Multistep Parallel Synthesis of Quinazoline-2,4-diones by a Fluorous Biphasic Concept without Perfluorinated Solvents

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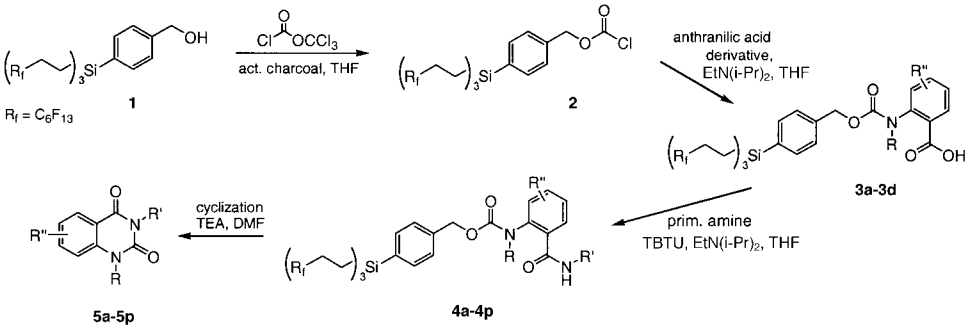
Based on perfluoro-tagged benzyl alcohol adsorbed *via* fluorous–fluorous interactions on fluorous reversed-phase silica gel (FRPSG), we have performed a multistep synthesis leading finally to a small library of quinazoline-2,4-diones. The whole reaction sequence runs without isolation of intermediates and most importantly, without the need of perfluorinated solvents.

1. Introduction. – Recently, fluorous chemistry techniques have emerged as an attractive approach for efficient separation and isolation steps in conducting solution chemistry [1]. Perfluoro-tagged compounds can be easily separated from organic compounds *via* liquid-liquid extraction between a common organic solvent and a perfluorinated solvent. Alternatively, solid-phase extraction on fluorous reversed-phase silica gel (FRPSG) can be performed. The easy workup procedures allow for efficient parallel synthesis and have, thus, found application in combinatorial chemistry and catalytic processes [2].

We have recently reported on the synthesis of a perfluoro-tagged (benzyloxy)carbonyl protecting group and its application in a fluorous biphasic system to the synthesis of two quinazoline-2,4-diones according to *Scheme 1* [3].

Scheme 1. *Synthesis of Quinazoline-2,4-diones* **5a**–**5p** *in Liquid Phase*



We had demonstrated that this multistep synthesis can be performed starting from **1** without isolation of intermediates, even if the individual steps do not proceed quantitatively. The quinazoline-2,4-diones **5a** and **5e** as desired products were obtained

by an intramolecular cyclization step induced by Et_3N [4][5]. All intermediates but the final quinazoline-2,4-diones were equipped with perfluoro tags and could, thus, be removed from the desired products by extraction between perfluorinated and organic medium without a chromatographic purification step.

Meanwhile, we have extended the approach to the synthesis of a small library of quinazoline-2,4-diones (*Table*). The overall yields for the desired target compounds were in the range from 35–90%.

Table. *Yields of Quinazoline-2,4-diones* **5a**–**5p** *Obtained by Employing Free Perfluoro Benzyl Alcohol* **1** *and FRPSG-Immobilized Linker Material* **6**

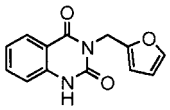
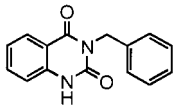
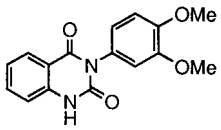
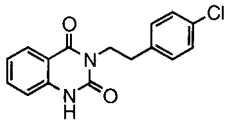
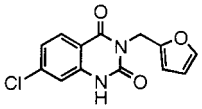
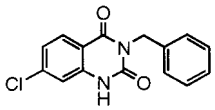
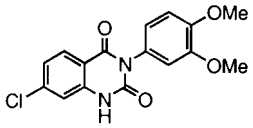
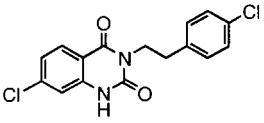
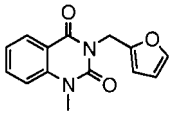
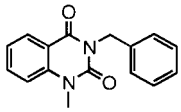
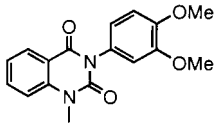
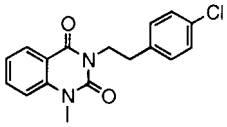
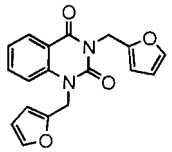
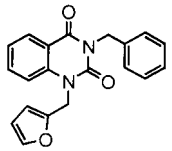
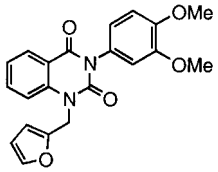
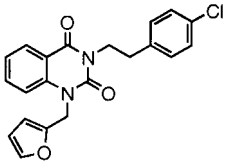
No.		Yield [%]	
		FBE[a])	FSPOS[b])
5a		66	47
5b		60	45
5c		75	30
5d		70	73
5e		90	29
5f		70	35
5g		43	77
5h		85	90

Table (cont.)

No.		Yield [%]	
		FBE[a])	FSPOS[b])
5i		67	52
5j		46	43
5k		54	83
5l		59	80
5m		46	52
5n		35	29
5o		51	42
5p		55	62

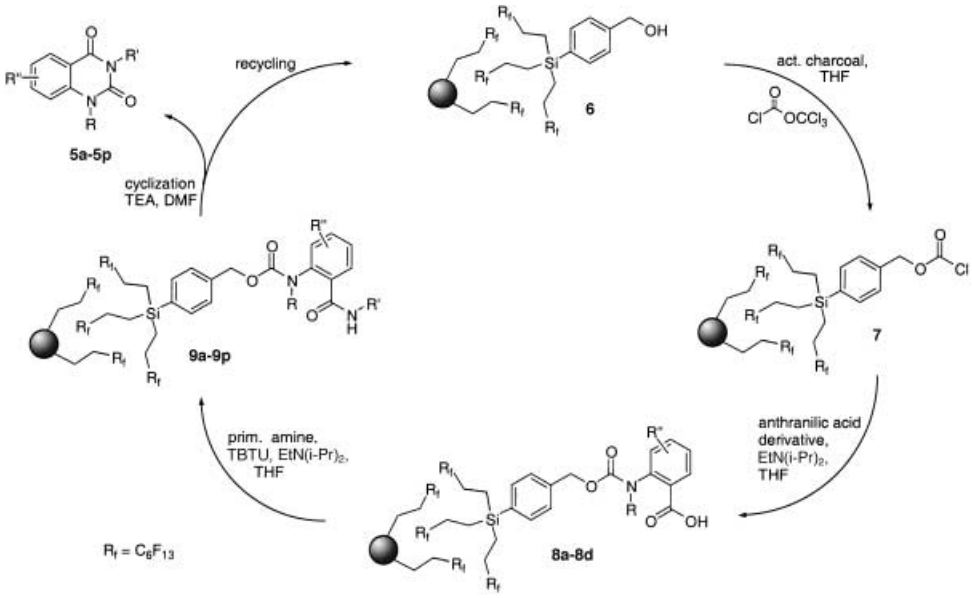
[a]) FBE = Fluorous biphasic extraction. [b]) FSPOS = Fluorous solid phase organic synthesis.

The applied perfluorinated solvents are regarded as benign but they have the disadvantage of being costly and environmentally persistent [6]. Thus, it would be of great value to make use of the fluorous–fluorous interactions without involvement of perfluorinated solvents [7].

Here, we would like to report on such an approach in which we have performed the synthesis of the quinazoline-2,4-dione library on perfluoro-tagged benzyl alcohol adsorbed on fluorous reversed-phase silica gel (FRPSG) by fluorous–fluorous interactions [8][9].

2. Results and Discussion. – The whole reaction sequence of the synthesis leading to the desired quinazoline-2,4-diones **5a**–**5p** is outlined in *Scheme 2*. Perfluoro-tagged benzyl alcohol **1** was immobilized on FRPSG by evaporating a solution of **1** (0.4 mmol) in Et_2O in the presence of 5 g of FRPSG to yield **6**.

Scheme 2. *Synthesis of Quinazoline-2,4-diones* **5a**–**5p** *Starting from FRPSG-Immobilized Benzyl Alcohol* **6**



For the coupling and (benzyloxy)carbonyl protection of anthranilic acids, immobilized alcohol **6** was first reacted with diphosgene to yield **7** [10]. This material was divided into four equal parts, and each part was reacted with a different anthranilic acid in the presence of *Hünig*'s base to yield intermediates **8a**–**8d**. Each intermediate of this material was again splitted into four equivalent portions each, and, again, each part was reacted with four amines with *O*-(benzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium-tetrafluoroborate (TBTU) as coupling reagent to produce the amides **9a**–**9p** ready for the cyclization step induced by Et_3N, leading to the envisaged target compounds **5a**–**5p** [11].

The reaction steps were carried out in THF, which leads to a substantial release of the perfluoro-tagged benzyl alcohol **1** into the solvent. Thus, the reaction takes place in solution as well as on solid support. After each reaction step, the solvent was

evaporated, and, then, the support was taken up in a mixture of MeCN/H_2O and filtered. The solvent switch caused a reattachment of the intermediates onto the FRPSG support. Control experiments had shown that more than 99% of the intermediates **1**–**4** remained on the FRPSG by applying this procedure.

In contrast, control experiments with unmodified silica gel and perfluoro-tagged benzyl alcohol **1** in MeCN/H_2O did not lead to a significant immobilization. More than 90% of **1** were found in solution.

After the final cyclization step the products **5a**–**5p** were obtained after separation from the FRPSG in pure form by crystallization out of the organic phase (see *General Procedure* in *Exper. Part*). The whole reaction sequence was performed without isolation of intermediates.

Yields of the 16 quinazoline-2,4-diones **5a**–**5p** are summarized in the *Table*. In essence, they correspond to those obtained in the parallel synthesis of **5a**–**5p** in a fluorous/organic biphasic system, followed by extraction with perfluorinated solvent.

The final cyclization step leads to regeneration of **6**. This recycled material could be re-used again for another round of synthesis according to *Scheme 2*. Compound **5p** was obtained in a yield of 35%.

The established system is a mimic of hydroxymethylated solid supports. Hence, it is amenable to a whole range of different heterocyclic core structures obtainable by a similar final intramolecular cyclization step [2]. Furthermore, the immobilized perfluoro-tagged benzyl alcohol can be adapted to a broad scope of reaction conditions without further evaluation, *e.g.*, of the swelling properties of the solid-support material.

Conclusions. – We were able to establish a straightforward multistep synthesis for quinazoline-2,4-diones without isolation of intermediates. The solution-phase synthesis started from the perfluoro-tagged benzyl alcohol **1**, and the final products **5a**–**5p** were isolated by liquid-liquid extraction between perfluorinated and organic solvent.

The solid-phase synthesis of **5a**–**5p** started from **6**, in which the perfluoro-tagged benzyl alcohol is attached to FRPSG by fluorous–fluorous interactions. The products were obtained in pure form after filtration from the FRPSG. This was possible, since all unreacted intermediates but the final products carry a perfluorinated unit, which renders them very lipophilic as compared to the quinazoline-2,4-diones. Most importantly, the latter approach does not involve the application of perfluorinated solvents. Furthermore, none of the individual steps has to go to completion. In addition, we were also able to demonstrate that recycled **6** from the first run could be used for another synthesis cycle (for **5p**). The approach is generally applicable to the rapid parallel multistep synthesis of different heterocyclic cores by cyclization protocols in analogy to existing protocols on solid phase for hydroxymethylated resins.

The principle of detachment and reattachment by solvent switch is a new method for solid-phase-supported synthesis. Since the attachment is based on fluorous–fluorous interactions, we would like to dub it as fluorous solid-phase organic synthesis (FSPOS).

We would like to thank Dr. *Keller*, Mrs. *Schonhard*, and Mr. *Reinbold* for NMR spectra, Mr. *Warth* and Mr. *Wörth* for mass spectra, and Mr. *Hickl* for elementary analysis. Furthermore, we would like to thank *Degussa AG* for a free gift of perfluoro(triethoxy)silane and *Byk Gulden Pharmaceuticals* for financial support.

Experimental Part

1. *General.* All reagents were obtained from *Acros* or *Aldrich* and were of highest purity available. THF was dried over Na and was freshly distilled before use. M.p.: electrothermal digital melting device *IA 9200*; uncorrected. NMR Spectra: at 250, 400 MHz (^{1}H) and 100 MHz (^{13}C); $CDCl_3$ and (D_6)DMSO solns.; chemical shifts δ in ppm rel. to Me_4Si (= 0 ppm) for ^{1}H and rel. to $CHCl_3$ (77,00 ppm) for ^{13}C as an internal reference; *J* in Hz. MS: *Finnigan MAT8200* (EI), *MAT312* (CI), and *TSQ-7000* (ESI) mass spectrometer.

2. *Synthesis.* A general procedure for rapid synthesis of quinazoline-2,4-diones with application of immobilized linker **1** on FRPSG is given below. For exper. data concerning the synthesis in fluorous biphasic system, see [3].

Preparation of FRPSG [12][13]. Silica gel (50 g; 35–70 μm; 550 m^2/g) was activated by treatment with 150 ml of conc. HCl. The supension was stirred for 2 h at r.t. and for 3 h at 50° in a rotary evaporator. Then the silica gel was filtered off, washed with 150 ml of MeOH/H_2O 1:1, 150 ml of MeOH, 150 ml of CH_2Cl_2, and 150 ml of Et_2O, and dried under high vacuum.

The activated silica gel was suspended in 150 ml of toluene (700 ppm H_2O), and 1.4 g (7 mmol) of TsOH and 35.8 g (0.07 mol) of (3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)(triethoxy)silane were added. The mixture was stirred for 12 h at r.t., then for 24 h at 100° in a rotary evaporator. The product was filtered off and washed with 300 ml of MeOH, 300 ml of CH_2Cl_2, 500 ml of Et_2O, and dried under high vacuum to give 74 g of FRPSG.

General Procedure for the Preparation of 4-[Tris(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)silyl]benzyl Alcohol Loaded Fluorous Reversed-Phase Silica Gel (FRPSG) (**6**). In a rotating flask, 0.43 mmol of **1** was thoroughly mixed with 5 g of FRPSG and Et_2O as a solvent. Et_2O was evaporated, and the resulting powder was treated with 3 × 20 ml of anh. MeCN to remove traces of H_2O.

Synthesis of **5a** *as an Example for the Preparation of Quinazoline-2,4-diones* **5a**–**5p**. A suspension of 0.1 g (0.51 mmol) of trichloromethyl chloroformate and 10 mg of activated charcoal in 50 ml anh. THF were shaken under Ar for 10 min. Within 10 min, 5.5 g of **6** were added to the suspension. After shaking at r.t. for 15 h, the solvent and reagent were evaporated to give **7**.

FRPSG-Bound chloroformate **7** (5.53 g), 0.28 g (2.0 mmol) of anthranilic acid, and 0.5 ml (3.0 mmol) of *Hünig*'s base were taken up in 50 ml anh. THF. The suspension was shaken at r.t. for 16 h. The solvent was removed *in vacuo*, and the residue was rinsed with 5 × 50 ml of MeCN/H_2O 8:1. The resulting powder was treated with 3 × 20 ml of anh. MeCN to remove traces of H_2O.

Under Ar, 5.56 g of the FRPSG-bound carbamate **8a**, 0.1 ml (1.0 mmol) furfurylamine, 0.3 ml (2.0 mmol) of *Hünig*'s base, and 0.32 g (1.0 mmol) of TBTU were suspended in 30 ml of anh. THF. The suspension was shaken at r.t. for 16 h. The solvent was removed *in vacuo*, and the FRPSG was rinsed with 5 × 50 ml of MeCN/H_2O 8:1 to give **9a**.

The FRPSG-bound amide **9a** (5.56 g) and 0.2 ml (2.0 mmol) of Et_3N were taken up in 10 ml of DMF. The suspension was heated in a sealed vial to 120° for 16 h. After cooling, the vial was carefully opened, and the mixture was washed with 100 ml of H_2O. The resulting slurry was filtered, and the FRPSG was rinsed with 5 × 40 ml of MeCN/H_2O 8:1 and concentrated *in vacuo*. During concentration, 48 mg (47%) of the desired quinazoline-2,4-dione **5a** precipitated from the aq./org. phase. The complete synthesis was performed in a straightforward manner without isolation of intermediates.

Data of the 16 Quinazoline-2,4-diones. 3-[(Furan-2-yl)methyl]quinazoline-2,4-dione (**5a**). Yield 48 mg (47%). M.p. 245°. ^{1}H-NMR ((D_6)DMSO, 400 MHz): 5.06 (*s*, CH_2); 6.29 (*d*, *J* = 2.6, 1 H (fur.)); 6.38 (*t*, *J* = 2.5, 1 H (fur.)); 7.20 (*m*, 2 arom. H); 7.52 (*s*, 1 H (fur.)); 7.65 (*t*, *J* = 7.8, 1 arom. H); 7.93 (*d*, *J* = 8.0, 1 arom. H); 11.00 (*s*, NH). ^{13}C-NMR ((D_6)DMSO, 100 MHz): 36.1; 108.1; 109.8; 113.6; 114.9; 122.0; 127.3; 134.3; 139.0; 141.2; 149.9; 150.0; 161.7. MS (70 eV): 242 (100, M^+), 213 (16), 146 (22), 81 (45). Anal. calc. for $C_{13}H_{10}N_2O_3$ (242.23): C 64.46, H 4.16, N 11.56; found: C 64.33, H 4.10, N 11.52.

3-Benzylquinazoline-2,4-dione (**5b**). Yield 48 mg (45%). M.p.: 229°. ^{1}H-NMR ($CDCl_3$, 400 MHz): 5.26 (*s*, CH_2); 7.02 (*d*, *J* = 7.3, 1 arom. H); 7.19–7.31 (*m*, 4 arom. H); 7.50 (*d*, *J* = 7.0, 2 arom. H); 7.58 (*t*, *J* = 10.0, 1 arom. H); 8.12 (*d*, *J* = 8.8, 1 arom. H); 9.65 (*s*, NH). ^{13}C-NMR ($CDCl_3$, 100 MHz): 44.3; 114.7; 114.9; 123.6; 127.8; 128.5; 129.0; 135.2; 136.9; 138.5; 151.8; 162.4. MS (70 eV): 252 (100, M^+), 235 (16), 147 (36), 91 (52). Anal. calc. for $C_{15}H_{12}N_2O_2 \cdot 0.2\ H_2O$ (255.69): C 70.46, H 4.81, N 10.95; found: C 70.16, H 4.90, N 10.78.

3-(3,4-Dimethoxyphenyl)quinazoline-2,4-dione (**5c**). Yield 38 mg (30%). M.p.: 260° (subl.). ^{1}H-NMR ((D_6)DMSO, 500 MHz): 3.70 (*s*, Me); 3.81 (*s*, Me); 6.82 (*dd*, *J* = 8.4, 2.1, 1 arom. H); 6.94 (*d*, *J* = 2.4, 1 arom. H); 7.01 (*d*, *J* = 8.5, 1 arom. H); 7.22 (*d*, *J* = 7.75, 2 arom. H); 7.68 (*t*, *J* = 8.6, 1 arom. H); 7.92 (*d*, *J* = 7.5, 1 arom. H); 11.47 (*s*, NH). ^{13}C-NMR ((D_6)DMSO, 125.7 MHz): 55.6; 111.5; 112.9; 114.3; 115.1; 121.1; 122.4; 127.5; 128.4; 135.1; 139.7; 148.5; 148.8 (12 arom. C); 150.3 (C(4)); 162.3 (C(2)). MS (70 eV): 298 (100, M^+), 146 (88), 119

(18), 97 (14), 81 (22), 71 (30), 69 (42), 57 (49). Anal. calc. for $C_{16}H_{14}N_2O_4$ (298.29): C 64.42, H 4.73, N 9.39; found: C 64.34, H 4.97, N 9.23.

3-[2-(4-Chlorophenyl)ethyl]aminazoline-2,4-dione (**5d**). Yield 93 mg (73%). M.p.: 232°. ^{1}H-NMR ((D$_6$)DMSO, 500 MHz): 2.88 (*t*, *J* = 7.9, CH_2); 4.09 (*t*, *J* = 8.0, CH_2); 7.16 (*d*, *J* = 8.2, 1 arom. H); 7.19 (*t*, *J* = 7.5, 1 arom. H); 7.24 (*d*, *J* = 8.5, 2 arom. H); 7.33 (*d*, *J* = 8.5, 2 arom. H); 7.64 (*t*, *J* = 7.7, 1 arom. H); 7.91 (*d*, *J* = 7.9, 1 arom. H); 11.41 (*s*, NH). ^{13}C-NMR ((D$_6$)DMSO, 125.7 MHz): 32.6; 41.0; 113.7; 115.1; 122.5; 127.3; 128.3; 130.5; 130.9; 135.0; 137.7; 139.3; 149.9; 161.7. MS (70 eV): 300 (19, M^+), 162 (28), 146 (46), 138 (100), 119 (23), 90 (16); Anal. calc. for $C_{16}H_{13}ClN_2O_2$ (300.74): C 63.90, H 4.36, N 9.31; found: C 63.53, H 4.48, N 9.33.

7-Chloro-3-[(furan-2-yl)methyl]quinazoline-2,4-dione (**5e**). Yield 34 mg (29%). M.p.: 256°. ^{1}H-NMR ((D$_6$)DMSO, 500 MHz): 5.05 (*s*, CH_2); 6.29 (*d*, *J* = 2.6, 1 H (fur.)); 6.37 (*t*, *J* = 2.5, 1 H (fur.)); 7.19 (*s*, 1 H (fur.)); 7.25 (*d*, *J* = 7.9, 1 arom. H); 7.53 (*s*, 1 arom. H); 7.92 (*d*, *J* = 8.0, 1 arom. H); 11.71 (*s*, NH). ^{13}C-NMR ((D$_6$)DMSO, 125.7 MHz): 42.7; 108.0; 110.5; 112.6; 114.6; 122.8; 129.5; 139.5; 140.5; 142.1; 149.6; 150.1; 160.8. MS (70 eV): 276 (100, M^+), 247 (17), 180 (36), 129 (76), 81 (91). Anal. calc. for $C_{13}H_9ClN_2O_3$ (276,67): C 56.43, H 3.28, N 10.13; found: C 55.98, H 3.02, N 9.82.

3-Benzyl-7-chloroquinazoline-2,4-dione (**5f**). Yield 43 mg (35%). M.p.: 271°. ^{1}H-NMR ((D$_6$)DMSO, 250 MHz): 4.98 (*s*, CH_2); 7.09–7.22 (*m*, 7 arom. H); 8.03 (*d*, *J* = 8.3, 1 arom. H); 11.55 (*s*, NH). ^{13}C-NMR ((D$_6$)DMSO, 100 MHz): 43.2; 112.7; 114.6; 122.8; 127.1; 127.5; 128.3; 129.5; 137.1; 139.5; 140.5; 150.1; 161.3. MS (70 eV): 286 (100, M^+), 269 (18), 181 (35), 154 (24), 132 (33), 91 (93), 65 (22). Anal. calc. for $C_{15}H_{11}ClN_2O_2$ (286.71): C 62.84, H 3.87, N 9.77; found: C 62.68, H 3.87, N 9.66.

7-Chloro-3-(3,4-dimethoxyphenyl)quinazoline-2,4-dione (**5g**). Yield 109 mg (77%). M.p.: 295° (dec.). ^{1}H-NMR ((D$_6$)DMSO, 250 MHz): 3.77 (*s*, Me); 3.87 (*s*, Me); 6.88 (*dd*, *J* = 8.4, 2.1, 1 arom. H); 7.01 (*d*, *J* = 2.4, 1 arom. H); 7.07 (*d*, *J* = 8.5, 1 arom. H); 7.28 (*m*, 2 arom. H); 7.33 (*d*, *J* = 2.5, 1 arom. H); 7.98 (*d*, *J* = 8.3, 1 arom. H); 11.67 (s, NH). ^{13}C-NMR ((D$_6$)DMSO, 100 MHz): 55.6; 111.5; 112.8; 113.3; 114.4; 121.0; 122.5; 128.1; 129.6; 139.3; 140.8; 148.5; 148.8; 150.1; 161.5. MS (70 eV): 332 (52, M^+), 317 (12), 286 (12), 180 (45) , 91 (100). Anal. calc. for $C_{16}H_{13}ClN_2O_4$ (332,74): C 57.75, H 3.94, N 8.42; found: C 57.88, H 4.13, N 8.28.

7-Chloro-3-[2-(4-chlorophenyl)ethyl]quinazoline-2,4-dione (**5h**). Yield 128 mg (90%). M.p. 240° (subl.). ^{1}H-NMR ((D$_6$)DMSO, 400 MHz): 2.98 (*t*, *J* = 7.9, CH_2); 4.20 (*t*, *J* = 8.0, CH_2); 7.29 (*d*, *J* = 2.0, 1 arom. H); 7.32–7.41 (*m*, 3 arom. H); 7.48 (*d*, *J* = 8.2, 2 arom. H); 11.68 (*s*, NH). ^{13}C-NMR ((D$_6$)DMSO, 100 MHz): 32.5; 41.1; 112.7; 114.4; 122.7; 128.3; 129.4; 130.5; 130.9; 137.6; 139.3; 149.8; 161.1. MS (70 eV): 334 (7, M^+), 180 (22), 138 (100), 103 (14). Anal. calc. for $C_{16}H_{12}Cl_2N_2O_2$ (335.18): C 57.33, H 3.61, N 8.36; found: C 57.11, H 3.44, N 7.97.

3-[(Furan-2-yl)methyl]-1-methylquinazoline-2,4-dione (**5i**). Yield 57 mg (52%). M.p. 186°. ^{1}H-NMR ((D$_6$)DMSO, 250 MHz): 3.46 (*s*, Me); 5.10 (*s*, CH_2); 6.25 (*d*, *J* = 3.4, 1 H (fur.)); 6.32 (*d*, *J* = 3.4, 1 H (fur.)); 7.25 (*t*, *J* = 7.9, 1 arom. H); 7.40 (*d*, *J* = 8.6, 1 arom. H); 7.47 (*s*, 1 H (fur.)); 7.73 (*t*, *J* = 8.1, 1 arom. H); 7.99 (*d*, *J* = 7.6, 1 arom. H). ^{13}C-NMR ((D$_6$)DMSO, 100 MHz): 30.7; 37.5; 95.8; 108.2; 110.5; 114.7; 122.9; 127.8; 135.6; 140.4; 142.1; 150.0; 150.2; 160.7. MS (70 eV): 256 (45, M^+), 227 (7), 177 (9), 104 (10), 81 (100). Anal. calc. for $C_{14}H_{12}N_2O_3$ (256.26): C 65.62, H 4.72, N 10.93; found: C 65.13, H 4.69, N 10.72.

3-Benzyl-1-methylquinazoline-2,4-dione (**5j**). Yield 49 mg (43%). M.p. 131°. ^{1}H-NMR ((D$_6$)DMSO, 250 MHz): 3.39 (*s*, Me); 5.00 (*s*, CH_2); 7.05–7.21 (*m*, 6 arom. H); 7.33 (*d*, *J* = 8.3, 1 arom. H); 7.65 (*t*, *J* = 7.9, 1 arom. H); 7.92 (*d*, *J* = 7.9, 1 arom. H). ^{13}C-NMR ((D$_6$)DMSO, 100 MHz): 30.7; 44.2; 114.6; 114.7; 122.8; 127.1; 127.6; 127.9; 128.3; 135.3; 137.2; 140.5; 150.1; 161.2. MS (70 eV): 266 (100, M^+), 161 (22), 132 (29), 105 (22), 91 (67), 77 (22). Anal. calc. for $C_{16}H_{14}N_2O_2 \cdot 0.2H_2O$ (269,89): C 71.20, H 5.30, N 10.37; found: C 70.72, H 5.32, N 10.14.

3-(3,4-Dimethoxyphenyl)-1-methylquinazoline-2,4-dione (**5k**). Yield 110 mg (83%). M.p. 240°. ^{1}H-NMR ((D$_6$)DMSO, 250 MHz): 3.43 (*s*, MeN); 3.60 (*s*, MeO); 3.71 (*s*, MeO); 6.71 (*dd*, *J* = 8.3, 2.2, 1 arom. H); 6.84 (*d*, *J* = 2.4, 1 arom. H); 6.92 (*d*, *J* = 8.9, 1 arom. H); 7.22 (*t*, *J* = 8.0, 1 arom. H); 7.40 (*d*, *J* = 8.5, 1 arom. H); 7.72 (*t*, *J* = 7.9, 1 arom. H); 7.94 (*d*, *J* = 7.9, 1 arom. H). ^{13}C-NMR ((D$_6$)DMSO, 100 MHz): 30.7; 55.6; 55.7; 111.5; 112.6; 114.6; 115.4; 120.9; 122.7; 128.0; 129.0; 135.5; 140.7; 148.5; 148.8; 150.6; 161.5. MS (70 eV): 312 (100, M^+), 297 (32), 266 (30), 159 (23), 132 (18), 104 (37), 91 (26), 77 (25). Anal. calc. for $C_{17}H_{16}N_2O_4$ (312.32): C 65.38, H 5.16, N 8.97; found: C 64.92, H 5.27, N 8.50.

3-[2-(4-Chlorophenyl)ethyl]-1-methylquinazoline-2,4-dione (**5l**). Yield 107 mg (80%). M.p. 164°. ^{1}H-NMR ((D$_6$)DMSO, 250 MHz): 2.87 (*t*, *J* = 7.9, CH_2); 3.44 (*s*, Me); 4.14 (*t*, *J* = 7.9, CH_2); 7.22–7.38 (*m*, 5 arom. H); 7.45 (*d*, *J* = 8.3, 1 arom. H); 7.78 (*t*, *J* = 8.0, 1 arom. H); 8.03 (*d*, *J* = 7.9, arom. H). ^{13}C-NMR ((D$_6$)DMSO, 100 MHz): 30.6; 32.5; 42.1; 114.6; 114.7; 122.7; 127.7; 128.4; 130.5; 131.0; 135.3; 137.7; 140.3; 150.1; 160.9. MS (70 eV): 314 (12, M^+), 189 (10), 176 (100), 138 (18), 105 (23), 77 (17). Anal. calc. for $C_{17}H_{15}ClN_2O_2 \cdot 0.2\,H_2O$ (317.68): C 64.27, H 4.82, N 8.82; found: C 63.97, H 5.18, N 8.81.

1,3-Bis[(furan-2-yl)methyl]quinazoline-2,4-dione (**5m**). Yield 71 mg (52%). M.p. 150°. ^{1}H-NMR ((D$_6$)DMSO, 400 MHz): 5.15 (*s*, CH$_2$); 5.36 (*s*, CH$_2$); 6.32 (*d*, *J* = 3.4, 1 H (fur.)); 6.35–6.41 (*m*, 2 H (fur.)); 6.45 (*d*, *J* = 3.4, 1 H (fur.)); 7.31 (*t*, *J* = 7.7, 1 arom. H); 7.52 (*s*, 1 H (fur.)); 7.57 (*s*, 1 H (fur.)); 7.59 (*d*, *J* = 8.6, 1 arom. H); 7.76 (*t*, *J* = 7.9, 1 arom. H); 8.07 (*d*, *J* = 8.1, 1 arom. H). ^{13}C-NMR ((D$_6$)DMSO, 100 MHz): 37.7; 39.0; 108.2; 108.8; 110.6; 110.7; 114.8; 115.0; 123.1; 128.1; 135.4; 139.4; 142.2; 142.8; 149.4; 149.9; 150.0; 160.6. MS (70 eV): 322 (37, M^+), 241 (58), 198 (48), 146 (74), 81 (100). Anal. calc. for C$_{18}$H$_{14}$N$_2$O$_4$ (322.31): calc: C 67.07, H 4.38, N 8.69; found: C 66.86, H 4.07, N 8.68.

3-Benzyl-1-[(furan-2-yl)methyl]quinazoline-2,4-dione (**5n**). Yield 41 mg (29%). M.p. 148°. ^{1}H-NMR ((D$_6$)DMSO, 400 MHz): 5.17 (*s*, CH$_2$); 5.38 (*s*, CH$_2$); 6.39 (*d*, *J* = 3.3, 1 H (fur.)); 6.43 (*d*, *J* = 3.3, 1 H (fur.)); 7.21–7.36 (*m*, 6 arom. H); 7.57 (*s*, 1 H (fur.)); 7.60 (*d*, *J* = 8.4, 1 arom. H); 7.76 (*t*, *J* = 8.1, 1 arom. H); 8.07 (*d*, *J* = 7.7, 1 arom. H). ^{13}C-NMR ((D$_6$)DMSO, 100 MHz): 38.9; 44.3; 108.6; 110.5; 114.8; 114.9; 123.1; 127.5; 128.0; 128.3; 135.3; 137.0; 139.4; 142.7; 149.4; 150.3; 160.9. MS (70 eV): 332 (47, M^+), 251 (12), 198 (16), 170 (7), 146 (30), 91 (14), 81 (100). Anal. calc. for C$_{20}$H$_{16}$N$_2$O$_3$ (332.35): calc: C 72.28, H 4.85, N 8.43; found: C 72.23, H 4.93, N 8.34.

3-(3,4-Dimethoxyphenyl)-1-[(furan-2-yl)methyl]quinazoline-2,4-dione (**5o**). Yield 68 mg (42%). M.p. 193°. ^{1}H-NMR ((D$_6$)DMSO, 250 MHz): 3.82 (*s*, Me); 3.77 (*s*, Me); 5.40 (*s*, CH$_2$); 6.44 (*d*, *J* = 3.3, 1 H (fur.)); 6.51 (*d*, *J* = 3.3, 1 H (fur.)); 6.88 (*d*, *J* = 8.5, 1 arom. H); 6.99–7.09 (*m*, 2 arom. H); 7.34 (*t*, *J* = 7.3, 1 arom. H); 7.61–7.69 (*m*, 1 arom. H, 1 H (fur.)); 7.81 (*t*, *J* = 7.9, 1 arom. H); 8.09 (*d*, *J* = 7.9, 1 arom. H). ^{13}C-NMR ((D$_6$)DMSO, 100 MHz): 38.9; 55.6; 108.7; 110.6; 111.5; 112.8; 114.8; 115.6; 120.9; 122.8; 128.1; 128.8; 135.2; 139.7; 142.7; 148.5; 148.8; 149.5; 150.4; 161.3. MS (70 eV): 378 (38, M^+), 153 (15), 138 (31), 81 (100). Anal. calc. for C$_{21}$H$_{18}$N$_2$O$_5$ (378.38): calc: C 66.66, H 4.79, N 7.40; found: C 66.60, H 5.03, N 7.48.

3-[2-(4-Chlorophenyl)ethyl]-1-[(furan-2-yl)methyl]quinazoline-2,4-dione (**5p**). Yield 100 mg (62%). M.p. 168°. ^{1}H-NMR ((D$_6$)DMSO, 500 MHz): 2.90 (*t*, *J* = 7.8, CH$_2$); 4.18 (*t*, *J* = 7.9, CH$_2$); 5.33 (*s*, CH$_2$); 6.37 (*d*, *J* = 3.4, 1 H (fur.)); 6.39 (*d*, *J* = 3.4, 1 H (fur.)); 7.21–7.33 (*m*, 5 arom. H); 7.55–7.59 (*m*, 1 arom. H, 1 H (fur.)); 7.74 (*t*, *J* = 7.7, 1 arom. H); 8.04 (*d*, *J* = 7.7, 1 arom. H). ^{13}C-NMR ((D$_6$)DMSO, 100 MHz): 32.4; 38.9; 42.1; 108.6; 110.5; 114.7; 114.8; 122.9; 127.9; 128.3; 130.5; 135.1; 137.5; 139.3; 142.7; 149.4; 150.0; 160.9. MS (70 eV): 380 (8, M^+), 242 (53), 146 (11), 138 (8), 81 (100). Anal. calc. for C$_{21}$H$_{17}$ClN$_2$O$_3$ (380.82): calc: C 66.23, H 4.50, N 7.36; found: C 66.38, H 4.54, N 6.94.

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Received August 16, 2002