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Access to Variously Substituted 5,6,7,8-Tetrahydro-3*H*-quinazolin-4-ones via Diels–Alder Adducts of Phenyl Vinyl Sulfone to Cyclobutene-Annelated Pyrimidinones[‡]

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Dedicated to Professor Tien-Yau Luh on the occasion of his 60th birthday

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Under basic conditions (Et_3N, dioxane), the aromatic amidines **4** and also *S*-methylisothiourea **4g** cleanly undergo Michael addition to methyl 2-chloro-2-cyclopropylideneacetate (**5**), followed by intramolecular nucleophilic substitution, cyclopropyl to cyclobutyl ring enlargement, deprotonation and cyclization with elimination of methanol to afford the cyclobutene-annelated pyrimidinones **6** in 43–83 % yield (7 examples). Thermal cyclobutene-ring opening of the latter at 175 °C followed by regioselective Diels–Alder cycloaddition with phenyl vinyl sulfone gives the 2-aryl-6-(phenylsulfonyl)-5,6,7,8-tetrahydroquinazolinone derivatives **12** in 39–83 % yield (7 examples). Base-induced elimination of benzenesulfinic acid and subsequent catalytic hydrogenation leads to the 2-aryltetrahydroquinazolinone derivatives **14** in excellent yields (6 examples). Deprotonation at the sulfonyl-substituted center, alkylation and subsequent elimination of benzenesulfinic acid followed by catalytic hydrogenation gives the 2,6-disubstituted tetrahydroquinazolinones **17a**-R. Nucleophilic substitution of the methylthio group in **12g** by secondary amines yields the 2-(dialkylamino)tetrahydroquinazolinones **14i–k**.

Introduction

Folic acid (**1**), one of the important B vitamins, is a precursor for the biosynthesis of the coenzyme tetrahydrofolic acid. The latter in turn serves both as a formyl and a hydroxymethyl transfer agent in a variety of biological systems.[1] The analogous 5,8-dideaza-5,6,7,8-tetrahydrofolic acid (**2**) and in general 2-substituted tetrahydroquinazolinones have attracted considerable attention in chemistry[2] and biology.[3] A wide range of biological activities has been discovered for such compounds: anticancer activity, antimicrobial activity against *Streptococcus faecium*, inhibition of dihydrofolate reductase and thymidilate synthase,[4] as well as an ability to be a good substrate for partially purified mouse liver folylpolyglutamate synthetase.[5] Although there are several known preparative routes to tetrahydroquinazolinone derivatives,[6] our recently discovered access to such compounds by way of Michael addition of amidines to methyl 2-chloro-2-cyclopropylidineacetate (**5**),[7] with ring-enlarging rearrangement to yield cyclobutene-annelated pyrimidinones **6**, which subsequently undergo thermal cyclobutene-ring opening followed by Diels–Alder reaction,[8] deserved further interest. In order to realize a substitution pattern as in **2** in a regioselective manner, we chose to test phenyl vinyl sulfone as a dienophile.[9] Although this sul-

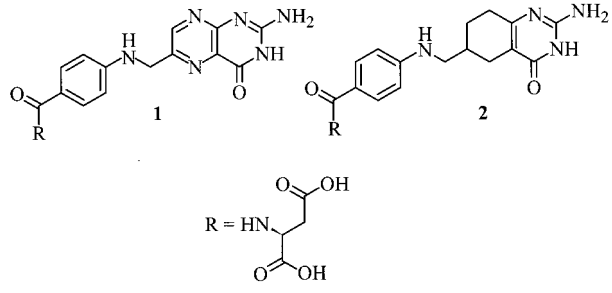

Figure 1. Coenzyme folic acid (**1**) and its dideazatetrahydro analogue **2**.

[‡] Cyclopropyl Building Blocks in Organic Synthesis, 124. Part 123: J. Revuelta, S. Cicchi, C. Faggi, S. I. Kozhushkov, A. de Meijere, A. Brandi, *J. Org. Chem.* **2006**, *71*, 2417–2423. Part 122: A. Zanobini, A. Brandi, A. de Meijere, *Eur. J. Org. Chem.* **2006**, 1251–1255.

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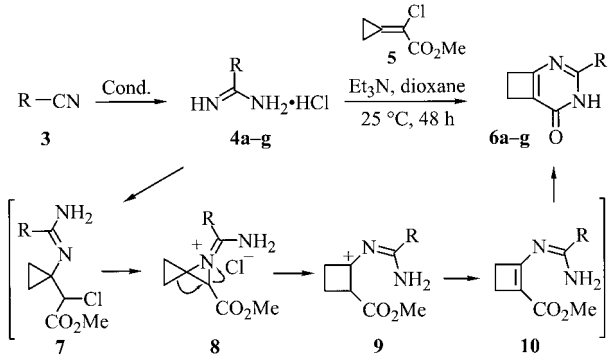
fone has been used as a dienophile in an intramolecular Diels–Alder reaction with an in situ opened cyclobutene ring,[10] a regioselective intermolecular addition of this kind has never been achieved (Figure 1).

Results and Discussion

Among the various known methods for the preparation of amidines from nitriles,[11] the one described by Reed et al.[11b] turned out to work best for the substrates employed here. Thus, upon treatment of tetrahydrofuran solutions of several aromatic nitriles **3b**–**e** with a 1 N solution of lithium bis(trimethylsilyl)amide (LiHMDS) in hexane followed by quenching with 5–6 N isopropanolic HCl, the corresponding amidines **4b**–**e** were formed and isolated in good to excellent yields (80–92%). Surprisingly, under these conditions *o*-phenylbenzonitrile failed to give amidine **4f**. This compound was eventually obtained by treatment with a freshly prepared solution of $MeAl(Cl)NH_2$ (from Me_3Al and NH_4Cl) in toluene according to a modified protocol developed by von der Saal et al., in 58% yield.[11e]

When a mixture of methyl 2-chloro-2-cyclopropylideneacetate (**5**) and 2 equiv. of benzamidine hydrochloride (**4a**) was stirred in dioxane in the presence of 4 equiv. of triethylamine at room temperature for 48 h, 3-phenyl-2,4-diazabicyclo[4.2.0]octa-1(6),2-diene-5-one (**6a**) was isolated in 83% yield. Similarly, under the same conditions the corresponding pyrimidinones **6b**–**f** were obtained in good yields (43–82%). The less reactive *S*-methylisothiourea hydrogensulfate (**4g**) produced the corresponding pyrimidinone **6g** at elevated temperature (50 °C) in 74% yield (Scheme 1).



Scheme 1. Michael addition of amidines **4** to methyl 2-chloro-2-cyclopropylideneacetate (**5**) to yield cyclobutene-annelated pyrimidinones **6**. Conditions **A**: $LiN(SiMe_3)_2$ (1 M, THF), THF, 25 °C, 4 h; conditions **B**: Me_3Al (2 M, toluene), NH_4Cl, toluene, 120 °C, 20 h (for further details see Table 1).

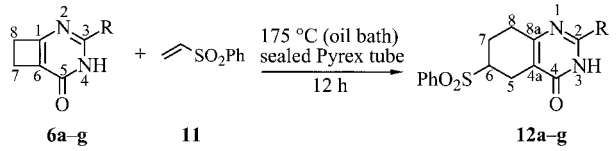
These cyclobutene-annelated pyrimidinones **6** resemble heteroanalogues of benzocyclobutene and, as expected, also undergo thermal ring opening and subsequent cycloaddition with dienophiles to give tetrahydroquinazolinone derivatives.[8] The reaction conditions for this transformation, applying phenyl vinyl sulfone (**11**), were optimized with

Table 1. Michael addition of amidines **4** to methyl 2-chloro-2-cyclopropylideneacetate (**5**) to yield cyclobutene-annelated pyrimidinones **6** (see Scheme 1).

Nitrile	R	Conditions	Amidine	Yield (%)	Product	Yield (%)
–[a]	Ph	–[a]	**4a**	–[a]	**6a**	83
3b	4-ClC_6H_4	**A**	**4b**	93	**6b**	78
3c	2-BrC_6H_4	**A**	**4c**	91	**6c**	76
3d	2-FC_6H_4	**A**	**4d**	82	**6d**	82
3e	4-(BnO)C_6H_4	**A**	**4e**	92	**6e**	68
3f	2-PhC_6H_4	**B**	**4f**	58	**6f**	43
–[b]	SMe	–[b]	**4g**	–[b]	**6g**	74[c]

[a] Compound **4a** was obtained from Acros Organics. [b] Compound **4g** was obtained from Aldrich. [c] Reaction was carried out with *S*-methylisothiourea hydrogensulfate at 50 °C.

compound **6a**. As reported before,[8] the reaction of **6a** with excess methyl acrylate or acrylonitrile led to inseparable mixtures of regioisomers. The first reactions of **6a** with an excess of phenyl vinyl sulfone (**11**) were carried out in toluene and in 1,2-dichlorobenzene solutions at 1 M concentrations and 175 °C in a sealed Pyrex tube for 12 h. Although they gave rather poor yields of the corresponding Diels–Alder adduct **12a** (Scheme 2 and Table 2, Entries 1, 2), the latter was obtained as a single regioisomer. The yields were significantly increased by carrying out the cycloaddition without any solvent. Because the melting point of the sulfone **11** is 68 °C, the cycloaddition to **6a** could be performed at 175 °C in molten **11** employing a tenfold excess. Thus, 2-phenyl-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (**12a**) was isolated in 84% yield as a single regioisomer (Entry 3). The structure was confirmed by ^1H NMR, ^{13}C NMR, HMBC (heteronuclear multiple bond coherence), HMQC (heteronuclear multiple quantum coherence) spectra as well as mass spectrometric data. Virtually the same yield (83%) was obtained with a fourfold excess of **11**, but with only 1.5 equiv. of **11** or at lower temperature (165 °C) the yield was substantially reduced (Entries 4–6).



Scheme 2. Regioselective Diels–Alder reactions of phenyl vinyl sulfone (**11**) with the cyclobutene-annelated pyrimidinones **6a**–**g**. For details see Table 2.

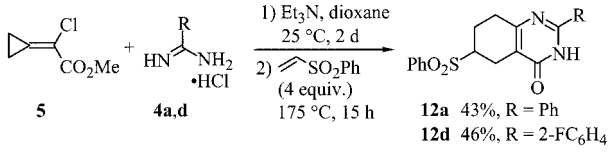
Once the optimal conditions had been found, the cyclobutene-annelated pyrimidinones **6b**–**g** were transformed in the same way to the corresponding adducts **12b**–**g** in good yields (Entries 7–12).

The overall transformations of **5** with the amidines **4a**,**d** and phenyl vinyl sulfone (**11**) were also successfully performed as one-pot operations in two steps by first treating **5** with **4a**,**d** in dioxane in the presence of Et_3N in a Pyrex

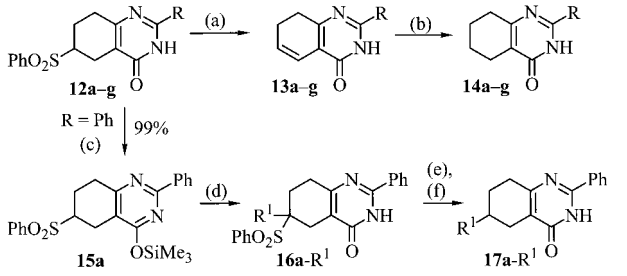
Table 2. Optimization of reaction conditions and regioselective Diels–Alder reactions of cyclobutene-annelated pyrimidinones **6a–g** with phenyl vinyl sulfone (**11**), reaction temperature 175 °C except for Entry 6 (165 °C), reaction time 12 h (see Scheme 2).

Entry	Starting material	R	Excess of **11**	Reaction conditions	Product	Yield (%)
1	**6a**	Ph	4	1,2-$Cl_2C_6H_4$	**12a**	25
2	**6a**	Ph	4	PhMe	**12a**	32
3	**6a**	Ph	10	neat	**12a**	84
4	**6a**	Ph	4	neat	**12a**	83
5	**6a**	Ph	1.5	neat	**12a**	49
6	**6a**	Ph	4	neat	**12a**	39
7	**6b**	4-ClC_6H_4	4	neat	**12b**	59
8	**6c**	2-BrC_6H_4	4	neat	**12c**	39
9	**6d**	2-FC_6H_4	4	neat	**12d**	76
10	**6e**	4-(BnO)C_6H_4	4	neat	**12e**	66
11	**6f**	2-PhC_6H_4	4	neat	**12f**	65
12	**6g**	SMe	4	neat	**12g**	56

bottle for 48 h, then adding **11** and heating the mixtures at 175 °C for 12 h. The products **12a** and **12d** could be isolated in 43 and 46% yield, respectively (Scheme 3).



Scheme 3. One-pot, two-step synthesis of tetrahydroquinazolinones **12a**,**d** from **5**, amidines **4a**,**d** and phenyl vinyl sulfone (**11**).



Scheme 4. Preparation of 2-substituted and 2,6-disubstituted tetrahydroquinazolines: (a) KO*t*Bu (3 equiv.), THF, 25 °C, 2 h; (b) Pd/C (10% Pd, w/w), H_2, MeOH or AcOH, 25 °C, 4–8 h; (c) $HN(SiMe_3)_2$, $(NH_4)_2SO_4$, 126 °C, 15 h; (d) *n*BuLi, THF, –78 °C, 30 min, then MeI or EtBr, 25 °C, 2 h; (e) KO*t*Bu, THF, 25 °C, 2 h; (f) Pd/C, H_2, MeOH, 25 °C, 4 h. For further details see Table 3.

Table 3. Preparation of 2-substituted and 2,6-disubstituted tetrahydroquinazolinones (see Scheme 4).

Entry	Starting material	Product	Yield (%)	Product	Yield (%)
1	**12a**	**13a**	94	**14a**	91
2	**12b**	**13b**	95	**14b**	94[a]
3	**12c**	**13c**	93	**14c**	92
4	**12d**	**13d**	92	**14d**	92
5	**12e**	**13e**	92	**14e**[b]	93[a,b]
6	**12f**	**13f**	87	**14f**	93
7	**12g**	**13g**	93	**14g**	n. r.[c]
8	**15a**	**16a**-Me	83	**17a**-Me	92
9	**15a**	**16a**-Et	86	**17a**-Et	90

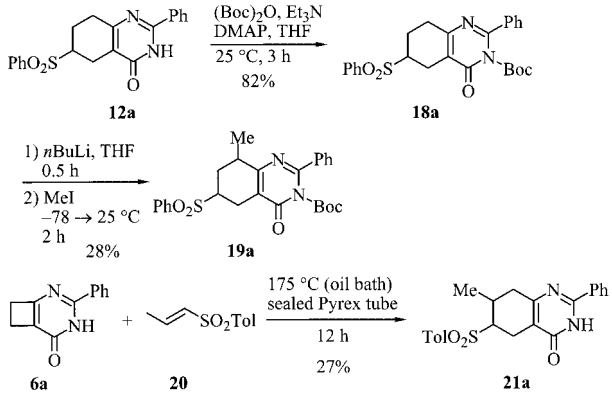
[a] Hydrogenation in AcOH. [b] Without *O*-benzyl group. [c] n. r. = no reaction.

The next issue was to remove the sulfonyl group from the products **12a–g**. Among the known methods for such a transformation treatment with sodium amalgam in the presence of Na_2HPO_4[12] has most widely been used. When **12a**, however, as well as its *O*-trimethylsilyl derivative **15a** or *N*-Boc-protected derivative **18a** was treated with Na/Hg and Na_2HPO_4 (4 equiv. each) in MeOH, only starting material **12a** was isolated in each case without any reduced material. Upon treatment with sodium sand and ethanol,[13] **12a** gave only a substantial amount of benzaldehyde. Eventually, a two-step procedure was employed. First, the $PhSO_2$ group was eliminated by treatment of **12a** with 3 equiv. of KO*t*Bu in tetrahydrofuran, then the elimination product **13a**, obtained in 96% yield after 2 h, was subjected to catalytic hydrogenation over palladium on charcoal in methanol to lead to the target 2-phenyl-5,6,7,8-tetrahydroquinazolinone (**14a**) in 91% yield. Analogously, **14c**,**d**,**f** were formed from **12c**,**d**,**f** in excellent yields (Scheme 4 and Table 3). Because of the low solubility of **13b** and **13e** in methanol, the hydrogenation had to be carried out in acetic acid to give **14b** and debenzylated **14e** (R = 4-HOC_6H_4) in 94 and 93% yield, respectively. In the case of **13g** the hydrogenation did not succeed, probably due to the presence of the methylthio group, which may have poisoned the catalyst. Instead of the desired product **14g**, some material without a methylthio group was isolated.

Reaction of **12a** with bis(trimethylsilyl)amine in the presence of ammonium sulfate gave the lactim silyl ether **15a** (99% yield), from which the sulfonyl-stabilized carbanion could be generated by treatment with *n*-butyllithium in tetrahydrofuran. Alkylation of this carbanion with methyl iodide or ethyl bromide gave, after work-up, the methyl- and ethyl-substituted derivatives **16a**-Me and **16a**-Et in 83 and 86% yield, respectively. Elimination of phenylsulfinic acid from **16a**-Me,Et and subsequent catalytic hydrogenation finally yielded the 5-alkyl-substituted tetrahydroquinazolinones **17a**-Me and **17a**-Et (92 and 90%), respectively (Scheme 4 and Table 3).

Surprisingly, when a tetrahydrofuran solution of the *N*-Boc-protected compound **18a**, prepared from **12a** in 82% yield, was treated with *n*-butyllithium and then with methyl iodide, methylation occurred only at C-8, not at C-6, to furnish *N*-Boc-8-methyl-2-phenyl-6-(phenylsulfonyl)tetrahydroquinazolin-4-one (**19a**) in poor yield (28%) only as a mixture of two diastereomers (*dr* 4:1). The yield was even lower, when lithium diisopropylamide or sodium bis(trimethylsilyl)amide were employed as base (19 and 14%), respectively (Scheme 5).

A tetrahydroquinazolinone with a substituent at C-7 was realized by the reaction of **6a** with (*E*)-1-propenyl *p*-tolyl sulfone (**20**). The corresponding cycloadduct **21a** (one diastereomer) was isolated, albeit in 27% yield only. The anal-

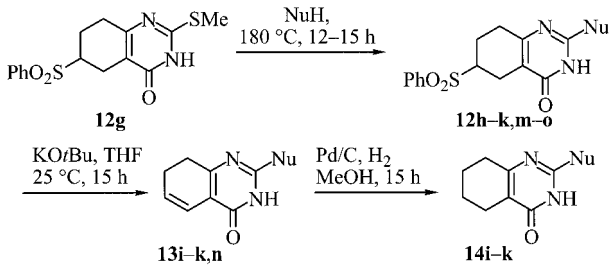


Scheme 5. Alkylation of the *N*-Boc-protected **18a** at C-8 and preparation of a 7-substituted tetrahydroquinazolinone **21a**.

ogous reaction with ethyl (*E*)-1-propenyl sulfone failed, because the sulfone polymerized under the reaction conditions (Scheme 5).

An option to prepare 8-substituted derivatives of **14**, which has not been tested yet, would be by employing the cyclobutene-annelated pyrimidinones of type **6** correspondingly substituted in the 8-position of the four-membered ring. These, along with their regioisomers should be accessible from amidines and 2′-substituted 2-chloro-2-cyclopropylideneacetates of type **5**.[14,15]

The 2-methylthio derivative **12g** was initially prepared mainly as a potential precursor to dialkylamino-substituted tetrahydroquinazolinone analogues of **12**, which ought to be accessible by nucleophilic substitution of the methylthio group in **12g** with secondary amines.[16] In an initial attempt, **12g** was heated with 2 equiv. of morpholine in DMF at 180 °C in a sealed Pyrex bottle for 12 h. This experiment did not afford the desired 2-morpholino-, but only the 2-(dimethylamino)-6-(phenylsulfonyl)tetrahydroquinazolinone (**12h**) in 78% yield. Obviously, this product was formed due to the liberation of dimethylamine from DMF at higher temperature and preferred substitution of the methylthio group by dimethylamine. This was confirmed by heating **12g** in an excess of DMF at 180 °C without morpholine, to give the same product in 86% yield. When **12g** was heated with an excess of neat morpholine at 180 °C for 12 h, **12i** was obtained in 93% yield (Scheme 6 and Table 4). Analogously, *N*-methyl- and *N*-benzylpiperazine furnished the corresponding substitution products **12j,k** in 91 and 92% yield, respectively. The elimination of $PhSO_2H$ from **12i–k** required a larger excess of KO*t*Bu (5 equiv.) and a longer period of time (15 h), but did furnish the dihydro derivatives **13i–k** in good yields (82–94%). Hydrogenation under the usual conditions provided the 2-morpholinyl-, 2-(*N*-methylpiperazinyl)-, and 2-piperazinyltetrahydroquinazolinone derivatives **14i–k** in 83–96% yield (Scheme 6).



Scheme 6. Nucleophilic substitution of the methylthio group in **12g** by amines. For details see Table 4.

Table 4. Preparation of 2-amino-substituted tetrahydroquinazolinones **14h–l** by nucleophilic substitution of the methylthio group in **12g** (see Scheme 6).

NuH	Product	Yield (%)	Product	Yield (%)	Product	Yield (%)
Me_2NH (DMF)	**12h**	86	–[a]	–[a]	–[a]	–[a]
	**12i**	93	**13i**	82	**14i**	96
	12j	91	**13j**	87	**14j**	83
	12k	92	**13k**	94	**14k**[b]	90
Bn_2NH	**12l**	n.r.[c]	–[a]	–[a]	–[a]	–[a]
$BnNH_2$	**12m**	65	**13m**	0[d]	–[a]	–[a]
NH(Me)Bn	**12n**	66	**13n**	94	–[a]	–[a]
Im-H	**12o**	63	–[a]	–[a]	–[a]	–[a]

[a] Not carried out. [b] Without *N*-benzyl group. [c] N. r. = no reaction. [d] Inseparable mixture of products.

Conclusions

In conclusion, cyclobutene-annelated pyrimidinones **6a–g** prepared by Michael addition of amidines to methyl 2-chloro-2-cyclopropylidineacetate (**5**) undergo thermal ring opening and regioselective Diels–Alder reaction with phenyl vinyl sulfone. The sulfonyl group was successfully removed by elimination under basic conditions and subsequent hydrogenation of the double bond. Thus, a method has been developed for transforming aromatic nitriles to 2-aryl-6-alkyltetrahydroquinazolinone derivatives (**17a**-R) in five simple steps with good overall yields.

Experimental Section

General Remarks: All reagents were used as purchased without further purification. All reactions in organic solvents were carried out using standard Schlenk techniques under dry nitrogen. Solvents were purified and dried prior to use according to conventional methods; tetrahydrofuran (THF), dioxane, toluene were freshly distilled from sodium/benzophenone. Solvents: C_5H_{12} stands for pentane. ^{1}H- and ^{13}C NMR spectra were recorded at ambient temperature with either Bruker AM 250 or Varian 200 or 300 instruments. Chemical shifts (δ) are given in ppm relative to residual resonances of solvents (^{1}H: 7.26 ppm for chloroform or 2.49 ppm for [D_6]-DMSO; ^{13}C: 77.0 ppm for $CDCl_3$, or 39.7 ppm for [D_6]DMSO). Coupling constants (J) are given in Hz. Multiplicities of signals are described as follows: s = singlet, br. s = broad singlet, d = doublet, t = triplet, m = multiplet, dt = doublet of triplets. The multiplicities of signals were determined by the DEPT (distortionless enhancement by polarization transfer) technique: + = primary (CH_3) or tertiary (CH) (positive DEPT signal), = secondary (CH_2) (negative DEPT signal), C_{quat} = quaternary C atoms. J values in ^{13}C NMR spectra refer to ^{13}C-^{19}F coupling. IR: Bruker IFS 66. MS: Finnigan MAT 95, 70 eV. Chromatographic separations were carried out on

Merck silica gel 60 (0.063–0.200 mm, 70–230 mesh ASTM). The dimensions of the columns are given in cm as "diameter × height of the silica gel layer". TLC: Macherey–Nagel, ready to use TLC plates Alugram® Sil G/UV_{254}. Detection under UV light at 254 nm. Melting points (uncorrected) were determind in capillaries with a Büchi 510 apparatus. Elemental analyses: Mikroanalytisches Laboratorium des Instituts für Organische und Biomolekulare Chemie der Universität Göttingen. Room temperature is abbreviated as room temp. Pd/C was purchased from Merck, Darmstadt. Benzamidine hydrochloride (**4a**) and *S*-methylisothiourea hemisulfate (**4g**) were purchased from Aldrich.

General Method (GP) 1. *p*-Chlorobenzamidine Hydrochloride (4b): Into a 50 mL dry reaction flask charged with 1 M $LiN(SiMe_3)_2$ in anhydrous THF (22 mmol), was added *p*-chlorobenzonitrile (2.76 g, 20.0 mmol) in 2 mL of THF, and the reaction mixture was kept stirring at room temp. for 4 h, at which point 5–6 N HCl (in *i*PrOH, 15 mL) was added. The crude reaction mixture was kept at 0 °C overnight. The precipitated product was filtered, washed with diethyl ether to yield **4b** (3.5 g, 93%) as a colorless solid, m.p. 238 °C (ref.[17] 243–245 °C). IR (KBr): $\tilde{\nu}$ = 3239 cm^{-1}, 3054, 1678, 1460, 1401, 1036, 715. ^1H NMR (250 MHz, [D_6]DMSO): δ = 7.60–7.77 (m, AA′ part of an AA′XX′ system, 2 H), 7.85–7.97 (m, XX′ part of an AA′XX′ system, 2 H), 8.40 (br. s, 4 H, NH) ppm. ^{13}C NMR (62.9 MHz, [D_6]DMSO): δ = 126.8 (C_{quat}), 129.4 (+), 130.6 (+), 139.1 (C_{quat}), 165.1 (NCN) ppm.

***o*-Bromobenzamidine Hydrochloride (4c):** According to GP 1, **4c** (4.3 g, 91%) was obtained from *o*-bromobenzonitrile (3.68 g, 20.2 mmol) and $LiN(SiMe_3)_2$ (22 mL, 1 M) as a colorless solid, m.p. > 250 °C. IR (KBr): $\tilde{\nu}$ = 3228 cm^{-1}, 3059, 1669, 1458, 1401, 1030, 728. ^1H NMR (250 MHz, [D_6]DMSO): δ = 7.42–7.64 (m, 3 H), 7.74–7.88 (m, 1 H), 9.55 (br. s, 4 H, NH) ppm. ^{13}C NMR (62.9 MHz, CD_3OD): δ = 121.1 (C_{quat}), 129.5 (+), 131.0 (+), 133.3 (C_{quat}), 134.8 (+), 135.0 (+), 168.4 (NCN) ppm. MS (DCI = 70 eV): *m/z* (%) = 397 (3)/399 (6)/401 (3) [2M – 2HCl + H^+], 216 (6) [M – HCl + NH_4^+], 199 (100) [M – HCl + H^+].

***o*-Fluorobenzamidine Hydrochloride (4d):** According to GP 1, **4d** (2.8 g, 82%) was obtained from *o*-fluorobenzonitrile (2.40 g, 19.8 mmol) and $LiN(SiMe_3)_2$ (22 mL, 1 M) as a colorless solid, m.p. 98–100 °C. IR (KBr): $\tilde{\nu}$ = 3477 cm^{-1}, 3144, 1701, 1674, 1476, 1401, 1228, 774, 684. ^1H NMR (250 MHz, [D_6]DMSO): δ = 7.32–7.49 (m, 2 H), 7.62–7.78 (m, 2 H), 9.31 (br. s, 4 H, NH) ppm. ^{13}C NMR (62.9 MHz, CD_3OD): δ = 118.2 (d, $^2J_{C-F}$ = 9.2 Hz, +), 118.8 (d, $^2J_{C-F}$ = 3.2 Hz, C_{quat}), 126.6 (+), 131.4 (+), 136.8 (+), 161.2 (d, $^1J_{C-F}$ = 253.7 Hz, C_{quat}), 164.9 (NCN) ppm.

***p*-Benzyloxybenzamidine Hydrochloride (4e):** According to GP 1, **4e** (2.42 g, 92%) was obtained from *p*-benzyloxybenzonitrile (2.09 g, 10 mmol) and $LiN(SiMe_3)_2$ (11 mL, 1 M) as a colorless solid, m.p. 181–182 °C (ref.[18] 179–180 °C). IR (KBr): $\tilde{\nu}$ = 3317 cm^{-1}, 3125, 1677, 1609, 1486, 1267, 1190, 1010, 837, 763. ^1H NMR (250 MHz, [D_6]DMSO): δ = 7.10–7.26 (m, 2 H), 7.28–7.52 (m, 5 H), 7.76–7.88 (m, XX′ part of an AA′XX′ system, 2 H), 9.08 (br. s, 2 H, NH), 9.26 (br. s, 2 H, NH) ppm. ^{13}C NMR (75.5 MHz, CD_3OD): δ = 71.4 (–, OCH_2), 116.7 (+), 121.14 (C_{quat}), 128.7 (+), 129.2 (+), 129.6 (+), 131.1 (+), 137.6 (C_{quat}), 164.9 (C_{quat}), 168.4 (NCN) ppm.

General Method (GP) 2. *o*-Phenylbenzamidine (4f): To a suspension of NH_4Cl (2.14 g, 40.0 mmol) in toluene (40 mL) was added at 5 °C Me_3Al (2 M in toluene, 40 mmol) over a period of 30 min. Then the temperature was allowed to reach 25 °C, and stirring was continued until the evolution of methane ceased (≈ 2 h). To this solution of $MeAl(Cl)NH_2$ was added *o*-biphenylnitrile (2.86 g, 16 mmol) in toluene (5 mL) within 5 min, and the resulting solution was heated under reflux for 20 h. After cooling to room temp., the crude reaction mixture was poured onto a suspension of SiO_2 (20 g) in CH_2Cl_2 (100 mL) and then filtered, the solid residue was washed with 2 × 50 mL of MeOH, and the solvent was removed in vacuo from the combined solutions. The residue was suspended in water (100 mL), HCl (30 mL, 2 N) was added, and the mixture extracted with ethyl acetate (2 × 50 mL). To the aq. layer was added NaOH (60 mL, 2 N), and the mixture extracted with CH_2Cl_2 (3 × 50 mL). This CH_2Cl_2 solution was dried with $MgSO_4$, filtered, and the solvent was removed in vacuo to yield **4f** (1.83 g, 58%) as a colorless solid, m.p. 148–150 °C (ref.[11e] 149–151 °C). IR (KBr): $\tilde{\nu}$ = 3408 cm^{-1}, 3059, 1674, 1639, 1600, 1427, 1199, 744, 701. ^1H NMR (250 MHz, [D_6]DMSO): δ = 6.7 (br. s, 3 H, NH), 7.22–7.64 (m, 9 H) ppm. ^{13}C NMR (62.9 MHz, [D_6]DMSO): δ = 127.3, 128.1, 128.3, 128.6, 129.0, 129.2, 136.2, 137.5, 139.0, 140.5, 165.9 (NCN) ppm. MS (70 eV): *m/z* (%) = 196 (10) [M^+], 195 (100) [M^+ – H], 178 (31), 77 (8).

General Procedure (GP) 3. 2,4-Diazabicyclo[4.2.0]octa-1(6),2-dien-5-ones (6): A solution of methyl 2-chloro-2-cyclopropylidineacetate (**5**), 2 equiv. of the respective amidine **4** and 4 equiv. of Et_3N was stirred in anhydrous dioxane at room temp. for 48 h. After filtration, the solid residue was suspended in CH_2Cl_2, the mixture washed with water, and the aq. layer was washed three times with CH_2Cl_2. The combined organic layers were dried with $MgSO_4$, evaporated in vacuo, and the crude product was subjected to column chromatography.

3-Phenyl-2,4-diazabicyclo[4.2.0]octa-1(6),2-dien-5-one (6a): The crude product obtained from **5** (365 mg, 2.5 mmol), benzamidine hydrochloride (**4a**, 793 mg, 5.00 mmol) and triethylamine (1.01 g, 10 mmol) in dioxane (25 mL) according to GP 3 was subjected to column chromatography (R_f = 0.3, Et_2O, 1.5 × 30 cm, 30 g SiO_2) to yield **6a** (411 mg, 83%) as a colorless solid, m.p. 191 °C. IR (KBr): $\tilde{\nu}$ = 3008 cm^{-1}, 2937, 1670, 1557, 1498, 1321, 1082, 838, 766. ^1H NMR (250 MHz, $CDCl_3$): δ = 3.01 (m, 2 H), 3.22 (m, 2 H), 7.47–7.53 (m, 3 H), 8.05–8.20 (m, 2 H), 12.54 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 25.7 (–), 33.7 (–), 124.1 (C_{quat}, C-6), 127.6 (+), 128.9 (+), 131.7 (+), 132.5 (C_{quat}), 158.6 (C_{quat}, C-1/C-3), 160.5 (C_{quat}, C-3/C-1), 171.9 (C_{quat}, C-5) ppm. MS (70 eV): *m/z* (%) = 198 (100) [M^+], 170 (7) [M^+ – CO], 104 (91) [HN=CPh^+], 77 (44) [Ph^+]. $C_{12}H_{10}N_2O$ (198.2): calcd. C 72.71, H 5.08, N 14.13; found C 72.44, H 5.38, N 14.03.

3-(*p*-Chlorophenyl)-2,4-diazabicyclo[4.2.0]octa-1(6),2-dien-5-one (6b): The crude product obtained from **5** (365 mg, 2.5 mmol), *p*-chlorobenzamidine hydrochloride (**4b**, 955 mg, 5.00 mmol) and triethylamine (1.01 g, 10 mmol) in dioxane (25 mL) according to GP 3 was subjected to column chromatography (R_f = 0.31, CH_2Cl_2/MeOH, 25:1, 1.5 × 20 cm, 25 g SiO_2) to yield **6b** (455 mg, 78%) as a colorless solid, m.p. 218–219 °C. IR (KBr): $\tilde{\nu}$ = 3078 cm^{-1}, 2938, 1668, 1520, 1491, 1322, 1092, 1076, 837, 760. ^1H NMR (250 MHz, [D_6]DMSO): δ = 2.90 (m, 2 H), 3.15 (m, XX′ part of an AA′XX′ system, 2 H), 7.60 (m, 2 H), 8.05 (m, AA′ part of an AA′XX′ system, 2 H), 11.80 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, [D_6]DMSO): δ = 25.1 (–), 33.6 (–), 126.1 (C_{quat}, C-6), 128.9 (+), 129.8 (+), 136.6 (C_{quat}), 152.1 (C_{quat}), 158.2 (C_{quat}, C-1/C-3), 159.6 (C_{quat}, C-3/C-1), 171.5 (C_{quat}, C-5) ppm. MS (70 eV): *m/z* (%) = 234/232 (33/100) [M^+], 204 (6) [M^+ – C_2H_4], 140/138 (18/57) [HN=$CC_6H_4Cl^+$], 111 (15). $C_{12}H_9ClN_2O$ (232.7): calcd. C 61.95, H 3.90, N 12.04; found C 61.63, H 3.78, N 11.83.

3-(*o*-Bromophenyl)-2,4-diazabicyclo[4.2.0]octa-1(6),2-dien-5-one (6c): The crude product obtained from **5** (1.1 g, 7.5 mmol), 2-bromobenzamidine hydrochloride (**4c**, 3.50 g, 14.9 mmol) and triethylamine (3.03 g, 30.0 mmol) in dioxane (60 mL) according to GP 3 was subjected to column chromatography (R_f = 0.35, Et_2O/MeOH,

50:1, 3 × 30 cm, 50 g SiO_2) to yield **6c** (1.59 g, 76%) as a colorless solid, m.p. 178–179 °C. IR (KBr): $\tilde{\nu}$ = 2925 cm^{-1}, 2847, 1662, 1540, 1472, 1326, 1089, 778, 762. ^1H NMR (200 MHz, $CDCl_3$): δ = 3.02 (m, 2 H), 3.22 (m, 2 H), 7.30–7.52 (m, 2 H), 7.52–7.78 (m, 2 H), 10.70 (br. s, 1 H, NH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 25.4 (–), 33.7 (–), 120.9 (C_{quat}), 125.1 (C_{quat}), 127.7 (+), 130.9 (+), 132.0 (+), 133.7 (+), 134.6 (C_{quat}), 157.6 (C_{quat}, C-1/C-3), 160.3 (C_{quat}, C-3/C-1), 171.2 (C_{quat}, C-5) ppm. MS (70 eV): *m/z* (%) = 279/277 (21/22) [M^+ + 1], 278/276 (97/100) [M^+], 184/182 (41/42) [$HNCC_6H_4Br^+$], 102 (58), 95 (79). $C_{12}H_9BrN_2O$ (277.1): calcd. C 52.01, H 3.27, N 10.11; found C 51.92, H 3.37, N 9.94.

3-(*o*-Fluorophenyl)-2,4-diazabicyclo[4.2.0]octa-1(6),2-dien-5-one (6d): The crude product obtained from **5** (730 mg, 5 mmol), *o*-fluorobenzamidine hydrochloride (**4d**, 1.75 g, 10.0 mmol) and triethylamine (2.02 g, 20.0 mmol) in dioxane (50 mL) according to GP 3 was subjected to column chromatography (R_f = 0.5, Et_2O/MeOH, 25:1, 3 × 30 cm, 50 g SiO_2) to yield **6d** (884 mg, 82%) as a colorless solid, m.p. 184–185 °C. IR (KBr): $\tilde{\nu}$ = 3095 cm^{-1}, 2976, 2947, 1668, 1617, 1532, 1319, 1223, 1084, 753. ^1H NMR (200 MHz, $CDCl_3$): δ = 3.04 (m, 2 H), 3.25 (m, 2 H), 7.16–7.42 (m, 2 H), 7.48–7.62 (m, 1 H), 8.10–8.32 (m, 1 H), 10.22 (br. s, 1 H, NH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 25.4 (–), 33.8 (–), 116.6 (+, d, $^2J_{C-F}$ = 23.1 Hz, C-3′), 120.1 (C_{quat}, d, $^2J_{C-F}$ = 9.1 Hz, C-1′), 124.99 (+, d, $^3J_{C-F}$ = 3.5 Hz, C-6′), 125.03 (C_{quat}, C-6), 130.9 (+, d, $^4J_{C-F}$ = 1.5 Hz, C-5′), 133.6 (+, d, $^3J_{C-F}$ = 9.1 Hz, C-4′), 156.7 (d, $^3J_{C-F}$ = 2.0 Hz, C-3), 156.8 (C_{quat}, C-1), 160.2 (C_{quat}, d, $^1J_{C-F}$ = 251.0 Hz, C-2′), 171.0 (C_{quat}, C-5) ppm. MS (70 eV): *m/z* (%) = 217 (17) [M^+ + 1], 216 (100) [M^+], 122 (42) [$HN{=}CC_6H_4F^+$], 102 (20), 95 (24) [$C_6H_4F^+$]. $C_{12}H_9FN_2O$ (216.2): calcd. C 66.66, H 4.20, N 12.96; found C 66.50, H 4.28, N 13.03.

3-(*p*-Benzyloxyphenyl)-2,4-diazabicyclo[4.2.0]octa-1(6),2-dien-5-one (6e): The crude product obtained from **5** (660 mg, 4.5 mmol), *p*-benzyloxybenzamidine hydrochloride (**4e**, 2.4 g, 9.13 mmol) and triethylamine (1.82 g, 18.0 mmol) in dioxane (50 mL) according to GP 3 was subjected to column chromatography (R_f = 0.34, CH_2Cl_2/MeOH, 25:1, 3 × 30 cm, 50 g SiO_2) to yield **6e** (930 mg, 68%) as a colorless solid, m.p. 212–213 °C. IR (KBr): $\tilde{\nu}$ = 3088 cm^{-1}, 2936, 1664, 1608, 1504, 1303, 1252, 1189, 843, 762. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.01 (m, 2 H), 3.20 (m, 2 H), 5.15 (s, 2 H, OCH_2), 7.04–7.12 (m, 2 H), 7.30–7.47 (m, 5 H), 7.95–8.22 (m, 2 H), 11.48 (br. s, 1 H, NH) ppm. ^{13}C NMR (50.3 MHz, [D_6]DMSO): δ = 24.6 (–), 32.9 (–), 69.4 (–, OCH_2), 114.7 (+), 122.5 (C_{quat}, C-6), 124.9 (C_{quat}), 127.6 (+), 127.8 (+), 128.4 (+), 129.4 (+), 136.5 (C_{quat}), 156.7 (C_{quat}), 159.9 (C_{quat}, C-1/C-3), 160.9 (C_{quat}, C-3/C-1), 169.9 (C-5) ppm. MS (70 eV): *m/z* (%) = 304 (8) [M^+], 91 (100) [$C_7H_7^+$]. $C_{19}H_{16}N_2O_2$ (304.4): calcd. C 74.98, H .30, N 9.20; found C 74.78, H 5.01, N 8.98.

3-(Biphenyl-2-yl)-2,4-diazabicyclo[4.2.0]octa-1(6),2-dien-5-one (6f): The crude product obtained from **5** (527 mg, 3.60 mmol), *o*-biphenylbenzamidine (**4f**, 1.40 g, 7.14 mmol) and triethylamine (1.44 g, 14.2 mmol) in dioxane (25 mL) according to GP 3 was subjected to column chromatography (R_f = 0.41, Et_2O, 1.5 × 20 cm, 20 g SiO_2) to yield **6f** (425 mg, 43%) of a colorless solid, m.p. 176–177 °C. IR (KBr): $\tilde{\nu}$ = 2928 cm^{-1}, 1675, 1540, 1478, 1323, 1088, 976, 745, 698. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.92 (m, 2 H), 3.18 (m, 2 H), 7.22–7.41 (m, 5 H, Ar-H), 7.44–7.78 (m, 4 H, Ar-H), 9.22 (br. s, 1 H, NH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 25.0 (–), 33.5 (–), 123.8 (C_{quat}, C-6), 127.7 (+), 128.1 (+), 128.75 (+), 128.79 (+), 129.8 (+), 130.68 (+), 130.71 (+), 132.3 (C_{quat}), 139.2 (C_{quat}), 140.6 (C_{quat}), 157.3 (C_{quat}, C-1/C-3), 161.9 (C_{quat}, C-3/C-1), 170.8 (C_{quat}, C-5) ppm. MS (70 eV): *m/z* (%) = 274 (42) [M^+], 273 (100) [M^+ – H], 245 (8), 178 (11).

3-Methylthio-2,4-diazabicyclo[4.2.0]octa-1(6),2-dien-5-one (6g): In a dry 50-mL round-bottomed flask were placed methyl 2-chloro-2-cyclopropylidineacetate (**5**) (365 mg, 2.50 mmol), *S*-methylisothiourea hemisulfate (**4g**, 1.39 g, 5.00 mmol) and triethylamine (1.52 g, 15.0 mmol) in anhydrous dioxane (25 mL), and the mixture was stirred at 50 °C for 48 h. After filtration, the solid residue was suspended in CH_2Cl_2 (25 mL) and the suspension washed with water. The aq. layer was extracted with CH_2Cl_2 (2 × 25 mL). After removing the solvent from the combined CH_2Cl_2 and dioxane layers in vacuo, the crude product was subjected to column chromatography (R_f = 0.3, CH_2Cl_2/MeOH, 25:1, 1.5 × 30 cm, 30 g SiO_2) to yield **6g** (310 mg, 74%) as a colorless solid, m.p. 215 °C. IR (KBr): $\tilde{\nu}$ = 2996 cm^{-1}, 2928, 1654, 1541, 1456, 1396, 1297, 1189, 922, 751. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.58 (s, 3 H, SMe), 2.95 (m, 2 H), 3.15 (m, 2 H), 11.5 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, [D_6]DMSO): δ = 13.4 (+), 24.9 (–), 33.2 (–), 120.4 (C_{quat}, C-6), 152.3 (C_{quat}, C-1/C-3), 156.6 (C_{quat}, C-3/C-1), 165.0 (C_{quat}, C-5) ppm. MS (70 eV): *m/z* (%) = 169 (12) [M^+ + 1], 168 (100) [M^+], 121 (14) [M^+ – *S*Me], 93 (22), 74 (16). $C_7H_8N_2OS$ (168.2): calcd. C 49.98, H 4.79, N 16.65; found C 49.66, H 5.14, N 16.50.

General Procedure (GP) 4: 6-(Phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12): In a sealed Pyrex tube, 1 equiv. of the respective 2,4-diazabicyclo[4.2.0]octa-1(6),2-dien-5-one (**6**) was stirred with 4 equiv. of phenyl vinyl sulfone at 175 °C for 12 h. The mixture was cooled to room temperature, dissolved in CH_2Cl_2/MeOH (10:1) and subjected to column chromatography.

2-Phenyl-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12a): The crude product obtained from 3-phenyl-2,4-diazabicyclo[4.2.0]octa-1(6),2-dien-5-one (**6a**, 198 mg, 1.00 mmol) and phenyl vinyl sulfone (670 mg, 4.00 mmol) according to GP 4 was subjected to column chromatography (R_f = 0.41, Et_2O/MeOH, 25:1, 1 × 30 cm, 25 g SiO_2) to yield **12b** (303 mg, 83%) as a colorless solid, m.p. > 250 °C. IR (KBr): $\tilde{\nu}$ = 2931 cm^{-1}, 1637, 1551, 1316, 1146, 1085, 699. ^1H NMR (200 MHz, [D_6]DMSO): δ = 1.60–1.83 (m, 1 H), 2.10–2.30 (m, 1 H), 2.30–2.45 (m, 1 H), 2.65–2.82 (m, 3 H), 3.60–3.80 (m, 1 H, 6-H), 7.4–7.6 (m, 3 H), 7.60–7.85 (m, 3 H), 7.85–8.10 (m, 4 H), 12.6 (br. s, 1 H, NH) ppm. ^{13}C NMR (50.3 MHz, [D_6]DMSO): δ = 21.1 (–), 21.7 (–), 29.8 (–), 57.4 (+, C-6), 115.9 (C_{quat}, C-4a), 127.5 (+), 128.46 (+), 128.49 (+), 129.5 (+), 131.3 (+), 132.2 (C_{quat}), 134.1 (+), 136.9 (C_{quat}), 153.9 (C_{quat}, C-2), 159.0 (C_{quat}, C-8a/C-4), 162.5 (C_{quat}, C-4/C-8a) ppm. MS (70eV): *m/z* (%) = 366 (2) [M^+], 225 (24) [M^+ – SO_2Ph], 224 (100) [M^+ – SO_2Ph – H], 180 (8), 104 (12), 77 (18) [Ph^+]. $C_{20}H_{18}N_2O_3S$ (366.5): calcd. C 65.56, H 4.95, N 7.64; found C 65.89, H 4.86, N 7.49.

2-(*p*-Chlorophenyl)-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12b): The crude product obtained from 3-(*p*-chlorophenyl)-2,4-diazabicyclo[4.2.0]octa-1(6),2-diene-5-one (**6b**, 400 mg, 1.72 mmol) and phenyl vinyl sulfone (1.15 g, 6.84 mmol) according to GP 4 was subjected to column chromatography (R_f = 0.41, CH_2Cl_2/MeOH, 25:1, 3 × 30 cm, 50 g SiO_2) to yield **12b** (410 mg, 59%) as a colorless solid, m.p. > 250 °C. IR (KBr): $\tilde{\nu}$ = 3067 cm^{-1}, 2946, 1655, 1548, 1506, 1321, 1146, 1087, 842, 749, 689. ^1H NMR (250 MHz, [D_6]DMSO): δ = 1.68–1.80 (m, 1 H), 2.20–2.75 (m, 5 H), 3.60–3.71 (m, 1 H, 6-H), 7.52–7.62 (m, 2 H), 7.71–7.80 (m, 3 H), 7.85–7.97 (m, 2 H), 8.02–8.11 (m, 2 H), 11.00 (br. s, 1 H, NH) ppm. ^{13}C NMR (63.9 MHz, [D_6]DMSO): δ = 21.5 (–), 22.0 (–), 30.0 (–), 57.5 (+, C-6), 117.0 (C_{quat}, C-4a), 128.8 (+), 128.9 (+), 129.5 (+), 129.8 (+), 131.0 (C_{quat}), 134.4 (+), 136.6 (C_{quat}), 137.1 (C_{quat}), 153.1 (C_{quat}, C-2), 159.6 (C_{quat}, C-8a/C-4), 162.5 (C_{quat}, C-4/C-8a) ppm. MS (70 eV): *m/z* (%) = 400 (1) [M^+], 261/

259 (10/36) [$M^+ - SO_2Ph$], 260/258 (32/100) [$M^+ - HSO_2Ph$], 140/138 (5/13) [$HN{=}CC_6H_4Cl^+$]. $C_{20}H_{17}ClN_2O_3S$ (400.9): calcd. C 59.92, H 4.27, N 6.99; found C 59.70, H 4.04, N 6.67.

2-(*o*-Bromophenyl)-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12c): The crude product obtained from 3-(*o*-bromophenyl)-2,4-diazabicyclo[4.2.0]octa-1(6),2-dien-5-one (**6c**, 1.10 g, 3.97 mmol) and phenyl vinyl sulfone (2.32 g, 13.8 mmol), according to GP 4 was subjected to column chromatography (R_f = 0.43, Et_2O/MeOH, 25:1, 3×30 cm, 50 g SiO_2) to yield **12c** (683 mg, 39%) as a colorless solid, m.p. 221–222 °C. IR (KBr): $\tilde{\nu}$ = 3064 cm^{-1}, 2932, 1653, 1604, 1544, 1447, 1301, 1147, 1084, 764, 690. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.80–2.01 (m, 1 H), 2.42–3.01 (m, 5 H), 3.20–3.35 (m, 1 H), 7.35–7.45 (m, 2 H), 7.53–7.75 (m, 5 H), 7.95–8.01 (m, 2 H), 11.04 (br. s, 1 H, NH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 21.5 (–), 22.1 (–), 30.6 (–), 58.6 (+, C-6), 117.6 (C_{quat}, C-4a), 120.9 (C_{quat}), 127.8 (+), 129.0 (+), 129.3 (+), 130.9 (+), 132.1 (+), 133.6 (+), 134.0 (+), 134.6 (C_{quat}), 136.8 (C_{quat}), 154.3 (C_{quat}, C-2), 160.3 (C_{quat}, C-8a/C-4), 162.4 (C_{quat}, C-4/C-8a) ppm. MS (70 eV): *m*/*z* (%) = 446/444 (1/1) [M^+], 318/316 (9/10), 304/302 (95/100) [$M^+ - HSO_2Ph$], 260/258 (11/11), 141 (18) [$PhSO_2^+$], 77 (52) [Ph^+]. $C_{20}H_{17}BrN_2O_3S$ (445.3): calcd. C 53.93, H 3.85, N 6.29; found C 54.22, H 3.71, N 6.34.

2-(*o*-Fluorophenyl)-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12d): The crude product obtained from 3-(*o*-fluorophenyl)-2,4-diazabicyclo[4.2.0]octa-1(6),2-dien-5-one (**6d**, 648 mg, 3 mmol) and phenyl vinyl sulfone (2.01 g, 12.0 mmol), according to GP 4 was subjected to column chromatography (R_f = 0.45, Et_2O/MeOH, 25:1, 3×30 cm, 50 g SiO_2) to yield **12d** (881 mg, 76%) as a colorless solid, m.p. 201–202 °C. IR (KBr): $\tilde{\nu}$ = 3073 cm^{-1}, 2941, 1672, 1603, 1558, 1449, 1308, 1146, 1084, 779, 689. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.81–2.12 (m, 1 H), 2.48–3.11 (m, 5 H), 3.22–3.40 (m, 1 H, 6-H), 7.10–7.38 (m, 3 H), 7.50–7.81 (m, 4 H), 7.95–8.20 (m, 2 H), 10.67 (br. s, 1 H, NH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 21.4 (–), 22.3 (–), 30.7 (–), 59.0 (+), 116.6 (+, d, $^2J_{C-F}$ = 22.9 Hz, C-3′), 117.7 (C_{quat}, C-4a), 119.4 (C_{quat}, d, $^2J_{C-F}$ = 9.2 Hz, C-1′), 125.1 (+, d, $^3J_{C-F}$ = 3.1 Hz, C-6′), 129.0 (+), 129.3 (+), 131.0 (+, d, $^4J_{C-F}$ = 1.1 Hz, C-5′), 133.7 (+, d, $^3J_{C-F}$ = 9.2 Hz, C-4′), 133.9 (+), 136.8 (C_{quat}), 150.5 (C_{quat}, d, $^3J_{C-F}$ = 1.5 Hz, C-2), 160.1 (C_{quat}, C-8a), 160.5 (C_{quat}, d, $^1J_{C-F}$ = 250.6 Hz, C-2′), 161.7 (C_{quat}, C-4) ppm. MS (70 eV): *m*/*z* (%) = 384 (1) [M^+], 243 (23) [$M^+ - SO_2Ph$], 242 (100) [$M^+ - HSO_2Ph$], 122 (16), 77 (22) [Ph^+]. $C_{20}H_{17}FN_2O_3S$ (384.4): calcd. C 62.49, H 4.46, N 7.29; found C 62.30, H 4.30, N 7.11.

2-[(*p*-Benzyloxy)phenyl]-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12e): The crude product obtained from 3-(*p*-benzyloxyphenyl)-2,4-diazabicyclo[4.2.0]octa-1(6),2-dien-5-one (**6e**, 652 mg, 2.1 mmol) and phenyl vinyl sulfone (1.43 g, 8.50 mmol), according to GP 4 was subjected to column chromatography (R_f = 0.40, CH_2Cl_2/MeOH, 25:1, 3×30 cm, 50 g SiO_2) to yield **12e** (670 mg, 66%) as a colorless solid, m.p. > 250 °C. IR (KBr): $\tilde{\nu}$ = 3072 cm^{-1}, 2939, 1649, 1607, 1547, 1516, 1304, 1259, 1144, 1085, 837, 742, 687. ^1H NMR (300 MHz, [D$_6$]DMSO): δ = 1.71–1.84 (m, 1 H), 2.18–2.31 (m, 1 H), 2.40–2.58 (m, 1 H), 2.64–2.78 (m, 3 H), 3.55–3.73 (m, 1 H, 6-H), 5.21 (s, 2 H), 7.05–7.12 (m, 2 H), 7.31–7.48 (m, 5 H), 7.64–7.8 (m, 3 H), 7.90–7.98 (m, 2 H), 8.04–8.11 (m, 2 H), 12.15 (br. s, 1 H, NH) ppm. ^{13}C NMR (50.3 MHz, [D$_6$]DMSO): δ = 21.1 (–), 22.0 (–), 29.7 (–), 57.4 (+), 69.3 (–), 114.7 (+), 114.9 (C_{quat}, C-4a), 124.3 (C_{quat}), 127.6 (+), 127.8 (+), 128.33 (C_{quat}), 128.36 (+), 128.41 (+), 129.2 (+), 129.5 (+), 134.0 (+), 136.5 (C_{quat}), 136.9 (C_{quat}), 153.8 (C_{quat}, C-2), 160.8 (C_{quat}, C-8a/C-4), 162.5 (C_{quat}, C-4/C-8a) ppm. MS (70eV): *m*/*z* (%) = 472 (2) [M^+], 330 (49) [$M^+ - HSO_2Ph$], 91 (100) [$C_7H_7^+$]. $C_{27}H_{24}N_2O_4S$ (472.6): calcd. C 68.63, H 5.12, N 5.93; found C 68.80, H 5.04, N 6.08.

2-(*o*-Biphenyl)-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12f): The crude product obtained from 3-(*o*-biphenyl)-2,4-diazabicyclo[4.2.0]octa-1(6),2-dien-5-one (**6f**, 501 mg, 1.83 mmol) and phenyl vinyl sulfone (1.23 g, 7.32 mmol), according to GP 4 was subjected to column chromatography (R_f = 0.31, Et_2O/MeOH, 25:1, 3×30 cm, 50 g SiO_2) to yield **12f** (522 mg, 65%) as a colorless solid, m.p. 194–195 °C. IR (KBr): $\tilde{\nu}$ = 3059 cm^{-1}, 3059, 2933, 1647, 1546, 1447, 1320, 1302, 1145, 1085, 742, 688. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.82–1.95 (m, 1 H), 2.42–2.95 (m, 5 H), 3.21–3.31 (m, 1 H, 6-H), 7.20–7.39 (m, 5 H), 7.42–7.78 (m, 7 H), 7.90–8.02 (m, 2 H), 9.1 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.3 (–), 22.1 (–), 30.5 (–), 59.1 (+), 116.5 (C_{quat}, C-4a), 127.7 (+), 128.1 (+), 128.4 (+), 128.9 (+), 129.0 (+), 129.1 (+), 130.0 (+), 130.9 (+), 131.0 (+), 131.7 (+), 133.9 (C_{quat}), 136.9 (C_{quat}), 139.2 (C_{quat}), 140.7 (C_{quat}), 155.7 (C_{quat}, C-8a), 160.1 (C_{quat}, C-2/C-4), 162.0 (C_{quat}, C-4/C-2) ppm. MS (70 eV): *m*/*z* (%) = 442 (4) [M^+], 300 (100) [$M^+ - HSO_2Ph$], 180 (16), 122 (17). $C_{26}H_{22}N_2O_3S$ (442.5): calcd. C 70.57, H 5.01, N 6.33; found C 70.53, H 4.98, N 6.04.

2-Methylthio-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12g): The crude product obtained from **6g** (168 mg, 1.00 mmol) and phenyl vinyl sulfone (672 g, 4.00 mmol), according to GP 4 was subjected to column chromatography (R_f = 0.41, CH_2Cl_2/MeOH, 25:1, 1.5×20 cm, 25 g SiO_2) to yield **12f** (189 mg, 56%) as a colorless solid, m.p. > 250 °C. IR (KBr): $\tilde{\nu}$ = 3059 cm^{-1}, 2918, 2847, 1644, 1576, 1448, 1315, 1150, 1088, 723, 689. ^1H NMR (200 MHz, [D$_6$]DMSO): δ = 1.57–1.79 (m, 1 H), 2.11–2.38 (m, 3 H), 2.43 (s, 3 H), 2.58–2.70 (m, 2 H), 3.52–3.73 (m, 1 H, 6-H), 7.60–7.81 (m, 3 H), 7.85–7.95 (m, 2 H), 12.56 (br. s, 1 H, NH) ppm. ^{13}C NMR (50.3 MHz, [D$_6$]DMSO): δ = 12.5 (+), 21.0 (–), 21.4 (–), 29.8 (–), 57.3 (+), 117.2 (C_{quat}, C-4a), 128.4 (+), 129.5 (+), 134.0 (+), 136.9 (C_{quat}), 154.3 (C_{quat}, C-8a), 159.8 (C_{quat}, C-2/C-4), 162.7 (C_{quat}, C-4/C-2) ppm. MS (70 eV): *m*/*z* (%) = 336 (2) [M^+], 195 (18), 194 (100) [$M^+ - HSO_2Ph$]. $C_{15}H_{16}N_2O_3S_2$ (336.4): calcd. C 53.55, H 4.79, N 8.33; found C 53.56, H 4.52, N 8.20.

General Procedure (GP) 5: 2-Aryl-7,8-dihydro-3*H*-quinazolin-4-one (13): To a suspension of sulfone **12** in THF, was added 3 equiv. of KO*t*Bu, and the resulting solution was stirred at room temp. for 2 h, poured into a separating funnel containing satd. aq. NH_4Cl solution (10 mL), and the mixture extracted with CH_2Cl_2 (3×20 mL). The organic layer was dried with $MgSO_4$, the solvent was evaporated in vacuo to yield **13**, which was used for the next reaction without further purification.

2-Phenyl-7,8-dihydro-3*H*-quinazolin-4-one (13a): According to GP 5 from the sulfone **12a** (366 mg, 1.00 mmol) and KO*t*Bu (336 mg, 3.00 mmol) was obtained **13a** (210 mg, 94%) as a pale yellow solid, m.p. 241 °C, R_f = 0.5 (hexane/ethyl acetate, 1:1). IR (KBr): $\tilde{\nu}$ = 3032 cm^{-1}, 2932, 1653, 1505, 1317, 930, 718. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.42–2.58 (m, 2 H, 7-H), 2.89 (m, 2 H, 8-H), 6.04 (dt, *J* = 9.7 and 4.3 Hz, 1 H, 6-H), 6.73 (dt, *J* = 9.7 and 1.8 Hz, 1 H, 5-H), 7.48–7.56 (m, 3 H), 8.14–8.22 (m, 2 H), 12.58 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.7 (–), 29.6 (–), 117.2 (C_{quat}, C-4a), 119.5 (+, C-5/C-6), 127.4 (+), 127.6 (+), 128.9 (+), 131.7 (+, C-6/C-5), 132.1 (C_{quat}), 154.6 (C_{quat}, C-2), 161.4 (C_{quat}, C-8a/C-4), 161.9 (C_{quat}, C-4/C-8a) ppm. MS (70 eV): *m*/*z* (%) = 224 (100) [M^+], 223 (98), 180 (19) [$M^+ - CONH_2$], 104 (14) [$PhCNH^+$], 77 (20) [Ph^+]. $C_{14}H_{12}N_2O$ (224.3): calcd. C 74.98, H 5.39, N 12.49; found C 74.71, H 5.31, N 12.31.

2-(*p*-Chlorophenyl)-7,8-dihydro-3*H*-quinazolin-4-one (13b): According to GP 5 from the sulfone **12b** (200 mg, 0.50 mmol) and KO*t*Bu (168 mg, 1.50 mmol) was obtained **13b** (123 mg, 95%) as a pale yellow solid, m.p. > 250 °C, R_f = 0.48 (hexane/ethyl acetate = 1:1). IR (KBr): $\tilde{\nu}$ = 3029 cm^{-1}, 2934, 1652, 1504, 1389, 1176, 1091, 738.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.42–2.56 (m, 2 H, 7-H), 2.87 (m, 2 H, 8-H), 6.06 (dt, J = 9.5 and 4.3 Hz, 1 H, 6-H), 6.71 (dt, J = 9.5 and 1.8 Hz, 1 H, 5-H), 7.48–7.56 (m, 2 H), 8.16–8.27 (m, 2 H), 13.1 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.3 (–), 28.7 (–), 116.8 (C_{quat}, C-4a), 119.6 (+, C-5/C-6), 127.7 (+), 128.9 (+), 129.5 (+), 131.7 (+, C-6/C-5), 136.5 (C_{quat}), 153.3 (C_{quat}, C-2), 159.6 (C_{quat}, C-8a/C-4), 162.5 (C_{quat}, C-4/C-8a) ppm. MS (70 eV): m/z (%) = 260/258 (32/100) [M^+], 259/257 (40/98) [M^+ – H], 216/214 (28/8), 104 (14), 77 (20) [Ph^+]. $C_{14}H_{11}ClN_2O$ (258.7): calcd. C 65.00, H 4.29, N 10.83; found C 64.93, H 4.08, N 10.99.

2-(*o*-Bromophenyl)-7,8-dihydro-3*H*-quinazolin-4-one (13c): According to GP 5 from the sulfone **12c** (400 mg, 0.90 mmol) and KO*t*Bu (302 mg, 2.70 mmol) was obtained **13c** (258 mg, 94%) as a pale yellow solid, m.p. 202 °C, R_f = 0.55 (Et_2O). IR (KBr): $\tilde{\nu}$ = 3035 cm^{-1}, 2836, 1665, 1491, 1324, 1183, 928, 767, 735. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.15–2.30 (m, 2 H, 7-H), 2.85 (m, 2 H, 8-H), 6.04 (dt, J = 9.6 and 4.4 Hz, 1 H, 6-H), 6.59 (dt, J = 9.6 and 1.7 Hz, 1 H, 5-H), 7.28–7.81 (m, 4 H), 11.55 (br. s, 1 H, N–H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 22.5 (–), 29.0 (–), 118.0 (C_{quat}, C-8a), 119.3 (+, C-5/C-6), 121.1 (C_{quat}), 127.7 (+), 127.9 (+), 131.1 (+), 131.8 (+), 133.7 (+), 134.3 (C_{quat}), 154.4 (C_{quat}, C-2), 160.56 (C_{quat}, C-8a/C-4), 160.64 (C_{quat}, C-4/C-8a) ppm. MS (70 eV): m/z (%) = 304/302 (96/100) [M^+], 203/201 (98/80), 259/257 (24/26), 102 (28). $C_{14}H_{11}BrN_2O$ (303.2): calcd. C 55.47, H 3.66, N 9.24; found C 55.22, H 3.70, N 9.03.

2-(*o*-Fluorophenyl)-7,8-dihydro-3*H*-quinazolin-4-one (13d): According to GP 5 from the sulfone **12d** (384 mg, 1.00 mmol) and KO*t*Bu (336 mg, 3.00 mmol) was obtained **13d** (223 mg, 92%) as a pale yellow solid, m.p. 191 °C, R_f = 0.51 (Et_2O). IR (KBr): $\tilde{\nu}$ = 3043 cm^{-1}, 2934, 2886, 1653, 1559, 1327, 1220, 1181, 1122, 774. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.38–2.52 (m, 2 H, 7-H), 2.85 (m, 2 H, 8-H), 5.98 (dt, ^3J = 9.5 and 4.4 Hz, 1 H, 6-H), 6.61 (dt, J = 9.5 and 1.7 Hz, 1 H, 5-H), 7.12–7.35 (m, 2 H), 7.41–7.54 (m, 1 H), 7.98–8.12 (m, 1 H), 11.51 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.5 (–), 29.0 (–), 116.5 (+, d, $^2J_{C-F}$ = 22.7 Hz, C-3′), 118.0 (C_{quat}, C-4a), 119.4 (+, C-5/C-6), 120.1 (C_{quat}, d, $^2J_{C-F}$ = 10.0 Hz, C-1′), 124.8 (+, d, $^3J_{C-F}$ = 3.3 Hz, C-6′), 127.8 (+, C-6/C-5), 130.9 (+, d, $^4J_{C-F}$ = 1.0 Hz, C-5′), 133.3 (+, d, $^3J_{C-F}$ = 9.0 Hz, C-4′), 150.6 (C_{quat}, d, $^3J_{C-F}$ = 1.0 Hz, C-2), 160.0 (C_{quat}, C-8a/C-4), 160.3 (C_{quat}, C-4/C-8a), 160.4 (C_{quat}, d, $^1J_{C-F}$ = 251.4 Hz, C-2′) ppm. MS (70 eV): m/z (%) = 242 (100) [M^+], 241 (85), 198 (24), 102 (12). $C_{14}H_{11}FN_2O$ (242.3): calcd. C 69.41, H 4.58, N 11.56; found C 69.22, H 4.83, N 11.45.

2-(*p*-Benzyloxyphenyl)-7,8-dihydro-3*H*-quinazolin-4-one (13e): According to GP 5 from the sulfone **12e** (400 mg, 0.85 mmol) and KO*t*Bu (285 mg, 2.54 mmol) was obtained **13e** (258 mg, 92%) as a pale yellow solid, m.p. 247 °C, R_f = 0.62 (CH_2Cl_2/MeOH, 25:1). IR (KBr): $\tilde{\nu}$ = 3032 cm^{-1}, 2943, 1646, 1606, 1512, 1305, 999, 753, 677. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.40–2.58 (m, 2 H), 2.85 (m, 2 H, 8-H), 5.15 (s, 2 H), 6.01 (dt, J = 9.6 and 4.4 Hz, 1 H, 6-H), 6.70 (dt, J = 9.6 and 1.7 Hz, 1 H, 5-H), 7.02–7.18 (m, 2 H),7.30–7.62 (m, 5 H), 8.06–8.22 (m, 2 H), 12.23 (br. s, 1 H, NH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 22.7 (–), 28.6 (–), 69.4 (–), 114.8 (C_{quat}, C-4a), 119.5 (+, C-5/C-6), 126.34 (+, C-6/C-5), 127.7 (+), 127.9 (+), 128.39 (+), 128.41 (+), 129.2 (+), 131.5 (C_{quat}), 136.5 (C_{quat}), 140.8 (C_{quat}), 155.9 (C_{quat}, C-2), 159.9 (C_{quat}, C-8a/C-4), 160.9 (C_{quat}, C-4/C-8a) ppm. MS (70 eV): m/z (%) = 330 (55) [M^+], 239 (8), 91 (100) [$C_7H_7^+$].

2-(*o*-Biphenyl)-7,8-dihydro-3*H*-quinazolin-4-one (13f): According to GP 5 from the sulfone **12f** (300 mg, 0.68 mmol) and KO*t*Bu (224 mg, 2.00 mmol) was obtained **13f** (177 mg, 87%) as a pale yellow solid, m.p. 193 °C, R_f = 0.55 (Et_2O). IR (KBr): $\tilde{\nu}$ = 3070 cm^{-1}, 2936, 1634, 1549, 1507, 1321, 1165, 979, 699. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.38–2.51 (m, 2 H, 7-H), 2.88 (m, 2 H, 8-H), 5.98 (dt, J = 9.5 and 4.4 Hz, 1 H, 6-H), 6.57 (dt, J = 9.5 and 1.7 Hz, 1 H, 5-H), 7.22–7.36 (m, 5 H), 7.44–7.62 (m, 3 H), 7.76–7.82 (m, 1 H) 9.51 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.5 (–), 38.7 (–), 117.2 (C_{quat}, C-4a), 119.3 (+, C-5/C-6), 127.8 (+, C-6/C-5), 127.9 (+), 128.6 (+), 129.0 (+), 129.1 (+), 130.2 (+), 130.9 (+), 131.1 (+), 131.5 (C_{quat}), 139.1 (C_{quat}), 140.8 (C_{quat}), 155.8 (C_{quat}, C-2), 159.8 (C_{quat}, C-8a/C-4), 160.0 (C_{quat}, C-4/C-8a) ppm. MS (70 eV): m/z (%) = 301 (28) [M^+ + 1], 300 (100) [M^+], 299 (40), 180 (38), 122 (43), 77 (78). $C_{20}H_{16}N_2O$ (300.4): calcd. C 79.98, H 5.37, N 9.33; found C 79.64, H 5.24, N 9.57.

2-Methylthio-7,8-dihydro-3*H*-quinazolin-4-one (13g): According to GP 5 from the sulfone **12g** (336 mg, 1.00 mmol) and KO*t*Bu (336 mg, 3.00 mmol) was obtained **13g** (181 mg, 93%) as a pale yellow solid, m.p. 214 °C, R_f = 0.45 (Et_2O). IR (KBr): $\tilde{\nu}$ = 2922 cm^{-1}, 2836, 1641, 1623, 1540, 1271, 1138, 1203, 943. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.38–2.49 (m, 2 H, 7-H), 2.60 (s, 3 H), 2.76 (m, 2 H, 8-H), 5.98 (dt, J = 9.7 and 4.3 Hz, 1 H, 6-H), 6.61 (dt, J = 9.7 and 1.8 Hz, 1 H, 5-H), 12.9 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.3 (+), 22.4 (–), 29.4 (–), 114.6 (C_{quat}, C-4a), 119.3 (+, C-5/C-6), 126.0 (+, C-6/C-5), 157.0 (C_{quat}, C-2), 161.2 (C_{quat}, C-8a/C-4), 162.2 (C_{quat}, C-4/C-8a) ppm. MS (70 eV): m/z (%) = 194 (100) [M^+], 147 (12), 121 (16), 92 (14). $C_9H_{10}N_2OS$ (194.3): calcd. C 55.65, H 5.19, N 14.42; found C 55.39, H 5.32, N 14.16.

General Procedure (GP) 6: 2-Aryl-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (14): A 50-mL flame-dried flask, flushed with nitrogen, was charged with Pd/C (10% Pd w/w) in 10 mL of MeOH. This mixture was stirred under H_2 for 30 min, at which point a solution of **13** in MeOH was added from a syringe, and stirring was continued, until the reaction was complete. The reaction mixture was filtered through a pad of Celite®, and the solvent was removed in vacuo to yield **14** as a colorless solid.

2-Phenyl-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (14a): According to GP 6 the crude reaction mixture obtained from **13a** (224 mg, 1.00 mmol), Pd/C (10% Pd w/w, 10 mg) in MeOH (20 mL) afforded after 4 h **14a** (206 mg, 91%) as a colorless solid, m.p. 224 °C. IR (KBr): $\tilde{\nu}$ = 2934 cm^{-1}, 2848, 1634, 1550, 1319, 1165, 979, 698. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.75–1.91 (m, 4 H), 2.50–2.65 (m, 2 H), 2.71–2.78 (m, 2 H), 7.40–7.58 (m, 3 H), 8.11–8.22 (m, 2 H), 12.38 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.8 (–), 21.9 (–), 22.3 (–), 31.9 (–), 120.2 (C_{quat}, C-4a), 127.5 (+), 128.8 (+), 131.4 (+), 132.5 (C_{quat}), 153.2 (C_{quat}, C-2), 162.5 (C_{quat}, C-8a/C-4), 164.5 (C_{quat}, C-4/C-8a) ppm. MS (70 eV): m/z (%) = 227 (19) [M^+ + 1], 226 (100) [M^+], 225 (51), 211 (31), 198 (10), 104 (21). $C_{14}H_{14}N_2O$ (226.3): calcd. C 74.31, H 6.24, N 12.38; found C 74.34, H 6.55, N 12.29.

2-(*p*-Chlorophenyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (14b): According to GP 6 the crude reaction mixture obtained from **13b** (51.6 mg, 0.20 mmol), Pd/C (10% Pd w/w, 20 mg) in AcOH (10 mL) afforded after 8 h **14b** (49 mg, 94%) as a colorless solid, m.p. 255 °C. IR (KBr): $\tilde{\nu}$ = 3070 cm^{-1}, 2936, 1634, 1549, 1507, 1321, 1014, 929, 699. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.74–1.93 (m, 4 H), 2.50–2.62 (m, 2 H), 2.66–2.79 (m, 2 H), 7.42–7.58 (m, 2 H), 8.13–8.24 (m, 2 H), 12.92 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.8 (–), 21.9 (–), 22.4 (–), 32.0 (–), 120.4 (C_{quat}, C-4a), 127.4 (+), 128.9 (+), 129.0 (C_{quat}), 131.4 (C_{quat}), 157.5 (C_{quat}, C-2/C-8a), 157.6 (C_{quat}, C-8a/C-2), 162.5 (C-4) ppm. MS (70 eV): m/z (%) = 262/260 (16/51) [M^+], 226 (100) [M^+ – C1 + 1], 225 (52) [M^+ – Cl], 211 (37), 104 (32), 77 (26).

2-(*o*-Bromophenyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (14c): According to GP 6 the crude reaction mixture obtained from **13c** (100 mg, 0.33 mmol) and Pd/C (10% Pd w/w, 20 mg) in MeOH (20 mL) was filtered through a pad of Celite® after 4 h and the solvent was removed in vacuo to yield **14b** (93 mg, 92%) as a colorless solid, m.p. 193 °C. IR (KBr): $\tilde{\nu}$ = 3035 cm^{-1}, 2944, 1648, 1559, 1319, 1227, 1031, 977, 927, 760, 728. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.72–1.91 (m, 4 H), 2.38–2.51 (m, 2 H), 2.60–2.78 (m, 2 H), 7.28–7.42 (m, 2 H), 7.51–7.68 (m, 2 H), 12.12 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.5 (–), 21.8 (–), 22.1 (–), 31.6 (–), 121.10 (C_{quat}), 121.14 (C_{quat}), 127.6 (+), 131.0 (+), 131.7 (+), 133.4 (+), 134.6 (C_{quat}), 156.2 (C_{quat}), 161.8 (C_{quat}), 163.6 (C-4) ppm. MS (70 eV): *m*/*z* (%) = 306/304 (95/100) [M^+], 291/289 (27/28), 225 (11) [M^+ – Br]. $C_{14}H_{13}BrN_2O$ (305.2): calcd. C 55.10, H 4.29, N 9.18; found C 55.32, H 4.14, N 8.97.

2-(*o*-Fluorophenyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (14d): According to GP 6 the crude reaction mixture obtained from **13d** (100 mg, 0.41 mmol), Pd/C (10% Pd w/w, 20 mg) in MeOH (20 mL) afforded **14d** (93 mg, 92%) after 4 h as a colorless solid, m.p. 170 °C. IR (KBr): $\tilde{\nu}$ = 3026 cm^{-1}, 2952, 1647, 1564, 1327, 1233, 1163, 979, 928, 761. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.66–1.92 (m, 4 H), 2.49–2.61 (m, 2 H), 2.63–2.74 (m, 2 H), 7.16–7.34 (m, 2 H), 7.22–7.58 (m, 1 H), 8.14–8.25 (m, 1 H), 10.2 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.6 (–), 21.9 (–), 22.2 (–), 31.7 (–), 116.4 (+, d, $^2J_{C-F}$ = 22.9 Hz), 120.3 (C_{quat}, d, $^2J_{C-F}$ = 9.2 Hz), 121.2 (C_{quat}, C-4a), 124.8 (+, d, $^3J_{C-F}$ = 3.1 Hz), 130.9 (+, d, $^4J_{C-F}$ = 1.5 Hz), 132.5 (+, d, $^3J_{C-F}$ = 9.1 Hz), 149.6 (C_{quat}, d, $^3J_{C-F}$ = 1.1 Hz, C-2), 160.4 (C_{quat}, d, $^1J_{C-F}$ = 250.7 Hz), 161.6 (C_{quat}, C-8a), 162.8 (C_{quat}, C-4) ppm. MS (70eV): *m*/*z* (%) = 244 (100) [M^+], 243 (48), 229 (28), 122 (16). $C_{14}H_{13}FN_2O$ (244.3): calcd. C 68.84, H 5.36, N 11.47; found C 69.09, H 5.21, N 11.61.

2-(*p*-Hydroxyphenyl)-5,6,7,8-tetrahydro-3*H*-quinazoline-4-one (14e, R = 4-HOC_6H_4): According to GP 6 the crude reaction mixture obtained from **13e** (165 mg, 0.50 mmol), Pd/C (10% Pd w/w, 25 mg) in AcOH (10 mL) afforded the title compound (113 mg, 93%) after 8 h as a colorless solid, m.p. > 250 °C. IR (KBr): $\tilde{\nu}$ = 3430 cm^{-1}, 2940, 1641, 1515, 1324, 1289, 1182, 1113, 932, 847, 768. ^1H NMR (300 MHz, [D_6]DMSO): δ = 1.61–1.80 (m, 4 H), 2.31–2.41 (m, 2 H), 2.54–2.61 (m, 2 H), 6.78–6.89 (m, 2 H), 7.88–7.99 (m, 2 H), 9.40–10.72 (2 × br. s, 2 H, NH, OH), ppm. ^{13}C NMR (75.5 MHz, [D_6]DMSO): δ = 21.5 (–), 21.6 (–), 21.9 (–), 31.1 (–), 115.2 (+), 115.3 (C_{quat}, C-4a), 117.8 (C_{quat}), 122.8 (C_{quat}), 129.1 (+), 153.0 (C_{quat}), 160.5 (C_{quat}), 162.9 (C_{quat}) ppm. MS (70 eV): *m*/*z* (%) = 242 (100) [M^+], 241 (44), 227 (27), 120 (31).

2-(*o*-Biphenyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (14f): According to GP 6 the crude reaction mixture obtained from **13f** (120 mg, 0.4 mmol), Pd/C (10% Pd w/w, 10 mg) in MeOH (20 mL) afforded **14f** (112 mg, 93%) after 4 h as a colorless solid, m.p. 190 °C. IR (KBr): $\tilde{\nu}$ = 3027 cm^{-1}, 2936, 1643, 1566, 1324, 1225, 1170, 978, 764. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.66–1.84 (m, 4 H), 2.38–2.48 (m, 2 H), 2.57–2.66 (m, 2 H), 7.21–7.42 (m, 5 H), 7.48–7.61 (m, 2 H), 7.72–7.79 (m, 2 H), 11.1 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.6 (–), 21.7 (–), 22.1 (–), 31.6 (–), 119.9 (C_{quat}, C-4a), 127.3 (+), 127.4 (+), 128.1 (+), 128.3 (+), 129.0 (+), 130.0 (+), 130.7 (+), 132.1 (C_{quat}), 139.5 (C_{quat}), 140.7 (C_{quat}), 156.1 (C_{quat}), 161.5 (C_{quat}), 163.3 (C_{quat}) ppm. MS (70 eV): *m*/*z* (%) = 302 (72) [M^+], 301 (35), 180 (58), 124 (100). $C_{20}H_{18}N_2O$ (302.4): calcd. C 79.44, H 6.00, N 9.26; found C 79.89, H 5.68, N 9.49.

One-Pot Synthesis of 2-Phenyl-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12a): A 10-mL Pyrex tube was charged with methyl 2-chloro-2-cyclopropylidineacetate **5** (147 mg, 1 mmol), benzamidine hydrochloride (**4a**, 313 mg, 2 mmol), triethylamine (405 mg, 4 mmol) and dioxane (5 mL), and the mixture was stirred at room temp. for 2 d, at which point phenyl vinyl sulfone (672 mg, 4 mmol) was added, the bottle was sealed and heated at 175 °C for 15 h. After cooling, the solvent was removed from the reaction mixture, and the residue was subjected to column chromatography (hexane/ethyl acetate = 1:2), to yield **12a** (157 mg, 43%) as a colorless solid.

Using the same method as above, 177 mg (46%) of **12d** was obtained from **5** (147 mg, 1 mmol), *o*-fluorobenzamidine hydrochloride **4d** (349 mg, 2 mmol), triethylamine (405 mg, 4 mol) and phenyl vinyl sulfone (672 mg, 4 mmol).

2-Phenyl-6-(phenylsulfonyl)-4-(trimethylsilyloxy)-5,6,7,8-tetrahydroquinazoline (15a): A dry 25-mL round-bottomed flask was charged with **12a** (1.6 g, 4.4 mmol), $HN(SiMe_3)_2$ (15 mL) and $(NH_4)_2SO_4$ (20 mg). This mixture was heated under reflux for 15 h. After cooling to room temp., the excess of $HN(SiMe_3)_2$ was removed in vacuo, the reaction mixture was diluted with CH_2Cl_2 (20 mg), the solution washed with water (5 mL) and dried with $MgSO_4$. Removal of the solvents yielded **15a** (1.91 g, 99%) as a colorless solid, m.p. >250 °C. IR (KBr): $\tilde{\nu}$ = 3012 cm^{-1}, 2943, 1652, 1552, 1502, 1321, 1145, 1082, 840, 752. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.45 (s, 9 H), 1.80–1.98 (m, 1 H), 2.35–2.51 (m, 1 H), 2.75–2.87 (m, 2 H), 3.02–3.21 (m, 2 H), 3.25–3.41 (m, 1 H), 7.18–7.32 (m, 3 H), 7.58–7.75 (m, 3 H), 7.95–8.03 (m, 2 H), 8.25–8.36 (m, 2 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 0.3 (+), 21.9 (–), 22.2 (–), 30.8 (–), 59.5 (+), 112.3 (C_{quat}, C-4a), 127.8 (+), 128.3 (+), 129.0 (+), 129.2 (+), 130.2 (+), 134.0 (+), 136.8 (C_{quat}), 137.5 (C_{quat}), 161.4 (C_{quat}), 164.1 (C_{quat}), 166.4 (C_{quat}) ppm. MS (70 eV): *m*/*z* (%) = 438 (2) [M^+], 296 (100) [M^+ – HSO_2Ph], 281 (23) [M^+ – HSO_2Ph – Me], 247 (63), 175 (25).

6-Methyl-2-phenyl-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4(3*H*)-one (16a-Me): To a cooled solution of the sulfone **15a** (439 mg, 1 mmol) in THF (15 mL) was added at –78 °C *n*BuLi (1.77 M in hexane, 0.62 mL) over a period of 15 min. The resulting mixture was stirred for an additional 15 min, at which point methyl iodide (156 mg, 1.1 mmol) in THF (1 mL) was added, the cooling bath was removed, and stirring was continued at room temp. for 2 h. The reaction mixture was poured into a separating funnel containing satd. aq. NH_4Cl solution (10 mL) and extracted with CH_2Cl_2 (3 × 15 mL). Removal of the solvents followed by column chromatography (R_f = 0.32, CH_2Cl_2/MeOH, 25:1, 1.5 × 30 cm, 25 g SiO_2) yielded **16a**-Me (315 mg, 83%) as a colorless solid, m.p. > 250 °C. IR (KBr): $\tilde{\nu}$ = 3057 cm^{-1}, 2943, 1644, 1553, 1447, 1300, 1153, 1088, 701. ^1H NMR (250 MHz, [D_6]DMSO): δ = 1.22 (s, 3 H), 1.84–2.10 (m, 2 H), 2.40–2.52 (m, 1 H), 2.62–2.83 (m, 3 H), 7.38–7.60 (m, 3 H), 7.63–8.10 (m, 7 H), 12.5 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, [D_6]DMSO): δ = 18.1 (+), 26.2 (–), 27.8 (–), 30.8 (–), 60.4 (C_{quat}), 115.7 (C_{quat}, C-4a), 127.8 (+), 128.8 (+), 129.6 (+), 130.5 (+), 131.8 (C_{quat}), 132.4 (+), 134.5 (C_{quat}), 134.6 (+), 154.1 (C_{quat}), 158.4 (C_{quat}), 164.2 (C_{quat}, C-4) ppm. MS (70 eV): *m*/*z* (%) = 380 (1) [M^+], 238 (100) [M^+ – HSO_2Ph], 77 (30). $C_{21}H_{20}N_2O_3S$ (380.5): calcd. C 66.30, H 5.30, N 7.36; found C 66.13, H 5.60, N 7.61.

6-Ethyl-2-phenyl-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (16a-Et): The crude mixture obtained from **15a** (439 mg, 1 mmol), *n*BuLi (1.77 M, 0.62 mL) and EtBr (119 mg, 1.1 mmol) according to the method described above, was subjected to column chromatography (R_f = 0.38, CH_2Cl_2/MeOH, 25:1, 1.5 × 30 cm, 25 g SiO_2) to afford **16a**-Et (339 mg, 86%) as a colorless solid, m.p. 242 °C. IR (KBr): $\tilde{\nu}$ = 3065 cm^{-1}, 2941, 1644, 1554, 1447, 1301, 1151, 1079, 763, 692. ^1H NMR (250 MHz, [D_6]DMSO): δ = 1.11

(t, J = 7.3, 3 H), 1.62–1.81 (m, 2 H), 2.12–2.44 (m, 2 H), 2.71–3.02 (m, 4 H), 7.41–7.74 (m, 6 H), 7.91–8.21 (m, 4 H), 12.6 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, [D$_6$]DMSO): δ = 8.6 (+), 23.3 (–), 24.4 (–), 27.5 (–), 28.4 (–), 63.6 (C_{quat}), 116.2 (C_{quat}, C-4a), 127.5 (+), 128.8 (+), 129.0 (+), 130.1 (C_{quat}), 130.2 (+), 131.8 (+), 133.8 (+), 135.7 (C_{quat}), 153.9 (C_{quat}), 160.7 (C_{quat}), 164.4 (C_{quat}) ppm. MS (70 eV): m/z (%) = 394 (1) [M$^+$], 253 (52) [M$^+$ – SO_2Ph], 252 (100) [M$^+$ – SO_2Ph – H], 237 (14), 211 (15), 104 (11).

6-Methyl-2-phenyl-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (17a-Me): According to the GP 5 from the sulfone **16a**-Me (265 mg, 0.7 mmol) and KO*t*Bu (235 mg, 2.1 mmol) was obtained 6-methyl-2-phenyl-7,8-dihydro-3*H*-quinazolin-4-one (160 mg, 96%) as a pale yellow solid, m.p. 218 °C, R_f = 0.6 (hexane/ethyl acetate, 1:2). IR (KBr): $\tilde{\nu}$ = 3031 cm^{-1}, 2924, 1636, 1506, 1436, 1314, 1182, 932, 772, 699. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.96 (s, 3 H), 2.39 (m, 2 H, 7-H), 2.89 (m, 2 H, 8-H), 6.46 (s, 1 H, 5-H), 7.42–7.61 (m, 3 H), 8.18–8.36 (m, 2 H), 13.3 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 23.4 (+), 28.3 (–), 29.9 (–), 114.3 (+, C-5), 117.8 (C_{quat}, C-4a), 127.5 (+), 128.8 (+), 131.3 (+), 132.3 (C_{quat}), 137.7 (C_{quat}, C-6), 153.4 (C_{quat}), 159.4 (C_{quat}), 161.9 (C_{quat}) ppm. MS (70 eV): m/z (%) = 238 (100) [M$^+$], 237 (38), 223 (50) [M$^+$ – Me], 194 (10) [M$^+$ – $CONH_2$], 104 (14), 77 (10) [Ph$^+$]. According to the GP 6 the crude reaction mixture obtained from 6-methyl-2-phenyl-7,8-dihydro-3*H*-quinazolin-4-one (100 mg, 0.42 mmol) and Pd/C (22 mg) in MeOH (25 mL) afforded **17a**-Me (97 mg, 96%) after 4 h as a pale yellow solid, m.p. 237 °C. IR (KBr): $\tilde{\nu}$ = 3072 cm^{-1}, 2948, 1641, 1507, 1316, 1073, 697. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.12 (d, ^3J = 6.5 Hz, 3 H), 1.38–1.56 (m, 1 H), 1.76–2.15 (m, 3 H), 2.68–2.86 (m, 3 H), 7.20–7.38 (m, 3 H), 8.02–8.14 (m, 2 H), 11.68 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.5 (+), 28.0 (+), 30.1 (–), 30.4 (–), 31.8 (–), 119.6 (C_{quat}, C-4a), 127.5 (+), 128.8 (+), 131.3 (+), 132.4 (C_{quat}), 153.3 (C_{quat}), 162.2 (C_{quat}), 164.8 (C_{quat}) ppm. MS (70 eV): m/z (%) = 240 (100) [M$^+$], 225 (90) [M$^+$ – Me], 198 (49), 104 (31), 77 (16). $C_{15}H_{16}N_2O$ (240.3): calcd. C 74.97, H 6.71, N 11.66; found C 74.77, H 6.99, N 11.53.

6-Ethyl-2-phenyl-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (17a-Et): According to the GP 5 from the sulfone **16a**-Et (197 mg, 0.5 mmol) and KO*t*Bu (168 mg, 1.5 mmol) was obtained 6-ethyl-2-phenyl-7,8-dihydro-3*H*-quinazolin-4-one (118 mg, 94%) as a pale yellow solid, m.p. 198 °C, R_f = 0.6 (hexane/ethyl acetate, 1:2). IR (KBr): $\tilde{\nu}$ = 3020 cm^{-1}, 2955, 2922, 1630, 1532, 1321, 1098, 922, 699. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.16 (t, J = 7.3 Hz, 3 H), 2.26 (q, J = 7.3 Hz, 2 H), 2.40 (m, 2 H, 7-H), 2.89 (m, 2 H, 8-H), 6.47 (s, 1 H, 5-H), 7.42–7.61 (m, 3 H), 8.22–8.38 (m, 2 H), 13.45 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 11.8 (+), 26.9 (–), 29.99 (–), 30.02 (–), 112.4 (+, C-5), 117.8 (C_{quat}, C-4a), 127.5 (+), 128.7 (+), 131.3 (+), 132.3 (C_{quat}), 143.2 (C_{quat}, C-6), 153.4 (C_{quat}), 159.7 (C_{quat}), 162.0 (C_{quat}) ppm. MS (70 eV): m/z (%) = 252 (100) [M$^+$], 237 (80) [M$^+$ – Me], 223 (25) [M$^+$ – Et], 180 (20). The crude reaction mixture obtained from 6-ethyl-2-phenyl-7,8-dihydro-3*H*-quinazolin-4-one (76 mg, 0.30 mmol) and 15 mg of Pd/C in 25 mL of MeOH after 4 h according to the GP 6 afforded 74 mg (96%) of **17a**-Et as a pale yellow solid, m.p. 221 °C. IR (KBr): $\tilde{\nu}$ = 2922 cm^{-1}, 1642, 1549, 1315, 919, 697. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.02 (t, J = 7.3 Hz, 3 H), 1.24–1.68 (m, 4 H), 1.80–2.15 (m, 2 H), 2.55–3.00 (m, 3 H), 7.36–7.60 (m, 3 H), 8.10–8.32 (m, 2 H), 13.12 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 11.5 (+), 27.9 (–), 28.1 (–), 28.8 (–), 31.8 (–), 34.7 (+), 119.6 (C_{quat}, C-4a), 127.5 (+), 128.7 (+), 131.3 (+), 132.4 (C_{quat}), 153.2 (C_{quat}, C-2/C-8a), 162.4 (C_{quat}, C-8a/C-2), 164.9 (C_{quat}, C-4) ppm. MS (70 eV): m/z (%) = 254 (80) [M$^+$], 225 (100) [M$^+$ – Et], 198 (36), 104 (22). $C_{16}H_{18}N_2O$ (254.3): calcd. C 75.56, H 7.13, N 11.01; found. C 75.36, H 7.45, N 10.88.

***tert*-Butyl 4-Oxo-2-phenyl-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-4*H*-quinazoline-3-carboxylate (18a):** To a suspension of **12a** (183 mg, 0.50 mmol) in THF (10 mL) was added $(Boc)_2O$ (218 mg, 1.0 mmol), Et_3N (50.6 mg, 0.5 mmol) and DMAP (122 mg, 0.5 mmol) at room temp., and the resulting solution was stirred at room temp. for 2 h. The reaction mixture was diluted with CH_2Cl_2 (25 mL) and the mixture washed with 1 N HCl (10 mL). The organic layer was separated, the aqueous layer extracted with CH_2Cl_2 (2×20 mL). The combined organic layers were dried with $MgSO_4$, the solvents removed, and the crude product was purified by column chromatography (R_f = 0.5, hexane/ethyl acetate, 2:1, 1×20 cm, flash SiO_2) to yield **18a** (191 mg, 82%) as a colorless solid, m.p. 153 °C. IR (KBr): $\tilde{\nu}$ = 3066 cm^{-1}, 2985, 1752, 1595, 1421, 1249, 1146. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.62 (s, 9 H), 1.84–2.04 (m, 1 H), 2.40–2.56 (m, 1 H), 2.79–3.25 (m, 4 H), 3.31–3.44 (m, 1 H, 6-H), 7.42–7.51 (m, 3 H), 7.58–7.78 (m, 3 H), 7.95–8.02 (m, 2 H), 8.28–8.39 (m, 2 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.8 (–), 22.0 (–), 27.5 (+), 31.0 (–), 58.9 (+), 85.2 (C_{quat}), 114.5 (C_{quat}, C-4a), 128.2 (+), 128.4 (+), 129.0 (+), 129.4 (+), 130.9 (+), 134.2 (C_{quat}), 136.4 (+), 136.5 (C_{quat}), 148.9 (C_{quat}), 162.6 (C_{quat}), 163.4 (C_{quat}) 167.0 (C=O) ppm. MS (70 eV): m/z (%) = 466 (1) [M$^+$], 225 (20), 224 (100) [M$^+$ – SO_2Ph – Boc], 57 (16). $C_{25}H_{26}N_2O_5S$ (466.6): calcd. C 64.36, H 5.62, N 6.00; found C 64.22, H 5.51, N 5.86.

***tert*-Butyl (6*R**,8*R**)-8-Methyl-4-oxo-2-phenyl-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-4*H*-quinazoline-3-carboxylate (19a):** To a solution of **18a** (233 mg, 0.5 mmol) in THF (10 mL) was added *n*BuLi (0.24 mL, 2.45 M in hexane) at –78 °C over a period of 15 min. The resulting dark red solution was stirred at this temp. for 15 min, at which point methyl iodide (92.3 mg, 0.65 mmol) in THF (1 mL) was added, the cooling bath was removed, and stirring was continued at room temp. for 2 h. The reaction mixture was poured into a separating funnel containing satd. aq. NH_4Cl solution (10 mL), and the mixture was extracted with Et_2O (3×15 mL). The combined organic solutions were dried with $MgSO_4$. Removal of the solvents followed by column chromatography (R_f = 0.55, hexane/ethyl acetate, 2:1, 1×20 cm, flash silica gel) yielded **19a** (mixture of diastereomers, ca. 4:1, 66 mg, 28%) as a colorless solid, m.p. 98 °C. IR (KBr): $\tilde{\nu}$ = 3029 cm^{-1}, 2981, 1762, 1540, 1410, 1243, 1148, 856. ^{1}H NMR (300 MHz, $CDCl_3$, major isomer): δ = 1.35 (d, J = 7.3 Hz, 3 H), 1.58 (s, 9 H), 2.04–2.32 (m, 2 H), 2.75–3.12 (m, 2 H), 3.25–3.39 (m, 1 H), 3.40–3.52 (m, 1 H, 6-H), 7.38–7.46 (m, 3 H), 7.58–7.77 (m, 3 H), 7.92–7.98 (m, 2 H), 8.30–8.39 (m, 2 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, major isomer): δ = 21.6 (+), 22.2 (–), 27.9 (+), 28.4 (–), 34.8 (+), 55.8 (+), 85.4 (C_{quat}), 114.0 (C_{quat}, C-4a), 128.1 (+), 128.3 (+), 129.1 (+), 129.5 (+), 131.2 (+), 134.2 (+), 136.36 (C_{quat}), 136.40 (C_{quat}), 149.2 (C_{quat}), 162.5 (C_{quat}), 163.4 (C_{quat}) 171.4 (C=O, Boc) ppm. MS (DCI = 70 eV): m/z (%) = 498 (5) [M + NH_4^+], 481 (100) [M + H$^+$], 381 (79), 341 (82). $C_{26}H_{28}N_2O_5S$ (480.6): calcd. C 64.98, H 5.87, N 5.83; found C 64.62, H 5.57, N 5.85.

(6*R,7*R**)-7-Methyl-2-phenyl-6-(*p*-tolylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (21a):** A 10-mL Pyrex tube was charged with **6a** (99 mg, 0.5 mmol) and (*E*)-1-propenyl-*p*-tolyl sulfone (**20**) (392 mg, 2 mmol), and the tube was heated at 175 °C for 12 h. After cooling down to room temp., the reaction mixture was dissolved in CH_2Cl_2/MeOH and subjected to column chromatography (R_f = 0.40, hexane/ethyl acetate, 1:2) to yield one of the diastereomers of **21a** (53 mg, 27%) as a colorless solid, m.p. 247 °C. IR (KBr): $\tilde{\nu}$ = 3034 cm^{-1}, 2927, 1653, 1507, 1302, 1142, 1018. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.26 (d, J = 7.8 Hz, 3 H), 2.42 (s, 3 H, Ts), 2.42–2.86 (m, 3 H), 2.88–3.04 (m, 1 H), 3.15–3.36 (m, 2 H), 7.30–7.90 (m, 7 H), 8.10–8.20 (m, 2 H, XX′ part of an AA′XX′ system),

12.8 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.4 (+), 21.7 (+), 27.2 (–), 37.3 (–), 63.2 (+), 115.6 (C_{quat}, C-4a), 127.5 (+), 128.7 (+), 128.88 (C_{quat}), 128.91 (+), 130.0 (+), 131.7 (+), 132.0 (C_{quat}), 135.2 (C_{quat}), 144.8 (C_{quat}), 154.1 (C_{quat}), 163.7 (C_{quat}) ppm. MS (70 eV): *m/z* (%) = 394 (2) [M^+], 239 (36), 238 (100), 223 (28), 180 (20).

2-Dimethylamino-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12h): A 10-mL Pyrex tube containing **12g** (168 mg, 0.5 mmol) in 2 mL of DMF was tightly sealed and heated at 180 °C for 12 h. The reaction mixture was cooled to room temp., the excess DMF was removed at reduced pressure, and the crude product was filtered through a pad of silica gel (2 × 3 cm, 10 g, CH_2Cl_2/MeOH, 10:1) to yield **12h** (143 mg, 86%) as a colorless solid, m.p. 249 °C. IR (KBr): $\tilde{\nu}$ = 2929 cm^{-1}, 1635, 1586, 1302, 1138, 1084. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.71–1.92 (m, 1 H), 2.31–2.87 (m, 4 H), 3.11 (s, 6 H), 3.13–3.26 (m, 1 H), 3.58–3.72 (m, 1 H), 7.53–7.74 (m, 3 H), 7.90–7.99 (m, 2 H), 11.59 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.5 (–), 22.0 (–), 31.1 (–), 37.4 (+), 59.9 (+), 104.1 (C_{quat}, C-4a), 129.0 (+), 129.1 (+), 133.8 (+), 137.1 (C_{quat}), 152.5 (C_{quat}), 161.9 (C_{quat}), 164.8 (C_{quat}) ppm. MS (70 eV): *m/z* (%) = 333 (6) [M^+], 192 (20), 191 (100), 162 (10), 77 (15). $C_{16}H_{19}N_3O_3S$ (333.4): calcd. C 57.64, H 5.74, N 12.60; found C 57.58, H 5.45, N 12.48.

2-(Morpholin-4-yl)-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12i): A 10-mL Pyrex tube containing **12g** (168 mg, 0.5 mmol) in morpholine (2 mL) was tightly sealed and heated at 180 °C for 15 h. The reaction mixture was cooled to room temp., the excess morpholine was removed in vacuo, and the crude product was filtered through a pad of silica gel (2 × 3 cm, 10 g, CH_2Cl_2/MeOH, 10:1) to yield **12i** (175 mg, 93%) as a colorless solid, m.p. > 250 °C. IR (KBr): $\tilde{\nu}$ = 2902 cm^{-1}, 2848, 1656, 1590, 1395, 1300, 1267, 1146, 1114, 979, 742, 722. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.55–1.72 (m, 1 H), 2.05–2.32 (m, 2 H), 3.41–3.72 (m, 12 H), 7.60–7.81 (m, 3 H), 7.82–7.92 (m, 2 H), 8.86 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, [D$_6$]DMSO): δ = 21.5 (–), 21.7 (–), 29.8 (–), 44.8 (–), 58.1 (+), 65.8 (–), 104.2 (C_{quat}, C-4a), 128.7 (+), 129.8 (+), 134.3 (+), 137.2 (C_{quat}), 151.9 (C_{quat}), 159.1 (C_{quat}), 163.4 (C_{quat}, C-4) ppm. MS (70 eV): *m/z* (%) = 375 (8) [M^+], 233 (100) [M^+ – HSO_2Ph], 202 (23), 176 (10). $C_{18}H_{21}N_3O_4S$ (375.5): calcd. C 57.58, H 5.64, N 11.19; found C 57.26, H 5.65, N 11.53.

2-(4-Methylpiperazin-1-yl)-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12j): According to the method described above, **12g** (336 mg, 1.00 mmol) and *N*-methylpiperazine (2 mL) gave **12j** (352 mg, 91%) as a colorless solid, m.p. > 250 °C. IR (KBr): $\tilde{\nu}$ = 3232 cm^{-1}, 2930, 2797, 1631, 1585, 1301, 1266, 1147, 1083, 1003, 721. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.78–1.92 (m, 1 H), 2.38 (s, 3 H), 2.41 (m, 4 H), 2.43–2.80 (m, 5 H), 3.13–3.26 (m, 1 H), 3.68–3.81 (m, 4 H), 7.52–7.71 (m, 3 H), 7.88–8.02 (m, 2 H), 11.42 (br. s, 1 H, NH) ppm. ^{13}C NMR (50.3 MHz, [D$_6$]-DMSO): δ = 21.0 (–), 21.2 (–), 29.6 (–), 43.8 (–), 45.1 (+), 53.7 (–), 58.0 (+), 104.4 (C_{quat}, C-4a), 128.0 (+), 129.0 (+), 133.4 (+), 137.1 (C_{quat}), 152.6 (C_{quat}, C-2), 159.3 (C_{quat}, C-8a), 163.2 (C_{quat}, C-4) ppm. MS (70 eV): *m/z* (%) = 388 (16) [M^+], 318 (100), 306 (24), 176 (74), 83 (55), 71 (26). $C_{19}H_{24}N_4O_3S$ (388.5): calcd. C 58.74, H 6.23, N 14.42; found C 58.64, H 6.14, N 14.29.

2-(4-Benzylpiperazin-1-yl)-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12k): According to the method described above, **12g** (750 mg, 2.23 mmol) and *N*-benzylpiperazine (1.57 g, 8.92 mmol) gave **12k** (953 mg, 92%) as a colorless solid, m.p. > 250 °C. IR (KBr): $\tilde{\nu}$ = 2937 cm^{-1}, 2816, 1653, 1576, 1304, 1262, 1144, 745. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.52–1.71 (m, 1 H), 2.08–2.42 (m, 7 H), 3.41–3.63 (m, 9 H), 7.17–7.38 (m, 5 H), 7.62–7.94 (m, 5 H), 9.26 (br. s, 1 H, NH) ppm. ^{13}C NMR (50.3 MHz, [D$_6$]DMSO): δ = 20.9 (–), 21.2 (–), 29.6 (–), 43.9 (–), 51.6 (–), 58.1 (+), 61.4 (–), 104.4 (C_{quat}, C-4a), 126.4 (+), 127.6 (+), 128.0 (+), 128.3 (+), 128.9 (+), 133.4 (+), 137.1 (C_{quat}), 137.5 (C_{quat}), 152.5 (C_{quat}), 159.4 (C_{quat}), 163.1 (C_{quat}, C-4) ppm. MS (70 eV): *m/z* (%) = 464 (14) [M^+], 429 (12), 412 (16), 318 (68), 159 (96), 91 (100). $C_{25}H_{28}N_4O_3S$ (464.6): calcd. C 64.63, H 6.07, N 12.06; found C 64.48, H 6.17, N 11.97.

2-Benzylamino-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12m): A 5-mL Pyrex tube was charged with **12g** (504 mg, 1.50 mmol) and 1.6 g (15 mmol) of benzylamine, the tube was tightly sealed and heated at 180 °C for 15 h. The reaction mixture was cooled to room temp., dissolved in CH_2Cl_2 and purified by column chromatography (1.5 × 15 cm, 25 g Al_2O_3, R_f = 0.4, CH_2Cl_2/MeOH, 25:1) to yield **12m** (385 mg, 65%) as a colorless solid, m.p. 115 °C. IR (KBr): $\tilde{\nu}$ = 3275 cm^{-1}, 3061, 2931, 1635, 1600, 1446, 1303, 1145, 1084, 750, 698. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.62–1.84 (m, 1 H), 2.20–2.62 (m, 5 H), 3.06–3.23 (m, 1 H), 4.58 (m, 2 H), 6.42 (m, 1 H), 7.18–7.38 (m, 5 H), 7.44–7.85 (m, 5 H), 9.80 (br. s, 1 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 21.4 (–), 22.0 (–), 30.9 (–), 44.2 (–), 59.6 (+), 105.4 (C_{quat}, C-4a), 126.7 (+), 127.2 (+), 128.5 (+), 128.9 (+), 129.1 (+), 133.8 (+), 136.8 (C_{quat}), 138.5 (C_{quat}), 143.1 (C_{quat}), 152.3 (C_{quat}), 164.5 (C_{quat}, C-4) ppm. MS (70 eV): *m/z* (%) = 395 (8) [M^+], 253 (80) [M^+ – HSO_2Ph], 106 (84), 91 (100).

2-[Benzyl(methyl)amino]-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12n): A 5-mL Pyrex tube was charged with **12g** (168 mg, 0.50 mmol) and *N*-methylbenzylamine (605 mg, 5 mmol), the tube was tightly sealed and heated at 180 °C for 15 h. The reaction mixture was cooled to room temp., dissolved in CH_2Cl_2/MeOH (10:1) and filtered through a pad of SiO_2 (2 × 3 cm, 10 g, DCM/MeOH, 25:1) to yield **12n** (134 mg, 66%) as a colorless solid, m.p. 220 °C. IR (KBr): $\tilde{\nu}$ = 3062 cm^{-1}, 2941, 1654, 1594, 1307, 1144, 1085. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.56–1.76 (m, 1 H), 2.08–2.35 (m, 3 H), 2.43–2.61 (m, 2 H), 2.92 (s, 3 H, CH_3), 3.50–3.62 (m, 1 H), 4.72 (s, 2 H, Bn-H), 7.14–7.40 (m, 5 H), 7.63–7.97 (m, 5 H), 10.76 (br. s, 1 H, NH) ppm. ^{13}C NMR (75.5 MHz, [D$_6$]DMSO): δ = 21.28 (–), 21.31 (–), 30.1 (–), 34.9 (+), 51.5 (–), 58.0 (+), 103.8 (C_{quat}, C-4a), 127.0 (+), 127.1 (+), 128.34 (+), 128.37 (+), 129.4 (+), 133.9 (+), 137.0 (C_{quat}), 137.4 (C_{quat}), 152.9 (C_{quat}), 160.0 (C_{quat}), 163.4 (C_{quat}) ppm. MS (DCI): *m/z* (%) = 410 (100) [M + H$^+$], 182 (57), 168 (70). $C_{22}H_{23}N_3O_3S$ (409.5): calcd. C 64.53, H 5.66, N 10.26; found C 64.20, H 5.63, N 10.06.

2-(Imidazol-1-yl)-6-(phenylsulfonyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (12o): A 5-mL Pyrex tube was charged with **12g** (168 mg, 0.50 mmol) and imidazole (340 mg, 5 mmol), the tube was tightly sealed and heated at 180 °C for 15 h. The reaction mixture was cooled to room temp., dissolved in CH_2Cl_2 and purified by column chromatography (1.5 × 15 cm, 25 g of silica gel, R_f = 0.45, Et_2O/MeOH, 10:1) to yield **12o** (112 mg, 63%) as a colorless solid, m.p. > 250 °C. IR (KBr): $\tilde{\nu}$ = 3160 cm^{-1}, 2892, 1844, 1601, 1479, 1426, 1308, 1151, 1086, 1016, 741. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.71–1.85 (m, 1 H), 2.18–2.31 (m, 1 H), 2.43–2.58 (m, 2 H), 2.68–2.83 (m, 2 H), 3.66–3.80 (m, 1 H), 7.02–7.19 (m, 1 H), 7.66–7.81 (m, 4 H), 7.90–7.98 (m, 2 H), 8.39 (s, 1 H), 10.80 (br. s, 1 H, NH) ppm. ^{13}C NMR (75.5 MHz, [D$_6$]DMSO): δ = 21.1 (–), 21.5 (–), 29.7 (–), 57.4 (+), 110.7 (C_{quat}, C-4a), 116.5 (+), 128.4 (+), 129.5 (+), 129.7 (+), 134.1 (+), 135.2 (+), 136.8 (C_{quat}), 150.1 (C_{quat}), 163.4 (C_{quat}), 167.8 (C_{quat}, C-4) ppm. MS (70 eV): *m/z* (%) = 356 (4) [M^+], 214 (100) [M^+ – HSO_2Ph], 113 (20). $C_{17}H_{16}N_4O_3S$ (356.5): calcd. C 57.29, H 4.53, N 15.72; found C 57.30, H 4.52, N 16.12.

2-(Morpholin-4-yl)-7,8-dihydro-3*H*-quinazolin-4-one (13i): To a suspension of **12i** (175 mg, 0.47 mmol) in THF (10 mL) was added KO*t*Bu (264 mg, 2.35 mmol), and the reaction mixture was stirred at room temp. for 15 h. Then it was poured into a separating funnel containing a satd. aq. NH_4Cl solution (10 mL), and the mixture was extracted with CH_2Cl_2 (3×15 mL). The organic solutions were dried with $MgSO_4$, and the solvent was removed in vacuo. The crude product was subjected to column chromatography (R_f = 0.45, Et_2O/MeOH, 25:1, 1.5×30 cm, 25 g of silica gel) to yield **13i** (90 mg, 82%) as a colorless solid, m.p. 228–230 °C. IR (KBr): $\tilde{\nu}$ = 2924 cm^{-1}, 2849, 1637, 1585, 1382, 1263, 1171, 1115, 987, 862, 729. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.28– 2.40 (m, 2 H), 2.62 (m, 2 H, 8-H), 3.81 (m, 8 H), 6.45 (dt, J = 9.7 and 4.3 Hz, 1 H, 6-H), 6.73 (dt, J = 9.7 and 1.8 Hz, 1 H, 5-H), 12.12 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.6 (–), 30.2 (–), 44.9 (–), 66.4 (–), 107.5 (C_{quat}, C-4a), 119.6 (+, C-5/C-6), 122.1 (+, C-6/C-5), 152.4 (C_{quat}), 162.5 (C_{quat}), 164.2 (C_{quat}) ppm. MS (70 eV): *m*/*z* (%) = 234/233 (11/100) [M^+ + 1], 233 (100) [M^+], 202 (62) [M^+ – CH_2OH], 188 (16), 176 (30). $C_{12}H_{15}N_3O_2$ (233.3): calcd. C 61.79, H 6.48, N 18.01; found C 61.54, H 6.72, N 17.91.

2-(4-Methylpiperazin-1-yl)-7,8-dihydro-3*H*-quinazolin-4-one (13j): The crude product obtained from **12j** (220 mg, 0.57 mmol) and KO*t*Bu (638 mg, 5.70 mmol) according to the method described above. Then it was subjected to column chromatography (R_f = 0.40, CH_2Cl_2/MeOH, 25:1, 1.5×20 cm, 25 g of Al_2O_3) to yield **13j** (121 mg, 87%) as a colorless solid, m.p. 188 °C. IR (KBr): $\tilde{\nu}$ = 3101 cm^{-1}, 2935, 2792, 1654, 1582, 1387, 1267, 1140, 1005, 727. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.21–2.38 (m, 5 H), 2.41–2.54 (m, 4 H), 2.55–2.66 (m, 2 H), 3.64–3.81 (m, 4 H), 5.72 (dt, J = 9.7 and 4.3 Hz, 1 H, 6-H), 6.48 (dt, J = 9.7 and 1.8 Hz, 1 H, 5-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.6 (–), 30.3 (–), 44.4 (–), 46.0 (+), 54.5 (–), 107.1 (C_{quat}, C-4a), 119.8 (+, C-5/C-6), 121.6 (+, C-6/C-5), 152.3 (C_{quat}), 162.5 (C_{quat}), 164.2 (C_{quat}) ppm. MS (70 eV): *m*/*z* (%) = 246 (49) [M^+], 189 (12), 176 (100). $C_{13}H_{18}N_4O$ (246.3): calcd. C 63.39, H 7.37, N 22.75; found C 63.37, H 7.23, N 22.59.

2-(4-Benzylpiperazin-1-yl)-7,8-dihydro-3*H*-quinazolin-4-one (13k): The crude product obtained from **12k** (200 mg, 0.43 mmol) and KO*t*Bu (480 mg, 4.280 mmol) according to the method described above, was subjected to column chromatography (R_f = 0.41, CH_2Cl_2/MeOH, 25:1, 1.5×30 cm, 25 g of silica gel) to yield **13k** (131 mg, 94%) as a colorless solid, m.p. 196–197 °C. IR (KBr): $\tilde{\nu}$ = 3040 cm^{-1}, 2953, 1636, 1576, 1388, 1311, 1277, 1170, 1005, 848, 726. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.22–2.40 (m, 2 H), 2.49–2.63 (m, 6 H), 3.54 (s, 2 H), 3.72–3.82 (m, 4 H), 5.68 (dt, J = 9.5 and 4.3 Hz, 1 H, 6-H), 6.42 (dt, J = 9.5 and 1.7 Hz, 1 H, 5-H), 7.26–7.38 (m, 5 H), 11.80 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.7 (–), 29.7 (–), 44.5 (–), 52.8 (–), 62.7 (–), 107.1 (C_{quat}, C-4a), 119.8 (+, C-5/C-6), 121.6 (+, C-6/C-5), 127.2 (+), 128.3 (+), 129.4 (+), 137.6 (C_{quat}), 152.2 (C_{quat}), 162.5 (C_{quat}), 164.2 (C_{quat}) ppm. MS (70 eV): *m*/*z* (%) = 322 (71) [M^+], 189 (30), 176 (100), 146 (38), 91 (53). $C_{19}H_{22}N_4O$ (322.4): calcd. C 70.78, H 6.88, N 17.38; found C 70.45, H 6.47, N 17.50.

2-[Benzyl(methyl)amino]-7,8-dihydro-3*H*-quinazolin-4-one (13n): To a suspension of **12n** (204 mg, 0.50 mmol) in THF (5 mL), KO*t*Bu (560 mg, 5.00 mmol) was added and the reaction mixture was stirred at room temp. for 15 h. Then it was poured into a separating funnel containing a satd. aq. NH_4Cl solution (10 mL) and extracted with CH_2Cl_2 (3×15 mL). The organic solutions were dried with $MgSO_4$, and the solvent was removed in vacuo to yield **13n** (121 mg, 90%) as a colorless solid, m.p. 166 °C. IR (KBr): $\tilde{\nu}$ = 2927 cm^{-1}, 2827, 1638, 1575, 1384, 1257, 1169, 1028, 731. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.25– 2.39 (m, 2 H), 2.61 (m, 2 H, 8-H), 3.11 (s, 3 H), 4.83 (s, 2 H), 5.64 (dt, J = 9.5 and 4.3 Hz, 1 H, 6-H), 6.42 (dt, J = 9.5 and 1.8 Hz, 1 H, 5-H), 7.20–7.37 (m, 5 H, aryl-H), 11.5 (br. s, 1 H, NH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 22.3 (–), 30.0 (–), 34.7 (+), 52.3 (–), 106.4 (C_{quat}, C-4a), 119.6 (+, C-5/C-6), 120.9 (+, C-6/C-5), 127.15 (+), 127.21 (+), 128.3 (+), 136.5 (C_{quat}), 152.6 (C_{quat}), 161.8 (C_{quat}), 163.8 (C_{quat}) ppm. MS (70 eV): *m*/*z* (%) = 267 (92) [M^+], 252 (67), 176 (52), 91 (100).

2-(Morpholin-4-yl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (14i): A 50-mL flame-dried round-bottomed flask flushed with nitrogen, was charged with MeOH (10 mL) and Pd/C (10% Pd w/w, 15 mg), and the mixture was stirred under H_2 for 30 min, at which point **13i** (100 mg, 0.43 mmol) in MeOH (15 mL) was added with a syringe, and stirring was continued at room temp. for 15 h. The mixture was filtered through a pad of Celite®, and the solvent was removed in vacuo to yield **14i** (97 mg, 96%) as a colorless solid, m.p. 204–205 °C. IR (KBr): $\tilde{\nu}$ = 2925 cm^{-1}, 2856, 1640, 1576, 1386, 1270, 1165, 1121, 1001, 877, 767. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.63–1.90 (m, 4 H), 2.30–2.42 (m, 2 H), 2.43–2.58 (m, 2 H), 3.56–3.92 (m, 8 H), 11.6 (br. s, 1 H, NH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 21.3 (–), 22.2 (–), 22.5 (–), 32.2 (–), 44.9 (–), 66.5 (–), 109.7 (C_{quat}, C-4a), 156.6 (C_{quat}), 163.6 (C_{quat}), 165.7 (C_{quat}) ppm. MS (70 eV): *m*/*z* (%) = 235 (84) [M^+], 204 (100) [M^+ – CH_2OH], 190 (40), 178 (90), 150 (47). $C_{12}H_{17}N_3O_2$ (235.3): calcd. C 61.26, H 7.28, N 17.86; found C 61.41, H 7.40, N 17.65.

2-(4-Methylpiperazin-1-yl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (14j): According to the method described above, **13j** (100 mg, 0.41 mmol) gave **14j** (84 mg, 83%) as a colorless solid, m.p. 210 °C. IR (KBr): $\tilde{\nu}$ = 3091 cm^{-1}, 2934, 2785, 1642, 1576, 1387, 1308, 1267, 1150, 1000, 845. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.61–1.80 (m, 4 H), 2.24–2.40 (m, 5 H), 2.42–2.58 (m, 6 H), 3.64–3.74 (m, 4 H), 11.81 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.3 (–), 22.3 (–), 22.6 (–), 32.3 (–), 44.5 (–), 46.0 (+), 54.6 (–), 109.3 (C_{quat}, C-4a), 151.7 (C_{quat}), 163.6 (C_{quat}), 165.6 (C_{quat}) ppm. MS (70 eV): *m*/*z* (%) = 248 (17) [M^+], 178 (100), 166 (12), 83 (28), 71 (19). $C_{13}H_{20}N_4O$ (248.3): calcd. C 62.88, H 8.12, N 22.56; found C 62.59, H 8.12, N 22.40.

2-(Piperazin-1-yl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one (14k): According to the method described above, **13k** (150 mg, 0.47 mmol) afforded **14k** (99 mg, 90%) as a colorless solid, m.p. 121 °C. IR (KBr): $\tilde{\nu}$ = 2930 cm^{-1}, 1700, 1635, 1576, 1437, 1398, 1267, 998. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.60–1.82 (m, 4 H), 2.28–2.54 (m, 4 H), 2.84–3.02 (m, 4 H), 3.62–3.71 (m, 4 H), 6.20 (br. s, 1 H, NH), 11.81 (br. s, 1 H, NH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.4 (–), 22.3 (–), 22.6 (–), 32.3 (–), 45.58 (–), 45.62 (–), 109.2 (C_{quat}, C-4a), 151.7 (C_{quat}), 163.5 (C_{quat}), 165.5 (C_{quat}) ppm. MS (70 eV): *m*/*z* (%) = 234 (21) [M^+], 192 (33), 178 (55), 166 (74), 72 (100).

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