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Synthesis of 5-thioxo-6*H*-imidazo[1,2-*c*]quinazolines and related compounds based on cyclocondensations of 2-isothiocyanatobenzonitrile (ITCB) with α-aminoketones

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Abstract—Pharmacologically relevant 5-thioxo-6*H*-imidazo[1,2-*c*]quinazolines and 5-oxo-6*H*-imidazo[1,2-*c*]quinazolines were prepared by sequential reactions of α-aminoketones with 2-isothiocyanatobenzonitrile (ITCB) and 2-isocyanatobenzonitrile (ICB), respectively. The functionalization of the thioxo moiety allowed the synthesis of 5-amino-6*H*-imidazo[1,2-*c*]quinazolines and of 1,2,4-triazolo[4,3-*a*]-imidazo[1,2-*c*]quinazolines.

1. Introduction

Isocyanates and isothiocyanates represent versatile 'relais species' in one-pot reactions. Carbanionic one-pot cyclizations of isocyanates and isothiocyanates with a nucleophile and an electrophile generally proceed as follows: the attack of the nucleophile onto the carbon atom of the cumulene gives rise to the formation of an ambident allyl-type anion. Subsequently, the nitrogen or the sulfur atom of the intermediate anion undergoes a nucleophilic attack onto the electrophile. A number of synthetically useful examples of this process have been reported in recent years.[1–9] 2-Isothiocyanatobenzonitrile (ITCB) and isocyanatobenzonitrile (ICB) represent versatile difunctional building blocks containing a nitrile and an isothiocyanate or an isocyanate function, respectively. 2-Isocyanatobenzonitrile can be prepared by reaction of 2-aminobenzonitrile with phosgene[10] or diphosgene[11] or by reaction of the oxime of isatine with thionyl chloride.[12] 2-Isothiocyanatobenzonitrile is available by reaction of 2-aminobenzonitrile with thiophosgene[13] and also by other methods.[14–16] The reaction of ITCB with butan-1-ol,[17] anilines[18] and acetamidines[19] was reported to give open-chained products. Zanardi et al. reported the manganese(III)acetate mediated oxidative dimerization[18] of ITCB and radical-type cyclizations.[1] The cyclization of ITCB with amines[20] and hydrazine[21] was reported to give 4-imino-1,2,3,4-tetrahydroquinazoline-2-thiones. We reported the synthesis of 4-alkylidene-3,4-dihydroquinazoline-2(1*H*)thiones by cyclization of ITCB with arylacetonitriles.[22] In addition, convenient syntheses of tricylic 1,2,3,4-tetrahydroquinazoline derivatives based on one-pot domino cyclizations of ITCB with carboxylic hydrazides[23] and α-aminoesters were developed.[24]

Recently, we reported the synthesis of 5-thioxo-6*H*-imidazo[1,2-*c*]quinazolines by one-pot cyclization of ITCB with α-aminoketones.[25] Herein, we report full details of these studies. With regard to our preliminary communication,[25] we extended the preparative scope and also studied the functionalization of the products based on reactions of the thioxo group. For example, tetracyclic 1,2,4-triazolo[4,3-*a*]-imidazo[1,2-*c*]quinazolines were prepared for the first time. The transformations reported herein provide a convenient access to a variety of 5-thioxo-6*H*-imidazo[1,2-*c*]quinazolines. It is noteworthy that related 1,2,4-triazolo[1,5-*c*]quinazolines possess interesting biological activity (antihypertonic, antirheumatic, antianaphylactic, antiasthmatic, tranquilizing, neuro-stimulating and benzodiazepine binding activity).[10,11,26–28] Benzimidazo[2,1-*b*]quinazoline-12(5*H*)-ones are potent immunosuppressors.[29]

Keywords: Cyclizations; *N*-Heterocycles; Isocyanates; Isothiocyanates; Sequential reactions.
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2. Results and discussion

2.1. Mechanism and optimization

During the optimization of the cyclization of α-aminoacetophenone hydrochloride (**2a**) with ITCB (**1**) the choice of the base proved to be an important parameter. The use of NEt_3 or piperidine (in CH_2Cl_2 or EtOH) resulted in the formation of complex mixtures. In contrast, employment of a two-phase system ($Na_2CO_3/H_2O/CH_2Cl_2$, 10 min, 20 °C) resulted in the clean formation of the open-chained condensation product **A** (90% yield). However, extension of the reaction time did not result in cyclization. In contrast, reflux of **A** for 10 min cleanly afforded quinazoline **B** (88%). The second cyclization could again not be realized by extension of the reaction time. A change of the solvent was mandatory: reflux of an EtOH solution of **B** for 8 h resulted in formation of 5-thioxo-6*H*-imidazo[1,2-*c*]quinazoline **3a** in 85% yield. Based on the optimization outlined above, we developed a sequential reaction of **1** with **2a**, which afforded **3a** in 73% yield. It is noteworthy that the crude quinazoline **B** had to be isolated during this process. A *one-pot* procedure (with addition of EtOH during the reaction but without isolation of **B**) was successfully applied to the synthesis of product **3d** (vide infra, Table 1). However, the yield decreased (31%) compared to the overall yield of the corresponding two-step procedure (80%).

The formation of **3a** can be explained by attack of the amino group onto the isothiocyanate (intermediate **A**), attack of the amino group onto the nitrile (intermediate **B**) and subsequent attack of the imino nitrogen onto the carbonyl group (Scheme 1). The formation of *iso*-**3a** is theoretically possible. Its formation may proceed by attack of the amino group onto the isothiocyanate, attack of the sulfur atom onto the nitrile (intermediate **C**), Dimroth rearrangement (intermediate **D**) and subsequent attack of the amino group onto the ketone. Products **3a** and *iso*-**3a** can theoretically undergo a Dimroth rearrangement to give products *Dimroth*-**3a** and *Dimroth-iso*-**3a** (Fig. 1). However, based on extensive structural investigations (vide infra), we believe that product **3a** is selectively formed in the reaction.

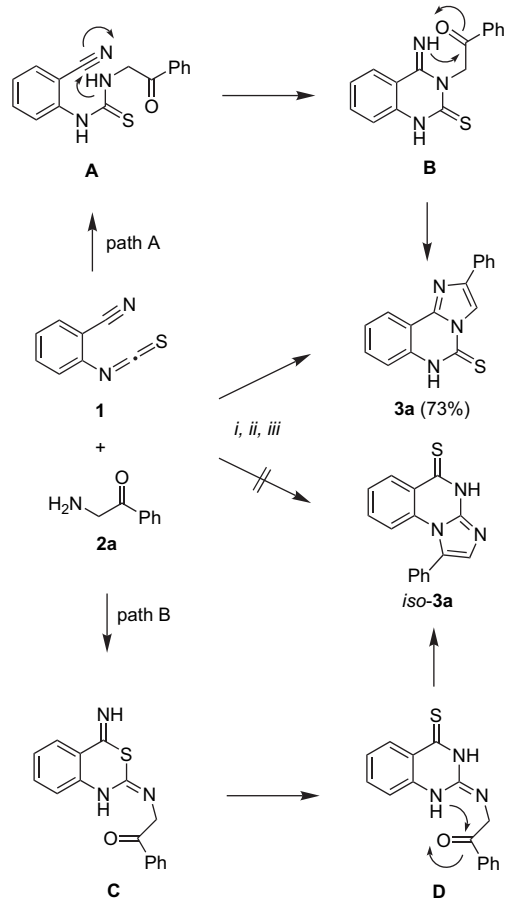
2.2. Preparative scope

The reaction of **1** with a variety of functionalized α-aminoacetophenones afforded the methyl-, methoxy-, bromo-, chloro-, fluoro- and nitro-substituted imidazo[1,2-*c*]quinazolines **3b–3g** (Scheme 2, Table 1). Quinazoline **3h** was

Table 1. Products and yields of **3a–k**

2	3	R^1	R^2	%[a]
a	**a**	Ph	H	73
b	**b**	4-MeC_6H_4	H	96
c	**c**	4-$(MeO)C_6H_4$	H	67
d	**d**	4-BrC_6H_4	H	80
e	**e**	4-ClC_6H_4	H	91
f	**f**	4-FC_6H_4	H	78
g	**g**	4-$(NO_2)C_6H_4$	H	34
h	**h**	2-Naphthyl	H	76
i	**i**	Me	H	37
j	**j**	*t*-Bu	H	53
k	**k**	Ph	Ph	79

[a] Isolated yields.



Scheme 1. Possible mechanistic pathways of the cyclization of ITCB (**1**) with phenacyl bromide: (i) Na_2CO_3, H_2O, CH_2Cl_2, 20 °C, 10 min; (ii) reflux, 20 min, isolation of crude intermediate **B**; (iii) *i*-PrOH, reflux, 10 h.

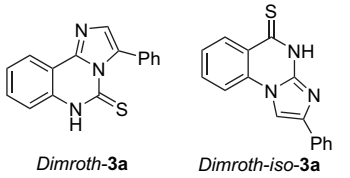
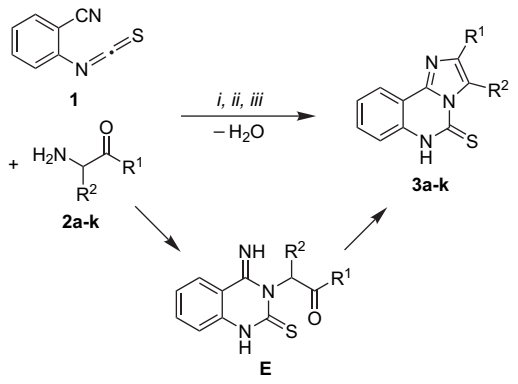


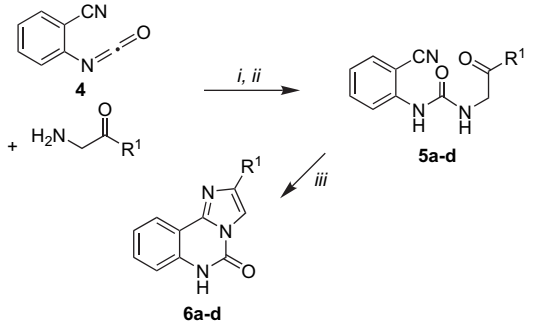
Figure 1. Structures of Dimroth-**3a** and Dimroth-*iso*-**3a**.



Scheme 2. Synthesis of 6*H*-imidazo[1,2-*c*]quinazolines **3a–3k**: (i) Na_2CO_3, H_2O, CH_2Cl_2, 20 °C, 10 min; (ii) reflux, 10 min, isolation of **E** and direct use for the next step; (iii) EtOH, reflux, 8–24 h.

prepared from 2-(α-aminoacetyl)naphthalene. The cyclization of **1** with α-aminoacetone and 1-amino-3,3-dimethylbutan-2-one afforded quinazolines **3i** and **3j**, respectively. Imidazo[1,2-*c*]quinazoline **3k** was prepared from α-amino-α-phenylacetophenone. All cyclizations proceeded with very good chemo- and regioselectivity and afforded the corresponding products in good to very good yields (except for **3g** and **3i**). The low yield of **3g** can be explained by the low nucleophilicity of the nitro-substituted α-aminoacetophenone **2g**. The low yield of **3i** can be explained by the high reactivity of aminoacetone (**2i**) which readily undergoes a dimerization under the reaction conditions employed.

The reaction of α-aminoacetophenone with isocyanatobenzonitrile (ICB, **4**)—the oxygen analogue of **1**—was previously studied by Zinner and Thom.[30] The application of the reaction conditions developed for the cyclization of aminoketones with ITCB (**1**) gave unsatisfactory results for **4**, due to hydrolysis of the isocyanate moiety. The best results were obtained when the reaction was carried out as follows: a CH_2Cl_2 solution of α-aminoacetophenone (**2a**), **4** and NEt_3 was stirred for 10 min at 20 °C and subsequently refluxed for 40 min to give **5a** in 90% isolated yield (Scheme 3). Reflux of an *i*-PrOH solution of **5a**, in the presence of NH_4OH, afforded the 5-oxo-6*H*-imidazo[1,2-*c*]quinazoline **6a** in 74% yield. The protocol was successfully applied to the cyclization of **4** with other α-aminoketones. These transformations afforded the imidazo[1,2-*c*]quinazolines **6a–6d** in good yields and with very good chemo- and regioselectivity (Table 2).



Scheme 3. Synthesis of 6*H*-imidazo[1,2-*c*]quinazolines **6a–6d**: *conditions*: (i) NEt_3, CH_2Cl_2, 20 °C, 10 min; (ii) reflux, 40 min, isolation of **A**; (iii) *i*-PrOH, NH_4OH, reflux, 8–32 h.

NOESY studies support the structure of 5-thioxo-6*H*-imidazo[1,2-*c*]quinazolines **3** based on interactions between the NH group and the neighbouring arene proton of the quinazoline moiety. The structures of **3b** and **3i** were independently confirmed by X-ray crystal structure analyses (Figs. 2 and 3).[31]

Table 2. Products and yields of **5a–d** and **6a–d**

5,**6**	R^1	% (**5**)[a]	% (**6**)[a]
a	C_6H_5	90	74
b	4-MeC_6H_4	88	78
c	4-BrC_6H_4	78	75
d	4-ClC_6H_4	75	61

[a] Isolated yields.

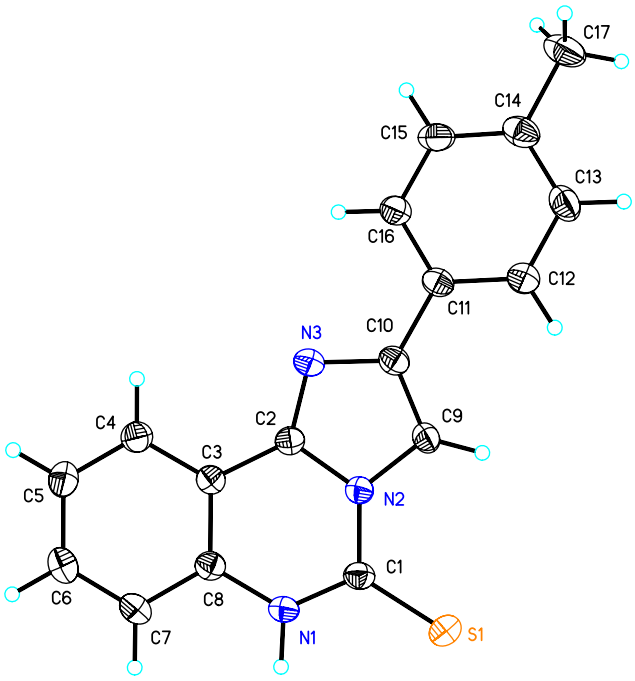


Figure 2. ORTEP plot of **3b**.

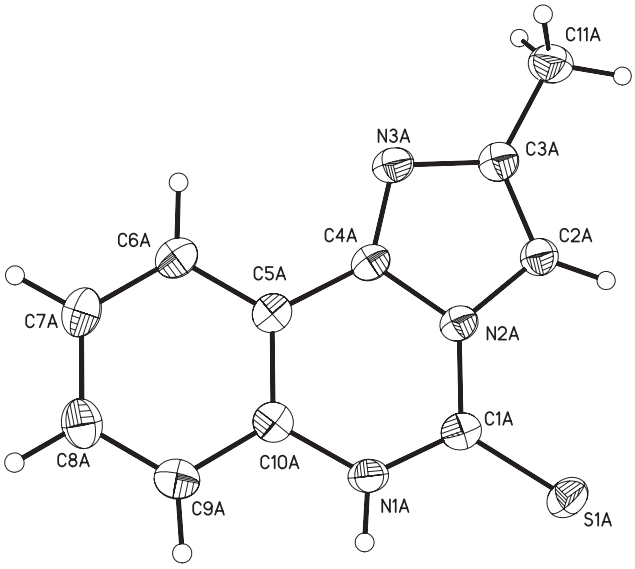
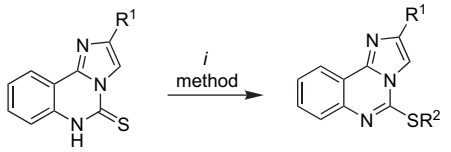


Figure 3. ORTEP plot of **3i**.

2.3. Reactions of 6*H*-imidazo[1,2-*c*]quinazolines

5-Thioxoquinazolines **3a–3k** represent versatile synthetic building blocks for further functionalizations. The NaOH or NaOMe mediated reaction of **3a**, **3d**, **3e** and **3k** with methyl iodide, allyl bromide and benzyl bromide resulted in S-alkylation and formation of imidazo[1,2-*c*]quinazolines **7a–7k** in good yields (Scheme 4, Table 3).

Detailed 2D NMR studies were carried out on **7k** and **7f**. For the CH_2 and the CH_3 groups located next to the sulfur atom a characteristic highfield shift was observed. The structure of **7k** was independently confirmed by X-ray crystal structure analysis (Fig. 4).[31]



Scheme 4. Synthesis of 6*H*-imidazo[1,2-*c*]quinazolines **7a–7k**: (i): method A: NaOH, R^3X, 60 °C; method B: NaOH, 20 °C, R^3X; method C: MeOH, NaOMe, R^3X, 2 h reflux (R^3X=MeI, H_2C=$CHCH_2Br$, BnBr).

Table 3. Synthesis of **7a–7k**

7	R^1	R^2	% (Method)[a]
a	Ph	Me	75 (A), 79 (B)
b	Ph	Allyl	76 (B), 80 (C)
c	Ph	Bn	71 (C)
d	Ph	$(CH_2)_2C_6H_5$	82 (C)
e	4-MeC_6H_4	Bn	75 (C)
f	4-BrC_6H_4	Me	74 (A), 77 (C)
g	4-BrC_6H_4	Allyl	76 (B), 81 (C)
h	4-BrC_6H_4	Bn	72 (C)
i	4-ClC_6H_4	Me	77 (C)
j	4-ClC_6H_4	Allyl	84 (B), 88 (C)
k	4-ClC_6H_4	Bn	76 (C)

[a] Yields of isolated products.

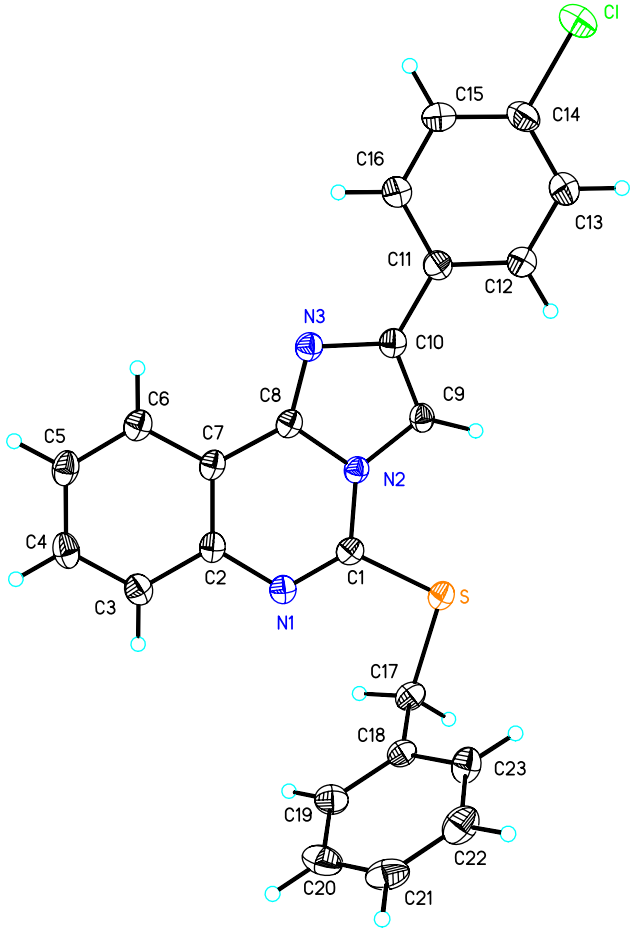
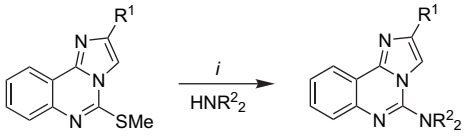


Figure 4. ORTEP plot of **7k**.

Reflux of 5-thiomethoxy-6*H*-imidazo[1,2-*c*]quinazolines **7a**, **7g** and **7j** with an excess of various secondary amines (neat) afforded the 5-amino-6*H*-imidazo[1,2-*c*]quinazolines **8a–8j** in very good yields (Scheme 5, Table 4).



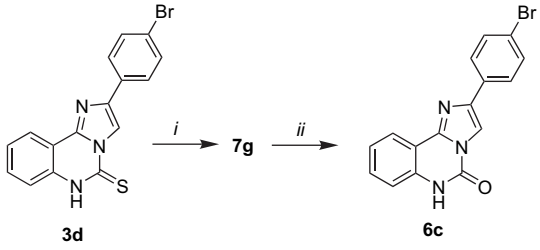
Scheme 5. Synthesis of 6*H*-imidazo[1,2-*c*]quinazolines **8a–8j**: *conditions*: (i) neat, reflux, 16 h.

Table 4. Synthesis of **8a–8j**

8	R^1	R^2	%[a]
a	Ph	$-(CH_2)_5-$	89
b	Ph	$-(CH_2)_2O(CH_2)_2-$	85
c	Ph	$-(CH_2)_4-$	83
d	4-BrC_6H_4	$-(CH_2)_5-$	79
e	4-BrC_6H_4	$-(CH_2)_2O(CH_2)_2-$	95
f	4-BrC_6H_4	$-(CH_2)_4-$	81
g	4-ClC_6H_4	$-(CH_2)_5-$	85
h	4-ClC_6H_4	$-(CH_2)_2O(CH_2)_2-$	93
i	4-ClC_6H_4	$-(CH_2)_4-$	86
j	4-ClC_6H_4	$-(CH_2)_2NMe(CH_2)_2-$	84

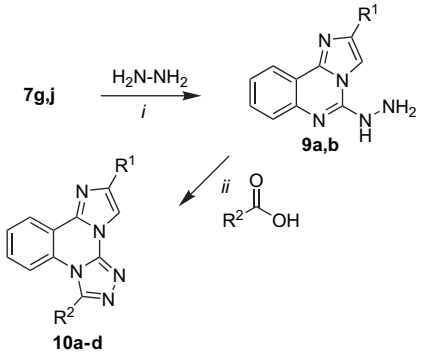
[a] Yields of isolated products.

5-Thioxo-6*H*-imidazo[1,2-*c*]quinazoline **3d** could be transformed, by oxidation of **7g**, into 5-oxo-6*H*-imidazo[1,2-*c*]quinazoline **6c** (Scheme 6). The spectroscopic data of compound **6c**, prepared from **3d**, were identical with those of the material obtained from **4** (vide supra). This experiment further supports the structure assigned for compounds **3**, **6** and **7**.



Scheme 6. Transformation of **3d** into **6c**: (i) NaOH, MeI; (ii) glacial AcOH, H_2O_2.

The reaction of 5-thiomethoxy-6*H*-imidazo[1,2-*c*]quinazolines **7g** and **7j** with hydrazine afforded the 5-hydrazino-6*H*-imidazo[1,2-*c*]quinazolines **9a** and **9b** in good yields (Scheme 7, Table 5). Reflux of **9a**, **9b** with formic or acetic



Scheme 7. Synthesis of **10a–10d**: *conditions*: (i) EtOH, reflux, 16 h; (ii) neat, reflux, 4 h.

Table 5. Synthesis of **10a–10d**

9,10	R^1	R^2	% (**9**)[a]	% (**10**)[a]
a	4-BrC_6H_4	H	79	79
b	4-ClC_6H_4	H	95	95
c	4-BrC_6H_4	Me	86	86
d	4-ClC_6H_4	Me	84	84

[a] Yields of isolated products.

acid afforded the 1,2,4-triazolo[4,3-*a*]-imidazo[1,2-*c*]quinazolines **10a–10d**. The synthesis of this heterocyclic core structure has, to the best of our knowledge, not yet been reported.

3. Conclusions

5-Thioxo-6*H*-imidazo[1,2-*c*]quinazolines and 5-oxo-6*H*-imidazo[1,2-*c*]quinazolines were prepared by sequential reactions of α-aminoketones with 2-isothiocyanatobenzonitrile (ITCB) and 2-isocyanatobenzonitrile (ICB), respectively. The functionalization of the thioxo moiety allowed the synthesis of 5-amino-6*H*-imidazo[1,2-*c*]quinazolines and of what are, to the best of our knowledge, the first 1,2,4-triazolo[4,3-*a*]-imidazo[1,2-*c*]quinazolines.

4. Experimental section

4.1. General

All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For ^1H and ^{13}C NMR, the deuterated solvents indicated were used. The ^1H NMR (300.13 MHz) and ^{13}C NMR (75.9 MHz) were recorded with a Bruker spectrometer ARX 300. In addition to the routine measurements, the ^1H NMR (500.13 MHz) and ^{13}C NMR (125.8 MHz) spectra of **7f**, **7k** were recorded on a Bruker spectrometer AVANCE 500 in $CDCl_3$ and DMSO-d_6, respectively, as solvents. Calibration of spectra was carried out on the solvent signals ($CDCl_3$: δ ^1H=7.25, δ ^{13}C=77.0; DMSO-d_6: δ ^1H=2.50, δ ^{13}C=39.7). The NMR signals were assigned by DEPT and two-dimensional ^1H,^1H COSY, ^1H,^1H NOESY and ^1H,^{13}C correlation spectra (HSQC, HMBC). Mass spectrometric data (MS) were obtained by electron ionization (70 eV), chemical ionization (CI, H_2O) or electrospray ionization (ESI). For preparative scale chromatography, silica gel (60–200 mesh) was used. Melting points are uncorrected.

4.2. Typical procedure for the synthesis of 5-thioxo-5,6-dihydro-imidazo[1,2-*c*]quinazolines (3a–3j)

To a CH_2Cl_2 suspension (40 mL) of isothiocyanatobenzonitrile (ITCB, 1.00 g, 6.4 mmol) and 4-(α-aminoacetyl)-1-fluorobenzene hydrochloride (1.21 g, 6.4 mmol) was added an aqueous solution (12 mL) of sodium carbonate (1.38 g) with stirring. The mixture was stirred for 10 min at 20 °C and for 10 min under reflux. After cooling to room temperature a colourless precipitate formed (intermediate **B**) which was filtered off. The organic and the aqueous layers of the filtrate were separated and the aqueous layer was extracted with CH_2Cl_2 (2×20 mL). The combined organic layers were concentrated at reduced pressure. The residue and the precipitate were suspended in EtOH (200 mL) and the mixture was refluxed for 12 h. The product **3f**, which crystallized upon cooling, was filtered off and dried in vacuo. The filtrate was concentrated at reduced pressure to give an additional amount of **3f** (combined yield: 1.48 g, 78%).

4.2.1. 2-Phenyl-6*H*-imidazo[1,2-*c*]quinazoline-5-thione (3a). From ITCB (1.00 g, 6.4 mmol) and α-aminothioacetophenone hydrochloride (0.95 g, 6.4 mmol), 8 h reflux. Yield: 1.30 g (73%), colourless prisms (2-propanol), mp 300–304 °C (decomp.). IR (KBr, cm^{-1}): $\tilde{\nu}$=3175, 3136, 3111, 3027, 2970, 1630 (m), 1537 (s), 1478, 1420 (m), 1357, 1302, 1190 (s), 1070, 973 (w), 774, 736, 695 (m). ^1H NMR (DMSO-d_6, 300 MHz): δ=7.34–7.71 (m, 6H, Ar), 8.08–8.12 (m, 2H, Ar), 8.29–8.32 (m, 1H, Ar), 8.66 (s, 1H, 3-H, Hetar), 13.81 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=112.6 (C-3), 113.6 (C, 10a), 116.4 (Ar-H, C-10), 123.0 (Ar-H, C-9), 125.5 (Ar-H, C-7), 125.8 (Ar-H, C-3′, C-5′), 128.3 (Ar-H, C-4′), 128.8 (Ar-H, C-2′, C-6′), 131.0 (Ar-H, C-8), 132.5 (C, C-1′), 134.5 (C, C-2), 139.9 (C, C-6a), 143.9 (C, C=N), 166.9 (C, C=S). MS (EI, 70 eV): *m*/*z* (%)=277 ([M]$^+$, 2), 261 (3), 245 (3), 127 (9), 105 (4). UV–vis (CH_3CN): λ_{max} (log ε)=213 (4.27), 225 (4.21), 259 (4.60), 285 (4.54), 323 (4.12), 340 (4.12), 354 (4.02). Anal. Calcd for $C_{16}H_{11}N_3S$ (277.35): C, 69.24; H, 4.00; N, 15.15; found: C, 69.55; H, 3.72; N, 15.12.

4.2.2. 2-Tolyl-6*H*-imidazo[1,2-*c*]quinazoline-5-thione (3b). From ITCB (1.00 g, 6.4 mmol) and α-amino-4-methylacetophenone hydrochloride (1.17 g, 6.4 mmol), 12 h reflux. Yield: 1.79 g (96%), colourless needles (2-propanol), mp 328–330 °C (decomp.). IR (KBr, cm^{-1}): $\tilde{\nu}$=3179, 3133, 3118, 3084, 3025, 2972, 1630 (m), 1536 (s), 1499 (w), 1474, 1418 (m), 1356 (s), 1324 (w), 1299 (m), 1186 (s), 772, 746 (m). ^1H NMR (DMSO-d_6, 300 MHz): δ=2.36 (s, 3H, CH_3), 7.28–7.31 (d, *J*=8.0 Hz, 2H, Ar), 7.48–7.71 (m, 3H, Ar), 7.97–8.00 (d, *J*=8.0 Hz, 2H, Ar), 8.29–8.31 (m, 1H, Ar), 8.60 (s, 1H, 3-H), 13.85 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=20.8 (CH_3), 111.9 (Ar-H, C-3), 113.5 (C, 10a), 116.3 (Ar-H, C-10), 122.9 (Ar-H, C-9), 125.4 (Ar-H, C-7), 125.6 (Ar-H, C-3′, C-5′), 129.3 (Ar-H, C-2′, C-6′), 129.6 (C, C-1′), 130.8 (Ar-H, C-8), 134.3 (C, C-2), 137.6 (C, C-4′), 139.7 (C, C-6a), 143.9 (C, C=N), 166.7 (C, C=S). MS (EI, 70 eV): *m*/*z* (%)=292 (23), 291 ([M]$^+$, 100), 290 (76), 275 (7), 103 (11). UV–vis (CH_3CN): λ_{max} (log ε)=219 (5.03), 262 (4.64), 286 (4.62), 325 (4.17), 341 (4.16), 355 (4.05). Anal. Calcd for $C_{17}H_{13}N_3S$ (291.38): C, 70.08; H, 4.50; N, 14.42; found: C, 69.80; H, 4.82; N, 14.52.

4.2.3. 2-(4-Methoxyphenyl)-6*H*-imidazo[1,2-*c*]quinazoline-5-thione (3c). From ITCB (0.50 g, 3.2 mmol) and α-amino-4-methoxyacetophenone hydrochloride (0.64 g, 3.2 mmol) and sodium carbonate (0.91 g), 16 h reflux. Yield: 0.66 g (67%), yellow prisms (2-propanol), mp 274–280 °C (decomp.). IR (KBr, cm^{-1}): $\tilde{\nu}$=3176, 3138, 3108, 3028, 2971 (w), 1628, 1615, 1537 (m), 1496 (s), 1475, 1421, 1355, 1301 (m), 1248, 1189 (s), 1172 (m), 1070 (w), 1030, 748 (m). ^1H NMR (DMSO-d_6, 300 MHz): δ=3.82 (s, 3H, CH_3), 7.02–7.05 (d, *J*=8.8 Hz, 2H, Ar), 7.46–7.66 (m, 3H, Ar), 7.99–8.03 (d, *J*=8.8 Hz, 2H, Ar), 8.27–8.30 (m, 1H, Ar), 8.53 (s, 1H, 3-H), 13.77 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=55.1 (OCH_3), 111.2 (Ar-H,

C-3), 113.4 (C, 10a), 114.1 (Ar-H, C-3′, C-5′), 116.4 (Ar-H, C-10), 122.9 (Ar-H, C-9), 125.0 (C, C-1′), 125.3 (Ar-H, C-7), 127.1 (Ar-H, C-2′, C-6′), 130.7 (Ar-H, C-8), 134.4 (C, C-2), 139.7 (C, C-6a), 143.8 (C, C=N), 159.3 (C, C-4′), 166.5 (C, C=S). MS (EI, 70 eV): *m/z* (%)=308 (18), 307 ([M]$^+$, 100), 306 (236), 293 (11), 265 (19). UV–vis (CH_3CN): λ_{max} (log ε)=267 (4.52), 289 (4.57), 300 (4.54), 327 (4.09), 342 (4.06). HRMS calcd for $C_{17}H_{13}N_3OS$ (307.37): [M]$^+$=307.0779; found: 307.0779.

4.2.4. 2-(4-Bromophenyl)-6*H*-imidazo[1,2-*c*]quinazoline-5-thione (3d). From ITCB (1.00 g, 6.4 mmol) and α-amino-4-bromoacetophenone hydrochloride (1.60 g, 6.4 mmol), 16 h reflux. Yield: 1.82 g (80%), colourless prisms (2-propanol), mp 344–346 °C (decomp.). IR (KBr, cm^{-1}): $\tilde{\nu}$=3177, 3143, 3114, 3029, 2975, 1630 (m), 1536, 1477 (s), 1418, 1404 (m), 1354 (s), 1315 (m), 1297 (s), 1266 (w), 1190 (s), 1070, 974, 833 (w), 748 (m). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=7.49–7.69 (m, 5H, Ar), 8.06–8.31 (m, 3H, Ar), 8.73 (s, 1H, 3-H), 13.82 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz, Cr(acac)$_3$): δ=113.3 (Ar-H, C-3), 113.6 (C, 10a), 116.5 (Ar-H, C-10), 121.3 (C, C-1′), 123.1 (Ar-H, C-9), 125.5 (Ar-H, C-7), 127.8 (Ar-H, C-3′, C-5′), 131.1 (Ar-H, C-8), 131.8 (Ar-H, C-2′, C-4′, C, C-6′), 134.7 (C, C-2), 140.1 (C, C-6a), 142.7 (C, C=N), 166.8 (C, C=S). MS (EI, 70 eV): *m/z* (%)=358 (25), 357 ([M]$^+$ (^{81}Br), 100), 356 (82), 355 ([M]$^+$ ^{79}Br, 97), 354 (68), 275 (25), 138 (38), 116 (21), 102 (21), 89 (47), 64 (12). UV–vis (CH_3CN): λ_{max} (log ε)=220 (4.92), 263 (4.61), 287 (4.59), 324 (4.19), 340 (4.15), 354 (4.02). Anal. Calcd for $C_{16}H_{10}BrN_3S$ (356.24): C, 53.95; H, 2.83; N, 11.80; found: C, 53.88; H, 2.98; N, 11.61.

4.2.5. 2-(4-Chlorophenyl)-6*H*-imidazo[1,2-*c*]quinazoline-5-thione (3e). From ITCB (1.00 g, 6.4 mmol) and α-amino-4-chloroacetophenone hydrochloride (1.32 g, 6.4 mmol), 24 h reflux. Yield: 1.81 g (91%), colourless prisms (2-propanol), mp 342–345 °C (decomp.). IR (KBr, cm^{-1}): $\tilde{\nu}$=3176, 3144, 3115, 3090, 3029, 2974 (m), 1632, 1537, 1481, 1476 (s), 1422, 1405 (m), 1355, 1315, 1302, 1290 (s), 1267, 1205 (w), 1190 (s), 1089, 1070, 974, 836 (m), 749 (s), 698 (w). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=7.48–7.71 (m, 5H, Ar), 8.12–8.31 (m, 3H, Ar), 8.73 (s, 1H, 3-H), 13.83 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz, Cr(acac)$_3$): δ=113.1 (Ar-H, C-3), 113.5 (C, 10a), 116.5 (Ar-H, C-10), 123.0 (Ar-H, C-9), 125.4 (Ar-H, C-7), 127.4 (Ar-H, C-3′, C-5′), 128.8 (Ar-H, C-2′, C-6′), 131.0 (Ar-H, C-8), 131.4 (Ar-H, C-4′), 132.6 (Ar-H, C-1′), 134.6 (C, C-2), 140.0 (C, C-6a), 142.6 (C, C=N), 166.8 (C, C=S). MS (EI, 70 eV): *m/z* (%)=313 ([M]$^+$ (^{37}Cl), 41), 312 (45), 311 ([M]$^+$ (^{35}Cl), 100), 310 (74), 275 (14), 138 (18), 89 (25). UV–vis (CH_3CN): λ_{max} (log ε)=220 (4.88), 262 (4.62), 286 (4.59), 324 (4.18), 340 (4.16), 354 (4.04). Anal. Calcd for $C_{16}H_{10}ClN_3S$ (311.79): C, 61.64; H, 3.23; N, 13.48; found: C, 61.92; H, 3.33; N, 13.51.

4.2.6. 2-(4-Fluorophenyl)-6*H*-imidazo[1,2-*c*]quinazoline-5-thione (3f). ITCB (1.00 g, 6.4 mmol) and α-amino-4-fluoroacetophenone hydrochloride (1.21 g, 6.4 mmol) were suspended in dichloromethane (40 mL). A solution of sodium carbonate (1.83 g in 12 mL of water) was added and the mixture was stirred for 10 min at ambient temperature and for 10 min at reflux. After cooling to room temperature a colourless precipitate formed. After filtration, the layers were separated and the aqueous layer was extracted with dichloromethane (2×20 mL). The organic layers were collected and the solvent was removed at reduced pressure. The residue and the precipitate were suspended in 2-propanol (200 mL) and the mixture was refluxed for 12 h. The product crystallized upon cooling. Concentration of the solution at reduced pressure gave a further amount of the product. Yield: 1.48 g (78%), colourless prisms (2-propanol), mp 327–332 °C (decomp.). IR (KBr, cm^{-1}): $\tilde{\nu}$=3179, 3141, 3113 (m), 3092, 3033, 2975 (m), 1634 (s), 1608 (m), 1566 (w), 1540, 1494, 1477 (s), 1467 (w), 1416, 1359, 1316 (s), 1303, 1295 (m), 1283 (w), 1230, 1219 (m), 1208 (w), 1193, 1156, 842, 747 (s). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=7.27–7.71 (m, 5H, Ar), 8.12–8.31 (m, 3H, Ar), 8.67 (s, 1H, 3-H), 13.82 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=112.6 (Ar-H, C-3), 113.5 (C, 10a), 115.7 (Ar-H, d, $J_{C,F}$=21 Hz, C-3′, C-5′), 116.4 (Ar-H, C-10), 123.1 (Ar-H, C-9), 125.5 (Ar-H, C-7), 127.8 (Ar-H, 2d, $J_{C,F}$=8 Hz, C-2′, C-6′), 129.0 (C, d, $J_{C,F}$=3 Hz, C-1′), 131.0 (Ar-H, C-8), 134.5 (C, C-2), 139.9 (C, C-6a), 142.9 (C, C=N), 162.1 (C, d, $J_{C,F}$=245 Hz, C-4′), 166.8 (C, C=S). MS (EI, 70 eV): *m/z* (%)=296 ([M+H]$^+$, 22), 295 (M$^+$, 100), 294 (83), 262 ([M−HS]$^+$, 3), 108 (17), 107 (16). UV–vis (CH_3CN): λ_{max} (log ε)= 220 (4.18), 259 (4.60), 283 (4.52), 323 (4.09), 340 (4.09), 354 (3.99). Anal. Calcd for $C_{16}H_{10}FN_3S$ (295.34): C, 65.07; H, 3.41; N, 14.23; found: C, 65.19; H, 3.54; N, 14.14.

4.2.7. 2-(4-Nitrophenyl)-6*H*-imidazo[1,2-*c*]quinazoline-5-thione (3g). From ITCB (1.00 g, 6.4 mmol) and α-amino-4-nitroacetophenone hydrochloride (1.39 g, 6.4 mmol), 24 h reflux. Yield: 0.70 g (34%), yellow prisms (2-propanol), mp 349–352 °C (decomp.). IR (KBr, cm^{-1}): $\tilde{\nu}$=3176, 3141, 3111, 3087, 3025, 2972, 1630, 1601 (m), 1534, 1514 (s), 1476, 1412 (m), 1336 (s), 1306, 1280 (m), 1292 (s), 1109, 856, 747 (m). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=7.49–7.70 (m, 3H, Ar), 8.30–8.41 (m, 5H, Ar), 8.95 (s, 1H, 3-H), 13.89 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz, Cr(acac)$_3$): δ=113.5 (Ar-H, C-3), 113.5 (C, C-10a), 116.5 (Ar-H, C-10), 123.0 (Ar-H, C-9), 125.4 (Ar-H, C-7), 127.4 (Ar-H, C-3′, C-5′), 128.8 (Ar-H, C-2′, C-6′), 131.0 (Ar-H, C-8), 131.4 (Ar-H, C-4′), 132.6 (Ar-H, C-1′), 134.6 (C, C-2), 140.0 (C, C-6a), 142.6 (C, C=N), 166.8 (C, C=S). MS (EI, 70 eV): *m/z* (%)=323 (20), 322 ([M]$^+$, 100), 321 (41), 276 ([M−NO$_2$]$^+$, 20), 275 (20), 116 (17), 89 (26). UV–vis (CH_3CN): λ_{max} (log ε)=223 (4.00), 243 (4.23), 279 (4.12), 334 (4.17). Anal. Calcd for $C_{16}H_{10}N_4O_2S$ (322.34): C, 59.62; H, 3.19; N, 17.38; found: C, 59.25; H, 3.33; N, 17.32.

4.2.8. 2-(Naphth-2-yl)-6*H*-imidazo[1,2-*c*]quinazoline-5-thione (3h). From ITCB (0.50 g, 3.2 mmol) and 2-(α-aminoacetyl)naphthalene hydrochloride (0.71 g, 3.2 mmol), 16 h reflux. Yield: 0.80 g (76%), colourless prisms (2-propanol), mp 328–335 °C (decomp.). IR (KBr, cm^{-1}): $\tilde{\nu}$=3177, 3142, 3111, 3056, 3024, 2973, 2939 (w), 1684, 1631, 1529 (m), 1476, 1419, 1418 (w), 1350, 1307 (m), 1285 (w), 1183, 1153, 749 (m). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=7.54–8.37 (m, 10H, Ar), 8.68, 8.81 (2s, 2H, 3-H, Ar), 13.81 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=113.5 (C, Ar-H), 116.4, 123.0, 123.9, 124.2, 125.4, 126.2, 126.4, 127.6, 128.1, 128.3 (Ar-H), 129.9 (C), 130.9

(Ar-H), 132.7, 133.1, 134.5, 140.0 (C), 143.7 (C, C=N), 166.7 (C, C=S). MS (EI, 70 eV): *m/z* (%)=328 (23), 327 ([M]$^+$, 100), 326 (59), 295 (4), 139 (14), 127 (4). UV–vis (CH_3CN): λ_{max} (log ε)=248 (4.83), 283 (4.20), 331 (3.59). HRMS (EI, 70 eV): calcd for $C_{20}H_{13}N_3S$ (327.41): [M]$^+$=327.0830; found: 327.0830.

4.2.9. 2-Methyl-6*H*-imidazo[1,2-*c*]quinazoline-5-thione (3i). From ITCB (1.00 g, 6.4 mmol) and aminoacetone hydrochloride (0.70 g, 6.4 mmol), 24 h reflux. Yield: 0.51 g (37%), colourless prisms (2-propanol/water), mp 263–273 °C (decomp.). IR (KBr, cm^{-1}): $\tilde{\nu}$=3171, 3029, 2954, 2930, 2865 (w), 1629, 1577, 1534, 1477, 1445, 1357, 1300, 1169 (m), 762 (w), 747 (m). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=2.36 (d, ^4J=0.9 Hz, 3H, CH_3), 7.44–7.65 (m, 3H, Ar), 7.97 (d, ^4J=0.9 Hz, 1H, 3-H), 8.17–8.20 (m, 1H, Ar), 13.65 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=13.8 (CH_3), 113.4 (C, 10a), 113.6 (Ar-H, C-3), 116.3 (Ar-H, C-10), 122.8 (Ar-H, C-9), 125.3 (Ar-H, C-7), 130.5 (Ar-H, C-8), 134.1 (C, C-2), 138.8 (C, C-6a), 142.0 (C, C=N), 166.5 (C, C=S). MS (EI, 70 eV): *m/z* (%)=216 (16), 215 ([M]$^+$, 100), 214 (40), 182 (17), 161 (10), 102 (10), 54 (11). UV–vis (CH_3CN): λ_{max} (log ε)= 239 (4.48), 278 (4.45), 296 (4.08), 308 (4.03), 336 (4.12), 351 (4.03). Anal. Calcd for $C_{11}H_9N_3S$ (215.28): C, 61.37; H, 4.21; N, 19.52; found: C, 61.00; H, 4.53; N, 19.42.

4.2.10. 2-*tert*-Butyl-6*H*-imidazo[1,2-*c*]quinazoline-5-thione (3j). From ITCB (1.00 g, 6.4 mmol) and 1-amino-3,3-dimethylbutan-2-one hydrochloride (1.00 g, 6.4 mmol), 24 h reflux. Yield: 0.87 g (53%), colourless prisms (2-propanol), mp 227–234 °C (decomp.). IR (KBr, cm^{-1}): $\tilde{\nu}$=3173, 3028 (w), 2963 (m), 1627 (s), 1563 (w), 1532 (s), 1475 (m), 1457, 1417 (w), 1352 (s), 1308 (m), 1287 (s), 1223, 1192, 1132, 748 (m). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=1.36 (s, 9H, 3CH_3), 7.44–7.65 (m, 3H, Ar), 7.87 (s, 1H, 3-H), 8.20–8.23 (m, 1H, Ar), 13.71 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=29.5 (CH_3), 31.9 ($C(CH_3)_3$), 110.5 (Ar-H, C-3), 113.5 (C, 10a), 116.3 (Ar-H, C-10), 122.8 (Ar-H, C-9), 125.3 (Ar-H, C-7), 130.5 (Ar-H, C-8), 134.1 (C, C-2), 138.9 (C, C-6a), 155.4 (C, C=N), 166.8 (C, C=S). MS (EI, 70 eV): *m/z* (%)=258 (8), 257 ([M]$^+$, 51), 242 ([M−CH_3]$^+$, 100), 202 (13). UV–vis (CH_3CN): λ_{max} (log ε)=239 (4.52), 278 (4.45), 295 (4.09), 308 (4.05), 335 (4.13), 349 (4.04). Anal. Calcd for $C_{14}H_{15}N_3S$ (257.36): C, 65.34; H, 5.87; N, 16.33; found: C, 64.89; H, 6.25; N, 16.29.

4.2.11. 2,3-Diphenyl-6*H*-imidazo[1,2-*c*]quinazoline-5-thione (3k). From ITCB (0.78 g, 5.0 mmol), α-amino-α-phenylacetophenone hydrochloride (1.24 g, 5.0 mmol) and sodium carbonate (1.43 g), 20 h reflux. Yield: 1.40 g (79%), colourless prisms (2-propanol), mp 283–288 °C (decomp.). IR (KBr, cm^{-1}): $\tilde{\nu}$=3183, 3123, 3028 (m), 2971 (w), 1631 (m), 1532 (s), 1479 (m), 1393, 1370 (w), 1324, 1276 (s), 1173, 774 (w), 749, 696 (m). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=7.22–7.68 (m, 13H, Ar), 8.34–8.37 (m, 1H, Ar), 13.34 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz, Cr(acac)$_3$): δ=114.0 (C, 10a), 116.0 (Ar-H, C-10), 123.0 (Ar-H, C-9), 124.9 (Ar-H, C-7), 127.3, 127.5, 128.1, 128.3, 130.8, 132.1 (Ar-H), 133.3 (C), 140.4 (C, C-6a), 141.3 (C, C=N), 168.1 (C, C=S). MS (EI, 70 eV): *m/z* (%)=354 (18), 353 ([M]$^+$, 76), 352 (45), 321 (5), 165 (33), 91 (30), 32 (22). UV–vis (CH_3CN): λ_{max} (log ε)=259 (4.58), 286 (4.50), 328 (4.14), 346 (4.16), 358 (4.10). Anal. Calcd for $C_{22}H_{15}N_3S$ (353.45): C, 74.76; H, 4.28; N, 11.89; found: C, 74.37; H, 4.57; N, 11.97.

4.3. Typical procedure for the synthesis of 5-oxo-5,6-dihydroimidazo[1,2-*c*]quinazolines (6a–6d)

To a CH_2Cl_2 suspension (40 mL) of isocyanatobenzonitrile (ICB, 325 mg, 2.4 mmol) and α-amino-4-methylacetophenone hydrochloride (520 mg, 2.4 mmol) was added dropwise a CH_2Cl_2 solution (10 mL) of NEt_3 (246 mg). The mixture was stirred for 10 min at 20 °C and for 40 min under reflux. Upon cooling to ambient temperature a colourless solid formed, which was filtered off and dried by exposure to air to give **5b** as a colourless solid (630 mg, 88%). An *i*-PrOH (100 mL) suspension of **5b** (360 mg, 1.2 mmol) and of ammonium hydroxide (20 mL) was refluxed for 20 h. The solution was cooled to ambient temperature and concentrated in vacuo to give a colourless precipitate which was filtered off and dried in vacuo. The solid was recrystallized from *i*-PrOH to give **6b** (255 mg, 78%) as colourless needles. ^{13}C NMR spectra of compounds **5a–5d** could not be obtained, due to their low solubility.

4.3.1. 2-Phenyl-6*H*-imidazo[1,2-*c*]quinazoline-5-one (6a). From ICB (0.72 g, 5.0 mmol), α-aminoacetophenone hydrochloride (0.85 g, 5.0 mmol) and triethylamine (0.50 g). Yield (**5a**): 0.95 g (90%). *Data of **5a***: IR (KBr, cm^{-1}): $\tilde{\nu}$=3334 (s, NH), 2224 (w, CN), 1692, 1652 (s), 1604 (m), 1576, 1554 (s), 1477, 1448, 1359, 1301, 1223, 761 (m), 688, 651 (w). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=4.72 (d, J=5.1 Hz, 2H, CH_2), 7.10–7.15 (m, 1H, Ar-H), 7.43 (t, J=5.1 Hz, 1H, N*H*CH_2), 7.56–7.72 (m, 4H, Ar-H), 8.01–8.04 (m, 3H, Ar-H), 8.98 (br s, 1H, NH). Reflux of **5a** (0.51 g, 1.8 mmol) in a mixture of 2-propanol (30 mL) and ammonium hydroxide (7 mL) for 2 h gave **6a** (0.35 g, 74%) as colourless prisms (2-propanol), mp 295–296 °C (decomp.). *Data of **6a***: IR (KBr, cm^{-1}): $\tilde{\nu}$=3211, 3152, 3084, 3059, 3001, 2938 (w), 1714 (s), 1598, 1557 (m), 1480 (w), 1408 (m), 1369 (w), 736 (m), 694 (w). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=7.31–7.61 (m, 6H, Ar-H), 8.05–8.23 (m, 3H, Ar-H), 8.41 (s, 1H, 3-H), 12.01 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=109.7 (Ar-H, C-3), 112.2 (C, 10a), 116.1 (Ar-H, C-10), 123.1 (Ar-H, C-9), 123.6 (Ar-H, C-7), 125.6 (Ar-H, C-3′, C-5′), 127.9 (Ar-H, C-4′), 128.8 (Ar-H, C-2′, C-6′), 130.7 (Ar-H, C-8), 133.0 (C, C-1′), 135.4 (C, C-2), 143.2 (C, C-6a), 143.7 (C, C=N), 145.0 (C, C=O). MS (EI, 70 eV): *m/z* (%)=262 (27), 261 ([M]$^+$, 100), 260 (10), 115 (10), 90 (20), 89 (18). UV–vis (CH_3CN): λ_{max} (log ε)=241 (4.61), 270 (4.20), 280 (4.18), 298 (4.12), 310 (4.12), 323 (4.13). Anal. Calcd for $C_{16}H_{11}N_3O$ (261.28): C, 73.55; H, 4.24; N, 16.08; found: C, 73.31; H, 4.41; N, 16.14.

4.3.2. 2-Tolyl-6*H*-imidazo[1,2-*c*]quinazoline-5-one (6b). Starting with ICB (0.32 g, 2.4 mmol), α-amino-4-methylacetophenone hydrochloride (0.52 g, 2.4 mmol) and triethylamine (0.25 g), **5b** (0.63 g, 88%) was isolated. *Data of **5b***: IR (KBr, cm^{-1}): $\tilde{\nu}$=3322 (s, NH), 2226 (w, CN), 1682, 1649, 1607, 1571, 1538 (s), 1476, 1450, 1414, 1358, 1298 (m), 1232 (s), 1184, 994, 815, 759, 639, 563 (m). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=2.40 (s, 3H, CH_3), 4.70

(d, J=5.1 Hz, 2H, CH_2), 7.09–7.14 (m, 1H, Ar-H), 7.36–7.38 (m, 2H, Ar-H), 7.42 (t, J=5.1 Hz, 1H, N*H*CH_2), 7.56–7.62 (m, 1H, Ar-H), 7.69–7.72 (m, 1H, Ar-H), 7.90–7.93 (m, 2H, Ar-H), 8.03–8.06 (m, 1H, Ar-H), 8.98 (br s, 1H, NH). Starting with an *i*-PrOH (100 mL) suspension of **5b** (360 mg, 1.2 mmol) and of ammonium hydroxide (20 mL) (reflux 20 h), **6b** (255 mg, 78%) was isolated as colourless prisms (2-propanol), mp 301–302 °C (decomp.). IR (KBr, cm^{-1}): $\tilde{\nu}$=3213 (w), 3155, 3077, 3064, 3053, 3015, 2943, 2923, 2894 (m), 1710, 1599, 1556 (s), 1497, 1483 (m), 1416 (s), 1371 (m), 1330 (w), 1296 (m), 1253, 1147, 830 (w), 822 (m), 747 (s), 737 (m). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=2.35 (s, 3H, CH_3), 7.25–8.22 (m, 8H, Ar-H), 8.34 (s, 1H, 3-H), 12.00 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=20.8 (CH_3), 108.9 (Ar-H, C-3), 112.0 (C, 10a), 115.8 (Ar-H, C-10), 122.8 (Ar-H, C-9), 123.3 (Ar-H, C-7), 125.4 (Ar-H, C-3′, C-5′), 129.2 (Ar-H, C-2′, C-6′), 130.1 (C, C-1′), 130.4 (Ar-H, C-8), 135.2 (C, C-2), 137.0 (C, C-4′), 143.1 (C, C-6a), 143.3 (C, C=N), 144.8 (C, C=O). MS (EI, 70 eV): m/z (%)=276 (19), 275 ([M]$^+$, 100), 247 ([M−CO]$^+$, 4), 130 (11). UV–vis (CH_3CN): λ_{max} (log ε)=242 (4.62), 249 (4.60), 273 (4.30), 312 (4.11), 324 (4.19). Anal. Calcd for $C_{17}H_{13}N_3O$ (275.31): C, 74.17; H, 4.76; N, 15.26; found: C, 74.14; H, 4.78; N, 15.14.

4.3.3. 2-(4-Bromophenyl)-6*H*-imidazo[1,2-*c*]quinazoline-5-one (6c). *Method A*. To a hot solution of **7g** (60 mg, 0.16 mmol) in glacial acetic acid (10 mL) was added H_2O_2 (5 mL). The mixture was stirred for 14 h at 20 °C and subsequently diluted with water to 50 mL to give a precipitate which was filtered off. Yield: 50 mg (91%). *Method B*. From ICB (0.72 g, 5.0 mmol), α-amino-4-chloroacetophenone hydrochloride (1.25 g, 5.0 mmol) and triethylamine (0.5 g). Yield (**5c**): 1.40 g (78%). IR (KBr, cm^{-1}): $\tilde{\nu}$=3341 (m, NH), 2223 (w, CN), 1690, 1651, 1584, 1546 (s), 1478, 1448, 1399, 1358, 1299, 1220, 1071, 992, 761 (m). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=4.72 (d, J=5.1 Hz, 2H, CH_2), 7.10–7.15 (m, 1H, Ar-H), 7.43 (t, J=5.1 Hz, 1H, N*H*CH_2), 7.56–7.79 (m, 4H, Ar-H), 7.94–8.05 (m, 3H, Ar-H), 8.98 (br s, 1H, NH). Reflux of **5c** (0.79 g, 2.2 mmol) in a mixture of 2-propanol (60 mL) and ammonium hydroxide (10 mL) for 24 h afforded **6c.** Yield: 0.56 g (75%), colourless prisms (2-propanol), mp 334–335 °C (decomp.). IR (KBr, cm^{-1}): $\tilde{\nu}$=3155, 3081, 3057, 3004, 2942 (w), 1712 (s), 1599, 1554, 1479 (m), 1406 (s), 1368, 829, 748 (m). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=7.32–7.67 (m, 5H, Ar-H), 8.00–8.22 (m, 3H, Ar-H), 8.49 (s, 1H, 3-H), 12.02 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=110.2 (Ar-H, C-3), 112.1 (C, 10a), 116.1 (Ar-H, C-10), 120.9 (C-1′), 123.0 (Ar-H, C-9), 123.6 (Ar-H, C-7), 127.6 (Ar-H, C-3′, C-5′), 130.8 (Ar-H, C-8), 131.7 (Ar-H, C-2′, C-6′), 132.3 (C, C-1′), 135.5 (C, C-4′), 135.3 (C, C-2), 142.0 (C, C-6a), 143.8 (C, C=N), 144.9 (C, C=O). MS (EI, 70 eV): m/z (%)=343 (16), 342 ([M]$^+$ (^{81}Br), 94), 341 (19), 340 ([M]$^+$ (^{79}Br), 100), 261 (7), 130 (18), 116 (14), 89 (25). UV–vis (CH_3CN): λ_{max} (log ε)=245 (4.58), 275 (4.30), 287 (4.30), 323 (4.19), 354 (3.99). Anal. Calcd for $C_{16}H_{10}BrN_3O$ (340.18): C, 56.49; H, 2.96; N, 12.35; found: C, 56.27; H, 3.35; N, 12.23.

4.3.4. 2-(4-Chlorophenyl)-6*H*-imidazo[1,2-*c*]quinazolin-5-one (6d). From ICB (0.72 g, 5.0 mmol), α-amino-4-chloroacetophenone hydrochloride (1.03 g, 5.0 mmol) and triethylamine (0.50 g). Yield (**5d**): 1.17 g (75%). IR (KBr, cm^{-1}): $\tilde{\nu}$=3330 (m, NH), 2224 (w, CN), 1689, 1649, 1586, 1551 (s), 1480, 1449, 1358, 1299, 1223, 1094, 994, 761 (m). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=4.74 (d, J=5.1 Hz, 2H, CH_2), 7.09–7.15 (m, 1H, Ar-H), 7.44 (t, J=5.1 Hz, 1H, N*H*CH_2), 7.53–7.72 (m, 4H, Ar-H), 8.00–8.06 (m, 3H, Ar-H), 8.98 (br s, 1H, NH). Reflux of **5d** (0.56 g, 1.8 mmol) in a mixture of 2-propanol (140 mL) and ammonium hydroxide (20 mL) for 32 h afforded **6d**. Yield: 0.32 g (61%), colourless prisms (2-propanol), mp 334–335 °C (decomp.). IR (KBr, cm^{-1}): $\tilde{\nu}$=3217, 3155, 3080, 3057, 3010, 2942, 2894 (w), 1708 (s), 1598, 1556, 1484, 1478 (m), 1407 (s), 1370 (m), 1295, 1147, 1089 (w), 835 (m), 750 (s). ^{1}H NMR (DMSO-d_6, 300 MHz): δ=7.33–7.64 (m, 5H, Ar-H), 8.07–8.25 (m, 3H, Ar-H), 8.48 (s, 1H, 3-H), 11.79 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=110.1 (Ar-H, C-3), 111.9 (C, 10a), 115.9 (Ar-H, C-10), 122.9 (Ar-H, C-9), 123.4 (Ar-H, C-7), 127.1 (Ar-H, C-3′, C-5′), 128.6 (Ar-H, C-2′, C-6′), 130.6 (Ar-H, C-8), 131.8 (C, C-1′), 132.1 (Ar-H, C-4′), 135.3 (C, C-2), 141.8 (C, C-6a), 143.6 (C, C=N), 144.7 (C, C=O). MS (EI, 70 eV): m/z (%)=298 ([M]$^+$ (^{37}Cl), 32), 297 (16), 296 ([M]$^+$ (^{35}Cl), 100), 89 (16). UV–vis (CH_3CN): λ_{max} (log ε)=245 (4.59), 274 (4.27), 286 (4.26), 310 (4.16), 323 (4.15). Anal. Calcd for $C_{16}H_{10}ClN_3O$ (295.73): C, 64.98; H, 3.41; N, 14.21; found: C, 65.00; H, 3.55; N, 14.13.

4.4. General procedure for the preparation of the alkylsulfanyl-imidazo[1,2-*c*]quinazolines (7a–7l)

Method A. Compounds **3a**, **3b**, **3d**, or **3e** (10.0 mmol) was dissolved in an aqueous solution of sodium hydroxide (0.02 M, 120 mL). The mixture was heated to 60 °C and methyl iodide (2.5 g, 16 mmol) was added dropwise over a period of 5 min. The colourless solid, which precipitated upon cooling, was filtered off and washed with water.

Method B. Compounds **3a**, **3d**, or **3e** (10.0 mmol) was dissolved in an aqueous solution of sodium hydroxide (0.02 M, 120 mL). Allyl bromide (1.44 g, 12.0 mmol) was added dropwise and the solution was stirred for 45 min at room temperature. The colourless solid, which precipitated upon cooling, was filtered off and washed with water.

Method C. A mixture of compound **3a**, **3b**, **3d**, or **3e** (10.0 mmol) and of NaOMe (0.54 g, 10.0 mmol) was dissolved in dry methanol (200 mL) and the solution was refluxed for 1 h. The alkyl halide (12.0 mmol) was added and the solution was heated at reflux for further 2 h. Upon cooling, a crystalline precipitate was formed, which was filtered off and washed with water.

4.4.1. 2-Phenyl-5-methylsulfanyl-imidazo[1,2-*c*]quinazoline (7a). Yield: method A: 2.18 g (75%); method C: 2.30 g (79%), yellow needles (EtOH), mp 182 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=724 (s), 768 (s), 955 (m), 1197 (s), 1273 (m), 1373 (s), 1474 (s), 1507 (s), 1593 (s). ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.87 (s, 3H, Me), 7.53–7.91 (m, 9H, Ar-H), 8.56 (s, 1H, Hetar). ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.7, 106.3, 117.3, 123.0, 126.2, 126.8, 126.9, 128.2, 128.8, 130.0, 133.1, 141.5, 143.4, 145.0, 147.2. MS (EI, 70 eV): m/z=291 (M$^+$, 100), 258 (25), 244 (20), 142

(4), 89 (12), 28 (9). Anal. Calcd for $C_{17}H_{13}N_3S$ (291.37): C, 70.08; H, 4.50; N, 14.42; found: C, 70.12; H, 4.65; N, 14.51.

4.4.2. 2-Phenyl-5-allylsulfanyl-imidazo[1,2-*c*]quinazoline (7b). Yield: method B: 2.41 g (76%); method C: 2.55 g (80%), yellow needles (EtOH), mp 90 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=766 (s), 955 (m), 1195 (s), 1372 (s), 1594 (s). ^1H NMR (300 MHz, $CDCl_3$): δ=4.14 (d, 2H, CH_2), 5.48 (d, 2H, CH_2), 6.03–6.09 (m, 1H, CH), 7.32–7.99 (m, 9H, Ar-H), 8.57 (s, 1H, Hetar). ^{13}C NMR (300 MHz, $CDCl_3$): δ=33.9, 106.4, 117.4, 119.3, 123.0, 126.2, 126.9, 128.2, 128.8, 130.0, 132.4, 133.1, 141.4, 143.5, 145.1, 146.0. MS (EI, 70 eV): *m*/*z*=317 (M^+, 100), 301 (51), 284 (44), 275 (27), 121 (12), 89 (15), 41 (11), 28 (35). Anal. Calcd for $C_{19}H_{15}N_3S$ (317.10): C, 71.48; H, 4.76; N, 13.29; found: C, 71.53; H, 4.81; N, 13.35.

4.4.3. 2-Phenyl-5-benzylsulfanyl-imidazo[1,2-*c*]quinazoline (7c). Yield: method A: 65%; method C: 2.60 g (71%), yellow prisms (EtOH), mp 188 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=766 (s), 956 (m), 1195 (s), 1374 (s), 1453 (s), 1474 (s), 1506 (s), 1594 (s). ^1H NMR (300 MHz, $CDCl_3$): δ=4.70 (s, 2H, CH_2, Bn), 7.30–7.98 (m, 14H, Ar-H), 8.52 (s, 1H, Hetar). ^{13}C NMR (75 MHz, $CDCl_3$): δ=35.4, 106.4, 117.4, 123.0, 126.1, 126.8, 128.9 127.8, 128.2, 128.7, 128.7, 129.3, 130.0, 133.0, 136.3, 141.3, 143.5, 145.1, 146.2. MS (EI, 70 eV): *m*/*z*=367 (M^+, 100), 276 (13), 245 (14), 91 (71), 59 (9), 28 (27). Anal. Calcd for $C_{23}H_{17}N_3S$ (367.47): C, 75.18; H, 4.66; N, 11.49; found: C, 75.07; H, 4.72; N, 11.51.

4.4.4. 2-Phenyl-5-phenylethylsulfanyl-imidazo[1,2-*c*]quinazoline (7d). Yield: method C: 3.12 g (82%), yellow prisms (EtOH), mp 221 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=759 (s), 9.56 (m), 1055 (m), 1192 (s), 1301 (s), 1475 (s), 1594 (m). ^1H NMR (300 MHz, CD_3OD): δ=3.22–3.23 (t, 2H, CH_2), 3.31–3.32 (t, 2H, CH_2), 7.29–7.99 (m 14H, Ar-H), 8.08 (s, 1H, Hetar). ^{13}C NMR (300 MHz, CD_3OD): δ=30.7, 36.6, 108.5, 116.4, 118.0, 123.1, 123.8, 125.4, 127.0, 128.2, 128.9, 129.8, 131.2, 134.1, 141.2, 142.1, 143.6, 144.1, 148.4, 166.5. MS (EI, 70 eV): *m*/*z*=381 (M^+, 16), 277 (100), 105 (13), 77 (11), 44 (11), 32 (13), 28 (54). Anal. Calcd for $C_{24}H_{19}N_3S$ (381.49): C, 75.56; H, 5.02; N, 11.01; found: C, 75.61; H, 5.21; N, 11.20.

4.4.5. 2-(4-Tolyl-5-benzylsulfanyl)-imidazo[1,2-*c*]quinazoline (7e). Yield: method C: 2.86 g (75%), yellow prisms (EtOH), mp 121 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=756 (m), 1018 (m), 1248 (m), 1402 (s), 1443 (s), 1474 (s), 1532 (s), 1628 (s), 1702 (m). ^1H NMR (300 MHz, DMSO-d_6): δ=2.35 (s, 3H, Me), 4.26 (s, 2H, CH_2), 7.21–7.97 (m, 13H, Ar-H), 8.39 (s, 1H, Hetar). MS (EI, 70 eV): *m*/*z*=381 (M^+, 14), 288 (100), 259 (44), 130 (30), 103 (29), 77 (17), 28 (4). Anal. Calcd for $C_{24}H_{19}N_3S$ (381.50): C, 75.56; H, 5.02; N, 11.01; found: C, 75.61; H, 5.08; N, 11.08.

4.4.6. 2-(4-Bromophenyl)-5-methylsulfanyl-imidazo[1,2-*c*]quinazoline (7f). Yield: method A: 2.74 g (74%); method C: 2.85 g (77%), colourless prisms (EtOH), mp 187 °C. IR (KBr, cm^{-1}) $\tilde{\nu}$=735 (m), 768 (m), 1197 (m), 1375 (s), 1475 (s), 1507 (s), 1593 (s). ^1H NMR (500 MHz, DMSO-d_6): δ=8.58 (s, 1H, H-2), 8.42 (ddd, 1H, $^3J_{8,9}$=8.0 Hz, $^4J_{7,9}$=1.6 Hz, $^5J_{6,9}$=0.6 Hz, H-9), 8.11 (m, 2H, *o*-C_6H_4Br), 7.86 (ddd, 1H, $^3J_{6,7}$=8.2 Hz, $^4J_{6,8}$=1.2 Hz, $^5J_{6,9}$=0.6 Hz, H-6), 7.75 (ddd, 1H, $^3J_{6,7}$=8.2 Hz, $^3J_{7,8}$=7.1 Hz, $^4J_{7,9}$= 1.6 Hz, H-7), 7.68 (m, 2H, *m*-C_6H_4Br), 7.64 (ddd, 1H, $^3J_{8,9}$= 8.0 Hz, $^3J_{7,8}$=7.1 Hz, $^4J_{6,8}$=1.2 Hz, H-8), 2.86 (s, 2H, SCH_3). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ=148.0 (C-5), 143.2 (C-3a), 142.7 (C-1), 141.0 (C-5a), 132.3 (*i*-C_6H_4Br), 131.8 (*m*-C_6H_4Br), 130.6 (C-7), 128.1 (*o*-C_6H_4Br), 127.3 (C-8), 127.0 (C-6), 122.6 (C-9), 121.4 (*p*-C_6H_4Br), 116.8 (C-9a), 108.6 (C-2), 13.6 (SCH_3). MS (70 eV): *m*/*z*=370 (M^+, 100), 368 (97), 274 (23), 256 (25), 144 (14), 102 (12), 88 (18), 28 (48). Anal. Calcd for $C_{17}H_{12}N_3S_1Br$ (370.28): C, 55.15; H, 3.27; N, 11.35; found: C, 55.18; H, 3.32; N, 11.38.

4.4.7. 2-(4-Bromophenyl)-5-allylsulfanyl-imidazo[1,2-*c*]quinazoline (7g). Yield: method B: 3.02 g (76%); method C: 3.20 g (81%), yellow prisms (EtOH), mp 145 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=736 (m), 768 (m), 955 (m), 1194 (m), 1374 (s), 1475 (s), 1508 (s), 1594 (s). ^1H NMR (300 MHz, $CDCl_3$): δ=4.15 (d, 2H, CH_2), 5.23–5.25 (d, 2H, CH_2), 6.12–6.15 (m, 1H, CH), 7.51–7.90 (m, 8H, Ar-H), 8.51 (s, 1H, Hetar). ^{13}C NMR (50 MHz, DMSO-d_6): δ= 33.1, 108.2, 116.6, 119.2, 121.1, 122.3, 126.7, 127.1, 127.8, 130.3, 131.5, 132.0, 132.6, 140.6, 142.5, 142.9, 146.3. MS (EI, 70 eV): *m*/*z*=397 (M^+, 100), 380 (53), 364 (35), 275 (97), 146 (11), 102 (11), 88 (11), 41 (14), 28 (23). Anal. Calcd for $C_{19}H_{15}N_3SBr$ (397.32): C, 57.88; H, 3.56; N, 10.60; found: C, 57.61; H, 3.62; N, 10.71.

4.4.8. 2-(4-Bromophenyl)-5-benzylsulfanyl-imidazo[1,2-*c*]quinazoline (7h). Yield: method C: 3.20 g (72%), colourless needles (EtOH), mp 195 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=701 (s), 768 (s), 955 (m), 1194 (s), 1373 (s), 1475 (s), 1508 (s), 1593 (m). ^1H NMR (300 MHz, DMSO-d_6): δ=4.79 (s, 2H, CH_2), 7.28–8.10 (m, 13H, Ar-H), 8.56 (s, 1H, Hetar). ^{13}C NMR (50 MHz, DMSO-d_6): δ=34.4, 108.3, 116.6, 121.2, 122.3, 126.7, 127.2, 127.5, 127.8, 128.4, 129.2, 130.4, 131.6, 132.0, 136.6, 140.7, 142.5, 142.9, 146.5. MS (EI, 70 eV): *m*/*z*=446 (M^+, 64), 412 (22), 322 (7), 275 (37), 91 (100), 66 (10), 28 (44). Anal. Calcd for $C_{23}H_{16}BrN_3S$ (445.36): C, 61.89; H, 3.61; N, 9.41; found: C, 62.02; H, 3.34; N, 9.43.

4.4.9. 2-(4-Chlorophenyl)-5-methylsulfanyl-imidazo[1,2-*c*]quinazoline (7i). Yield: method A: 2.34 g (72%); method C: 2.50 g (77%), colourless needles (EtOH), mp 135 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=737 (s), 765 (s), 955 (m), 1196 (s), 1272 (m), 1374 (s), 1475 (s), 1507 (s), 1593 (s). ^1H NMR (300 MHz, $CDCl_3$): δ=2.87 (s, 3H, Me), 7.41–7.97 (m, 8H, Ar-H), 8.56 (s, 1H, Hetar). ^{13}C NMR (50 MHz, DMSO-d_6): δ=13.3, 108.2, 116.5, 122.3, 126.7, 127.0, 127.5, 128.6, 130.3, 131.7, 132.5, 140.7, 142.4, 142.8, 147.7. MS (EI, 70 eV): *m*/*z*=325 (M^+, 71), 205 (100), 145 (12), 123 (15), 107 (12), 95 (35), 81 (17), 55 (18), 28 (25). Anal. Calcd for $C_{17}H_{12}N_3SCl$ (325.82): C, 62.67; H, 3.71; N, 12.90; found: C, 62.66; H, 3.70; N, 12.89.

4.4.10. 2-(4-Chlorophenyl)-5-allylsulfanyl-imidazo[1,2-*c*]quinazoline (7j). Yield: method B: 2.96 g (84%); method C: 3.10 g, (88%), colourless needles (EtOH), mp 117 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=736 (s), 768 (s), 634 (m), 955 (m), 1091 (m), 1195 (s), 1375 (s), 1476 (s), 1508 (s), 1595 (s). ^1H NMR (300 MHz, $CDCl_3$): δ=4.15–4.18 (d, 2H, CH_2), 5.23–5.26 (d, 2H, CH_2), 6.07–6.13 (m, 1H, CH), 7.40–7.98 (m, 8H,

Ar-H), 8.55 (s, 1H, Hetar). ^{13}C NMR (300 MHz, $CDCl_3$): δ=34.1, 106.7, 117.5, 119.5, 123.1, 127.1, 127.2, 127.6, 129.1, 130.3, 131.8, 132.5, 134.2, 141.6, 147.6, 144.1, 146.1. MS (EI, 70 eV): *m*/*z*=351/353 (M^+, 100/39), 318 (47), 275 (84), 123 (11), 102 (9), 32 (14), 28 (75). Anal. Calcd for $C_{19}H_{14}N_3SCl$ (351.85): C, 64.84; H, 4.01; N, 11.94; found: C, 64.91; H, 4.20; N, 11.81.

4.4.11. 2-(4-Chlorophenyl)-5-benzylsulfanyl-imidazo-[1,2-*c*]quinazoline (7k). Yield: method C: 3.06 g (76%). ^{1}H NMR (500 MHz, DMSO-d_6): δ=13.80 (br s, 1H, NH), 8.72 (s, 1H, H-2), 8.28 (dd, 1H, $^3J_{8,9}$=8.0 Hz, $^4J_{7,9}$=1.5 Hz, H-9), 8.13 (m, 2H, *o*-C_6H_4Cl), 7.67 (ddd, 1H, $^3J_{6,7}$=8.2 Hz, $^3J_{7,8}$=7.0 Hz, $^4J_{7,9}$=1.2 Hz, H-7), 7.62 (dd, 1H, $^3J_{6,7}$=8.2 Hz, $^4J_{6,8}$=1.2 Hz, H-6), 7.52 (m, 2H, *m*-C_6H_4Cl), 7.50 (ddd, 1H, $^3J_{8,9}$=8.0 Hz, $^3J_{7,8}$=7.0 Hz, $^4J_{6,8}$=1.2 Hz, H-8). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ=166.9 (C-5), 142.7 (C-1), 140.3 (C-3a), 135.0 (C-5a), 132.8 (*p*-C_6H_4Cl), 131.7 (*i*-C_6H_4Cl), 131.1 (C-7), 129.0 (*m*-C_6H_4Cl), 127.6 (*o*-C_6H_4Cl), 125.5 (C-8), 123.1 (C-9), 116.9 (C-6), 113.2 (C-2), 113.8 (C-9a). Anal. Calcd for $C_{23}H_{16}ClN_3S$ (401.92): C, 68.73; H, 4.01; N, 10.45; found: C, 68.62; H, 4.21; N, 10.43.

4.5. General procedure for the preparation of 5-amino-imidazo[1,2-*c*]quinazolines (8a–8j)

Compound **8a**, **8g**, or **8j** (10.0 mmol) was dissolved at 70 °C in the respective secondary amine (10–12 mL) and the solution was refluxed for 16 h. After cooling to room temperature, the precipitated product was filtered off and washed with methanol.

4.5.1. 2-Phenyl-5-piperidino-imidazo[1,2-*c*]quinazoline (8a). Yield: 2.92 g (89%), colourless rods (EtOH), mp 152 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=727 (m), 767 (m), 994 (m), 1235 (m), 1392 (s), 1452 (m), 1524 (s), 1562 (m), 1606 (s), 2838 (m), 2934 (m). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.75–1.89 (m, 6H, 3×CH_2), 3.44–3.47 (t, 4H, 2×CH_2), 7.35–8.02 (m, 9H, Ar-H), 8.55 (s, 1H, Hetar). ^{13}C NMR (75 MHz, $CDCl_3$): δ=24.4, 25.5, 50.0, 106.9, 117.1, 122.8, 125.5, 126.0, 126.6, 128.0, 128.6, 129.8, 133.4, 141.9, 144.4, 145.7, 147.2. MS (EI, 70 eV): *m*/*z*=328 (M^+, 100), 299 (24), 285 (20), 272 (36), 259 (23), 245 (62), 218 (9), 102 (4), 84 (9), 41 (5), 28 (3). Anal. Calcd for $C_{21}H_{20}N_4$ (328.41): C, 76.80; H, 6.14; N, 17.06; found: C, 76.80; H, 6.14; N, 17.10.

4.5.2. 2-Phenyl-5-morpholino-imidazo[1,2-*c*]quinazoline (8b). Yield: 2.81 g (85%), yellow prisms (EtOH), mp 205 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=769 (s), 1115 (s), 1231 (m), 1393 (s), 1455 (m), 1523 (s), 1611 (s). ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.49–3.52 (t, 4H, 2×CH_2), 3.94–3.97 (t, 4H, 2×CH_2), 7.31–8.01 (m, 9H, Ar-H), 8.54 (s, 1H, Hetar). ^{13}C NMR (50 MHz, DMSO-d_6): δ=49.1, 66.3, 106.4, 117.2, 122.8, 126.06, 126.07, 126.7, 128.1, 128.7, 130.0, 133.1, 141.5, 144.8, 145.7, 146.1. MS (EI, 70 eV): *m*/*z*=330 (M^+, 100), 285 (27), 273 (65), 245 (34), 143 (3), 116 (6), 90 (6), 28 (5). Anal. Calcd for $C_{20}H_{18}N_4O$ (330.38): C, 72.71; H, 5.49; N, 16.96; found: C, 72.77; H, 5.51; N, 16.91.

4.5.3. 2-Phenyl-5-pyrrolidino-imidazo[2,1-*c*]quinazoline (8c). Yield: 2.61 g (83%), colourless rods (EtOH), mp 211 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=718 (s), 765 (m), 1341 (m), 1414 (s), 1483 (m), 1522 (s), 1564 (s), 1600 (s), 2873 (m), 2969 (m). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.98–2.03 (m, 4H, 2×CH_2), 3.81–3.85 (t, 4H, 2×CH_2), 7.31–7.97 (m, 9H, Ar-H), 8.46 (s, 1H, Hetar). ^{13}C NMR (75 MHz, $CDCl_3$): δ=25.6, 49.9, 107.4, 115.8, 122.7, 123.7, 125.9, 127.8, 128.6, 130.0, 133.4, 142.8, 143.9, 144.5, 146.6. MS (EI, 70 eV): *m*/*z*=314 (M^+, 90), 285 (86), 259 (38), 245 (70), 244 (56), 142 (26), 115 (28), 102 (24), 91 (15), 90 (30), 77 (17), 71 (14), 28 (100). Anal. Calcd for $C_{20}H_{18}N_4$ (314.38): C, 76.41; H, 5.77; N, 17.82; found: C, 76.45; H, 5.81; N, 17.81.

4.5.4. 2-(4-Bromophenyl)-5-piperidino-imidazo[1,2-*c*]quinazoline (8d). Yield: 3.22 g (79%), colourless rods (EtOH), mp 196 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=766 (m), 834 (m), 1235 (m), 1394 (s), 1523 (s), 1606 (s), 2838 (s), 2933 (m). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.64–1.90 (m, 6H, 3×CH_2), 3.44–3.47 (t, 4H, 2×CH_2), 7.45–7.92 (m, 8H, Ar-H), 8.52 (s, 1H, Hetar). ^{13}C NMR (75 MHz, $CDCl_3$): δ=24.9, 25.6, 50.1, 107.1, 117.0, 121.9, 122.8, 125.8, 126.7, 127.6, 130.1, 131.8, 132.4, 142.0, 143.4, 146.0, 147.2. MS (EI, 70 eV): *m*/*z*=406/408 (M^+ 74/70), 350 (11), 325 (21), 323 (20), 244 (7), 114 (5), 84 (21), 41 (11), 32 (29), 28 (100). Anal. Calcd for $C_{21}H_{19}BrN$ (407.31): C, 61.93; H, 4.70; N, 13.76; found: C, 61.90; H, 4.70; N, 13.75.

4.5.5. 2-(4-Bromophenyl)-5-morpholino-imidazo[1,2-*c*]quinazoline (8e). Yield: 3.90 g (95%), yellow prisms (EtOH), mp 235 °C. IR (KBr, cm^{-1}) $\tilde{\nu}$=767 (m), 1004 (m), 1114 (s), 1391 (s), 1476 (s), 1525 (s), 1609 (s), 2857 (m). ^{1}H NMR (300 MHz, DMSO-d_6): δ=3.47–3.48 (t, 8H, 4×CH_2), 7.51–8.37 (m, 8H, Ar-H), 8.46 (s, 1H, Hetar). ^{13}C NMR (75 MHz, $CDCl_3$): δ=49.2 (CH_2), 66.4 (CH_2), 106.6, 117.7, 122.2, 122.9, 126.3, 126.9, 127.7, 130.3, 131.9, 132.2, 141.6, 143.8, 146.0, 146.1. MS (EI, 70 eV): *m*/*z*=410 (M^+, 100), 408 (95), 364 (23), 351 (60), 322 (24), 243 (14), 142 (28), 129 (15), 102 (34), 89 (24), 28 (25). Anal. Calcd for $C_{20}H_{17}N_4BrO$ (409.28): C, 58.69; H, 4.19; N, 13.69; found: C 58.21; H, 4.20; N, 13.70.

4.5.6. 2-(4-Bromophenyl)-5-pyrrolidino-imidazo[1,2-*c*]quinazoline (8f). Yield: 3.07 g (81%), yellow needles (EtOH), mp 201 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=764 (m), 834 (m), 1010 (m), 1277 (m), 1407 (s), 1480 (m), 1522 (s), 1599 (s), 2876 (m), 2908 (m). ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.06–2.11 (m, 4H, 2×CH_2), 3.89–3.94 (t, 4H, 2×CH_2), 7.19–7.90 (m, 8H, Ar-H), 8.46 (s, 1H, Hetar). ^{13}C NMR (75 MHz, $CDCl_3$): δ=25.7 (CH_2), 50.1 (CH_2), 107.6 (C-3), 115, 121.8, 122.8, 124.0, 125.5, 127.5, 130.2, 131.8, 132.4, 142.8, 142.9, 144.6, 146.8. MS (70 eV): *m*/*z*=392 (M^+, 100), 364 (54), 339 (17), 324 (24), 284 (15), 244 (14), 142 (6), 102 (4). Anal. Calcd for $C_{20}H_{17}BrN_4$ (393.28): C, 61.08; H, 4.36; N, 14.25; found: C, 61.10; H, 4.41; N, 14.25.

4.5.7. 2-(4-Chlorophenyl)-5-piperidino-imidazo[1,2-*c*]quinazoline (8g). Yield: 3.08 g (85%), colourless needles (EtOH), mp 180 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=765 (m), 836 (m), 994 (m), 1094 (m), 1235 (m), 1273 (m), 1393 (m), 1476 (m), 1524 (s), 1606 (s), 2838 (m), 2933 (m). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.76–1.87 (m, 6H, 3×CH_2), 3.44–3.48 (t, 4H, 2×CH_2), 7.41–7.97 (m, 8H, Ar-H), 8.52 (s, 1H, Hetar). ^{13}C NMR (50 MHz, DMSO-d_6): δ=23.8, 24.8, 49.5, 108.6, 116.2, 122.1, 125.3, 126.2, 127.5, 128.4,

129.9, 132.0, 132.2, 141.3, 142.0, 144.7, 146.8. MS (EI, 70 eV): m/z=362 (M^+, 100), 333 (20), 319 (16), 306 (28), 279 (45), 84 (25), 28 (5). Anal. Calcd for $C_{21}H_{19}N_4Cl$ (362.86): C, 69.51; N, 5.28; N, 15.44; found: C, 69.62; H, 5.35; N, 15.47.

4.5.8. 2-(4-Chlorophenyl)-5-morpholino-imidazo[1,2-*c*]quinazoline (8h). Yield: 3.40 g (93%), yellow needles (EtOH), mp 217 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=767 (m), 837 (m), 1114 (s), 1230 (m), 1359 (m), 1390 (s), 1478 (s), 1526 (s), 1609 (s), 2858 (m), 3140 (m). ^1H NMR (300 MHz, DMSO-d_6): δ=3.26–3.49 (m, 8H, 4×CH_2), 7.51–8.37 (m, 8H, Ar-H), 8.47 (s, 1H, Hetar). ^{13}C NMR (50 MHz, DMSO-d_6): δ=48.8, 65.6, 113.4, 125.7 (Ar), 126.3 (Ar), 127.3 (Ar), 128.5 (Ar), 128.6 (Ar), 130.0 (Ar), 131.3 (Ar), 132.0 (Ar), 134.4 (Ar), 141.0, 142.2, 146.2, 166.7. MS (EI, 70 eV): m/z=364 (M^+, 100), 321 (18), 319 (30), 311 (35), 307 (76), 279 (46), 149 (19), 142 (22), 129 (8), 102 (14), 89 (11), 28 (19). Anal. Calcd for $C_{20}H_{17}N_4OCl$ (364.83): C, 65.85; H, 4.70; N, 15.36; found: C, 65.81; H, 4.70; N, 15.40.

4.5.9. 2-(4-Chlorophenyl)-5-pyrrolidino-imidazo[1,2-*c*]quinazoline (8i). Yield: 2.99 g (86%), yellow rods (EtOH), mp 221 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=765 (m), 1012 (m), 1091 (m), 1278 (m), 1408 (s), 1481 (s), 1523 (s), 1599 (s), 2877 (m), 2969 (m). ^1H NMR (300 MHz, $CDCl_3$): δ=2.06–2.10 (m, 4H, 2×CH_2), 3.91–3.92 (t, 4H, 2×CH_2), 7.32 (m, 8H, Ar), 8.46 (s, 1H, Hetar). ^{13}C NMR (75 MHz, $CDCl_3$): δ=25.7 (CH_2), 50.1 (CH_2), 107.6 (C-2), 115.8 (Ar), 122.8 (CH, Ar), 124.0 (CH, Ar), 125.5 (CH, Ar), 127.2 (CH, Ar), 128.9 (CH, Ar), 130.2 (CH, Ar), 132.0 (Ar), 133.6 (Ar), 142.8 (C-7a), 142.9 (C-2), 144.6 (C-5), 146.8 (C-10a). MS (EI, 70 eV): m/z=348 (M^+, 100), 319 (69), 293 (22), 279 (49), 149 (20), 142 (26), 123 (15), 113 (15), 101 (15), 89 (35), 71 (52), 41 (25), 28 (14). Anal. Calcd for $C_{20}H_{17}N_4Cl$ (348.83): C, 68.86; H, 4.91; N, 16.06; found: C, 68.86; H, 4.92; N, 16.05.

4.5.10. 2-(4-Chlorophenyl)-5-(*N*-methylpiperazino)-imidazo[1,2-*c*]quinazoline (8j). Yield: 3.17 g (84%), yellow needles (EtOH), mp 284 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=748 (m), 833 (m), 1092 (m), 1191 (s), 1296 (m), 1355 (s), 1478 (s), 1533 (s), 1630 (m), 3027 (m), 3178 (m). ^1H NMR (300 MHz, DMSO-d_6): δ=3.29–3.45 (m, 4H, 2×CH_2), 4.37 (s, 1H, CH_3), 7.51–8.31 (m, 8H, Ar-H), 8.72 (s, 1H, Hetar). ^{13}C NMR (75 MHz, DMSO-d_6): δ=113.0, 113.4, 116.3, 122.9, 125.3, 127.3, 128.7, 130.9, 131.3, 132.6, 134.5, 139.9, 142.6, 166.8. MS (EI, 70 eV): m/z=377 (M^+, 39), 311 (99), 307 (82), 294 (28), 142 (12), 102 (17), 83 (69), 71 (100), 42 (50), 28 (67). Anal. Calcd for $C_{21}H_{20}HN_5$ (377.87): C, 66.75; H, 5.33; N, 18.53; found: C, 66.71; H, 5.30; N, 18.51.

4.5.11. 2-(4-Bromophenyl)-5-hydrazino-imidazo[1,2-*c*]quinazoline (9a). Compound **7g** (1.85 g, 5.0 mmol) was refluxed in an ethanol solution (80 mL) of hydrazine hydrate (15 mL) for 16 h. After cooling, a precipitate formed which was separated by filtration, washed with water and dried in vacuo. Yield: 1.45 g (82%), yellow rods (EtOH), mp 254 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=759 (s), 830 (m), 1008 (m), 1284 (m), 1427 (s), 1475 (s), 1521 (s), 1653 (s), 3139 (m). ^1H NMR (300 MHz, DMSO-d_6): δ=7.31–7.91 (m, 8H, Ar-H), 8.56 (s, 1H, 3-H, Hetar), 10.15 (s, br, 2H, NH_2). ^{13}C NMR (50 MHz, DMSO-d_6): δ=114.6, 120.7, 122.2, 122.8, 124.3, 127.2, 129.2, 131.3, 132.6, 142.0, 143.2, 144.1. MS (EI, 70 eV): m/z=354 (M^+), 339 (82), 258 (25), 129 (33), 102 (18), 32 (23), 28 (100). Anal. Calcd for $C_{16}H_{12}N_5Br$ (354.20): C, 54.25; H, 3.41; N, 19.77; found: C, 54.31; H, 3.52; N, 19.82.

4.5.12. 2-(4-Chlorophenyl)-5-hydrazino-imidazo[1,2-*c*]quinazoline (9b). Compound **7j** (3.25 g, 10.0 mmol) was refluxed in an ethanol solution (160 mL) of hydrazine hydrate (30 mL) for 16 h. After cooling, a precipitate formed which was separated by filtration, washed with water and dried in vacuo. Yield: 2.50 g (81%), colourless prisms (EtOH), mp 231 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=763 (m), 835 (m), 1091 (m), 1283 (m), 1386 (m), 1431 (m), 1477 (s), 1526 (s), 1565 (m), 1620 (s), 1650 (s), 3061 (m), 3328 (m). ^1H NMR (300 MHz, $CDCl_3$): δ=7.33–7.97 (m, 8H, Ar-H), 8.49 (s, 1H, 3-H, Hetar). ^{13}C NMR (50 MHz, DMSO-d_6): δ=114.6, 122.8, 124.5, 126.9, 128.79, 128.83, 129.9, 132.1, 132.2, 142.0, 143.2, 144.2. MS (EI, 70 eV): m/z=309 (M^+, 15), 293 (100), 258 (18), 129 (25), 117 (12), 102 (13), 90 (22), 32 (15), 28 (69). Anal. Calcd for $C_{16}H_{12}N_5Cl$ (309.75): C, 62.04; H, 3.90; N, 22.61; found: C, 62.15; H, 4.01; N, 22.81.

4.5.13. 6-(4-Bromophenyl)-1,2,4-triazolo[4,3-*a*]-imidazo[1,2-*c*]quinazoline (10a). Compound **9a** (3.54 g, 10.0 mmol) was refluxed in formic acid (30 mL) for 4 h. The solution was concentrated under reduced vacuum to 10 mL. On cooling, a colourless solid precipitated, which was filtered off. The product was washed with water and recrystallized from EtOH. Yield: 2.98 g (82%), colourless prisms (EtOH), mp 246 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=747 (s), 1071 (m), 1135 (m), 1229 (s), 1478 (s), 2801 (s), 2916 (s), 3113 (s). ^1H NMR (300 MHz, $CDCl_3$): δ=7.55–7.93 (m, 8H, Ar-H), 8.35 (s, 1H, Hetar), 8.99 (s, 1H, 3-H, Hetar). ^{13}C NMR (50 MHz, DMSO-d_6): δ=116.5, 120.9, 127.3, 127.3, 127.4, 128.7, 131.6, 131.8, 140.5, 142.5, 142.9, 158.9, 161.5, 166.7, 167.0. MS (EI, 70 eV): m/z=363/365 (M^+ 100/96), 337, 339 (46/46), 257 (38), 129 (12), 102 (12), 28 (4). Anal. Calcd for $C_{17}H_{10}N_5Br$ (364.20): C, 56.06; H, 2.77; N, 19.23; found: C, 56.12; H, 2.98; N, 19.25.

4.5.14. 6-(4-Chlorophenyl)-1,2,4-triazolo[4,3-*a*]-imidazo[1,2-*c*]quinazoline (10b). Compound **9b** (3.09 g, 10.0 mmol) was refluxed in formic acid (30 mL) for 4 h. The workup was carried out as described for compound **10a**. Yield: 2.78 g (87%), colourless needles (EtOH), mp 295 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=742 (s), 765 (s), 837 (m), 1091 (m), 1476 (s), 1503 (s), 1609 (s). ^1H NMR (300 MHz, $CDCl_3$): δ=7.43–7.96 (m, 8H, Ar-H), 8.34 (s, 1H, Hetar), 8.99 (s, 1H, 3-H, Hetar). MS (EI, 70 eV): m/z=319 (M^+, 100), 257 (24), 129 (6), 101 (3), 28 (24). Anal. Calcd for $C_{17}H_{10}N_5Cl$ (319.75): C, 63.86; H, 3.15; N, 21.90; found: C, 63.81; H, 3.70; N, 21.91.

4.5.15. 1-Methyl-6-(4-bromophenyl)-1,2,4-triazolo-[4,3-*a*]-imidazo[1,2-*c*]quinazoline (10c). Compound **9a** (3.54 g, 10.0 mmol) was refluxed in glacial AcOH (30 mL) for 4 h. The workup was carried out as described for compound **10a**. Yield: 3.21 g (85%), colourless prisms (EtOH), mp 338 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=743 (m), 834 (m), 1007 (m), 1443 (m), 1476 (s), 1549 (s), 1593 (m), 1615 (s), 1638 (s), 3102 (m). ^1H NMR (300 MHz, $CDCl_3$): δ=2.17

(s, 1H, Me), 7.59–7.90 (m, 8H, Ar-H), 8.50 (s, 1H, 3-H, Hetar). ^{13}C NMR (50 MHz, DMSO-d_6): δ=21.0, 107.3 114.6, 120.7, 12.2, 122.9, 124.5, 127.2, 130.0, 131.8, 132.6, 142.0, 143.2, 144.2, 144.3, 171.8. MS (EI, 70 eV): m/z=377 (M^+, 100), 257 (84), 129 (16), 114 (7), 102 (22), 77 (10), 28 (2). Anal. Calcd for $C_{18}H_{12}N_5Br$ (378.23): C, 57.16; H, 3.10; N, 18.52; found: C, 57.18; H, 3.23; N, 18.52.

4.5.16. 1-Methyl-6-(4-chlorophenyl)-1,2,4-triazolo-[4,3-*a*]-imidazo[1,2-*c*]quinazoline (10d). Compound **9b** (3.54 g, 10.0 mmol) in glacial AcOH (30 mL) was refluxed for 4 h. The workup was carried out as described for compound **10a**. Yield: 2.86 g (86%), yellow needles (EtOH), mp 267 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$=762 (m), 834 (m), 1013 (m), 1090 (m), 1431 (s), 1475 (s), 1527 (s), 1648 (s), 3263 (m). ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.12 (s, 3H, Me), 7.42–8.08 (m, 8H, Ar-H), 8.31 (s, 1H, 3-H, Hetar). ^{13}C NMR (50 MHz, DMSO-d_6): δ=107.8, 114.5, 122.1, 122.8, 124.4, 126.9, 127.1, 128.6, 128.8, 129.9, 132.2, 142.0, 143.0, 144.1, 144.2. MS (EI, 70 eV): m/z=334 (M^+, 7), 332 (29), 294 (9), 293 (16), 292 (21), 256 (10), 123 (21), 82 (10), 44 (44), 28 (100). Anal. Calcd for $C_{18}H_{12}N_5Cl$ (333.72): C, 64.77; H, 3.62; N, 20.98; found: C, 64.68; H, 3.75; N, 21.01.

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