Two-Step Synthesis of 1,3-Disubstituted 3,4-Dihydro-4-thioxoquinazolin-2(1*H*)-ones from 1-Bromo-2-fluorobenzenes

by **Kazuhiro Kobayashi***, **Toshihide Komatsu**, **Yuki Yokoi**, and **Hisatoshi Konishi**

Division of Applied Chemistry, Department of Chemistry and Biotechnology, Graduate School of Engineering, Tottori University, 4-101 Koyama-minami, Tottori 680-8552, Japan (phone/fax: +81-857-315263; e-mail: kkoba@chem.tottori-u.ac.jp)

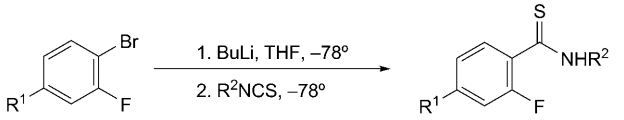
An efficient synthesis of 3-alkyl-3,4-dihydro-4-thioxobenzoquinazolin-2(1*H*)-ones **3** has been accomplished in two steps and in satisfactory yields from 1-bromo-2-fluorobenzenes **1**. Thus, the reaction of 1-fluoro-2-lithiobenzenes, generated by the Br/Li exchange between **1** and BuLi, with alkyl isothiocyanates, gives *N*-alkyl-2-fluorobenzothioamides **2**, which, in turn, react with a series of isocyanates in the presence of NaH to give the desired products **3**.

Introduction. – Some compounds having the 3,4-dihydro-4-thioxobenzoquinazolin-2(1*H*)-one skeleton have been reported to exhibit biological activities [1][2]. Perhaps the most common approach for their synthesis [1][3] to date is that reported by *Billon et al.* [1], involving a direct monothiation of the respective 1,2,3,4-tetrahydroquinazoline-2,4-diones with P_2S_5 [2b]. Development of a new and facile methodology for the preparation of these derivatives is, therefore, of considerable interest. The results of our investigation, which offer a two-step preparation of 1,3-disubstituted 3,4-dihydro-4-thioxobenzoquinazolin-2(1*H*)-ones **3** from commercially available 1-bromo-2-fluorobenzenes **1**, are described herein. It was predicted that Br/Li exchange between **1** and BuLi would generate 1-fluoro-2-lithiobenzenes. Subsequent treatment with isothiocyanates would give secondary 2-fluorobenzothioamides **2**, which, after deprotonation of the amide NH with an appropriate base and subsequent treatment with isocyanates, would furnish the desired compounds **3**.

Results and Discussion. – 1-Bromo-2-fluorobenzene (**1a**) was treated with BuLi under conditions reported previously by *Gilmann* and *Gorsich* [4] to generate 1-fluoro-2-lithiobenzene. Treatment of this lithiated product with EtNCS and subsequent usual aqueous workup gave the expected *N*-ethyl-2-fluorobenzothioamide (**2a**) in moderate-to-fair yield (*Scheme 1*). We reasoned that introduction of an electron-withdrawing group into the benzene nucleus would enable the stabilization of the corresponding Li product and give the desired benzothioamides in much better yields. As expected, 1-bromo-4-chloro-2-fluorobenzene (**1b**) delivered the corresponding desired products **2b**–**2d** in excellent yields, as indicated in *Scheme 1*, by treating its lithiated derivative with EtNCS, BnNCS, and PhNCS, respectively.

With *N*-monosubstituted 2-fluorobenzothioamides **2** in hand, we then conducted the reactions leading to 1,3-disubstituted 3,4-dihydro-4-thioxoquinazolin-2(1*H*)-ones **3**. The reaction conditions for the preparation of **3** involved adding isocyanates to a

Scheme 1

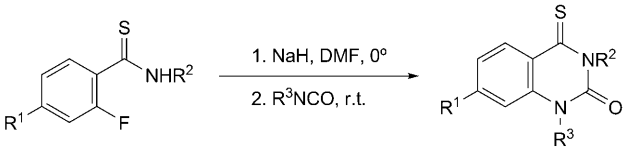


1a R^1 = H
1b R^1 = Cl

	R^1	R^2	Yield [%]
2a	H	Et	62
2b	Cl	Et	97
2c	Cl	Bn	92
2d	Cl	Ph	86

solution of the thioamide anion at room temperature, generated by treating **2** with NaH at 0° in DMF, as shown in *Scheme 2*, and the reactions were continued at the same temperature for the times listed in the *Table*. Addition of the thioamide anion to the isocyanate C-atom generates a carbamoyl amide anion intermediate, which undergoes intramolecular substitution of the F-atom in *ortho*-position to provide **3**. When the addition of isocyanates was carried out at 0°, the yield of the product decreased considerably in each case; the reason for this observation is not clear. With a Cl-atom at

Scheme 2



2 **3**

Table. *Preparation of 3,4-Dihydro-4-thioxoquinazolin-2(1*H*)-ones* **3**

Entry	**2**	Time	**3**	R^1	R^2	R^3	Yield[a]) [%]
1	**2a**	2 h	**3a**	H	Et	Ph	63
2	**2a**	2 h	**3b**	H	Et	3-Me–C_6H_4	66
3	**2a**	3 h	**3c**	H	Et	4-Cl–C_6H_4	53
4	**2b**	1 h	**3d**	Cl	Et	Ph	80
5	**2b**	1 h	**3e**	Cl	Et	3-Me–C_6H_4	76
6	**2b**	3 h	**3f**	Cl	Et	4-Br–C_6H_4	68
7	**2b**	overnight	**3g**	Cl	Et	4-MeO–C_6H_4	46
8	**2b**	30 min	**3h**	Cl	Et	Naphthalen-1-yl	80
9	**2b**	20 h	**3i**	Cl	Et	Bu	80
10	**2c**	1.5 h	**3j**	Cl	Bn	Ph	65
11	**2c**	10 min	**3k**	Cl	Bn	4-CF_3–C_6H_4	56
12	**2c**	24 h	**3l**	Cl	Bn	Bu	72
13	**2c**	1 d	**3m**	Cl	Bn	*t*-Bu	0[b])
14	**2d**	1 d	**3n**	Cl	Ph	Ph	0[b])

[a]) Yields of isolated products. [b]) The starting thioamides were recovered almost quantitatively.

C(4) of the *N*-ethyl-2-fluorobenzothioamide, the reaction times were shorter, and, in general, the product yields increased fairly (*Entries 4*, *5*, and *8*). The slight decrease in the yield of product **3f** by the use of 4-bromophenyl isocyanate is ascribed to a loss of material during the purification procedure due to its lower solubility in volatile organic solvents (*Entry 6*). An electron-rich isocyanate, such as 4-methoxyphenyl isocyanate, resulted in a somewhat poor yield of the desired product **3g** (*Entry 7*). Naphthalen-1-yl isocyanate also reacted well to give the corresponding product **3h** in good yield (*Entry 8*). Although the reaction with an aliphatic isocyanate, such as BuNCO, required a prolonged reaction time, it furnished the desired product **3i** in good yield (*Entry 9*). *N*-Benzyl-4-chloro-2-fluorobenzamide (**2c**) was successfully employed in the present reaction to give the corresponding products **3j**–**3l**, but in somewhat lower yields compared to those using **1b** (*Entries 10* and *12*); an inductively electron-withdrawing CF_3 substituent had a strong effect on the reaction rate, but the yield of the product **3k** was moderate (*Entry 11*). However, the use of *t*-BuNCO did not give the desired product **3m** at all, and the starting amide **2c** was recovered almost quantitatively (*Entry 13*). This is ascribed to the lower reactivity of *t*-BuNCO due to its steric bulkiness. The attempted preparation of 6-chloro-3,4-dihydro-1,3-diphenyl-4-thioxo-benzoquinazolin-2(1*H*)-one (**3n**) by reacting the amide anion intermediate generated from 4-chloro-2-fluoro-*N*-phenylbenzamide (**2d**) with PhNCO resulted in an almost quantitative recovery of the starting **2d**, even after an extended reaction time (*Entry 14*).

In conclusion, we have demonstrated that the reaction of 1-fluoro-2-lithiobenzenes with aliphatic isothiocyanates, followed by the addition–substitution reaction between the resulting *N*-alkyl-2-fluorobenzothioamides and a range of isocyanates, enables the efficient synthesis of 3-alkyl-3,4-dihydro-4-thioxoquinazolin-2(1*H*)-ones in two steps in satisfactory overall yields from commercially available 1-bromo-2-fluorobenzenes. The products of these reactions are of potential medicinal interest. The present approach offers significant advantages over the previously described methods because of the ready availability of the starting materials and simple operations.

Experimental Part

General. All of the org. solvents used in this study were dried on appropriate drying agents and distilled prior to use. All chemicals used in this study were commercially available. TLC: *Merck Kieselgel 60 PF_{254}*. Column chromatography (CC): *Wako Gel C-200E*. M.p.: *Laboratory Devices MEL-TEMP II* melting apparatus; uncorrected. IR Spectra: *Shimadzu FTIR-8300* spectrophotometer. ^{1}H-NMR Spectra: in $CDCl_3$ with TMS as an internal reference; *JEOL ECP500* FT NMR spectrometer operating at 500 MHz, or *JEOL LA400* FT NMR spectrometer operating at 400 MHz; ^{13}C-NMR spectra: in $CDCl_3$ with TMS as an internal reference; *JEOL ECP500* FT NMR spectrometer operating at 125 MHz. Low-resolution (LR) MS (EI, 70 eV): *JEOL JMS AX505 HA* spectrometer.

N-*Alkyl-2-fluorobenzothioamides* **2**. These compounds were prepared by reacting 1-fluoro-2-lithiobenzenes, generated from the respective 1-bromo-2-fluorobenzenes according to the procedure of *Gilmann et al.* [4], with the corresponding alkyl isothiocyanates in Et_2O at $-78°$, followed by usual aq. workup and subsequent purification by CC on silica gel.

N-*Ethyl-2-fluorobenzenecarbothioamide* (**2a**). Yellow solid. R_f (THF/hexane 1:7) 0.37. M.p. 62–64° (hexane). IR (KBr): 3235, 1221. ^{1}H-NMR (500 MHz): 1.38 (*t*, *J* = 7.3, 3 H); 3.86–3.92 (*m*, 2 H); 7.07 (*ddd*, *J* = 9.6, 8.2, 1.4, 1 H); 7.20 (*td*, *J* = 7.8, 1.4, 1 H); 7.38–7.42 (*m*, 1 H); 7.91 (br. *s*, 1 H); 8.15 (*ddd*, *J* = 8.2, 7.8, 1.4, 1 H). Anal. calc. for $C_9H_{10}FNS$ (183.25): C 58.99, H 5.50, N 7.64; found: C 58.88, H 5.51, N 7.47.

4-Chloro-N-*ethyl-2-fluorobenzenecarbothioamide* (**2b**). Yellow oil. R_f (THF/hexane 1:7) 0.29. IR (neat): 3239, 1605, 1219. ^{1}H-NMR (500 MHz): 1.37 (*t*, *J* = 7.3, 3 H); 3.84 – 3.89 (*m*, 2 H); 7.11 (*dd*, *J* = 11.9, 1.8, 1 H); 7.19 (*dd*, *J* = 8.7, 1.8, 1 H); 7.88 (br. *s*, 1 H); 8.12 (*t*, *J* = 8.7, 1 H). Anal. calc. for C_9H_9ClFNS (217.69): C 49.66, H 4.17, N 6.43; found: C 49.58, H 4.29, N 6.20.

4-Chloro-2-fluoro-N-*(phenylmethyl)benzenecarbothioamide* (**2c**). Yellow oil. R_f (THF/hexane 1:7) 0.27. IR (neat): 3231, 1605, 1217. ^{1}H-NMR (500 MHz): 5.00 (*d*, *J* = 5.0, 2 H); 7.09 (*dd*, *J* = 11.5, 1.8, 1 H); 7.20 (*dd*, *J* = 8.7, 1.8, 1 H); 7.34 – 7.39 (*m*, 5 H); 8.09 (br. *s*, 1 H); 8.13 (*t*, *J* = 8.7, 1 H). Anal. calc. for $C_{14}H_{11}ClFNS$ (279.76): C 60.10, H 3.96, N 5.01; found: C 60.15, H 4.06, N 4.96.

4-Chloro-2-fluoro-N-*phenylbenzenecarbothioamide* (**2d**). Yellow solid. R_f (Et_2O/hexane 1:2) 0.39. M.p. 106 – 108° (hexane/Et_2O). IR (KBr): 3246, 1604, 1209. ^{1}H-NMR (500 MHz): 7.18 (*dd*, *J* = 11.4, 1.4, 1 H); 7.25 (*d*, *J* = 8.7, 1 H); 7.33 (*t*, *J* = 7.3, 1 H); 7.46 (*dd*, *J* = 7.8, 7.3, 2 H); 7.75 (*d*, *J* = 7.8, 2 H); 8.15 (*t*, *J* = 8.7, 1 H); 9.26 (br. *s*, 1 H). Anal. calc. for $C_{13}H_9ClFNS$ (265.73): C 58.76, H 3.41, N 5.27; found: C 58.48, H 3.49, N 5.18.

*3-Ethyl-3,4-dihydro-1-phenyl-4-thioxoquinazolin-2(1*H*)-one* (**3a**). *General Procedure.* To a stirred suspension of NaH (60% in mineral oil; 33 mg, 0.84 mmol) in DMF (3 ml) at 0° was added a soln. of **2a** (0.15 g, 0.76 mmol) in DMF (1 ml). After the evolution of H_2 gas had ceased, PhNCO (91 mg, 0.79 mmol) was added, the mixture was stirred for 2 h at r.t., sat. aq. NH_4Cl (10 ml) was added, and the org. products were extracted with AcOEt three times (8 ml each). The combined extracts were washed with brine, dried (anh. Na_2SO_4), and concentrated by evaporation. The residual solid was recrystallized from hexane/CH_2Cl_2 to give **3a** (0.14 g, 63%). Yellow solid. M.p. 200 – 202°. IR (KBr): 1684, 1248. ^{1}H-NMR (500 MHz): 1.40 (*t*, *J* = 7.3, 3 H); 4.79 (*q*, *J* = 7.3, 2 H); 6.49 (*d*, *J* = 7.8, 1 H); 7.21 (*ddd*, *J* = 8.2, 7.3, 1.4, 1 H); 7.33 (*dd*, *J* = 8.2, 1.4, 2 H); 7.42 (*ddd*, *J* = 7.8, 7.3, 1.4, 1 H); 7.55 (*tt*, *J* = 7.3, 1.4, 1 H); 7.61 (*dd*, *J* = 8.2, 7.3, 2 H); 8.76 (*dd*, *J* = 8.2, 1.4, 1 H). ^{13}C-NMR: 11.48; 44.25; 115.49; 121.96; 123.78; 128.77; 129.46; 130.37; 133.35; 134.33; 136.41; 138.24; 148.03; 190.96. MS: 282 (100, M^+). Anal. calc. for $C_{16}H_{14}N_2OS$ (282.36): C 68.06, H 5.00, N 9.92; found: C 67.83, H 5.24, N 9.75.

*3-Ethyl-3,4-dihydro-1-(3-methylphenyl)-4-thioxoquinazolin-2(1*H*)-one* (**3b**). Yellow solid. M.p. 120 – 122° (hexane/CH_2Cl_2). IR (KBr): 1690, 1250. ^{1}H-NMR (500 MHz): 1.40 (*t*, *J* = 7.3, 3 H); 2.44 (*s*, 3 H); 4.78 (*q*, *J* = 7.3, 2 H); 6.51 (*d*, *J* = 8.2, 1 H); 7.12 (*d*, *J* = 8.7, 1 H); 7.13 (*s*, 1 H); 7.20 (*ddd*, *J* = 8.2, 7.3, 0.9, 1 H); 7.35 (*d*, *J* = 7.8, 1 H); 7.42 (*ddd*, *J* = 7.8, 7.3, 1.4, 1 H); 7.48 (*dd*, *J* = 7.8, 7.3, 1 H); 8.75 (*dd*, *J* = 8.2, 1.4, 1 H). ^{13}C-NMR: 11.46; 21.34; 44.23; 115.60; 121.90; 123.70; 125.62; 129.16; 130.13; 130.25; 133.26; 134.29; 136.27; 138.28; 140.60; 148.03; 190.94. MS: 296 (100, M^+). Anal. calc. for $C_{17}H_{16}N_2OS$ (296.39): C 68.89, H 5.44, N 9.45; found: C 68.70, H 5.61, N 9.20.

*1-(4-Chlorophenyl)-3-ethyl-3,4-dihydro-4-thioxoquinazolin-2(1*H*)-one* (**3c**). Yellow solid. M.p. 142 – 145° (MeOH). IR (KBr): 1688, 1248. ^{1}H-NMR (400 MHz): 1.39 (*t*, *J* = 7.3, 3 H); 4.77 (*q*, *J* = 7.3, 2 H); 6.50 (*dd*, *J* = 8.4, 0.7, 1 H); 7.23 (*ddd*, *J* = 8.4, 6.9, 1.1, 1 H); 7.29 (*d*, *J* = 8.8, 2 H); 7.45 (*ddd*, *J* = 8.4, 6.9, 1.4, 1 H); 7.59 (*d*, *J* = 8.8, 2 H); 8.75 (*dd*, *J* = 8.4, 1.4, 1 H). ^{13}C-NMR: 11.47; 44.26; 115.21; 122.01; 123.98; 130.28; 130.66; 133.50; 134.41; 134.85; 135.54; 137.92; 147.88; 190.86. MS: 316 (100, M^+). Anal. calc. for $C_{16}H_{13}ClN_2OS$ (316.81): C 60.66, H 4.14, N 8.84; found: C 60.42, H 4.21, N 8.91.

*7-Chloro-3-ethyl-3,4-dihydro-1-phenyl-4-thioxoquinazolin-2(1*H*)-one* (**3d**). Yellow solid. M.p. 142 – 145° (hexane/Et_2O). IR (KBr): 1688, 1250. ^{1}H-NMR (500 MHz): 1.39 (*t*, *J* = 7.3, 3 H); 4.75 (*q*, *J* = 7.3, 2 H); 6.48 (*d*, *J* = 1.8, 1 H); 7.17 (*dd*, *J* = 8.7, 1.8, 1 H); 7.32 (*d*, *J* = 7.3, 2 H); 7.58 (*t*, *J* = 7.3, 1 H); 7.63 (*t*, *J* = 7.3, 2 H); 8.69 (*d*, *J* = 8.7, 1 H). ^{13}C-NMR: 11.42; 44.31; 115.21; 120.47; 124.33; 128.63; 129.81; 130.60; 134.86; 135.90; 138.92; 141.10; 147.82; 189.87. MS: 316 (100, M^+). Anal. calc. for $C_{16}H_{13}ClN_2OS$ (316.81): C 60.66, H 4.14, N 8.84; found: C 60.71, H 4.19, N 8.79.

*7-Chloro-3-ethyl-3,4-dihydro-1-(3-methylphenyl)-4-thioxoquinazolin-2(1*H*)-one* (**3e**). Yellow solid. M.p. 135 – 137° (hexane/Et_2O). IR (KBr): 1701, 1250. ^{1}H-NMR (400 MHz): 1.38 (*t*, *J* = 7.3, 3 H); 2.46 (*s*, 3 H); 4.75 (*q*, *J* = 7.3, 2 H); 6.50 (*d*, *J* = 2.2, 1 H); 7.10 – 7.12 (*m*, 2 H); 7.16 (*dd*, *J* = 8.7, 2.2, 1 H); 7.37 (*dd*, *J* = 7.3, 0.7, 1 H); 7.51 (*ddd*, *J* = 7.8, 7.3, 1.1, 1 H); 8.68 (*d*, *J* = 8.7, 1 H). ^{13}C-NMR: 11.40; 21.37; 44.26; 115.28; 120.40; 124.24; 125.43; 129.00; 130.32; 130.61; 134.76; 135.75; 138.95; 140.86; 141.02; 147.81; 189.83. MS: 330 (100, M^+). Anal. calc. for $C_{17}H_{15}ClN_2OS$ (330.83): C 61.72, H 4.57, N 8.47; found: C 61.77, H 4.55, N 8.53.

*1-(4-Bromophenyl)-7-chloro-3-ethyl-3,4-dihydro-4-thioxoquinazolin-2(1*H*)-one* (**3f**). Yellow solid. M.p. 151 – 154° (hexane/Et_2O). IR (KBr): 1699, 1248. ^{1}H-NMR (500 MHz): 1.37 (*t*, *J* = 7.3, 3 H); 4.72 (*q*,

$J = 7.3$, 2 H); 6.48 (*d*, $J = 1.4$, 1 H); 7.17 (*dd*, $J = 9.2$, 1.4, 1 H); 7.21 (*d*, $J = 7.8$, 2 H); 7.76 (*d*, $J = 7.8$, 2 H); 8.67 (*d*, $J = 9.2$, 1 H). ^{13}C-NMR: 11.41; 44.31; 114.90; 120.49; 123.99; 124.54; 130.43; 133.89; 134.86; 134.99; 138.50; 141.22; 147.60; 189.73. MS: 394 (100, M^+). Anal. calc. for $C_{16}H_{12}BrClN_2OS$ (395.70): C 48.56, H 3.06, N 7.08; found: C 48.68, H 2.98, N 6.97.

*7-Chloro-3-ethyl-3,4-dihydro-1-(4-methoxyphenyl)-4-thioxoquinazolin-2(1*H*)-one* (**3g**). Yellow solid. M.p. 153–155° (hexane/CH_2Cl_2). IR (KBr): 1686, 1248. ^{1}H-NMR (500 MHz): 1.38 (*t*, $J = 7.3$, 3 H); 3.90 (*s*, 3 H); 4.74 (*q*, $J = 7.3$, 2 H); 6.54 (*d*, $J = 1.8$, 1 H); 7.10 (*d*, $J = 8.2$, 2 H); 7.15 (*dd*, $J = 8.2$, 1.8, 1 H); 7.22 (*d*, $J = 8.2$, 2 H); 8.17 (*d*, $J = 8.2$, 1 H). ^{13}C-NMR: 11.42; 44.34; 55.61; 115.31; 115.76; 120.46; 124.23; 128.30; 129.63; 134.82; 139.29; 141.08; 148.06; 160.27; 189.88. MS: 346 (100, M^+). Anal. calc. for $C_{17}H_{15}ClN_2O_2S$ (346.83): C 58.87, H 4.36, N 8.08; found: C 58.88, H 4.27, N 7.92.

*7-Chloro-3-ethyl-3,4-dihydro-1-(naphthalen-1-yl)-4-thioxoquinazolin-2(1*H*)-one* (**3h**). Yellow solid. M.p. 150–153° (hexane/Et_2O). IR (KBr): 1688, 1233. ^{1}H-NMR (500 MHz): 1.41 (*t*, $J = 7.3$, 3 H); 4.74–4.84 (*m*, 2 H); 6.30 (*d*, $J = 1.8$, 1 H); 7.16 (*dd*, $J = 9.2$, 1.8, 1 H); 7.46–7.52 (*m*, 3 H); 7.58 (*dd*, $J = 7.8$, 7.3, 1 H); 7.67 (*dd*, $J = 8.2$, 7.3, 1 H); 8.01 (*d*, $J = 8.2$, 1 H); 8.08 (*d*, $J = 8.2$, 1 H); 8.73 (*d*, $J = 8.7$, 1 H). ^{13}C-NMR: 11.49; 44.30; 115.28; 120.43; 121.49; 124.51; 126.02; 127.07; 127.11; 128.05; 128.96; 129.58; 130.49; 132.22; 134.87; 134.94; 139.05; 141.33; 147.71; 189.96. MS: 366 (100, M^+). Anal. calc. for $C_{20}H_{15}ClN_2OS$ (366.86): C 65.48, H 4.12, N 7.64; found: C 65.40, H 4.16, N 7.77.

*1-Butyl-7-chloro-3-ethyl-3,4-dihydro-4-thioxoquinazolin-2(1*H*)-one* (**3i**). Yellow solid. M.p. 61–64° (hexane). IR (neat): 1693, 1246. ^{1}H-NMR (500 MHz): 1.02 (*t*, $J = 7.3$, 3 H); 1.35 (*t*, $J = 7.3$, 3 H); 1.48 (*sext.*, $J = 7.3$, 2 H); 1.73 (*quint.*, $J = 7.3$, 2 H); 4.10 (*t*, $J = 7.3$, 2 H); 4.73 (*q*, $J = 7.3$, 2 H); 7.13 (*d*, $J = 1.8$, 1 H); 7.18 (*dd*, $J = 8.7$, 1.8, 1 H); 8.70 (*d*, $J = 8.7$, 1 H). ^{13}C-NMR: 11.39; 13.71; 20.03; 29.13; 44.20; 44.42; 113.59; 120.93; 122.87; 135.45; 137.33; 141.52; 147.92; 189.39. MS: 296 (100, M^+). Anal. calc. for $C_{14}H_{17}ClN_2OS$ (296.82): C 56.65, H 5.77, N 9.44; found: C 56.56, H 5.80, N 7.26.

*7-Chloro-3,4-dihydro-1-phenyl-3-(phenylmethyl)-4-thioxoquinazolin-2(1*H*)-one* (**3j**). Yellow solid. M.p. 188–191° (hexane/CH_2Cl_2). IR (KBr): 1688, 1204. ^{1}H-NMR (500 MHz): 5.94 (*s*, 2 H); 6.49 (*d*, $J = 1.8$, 1 H); 7.16 (*dd*, $J = 8.7$, 1.7, 1 H); 7.25 (*t*, $J = 7.3$, 1 H); 7.27–7.31 (*m*, 4 H); 7.53 (*d*, $J = 7.8$, 2 H); 7.56 (*t*, $J = 7.3$, 1 H); 7.61 (*dd*, $J = 7.8$, 7.3, 2 H); 8.67 (*d*, $J = 8.7$, 1 H). ^{13}C-NMR: 51.32; 115.28; 120.47; 124.45; 127.58; 128.30; 128.63; 128.81; 129.85; 130.61; 135.27; 135.86; 135.94; 138.91; 141.27; 148.39; 190.45. MS: 378 (100, M^+). Anal. calc. for $C_{21}H_{15}ClN_2OS$ (378.87): C 66.57, H 3.99, N 7.39; found: C 66.33, H 4.07, N 7.27.

*7-Chloro-3,4-dihydro-3-(phenylmethyl)-4-thioxo-1-[4-(trifluoromethyl)phenyl]quinazolin-2(1*H*)-one* (**3k**). Yellow solid. M.p. 221–223° (hexane/CH_2Cl_2). IR (KBr): 1703, 1126. ^{1}H-NMR (500 MHz): 5.92 (*s*, 2 H); 6.44 (*d*, $J = 1.8$, 1 H); 7.19 (*dd*, $J = 8.7$, 1.8, 1 H); 7.24–7.31 (*m*, 3 H); 7.47 (*d*, $J = 8.7$, 2 H); 7.52 (*d*, $J = 8.2$, 2 H); 7.89 (*d*, $J = 8.7$, 2 H); 8.68 (*d*, $J = 8.7$, 1 H). ^{13}C-NMR: 51.32; 114.85; 120.56; 124.84; 127.73; 127.81; 127.84; 128.36; 128.83; 129.56; 132.26; 135.54; 135.76; 138.21; 138.98; 141.50; 148.13; 190.27. MS: 446 (100, M^+). Anal. calc. for $C_{22}H_{14}ClF_3N_2OS$ (446.87): C 59.13, H 3.16, N 6.27; found: C 58.97, H 3.26, N 6.45.

*1-Butyl-7-chloro-3,4-dihydro-3-(phenylmethyl)-4-thioxoquinazolin-2(1*H*)-one* (**3l**). Yellow solid. M.p. 112–114° (hexane/CH_2Cl_2). IR (KBr): 1674, 1217. ^{1}H-NMR (500 MHz): 1.00 (*t*, $J = 7.3$, 3 H); 1.46 (*sext.*, $J = 7.3$, 2 H); 1.72 (*quint.*, $J = 7.3$, 2 H); 4.10 (*t*, $J = 7.3$, 2 H); 5.92 (*s*, 2 H); 7.14 (*s*, 1 H); 7.18 (*dd*, $J = 8.7$, 1.4, 1 H); 7.24 (*t*, $J = 7.3$, 1 H); 7.29 (*dd*, $J = 7.8$, 7.3, 2 H); 7.44 (*d*, $J = 7.8$, 2 H); 8.69 (*d*, $J = 8.7$, 1 H). ^{13}C-NMR: 13.70; 19.99; 29.09; 44.36; 51.52; 113.67; 120.91; 124.00; 127.46; 128.23; 128.31; 135.85; 135.97; 137.32; 141.72; 148.42; 190.03. MS: 358 (100, M^+). Anal. calc. for $C_{19}H_{19}ClN_2OS$ (358.89): C 63.59, H 5.34, N 7.81; found: C 63.81, H 5.30, N 7.69.

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REFERENCES

[1] F. Billon, C. Delchambre, A. Cloarec, E. Sartori, J.-M. Teulon, *Eur. J. Med. Chem*. **1990**, *25*, 121.
[2] a) M. S. Malamas, J. Millen, *J. Med. Chem*. **1991**, *34*, 1492; b) H. Kakuta, A. Tanatani, K. Hasegawa, Y. Hashimoto, *Chem. Pharm. Bull*. **2003**, *51*, 1273.
[3] G. Wagner, L. Rothe, *Pharmazie* **1971**, *26*, 271.
[4] H. Gilmann, R. D. Gorsich, *J. Am. Chem. Soc*. **1955**, *77*, 3919.

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