Synthesis of 1-Acyl-3,4-dihydroquinazoline-2(1*H*)-thiones by Cyclization of *N*-[2-(Isothiocyanatomethyl)phenyl] Amides Generated *in situ* from *N*-[2-(Azidomethyl)phenyl] Amides

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An efficient method for the preparation of 1-acyl-3,4-dihydroquinazoline-2(1*H*)-thiones **5** has been developed. The reaction of *N*-[2-(azidomethyl)phenyl] amides **3**, easily prepared by a three-step sequence starting with (2-aminophenyl)methanols, with Ph_3P, followed by CS_2, allowed generation of *N*-[2-(isothiocyanatomethyl)phenyl]-amide intermediates **4**, which underwent cyclization on treatment with NaH to furnish the corresponding desired products in generally good yields.

Introduction. – 3,4-Dihydroquinazoline-2(1*H*)-thione derivatives have attracted much attention, because some of them have been reported to exhibit biological activities [1]. This type of heterocycles have commonly been prepared by the reaction of 2-(aminomethyl)benzenamines with $CSCl_2$ [2]. Recently, a new type of derivatives, 4-alkylidene-3,4-dihydroquinazoline-2(1*H*)-thiones, have been synthesized by the reaction of 2-isothiocyanatobenzonitriles with carbon nucleophiles [3]. Some biologically active 1-acyl derivatives have also been prepared [4]. However, no general methods for the synthesis of 1-acyl derivatives have been reported so far. We envisaged that *N*-[2-(azidomethyl)phenyl] amides **3** could generate *N*-[2-(isothiocyanatomethyl)-phenyl] amides **4**, which would undergo cyclization to 1-acyl-3,4-dihydroquinazoline-2(1*H*)-thiones **5** on treatment with a base. Herein, we report the results of our study, providing a convenient synthetic approach to **5**. We have found that the azido precursors **3** can be easily prepared by a three-step sequence starting with (2-aminophenyl)methanols, and that the desired product **5** can be obtained form **3** in a one-pot reaction through treatment of the isothiocyanate intermediates **4** with NaH.

Results and Discussion. – *N*-[2-(hydroxymethyl)phenyl] amides **1** were readily prepared in good yields (see *Exper. Part*) by reacting (2-aminophenyl)methanols with appropriate acylating agents. These amides **1** were chlorinated with $SOCl_2$ in THF at $-40°$ to room temperature to afford *N*-[2-(chloromethyl)phenyl] amides **2** in fair-to-good yields. Replacement of the Cl group of **2** with NaN_3 in DMF at room temperature proceeded smoothly and cleanly to afford the corresponding *N*-[2-(azidomethyl)-phenyl] amides **3** in good yields (*Table*).

The desired products **5** could be obtained in a one-pot reaction from **3**, as illustrated in the *Scheme* as well. Thus, treatment of **3** with Ph_3P in CH_2Cl_2 at room temperature afforded the corresponding aza-ylide intermediates. After replacement of the solvent

Scheme

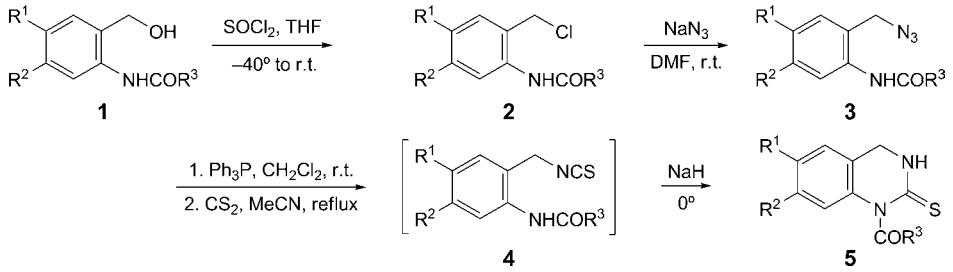

Table. *Preparation of 3,4-Dihydroquinazoline-2(1*H*)-thiones* **5**

Entry	**1**	**2**	Yield[a]) [%]	**3**	Yield[a]) [%]	**5**	Yield[a]) [%]
1	**1a** ($R^1 = R^2 = H$, $R^3 = Me$)	**2a**	87	**3a**	73	**5a**	64
2	**1b** ($R^1 = R^2 = H$, $R^3 = Ph$)	**2b**	95	**3b**	82	**5b**	78
3	**1c** ($R^1 = R^2 = H$, $R^3 = 2\text{-Me–}C_6H_4$)	**2c**	73	**3c**	97	**5c**	54
4	**1d** ($R^1 = R^2 = H$, $R^3 = 3\text{-Cl–}C_6H_4$)	**2d**	71	**3d**	93	**5d**	81
5	**1e** ($R^1 = R^2 = H$, $R^3 = 4\text{-Cl–}C_6H_4$)	**2e**	60	**3e**	78	**5e**	75
6	**1f** ($R^1 = R^2 = H$, $R^3 = 4\text{-MeO–}C_6H_4$)	**2f**	60	**3f**	91	**5f**	62
7	**1g** ($R^1 = R^2 = H$, $R^3 = EtO$)	**2g**	87	**3g**	92	**5g**	86
8	**1h** ($R^1 = H$, $R^2 = Cl$, $R^3 = Me$)	**2h**	60	**3h**	97	**5h**	62
9	**1i** ($R^1 = H$, $R^2 = Cl$, $R^3 = Ph$)	**2i**	59	**3i**	87	**5i**	76
10	**1j** ($R^1 = R^2 = MeO$, $R^3 = Ph$)	**2j**	91	**3j**	78	**5j**	74

[a]) Yields of isolated products.

by MeCN, the intermediates were reacted with CS_2 at reflux temperature to generate the corresponding isothiocyanato intermediates **4**. Subsequently, these intermediates were treated with NaH. Cyclization took place immediately to give, after usual aqueous workup and the subsequent purification of the crude products by column chromatography on SiO_2, the desired products **5**. The results compiled in the *Table* indicate that the yields of **5** are generally fair-to-good, though the yield of the 1-(2-methylbenzoyl) derivative **5c** is somewhat lower than those of the others, probably due to steric reasons. It should be noted that the use of ClCOOEt as an acylating agent for the first step of the present synthetic sequence has proved to be effective. *Entry 7* indicates that the yields of each step of this sequence are comparable to those of the others.

In conclusion, we have developed a convenient sequence for the preparation of 1-acyl-3,4-dihydroquinazoline-2(1*H*)-thiones **5** from (2-aminophenyl)methanols. The present method may be of value in organic synthesis because of the operational simplicity, as well as the good availability of the starting materials.

Experimental Part

General. All org. solvents were dried over appropriate drying agents and distilled prior to use. All chemicals were commercially available. TLC: *Merck* silica gel *60 PF_{254}*. Column chromatography (CC): *Wako Gel C-200E.* M.p.: *Laboratory Devices MEL-TEMP II* melting-point apparatus; uncorrected. IR

Spectra: *PerkinElmer Spectrum65* FTIR spectrophotometer; $\tilde{\nu}$ in cm^{-1}. ^{1}H-NMR Spectra: *JEOL ECP500* FT NMR or *JEOL LA400* FT NMR spectrometer (at 500 or 400 MHz, resp.); in $CDCl_3$, δ in ppm rel. to Me_4Si as internal standard, J in Hz. ^{13}C-NMR Spectra: *JEOL ECP500* FT NMR spectrometer, at 125 MHz; in $CDCl_3$, δ in ppm rel. to Me_4Si as internal standard. HR-MS (DART, positive-ion mode): *Thermo Scientific Exactive* spectrometer; in *m*/*z*.

(2-Amino-4,5-dimethoxyphenyl)methanol. A soln. of (4,5-dimethoxy-2-nitrophenyl)methanol (1.1 g, 5.2 mmol) in AcOEt (30 ml) containing 10% Pd/C (0.19 g, 0.16 mmol) was stirred under H_2 at r.t. for 1 d. After filtration under reduced pressure through a *Celite* pad, the filtrate was concentrated by evaporation to give a residue, separation of which by CC (SiO_2; AcOEt) afforded the product (0.83 g, 87%). White solid. M.p. 75–76° (hexane/Et_2O). IR (KBr): 3368, 1619, 1519. ^{1}H-NMR (500 MHz): 1.60 (br. *s*, 1 H); 3.79–3.86 (including 2 br. *s* at 3.81, 3.84, 8 H); 4.61 (*s*, 2 H); 6.32 (*s*, 1 H); 6.66 (*s*, 1 H). Anal. calc. for $C_9H_{13}NO_3$ (183.20): C 59.00, H 7.15, N 7.65; found: C 59.03, H 7.22, N 7.42.

N-*[2-(Hydroxymethyl)phenyl]acetamide* (**1a**). To a stirred soln. of (2-aminophenyl)methanol (0.62 g, 5.0 mmol) in Et_2O (10 ml) at 0° was added Ac_2O (1.5 g, 15 mmol) dropwise. After 5 min stirring at the same temp., the precipitate was collected by filtration under reduced pressure: 0.72 g (87%). White solid. M.p. 116–117° (hexane/CH_2Cl_2) ([5]: 114–115°). The IR and ^{1}H-NMR data for this compound were identical to those reported in [6].

N-*[2-(Hydroxymethyl)phenyl]benzamide* (**1b**). To a stirred mixture of 2-(aminophenyl)methanol (0.31 g, 2,5 mmol) in sat. aq. $NaHCO_3$ (12 ml) at r.t. was added BzCl (0.42 g, 3.0 mmol) dropwise. After 30 min stirring at the same temp., the precipitate was collected by filtration under reduced pressure and washed with hexane/Et_2O 20:1 to give **1b** (0.54 g, 95%). Colorless needles. M.p. 93–94° (hexane/CH_2Cl_2; [7]: 95–96°). IR (KBr): 3361, 3309, 1645. ^{1}H-NMR (500 MHz): 2.33 (*t*, *J* = 5.9, 1 H); 4.81 (*d*, *J* = 5.9, 2 H); 7.11 (*dd*, *J* = 7.8, 6.8, 1 H); 7.21 (*d*, *J* = 7.8, 1 H); 7.40 (*ddd*, *J* = 7.8, 6.8, 2.0, 1 H); 7.48–7.58 (*m*, 3 H); 7.95 (*dd*, *J* = 8.8, 2.0, 2 H); 8.31 (*d*, *J* = 7.8, 1 H); 9.57 (br. *s*, 1 H).

N-*[2-(Hydroxymethyl)phenyl]-2-methylbenzamide* (**1c**) was prepared from (2-aminophenyl)methanol and 2-methylbenzoyl chloride as described for **1b**. Yield: 73%. Colorless crystals. M.p. 127–128° (hexane/CH_2Cl_2). IR (KBr): 3249, 1644. ^{1}H-NMR (400 MHz): 2.16 (*t*, *J* = 4.9, 1 H); 2.56 (*s*, 3 H); 4.75 (*d*, *J* = 4.9, 2 H); 7.13 (*t*, *J* = 7.8, 1 H); 7.22–7.29 (*m*, 3 H); 7.35–7.42 (*m*, 2 H); 7.55 (*d*, *J* = 7.8, 1 H); 8.25 (*d*, *J* = 7.8, 1 H); 8.90 (br. *s*, 1 H). Anal. calc. for $C_{15}H_{15}NO_2$ (241.29): C 74.67, H 6.27, N 5.81; found: C 74.26, H 6.31, N 5.52.

3-Chloro-N-*[2-(hydroxymethyl)phenyl]benzamide* (**1d**) was prepared from (2-aminophenyl)methanol and 3-chlorobenzoyl chloride as described for **1b**. Yield: 86%. Colorless crystals. M.p. 120–121° (hexane/CH_2Cl_2). IR (KBr): 3251, 1657. ^{1}H-NMR (400 MHz): 2.41 (br. *s*, 1 H); 4.82 (*s*, 2 H); 7.11 (*dd*, *J* = 7.8, 6.8, 1 H); 7.21 (*d*, *J* = 7.8, 1 H); 7.39 (*t*, *J* = 7.8, 1 H); 7.42 (*dd*, *J* = 8.8, 6.8, 1 H); 7.53 (*d*, *J* = 6.8, 1 H); 7.79 (*d*, *J* = 7.8, 1 H); 7.94 (*d*, *J* = 2.0, 1 H); 8.28 (*d*, *J* = 7.8, 1 H); 9.63 (br. *s*, 1 H). Anal. calc. for $C_{14}H_{12}ClNO_2$ (261.70): C 64.25, H 4.62, N 5.35; found: C 64.20, H 4.50, N 5.32.

4-Chloro-N-*[2-(hydroxymethyl)phenyl]benzamide* (**1e**) was prepared from (2-aminophenyl)methanol and 4-chlorobenzoyl chloride as described for **1b**. Yield: 92%. Colorless crystals. M.p. 121–124° (hexane/CH_2Cl_2). IR (KBr): 3284, 1663, 1614. ^{1}H-NMR (500 MHz): 2.32 (*t*, *J* = 5.7, 1 H); 4.82 (*d*, *J* = 5.7, 2 H); 7.11 (*t*, *J* = 7.4, 1 H); 7.21 (*d*, *J* = 7.4, 1 H); 7.40 (*dd*, *J* = 8.0, 7.4, 1 H); 7.46 (*d*, *J* = 8.6, 2 H); 7.88 (*d*, *J* = 8.6, 2 H); 8.30 (*d*, *J* = 8.0, 1 H); 9.61 (br. *s*, 1 H). Anal. calc. for $C_{14}H_{12}ClNO_2$ (261.70): C 64.25, H 4.62, N 5.35; found: C 64.29, H 4.70, N 5.31.

N-*[2-(Hydroxymethyl)phenyl]-4-methoxybenzamide* (**1f**) was prepared from (2-aminophenyl)methanol and 4-methoxybenzoyl chloride as described for **1b**. Yield: 71%. Colorless crystals. M.p. 144–146° (hexane/CH_2Cl_2). IR (KBr): 3264, 1642, 1608. ^{1}H-NMR (500 MHz): 2.39 (*t*, *J* = 5.7, 1 H); 3.87 (*s*, 3 H); 4.80 (*d*, *J* = 5.7, 2 H); 6.98 (*d*, *J* = 9.2, 2 H); 7.09 (*t*, *J* = 7.4, 1 H); 7.20 (*d*, *J* = 7.4, 1 H); 7.38 (*ddd*, *J* = 8.0, 7.4, 1.1, 1 H); 7.91 (*d*, *J* = 9.2, 2 H); 8.28 (*d*, *J* = 8.0, 1 H); 9.47 (br. *s*, 1 H). Anal. calc. for $C_{15}H_{15}NO_3$ (257.28): C 70.02, H 5.88, N 5.44; found: C 69.74, H 5.90, N 5.26.

Ethyl 2-(Hydroxymethyl)phenylcarbamate (**1g**) [8] was prepared from (2-aminophenyl)methanol and ClCOOEt as described for the preparation of **1b**. Yield: 95%. Colorless oil. R_f (AcOEt/hexane 3:2) 0.48. IR (neat): 3352, 1710. ^{1}H-NMR (500 MHz): 1.32 (*t*, *J* = 7.4, 3 H); 2.05 (*t*, *J* = 5.7, 1 H); 4.22 (*q*, *J* = 7.4, 2 H); 4.71 (*d*, *J* = 5.7, 2 H); 7.03 (*t*, *J* = 7.4, 1 H); 7.17 (*d*, *J* = 7.4, 1 H); 7.33 (*d*, *J* = 7.4, 1 H); 7.84 (br. *s*, 1 H); 7.94 (*d*, *J* = 7.4, 1 H).

N-*[5-Chloro-2-(hydroxymethyl)phenyl]acetamide* (**1h**) was prepared from (2-amino-4-chlorophenyl)methanol and Ac_2O as described for **1a**. Yield: 84%. White solid. M.p. 129–131° (hexane/CH_2Cl_2). IR (KBr): 3266, 1658, 1605. ^{1}H-NMR (500 MHz): 2.19 (*s*, 3 H); 2.20 (*t*, *J* = 5.9, 1 H); 4.69 (*d*, *J* = 5.9, 2 H); 7.04 (*d*, *J* = 8.8, 1 H); 7.09 (*d*, *J* = 8.8, 1 H); 8.18 (*s*, 1 H); 8.61 (br. *s*, 1 H). Anal. calc. for $C_9H_{10}ClNO_2$ (199.63): C 54.15, H 5.05, N 7.02; found: C 54.18, H 5.34, N 6.80.

N-*[5-Chloro-2-(hydroxymethyl)phenyl]benzamide* (**1i**) [9] was prepared from (2-amino-4-chlorophenyl)methanol and BzCl as described for **1b**. Yield: 87%. White solid. M.p. 129–131° (hexane/CH_2Cl_2). IR (KBr): 3415, 3312, 1666, 1614. ^{1}H-NMR (500 MHz): 2.32 (*t*, *J* = 5.7, 1 H); 4.80 (*d*, *J* = 5.7, 2 H); 7.06 (*dd*, *J* = 8.0, 1.7, 1 H); 7.11 (*d*, *J* = 8.0, 1 H); 7.50 (*dd*, *J* = 8.0, 7.4, 2 H); 7.57 (*t*, *J* = 7.4, 1 H); 7.93 (*d*, *J* = 8.0, 2 H); 8.45 (*s*, 1 H); 9.68 (br. *s*, 1 H). Anal. calc. for $C_{14}H_{12}ClNO_2$ (261.70): C 64.25, H 4.62, N 5.35; found: C 64.19, H 4.78, N 5.30.

N-*[2-(Hydroxymethyl)-4,5-dimethoxyphenyl]benzamide* (**1j**) was prepared from (2-amino-4,5-dimethoxyphenyl)methanol and BzCl as described for **1b**. Yield: 83%. White solid. M.p. 138–139° (hexane/CH_2Cl_2). IR (KBr): 3396, 3292, 1646, 1619. ^{1}H-NMR (500 MHz): 2.39 (*t*, *J* = 5.9, 1 H); 3.87 (*s*, 3 H); 3.94 (*s*, 3 H); 4.74 (*d*, *J* = 5.9, 2 H); 6.73 (*s*, 1 H); 7.50 (*ddd*, *J* = 8.8, 7.6, 2.0, 2 H); 7.56 (*td*, *J* = 7.6, 2.0, 1 H); 7.92 (*s*, 1 H); 7.94 (*d*, *J* = 8.8, 2 H); 9.35 (br. *s*, 1 H). Anal. calc. for $C_{16}H_{17}NO_4$ (287.31): C 66.89, H 5.96, N 4.88; found: C 66.64, H 5.93, N 4.75.

N-*[2-(Chloromethyl)phenyl]acetamide* (**2a**) [10]. *Representative Procedure.* To a stirred soln. of **1a** (0.41 g, 2.5 mmol) in THF (7 ml) at −40° was added a soln. of $SOCl_2$ (0.31 g, 2.6 mmol) in THF (1.5 ml) during 6 min. The temp. was raised gradually to r.t., and stirring was continued overnight, then Na_2CO_3 (1.5 g) was added. After stirring for 30 min, the mixture was filtered under reduced pressure. The filtrate was concentrated by evaporation to give a residue, purification of which by CC (SiO_2; AcOEt/hexane 3:2) furnished **2a** (0.40 g, 88%). Colorless needles. M.p. 114–115° (hexane/CH_2Cl_2). IR (KBr): 3254, 1654. ^{1}H-NMR (400 MHz): 2.25 (*s*, 3 H); 4.62 (*s*, 2 H); 7.15 (*t*, *J* = 7.8, 1 H); 7.32 (*d*, *J* = 7.8, 1 H); 7.38 (*t*, *J* = 7.8, 1 H); 7.52 (br. *s*, 1 H); 7.86 (*d*, *J* = 7.8, 1 H).

N-*[2-(Chloromethyl)phenyl]benzamide* (**2b**). White solid. M.p. 122–124° (hexane/CH_2Cl_2). IR (KBr): 3253, 1647, 1601. ^{1}H-NMR (400 MHz): 4.70 (*s*, 2 H); 7.19 (*dd*, *J* = 8.8, 7.8, 1 H); 7.35 (*dd*, *J* = 7.8, 2.0, 1 H); 7.45 (*t*, *J* = 7.8, 1 H); 7.53 (*t*, *J* = 7.8, 2 H); 7.60 (*t*, *J* = 7.8, 1 H); 7.96 (*dd*, *J* = 7.8, 2.0, 2 H); 8.10 (*d*, *J* = 8.8, 1 H); 8.41 (br. *s*, 1 H). Anal. calc. for $C_{14}H_{12}ClNO$ (245.70): C 68.44, H 4.92, N 5.70; found: C 68.28, H 4.98, N 5.65.

N-*[2-(Chloromethyl)phenyl]-2-methylbenzamide* (**2c**). Colorless crystals. M.p. 148–149° (hexane/CH_2Cl_2). IR (KBr): 3252, 1648. ^{1}H-NMR (500 MHz): 2.58 (*s*, 3 H); 4.67 (*s*, 2 H); 7.20 (*dd*, *J* = 8.0, 7.4, 1 H); 7.29–7.32 (*m*, 2 H); 7.36 (*dd*, *J* = 7.4, 1.1, 1 H); 7.41 (*t*, *J* = 7.4, 1 H); 7.45 (*dd*, *J* = 8.0, 7.4, 1 H); 7.60 (*d*, *J* = 8.0, 1 H); 7.91 (br. *s*, 1 H); 8.09 (*d*, *J* = 7.4, 1 H). Anal. calc. for $C_{15}H_{14}ClNO$ (259.73): C 69.36, H 5.43, N 5.39; found: C 69.20, H 5.59, N 5.39.

3-Chloro-N-*[2-(chloromethyl)phenyl]benzamide* (**2d**). Colorless crystals. M.p. 121–123° (hexane/CH_2Cl_2). IR (KBr): 3236, 1646. ^{1}H-NMR (500 MHz): 4.70 (*s*, 2 H); 7.21 (*t*, *J* = 7.4, 1 H); 7.36 (*d*, *J* = 7.4, 1 H); 7.44–7.49 (*m*, 2 H); 7.57 (*d*, *J* = 8.0, 1 H); 7.81 (*d*, *J* = 8.0, 1 H); 7.97 (*s*, 1 H); 8.06 (*d*, *J* = 8.6, 1 H); 8.36 (br. *s*, 1 H). Anal. calc. for $C_{14}H_{11}Cl_2NO$ (280.15): C 60.02, H 3.96, N 5.00; found: C 59.95, H 3.74, N 5.24.

4-Chloro-N-*[2-(chloromethyl)phenyl]benzamide* (**2e**). Colorless crystals. M.p. 128–130° (hexane/CH_2Cl_2). IR (KBr): 3279, 1648. ^{1}H-NMR (500 MHz): 4.70 (*s*, 2 H); 7.19 (*td*, *J* = 7.4, 1.1, 1 H); 7.36 (*dd*, *J* = 7.4, 1.1, 1 H); 7.45 (*ddd*, *J* = 8.0, 7.4, 1.1, 1 H); 7.50 (*d*, *J* = 8.6, 2 H); 7.90 (*d*, *J* = 8.6, 2 H); 8.07 (*d*, *J* = 8.0, 1 H); 8.37 (br. *s*, 1 H). Anal. calc. for $C_{14}H_{11}Cl_2NO$ (280.15): C 60.02, H 3.96, N 5.00; found: C 59.97, H 4.04, N 4.91.

N-*[2-(Chloromethyl)phenyl]-4-methoxybenzamide* (**2f**). Colorless crystals. M.p. 142–144° (hexane/CH_2Cl_2). IR (KBr): 3269, 1640, 1607. ^{1}H-NMR (500 MHz): 3.99 (*s*, 3 H); 4.70 (*s*, 2 H); 7.02 (*d*, *J* = 8.6, 2 H); 7.17 (*t*, *J* = 7.8, 1 H); 7.34 (*d*, *J* = 7.8, 2.0, 1 H); 7.44 (*t*, *J* = 7.8, 1 H); 7.93 (*d*, *J* = 8.6, 2 H); 8.09 (*d*, *J* = 7.8, 1 H); 8.33 (br. *s*, 1 H). Anal. calc. for $C_{15}H_{14}ClNO_2$ (275.73): C 65.34, H 5.12, N 5.08; found: C 65.26, H 5.26, N 5.04.

Ethyl 2-(Chloromethyl)phenylcarbamate (**2g**). White solid. M.p. 86–87° (hexane/CH_2Cl_2). IR (KBr): 3287, 1691. ^{1}H-NMR (500 MHz): 1.34 (*t*, *J* = 7.4, 3 H); 4.25 (*q*, *J* = 7.4, 2 H); 4.62 (*s*, 2 H); 6.89 (br.

s, 1 H); 7.10 (*t*, *J* = 7.4, 1 H); 7.29 (*d*, *J* = 8.0, 1 H); 7.38 (*dd*, *J* = 8.0, 7.4, 1 H); 7.86 (*d*, *J* = 7.4, 1 H). Anal. calc. for $C_{10}H_{12}ClNO_2$ (213.66): C 56.21, H 5.66, N 6.56; found: C 56.06, H 5.78, N 6.32.

N-*[5-Chloro-2-(chloromethyl)phenyl]acetamide* (**2h**) [11]. White solid. M.p. 155–156° (hexane/CH_2Cl_2). IR (KBr): 3259, 1661. ^{1}H-NMR (500 MHz): 2.25 (*s*, 3 H); 4.58 (*s*, 2 H); 7.12 (*d*, *J* = 8.6, 1 H); 7.23 (*d*, *J* = 8.6, 1 H); 7.53 (br. *s*, 1 H); 8.01 (br. *s*, 1 H).

N-*[5-Chloro-2-(chloromethyl)phenyl]benzamide* (**2i**). White solid. M.p. 137–139° (hexane/CH_2Cl_2). IR (KBr) 3265, 1646. ^{1}H-NMR (400 MHz): 4.66 (*s*, 2 H); 7.15 (*dd*, *J* = 7.8, 2.0, 1 H); 7.28 (*d*, *J* = 7.8, 1 H); 7.54 (*t*, *J* = 7.8, 2 H); 7.61 (*t*, *J* = 7.8, 1 H); 7.95 (*d*, *J* = 7.8, 2 H); 8.24 (*d*, *J* = 2.0, 1 H); 8.43 (br. *s*, 1 H). Anal. calc. for $C_{14}H_{11}Cl_2NO$ (280.15): C 60.02, H 3.96, N 5.00; found: C 59.81, H 4.00, N 4.80.

N-*[2-(Chloromethyl)-4,5-dimethoxyphenyl]benzamide* (**2j**). White solid. M.p. 160–162° (hexane/CH_2Cl_2). IR (KBr): 3274, 1642, 1612. ^{1}H-NMR (400 MHz): 3.91 (*s*, 3 H); 3.94 (*s*, 3 H); 4.68 (*s*, 2 H); 8.34 (*s*, 1 H); 7.54 (*dd*, *J* = 7.8, 6.9, 2 H); 7.60 (*t*, *J* = 6.9, 1 H); 7.67 (*s*, 1 H); 7.96 (*d*, *J* = 7.8, 2 H); 8.26 (br. *s*, 1 H). Anal. calc. for $C_{16}H_{16}ClNO_3$ (305.76): C 62.85, H 5.27, N 4.58; found: C 62.82, H 5.26, N 4.55.

N-*[2-(Azidomethyl)phenyl]acetamide* (**3a**). *Representative Procedure.* To a stirred soln. of NaN_3 (72 mg, 1.1 mmol) in DMF (1 ml) at r.t. was added a soln. of **2a** (0.18 g, 1.0 mmol) in DMF (1.5 ml). Stirring was continued for 1.5 h at the same temp., before H_2O (15 ml) was added. The mixture was extracted with AcOEt (3 × 10 ml), and the combined extracts were washed with H_2O (3 × 10 ml) and brine (10 ml), dried (Na_2SO_4), and concentrated by evaporation. The residual solid was recrystallized from hexane/CH_2Cl_2 to give **3a** (0.14 g, 73%). White solid. M.p. 92–94°. IR (KBr): 3275, 2117, 2092, 1657. ^{1}H-NMR (400 MHz): 2.22 (*s*, 3 H); 4.34 (*s*, 2 H); 7.16 (*dd*, *J* = 7.8, 6.8, 1 H); 7.27 (*d*, *J* = 7.8, 1 H); 7.39 (*dd*, *J* = 7.8, 6.8, 1 H); 7.58 (br. *s*, 1 H); 7.91 (*d*, *J* = 7.8, 1 H). Anal. calc. for $C_9H_{10}N_4O$ (190.20): C 56.83, H 5.30, N 29.46; found: C 56.70, H 5.59, N 29.17.

N-*[2-(Azidomethyl)phenyl]benzamide* (**3b**) [12]. Colorless crystals. M.p. 88–89° (hexane/CH_2Cl_2). IR (KBr): 3289, 2101, 1654. ^{1}H-NMR (500 MHz): 4.42 (*s*, 2 H); 7.19 (*td*, *J* = 7.4, 1.1, 1 H); 7.30 (*dd*, *J* = 7.4, 1.1, 1 H); 7.45 (*ddd*, *J* = 8.0, 7.4, 1.1, 1 H); 7.53 (*t*, *J* = 7.4, 2 H); 7.59 (*tt*, *J* = 7.4, 1.1, 1 H); 7.94 (*dd*, *J* = 7.0, 1.1, 2 H); 8.16 (*d*, *J* = 8.0, 1 H); 8.50 (br. *s*, 1 H).

N-*[2-(Azidomethyl)phenyl]-2-methylbenzamide* (**3c**). Colorless crystals. M.p. 103–105° (Et_2O). IR (KBr): 3250, 2105, 1650. ^{1}H-NMR (500 MHz): 2.56 (*s*, 3 H); 4.39 (*s*, 2 H); 7.20 (*t*, *J* = 7.4, 1 H); 7.29–7.32 (*m*, 3 H); 7.40 (*dd*, *J* = 7.4, 6.9, 1 H); 7.45 (*dd*, *J* = 8.0, 7.4, 1 H); 7.56 (*d*, *J* = 7.4, 1 H); 7.97 (br. *s*, 1 H); 8.14 (*d*, *J* = 7.4, 1 H). Anal. calc. for $C_{15}H_{14}N_4O$ (266.30): C 67.65, H 5.30, N 21.04; found: C 67.61, H 5.49, N 20.95.

N-*[2-(Azidomethyl)phenyl]-3-chlorobenzamide* (**3d**). Colorless crystals. M.p. 96–97° (hexane/Et_2O). IR (KBr) 3251, 2102, 1647. ^{1}H-NMR (500 MHz): 4.42 (*s*, 2 H); 7.21 (*dd*, *J* = 7.4, 6.9, 1 H); 7.31 (*dd*, *J* = 7.4, 1.1, 1 H); 7.44–7.48 (*m*, 2 H); 7.56 (*dt*, *J* = 8.0, 1.1, 1 H); 7.78 (*d*, *J* = 8.0, 1 H); 7.94 (*t*, *J* = 1.7, 1 H); 8.12 (*d*, *J* = 8.0, 1 H); 8.49 (br. *s*, 1 H). Anal. calc. for $C_{14}H_{11}ClN_4O$ (286.72): C 58.65, H 3.87, N 19.54; found: C 58.50, H 4.06, N 19.31.

N-*[2-(Azidomethyl)phenyl]-4-chlorobenzamide* (**3e**). Colorless needles. M.p. 97–99° (hexane/CH_2Cl_2). IR (KBr): 3287, 2093, 1650. ^{1}H-NMR (500 MHz): 4.42 (*s*, 2 H); 7.20 (*td*, *J* = 7.4, 1.1, 1 H); 7.30 (*dd*, *J* = 7.4, 1.1, 1 H); 7.45 (*ddd*, *J* = 8.0, 7.4, 1.1, 1 H); 7.50 (*d*, *J* = 8.6, 2 H); 7.87 (*d*, *J* = 8.6, 2 H); 8.14 (*d*, *J* = 8.0, 1 H); 8.50 (br. *s*, 1 H). Anal. calc. for $C_{14}H_{11}ClN_4O$ (286.72): C 58.65, H 3.87, N 19.54; found: C 58.53, H 3.97, N 19.49.

N-*[2-(Azidomethyl)phenyl]-4-methoxybenzamide* (**3f**). Colorless crystals. M.p. 118–119° (Et_2O). IR (KBr): 3289, 2097, 1641, 1606. ^{1}H-NMR (500 MHz): 3.89 (*s*, 3 H); 4.42 (*s*, 2 H); 7.01 (*d*, *J* = 8.8, 2 H); 7.17 (*dd*, *J* = 8.8, 7.8, 1 H); 7.30 (*d*, *J* = 8.8, 1 H); 7.44 (*ddd*, *J* = 8.8, 7.8, 2.0, 1 H); 7.90 (*d*, *J* = 8.8, 2 H); 8.15 (*d*, *J* = 8.8, 1 H); 8.44 (br. *s*, 1 H). Anal. calc. for $C_{15}H_{14}N_4O_2$ (282.30): C 63.82, H 5.00, N 19.85; found: C 63.73, H 5.05, N 19.79.

Ethyl 2-(Azidomethyl)phenylcarbamate (**3g**). Colorless oil. R_f (AcOEt/hexane 1:4) 0.48. IR (neat): 3320, 2101, 1717. ^{1}H-NMR (500 MHz): 1.33 (*t*, *J* = 7.4, 3 H); 4.24 (*q*, *J* = 7.4, 2 H); 4.35 (*s*, 2 H); 6.96 (br. *s*, 1 H); 7.11 (*t*, *J* = 7.4, 1 H); 7.24 (*d*, *J* = 7.4, 1 H); 7.38 (*t*, *J* = 7.4, 1 H); 7.89 (*d*, *J* = 7.4, 1 H). Anal. calc. for $C_{10}H_{12}N_4O_2$ (220.23): C 54.54, H 5.49, N 25.44; found: C 54.40, H 5.53, N 25.31.

N-*[2-(Azidomethyl)-5-chlorophenyl]acetamide* (**3h**). White solid. M.p. 105–106° (hexane/CH_2Cl_2). IR (KBr): 3245, 2096, 1661. ^{1}H-NMR (500 MHz): 2.23 (*s*, 3 H); 4.32 (*s*, 2 H); 7.13 (*d*, *J* = 8.0, 1 H); 7.19 (*d*,

$J = 8.0$, 1 H); 7.65 (br. *s*, 1 H); 8.07 (br. *s*, 1 H). Anal. calc. for $C_9H_9ClN_4O$ (224.65): C 48.12, H 4.04, N 24.94; found: C 47.97, H 4.07, N 24.77.

N-*[2-(Azidomethyl)-5-chlorophenyl]benzamide* (**3i**). White solid. M.p. 94–96° (hexane/CH_2Cl_2). IR (KBr): 3287, 2104, 1652, 1601. ^{1}H NMR (500 MHz): 4.40 (*s*, 2 H); 7.15 (*dd*, $J = 8.0$, 2.3, 1 H); 7.22 (*d*, $J = 8.0$, 1 H); 7.54 (*dd*, $J = 8.0$, 7.4, 2 H); 7.60 (*tt*, $J = 7.4$, 1.1, 1 H); 7.92 (*dd*, $J = 8.0$, 1.1, 2 H); 8.32 (*d*, $J =$ 2.3, 1 H); 8.59 (br. *s*, 1 H). Anal. calc. for $C_{14}H_{11}ClN_4O$ (286.72): C 58.65, H 3.87, N 19.54; found: C 58.70, H 3.72, N 19.27.

N-*[2-(Azidomethyl)-4,5-dimethoxyphenyl]benzamide* (**3j**). White solid. M.p. 127–129° (hexane/CH_2Cl_2). IR (KBr): 3185, 2089, 1634. ^{1}H-NMR (400 MHz): 3.91 (*s*, 3 H); 3.94 (*s*, 3 H); 4.37 (*s*, 2 H); 6.80 (*s*, 1 H); 7.53 (*dd*, $J = 7.8$, 6.8, 2 H): 7.59 (*t*, $J = 6.8$, 1 H); 7.72 (*s*, 1 H); 7.92 (*d*, $J = 7.8$, 2 H); 8.35 (br. *s*, 1 H). Anal. calc. for $C_{16}H_{16}N_4O_3$ (312.32): C 61.53, H 5.16, N 17.94; found: C 61.41, H 5.27, N 17.89.

*1-(3,4-Dihydro-2-thioxoquinazolin-1(2*H*)-yl)ethanone* (**5a**). *Representative Procedure.* A mixture of **3a** (0.13 g, 0.70 mmol) and PPh_3 (0.19 g, 0.84 mmol) in CH_2Cl_2 was stirred at r.t. for 2 h. After removal of CH_2Cl_2 under reduced pressure, MeCN and CS_2 (1.6 ml each) were added. The mixture was heated at reflux temp. for 1 h, and then it was cooled to 0°. NaH (60% in mineral oil; 28 mg, 0.70 mmol) was added, and stirring was continued for 10 min before sat. aq. NH_4Cl (15 ml) was added. The resulting mixture was extracted with AcOEt (3×10 ml). The combined extracts were washed with brine (10 ml), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by CC (SiO_2; CH_2Cl_2) to give **5a** (92 mg, 64%). White solid. M.p. 157–159° (hexane/CH_2Cl_2). IR (KBr): 3178, 1702, 1621, 1246. ^{1}H-NMR (500 MHz): 2.76 (*s*, 3 H); 4.89 (*s*, 2 H); 6.87 (*d*, $J = 8.0$, 1 H); 7.13 (*t*, $J = 7.4$, 1 H); 7.21 (*d*, $J = 7.4$, 1 H); 7.29 (*dd*, $J = 8.0$, 7.4, 1 H); 8.98 (br. *s*, 1 H). ^{13}C-NMR: 27.8; 44.4; 113.8; 122.0; 125.1; 126.0; 128.9; 134.7; 173.6; 179.6. HR-MS: 207.0585 ($[M+H]^+$, $C_{10}H_{11}N_2OS^+$; calc. 207.0587). Anal. calc. for $C_{10}H_{10}N_2OS$ (206.26): C 58.23, H 4.89, N 13.58; found: C 58.12, H 5.03, N 13.42.

*(3,4-Dihydro-2-thioxoquinazolin-1(2*H*)-yl)(phenyl)methanone* (**5b**). Colorless crystals. M.p. 193–194° (hexane/CH_2Cl_2). IR (KBr): 3169, 1691, 1616, 1242. ^{1}H-NMR (500 MHz): 4.86 (*s*, 2 H); 6.89 (*d*, $J = 8.0$, 1 H); 7.16 (*dd*, $J = 8.0$, 7.4, 1 H); 7.24 (*d*, $J = 7.4$, 1 H); 7.32 (*t*, $J = 7.4$, 1 H); 7.37 (*dd*, $J = 8.0$, 7.4, 2 H); 7.49 (*t*, $J = 7.4$, 1 H); 7.69 (*dd*, $J = 8.0$, 1.1, 2 H); 9.01 (br. *s*, 1 H). ^{13}C-NMR: 46.81; 114.25; 121.16; 124.99; 126.05; 128.26; 128.97; 129.04; 132.04; 134.48; 135.64; 173.38; 179.71. HR-MS: 269.0728 ($[M+H]^+$, $C_{15}H_{13}N_2OS^+$; calc. 269.0743). Anal. calc. for $C_{15}H_{12}N_2OS$ (268.33): C 67.14, H 4.51, N 10.44; found: C 67.09, H 4.50, N 10.38.

*(3,4-Dihydro-2-thioxoquinazolin-1(2*H*)-yl)(2-methylphenyl)methanone* (**5c**). Pale-yellow crystals. M.p. 185–187° (hexane/CH_2Cl_2). IR (KBr) 3170, 1691, 1620, 1251. ^{1}H-NMR (500 MHz): 2.47 (*s*, 3 H); 4.90 (*s*, 2 H); 6.79 (*d*, $J = 8.0$, 1 H); 7.08 (*t*, $J = 7.4$, 1 H); 7.14–7.32 (*m*, 6 H); 7.59 (br. *s*, 1 H). ^{13}C-NMR: 20.00; 45.66; 114.17; 121.32; 125.02; 125.25; 126.06; 127.28; 128.93; 130.34; 131.03; 134.39; 136.50; 137.74; 173.25; 179.24. HR-MS: 283.0886 ($[M+H]^+$, $C_{16}H_{15}N_2OS^+$; calc. 283.0900). Anal. calc. for $C_{16}H_{14}N_2OS$ (282.36): C 68.06, H 5.00, N 9.92; found: C 67.84, H 5.01, N 9.73.

*(3-Chlorophenyl)(3,4-dihydro-2-thioxoquinazolin-1(2*H*)-yl)methanone* (**5d**). Colorless crystals. M.p. 195–198° ($CHCl_3$). IR (KBr): 3168, 1704, 1615, 1246. ^{1}H-NMR (500 MHz): 4.86 (*s*, 2 H); 6.91 (*d*, $J = 8.0$, 1 H); 7.18 (*td*, $J = 7.4$, 1.1, 1 H); 7.25 (*d*, $J = 7.4$, 1 H); 7.30 (*dd*, $J = 8.0$, 7.4, 1 H); 7.33 (*ddd*, $J =$ 8.0, 7.4, 1.1, 1 H); 7.44 (*dt*, $J = 8.0$, 1.1, 1 H); 7.54 (*ddd*, $J = 8.0$, 1.7, 1.1, 1 H); 7.65 (*t*, $J = 1.7$, 1 H); 9.17 (br. *s*, 1 H). ^{13}C-NMR: 46.73; 114.19; 121.08; 125.17; 126.17; 126.97; 128.77; 129.15; 129.49; 131.95; 134.28; 134.31; 137.47; 172.09; 179.42. HR-MS: 303.0357 ($[M+H]^+$, $C_{15}H_{12}ClN_2OS^+$; calc. 303.0353). Anal. calc. for $C_{15}H_{11}ClN_2OS$ (302.78): C 59.50, H, 3.66, N 9.25; found: C 59.22, H 3.69, N 9.19.

*(4-Chlorophenyl)(3,4-dihydro-2-thioxoquinazolin-1(2*H*)-yl)methanone* (**5e**). Colorless crystals. M.p. 169–172° (hexane/$CHCl_3$). IR (KBr): 3190, 1696, 1622, 1231. ^{1}H-NMR (500 MHz): 4.85 (*s*, 2 H); 6.89 (*d*, $J = 7.4$, 1 H); 7.17 (*td*, $J = 7.4$, 1.1, 1 H); 7.23 (*d*, $J = 7.4$, 1 H); 7.30–7.35 (*m*, 3 H); 7.62 (*d*, $J = 8.0$, 2 H); 9.48 (br. *s*, 1 H). ^{13}C-NMR (125 MHz): 46.79; 114.23; 121.08; 125.15; 126.12; 128.60; 129.10; 130.33; 134.13; 134.33; 138.35; 172.38; 179.54. HR-MS: 303.0344 ($[M+H]^+$, $C_{15}H_{12}ClN_2OS^+$; calc. 303.0353). Anal. calc. for $C_{15}H_{11}ClN_2OS$ (302.78): C 59.50, H 3.66, N 9.25; found: C 59.25, H 3.63, N 9.28.

*(3,4-Dihydro-2-thioxoquinazolin-1(2*H*)-yl)(4-methoxyphenyl)methanone* (**5f**). Pale-yellow solid. M.p. 159–162° (hexane/CH_2Cl_2). IR (KBr): 3186, 1670, 1623, 1257. ^{1}H-NMR (500 MHz): 3.84 (*s*, 3 H); 4.81 (*s*, 2 H); 6.87 (*d*, $J = 9.2$, 2 H); 6.89 (*d*, $J = 8.0$, 1 H); 7.15 (*t*, $J = 7.4$, 1 H); 7.21 (*d*, $J = 7.4$, 1 H); 7.31 (*dd*, $J = 8.0$, 7.4, 1 H); 7.72 (*d*, $J = 9.2$, 2 H); 9.07 (br. *s*, 1 H). ^{13}C-NMR: 47.15; 55.41; 113.66; 114.00;

120.96; 124.84; 126.09; 127.49; 128.97; 131.65; 134.46; 163.20; 172.71; 179.82. HR-MS: 299.0849 ($[M+H]^+$, $C_{16}H_{15}N_2O_2S^+$; calc. 299.0849). Anal. calc. for $C_{16}H_{14}N_2O_2S$ (298.36): C 64.41, H 4.73, N 9.39; found: C 64.20, H 4.84, N 9.25.

*Ethyl 3,4-Dihydro-2-thioxo-2*H*-quinazoline-1-carboxylate* (**5g**). White solid. M.p. 128–131° (hexane/CH_2Cl_2). IR (KBr): 3285, 1713, 1601, 1229. ^{1}H-NMR (500 MHz): 1.45 (*t*, *J* = 7.4, 3 H); 4.45 (*d*, *J* = 2.3, 2 H); 4.49 (*q*, *J* = 7.4, 2 H); 7.08 (*d*, *J* = 7.4, 1 H); 7.13 (*t*, *J* = 7.4, 2 H); 7.27 (*t*, *J* = 7.4, 1 H); 7.82 (br. *s*, 1 H). ^{13}C-NMR: 13.72; 44.05; 65.07; 116.02; 119.94; 125.13; 125.89; 128.50: 134.07; 152.44; 177.65. HR-MS: 237.0693 ($[M+H]^+$, $C_{11}H_{13}N_2O_2S^+$; calc. 237.0692). Anal. calc. for $C_{11}H_{12}N_2O_2S$ (236.29): C 55.91, H 5.12, N 11.86; found: C 55.77, H 5.05, N 11.83.

*1-(7-Chloro-3,4-dihydro-2-thioxoquinazolin-1(2*H*)-yl)ethanone* (**5h**). White solid. M.p. 187–189° (hexane/$CHCl_3$). IR (KBr): 3184, 1707, 1614, 1242. ^{1}H-NMR (500 MHz): 2.76 (*s*, 3 H); 4.85 (*s*, 2 H); 6.93 (br. *s*, 1 H); 7.10 (*dd*, *J* = 8.0, 1.7, 1 H); 7.14 (*d*, *J* = 8.0, 1 H); 9.31 (br. *s*, 1 H). ^{13}C NMR: 27.7; 44.01; 113.94; 120.20; 124.84; 127.10; 134.53; 135.51; 173.53; 179.68. HR-MS: 241.0189 ($[M+H]^+$, $C_{10}H_{10}ClN_2OS^+$; calc. 241.0197). Anal. calc. for $C_{10}H_9ClN_2OS$ (240.71): C 49.90, H 3.77, N 11.64; found: C 49.80, H 3.92, N 11.36.

*(7-Chloro-3,4-dihydro-2-thioxoquinazolin-1(2*H*)-yl)(phenyl)methanone* (**5i**). White solid. M.p. 176–178° (hexane/$CHCl_3$). IR (KBr): 3162, 1694, 1611, 1241. ^{1}H-NMR (500 MHz): 4.82 (*s*, 2 H); 6.90 (*d*, *J* = 1.7, 1 H); 7.14 (*dd*, *J* = 8.0, 1.7, 1 H); 7.18 (*d*, *J* = 8.0, 1 H); 7.38 (*dd*, *J* = 8.0, 7.4, 2 H); 7.50 (*t*, *J* = 7.4, 1 H); 7.68 (*d*, *J* = 8.0, 2 H); 8.99 (br. *s*, 1 H). ^{13}C-NMR: 46.41; 114.32; 119.50; 124.88; 127.20; 128.35; 129.02; 132.46; 134.67; 135.27; 135.36; 173.27; 179.84. HR-MS: 303.0348 ($[M+H]^+$, $C_{15}H_{12}ClN_2OS^+$; calc. 303.0353). Anal. calc. for $C_{15}H_{11}ClN_2OS$ (302.78): C 59.50, H 3.66, N 9.25; found: C 59.20, H 3.66, N 8.95.

*(3,4-Dihydro-6,7-dimethoxy-2-thioxoquinazolin-1(2*H*)-yl)(phenyl)methanone* (**5j**). Pale-yellow solid. M.p. 219–221° (hexane/CH_2Cl_2). IR (KBr): 3176; 1682; 1629; 1242. ^{1}H-NMR (500 MHz): 3.82 (*s*, 3 H); 3.88 (*s*, 3 H); 4.80 (*s*, 2 H); 6.48 (*s*, 1 H); 6.71 (*s*, 1 H); 7.35 (*t*, *J* = 7.4, 2 H); 7.46 (*t*, *J* = 7.4, 1 H); 7.68 (*d*, *J* = 7.4, 2 H); 9.51 (br. *s*, 1 H). ^{13}C-NMR: 46.53; 56.22; 56.37; 98.96; 109.02; 112.70; 128.17; 128.98; 132.00; 133.74; 135.811; 146.49; 149.41; 173.42; 178.85. HR-MS: 329.0947 ($[M+H]^+$, $C_{17}H_{17}N_2O_3S^+$; calc. 329.0954). Anal. calc. for $C_{17}H_{16}N_2O_3S$ (328.39): C 62.18, H 4.91, N 8.53; found: C 62.02, H 4.84, N 8.45.

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