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Synthesis of 2-oxo-2,3,5,6-tetrahydro-5-thioxoimidazo[1,2-*c*]-quinazolines by one-pot cyclization of α-aminocarboxylic esters with 2-(isothiocyanato)benzonitrile (ITCB)

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Abstract—The cyclization of 2-(isothiocyanato)benzonitrile with α-aminocarboxylic esters and acids afforded a variety of 2-oxo-2,3,5,6-tetrahydro-5-thioxo-imidazo[1,2-*c*]quinazolines with very good regioselectivity.

1. Introduction

2-(Isothiocyanato)benzonitrile (ITCB) represents a versatile synthetic building block.[1] In recent years, one-pot cyclizations of ITCB with a number of nucleophiles have been reported. Recently, we and others have reported one-pot cyclizations of ITCB with hydrazine,[2] carboxylic hydrazides,[3,4] α-aminoketones,[5] and carbon nucleophiles.[6] In addition, one-pot cyclizations of ITCB-derived dichloroisocyanides have been reported.[7,8] Recently, we reported the synthesis of 2-oxo-2,3,5,6-tetrahydro-5-thioxo-imidazo[1,2-*c*]quinazolines by one-pot cyclization of ITCB with α-aminocarboxylic esters.[9] Herein, we report full details of this work and studies related to the preparative scope. Notably, functionalized quinazolines are of pharmacological relevance and show antihypertonic, antirheumatic, antianaphylactic, antiasthmatic, tranquilizing, neuro-stimulating, and benzodiazepine binding activity.[10] In addition, they represent useful synthetic building blocks.

2. Mechanism and optimization

The reaction of ethyl glycinate (**2a**) with ITCB (**1a**) afforded—based on MS data and elemental analysis—a tricyclic cyclization product. The formation of 2-oxo-2,3,5,6-tetrahydro-5-thioxoimidazo[1,2-*c*]quinazoline **3a** or its isomer *iso*-**3a** can be discussed. 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 group onto the ester group (Scheme 1). The formation of *iso*-**3a** 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 ester. Based on structural investigations (vide infra), we believe that **3a** is formed in the reaction, although the structure *iso*-**3a** cannot be completely ruled out.

The best yields were obtained when a two phase system of a CH_2Cl_2 solution of the starting materials and of an aqueous solution of Na_2CO_3 was stirred for 10 min at 20 °C (formation of **A**) and subsequently refluxed for 20 min (formation of **B**). After aqueous work-up, an *i*PrOH solution of **B** was refluxed (formation of **3a**). The yield of **3a** decreased when the CH_2Cl_2 solution was refluxed immediately without stirring at 20 °C. In contrast, intermediate **A** was isolated when the reaction was carried out at 20 °C without reflux. The yield of **3a** dropped and intermediate **B** was isolated when the *i*PrOH solution was not refluxed for sufficient time. The reaction could be also carried out as a one-pot reaction without isolation of **B**. However, the yield dropped (36%) compared to the sequential procedure (58%).

Keywords: Amino acids; Cyclizations; Domino reactions; Isothiocyanates; Regioselectivity.
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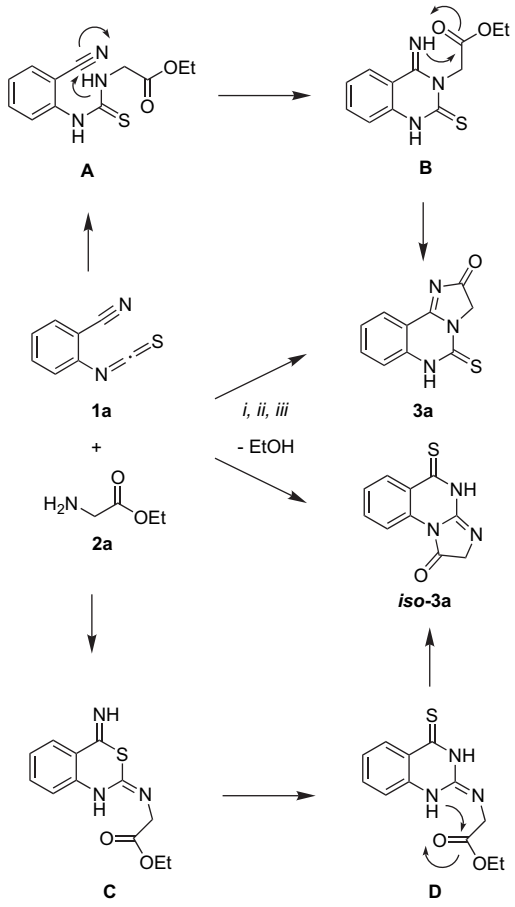
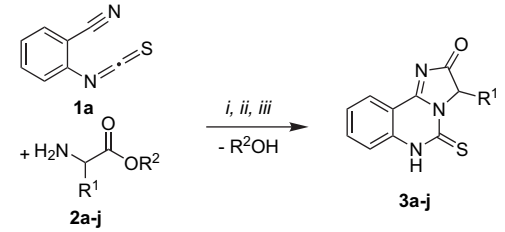


Scheme 1. Possible mechanistic pathways of the cyclization of ITCB (**1a**) with ethyl glycinate: (i) Na_2CO_3, H_2O, CH_2Cl_2, 20 °C, 10 min; (ii) reflux, 20 min, isolation of crude intermediate **B**; (iii) *i*PrOH, reflux, 10 h.

3. Scope and limitations

The reaction of ITCB with ethyl alanate furnished the 2-oxo-2,3,5,6-tetrahydro-5-thioxoimidazo[1,2-*c*]quinazoline **3b**, albeit in only 21% yield (Scheme 2, Table 1). The cyclization of ITCB with the amino acid alanine gave **3b** in 45% yield. The cyclization of ITCB with methyl 2-aminobutyrate afforded **3c**. The cyclization of ITCB with ethyl valinate and valine afforded **3d** in 77 and 43% yield, respectively. 5-Thioxoimidazo[1,2-*c*]quinazoline **3e** was prepared from methyl leucinate. The cyclization of ITCB with ethyl 2-amino-4-cyclohexylbutyrate gave the quinazoline **3f**. Heterocycles **3g** and **3h** were prepared from methyl phenylalanate ester and ethyl 2-phenylglycinate, respectively. The reaction of



Scheme 2. Synthesis of **3a–j**: (i) Na_2CO_3, H_2O, CH_2Cl_2, 20 °C, 10 min; (ii) reflux, 20 min, isolation of crude **B**; (iii) *i*PrOH, reflux, 10 h.

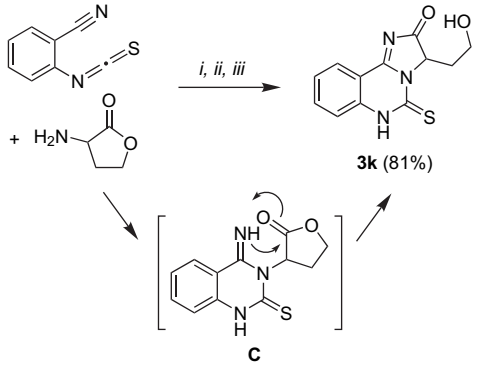
Table 1. Products and yields

3	R^1	R^2	% (3)[a]
a	H	Et	58
b	Me	Et	21
b	Me	H	45
c	Et	Me	20
d	*i*Pr	Et	77
d	*i*Pr	H	43
e	*i*Bu	Me	86
f	$(CH_2)_2$(*c*Hex)	Et	81
g	Bn	Me	35
h	Ph	Et	62
i	CO_2Et	Et	60
j	CH_2CO_2Bn	Bn	84

[a] Yields of isolated products.

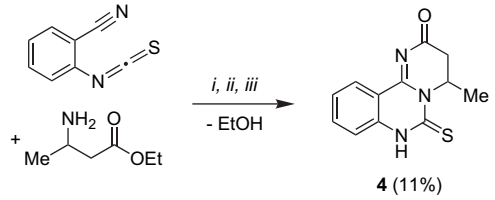
ITCB with diethyl 2-aminomalonate and dibenzyl aspartate gave the ester substituted quinazolines **3i** and **3j**, respectively. Notably, racemic products were isolated when enantiomerically pure starting materials were used, due to racemization.

The reaction of α-amino-γ-butyrolactone with ITCB afforded 3-(2-hydroxyethyl)-5-thioxoimidazo[1,2-*c*]quinazolin-2-one **3k**. The formation of **3k** can be explained by attack of the amino group onto the isothiocyanate, subsequent cyclization by attack of the amino group onto the nitrile (intermediate **C**), and subsequent nucleophilic attack of the imino group onto the lactone ring and cleavage of the latter (Scheme 3).



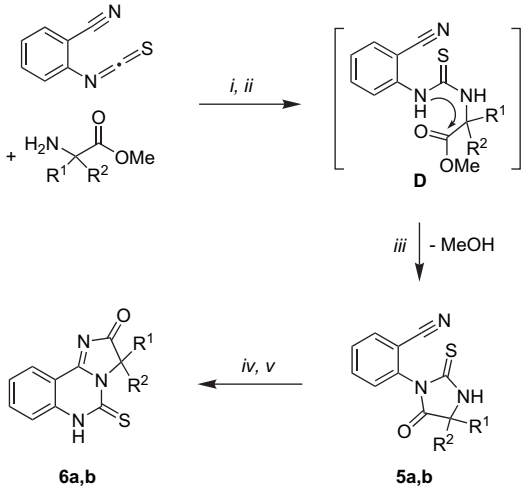
Scheme 3. Synthesis of **3k**: (i) Na_2CO_3, H_2O, CH_2Cl_2, 20 °C, 10 min; (ii) reflux, 20 min, isolation of crude **C**; (iii) *i*PrOH, reflux, 10 h.

The reaction of ITCB with racemic ethyl 3-aminobutyrate (**4**) afforded the racemic pyrimidinone **5**, albeit, in only 11% yield (Scheme 4). The final cyclization step (attack of the imino group onto the ester group) proved to be problematic. The yield could *not* be improved by extension of the reaction time or by variation of the concentration.



Scheme 4. Synthesis of **4**, conditions: (i) Na_2CO_3, H_2O, CH_2Cl_2, 20 °C, 10 min; (ii) reflux, 20 min; (iii) *i*PrOH, reflux, 10 h.

The reaction of ITCB with methyl 2-amino-2-methylpropionate and methyl 1-aminocyclohexylcarboxylate afforded 2-thioxoimidazolidinones **5a** and **5b** (Scheme 5, Table 2). The formation of **5a**,**b** can be explained by attack of the amino group onto the isothiocyanate and subsequent cyclization by attack of the ITCB-derived amino group onto the ester. The change in the mechanism can be explained by (a) the steric hindrance of the 2-amino-2-methylpropionate and (b) Thorpe–Ingold effect. Treatment of **5a**,**b** with an aqueous solution of sodium hydroxide afforded 2-oxoimidazo[1,2-*c*]-quinazolines **6a**,**b** by ring cleavage to give a carboxylic acid, attack of the amino group onto the nitrile, and subsequent attack of the imino group onto the carboxylic acid.



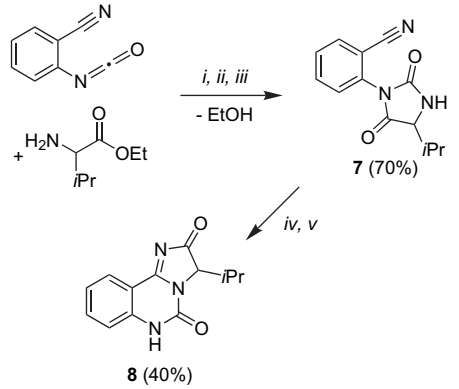
Scheme 5. Synthesis of **5a**,**b** and **6a**,**b**: (i) Na_2CO_3, H_2O, CH_2Cl_2, 20 °C, 10 min; (ii) reflux, 20 min, isolation of **D**; (iii) *i*PrOH, reflux, 10 h; (iv) NaOH, H_2O (4%), 20 °C, 24 h; (v) H_2O, HCl.

Table 2. Products and yields

5,6	R^1	R^2	% (**5**)[a]	% (**6**)[a]
a	Me	Me	40	80
b	–$(CH_2)_5$–		40	35

[a] Isolated yields.

The reaction of ethyl valinate with 2-isocyanatobenzonitrile—the oxa-analog of ITCB—afforded the imidazolidine-2,5-dione **7** (Scheme 6). Treatment of **7** with an aqueous solution of NaOH afforded the 2,5-dioxo-imidazo[1,2-*c*]quinazoline **8**. The formation of **7** and **8** follows the mechanism as discussed for the formation of **5a**,**b** and **6a**,**b**.



Scheme 6. Synthesis of **8**: (i) NEt_3, CH_2Cl_2, 20 °C, 10 min; (ii) reflux, 40 min, isolation of intermediate; (iii) *i*PrOH, NH_4OH, reflux, 48 h; (iv) NaOH, H_2O (4%), 20 °C, 24 h; (v) HCl, H_2O.

4. Structure elucidation

The structures of products **3a**–**j** were assigned based on the similarity of their NMR spectroscopic data, on a detailed structural analysis of **3g** and **6a**, and on an X-ray crystal structure analysis of **6a** (vide infra). The NMR signals of **3g** were assigned by DEPT and two-dimensional ^{1}H–^{1}H COSY, ^{1}H–^{1}H NOESY, and ^{1}H–^{13}C correlation spectra (HSQC, HMBC). In the HMBC spectrum cross peaks were found for C-11 with H-3, H-7, and H-10; as well as NH with CS and C-10a, which confirm the given structure. The alternative structure given in Figure 1 can be excluded based on the HMBC spectrum in which a correlation was found between the NH proton and the signal for the quaternary aromatic carbon atom C-10a at δ=110.7. Furthermore, the NMR data of **3g** are in best agreement with those assigned for compound **6a**. All derivatives **3a**–**k** exhibit very similar IR absorptions (C=O), ^{13}C NMR data (C=O and C=S groups and carbon atoms C-6a, C-8, C-9, C-7, C-10a, and C-3 of the quinazoline moiety), and ^{1}H NMR data (protons 3-H and NH) (Fig. 1, Table 3).

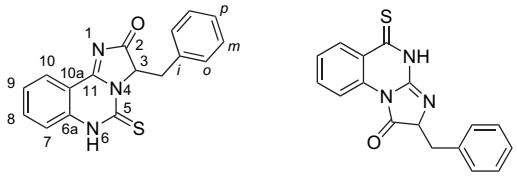


Figure 1. Atom numbering of **3g** for NMR signal assignment.

The structures of products **6a**,**b** were assigned based on the similarity of their NMR spectroscopic data, on a detailed structural analysis of **6a**, and on an X-ray crystal structure analysis of **6a**. The NMR signals of **6a** were assigned by DEPT and two-dimensional ^{1}H–^{1}H COSY, ^{1}H–^{1}H NOESY, and ^{1}H–^{13}C correlation spectra (HSQC, HMBC). In the HMBC spectrum cross peaks were found for NH with C=S, C-7, C-10a, and C-6a; C-11 with H-10 and H-7 (^4J); and Me (protons) with C-2 and C-3 (Fig. 2). In the NOESY spectrum cross peaks were found for the NH proton with H-7. No other correlations besides this for the aromatic protons were observed. The structure of **6a** was independently confirmed by X-ray crystal structure analysis (Fig. 3).[11]

In conclusion, we have reported the synthesis of 2-oxo-2,3,5,6-tetrahydro-5-thioxoimidazo[1,2-*c*]quinazolines based on the cyclization reactions of 2-(isothiocyanato)benzonitrile with α-aminocarboxylic esters.

5. Experimental

5.1. General

All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For ^{1}H and ^{13}C

Table 3. Characteristic spectroscopic features of **3a–k**, **6a**, and **8**

Nr.	$\tilde{\nu}$(C=O) (cm^{-1})	δ (ppm) 3-H	δ (ppm) NH	δ (ppm) C-3	δ (ppm) C=O	δ (ppm) C=S	δ (ppm) C-6a	δ (ppm) C-8	δ (ppm) C-9	δ (ppm) C-7	δ (ppm) C-10a
3a	1746, 1627	4.48	13.85	53.6	184.4	168.3	139.8	137.0	125.6	116.3	111.0
3b	1743, 1624	4.57	13.24	59.7	188.4	168.5	139.6	137.0	125.0	115.9	111.2
3c	1741, 1624	4.64	13.20	64.4	187.6	168.8	139.7	137.1	125.1	116.0	110.8
3d	1733, 1627	4.51	13.25	67.9	186.5	168.5	139.7	137.1	125.2	116.1	110.9
3e	1746, 1627	4.62	13.25	62.4	187.9	168.5	139.6	137.0	125.1	115.9	110.9
3f	1752, 1624	4.63	13.25	63.8	187.7	168.6	139.6	137.1	125.1	116.0	110.8
3g	1736, 1624	4.89	13.30	64.8	187.2	169.1	139.6	137.5	125.5	116.2	110.7
3h	1743	5.64	13.28	67.2	185.1	169.4	139.9	137.3	125.1	116.0	111.0
3i	1752, 1625	5.38	13.65	66.2	179.1	169.1	139.9	138.1	125.7	116.4	110.2
3j	1744, 1625	4.83	13.26	60.0	186.6	168.8	139.5	137.1	125.2	116.0	111.0
3k	1717, 1624	4.64	13.18	61.7	187.8	168.7	139.5	136.9	125.0	115.8	111.0
6a	1729, 1627	—	13.13	67.4	191.6	169.0	139.8	136.8	125.3	115.9	111.7
8	1745/1728, 1628	4.39	13.79	64.7	187.2	171.9	141.2	136.7	123.3	115.8	109.1

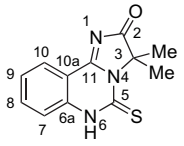


Figure 2. Atom numbering of **6a** for NMR signal assignment.

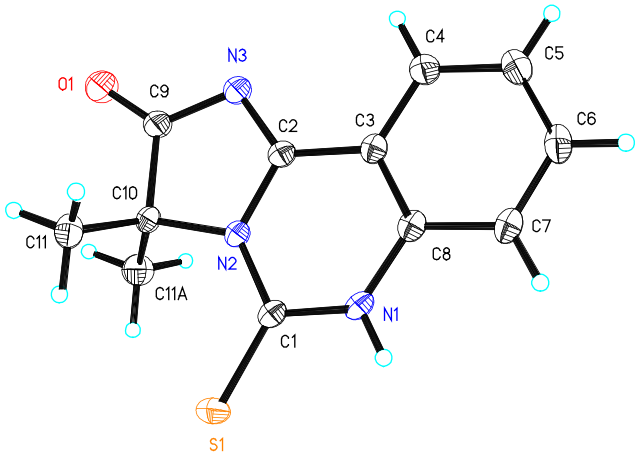


Figure 3. ORTEP plot of **6a**. The thermal ellipsoids of 50% probability are shown for the non-hydrogen atoms.

NMR, the deuterated solvents indicated were used. The ^{1}H NMR (300.13 MHz) and ^{13}C NMR (75.9 MHz) were recorded on a Bruker spectrometer ARX 300. In addition to the routine measurements, spectra of **3g** and **6a** were measured on a Bruker Spectrometer AVANCE 500 (^{1}H: 500.13 MHz and ^{13}C: 125.8 MHz). Calibration of spectra was carried out on the solvent signals (DMSO-d_6: δ ^{1}H=2.50, δ ^{13}C=39.7). 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.

5.1.1. 5-Thioxo-5,6-dihydroimidazo[1,2-*c*]quinazolin-2-one (3a). 2-(Isothiocyanato)benzonitrile (1.00 g, 6.4 mmol) and ethyl glycinate hydrochloride (1.21 g, 6.4 mmol) were suspended in dichloromethane (40 ml). A solution of sodium carbonate (1.83 g in 12 ml water) was added and the mixture was stirred for 10 min at ambient temperature and for 10 min under reflux. After cooling to room temperature, a colorless precipitate was formed. The latter was filtered off, the organic and the aqueous layer were separated, and the latter was extracted with dichloromethane (2×20 ml). The combined organic layers were dried (Na_2SO_4), filtered, and the solvent of the filtrate was removed at reduced pressure. The residue and the precipitate were suspended in isopropanol (200 ml) and the mixture was refluxed for 12 h. The product was crystallized after cooling. Concentration of the mother liquor at reduced pressure gave a further amount of the product. Yield: 0.80 g (58%), brown roods (acetone), mp 320–323 °C (decomp.). IR (KBr): $\tilde{\nu}$=3105, 3071 (w), 3013, 2993, 2928, 2922, 2847 (m), 1746, 1636, 1627, 1601, 1554, 1529, 1479, 1424, 1342, 1306, 1255, 1226, 1175, 1067 (s), 945 (w), 756, 543 (s) cm^{-1}. ^{1}H NMR (DMSO-d_6, 300 MHz): δ=4.48 (s, 2H, CH_2), 7.41–7.48 (m, 2H, Ar), 7.84–8.07 (m, 2H, Ar), 13.85 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=53.6 (CH_2), 111.0 (C), 116.3, 125.6, 127.5, 137.0 (CH), 139.8, 168.1, 168.3 (C), 184.4 (C=O). MS (EI, 70 eV): *m/z* (%)=218 (13), 217 (M^+, 100), 171 (23), 161 (11), 160 (13), 143 (19), 129 (12), 102 (21). UV–vis (CH_3CN): λ_{max} (log ε)=246 (4.22), 249 (4.22), 267 (4.45), 292 (4.48), 350 (3.68). Anal. Calcd for $C_{10}H_7N_3OS$ (217.25): C, 55.29; H, 3.25; N, 19.34; found: C, 55.35; H, 3.33; N, 19.32.

5.1.2. 3-Methyl-5-thioxo-5,6-dihydroimidazo[1,2-*c*]-quinazolin-2-one (3b). Method A: from alanine (285 mg, 3.2 mmol), 2-(isothiocyanato)benzonitrile (500 mg, 3.2 mmol), TEA (1 ml) in ethanol/water (50 ml/5 ml), and 15 h reflux. Yield: 330 mg (45%). Method B: from ethyl alaninate hydrochloride (0.98 g, 6.4 mmol) and 2-(isothiocyanato)-benzonitrile (1.000 g, 6.4 mmol). Yield: 0.300 g (21%), yellow prisms (ethanol), mp 314 °C (decomp.). IR (KBr): $\tilde{\nu}$=3016, 2982, 2938, 2912 (w), 1743, 1633, 1624 (s), 1600 (m), 1560, 1536, 1533, 1530, 1527, 1478 (s), 1459 (m), 1405, 1351, 1331, 1304 (s), 1284 (m), 1252, 1213, 1161, 1152 (s) cm^{-1}. ^{1}H NMR (DMSO-d_6, 300 MHz): δ=1.69 (d, J=7.1 Hz, 3H, CH_3), 4.57 (q, J=7.1 Hz, 1H, 3-H), 7.41–8.09 (m, 4H, Ar), 13.24 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=14.9 (CH_3), 59.7 (C-3), 111.2 (C), 115.9, 125.0, 127.4, 137.0 (CH), 139.6, 168.0, 168.5 (C), 188.4 (C=O). MS (EI, 70 eV): *m/z* (%)=232 (16), 231 (M^+, 100), 216 (17), 198 (39), 171 (22), 161 (20), 160 (18), 143 (24), 102 (18). UV–vis (CH_3CN): λ_{max} (log ε)=251 (4.18), 268 (4.42), 295 (4.49), 352 (3.60). Anal. Calcd for

$C_{11}H_9N_3OS$ (231.28): C, 57.13; H, 3.92; N, 18.17; found: C, 57.02; H, 4.12; N, 17.73.

5.1.3. 3-Ethyl-5-thioxo-5,6-dihydroimidazo[1,2-*c*]quinazolin-2-one (3c). Method B: from methyl 2-aminobutyrate hydrochloride (0.49 g, 3.2 mmol) and 2-(isothiocyanato)-benzonitrile (0.500 g, 3.2 mmol). Yield: 0.15 g (20%), colorless prisms (ethanol), mp 260–264 °C (decomp.). IR (KBr): $\tilde{\nu}$=3075, 3017 (w), 2965, 2938, 2918, 2879 (m), 1741, 1624 (s), 1602 (m), 1526, 1477 (s), 1465 (m), 1405 (s), 1351, 1338 (m), 1280 (s), 1257 (m), 1234 (w), 1210 (s), 1154 (m), 1078 (w) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ=0.67 (t, J=7.4 Hz, 3H, CH_3), 2.11 (m, 1H, CH_2), 2.71 (m, 1H, CH_2), 4.64 (dd, J=6.3, 2.7 Hz, 1H, 3-H), 7.43–7.48 (m, 2H, Ar), 7.85–8.09 (m, 2H, Ar), 13.20 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=6.6 (CH_3), 21.0 (CH_2), 64.4 (C-3), 110.8 (C), 116.0, 125.1, 127.5, 137.1 (CH), 139.7, 168.5, 168.8 (C), 187.6 (C=O). MS (EI, 70 eV): *m*/*z* (%)=246 (16), 245 (M^+, 100), 230 ([M−CH_3]$^+$, 50), 217 (71), 216 ([M−C_2H_5]$^+$, 32), 212 (42), 204 (20), 203 (27), 171 (22), 161 (51), 145 (10), 144 (13), 143 (26), 134 (13), 129 (17), 102 (20). UV–vis (CH_3CN): λ_{max} (log ε)=209 (4.38), 252 (4.20), 269 (4.44), 295 (4.51), 352 (3.63). Anal. Calcd for $C_{12}H_{11}N_3OS$ (245.30): C, 58.76; H, 4.52; N, 17.13; found: C, 58.84; H, 4.91; N, 17.07.

5.1.4. 3-Isopropyl-5-thioxo-5,6-dihydroimidazo[1,2-*c*]-quinazolin-2-one (3d). Method A: from valine (375 mg, 3.2 mmol), 2-(isothiocyanato)benzonitrile (500 mg, 3.2 mmol), TEA (1 ml) in ethanol/water (50 ml/5 ml), and 16 h reflux. Yield: 357 mg (43%). Method B: from ethyl valinate hydrochloride (1.16 g) and 2-(isothiocyanato)benzonitrile (1.000 g, 6.4 mmol). Yield: 1.28 g (77%), colorless prisms (isopropanol), mp 278–288 °C (decomp.). IR (KBr): $\tilde{\nu}$=3171, 3113, 3079, 3027, 2968 (m), 1733, 1627, 1557, 1529, 1476 (s), 1413 (m), 1348 (s), 1295 (m), 1260, 1207, 1149 (s), 1067, 969, 762 (m) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ=0.63 (d, J=6.8 Hz, 3H, CH_3), 1.20 (d, J=7.1 Hz, 3H, CH_3), 3.34–3.38 (m, 1H, C*H*(CH_3)$_2$), 4.51 (d, J=3.3 Hz, 1H, 3-H), 7.41–7.48 (m, 2H, Ar), 7.84–8.07 (m, 2H, Ar), 13.25 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=14.9 (CH_3), 16.9 (CH_3), 25.9 (*C*H(CH_3)$_2$), 67.9 (C-3), 110.9 (C), 116.1, 125.2, 127.6, 137.1 (CH), 139.7, 168.51, 168.52 (C), 186.5 (C=O). MS (EI, 70 eV): *m*/*z* (%)=260 (18), 259 (M^+, 100), 244 (38), 226 (23), 218 (11), 217 (70), 216 (55), 204 (36), 203 (82), 178 (36), 177 (15), 171 (11), 162 (25), 161 (59), 160 (10), 145 (19), 144 (15), 134 (14), 129 (15), 102 (25), 39 (10). UV–vis (CH_3CN): λ_{max} (log ε)=210 (4.52), 248 (4.20), 253 (4.21), 269 (4.44), 296 (4.51), 352 (3.63). Anal. Calcd for $C_{13}H_{13}N_3OS$ (259.33): C, 60.21; H, 5.05; N, 16.20; found: C, 60.61; H, 5.48; N, 16.46.

5.1.5. 3-Isobutyl-5-thioxo-5,6-dihydroimidazo[1,2-*c*]-quinazolin-2-one (3e). Method B: from methyl leucinate hydrochloride (1.16 g, 6.4 mmol) and 2-(isothiocyanato)-benzonitrile (1 g, 6.4 mmol). Yield: 1.51 g (86%), colorless prisms (isopropanol), mp 250–264 °C (decomp.). IR (KBr): $\tilde{\nu}$=3176, 3108, 3022 (w), 2960 (m), 1746, 1627 (s), 1601 (m), 1550, 1520, 1474 (s), 1402, 1346, 1334, 1221, 1195 (m), 1151 (s) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ=0.82 (d, J=6.7 Hz, 3H, CH_3), 0.89 (d, J=6.5 Hz, 3H, CH_3), 1.86 (m, 1H, C*H*(CH_3)$_2$), 2.10–2.26 (m, 2H, CH_2), 4.62 (dd, J=8.2, 3.4 Hz, 1H, 3-H), 7.42–7.47 (m, 2H, Ar), 7.84–8.09 (m, 2H, Ar), 13.25 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=21.8, 23.21 (CH_3), 23.22 (CH), 36.1 (CH_2), 62.4 (C-3), 110.9 (C), 115.9, 125.1, 127.4, 137.0 (CH), 139.6, 168.2, 168.5 (C), 187.9 (C=O). MS (EI, 70 eV): *m*/*z* (%)=273 (M^+, 5), 230 (34), 217 (100), 161 (22), 102 (11), 71 (13). UV–vis (CH_3CN): λ_{max} (log ε)=247 (4.21), 252 (4.21), 269 (4.44), 296 (4.50), 353 (3.63). Anal. Calcd for $C_{14}H_{15}N_3OS$ (273.36): C, 61.51; H, 5.53; N, 15.37; found: C, 61.47; H, 5.70; N, 15.47.

5.1.6. 3-(2-Cyclohexylethyl)-5-thioxo-5,6-dihydroimidazo[1,2-*c*]quinazolin-2-one (3f). Method B: from ethyl 2-amino-4-cyclohexylbutyrate hydrochloride (1.60 g) and 2-(isothiocyanato)benzonitrile (1.000 g, 6.4 mmol). Yield: 1.69 g (81%), colorless prisms (ethanol), mp 278–295 °C (decomp.). IR (KBr): $\tilde{\nu}$=3105, 3016 (w), 2921, 2850, 1752, 1629, 1624 (s), 1602 (m), 1527, 1478 (s), 1449 (m), 1405, 1350 (s), 1336, 1289, 1264 (m), 1215, 1199 (s), 1153, 1072, 756 (m) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ=0.78–1.16 (m, 8H, CH_2), 1.59–1.63 (m, 5H, 2CH_2, CH), 2.11 (m, 1H, CH_2 ethyl), 2.65 (m, 1H, CH_2 ethyl), 4.63 (dd, J=6.5, 2.7 Hz, 1H, 3-H), 7.42–7.48 (m, 2H, Ar), 7.85–8.08 (m, 2H, Ar), 13.25 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=25.1, 25.6, 25.6, 25.9, 29.2, 32.4, 32.6 (CH_2), 36.6 (CH), 63.8 (C-3), 110.8 (C), 116.0, 125.1, 127.4, 137.1 (CH), 139.6, 168.5, 168.6 (C), 187.7 (C=O). MS (EI, 70 eV): *m*/*z* (%)=327 (M^+, 25), 295 (21), 294 (100), 232 (12), 230 (44), 219 (13), 218 (24), 217 (96), 204 (21), 203 (21), 198 (12), 178 (13), 161 (26), 55 (17), 41 (20). UV–vis (CH_3CN): λ_{max} (log ε)=247 (4.22), 252 (4.22), 269 (4.44), 295 (4.50), 352 (3.64). Anal. Calcd for $C_{18}H_{21}N_3OS$ (327.45): C, 66.03; H, 6.46; N, 12.83; found: C, 66.22; H, 6.45; N, 12.45.

5.1.7. 3-Benzyl-5-thioxo-5,6-dihydroimidazo[1,2-*c*]-quinazolin-2-one (3g). Method B: from methyl phenyl alaninate hydrochloride (1.38 g, 6.4 mmol) and 2-(isothiocyanato)benzonitrile (1.000 g, 6.4 mmol). Yield: 0.68 g (35%), yellow prisms (ethanol), mp 246–252 °C (decomp.). IR (KBr): $\tilde{\nu}$=3185, 3145, 3111, 3095, 3071, 3027, 2934 (w), 1736, 1624, 1550, 1521, 1478, 1404, 1342, 1216 (s), 1153 cm^{-1}. The atom numbering for NMR signal assignment is given in Figure 1. ^1H NMR (DMSO-d_6, 500 MHz): δ=3.28 (dd, $^2J_{CH_{2(a)},CH_{2(b)}}$=13.6 Hz, $^3J_{3,CH_{2(b)}}$= 2.5 Hz, 1H, $CH_{2(b)}$), 4.15 (dd, $^2J_{CH_{2(a)},CH_{2(b)}}$=13.6 Hz, $^3J_{3,CH_{2(a)}}$=6.3 Hz, 1H, $CH_{2(a)}$), 4.89 (dd, $^3J_{3,CH_{2(a)}}$= 6.3 Hz, $^3J_{3,CH_{2(b)}}$=2.5 Hz, 1H, 3-H), 7.03–7.15 (m, 5H, Ph), 7.34 (ddd, $^3J_{9,10}$=8.0 Hz, $^3J_{8,9}$=7.2 Hz, $^4J_{7,9}$=1.0 Hz, 1H, H-9), 7.41 (br d, $^3J_{7,8}$=8.2 Hz, 1H, H-7), 7.81 (ddd, $^3J_{7,8}$=8.2 Hz, $^3J_{8,9}$=7.2 Hz, $^4J_{8,10}$=1.5 Hz, 1H, H-8), 7.83 (dd, $^3J_{9,10}$=8.0 Hz, $^4J_{8,10}$=1.5 Hz, 1H, H-10), 13.30 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 125.8 MHz): δ=33.3 (CH_2), 64.8 (C-3), 110.7 (C-10a), 116.2 (C-7), 125.5 (C-9), 127.3 (*p*-Ph), 127.7 (C-10), 128.4 (*m*-Ph), 129.3 (*o*-Ph), 134.5 (*i*-Ph), 137.5 (C-8), 139.6 (C-6a), 168.8 (C-11), 169.1 (C=S), 187.2 (C-2). MS (EI, 70 eV): *m*/*z* (%)=308 (21), 307 (M^+, 100), 274 (17), 216 (71), 204 (20), 203 (61), 161 (20), 143 (12), 103 (19), 102 (18), 91 (31), 77 (15). UV–vis (CH_3CN): λ_{max} (log ε)=252 (4.20), 270 (4.42), 296 (4.46), 354 (3.60). Anal. Calcd for $C_{17}H_{13}N_3OS$ (307.36): C, 66.43; H, 4.26; N, 13.67; found: C, 66.19; H, 4.29; N, 13.98.

5.1.8. 3-Phenyl-5-thioxo-5,6-dihydroimidazo[1,2-*c*]quinazolin-2-one (3h). Method B: from ethyl phenyl glycinate hydrochloride (1.29 g, 6.4 mmol) and 2-(isothiocyanato)-benzonitrile (1.000 g, 6.4 mmol). Yield: 1.16 g (62%), colorless prisms (isopropanol), mp 295 °C (decomp.). IR (KBr): $\tilde{\nu}$=3164, 3109, 3073, 3026, 2962, 2956, 2922 (w), 1743, 1677, 1602, 1558, 1526, 1479 (s), 1455 (w), 1403, 1345, 1325 (m), 1296 (s), 1254, 1236 (w), 1210, 1186 (s), 1152 (s), 1061 (w) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ=5.64 (s, 1H, 3-H), 7.23–7.51 (m, 7H, Ar), 7.89–8.17 (m, 2H, Ar), 13.28 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=67.2 (C-3), 111.0 (C), 116.0, 125.1, 126.5, 127.7, 127.8, 128.5 (CH), 133.4 (C), 137.3 (CH), 139.9, 168.2, 169.4 (C), 185.1 (C=O). MS (EI, 70 eV): *m/z* (%)=294 (19), 293 (M^+, 100), 261 (13), 260 (63), 171 (15), 143 (21), 129 (10), 104 (12), 102 (15), 91 (11), 77 (13). UV–vis (CH_3CN): λ_{max} (log ε)=247 (4.28), 269 (4.47), 295 (4.50), 357 (3.66). Anal. Calcd for $C_{16}H_{11}N_3OS$ (293.35): C, 65.51; H, 3.78; N, 14.32; found: C, 65.82; H, 4.11; N, 14.34.

5.1.9. Ethyl 2-oxo-5-thioxo-2,3,5,6-tetrahydroimidazo[1,2-*c*]quinazolin-3-carboxylate (3i). Method B: from diethyl 2-aminomalonate hydrochloride (1.35 g, 6.4 mmol) and 2-(isothiocyanato)benzonitrile (1.000 g, 6.4 mmol). Yield: 1.11 g (60%), colorless prisms (isopropanol), mp 229–239 °C (decomp.). IR (KBr): $\tilde{\nu}$=3185 (m), 3121, 3081, 3022, 2982, 2959, 2934 (w), 1752, 1724, 1625 (s), 1598 (m), 1549, 1518 (s), 1479, 1409, 1345 (m), 1301 (s), 1241 (m), 1202, 1143 (s), 1078, 1023, 762, 565 (m) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ=1.22 (t, J=7.2 Hz, 3H, CH_3), 4.23 (q, J=7.2 Hz, 2H, CH_2), 5.38 (s, 1H, 3-H), 7.48–7.53 (m, 2H, Ar), 7.93–8.12 (m, 2H, Ar), 13.65 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=13.8 (CH_3), 62.1 (CH_2), 66.2 (C-3), 110.2 (C), 116.4, 125.7, 127.8, 138.1 (CH), 139.9, 162.4, 167.7 (C), 169.1, 179.1 (C=O). MS (EI, 70 eV): *m/z* (%)=290 (17), 289 (M^+, 100), 243 ([M−C_2H_6O]$^+$, 31), 217 (41), 216 ([M−$COOC_2H_5$]$^+$, 93), 215 (39), 171 (14), 160 (28), 143 (15), 134 (13), 129 (18), 103 (13), 102 (57), 90 (16), 76 (31), 65 (11), 64 (12). UV–vis (CH_3CN): λ_{max} (log ε)=209 (4.29), 247 (4.18), 269 (4.50), 294 (4.46), 358 (3.62). Anal. Calcd for $C_{13}H_{11}N_3O_3S$ (289.31): C, 53.97; H, 3.83; N, 14.52; found: C, 54.02; H, 4.26; N, 14.64.

5.1.10. Benzyl (2-oxo-5-thioxo-2,3,5,6-tetrahydroimidazo[1,2-*c*]quinazolin-3-yl)acetate (3j). Method A: from dibenzyl aspartate (714 mg, 3.2 mmol), 2-(isothiocyanato)-benzonitrile (500 mg, 3.2 mmol), TEA (1 ml) in ethanol/water (50 ml/5 ml), and 15 h reflux. Yield: 350 mg (30%). Method B: from dibenzyl aspartate toluenesulfonate (3.10 g, 6.4 mmol) and 2-(isothiocyanato)benzonitrile (1.000 g, 6.4 mmol). Yield: 1.97 g (84%), colorless platelets (ethanol), mp 233–234 °C (decomp.). ^1H NMR (DMSO-d_6, 300 MHz): δ=3.35–3.52 (m, 1H, CH_2COO), 3.90 (m, J=17.3, 5.9 Hz, 1H, CH_2COO), 4.83 (m, J=5.9, 3.3 Hz, 1H, 3-H), 4.95–5.07 (q(AB), J=12.4 Hz, 2H, OCH_2), 7.22–7.25 (m, 5H, phenyl), 7.43–7.48 (m, 2H, CH), 7.85–8.05 (m, 2H, CH), 13.26 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=32.9 (CH_2), 60.0 (C-3), 65.9 (OCH_2), 111.0 (C), 116.0, 125.2, 127.5, 127.7, 127.9, 128.2 (Ar–H), 135.4 (C), 137.1 (Ar–H), 139.5, 168.6, 168.8 (C), 169.0, 186.6 (C=O). IR (KBr): $\tilde{\nu}$=3175, 3116, 3082, 3031, 2979, 2953 (w), 1744, 1625 (s), 1603 (m), 1558, 1554, 1526 (s), 1479, 1406, 1355 (m), 1333 (s), 1283, 1254 (m), 1220, 1176 (s), 1146 (m), 1073 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=365 (M^+, 17), 274 (70), 260 (14), 259 (93), 257 (13), 256 (49), 232 (11), 231 (56), 230 (94), 229 (13), 228 (14), 217 (40), 204 (11), 203 (12), 202 (13), 198 (11), 161 (42), 143 (10), 102 (18), 91 (100), 71 (21), 66 (19), 43 (11). UV–vis (CH_3CN): λ_{max} (log ε)=269 (4.45), 295 (4.48), 354 (4.44). Anal. Calcd for $C_{19}H_{15}N_3O_3S$ (365.41): C, 62.45; H, 4.14; N, 11.50; found: C, 62.38; H, 4.29; N, 11.28.

5.1.11. 3-(2-Hydroxyethyl)-5-thioxo-5,6-dihydroimidazo[1,2-*c*]quinazolin-2-one (3k). Method B: from α-amino-γ-butyrolactone hydrobromide (1.16 g, 6.4 mmol) and 2-(isothiocyanato)benzonitrile (1.000 g, 6.4 mmol). Yield: 1.69 g (81%), colorless prisms (ethanol), mp 263–265 °C (decomp.). IR (KBr): $\tilde{\nu}$=3410, 3254, 3018 (w), 2962, 2940, 2918, 2860 (m), 1717, 1624 (s), 1602 (m), 1533 (s), 1480, 1426, 1405 (m), 1329 (s), 1286, 1238, 1221, 1201, 1156, 1084, 752 (m) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ=2.27–2.38 (m, 1H, CH_2), 2.70–2.81 (m, 1H, CH_2), 3.36–3.44 (m, 1H, CH_2), 4.47–4.50 (m, 1H, CH_2), 4.64 (dd, J=7.1, 2.6 Hz, 1H, 3-H), 7.41–7.47 (m, 2H, Ar–H), 7.83–8.08 (m, 2H, Ar–H), 13.18 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=30.6, 56.0 (CH_2), 61.7 (C-3), 111.0 (C), 115.8, 125.0, 127.5, 136.9 (CH), 139.5, 168.4, 168.7 (C), 187.8 (C=O). MS (EI, 70 eV): *m/z* (%)=261 ([M]$^+$, 1), 243 ([M−H_2O]$^+$, 4), 230 ([M−CH_2OH]$^+$, 6), 217 ([M−C_2H_3OH]$^+$, 25), 143 (2), 129 (3). UV–vis (CH_3CN): λ_{max} (log ε)=207 (4.33), 231 (4.07), 248 (4.18), 251 (4.18), 269 (4.37), 295 (4.40), 349 (3.64). Anal. Calcd for $C_{12}H_{11}N_3O_2S$ (261.30): C, 55.16; H, 4.24; N, 16.08; found: C, 55.35; H, 4.48; N, 15.79.

5.1.12. 4-Methyl-6-thioxo-3,4,5,6-tetrahydropyrimidino[2,3-*c*]quinazolin-2-one (4). Method B: from ethyl 3-aminobutyrate hydrochloride (0.84 g, 6.4 mmol) and 2-(isothiocyanato)benzonitrile (1.000 g, 6.4 mmol). Yield: 0.18 g (11%), colorless prisms (ethanol), mp 290–307 °C (decomp.). IR (KBr): $\tilde{\nu}$=3243, 3209, 3129, 3073, 3033, 2978, 2962 (w), 1687, 1621, 1606, 1549, 1528, 1510, 1486 (s), 1447 (m), 1403 (s), 1311, 1278 (m), 1261, 1175, 1155 (s), 1125, 1095 (m), 1081 (w), 1005 (m) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ=1.26 (d, J=6.6 Hz, 3H, CH_3), 2.45 (dd, J=15.0, 1.6 Hz, 1H, CH_2), 2.93 (dd, J=15.0, 6.6 Hz, 1H, CH_2), 5.78 (dq, J=6.6, 1.6 Hz, 1H, C*H*CH_3), 7.34–7.40 (m, 2H, Ar), 7.74–7.79 (m, 1H, Ar), 8.17–8.20 (m, 1H, Ar), 13.25 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=15.8 (CH_3), 35.8 (CH_2), 51.5 (*C*HCH_3), 115.5, 124.9 (CH), 127.0 (C), 127.2, 135.7 (CH), 138.6, 153.2, 172.2 (C), 175.8 (C=O). MS (EI, 70 eV): *m/z* (%)=246 (12), 245 ([M]$^+$, 87), 230 ([M−CH_3]$^+$, 7), 212 (21), 204 (30), 203 (100), 161 (30), 145 (26), 144 (14), 143 (12). UV–vis (CH_3CN): λ_{max} (log ε)=209 (4.44), 231 (3.82), 252 (4.14), 271 (4.35), 298 (4.54), 349 (3.74). Anal. Calcd for $C_{12}H_{11}N_3OS$ (245.30): C, 58.76; H, 4.52; N, 17.13; found: C, 58.82; H, 4.88; N, 17.53.

5.1.13. 2-(4,4-Dimethyl-5-oxo-2-thioxoimidazolidin-1-yl)-benzonitrile (5a). Method B: from methyl 2-amino-isobutyrate hydrochloride (0.49 g, 3.2 mmol) and 2-(isothiocyanato)benzonitrile (0.50 g, 3.2 mmol). Yield: 0.31 g (39%), colorless prisms (ethanol), mp 260–264 °C

(decomp.). IR (KBr): $\tilde{\nu}$=3304 (s), 3114 (w), 2237 (m), 1764 (s), 1600 (w), 1517, 1460 (s), 1402 (m), 1278, 1183 (s), 1131, 766 (m), 634 (w), 599 (m) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ=1.46 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 7.65–8.06 (m, 4H, Ar), 10.91 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=22.9 (CH_3), 24.1 (CH_3), 61.4 ($C(CH_3)_2$), 112.4 (CN), 115.4 (C), 130.2, 131.2, 133.1, 134.1 (CH), 135.7, 176.4 (C), 179.2 (C=O). MS (EI, 70 eV): *m/z* (%)=246 (12), 245 (M^+, 100), 161 (48), 160 (80), 143 (8), 129 (11), 115 (10), 102 (24), 100 (16). Anal. Calcd for $C_{12}H_{11}N_3OS$ (245.30): C, 58.76; H, 4.52; N, 17.13; found: C, 58.71; H, 4.62; N, 17.18.

5.1.14. 3,3-Dimethyl-5-thioxo-5,6-dihydroimidazo[1,2-*c*]-quinazolin-2-one (6a). Compound **5a** (100 mg, 0.4 mmol) was dissolved in a mixture of an aqueous solution of sodium hydroxide (2%, 30 ml) and isopropanol (2 ml). The mixture was stirred for 12 h at room temperature, diluted with water, and acidified with concd hydrochloric acid. The solid precipitate was collected and dried. Yield: 65 mg (65%), colorless prisms (ethanol), mp 320–327 °C (decomp.). IR (KBr): $\tilde{\nu}$=3437 (w), 3246 (s), 3124, 2978 (w), 1729, 1627, 1601, 1543, 1510 (s), 1474, 1392, 1374, 1348 (m), 1303 (s), 1273, 1245 (m), 1210 (s), 1157 (m), 1135 (s), 1100 (m) cm^{-1}. The atom numbering for NMR signal assignment is given in Figure 2. ^1H NMR (DMSO-d_6, 500 MHz): δ=1.74 (s, 6H, 2Me), 7.42 (dt, $^3J_{9,10}$=8.0 Hz, $^3J_{8,9}$=7.2 Hz, $^4J_{7,9}$= 1.0 Hz, 1H, H-9), 7.43 (d, $^3J_{7,8}$=8.2 Hz, 1H, H-7), 7.84 (ddd, $^3J_{7,8}$=8.2 Hz, $^3J_{8,9}$=7.2 Hz, $^4J_{8,10}$=1.5 Hz, 1H, H-8), 8.11 (dd, $^3J_{9,10}$=8.0 Hz, $^4J_{8,10}$=1.5 Hz, 1H, H-10), 13.13 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 125.8 MHz): δ=21.1 (2Me), 67.4 (C-3), 111.7 (C-10a), 115.9 (C-7), 125.3 (C-9), 128.0 (C-10), 137.3 (C-8), 139.8 (C-6a), 168.1 (C-11), 169.0 (C=S), 191.6 (C-2). MS (EI, 70 eV): *m/z* (%)=246 (12), 245 (M^+, 100), 230 ([M−CH_3]$^+$, 32), 213 (13), 212 (84), 204 (14), 171 (39), 161 (31), 160 (11), 143 (32), 102 (21). UV–vis (CH_3CN): λ_{max} (log ε)=209 (4.44), 252 (4.18), 269 (4.40), 299 (4.51), 354 (3.60). $C_{12}H_{11}N_3OS$ (245.30).

5.1.15. 3-(2-Cyanophenyl)-2-thioxo-1,3-diazaspiro[4,5]-decan-4-one (5b). Method A: from 1-aminocyclohexanoic acid (460 mg, 3.2 mmol), 2-(isothiocyanato)benzonitrile (500 mg, 3.2 mmol), TEA (320 mg) in ethanol/water (50 ml/5 ml), and 16 h reflux. Yield: 0.32 g (35%), colorless prisms (isopropanol), mp 302–312 °C (decomp.). IR (KBr): $\tilde{\nu}$=3293, 3179, 2941, 2859, 2234 (w), 1767, 1513 (s), 1457, 1401, 1262 (m), 1225 (s), 1074 (m) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ=1.38–1.83 (m, 10H, 5CH_2), 7.64–7.72 (m, 2H, Ar), 7.86–8.05 (m, 2H, Ar), 11.21 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=20.4 (2CH_2), 24.2 (CH_2), 32.0 (CH_2), 33.3 (CH_2), 64.6 (C-3), 112.5 (CN), 115.6 (C), 130.3, 131.4, 133.3, 134.2 (CH), 135.8, 175.9 (C), 179.7 (C=O). MS (EI, 70 eV): *m/z* (%)=286 (17), 285 ([M]$^+$, 100), 256 (16), 230 (53), 229 (13), 161 (52), 160 (18), 143 (12), 129 (16), 102 (22), 97 (18), 96 (11). Anal. Calcd for $C_{15}H_{15}N_3OS$ (285.37): C, 63.13; H, 5.30; N, 14.73; found: C, 62.80; H, 5.72; N, 14.35.

5.1.16. Spirocyclohexan-1,3′-2-oxo-2-thioxo-4,5-dihydroimidazo[1,2-*c*]quinazoline (6b). Compound **5b** (100 mg, 0.35 mmol) was dissolved in a mixture of an aqueous solution of sodium hydroxide (2%, 50 ml) and of isopropanol (5 ml). The solution was stirred for 12 h at room temperature, diluted with water, and acidified with concd hydrochloric acid. The solid precipitate was collected and dried. Yield: 0.40 g (40%), colorless prisms (ethanol), mp 363–370 °C (decomp.). IR (KBr): $\tilde{\nu}$=3244, 3230 (m), 2930, 2863 (w), 1724, 1626, 1544, 1517 (s), 1482, 1454, 1391, 1354, 1323 (m), 1276, 1207, 1167, 1141, 1082 (m) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ=1.24–1.29 (m, 1H, CH_2), 1.54–1.71 (m, 5H, CH_2), 2.07–2.11 (m, 2H, CH_2), 3.52–3.60 (m, 2H, CH_2), 7.37–7.42 (m, 2H, Ar), 7.80–7.84 (m, 1H, Ar), 8.06–8.09 (m, 1H, Ar), 13.06 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=19.5 (2CH_2), 23.8 (CH_2), 25.7 (2CH_2), 68.8 (C-3), 111.5, 115.7 (C), 125.0, 127.6, 130.5, 136.9 (CH), 167.5 (C=N), 168.7 (C), 190.3 (C=O). MS (EI, 70 eV): *m/z* (%)=285 ([M]$^+$, 4), 198 (13), 118 (100), 91 (38). UV–vis (CH_3CN): λ_{max} (log ε)=211 (4.36), 254 (4.14), 270 (4.34), 301 (4.47), 354 (3.57). $C_{15}H_{15}N_3OS$ (285.37).

5.1.17. 2-(4-Isopropyl-2,5-dioxoimidazolidin-1-yl)benzonitrile (7). 2-(Isocyanato)benzonitrile (1.44 g, 10.0 mmol) and ethyl valinate hydrochloride (1.81 g 10.0 mmol) were suspended in 40 ml of dry dichloromethane. A dichloromethane solution (20 ml) of TEA (1.01 g, 10.0 mmol) was dropwise added with stirring. The mixture was stirred for 10 min at 20 °C and for 1 h under reflux. The solvent was removed in vacuo and the residue was washed with water (100 ml) and dried by exposure to air. Yield of noncyclized intermediate: 2.07 g (79%), colorless solid. IR (KBr): $\tilde{\nu}$=3329 (m), 2969, 2876 (w), 2219 (w, CN), 1739 (s), 1708 (m), 1655 (s), 1608, 1582 (m), 1555 (s), 1474, 1451, 1301, 1238, 1208, 1157 (m) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ=0.91 (d, J=7.2 Hz, 3H, CH_3), 0.93 (d, J=7.1 Hz, 3H, CH_3), 1.22 (t, J=7.1 Hz, 3H, CH_3 ester), 2.07–2.13 (m, 1H, CH), 4.11–4.20 (m, 3H, CH_2 ester, CH), 7.09–7.14 (m, 1H, Ar), 7.44 (d, J=8.3 Hz, 1H, NH), 7.56–7.71 (m, 2H, Ar), 8.09–8.11 (m, 1H, Ar), 8.72 (s, 1H, NH). An isopropanol solution (100 ml) of the open-chained product (1.200 g, 4.6 mmol) and TEA (3 ml) was refluxed for 24 h. The solvent was removed in vacuo. A few drops of methanol were added to the residue to give product **7** as a precipitate, which was filtered off. Yield: 0.78 g (70%), colorless prisms (isopropanol), mp 129.0–133.0 °C (decomp.). IR (KBr): $\tilde{\nu}$=3243, 3129, 2968 (m), 2233 (w, CN), 1778 (m), 1727 (s), 1497, 1459 (m), 1415 (s), 1350, 1297, 1237, 1177 (m) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ=0.95 (d, J=6.8 Hz, 3H, CH_3), 1.09 (d, J=7.0 Hz, 3H, CH_3), 2.11–2.19 (m, 1H, CH), 4.25 (m, 1H, CH), 7.55–7.69 (m, 2H, Ar), 7.84–7.89 (m, 1H, Ar), 8.00–8.03 (m, 1H, Ar), 8.74 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=15.9 (CH_3), 18.4 (CH_3), 29.8, 61.9 (CH), 111.4 (CN), 115.8 (C), 129.5, 129.8, 133.4, 134.1 (CH), 134.3 (C), 154.8, 172.1 (C, C=O). MS (EI, 70 eV): *m/z* (%)=243 ([M]$^+$, 9), 202 (11), 201 (100), 145 (32), 144 (17). 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 $C_{13}H_{13}N_3O_2$ (243.26): C, 64.19; H, 5.39; N, 17.27; found: C, 64.58; H, 5.48; N, 17.14.

5.1.18. 3-Isopropyl-2,5-dioxo-5,6-dihydroimidazo[1,2-*c*]quinazoline (8). Compound **7** (0.500 g, 2.0 mmol) was dissolved in a mixture of an aqueous solution of sodium hydroxide (4%, 100 ml) and isopropanol (5 ml). The mixture was stirred over night at room temperature, diluted with water, and acidified with concd hydrochloric acid. The solid

precipitate was collected and dried. Yield: 0.34 g (68%), colorless prisms (isopropanol), mp 258–265 °C (decomp.). IR (KBr): $\tilde{\nu}$=3211, 3154 (w), 3101, 3085, 3058, 3019, 2966, 2907, 2882 (m), 1745, 1728, 1705, 1628, 1601, 1562, 1519, 1487, 1449 (s), 1353 (m), 1317 (s), 1258 (w), 1189, 1147 (m) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ=0.74 (d, J=6.9 Hz, 3H, CH_3), 1.15 (d, J=7.1 Hz, 3H, CH_3), 2.74–2.80 (m, 1H, CH), 4.39 (d, J=3.3 Hz, 1H, 3-H), 7.26–7.35 (m, 2H, Ar), 7.76–7.82 (m, 1H, Ar), 8.01–8.04 (m, 1H, Ar), 11.79 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ=16.0 (CH_3), 17.0 (CH_3), 27.4 ($CH(CH_3)_2$), 64.7 (CH, C-3), 109.1 (C), 115.8, 123.3, 127.7, 136.7 (CH), 141.2, 145.6 (C), 171.9, 187.2 (C=O). MS (EI, 70 eV): m/z (%)=243 (M^+, 0.4), 228 (12), 201 (75), 188 (14), 145 (15). UV–vis (CH_3CN): λ_{max} (log ε)= 231 (4.70), 252 (3.93), 262 (3.98), 277 (3.99), 290 (3.85), 335 (3.69). Anal. Calcd for $C_{13}H_{13}N_3O_2$ (243.26): C, 64.15; H, 5.35; N, 17.28; found: C, 64.29; H, 5.37; N, 17.46.

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References and notes

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11. Crystallographic data (excluding structure factors) for the structure in this paper (**6a**) have been deposited in the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-603359. Copies of these data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk or via www.ccdc.cam.ac.uk/conts/retrieving.html.