,4-triazol-3-yl)benzamides with Pb(OAc)<sub>4</sub> and NaOBr<sup>[4]</sup> and by oxidative cyclization of 4-quinazolinecarbaldehyde hydrazones.<sup>[7]</sup>

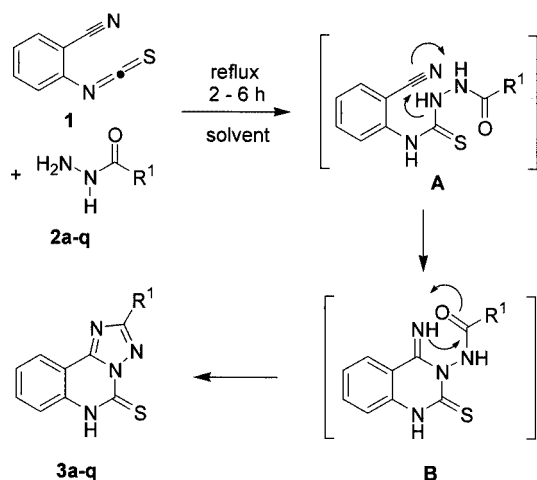
In recent years, we have reported a number of cyclization reactions of dianions and electroneutral dinucleophiles with 1,2-dielectrophiles for the synthesis of heterocyclic frameworks.<sup>[11]</sup> Here we wish to report cyclizations between carboxylic hydrazides and 2-isothiocyanatobenzonitrile (**1**) – a new and interesting type of 1,5-dielectrophile.<sup>[12]</sup> The cyclization proceeds by a domino process that, to the best of our knowledge, has not yet been reported.<sup>[13–16]</sup> We have studied this reaction widely, and it has allowed efficient one-pot syntheses of a great variety of pharmacologically relevant 1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thiones.

## Results and Discussion

Treatment of acetic hydrazide (**2b**) with 2-isothiocyanatobenzonitrile (**1**) at room temperature resulted in the formation of an open-chain product. Heating of a solution of the starting materials at reflux afforded the 1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione **3b** in up to 88% yield. The formation of **3b** can be explained by attack of the hydrazide onto the central carbon of the isothiocyanate (intermediate **A**), subsequent cyclization by attack of the hydrazide nitrogen onto the nitrile to give intermediate **B**, attack of the amidine nitrogen onto the carbonyl group and, finally, extrusion of water (Scheme 1). In this reaction, three new bonds were formed in only one synthetic operation. The reaction was monitored by TLC and IR (analysis of the diagnostic C≡N and C=O absorptions): intermediate **A** was formed predominantly when the reaction was carried out at 0 °C rather than under reflux, while intermediate **B** was formed predominantly when the reaction time (reflux) was too short.

The structures of heterocycles **3** were confirmed by spectroscopic methods, by comparison of their data with those

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Scheme 1. Synthesis of 1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thiones **3a–q** (solvent = EtOH, *i*PrOH, or CH<sub>2</sub>Cl<sub>2</sub>)

of independently prepared products and by their chemical behaviour (vide infra). All products were isolated as colourless solids, showing very strong UV absorptions in 220–267 nm range (first absorption) and the 246–340 nm range (second absorption).

For the optimization, the choice of solvent (EtOH, *i*PrOH, or CH<sub>2</sub>Cl<sub>2</sub>), temperature (reflux), reaction time (2–6 h) and concentration (0.25–0.025 M) proved to be important parameters. This can be explained by the influence of these parameters on the solubility of the starting materials and of intermediate **B**. This usually precipitated during the reaction and slowly dissolved upon cyclization to give **3**. The reaction time was generally shorter for aliphatic hydrazides than for their aromatic counterparts, which can be explained by the higher electrophilicity of aliphatic carbonyl derivatives relative to aromatic carbonyl derivatives and by the higher solubility of aliphatic starting materials and intermediates relative to the aromatic derivatives.

To study the preparative scope of the reaction, the hydrazide component was varied systematically (Scheme 1, Table 1). Treatment of formyl hydrazide **2a** with **1** afforded the unsubstituted parent 1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (**3a**). From acetyl and hexadecanoic hydrazides, the methyl- and pentadecyl-substituted quinazolines **3b** and **3c**, respectively, were obtained. Cyclization of **1** with cyanomethyl, benzyl, and phenoxymethyl hydrazides afforded the corresponding quinazolines **3d–f**. By starting with **2g–m**, the aryl-substituted quinazolines **3g–m** were formed. Treatment of **1** with hydrazides **2n–q** gave the pyridyl- and furyl-substituted 1,2,4-triazolo[1,5-*c*]quinazolines **3n–q**. The products, which in most cases had not previously been prepared, were isolated in good to excellent yields (67–99%).

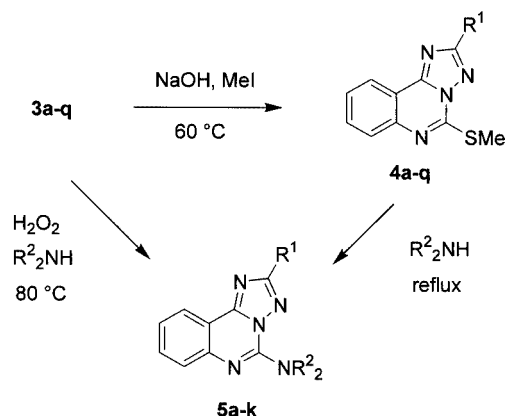
Quinazolines **3a–q** were next transformed into the corresponding thioethers **4a–q** by a procedure recently reported by us.<sup>[14]</sup> These compounds represent excellent starting materials for nucleophilic displacement reactions (vide infra) and are much more soluble than the thioxo derivatives **3** in many solvents.

Table 1. Products and yields

| Entry    | R <sup>1</sup>                                       | <b>3</b> [%] <sup>[a]</sup> | <b>4</b> [%] <sup>[a]</sup> |
|----------|------------------------------------------------------|-----------------------------|-----------------------------|
| <b>a</b> | H                                                    | 73                          | 99                          |
| <b>b</b> | CH <sub>3</sub>                                      | 88                          | 91                          |
| <b>c</b> | CH <sub>3</sub> (CH <sub>2</sub> ) <sub>14</sub>     | 96                          | 93                          |
| <b>d</b> | (NC)CH <sub>2</sub>                                  | 80                          | 72                          |
| <b>e</b> | (C <sub>6</sub> H <sub>5</sub> )CH <sub>2</sub>      | 73                          | 74                          |
| <b>f</b> | (C <sub>6</sub> H <sub>5</sub> )OCH <sub>2</sub>     | 99                          | 87                          |
| <b>g</b> | C <sub>6</sub> H <sub>5</sub>                        | 67                          | 96                          |
| <b>h</b> | 4-CH <sub>3</sub> (C <sub>6</sub> H <sub>4</sub> )   | 73                          | 83                          |
| <b>i</b> | 4-Br(C <sub>6</sub> H <sub>4</sub> )                 | 93                          | 87                          |
| <b>j</b> | 4-Cl(C <sub>6</sub> H <sub>4</sub> )                 | 71                          | 95                          |
| <b>k</b> | 2,4-Cl <sub>2</sub> (C <sub>6</sub> H <sub>3</sub> ) | 98                          | 79                          |
| <b>l</b> | 3,5-Cl <sub>2</sub> (C <sub>6</sub> H <sub>3</sub> ) | 96                          | 76                          |
| <b>m</b> | 4-NO <sub>2</sub> (C <sub>6</sub> H <sub>4</sub> )   | 76                          | 75                          |
| <b>n</b> | 2-Pyridyl                                            | 94                          | 83                          |
| <b>o</b> | 3-Pyridyl                                            | 95                          | 74                          |
| <b>p</b> | 4-Pyridyl                                            | 82                          | 79                          |
| <b>q</b> | 2-Furyl                                              | 72                          | 82                          |

<sup>[a]</sup> Isolated yields (by methods A and B, see Exp. Sect. for details).

Unlike the corresponding oxo derivatives, 5-thioxo-substituted quinazolines **3** can be used as starting materials for the synthesis of 5-substituted quinazolines, since the thio-carbonyl group can readily be transformed into an excellent leaving group. This was demonstrated by transformation of heterocycles **3** into 5-amino-1,2,4-triazolo[1,5-*c*]quinazolines **5**, via the corresponding thioethers **4**.<sup>[14]</sup> Treatment of selected thioethers **4** with secondary amines (such as morpholine, piperidine, and pyrrolidine) afforded the 5-amino-quinazolines **5a–k** in high yields (Scheme 2, Table 2). From previous findings,<sup>[14]</sup> compounds **5a–k** could also be prepared directly from **3**: treatment of the latter with H<sub>2</sub>O<sub>2</sub> gave sulfonic acid intermediates, which reacted with the nucleophile.<sup>[17]</sup> However, the reactions proceeded less cleanly and yields were lower than those obtained by the stepwise procedure. This can be explained by hydrolysis of the sulfonic acid intermediates under the reaction conditions to give oxo-analogues of **3**. Heterocycles **4** and **5** were isolated as colourless solids that showed very strong UV absorptions in similar ranges to quinazolines **3**. Amino-substituted 1,2,4-triazolo[1,5-*c*]quinazolines related to **5** are adenosine



Scheme 2. Functionalization of quinazolines **3** by treatment with amines

antagonists selective to the human A<sub>3</sub> receptor, which mediates processes of inflammation, hypotension, and mast cell degranulation and plays an important role in the central nervous system.<sup>[18]</sup>

Table 2. Synthesis of amino-substituted quinazolines **5a–k**

| 4        | 5        | R <sup>1</sup>                                   | R <sup>2</sup>                                                      | A [%] <sup>[a]</sup> | B [%] <sup>[a]</sup> |
|----------|----------|--------------------------------------------------|---------------------------------------------------------------------|----------------------|----------------------|
| <b>b</b> | <b>a</b> | CH <sub>3</sub>                                  | –(CH <sub>2</sub> ) <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub> – | 86                   | 85                   |
| <b>g</b> | <b>b</b> | C <sub>6</sub> H <sub>5</sub>                    | –(CH <sub>2</sub> ) <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub> – | 74                   | 73                   |
| <b>p</b> | <b>c</b> | 4-Pyridyl                                        | –(CH <sub>2</sub> ) <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub> – | 90                   | 34                   |
| <b>c</b> | <b>d</b> | CH <sub>3</sub> (CH <sub>2</sub> ) <sub>14</sub> | –(CH <sub>2</sub> ) <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub> – | 90                   | 96                   |
| <b>b</b> | <b>e</b> | CH <sub>3</sub>                                  | –(CH <sub>2</sub> ) <sub>5</sub> –                                  | 92                   | 88                   |
| <b>g</b> | <b>f</b> | C <sub>6</sub> H <sub>5</sub>                    | –(CH <sub>2</sub> ) <sub>5</sub> –                                  | 86                   | 83                   |
| <b>p</b> | <b>g</b> | 4-Pyridyl                                        | –(CH <sub>2</sub> ) <sub>5</sub> –                                  | 73                   | 67                   |
| <b>c</b> | <b>h</b> | CH <sub>3</sub> (CH <sub>2</sub> ) <sub>14</sub> | –(CH <sub>2</sub> ) <sub>5</sub> –                                  | 97                   | 95                   |
| <b>b</b> | <b>i</b> | CH <sub>3</sub>                                  | –(CH <sub>2</sub> ) <sub>4</sub> –                                  | 89                   | 86                   |
| <b>g</b> | <b>j</b> | C <sub>6</sub> H <sub>5</sub>                    | –(CH <sub>2</sub> ) <sub>4</sub> –                                  | 95                   | 97                   |
| <b>p</b> | <b>k</b> | 4-Pyridyl                                        | –(CH <sub>2</sub> ) <sub>4</sub> –                                  | 98                   | 92                   |

In summary, we report a new and efficient one-pot synthesis of a variety of 1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thiones. These products are of great pharmacological relevance and can be functionalized further by treatment with amines.

## Experimental Section

**General:** All solvents were distilled prior to use. Melting points are uncorrected. The NMR measurements were carried out on a Bruker Model ARX 300 spectrometer. The deuterated solvents indicated were used. Elemental analyses were performed on a Leco CHNS-932 elemental analyser. For UV/Vis spectra a Perkin–Elmer Lambda 19 UV/Vis/NIR spectrometer was used. IR Spectra were obtained on a Nicolet 205 FT-IR spectrometer.

**General Procedure for the Synthesis of 1,2,4-Triazolo[1,5-*c*]quinazoline-5(6*H*)-thiones **3a–q**:** A solution of the appropriate carboxylic hydrazide **2a–q** (10 mmol) was added to a solution of 2-isothiocyanatobenzonitrile (**1**) (1.60 g, 10 mmol) in EtOH, *i*PrOH, or CH<sub>2</sub>Cl<sub>2</sub> (40–400 mL). The mixture was heated at reflux for 2–6 h. After cooling, a colourless precipitate formed, and this was filtered off and recrystallized from EtOH, *i*PrOH, or DMF. Compounds **3n–p** were dried in vacuo at 100 °C over phosphorus pentoxide. For the synthesis of **3a** and **3b**, **1** (10 mmol) and **2a** or **2b** were dissolved in CH<sub>2</sub>Cl<sub>2</sub> (50 mL). The mixture was heated at reflux for 165 min (**3a**) or for 105 min (**3b**). In the case of **3c–3q** the reaction mixture was heated at reflux for 6 h.

**1,2,4-Triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (**3a**):** This product was obtained from **1** in EtOH (40 mL) and **2a** in EtOH (300 mL). Yield: 1.47 g (73%), colourless prisms (EtOH), m.p. 335 °C. IR (KBr):  $\tilde{\nu}$  = 3177 (m), 3108 (m), 3027 (m), 2954 (m), 1639 (s), 1541 (s), 1477 (s), 1343 (s), 1283 (m), 1261 (m), 1226 (m), 1165 (s), 1087 (s) cm<sup>–1</sup>. UV (*i*PrOH):  $\lambda_{\text{max}}$  (lgε) = 226.47 (4.53), 246.29 (4.09), 256.90 (4.07), 264.93 (4.03), 274.33 (3.99), 301.53 (4.30), 336.12 (4.02) nm. <sup>1</sup>H NMR ([D<sub>6</sub>]DMSO, 300 MHz):  $\delta$  = 2.63 (s, 3 H, CH<sub>3</sub>), 7.43–7.77 (m, 3 H, ArH), 8.22 (d, 1 H, C<sub>10</sub>-H, *J* = 8.1 Hz), 13.80 (s, 1 H, NH) ppm. <sup>13</sup>C NMR ([D<sub>6</sub>]DMSO, 75 MHz):  $\delta$  = 112.3, 116.3, 123.9, 125.4, 133.0, 136.2, 148.3, 154.5, 166.8 ppm. MS: *m/z* = 202 (100) [M<sup>+</sup>], 161 (20), 129 (10), 120 (9), 102 (10).

C<sub>9</sub>H<sub>6</sub>N<sub>4</sub>S (202.24): calcd. C 53.45, H 2.99, N 27.7; found C 53.69, H 2.83, N 27.57.

**2-Methyl-1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (**3b**):** This product was obtained from **1** in EtOH (40 mL) and **2b** in EtOH (10 mL). Yield: 1.90 g (88%), colourless needles (EtOH), m.p. 282–284 °C. IR (KBr):  $\tilde{\nu}$  = 3185 (m), 3113 (m), 2936 (m), 1629 (s), 1548 (s), 1476 (s), 1386 (s), 1340 (s), 1298 (s), 1253 (m), 1230 (m), 1099 (m) cm<sup>–1</sup>. UV (*i*PrOH):  $\lambda_{\text{max}}$  (lgε) = 227.85 (4.61), 300.8 (4.31), 336.6 (4.01) nm. <sup>1</sup>H NMR ([D<sub>6</sub>]DMSO, 300 MHz):  $\delta$  = 2.63 (s, 3 H, CH<sub>3</sub>), 7.43–8.22 (m, 4 H, Ar-H), 13.80 (s, 1 H, NH) ppm. <sup>13</sup>C NMR ([D<sub>6</sub>]DMSO, 75 MHz):  $\delta$  = 12.9, 14.1, 111.85, 116.2, 123.9, 125.3, 132.9, 136.1, 148.6, 166.3 ppm. MS: *m/z* = 216 (100) [M<sup>+</sup>], 146 (17), 145 (18), 144 (27), 120 (16), 102 (13) ppm. C<sub>10</sub>H<sub>8</sub>N<sub>4</sub>S (216.25): calcd. C 55.54, H 3.73, N 25.91; found C 55.49, H 3.85, N 25.86.

**2-Pentadecan-1-yl-1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (**3c**):** This product was obtained from **1** in EtOH (40 mL) and **2c** in EtOH (20 mL). Yield: 3.96 g (96%), colourless needles (EtOH), m.p. 156 °C. IR (KBr):  $\tilde{\nu}$  = 3205 (m), 2948 (s), 2850 (s), 1632 (s), 1601 (s), 1563 (m), 1488 (m), 1440 (m), 1337 (m), 1322 (m), 1300 (m), 1229 (m), 1114 (m), 1099 (m) cm<sup>–1</sup>. UV (EtOH):  $\lambda_{\text{max}}$  (lgε) = 228.37 (4.60), 256.85 (4.14), 277.24 (4.02), 301.12 (4.30), 335.37 (3.97) nm. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  = 0.85–0.90 (t, 3 H, CH<sub>3</sub>), 1.25–1.41 (m, 26 H, CH<sub>2</sub>), 2.96–3.02 (t, 2 H, CH<sub>2</sub>), 7.48–8.37 (m, 4 H, ArH), 11.21 (s, 1 H, NH) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  = 14.1, 22.7, 28.3, 28.9, 29.4, 29.5, 29.7, 31.9, 112.5, 115.2, 125.2, 126.0, 133.2, 135.5, 149.0, 167.1, 169.8 ppm. MS: *m/z* = 413 (62) [M<sup>+</sup>], 412 (34), 379 (17), 271 (21), 229 (100), 216 (95). C<sub>24</sub>H<sub>36</sub>N<sub>4</sub>S (412.64): calcd. C 69.86, H 8.79, N 13.58; found C 69.88, H 9.07, N 13.16.

**2-Cyanomethyl-1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (**3d**):** This product was obtained from **1** in EtOH (40 mL) and **2d** in EtOH (20 mL). Yield: 1.93 g (80%), colourless prisms (EtOH), m.p. 316 °C. IR (KBr):  $\tilde{\nu}$  = 3188 (m), 3166 (m), 3105 (m), 3074 (m), 3004 (m), 2910 (s), 2256 (w), 1630 (s), 1601 (m), 1548 (s), 1546 (s), 1300 (s), 1252 (s), 1241 (m), 1118 (m) cm<sup>–1</sup>. UV (*i*PrOH):  $\lambda_{\text{max}}$  (lgε) = 227.49 (4.59), 302.09 (4.30), 338.66 (3.96) nm. <sup>1</sup>H NMR ([D<sub>6</sub>]DMSO, 300 MHz):  $\delta$  = 4.52 (s, 2 H, CH<sub>2</sub>CN), 7.51–8.22 (m, 4 H, ArH), 14.09 (s, 1 H, NH) ppm. <sup>13</sup>C NMR ([D<sub>6</sub>]DMSO, 75 MHz):  $\delta$  = 17.86, 112.0, 116.4, 116.6, 124.1, 125.7, 133.4, 136.5, 149.6, 158.7, 166.4 ppm. MS: *m/z* = 241 (100) [M<sup>+</sup>], 214 (75), 161 (14), 146 (9), 143 (8), 102 (18). C<sub>11</sub>H<sub>7</sub>N<sub>5</sub>S (241.27): calcd. C 54.76, H 2.92, N 29.03; found C 54.63, H 2.67, N 28.92.

**2-Benzyl-1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (**3e**):** This product was obtained from **1** in EtOH (40 mL) and **2e** in EtOH (450 mL). Yield: 2.13 g (73%), colourless prisms (EtOH), m.p. 222 °C. IR (KBr):  $\tilde{\nu}$  = 3183 (m), 3024 (m), 1632 (s), 1561 (s), 1542 (s), 1476 (s), 1380 (s), 1322 (s), 1300 (s), 1254 (m), 1157 (m), 1115 (m), 1099 (m) cm<sup>–1</sup>. UV (EtOH):  $\lambda_{\text{max}}$  (lgε) = 229.45 (4.63), 247.96 (4.21), 277.72 (4.03), 301.52 (4.33), 335.65 (3.98) nm. <sup>1</sup>H NMR ([D<sub>6</sub>]DMSO, 300 MHz):  $\delta$  = 4.26 (s, 2 H, CH<sub>2</sub>), 7.24–8.19 (m, 9 H, ArH), 13.94 (s, 1 H, NH) ppm. <sup>13</sup>C NMR ([D<sub>6</sub>]DMSO, 75 MHz):  $\delta$  = 34.17, 111.9, 116.2, 123.9, 125.3, 126.5, 128.4, 128.8, 132.9, 136.2, 137.2, 148.9, 166.1, 166.5 ppm. MS: *m/z* = 292 (100) [M<sup>+</sup>], 131 (9), 115 (8), 103 (12), 91 (18). C<sub>16</sub>H<sub>12</sub>N<sub>4</sub>S (292.36): calcd. C 65.73, H 4.14, N 19.16; found C 65.79, H 4.40, N 18.96.

**2-Phenoxymethyl-1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (**3f**):** This product was obtained from **1** in *i*PrOH (80 mL) and **2f** in *i*PrOH (70 mL). Yield: 3.05 g (99%), colourless needles (EtOH), m.p. 251 °C. IR (KBr):  $\tilde{\nu}$  = 3193 (m), 3147 (m), 3058 (m), 1632 (s), 1600 (s), 1588 (m), 1567 (m), 1541 (s), 1496 (m), 1476 (s), 1247

(s), 1223 (s), 1099 (m)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 228.29 (4.67), 302.50 (4.25), 337.38 (3.96) nm.  $^1\text{H}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 300 MHz):  $\delta$  = 5.36 (s, 2 H,  $\text{CH}_2$ ), 7.55–8.25 (m, 9 H, ArH), 14.05 (s, 1 H, NH) ppm.  $^{13}\text{C}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 75 MHz):  $\delta$  = 63.2, 112.3, 115.0, 116.7, 121.6, 124.4, 126.0, 130.0, 133.7, 136.7, 149.5, 158.2, 163.2, 166.9 ppm. MS:  $m/z$  = 308 (86)  $[\text{M}^+]$ , 215 (100), 161 (42), 102 (13), 66 (17).  $\text{C}_{16}\text{H}_{12}\text{N}_4\text{OS}$  (308.36): calcd. C 62.32, H 3.92, N 18.17; found C 62.10, H 3.87, N 17.92.

**2-Phenyl-1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (3g):** This product was obtained from **1** in EtOH (40 mL) and **2g** in EtOH (250 mL). Yield: 1.86 g (67%), colourless prisms (EtOH), m.p. 311 °C. IR (KBr):  $\tilde{\nu}$  = 3197 (m), 3141 (m), 3031 (m), 1631 (s), 1530 (s), 1473 (s), 1446 (s), 1325 (s), 1253 (m), 1233 (m), 1132 (m), 1080 (m)  $\text{cm}^{-1}$ . UV (EtOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 251.85 (4.70), 278.53 (4.39), 290.31 (4.36), 307.49 (4.21), 338.20 (4.05) nm.  $^1\text{H}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 300 MHz):  $\delta$  = 7.56–8.32 (m, 9 H, ArH), 14.01 (s, 1 H, NH) ppm.  $^{13}\text{C}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 75 MHz):  $\delta$  = 112.1, 116.3, 124.1, 125.4, 126.9, 129.0, 129.4, 130.7, 133.7, 133.1, 136.3, 149.4, 163.5, 166.5 ppm. MS:  $m/z$  = 278 (100)  $[\text{M}^+]$ , 277 (86), 146 (12), 120 (11), 118 (18), 103 (12).  $\text{C}_{15}\text{H}_{10}\text{N}_4\text{S}$  (278.33): calcd. C 64.73, H 3.62, N 20.13; found C 64.58, H 3.52, N 19.92.

**2-Tolyl-1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (3h):** This product was obtained from **1** in *i*PrOH (80 mL) and **2h** in *i*PrOH (120 mL). Yield: 2.13 g (73%), colourless prisms (EtOH), m.p. 315 °C. IR (KBr):  $\tilde{\nu}$  = 3192 (m), 3139 (m), 3068 (m), 1631 (s), 1611 (m), 1536 (s), 1469 (s), 1299 (s), 1253 (m), 1131 (m), 982 (m), 750 (s)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 220.04 (4.26), 255.04 (4.61), 293.85 (4.40), 339.11 (3.92) nm.  $^1\text{H}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 300 MHz):  $\delta$  = 1.03–1.08 (s, 3 H,  $\text{CH}_3$ ), 7.39–8.31 (m, 8 H, ArH), 13.99 (s, 1 H, NH) ppm.  $^{13}\text{C}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 75 MHz):  $\delta$  = 21.0, 112.1, 116.3, 124.1, 125.4, 126.8, 127.0, 129.7, 133.1, 136.9, 140.7, 149.5, 163.6, 166.4 ppm. MS:  $m/z$  = 292 (100)  $[\text{M}^+]$ , 291 (89), 146 (15), 132 (15), 20 (11).  $\text{C}_{16}\text{H}_{12}\text{N}_4\text{S}$  (292.36): calcd. C 65.73, H 4.14, N 19.16; found C 65.91, H 4.29, N 19.54.

**2-(4-Bromophenyl)-1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (3i):** This product was obtained from **1** in *i*PrOH (80 mL) and **2i** in *i*PrOH (50 mL). Yield: 3.32 g (93%), colourless needles (DMF), m.p. 342 °C. IR (KBr):  $\tilde{\nu}$  = 3114 (m), 3086 (m), 3068 (m), 1631 (s), 1536 (s), 1405 (s), 1299 (s), 1131 (m), 1081 (m), 1012 (m), 982 (m), 753 (s)  $\text{cm}^{-1}$ . UV (DMF):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 277.23 (4.54), 338.57 (4.16) nm.  $^1\text{H}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 300 MHz):  $\delta$  = 7.54–8.32 (m, 8 H, ArH), 13.94 (s, 1 H, NH) ppm.  $^{13}\text{C}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 75 MHz):  $\delta$  = 112.1, 116.5, 124.1, 124.3, 125.5, 128.6, 128.9, 132.1, 133.2, 136.6, 149.6, 162.6, 166.4 ppm. MS:  $m/z$  = 357 (100)  $[\text{M}^+]$ , 356 (94), 355 (58), 196 (11), 146 (13), 138 (13), 120 (12).  $\text{C}_{15}\text{H}_9\text{BrN}_4\text{S}$  (357.24): calcd. C 50.43, H 2.54, N 15.68; found C 50.33, H 2.36, N 15.62.

**2-(4-Chlorophenyl)-1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (3j):** This product was obtained from **1** in *i*PrOH (80 mL) and **2j** in *i*PrOH (70 mL). Yield: 2.22 g (71%), colourless needles (EtOH), m.p. 345 °C. IR (KBr):  $\tilde{\nu}$  = 3200 (m), 3139 (m), 3118 (m), 3068 (m), 3027 (m), 1632 (s), 1536 (s), 1447 (s), 1409 (s), 1315 (s), 1299 (s), 1253 (m), 1132 (m), 753 (s)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 267.23 (3.48), 338.19 (3.96) nm.  $^1\text{H}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 300 MHz):  $\delta$  = 7.56–8.31 (m, 8 H, ArH), 13.91 (s, 1 H, NH) ppm.  $^{13}\text{C}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 75 MHz):  $\delta$  = 55.9, 112.1, 116.3, 124.1, 125.4, 128.3, 128.7, 129.2, 133.2, 135.4, 136.4, 149.6, 162.5, 166.4 ppm. MS:  $m/z$  = 313 (45)  $[\text{M}^+]$ , 312 (100), 311 (74), 151 (17), 146 (15), 120 (16), 102 (16).  $\text{C}_{15}\text{H}_9\text{ClN}_4\text{S}$  (312.78): calcd. C 57.60, H 2.90, N 17.91; found C 57.87, H 2.88, N 18.02.

**2-(2,4-Dichlorophenyl)-1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (3k):** This product was obtained from **1** in *i*PrOH (80 mL) and **2k**

in *i*PrOH (70 mL). Yield: 3.40 g (98%), colourless needles (DMF), m.p. 287 °C. IR (KBr):  $\tilde{\nu}$  = 3107 (m), 3087 (m), 3016 (m), 1633 (s), 1540 (s), 1302 (s), 1231 (m), 1137 (m), 1106 (m), 1089 (m), 980 (m), 756 (s)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 203.07 (4.49), 225.76 (4.52), 253.15 (4.60) nm.  $^1\text{H}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 300 MHz):  $\delta$  = 7.57–8.34 (m, 7 H, ArH), 13.91 (s, 1 H, NH) ppm.  $^{13}\text{C}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 75 MHz):  $\delta$  = 112.0, 116.4, 124.2, 125.5, 127.7, 130.2, 133.2, 133.3, 135.6, 136.5, 148.8, 161.6, 166.5 ppm. MS:  $m/z$  = 348 (14)  $[\text{M}^+]$ , 346 (22), 313 (38), 312 (19), 311 (100).  $\text{C}_{15}\text{H}_8\text{Cl}_2\text{N}_4\text{S}$  (347.22): calcd. C 51.89, H 2.32, N 16.14; found C 51.94, H 2.02, N 16.13.

**2-(3,5-Dichlorophenyl)-1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (3l):** This product was obtained from **1** in *i*PrOH (80 mL) and **2l** in *i*PrOH (220 mL). Yield: 3.33 g (96%), colourless prisms (DMF), m.p. 360 °C. IR (KBr):  $\tilde{\nu}$  = 3111 (m), 3080 (m), 3016 (m), 1632 (s), 1541 (s), 1503 (s), 1475 (m), 1301 (s), 1232 (m), 1085 (m), 976 (m), 756 (m)  $\text{cm}^{-1}$ . UV (DMF):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 303.03 (4.28), 342.81 (4.02) nm.  $^1\text{H}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 300 MHz):  $\delta$  = 7.57–8.34 (m, 7 H, ArH), 14.15 (s, 1 H, NH) ppm.  $^{13}\text{C}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 75 MHz):  $\delta$  = 5.3, 6.9, 55.9, 125.2, 130.1, 133.4, 134.9, 136.6, 149.8, 166.4, 221.2 ppm. MS:  $m/z$  = 347 (65)  $[\text{M}^+]$ , 346 (100), 345 (72), 186 (14), 146 (22), 120 (24).  $\text{C}_{15}\text{H}_8\text{Cl}_2\text{N}_4\text{S}$  (347.22): calcd. C 51.89, H 2.32, N 16.14; found C 52.08, H 2.17, N 16.52.

**2-(4-Nitrophenyl)-1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (3m):** This product was obtained from **1** in *i*PrOH (80 mL) and **2m** in *i*PrOH (130 mL). Yield: 2.46 g (76%), colourless rods (EtOH), m.p. 335 °C. IR (KBr):  $\tilde{\nu}$  = 3103 (m), 3068 (m), 2981 (m), 1632 (s), 1603 (s), 1551 (s), 1536 (s), 1472 (s), 1343 (s), 1313 (s), 1247 (m), 1107 (m)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 235.98 (4.43), 282.04 (4.25) nm.  $^1\text{H}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 300 MHz):  $\delta$  = 7.55–8.51 (m, 8 H, ArH), 14.12 (s, 1 H, NH) ppm.  $^{13}\text{C}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 75 MHz):  $\delta$  = 112.1, 116.4, 124.1, 124.3, 125.5, 128.1, 133.3, 135.3, 136.5, 148.6, 149.9, 161.6, 166.5 ppm. MS:  $m/z$  = 323 (100)  $[\text{M}^+]$ , 322 (43), 175 (63), 149 (36), 120 (43), 104 (19).  $\text{C}_{15}\text{H}_9\text{N}_5\text{O}_2\text{S}$  (323.33): calcd. C 55.72, H 2.81, N 21.66; found C 55.73, H 2.45, N 21.65.

**2-(2-Pyridyl)-1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (3n):** This product was obtained from **1** in *i*PrOH (80 mL) and **2n** in *i*PrOH (50 mL). Yield: 2.62 g (94%), colourless prisms (DMF), m.p. 374 °C. IR (KBr):  $\tilde{\nu}$  = 3148 (w), 3108 (w), 3090 (w), 3019 (w), 1637 (s), 1600 (m), 1561 (s), 1552 (s), 1475 (s), 1419 (s), 1256 (m), 1244 (m), 1155 (m), 1114 (m), 1081 (m)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 245.07 (4.58), 339.98 (3.50) nm.  $^1\text{H}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 300 MHz):  $\delta$  = 7.57–8.80 (m, 8 H, ArH, pyridyl) ppm.  $^{13}\text{C}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 75 MHz):  $\delta$  = 112.3, 123.0, 124.1, 125.2, 125.5, 133.1, 136.4, 137.3, 148.2, 149.4, 150.0, 163.2, 166.7 ppm. MS:  $m/z$  = 279 (100)  $[\text{M}^+]$ , 251 (39), 250 (14), 123 (22), 102 (14), 78 (29).  $\text{C}_{14}\text{H}_9\text{N}_5\text{S}$  (279.32): calcd. C 60.20, H 3.25, N 25.07; found C 60.13, H 2.83, N 24.97.

**2-(3-Pyridyl)-1,2,4-triazolo[1,5-*c*]quinazoline-5(6*H*)-thione (3o):** This product was obtained from **1** in *i*PrOH (80 mL) and **2o** in *i*PrOH (40 mL). Yield: 2.65 g (95%), colourless rods (DMF), m.p. 347 °C. IR (KBr):  $\tilde{\nu}$  = 3108 (w), 3062 (w), 1636 (s), 1601 (m), 1562 (s), 1548 (s), 1477 (s), 1412 (s), 1380 (s), 1307 (s), 1299 (s), 1140 (s), 1088 (m)  $\text{cm}^{-1}$ . UV (DMF):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 266.60 (4.42), 338.62 (4.14) nm.  $^1\text{H}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 300 MHz):  $\delta$  = 7.57–9.40 (m, 8 H, ArH, pyridyl), 14.08 (s, 1 H, NH) ppm.  $^{13}\text{C}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 75 MHz):  $\delta$  = 112.1, 116.3, 124.2, 125.4, 133.2, 134.4, 136.4, 147.7, 149.6, 151.4, 161.5, 166.4 ppm. MS:  $m/z$  = 279 (100)  $[\text{M}^+]$ , 278 (82), 146 (15), 119 (17), 102 (13).  $\text{C}_{14}\text{H}_9\text{N}_5\text{S}$  (279.32): calcd. C 60.20, H 3.25, N 25.07; found C 60.26, H 3.28, N 25.10.

**2-(4-Pyridyl)-1,2,4-triazolo[1,5-c]quinazoline-5(6H)-thione (3p):**

This product was obtained from **1** and **2p** in DMF (50 mL). Yield: 2.29 g (82%), colourless needles (DMF), m.p. 335 °C. IR (KBr):  $\tilde{\nu}$  = 3195 (m), 3012 (m), 2956 (m), 1636 (s), 1538 (s), 1485 (s), 1377 (m), 1328 (m), 1302 (s), 1261 (m), 1238 (m), 1139 (m), 1085 (m)  $\text{cm}^{-1}$ . UV (EtOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 249.86 (4.62), 310.55 (4.03), 341.18 (4.02) nm.  $^1\text{H}$  NMR ([D<sub>6</sub>]DMSO, 300 MHz):  $\delta$  = 7.57–8.83 (m, 8 H, ArH, pyridyl), 14.12 (s, 1 H, NH) ppm.  $^{13}\text{C}$  NMR ([D<sub>6</sub>]DMSO, 75 MHz):  $\delta$  = 112.1, 116.3, 124.2, 125.5, 133.2, 134.4, 136.4, 147.7, 149.6, 151.4, 161.5, 166.4 ppm. MS:  $m/z$  = 279 (100) [ $\text{M}^+$ ], 278 (75), 146 (14), 120 (12), 102 (10). C<sub>14</sub>H<sub>9</sub>N<sub>5</sub>S (279.32): calcd. C 60.20, H 3.25, N 25.07; found C 60.49, H 3.47, N 24.98.

**2-(2-Furyl)-1,2,4-triazolo[1,5-c]quinazoline-5(6H)-thione (3q):**

This product was obtained from **1** in *i*PrOH (80 mL) and **2q** in *i*PrOH (30 mL). Yield: 1.93 g (72%), colourless rods (*i*PrOH), m.p. 333 °C. IR (KBr):  $\tilde{\nu}$  = 3190 (m), 3146 (m), 3117 (m), 1633 (s), 1620 (s), 1530 (s), 1509 (s), 1429 (m), 1316 (s), 1300 (s), 1181 (m), 1131 (m), 755 (s)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 233.76 (4.14), 231.11 (4.15), 259.51 (4.48), 278.46 (4.37), 297.37 (4.45), 341.21 (3.86) nm.  $^1\text{H}$  NMR ([D<sub>6</sub>]DMSO, 300 MHz):  $\delta$  = 6.77–8.29 (m, 7 H, ArH, furfuryl), 14.02 (s, 1 H, NH) ppm.  $^{13}\text{C}$  NMR ([D<sub>6</sub>]DMSO, 75 MHz):  $\delta$  = 112.3, 112.7, 113.2, 116.8, 124.5, 125.9, 133.7, 137.0, 145.0, 146.0, 149.7, 156.8, 166.7 ppm. MS:  $m/z$  = 268 (100) [ $\text{M}^+$ ], 240 (24), 210 (25), 120 (12), 107 (21). C<sub>13</sub>H<sub>8</sub>N<sub>4</sub>OS (268.29): calcd. C 58.20; H 3.01, N 20.88; found C 58.21, H 2.89, N 20.61.

**General Procedure for the Preparation of the 5-Methylsulfanyl-1,2,4-triazolo[1,5-c]quinazolines (4a–4q):** Compounds **3a–3q** (5 mmol) were dissolved in aqueous sodium hydroxide (0.02 M, 60 mL). Methyl iodide (1.00 g, 7.00 mmol) was added dropwise, and the mixture was heated to 60 °C over a period of 5 minutes. The colourless precipitate formed on cooling was filtered off, washed with water, and recrystallized from ethanol.

**5-Methylsulfanyl-1,2,4-triazolo[1,5-c]quinazoline (4a):** Yield: 1.07 g (99%), colourless rods (EtOH), m.p. 135 °C. IR (KBr):  $\tilde{\nu}$  = 3015 (w), 2927 (w), 1620 (s), 1589 (s), 1505 (s), 1463 (s), 1380 (s), 1310 (s), 1276 (m), 1198 (m), 1166 (m), 1075 (s)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 220.92 (4.58), 248.47 (4.46), 279.52 (4.11), 308.07 (3.51), 322.07 (3.58) nm.  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  = 2.79 (s, 3 H, SCH<sub>3</sub>), 7.30–7.87 (m, 4 H, ArH), 8.39 (s, 1 H, C<sup>2</sup>-H) ppm.  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  = 13.4, 115.9, 123.5, 127.0, 127.1, 131.9, 143.3, 149.6, 150.1, 154.4 ppm. MS:  $m/z$  = 216 (100) [ $\text{M}^+$ ], 215 (33), 189 (34), 145 (24), 114 (19), 102 (17). C<sub>10</sub>H<sub>8</sub>N<sub>4</sub>S (216.26): calcd. C 55.54, H 3.73, N 25.91; found C 55.83, H 3.72, N 25.88.

**2-Methyl-5-methylsulfanyl-1,2,4-triazolo[1,5-c]quinazoline (4b):**

Yield: 1.02 g (91%), colourless needles (EtOH), m.p. 151 °C. IR (KBr):  $\tilde{\nu}$  = 3005 (w), 2929 (w), 1624 (m), 1592 (s), 1559 (m), 1516 (s), 1509 (s), 1491 (s), 1468 (m), 1369 (m), 1303 (s)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 223.09 (4.47), 248.99 (4.57), 278.60 (4.08), 285.92 (4.05), 309.12 (3.59), 323.09 (3.63) nm.  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  = 2.69 (s, 3 H, CH<sub>3</sub>), 2.81 (s, 3 H, SCH<sub>3</sub>), 7.55–8.41 (m, 4 H, ArH) ppm.  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  = 13.4, 14.6, 115.7, 123.6, 127.0, 127.3, 131.9, 143.5, 149.2, 150.7, 163.9 ppm. MS:  $m/z$  = 230 (100) [ $\text{M}^+$ ], 229 (22), 189 (62), 188 (38), 184 (30), 145 (29), 114 (23). C<sub>11</sub>H<sub>10</sub>N<sub>4</sub>S (230.29): calcd. C 57.37, H 4.38, N 24.33; found C 57.42, H 4.51, N 24.17.

**5-Methylsulfanyl-2-pentadecanyl-1,2,4-triazolo[1,5-c]quinazoline (4c):**

Yield: 1.98 g (93%), colourless rods (EtOH), m.p. 85 °C. IR (KBr):  $\tilde{\nu}$  = 2949 (m), 2917 (s), 2850 (s), 1623 (m), 1592 (m), 1509 (s), 1492 (m), 1472 (m), 1372 (m), 1316 (m), 1088 (m)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 224.13 (4.45), 248.96 (4.62), 278.90 (4.08), 309.14 (3.59), 323.09 (3.64) nm.  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  =

0.85–0.90 (t, 3 H, CH<sub>3</sub>), 1.25–1.92 (m, 26 H, CH<sub>2</sub>), 2.81 (s, 3 H, SCH<sub>3</sub>), 2.96–3.01 (t, 2 H, CH<sub>2</sub>), 7.57–8.46 (m, 4 H, ArH) ppm.  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  = 13.4, 14.1, 22.7, 28.5, 28.9, 29.4, 29.5, 29.7, 31.9, 115.8, 123.7, 126.9, 127.2, 131.8, 143.5, 150.6, 167.9 ppm. MS:  $m/z$  = 427 (6) [ $\text{M}^+$ ], 285 (18), 243 (44), 231 (13), 230 (100). C<sub>25</sub>H<sub>38</sub>N<sub>4</sub>S (426.67): calcd. C 70.38, H 8.98, N 13.13; found C 70.29, H 8.76, N 13.32.

**2-Cyanomethyl-5-methylsulfanyl-1,2,4-triazolo[1,5-c]quinazoline (4d):**

Yield: 0.92 g (72%), colourless prisms (EtOH), m.p. 190 °C. IR (KBr):  $\tilde{\nu}$  = 2968 (m), 2256 (w), 1622 (s), 1592 (m), 1506 (s), 1490 (m), 1375 (m), 1356 (m), 1314 (m), 1088 (m), 966 (m), 767 (m)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 222.18 (4.50), 249.38 (4.58), 279.64 (4.10), 309.23 (3.58), 323.24 (3.59) nm.  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  = 2.8 (s, 3 H, SCH<sub>3</sub>), 4.1 (s, 3 H, CN-CH<sub>3</sub>), 7.28–8.39 (m, 4 H, ArH) ppm.  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  = 13.4, 18.7, 115.0, 115.4, 123.7, 127.3, 127.4, 132.5, 143.4, 149.3, 151.3, 157.1 ppm. MS:  $m/z$  = 255 (48) [ $\text{M}^+$ ], 215 (19), 102 (5), 57 (10), 32 (25), 28 (100). C<sub>12</sub>H<sub>9</sub>N<sub>5</sub>S (255.3): calcd. C 56.45, H 3.55, N 27.43; found C 56.69, H 3.41, N 27.70.

**2-Benzyl-5-methylsulfanyl-1,2,4-triazolo[1,5-c]quinazoline (4e):**

Yield: 1.13 g (74%), colourless needles (EtOH), m.p. 130 °C. IR (KBr):  $\tilde{\nu}$  = 2923 (w), 1622 (m), 1589 (s), 1504 (s), 1487 (s), 1460 (m), 1372 (s), 1308 (m), 1275 (m), 1149 (w), 1087 (m), 965 (m), 768 (m)  $\text{cm}^{-1}$ . UV (DMF):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 265.60 (4.09), 280.54 (4.06), 309.71 (3.58), 323.76 (3.62) nm.  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  = 2.81 (s, 3 H, CH<sub>3</sub>), 4.35 (s, 2 H, CH<sub>2</sub>), 7.24–8.43 (m, 9 H, ArH) ppm.  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  = 13.4, 35.1, 115.8, 123.8, 126.7, 126.9, 127.2, 128.6, 129.0, 131.9, 137.2, 143.5, 149.4, 166.0 ppm. MS:  $m/z$  = 306 (100) [ $\text{M}^+$ ], 305 (12), 259 (30), 215 (58), 189 (12), 91 (23). C<sub>17</sub>H<sub>14</sub>N<sub>4</sub>S (306.39): calcd. C 66.64, H 4.61, N 18.29; found C 66.47, H 4.48, N 18.32.

**5-Methylsulfanyl-2-phenoxyethyl-1,2,4-triazolo[1,5-c]quinazoline (4f):**

Yield: 1.40 g (87%), colourless prisms (EtOH), m.p. 163 °C. IR (KBr):  $\tilde{\nu}$  = 2931 (w), 1620 (m), 1597 (m), 1588 (s), 1496 (s), 1461 (m), 1364 (m), 1309 (m), 1238 (s), 1224 (s), 1088 (m), 1033 (m)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 223.49 (4.60), 249.53 (4.61), 270.00 (4.13), 277.15 (4.16), 309.02 (3.65), 323.06 (3.65) nm.  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  = 2.83 (s, 3 H, SCH<sub>3</sub>), 5.41 (s, 2 H, OCH<sub>2</sub>), 7.28–8.51 (m, 9 H, ArH) ppm.  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  = 13.4, 25.3, 63.5, 90.1, 115.0, 115.8, 121.4, 123.9, 127.2, 127.3, 129.5, 132.3, 143.5, 149.6, 151.2, 158.3, 162.6 ppm. MS:  $m/z$  = 322 (87) [ $\text{M}^+$ ], 230 (31), 229 (100), 188 (33), 186 (39), 160 (13). C<sub>17</sub>H<sub>14</sub>N<sub>4</sub>OS (322.40): calcd. C 63.34, H 4.38, N 17.38; found C 63.27, H 4.18, N 17.13.

**5-Methylsulfanyl-2-phenyl-1,2,4-triazolo[1,5-c]quinazoline (4g):**

Yield: 1.40 g (96%), colourless rods (EtOH), m.p. 170 °C. IR (KBr):  $\tilde{\nu}$  = 1621 (m), 1596 (s), 1585 (m), 1521 (m), 1499 (s), 1476 (s), 1444 (s), 1366 (s), 1317 (m), 1131 (m), 1069 (m), 964 (m)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 211.64 (4.37), 252.51 (4.70), 258.58 (4.73), 311.67 (3.82), 325.92 (3.67) nm.  $^1\text{H}$  NMR ([D<sub>6</sub>]DMSO, 300 MHz):  $\delta$  = 2.81 (s, 3 H, S-CH<sub>3</sub>), 7.60–8.30 (m, 9 H, ArH) ppm.  $^{13}\text{C}$  NMR ([D<sub>6</sub>]DMSO, 75 MHz):  $\delta$  = 12.9, 115.4, 123.4, 127.0, 127.3, 129.0, 129.5, 130.7, 132.4, 142.8, 149.5, 150.6, 156.4, 162.9, 180.6, 238.1 ppm. MS:  $m/z$  = 292 (100) [ $\text{M}^+$ ], 291 (20), 245 (24), 189 (34), 188 (13), 145 (15), 118 (9). C<sub>16</sub>H<sub>12</sub>N<sub>4</sub>S (292.35): calcd. C 65.73, H 4.14, N 19.16; found C 65.82, H 4.47, N 19.03.

**5-Methylsulfanyl-2-tolyl-1,2,4-triazolo[1,5-c]quinazoline (4h):**

Yield: 1.27 g (83%), colourless prisms (EtOH), m.p. 194 °C. IR (KBr):  $\tilde{\nu}$  = 2925 (w), 1616 (s), 1591 (s), 1573 (m), 1557 (m), 1497 (s), 1477 (s), 1446 (s), 1364 (s), 1313 (m), 1130 (m), 1072 (m)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 217.59 (4.38), 261.09 (4.72), 271.30 (4.66),

312.60 (3.62), 326.13 (3.47) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 1.22 (s, 3 H,  $\text{CH}_3$ ), 2.83 (s, 3 H,  $\text{SCH}_3$ ), 7.61–8.54 (m, 8 H, ArH) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 13.4, 21.6, 25.4, 116.0, 123.9, 126.9, 127.2, 127.3, 127.6, 129.4, 131.9, 140.7, 143.5, 149.7, 151.0, 164.3 ppm. MS:  $m/z$  = 306 (100) [ $\text{M}^+$ ], 305 (18), 259 (26), 189 (45), 188 (17), 145 (18).  $\text{C}_{17}\text{H}_{14}\text{N}_4\text{S}$  (306.37): calcd. C 66.64, H 4.61, N 18.29; found C 66.48, H 4.67, N 17.96.

**2-(4-Bromophenyl)-5-methylsulfanyl-1,2,4-triazolo[1,5-*c*]quinazoline (4i):** Yield: 1.61 g (87%), colourless prisms (EtOH), m.p. 204 °C. IR (KBr):  $\tilde{\nu}$  = 1623 (m), 1591 (s), 1572 (m), 1561 (m), 1500 (s), 1476 (m), 1459 (m), 1441 (s), 1367 (m), 1308 (m), 1274 (m), 1131 (m)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  ( $\lg\epsilon$ ) = 217.65 (4.32), 261.96 (4.75), 273.52 (4.68), 326.20 (3.45) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 2.82 (s, 3 H,  $\text{SCH}_3$ ), 7.61–8.50 (m, 8 H, ArH) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 13.4, 115.9, 123.8, 125.0, 127.0, 127.3, 129.1, 129.2, 131.9, 132.1, 143.5, 149.6, 151.1, 163.3 ppm. MS:  $m/z$  = 372 (100) [ $\text{M}^+$ ], 370 (67), 325 (17), 323 (15), 189 (68), 188 (27), 145 (29), 102 (39).  $\text{C}_{16}\text{H}_{11}\text{BrN}_4\text{S}$  (371.26): calcd. C 51.76, H 2.99, N 15.09; found C 51.90, H 2.96, N 15.13.

**2-(4-Chlorophenyl)-5-methylsulfanyl-1,2,4-triazolo[1,5-*c*]quinazoline (4j):** Yield: 1.55 g (95%), colourless needles (EtOH), m.p. 400 °C. IR (KBr):  $\tilde{\nu}$  = 2926 (w), 1623 (m), 1593 (m), 1572 (m), 1503 (s), 1476 (m), 1442 (s), 1362 (m), 1309 (m), 1130 (m), 1087 (m), 1072 (m), 969 (m), 746 (s)  $\text{cm}^{-1}$ . UV (DMF):  $\lambda_{\text{max}}$  ( $\lg\epsilon$ ) = 266.78 (4.50), 336.11 (4.03) nm.  $^1\text{H}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 300 MHz):  $\delta$  = 2.82 (s, 3 H,  $\text{SCH}_3$ ), 7.29–8.27 (m, 8 H, ArH) ppm.  $^{13}\text{C}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 75 MHz):  $\delta$  = 114.0, 122.3, 122.9, 124.3, 128.3, 128.8, 129.2, 130.0, 131.0, 134.1, 144.4, 149.9, 159.5, 165.9 ppm. MS:  $m/z$  = 326 (100) [ $\text{M}^+$ ], 325 (14), 279 (21), 189 (52), 188 (18), 145 (17), 102 (14).  $\text{C}_{16}\text{H}_{11}\text{ClN}_4\text{S}$  (326.80): calcd. C 58.80, H 3.39, N 17.15; found C 58.53, H 3.28, N 17.27.

**2-(2,4-Dichlorophenyl)-5-methylsulfanyl-1,2,4-triazolo[1,5-*c*]quinazoline (4k):** Yield: 1.43 g (79%), colourless needles (EtOH), m.p. 227 °C. IR (KBr):  $\tilde{\nu}$  = 1621 (m), 1593 (s), 1500 (s), 1473 (m), 1459 (m), 1442 (m), 1363 (m), 1301 (m), 1104 (m), 1047 (m), 965 (m), 765 (m)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  ( $\lg\epsilon$ ) = 222.70 (4.58), 253.72 (4.70), 324.69 (3.55) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 2.84 (s, 3 H,  $\text{SCH}_3$ ), 7.39–8.54 (m, 7 H, ArH) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 13.43, 115.9, 123.9, 127.2, 127.4, 128.0, 130.7, 132.2, 133.0, 134.4, 136.4, 143.6, 150.5, 161.9, 165.3 ppm. MS:  $m/z$  = 361 (24) [ $\text{M}^+$ ], 360 (100), 327 (36), 325 (96), 315 (26), 313 (32), 294 (22), 292 (63), 189 (57), 146 (33).  $\text{C}_{16}\text{H}_{10}\text{Cl}_2\text{N}_4\text{S}$  (361.26): calcd. C 53.19, H 2.79, N 15.51; found C 53.06, H 2.87, N 15.48.

**2-(3,5-Dichlorophenyl)-5-methylsulfanyl-1,2,4-triazolo[1,5-*c*]quinazoline (4l):** Yield: 1.37 g (76%), colourless needles (EtOH), m.p. 245 °C. IR (KBr):  $\tilde{\nu}$  = 2931 (w), 1620 (m), 1594 (s), 1503 (s), 1432 (m), 1397 (s), 1365 (m), 1357 (m), 1301 (m), 1078 (m), 966 (m), 801 (m)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  ( $\lg\epsilon$ ) = 222.20 (4.59), 235.08 (4.59), 259.56 (4.70), 311.75 (3.73), 326.65 (3.48) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 2.85 (s, 3 H,  $\text{SCH}_3$ ), 7.47–8.53 (m, 7 H, ArH) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 13.5, 115.8, 123.8, 126.0, 127.2, 127.4, 130.3, 132.3, 133.1, 135.5, 143.6, 149.7, 151.3, 161.8 ppm. MS:  $m/z$  = 361 (30) [ $\text{M}^+$ ], 360 (90), 315 (21), 313 (22), 189 (100), 188 (37), 145 (27).  $\text{C}_{16}\text{H}_{10}\text{Cl}_2\text{N}_4\text{S}$  (361.26): calcd. C 53.20, H 2.79, N 15.51; found C 53.32, H 2.68, N 15.63.

**5-Methylsulfanyl-2-(4-nitrophenyl)-1,2,4-triazolo[1,5-*c*]quinazoline (4m):** Yield: 1.26 g (75%), colourless needles (EtOH), m.p. 265 °C. IR (KBr):  $\tilde{\nu}$  = 1622 (m), 1608 (m), 1590 (m), 1561 (w), 1519 (s), 1502 (s), 1476 (m), 1460 (m), 1419 (m), 1343 (s), 1308 (m), 724 (s)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  ( $\lg\epsilon$ ) = 242.82 (4.59), 252.90 (4.49), 295.92 (4.48) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 2.86 (s, 3 H,

$\text{SCH}_3$ ), 7.67–8.59 (m, 8 H, ArH) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 13.5, 25.4, 115.8, 123.9, 124.0, 127.3, 127.5, 128.5, 132.4, 136.2, 143.6, 149.1, 149.7, 151.4, 162.0 ppm. MS:  $m/z$  = 337 (100) [ $\text{M}^+$ ], 336 (14), 290 (12), 189 (37), 188 (21), 145 (15).  $\text{C}_{16}\text{H}_{11}\text{O}_2\text{N}_5\text{S}$  (337.36): calcd. C 56.97, H 3.29, N 20.76; found C 56.68, H 3.03, N 20.47.

**5-Methylsulfanyl-2-(2-pyridyl)-1,2,4-triazolo[1,5-*c*]quinazoline (4n):** Yield: 1.22 g (83%), colourless rods (EtOH), m.p. 226 °C. IR (KBr):  $\tilde{\nu}$  = 1620 (m), 1592 (s), 1499 (s), 1475 (m), 1461 (m), 1420 (s), 1365 (s), 1309 (m), 1275 (m), 1158 (m), 1075 (m), 964 (s)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  ( $\lg\epsilon$ ) = 239.50 (4.60), 249.33 (4.60), 275.17 (4.43), 325.94 (3.64) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 2.85 (s, 3 H,  $\text{SCH}_3$ ), 7.41–8.88 (m, 8 H, ArH, pyridyl) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 13.5, 116.1, 123.2, 124.2, 124.9, 127.2, 128.8, 130.1, 132.2, 136.9, 143.6, 149.0, 150.3, 151.4, 163.4 ppm. MS:  $m/z$  = 293 (100) [ $\text{M}^+$ ], 260 (50), 218 (10), 189 (12), 145 (17), 143 (14), 105 (28).  $\text{C}_{15}\text{H}_{11}\text{N}_5\text{S}$  (293.35): calcd. C 61.42, H 3.78, N 23.87; found C 61.63, H 3.64, N 23.93.

**5-Methylsulfanyl-2-(3-pyridyl)-1,2,4-triazolo[1,5-*c*]quinazoline (4o):** Yield: 1.08 g (74%), colourless needles (EtOH), m.p. 209 °C. IR (KBr):  $\tilde{\nu}$  = 1620 (m), 1589 (s), 1573 (s), 1561 (s), 1498 (s), 1475 (m), 1443 (m), 1363 (s), 1294 (m), 1139 (m), 1174 (m), 769 (s)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  ( $\lg\epsilon$ ) = 255.08 (4.66), 311.42 (3.71), 326.16 (3.55) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 2.83 (s, 3 H,  $\text{SCH}_3$ ), 7.44–9.59 (m, 8 H, ArH, pyridyl) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 13.4, 115.8, 123.5, 123.9, 126.3, 127.1, 127.4, 132.2, 134.9, 143.5, 149.0, 149.7, 151.2, 151.3, 161.9 ppm. MS:  $m/z$  = 293 (100) [ $\text{M}^+$ ], 292 (18), 260 (17), 246 (21), 189 (835), 188 (18), 145 (18).  $\text{C}_{15}\text{H}_{11}\text{N}_5\text{S}$  (293.35): calcd. C 61.42, H 3.78, N 23.87; found C 61.63, H 3.79, N 23.94.

**5-Methylsulfanyl-2-(4-pyridyl)-1,2,4-triazolo[1,5-*c*]quinazoline (4p):** Yield: 1.16 g (79%), colourless rods (EtOH), m.p. 69 °C. IR (KBr):  $\tilde{\nu}$  = 1620 (s), 1606 (m), 1593 (s), 1519 (m), 1497 (s), 1476 (s), 1448 (m), 1418 (m), 1366 (s), 1355 (m), 1293 (m), 996 (s)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  ( $\lg\epsilon$ ) = 234.95 (4.53), 244.37 (4.52), 252.99 (4.54), 258.44 (4.55), 311.64 (3.71), 326.48 (3.52) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 2.83 (s, 3 H,  $\text{SCH}_3$ ), 7.63–8.80 (m, 8 H, ArH, pyridyl) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 13.4, 115.8, 121.6, 123.8, 127.2, 127.4, 132.3, 137.6, 143.5, 149.7, 150.5, 151.3, 161.9 ppm. MS:  $m/z$  = 293 (100) [ $\text{M}^+$ ], 292 (19), 246 (13), 189 (42), 188 (21), 145 (22).  $\text{C}_{15}\text{H}_{11}\text{N}_5\text{S}$  (293.35): calcd. C 61.42, H 3.78, N 23.87; found C 61.27, H 3.83, N 23.69.

**2-(2-Furyl)-5-methylsulfanyl-1,2,4-triazolo[1,5-*c*]quinazoline (4q):** Yield: 1.16 g (82%), colourless needles (EtOH), m.p. 194 °C. IR (KBr):  $\tilde{\nu}$  = 1616 (s), 1589 (s), 1556 (m), 1510 (s), 1499 (s), 1474 (m), 1429 (s), 1362 (s), 1306 (s), 1078 (s), 964 (s), 753 (s)  $\text{cm}^{-1}$ . UV (DMF):  $\lambda_{\text{max}}$  ( $\lg\epsilon$ ) = 277.99 (4.63), 327.33 (3.39) nm.  $^1\text{H}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 300 MHz):  $\delta$  = 2.81 (s, 3 H,  $\text{SCH}_3$ ), 6.77–8.45 (m, 7 H, ArH, furfuryl) ppm.  $^{13}\text{C}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 75 MHz):  $\delta$  = 13.3, 112.7, 113.3, 115.5, 123.8, 127.4, 127.9, 133.1, 143.3, 145.1, 145.9, 149.9, 150.8, 156.1 ppm. MS:  $m/z$  = 282 ( $\text{M}^+$ , 100), 265 (51), 254 (11), 253 (18), 236 (9), 160 (9), 102 (11).  $\text{C}_{14}\text{H}_{10}\text{N}_4\text{O}_2\text{S}$  (282.32): calcd. C 59.56, H 3.57, N 19.85; found C 59.86, H 3.57, N 19.67.

**General Procedures for the Preparation of the 1,2,4-Triazolo[1,5-*c*]quinazolines (5a–5k)**

**Method A:** Compounds **4b**, **4g**, or **4p** (10 mmol) were dissolved at 70 °C in the respective secondary amine (12–14 mL) and the solution was refluxed for 16 hours. After cooling to room temperature, the precipitated product was filtered and washed with methanol.

**Method B:** Compounds **3b**, **3c**, **3g**, or **3p** (10 mmol) were dissolved in the respective secondary amine (8 mL) at 80 °C. To the solution was added hydrogen peroxide (30%, 5 mL). After cooling the precipitate was filtered, washed with water and recrystallized from methanol or ethanol.

**2-Methyl-5-morpholino-1,2,4-triazolo[1,5-*c*]quinazoline (5a):** Yield A: 2.32 g (86%), B: 2.29 g (85%), colourless prisms (MeOH), m.p. 126–127 °C. IR (KBr):  $\tilde{\nu}$  = 3021 (w), 2958 (m), 2856 (m), 1621 (s), 1602 (s), 1562 (s), 1526 (s), 1503 (m), 1474 (m), 1465 (m), 1446 (s), 1309 (m), 1253 (s), 1200 (s), 1177 (s)  $\text{cm}^{-1}$ . UV (EtOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 221.43 (4.42), 245.42 (4.59), 276.74 (4.15), 285.16 (4.16), 324.74 (3.62) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 2.64 (s, 3 H,  $\text{CH}_3$ ), 3.92–3.96 (m, 4 H,  $\text{N-CH}_2$ ), 4.01–4.05 (m, 4 H,  $\text{OCH}_2$ ), 7.41–8.33 (m, 4 H, ArH) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 14.5, 48.2, 66.6, 114.7, 123.4, 124.9, 126.2, 131.9, 143.7, 144.7, 153.8, 162.6 ppm. MS:  $m/z$  = 269 (100) [ $\text{M}^+$ ], 268 (46), 239 (22), 238 (30), 224 (54), 212 (61), 199 (23), 185 (25).  $\text{C}_{14}\text{H}_{15}\text{N}_5\text{O}$  (269.31): calcd. C 62.44, H 5.61, N 26.01; found C 62.51, H 5.65, N 26.28.

**5-Morpholino-2-phenyl-1,2,4-triazolo[1,5-*c*]quinazoline (5b):** Yield A: 2.45 g (74%), B: 2.42 g (73%), colourless prisms (EtOH), m.p. 182 °C. IR (KBr):  $\tilde{\nu}$  = 3060 (w), 2959 (w), 2901 (w), 2860 (m), 1625 (s), 1604 (s), 1528 (s), 1443 (s), 1399 (s), 1377 (m), 1333 (m), 1202 (s), 1119 (s), 1002 (s)  $\text{cm}^{-1}$ . UV (EtOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 252.78 (4.68), 326.27 (3.56) nm.  $^1\text{H}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 300 MHz):  $\delta$  = 3.86–3.89 (t, 4 H,  $\text{N-CH}_2$ ), 4.04–4.07 (t, 4 H,  $\text{O-CH}_2$ ), 7.54–8.38 (m, 9 H, Ar-H) ppm.  $^{13}\text{C}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 75 MHz):  $\delta$  = 47.9, 65.7, 114.3, 123.3, 124.8, 125.9, 126.9, 128.9, 129.7, 130.5, 132.3, 143.3, 144.6, 153.6, 161.7, 178.0 ppm. MS:  $m/z$  = 331 (100) [ $\text{M}^+$ ], 330 (44), 301 (20), 300 (24), 288 (19), 286 (36), 274 (42), 245 (52).  $\text{C}_{19}\text{H}_{17}\text{N}_5\text{O}$  (331.38): calcd. C 68.87, H 5.17, N 21.13; found C 69.15, H 5.42, N 21.18.

**5-Morpholino-2-(4-pyridyl)-1,2,4-triazolo[1,5-*c*]quinazoline (5c):** Yield A: 3.0 g (90%), B: 1.13 g (34%), colourless prisms (EtOH), m.p. 217 °C. IR (KBr):  $\tilde{\nu}$  = 2966 (w), 2912 (w), 2859 (w), 1625 (s), 1605 (s), 1567 (m), 1527 (s), 1448 (m), 1416 (m), 1371 (m), 1262 (m), 1202 (m), 1119 (s), 1003 (m)  $\text{cm}^{-1}$ . UV (EtOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 245.01 (4.69), 330.00 (3.66) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 3.97–4.00 (t, 4 H,  $\text{N-CH}_2$ ), 4.10–4.13 (m, 4 H,  $\text{O-CH}_2$ ), 7.48–8.80 (m, 8 H, ArH, pyridyl) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 48.4, 66.6, 114.9, 121.4, 123.8, 125.2, 126.4, 132.4, 137.8, 144.6, 150.5, 154.6, 160.9, 182.3 ppm. MS:  $m/z$  = 332 (100) [ $\text{M}^+$ ], 331 (31), 301 (17), 288 (33), 275 (45), 247 (20), 246 (17).  $\text{C}_{18}\text{H}_{16}\text{N}_6\text{O}$  (332.37): calcd. C 65.05, H 4.85, N 25.29; found C 65.19, H 5.06, N 25.17.

**5-Morpholino-2-pentadecanyl-1,2,4-triazolo[1,5-*c*]quinazoline (5d):** Yield A: 4.20 g (90%), B: 4.47 g (96%), colourless prisms (EtOH), m.p. 85 °C. IR (KBr):  $\tilde{\nu}$  = 3228 (w), 2953 (m), 2922 (s), 2850 (s), 1627 (m), 1604 (s), 1566 (m), 1530 (s), 1466 (m), 1404 (m), 1378 (m), 1335 (m)  $\text{cm}^{-1}$ . UV (*i*PrOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 223.37 (4.45), 245.14 (4.54), 277.18 (4.12), 324.09 (3.59) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 0.85–0.90 (t, 3 H,  $\text{CH}_3$ ), 1.21–1.91 (m, 26 H,  $\text{CH}_2$ ), 2.92–2.97 (t, 2 H,  $\text{CH}_2$ ), 3.93–3.96 (m, 4 H,  $\text{N-CH}_2$ ), 4.05–4.08 (m, 4 H,  $\text{CH}_2$ ), 7.40–8.38 (m, 4 H, ArH) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 14.1, 22.7, 28.3, 28.9, 29.4, 29.5, 29.6, 29.7, 29.7, 31.9, 48.2, 66.6, 112.5, 114.9, 123.6, 124.9, 125.2, 125.9, 126.3, 131.9, 135.7, 143.7, 144.9, 153.8, 166.5 ppm. MS:  $m/z$  = 465 (100) [ $\text{M}^+$ ], 424 (14), 408 (19), 338 (11), 324 (17), 282 (42), 269 (86).  $\text{C}_{28}\text{H}_{43}\text{N}_5\text{O}$  (465.66): calcd. C 72.22, H 9.31, N 15.04; found C 71.90, H 8.98, N 14.91.

**2-Methyl-5-piperidino-1,2,4-triazolo[1,5-*c*]quinazoline (5e):** Yield A: 2.46 g (92%), B: 2.35 g (88%), colourless rods (MeOH), m.p. 130

°C. IR (KBr):  $\tilde{\nu}$  = 3035 (w), 2937 (m), 2929 (m), 2853 (m), 1620 (s), 1600 (s), 1563 (s), 1524 (s), 1502 (m), 1473 (m), 1463 (s), 1410 (m), 1382 (s), 1302 (s), 1237 (s)  $\text{cm}^{-1}$ . UV (EtOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 222.17 (4.44), 246.41 (4.58), 253.29 (4.53), 287.57 (4.21), 326.10 (3.57) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 1.70–1.84 (m, 6 H,  $\text{CH}_2$ ), 2.65 (s, 3 H,  $\text{CH}_3$ ), 3.92–3.96 (t, 4 H,  $\text{N-CH}_2$ ), 7.36–8.33 (m, 4 H, ArH) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 14.6, 24.7, 25.6, 49.1, 114.6, 123.4, 124.4, 126.1, 131.8, 144.1, 145.4, 153.9, 162.4 ppm. MS:  $m/z$  = 267 (100) [ $\text{M}^+$ ], 266 (32), 252 (17), 238 (24), 226 (34), 225 (10), 799 (18), 198 (21).  $\text{C}_{15}\text{H}_{17}\text{N}_5$  (267.33): calcd. C 67.39, H 6.41, N 26.20; found C 67.45, H 6.52, N 26.31.

**2-Phenyl-5-piperidino-1,2,4-triazolo[1,5-*c*]quinazoline (5f):** Yield A: 2.83 g (86%), B: 2.73 g (83%), colourless needles (EtOH), m.p. 129.5 °C. IR (KBr):  $\tilde{\nu}$  = 2935 (m), 2849 (m), 1625 (s), 1583 (m), 1564 (s), 1530 (s), 1484 (m), 1463 (m), 1444 (s), 1407 (m), 1381 (m), 1329 (m), 1303 (m), 1230 (m), 1194 (m)  $\text{cm}^{-1}$ . UV (EtOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 254.15 (4.70) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 1.77–1.87 (m, 6 H,  $\text{CH}_2$ ), 4.02–4.05 (t, 4 H,  $\text{NH}_2$ ), 7.41–8.43 (m, 9 H, ArH) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 2.47, 25.7, 49.2, 114.9, 123.8, 124.3, 126.1, 127.5, 128.7, 130.2, 130.5, 131.9, 144.2, 145.5, 154.3, 162.8 ppm. MS:  $m/z$  = 329 (100) [ $\text{M}^+$ ], 300 (14), 273 (16), 247 (15), 245 (25), 226 (36), 118 (24).  $\text{C}_{20}\text{H}_{19}\text{N}_5$  (329.39): calcd. C 72.92, H 5.82, N 21.26; found C 73.20, H 6.29, N 21.23.

**5-Piperidino-2-(4-pyridyl)-1,2,4-triazolo[1,5-*c*]quinazoline (5g):** Yield A: 2.41 g (73%), B: 2.21 g (67%), colourless prisms (EtOH), m.p. 163–164 °C. IR (KBr):  $\tilde{\nu}$  = 2975 (m), 2945 (m), 2873 (m), 1623 (s), 1605 (s), 1567 (s), 1538 (s), 1510 (m), 1502 (m), 1479 (s), 1456 (m), 1430 (s), 1343 (s), 1268 (m)  $\text{cm}^{-1}$ . UV (EtOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 219.93 (4.42), 245.60 (4.64), 253.07 (4.64), 279.51 (4.28), 288.19 (4.33), 333.61 (3.72) nm.  $^1\text{H}$  NMR ( $[\text{D}_6]\text{DMSO}$ , 300 MHz):  $\delta$  = 1.25–2.34 (m, 6 H,  $\text{CH}_2$ ), 4.00–4.03 (t, 4 H,  $\text{N-CH}_2$ ), 7.42–8.79 (m, 8 H, ArH, pyridyl) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 24.7, 25.7, 49.2, 114.7, 121.4, 123.7, 124.6, 126.2, 132.2, 140.0, 144.2, 145.2, 150.4, 154.6, 160.6 ppm. MS:  $m/z$  = 330 (100) [ $\text{M}^+$ ], 329 (34), 301 (19), 274 (12), 248 (19), 226 (28), 118 (24).  $\text{C}_{19}\text{H}_{18}\text{N}_6$  (330.38): calcd. C 69.07, H 5.49, N 25.44; found C 68.57, H 6.01, N 25.82.

**2-Pentadecanyl-5-piperidino-1,2,4-triazolo[1,5-*c*]quinazoline (5h):** Yield A: 4.50 g (97%), B: 4.41 g (95%), colourless rods (EtOH), m.p. 68 °C. IR (KBr):  $\tilde{\nu}$  = 2918 (s), 2850 (s), 1622 (m), 1600 (s), 1566 (s), 1529 (s), 1467 (m), 1415 (m), 1385 (m), 1337 (m), 1304 (m), 1234 (m), 1134 (m)  $\text{cm}^{-1}$ . UV (EtOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 246.63 (4.55), 252.93 (4.50), 287.77 (4.16), 325.92 (3.46) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 0.85–0.90 (t, 3 H,  $\text{CH}_3$ ), 1.20–1.89 (m, 32 H,  $\text{CH}_2$ ), 2.92–2.97 (t, 2 H,  $\text{CH}_2$ ), 3.94–3.98 (t, 4 H,  $\text{N-CH}_2$ ), 7.38–8.35 (m, 4 H, ArH) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 14.1, 22.7, 24.7, 25.4, 25.6, 27.4, 28.3, 28.9, 29.3, 29.4, 29.5, 29.6, 29.7, 31.9, 49.1, 114.7, 123.5, 124.2, 126.1, 131.7, 144.1, 145.5, 153.8, 166.2 ppm. MS:  $m/z$  = 463 (100) [ $\text{M}^+$ ], 322 (11), 280 (24), 267 (46), 266 (16).  $\text{C}_{29}\text{H}_{45}\text{N}_6$  (463.69): calcd. C 75.11, H 9.78, N 15.11; found C 75.14, H 9.42, N 14.89.

**2-Methyl-5-pyrrolidino-1,2,4-triazolo[1,5-*c*]quinazoline (5i):** Yield A: 2.25 g (89%), B: 2.18 g (86%), colourless prisms (MeOH), m.p. 166–167 °C. IR (KBr):  $\tilde{\nu}$  = 2965 (m), 2952 (m), 2870 (m), 1626 (s), 1605 (s), 1568 (s), 1538 (s), 1504 (m), 1476 (s), 1459 (s), 1441 (m), 1420 (m), 1342 (s), 1315 (m), 1297 (m)  $\text{cm}^{-1}$ . UV (EtOH):  $\lambda_{\text{max}}$  (lg $\epsilon$ ) = 218.78 (4.40), 245.55 (4.60), 253.04 (4.60), 279.29 (4.23), 287.90 (4.28), 333.44 (3.65) nm.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 1.98–2.03 (m, 4 H,  $\text{CH}_2$ ), 2.58 (s, 3 H,  $\text{CH}_3$ ), 4.04–4.09 (m, 4 H,  $\text{N-CH}_2$ ), 7.23–8.24 (m, 4 H, ArH) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  = 14.5, 25.5, 50.1, 113.6, 123.0, 123.4,

125.3, 131.8, 143.5, 145.2, 153.8, 162.0 ppm. MS:  $m/z$  = 253 (100) [ $M^+$ ], 252 (27), 238 (18), 225 (60), 224 (34), 184 (56).  $C_{14}H_{15}N_5$  (253.31): calcd. C 66.38, H 5.97, N 27.65; found C 66.51, H 6.01, N 27.53.

**2-Phenyl-5-pyrrolidino-1,2,4-triazolo[1,5-c]quinazoline (5j):** Yield A: 3.00 g (95%), B: 3.06 g (97%), colourless prisms (EtOH), m.p. 182 °C. IR (KBr):  $\tilde{\nu}$  = 3062 (w), 3041 (s), 2969 (w), 2954 (w), 2874 (w), 1624 (s), 1606 (s), 1563 (s), 1530 (s), 1445 (s), 1359 (m), 1295 (m), 1217 (m), 1252 (m), 1070 (s)  $cm^{-1}$ . UV (iPrOH):  $\lambda_{max}$  (lg $\epsilon$ ) = 203.58 (4.49), 254.66 (4.71), 333.05 (3.71) nm.  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  = 1.98–2.03 (m, 4 H,  $CH_2$ ), 4.08–4.13 (t, 4 H, N- $CH_2$ ), 7.29–8.34 (m, 9 H, ArH) ppm.  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz):  $\delta$  = 25.5, 50.1, 113.8, 122.9, 123.7, 125.3, 127.3, 128.6, 130.0, 130.6, 131.8, 143.5, 145.3, 154.1, 162.5 ppm. MS:  $m/z$  = 315 (100) [ $M^+$ ], 314 (37), 287 (49), 286 (20), 260 (24), 245 (27), 184 (31).  $C_{19}H_{17}N_5$  (315.37): calcd. C 72.36, H 5.43, N 22.21; found C 72.31, H 5.83, N 22.21.

**2-(4-Pyridyl)-5-pyrrolidino-1,2,4-triazolo[1,5-c]quinazoline (5k):** Yield A: 3.10 g (98%), B: 2.91 g (92%), colourless prisms (EtOH), m.p. 233 °C. IR (KBr):  $\tilde{\nu}$  = 2969 (m), 2878 (m), 1623 (s), 1567 (s), 1533 (s), 1481 (s), 1456 (s), 1410 (m), 1343 (m), 1294 (m), 1109 (m), 1011 (w)  $cm^{-1}$ . UV (EtOH):  $\lambda_{max}$  (lg $\epsilon$ ) = 249.08 (4.70), 333.38 (3.73) nm.  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  = 2.01–2.16 (m, 4 H,  $CH_2$ ), 4.11–4.15 (m, 4 H, 2N- $CH_2$ ), 7.27–8.77 (m, 8 H, ArH, pyridyl) ppm.  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz):  $\delta$  = 25.5, 50.0, 113.7, 121.3, 123.2, 123.7, 125.4, 132.2, 138.1, 143.3, 145.3, 150.4, 154.4, 160.4 ppm. MS:  $m/z$  = 316 (100) [ $M^+$ ], 315 (26), 288 (43), 287 (23), 261 (18), 247 (14), 184 (17).  $C_{18}H_{16}N_6$  (316.36): calcd. C 68.33, H 5.10, N 26.57; found C 68.11, H 5.30, N 26.65.

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