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Ring-chain tautomerism in 2-substituted 1,2,3,4-tetrahydroquinazolines A ^{1}H, ^{13}C and ^{15}N NMR study

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Abstract—In this work 32 1,2,3,4-tetrahydroquinazoline derivatives were synthesized by the reaction of 2-aminomethylaniline with aldehydes and ketones and their ring-chain tautomerism studied by ^{1}H, ^{13}C and ^{15}N NMR spectroscopy. The ketone, as well as the alkyl aldehyde, derivatives were found to favor exclusively ring forms, whereas tautomeric equilibria were observed for aryl aldehyde derivatives. For *para*-phenyl substituted compounds, good linear correlations were found between the Hammett–Brown σ^{+} parameter and log K (K=[ring]/[chain]) and also between σ^{+} and $\delta_{N=C}$ (N=C nitrogen chemical shift). An excellent correlation was also found between log K and $\delta_{N=C}$, which shows that the electronic character of the aryl substituent is carried by the conjugation effect to the environment of the nitrogen atom.

1. Introduction

The structural properties, especially ring-chain tautomerism, of five- and six-membered 1,3-X,Y-heterocycles (X, Y=O, S, NR) have been under active study in recent years.[1] Ring-chain tautomerism is known to occur in heterocyclic systems closely related to quinazolines, such as 1,3-imidazolidines[2] and piperimidines,[3] as well as in their oxygen-containing analogs, 1,3- and 3,1-benzoxazines,[4–9] which have been subjected to numerous studies during last decades. Tetrahydroquinazolines have been investigated in several studies,[10–14] but only very recently, the ring-chain tautomerism of 3-substituted tetrahydro-[15] and decahydroquinazolines[16] has been found by Fülöp and co-workers.

The ring-chain tautomeric equilibrium depends greatly on the substituent at position 2. In 2-aryl substituted compounds the ring-chain ratio has been found to depend on the electronic character of the substituent on the aromatic ring.[1,3–8,15,16] In these cases a linear correlation has been found between the logarithm of equilibrium constant K_X (K=[ring]/[chain]) and the Hammett-Brown parameter σ^{+} that describes the electronic character of the substituent X on the phenyl ring (Eq. (1)).

$$\log K_X = \rho\sigma^{+} + \log K_H \quad (1)$$

The value ρ has been found to be dependent on the ring system as well as on the circumstances during measurement, i.e. on the solvent and temperature. A good linear correlation has been found also between the N=C nitrogen chemical shifts and Hammett's parameters in compounds having structure X–C_6H_4–C=N–R[17] (Eq. (2)).

$$\delta_{N=C} = a\sigma^{+} + b \quad (2)$$

The chain form, Schiff base, has a structure like that above, which allows us to expect that the dependence in Eq. (2) is valid also in this case for tetrahydroquinazolines. Thus, we should, by combining Eqs. (1) and (2), be able to find a new linear correlation between log K and the N=C nitrogen chemical shifts (Eq. (3)).

$$\log K_X = A\delta_{N=C} + B \quad (3)$$

In this case dependence between two real physical quantities would exist without involving the Hammett's parameter.

In this work, a set of 2-substituted 1,2,3,4-tetrahydroquinazolines was synthesized from 2-aminomethylaniline and corresponding carbonyl compounds (Table 1). Structure determination and the analysis of tautomeric equilibria were performed by NMR spectroscopy mainly in DMSO-d_6. In addition to ^{1}H and ^{13}C NMR results, ^{15}N spectra were also measured for selected compounds. The aims of the work were to determine the structures by NMR, to study the effect of the substituent(s) at position 2 on the tautomeric equilibrium and to investigate the suitability of the linear correlations (Eqs. (1)–(3)) for 2-aryl-substituted compounds.

Keywords: 1,2,3,4-tetrahydroquinazolines; ring-chain tautomerism; NMR spectroscopy; Hammett's equation.

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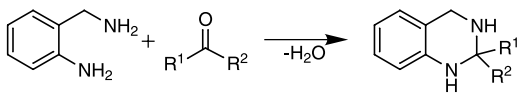
Table 1. Structures of studied compounds with the percentage amounts of the ring form in DMSO-d_6 at 30°C

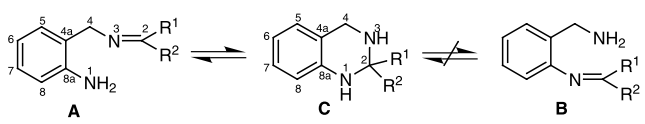


Compound	R^1	R^2	Ring (%)
1a	H	Me	100
1b	H	Pr	100
1c	H	*i*-Pr	100
1d	Me	Me	100
1e	$-(CH_2)_5-$		100
2a	Me	C_6H_5	100
2b	Me	4-Me-C_6H_4	100
2c	Me	4-NO_2-C_6H_4	100
2d	Me	4-OMe-C_6H_4	100
3	Me	2-Naphthyl	100
4a	H	4-NO_2-C_6H_4	100
4b	H	4-Cl-C_6H_4	96.2
4c	H	C_6H_5	95.2
4d	H	4-F-C_6H_4	95.2
4e	H	4-OMe-C_6H_4	85.5
4f	H	4-OEt-C_6H_4	84.0
4g	H	4-OH-C_6H_4	76.9
4h	H	4-NMe_2-C_6H_4	55.6
4i	H	4-NEt_2-C_6H_4	50.0
5a	H	2-OH-C_6H_4	38.0
5b	H	3-NO_2-C_6H_4	100
5c	H	3-I-C_6H_4	100
6a	H	2-OMe-5-NO_2-C_6H_3	100
6b	H	2,4-Cl_2-C_6H_3	98.0
6c	H	2-Cl-6-NO_2-C_6H_3	96.2
6d	H	3,4-$(OMe)_2$-C_6H_3	83.3
6e	H	2-OH-3,5-Cl_2-C_6H_2	75.2
6f	H	2-OH-5-OMe-C_6H_3	47.6
7	H	2-OH-1-Naphthyl	0

2. Results and discussion

2.1. NMR analysis and structure determination

The NMR measurements were made mainly in DMSO-d_6 and for compounds **4** also in $CDCl_3$. Initially, the proton spectra were measured as quickly as possible after dissolving the compound (usually within 15 min). The spectra were taken again after one day but no change was found in tautomeric ratios, so the equilibrium is reached quickly in solution. Chemical shift assignments were based, in addition to information from normal proton and carbon measurements, mainly on DEPT 135°, phase-sensitive DQF-COSY and f1-decoupled CH-shift correlation spectra. Long-range correlation spectra (long-range DQF-COSY and HMBC or COLOC) were also measured when more information was needed for assignments. Nitrogen spectra were measured using $^1H-^{15}N$-HMQC and -HMBC experiments. The ring-chain ratios were determined from the integrals of the 4-CH_2 protons (Scheme 1). In some cases other well-separated peaks were used to calculate the ring-chain ratios. NMR data for all compounds are provided in Section 4.



Scheme 1. Ring-chain equilibrium including numbering for compounds studied. **A** and **B** refer to aniline and benzylamine type chain forms, respectively.

In 1,3-unsubstituted tetrahydroquinazolines can occur chain-ring-chain tautomeric equilibria containing one cyclic form and two linear forms: aniline (A, Scheme 1) and benzylamine (B, Scheme 1) type structures. The chain form is easy to differentiate from the ring form based on the proton and carbon signals (δ_H 8.3–8.7 and δ_C 160–166 ppm, respectively) of sp^2-hybridized C=N carbon and proton attached to it. In addition, the cyclic form can be easily identified from magnetically nonequivalent methylene protons at position 4 (C, Scheme 1). In the spectra only the aniline type chain form (A) was observed. It can be identified from the long-range heteronuclear correlations observed between the methylene carbon/protons and H–C=N proton/carbon in HMBC spectrum, which are possible only in the aniline type linear forms. The preference of chain form (A) is explained by the difference in chemical nature of N-1 and N-3. N-1, which is directly attached to phenyl ring, is much more acidic (pK_a(aniline)=4.6 and pK_a(benzylamine)=9.3) than N-3. Thus its ability to form stabilizing intramolecular hydrogen bond with N=C nitrogen in linear form is much stronger than the one of N-3. Furthermore, the formation of the intramolecular hydrogen bond is also sterically favored in aniline type chain form. A similar behavior has been observed also for oxygen analogs. The 1,3-benzoxazines have been found to favor chain form more than the 3,1-benzoxazines.[7]

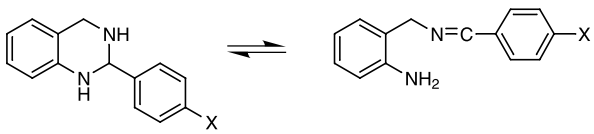
2.2. Compounds 1–3

These compounds include the products of the alkyl aldehydes and ketones (**1**) as well as of the aromatic ketones (**2**,**3**). The common factor for these compounds is that they do not contain observable amounts of forms other than ring forms. For alkyl substituted compounds **1**, the reason for this is most likely the lack of steric hindrance around position 2 that makes molecules very stable in cyclic form. The analogous 1,3-benzoxazines were also found to exhibit only ring form.[4] The aromatic ketone products **2**,**3**, unlike their aldehyde analogs (vide infra) are also completely cyclic. Undoubtedly, the methyl substituent is responsible for this fact. A similar effect has also been observed in 2-aryl-2-methyl-1,3-oxazolidines.[6] The effect can be explained either by the increase of the ring stability, or by the growth of n,π-repulsive interactions, which destabilizes the linear form. Likely, both phenomena are, in some degree, responsible for the preference of ring form in acetophenone derivatives. However, the linear forms have been recently observed in 2-methyl substituted amide derivatives.[18]

2.3. Compounds 4–7

These compounds include the aromatic aldehyde products. Compounds **4** consist of a set of *para*-substituted, compounds **5** of *ortho*- or *meta*-substituted and compounds **6** of di- or trisubstituted phenyl substituents. Compound **7** is somewhat different from others being the only naphthyl derivative. Most of these compounds were found to exhibit ring-chain tautomeric equilibria between the cyclic and the aniline type linear forms.

Table 2. Ring proportions (in DMSO-d_6 at 30°C and $CDCl_3$ at 25°C) and ^{15}N shifts (C=N, chain form, in DMSO-d_6) for *para*-substituted 2-phenyl-1,2,3,4-tetrahydroquinazolines (**4**) and Hammett–Brown parameters (σ^+) for substituents X



Compound	X	σ^+	Ring(%) in DMSO-d_6	Ring (%) in $CDCl_3$	$\delta_{N=C}$ (ppm) in DMSO-d_6
4a	NO_2	0.79	100	97.1	–
4b	Cl	0.11	96.2	94.3	−50.5
4c	H	0	95.2	94.3	−52.4
4d	F	−0.07	95.2	93.5	−54.1
4e	OMe	−0.78	85.5	86.2	−61.1
4f	OEt	−0.83	84.0	85.5	−61.1
4g	OH	−0.92	76.9	87.7	−64.9
4h	NMe_2	−1.70	55.6	69.4	−70.5
4i	NEt_2	−2.09	50.0	64.5	−72.6

The relative amount of the linear form in compounds **4** was found to increase with the Hammett-Brown σ^+ parameter of the *para*-substituent X (Table 2). To investigate the solvent dependence of the tautomeric equilibria, measurements were also made in $CDCl_3$. The plots based on Eq. (1) were made in both solvents and good linear correlations were found (Fig. 1 and Table 3). It can be noted that the solvent has a clear effect on the slope, however, the effect to the intercept is rather small. The linear correlation in DMSO-d_6 is steeper than the one in $CDCl_3$. These results are opposite to those obtained for 2-aryl substituted 1,3-oxazolidines,[1,6] in which the slope of the Hammett plot was observed to be fairly independent of solvent, especially in the case of DMSO-d_6 (0.48) and $CDCl_3$ (0.47). Furthermore K_H was found to be very dependent on solvent, DMSO-d_6 (0.11) and $CDCl_3$ (1.59), i.e. increasing solvent proton-accepting ability stabilized the open-chain tautomer.[1] In the case of our compounds we explained the preference of the aniline type chain form by intramolecular hydrogen bonding (see above). Thus, polar DMSO-d_6, by forming intermolecular hydrogen bonds, inhibits the formation of intramolecular hydrogen bonding and makes

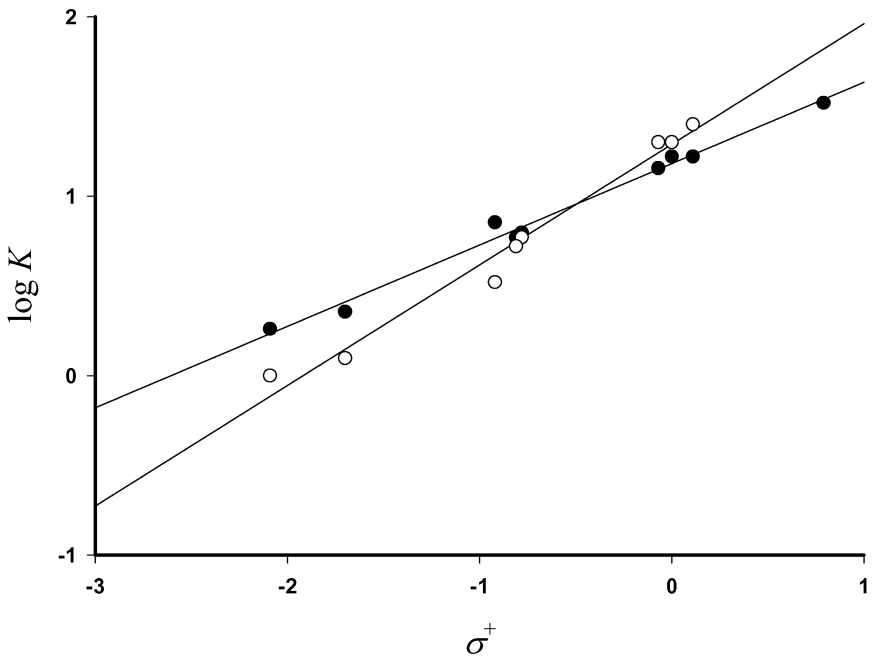


Figure 1. Plots of log K (K=[ring]/[chain]) in DMSO-d_6 (●) and in $CDCl_3$ (○) versus Hammett–Brown parameter σ^+.

Table 3. Linear regression analysis data for compounds **4a–i** (see Figs. 1–3 for plots)

Plot	Number of points	Slope[a]	Intercept[a]	Correlation coefficient
log K_{DMSO} vs σ^+	8	0.67 (4)	1.29 (5)	0.989
log K_{CDCl3} vs σ^+	9	0.45 (2)	1.18 (2)	0.993
$\delta_{N=C}$ vs σ^+	8	10.1 (7)	−53.0 (8)	0.987
log K_{DMSO} vs $\delta_{N=C}$	8	0.066 (3)	4.78 (13)	0.996

[a] Standard deviations are given in parentheses.

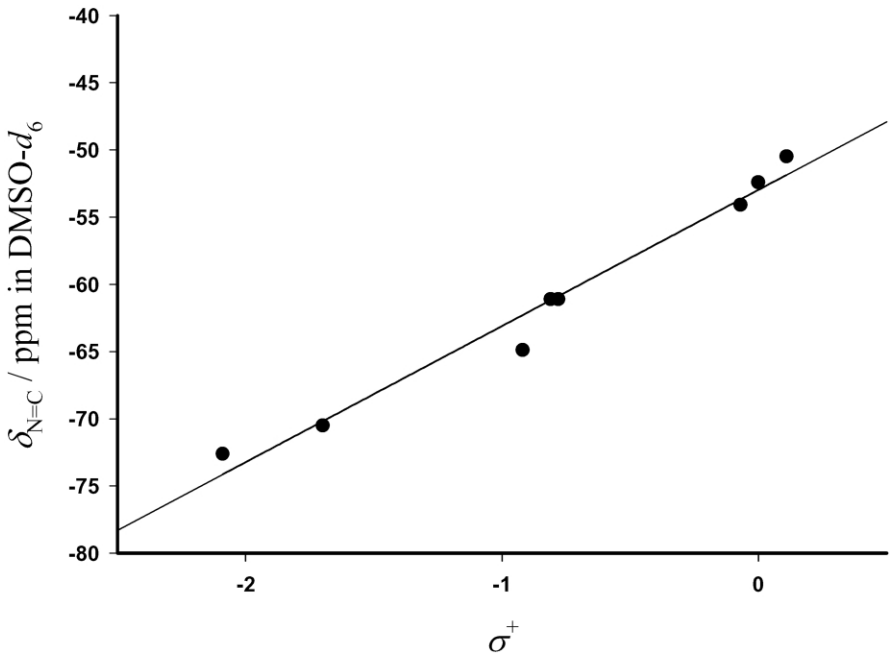


Figure 2. Plot of chemical shift of double-bond nitrogen $\delta_{N=C}$ in chain form (ppm in DMSO-d_6 at 30°C) versus Hammett–Brown parameter σ^+.

the linear form less favored than expected based on data for 1,3-oxazolidines, in which the intramolecular hydrogen bonds does not play an important role in the equilibrium.

The differences in stabilities of the closed ring forms can be discussed based on the value of *c*, which is the intercept for the 2-aryl-1,3-*O*,*N*-heterocycle subtracted from the one for the corresponding 2-aryl-1,3-*N*,*N*-heterocycle. Thus a positive *c* value means a more stable ring form than that for the oxygen analog. For compounds **4** (in $CDCl_3$), $c=0.45-(-0.66)=1.11$, where the −0.66 is the intercept for the 2-aryl-3,4-dihydro-2*H*-1,3-benzoxazines.[7,15] It is interesting to calculate the value *c* also for 2-aryl-hexahydropyrimidines:[3] $c=0.93-(-0.15)=1.08$, where the −0.15 is the intercept for the 2-aryl-1,3-oxazines.[7] Thus the increase in the stability of the ring form is almost equal when replacing the O by NH, whether there is a benzene ring condensed to the structure or not. For 3-substituted *N*,*N*-analogs it has been observed that the larger the substituent the less stable is the ring form.[15]

Also ^{15}N NMR spectra (in DMSO-d_6) were measured for compounds **4**. For NH-nitrogens no significant difference was noted depending on the tautomeric ratio. However, a clear effect was observed on the chemical shifts of N=C-nitrogen in chain form ranging from −72.6 (NEt_2) to

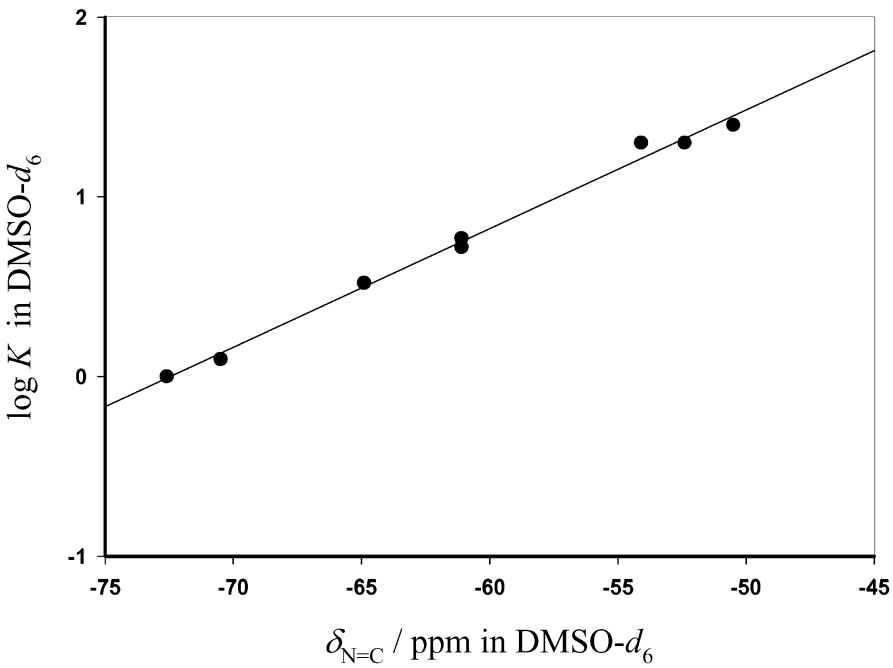


Figure 3. Plot of log *K* (*K*=[ring]/[chain]) versus chemical shift of double-bond nitrogen $\delta_{N=C}$ in chain form (ppm in DMSO-d_6 at 30°C).

−50.5 ppm (Cl) (Table 2). A linear fit according to Eq. (2) was made and a fairly good correlation was found (Fig. 2 and Table 3). This correlation can be explained by the electron-donating/electron-withdrawing character of the substituent X that affects the charge density of the conjugated C=N unit.[17] Thus, for example, electron-donating substituent NEt_2 increases the charge density on C=N nitrogen, which also increases the shielding of the nitrogen causing the upfield chemical shift.

After the correlations above, it was natural to make the linear fit also between the logarithm of the equilibrium constant K and ^{15}N chemical shift (Eq. (3). A very good correlation was found for this fit (Fig. 3 and Table 3). As far as we know, this is the first time that this correlation has been found in ring-chain tautomeric systems. It gives a direct link between the K and $\delta_{N=C}$ without involving the Hammett's constant.

It has been found for 1,3-*O*,*N*-heterocyclic systems, based on the theoretical charge calculations, that electron-donating substituents stabilize the chain tautomer by increasing its resonance stabilization via polarization of the C=N unit and by strengthening the intramolecular hydrogen bond.[19] This observation is in harmony with our results, that provide the experimental proof for these theoretical conclusions. It is very probable that a correlation in Eq. (3) would also be found for other, e.g. 1,3-*O*,*N*-heterocyclic ring-chain tautomeric systems.

The *meta*-substituted compounds **5b**,**c** did not contain observable amounts of the chain form in DMSO-d_6 (Table 1) due to the large values of the Hammett's constant for *m*-NO_2 (0.71) and *m*-I (0.35). Hence they were excluded from correlation studies, although *meta*-substituted compounds usually behave similarly to *para*-substituted ones. Compound **5a** (*o*-hydroxy-substituted) was found to be predominantly in the chain form. The ^{15}N shift for C=N was also measured for this compound (−86.2 ppm), but it did not fit to the straight line in Figure 3. This demonstrates that Eq. (3) is not valid for *ortho*-substituted compounds where steric effects also strongly affect the ring-chain ratio. In this sense, Eq. (3) does not provide anything new compared with Hammett's relations.

The ring-chain tautomeric ratios in di- or tri-substituted compounds **6** depend greatly on the substituents. The structures containing the electron-withdrawing NO_2 group tend to prefer the ring form in spite of the position of substitution, whereas the structures containing hydroxyl group at the *ortho* position favor chain forms. Compound **6c** provides the chance to discuss the conformations of the heteroring, since it was the only compound where the NH-3 signal was not broadened and the $^1H-^1H$ coupling constants were extractable from the proton spectrum. This follows most likely from the oxygen(s) of the *o*-NO_2 substituent that can form a tight hydrogen bond with NH-3 and prevent rapid exchange. The following J-values (in Hz) are found (Section 4): $J_{NH\text{-}3,H\text{-}4x}$=3.2, $J_{NH\text{-}3,H\text{-}4y}$=10.2, $J_{NH\text{-}3,H\text{-}2}$=11.3 and $J_{NH\text{-}1,H\text{-}2}$ small (not resolved). These values are in agreement with the torsion angles for half-chair structure, in which atoms 1 and 4 are in plane with condensed benzene ring. Therefore, protons H-2, NH-3 and H-4y can be identified as (pseudo)axial and NH-1 and H-4x as (pseudo) equatorial. The large aryl substituent therefore adopts equatorial orientation as was expected.

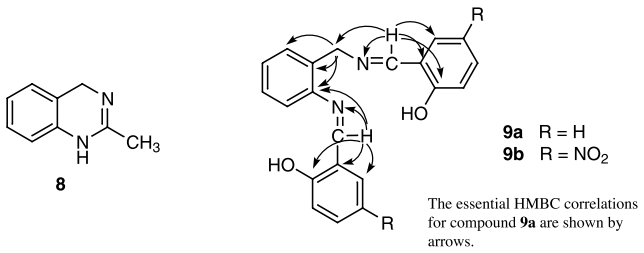


Figure 4. The structures of compounds **8** and **9**.

Hydroxynaphthyl derivative **7** was found to be completely in the chain form. The strong preference of the linear form can be explained not only by the steric factors but also by the existence of rapidly exchanging equilibrium of the enolimine and ketoenamine forms[20] that stabilizes the linear form. The results are in agreement with literature.[20–22]

2.4. Compounds 8–9

This set contains compounds that clearly differ from the previous ones (Fig. 4). These compounds were obtained when the non-equimolar solution of the reactants was boiled for one week (**8**) or 48 h (**9**) instead of letting it be at room temperature (Section 4). Compound **8** was easy to identify from its NMR data, especially from the C-2 shift (173.47 ppm). The bilinear compounds **9** were formed when a 2:1 mole ratio of aldehyde and 2-aminomethylaniline was used. For the identification of **9a** the long-range HMBC correlations (Fig. 4) proved a useful method.

3. Conclusion

A set of 2-substituted 1,2,3,4-tetrahydroquinazolines was prepared from 2-aminomethylaniline and corresponding aldehyde or ketone and their properties, especially ring-chain tautomerism, were studied by ^1H, ^{13}C and ^{15}N NMR spectroscopy. All 2-alkyl-substituted (**1**) as well as all 2,2-disubstituted (**2**,**3**) compounds were found to be completely in the ring form. However, the 2-aryl-substituted (**4**–**7**) compounds displayed ring-chain tautomeric equilibria containing one ring and one chain form. The chain form was concluded to be the aniline type linear form based on HMBC long-range correlations observed between the methylene carbon/protons and H–C=N proton/carbon. The preference for the aniline type linear form can be explained by the intramolecular hydrogen bonding between the NH_2 proton(s) and C=N nitrogen. In some cases (**9**), the formation of the bilinear form was also observed when a 2:1 mole ratio between the aldehyde and 2-aminomethylaniline was used.

For *para*-substituted 2-aryl-1,2,3,4-tetrahydroquinazolines (**4**) log K and $\delta_{N=C}$ gave good linear correlations with the Hammett–Brown parameter σ^+ that describes the electronic character of the substituent on the phenyl ring (Eqs. (1) and (2)). Furthermore, an excellent linear correlation was found between log K and $\delta_{N=C}$. This

shows that ring-chain equilibrium ratio depends on the charge density, or nuclear shielding, of the C=N nitrogen atom. Thus the substituent's electronic character plays an essential role at the stability of the linear form affecting nitrogen's charge density through the conjugated C=N double bond.

4. Experimental

4.1. General

NMR-spectra were acquired using a JEOL JNM-A-500 spectrometer operating at 500.16 MHz for ^{1}H, 125.78 MHz for ^{13}C and 50.69 MHz for ^{15}N or a JEOL JNM-L-400 spectrometer operating at 399.78 MHz for ^{1}H and 100.54 MHz for ^{13}C. Spectra were recorded at 30°C in DMSO-d_6 and at 25°C in $CDCl_3$. Proton and carbon spectra in DMSO-d_6 were referenced internally to the solvent signals using values 2.49 ppm for ^{1}H and 39.50 ppm for ^{13}C. Nitrogen spectra were referenced externally to the standard sample of nitromethane (10% deuterated) using a value of 0.00 ppm.

^{1}H spectra were acquired with normal single-pulse excitation, 45° flip-angle consisting of 32k data points. 1D carbon spectra were acquired with normal single-pulse excitation, broad-band proton decoupling, 45° flip-angle and with spectral widths of 30 kHz consisting of 65k data points and with 0.3–0.5 Hz exponential weighting applied prior to Fourier transformation. DEPT spectra were acquired as carbon spectra. 2D heteronuclear correlation experiments were acquired using either carbon detected CH-shift correlation with partial homonuclear decoupling in the f1 dimension or proton detected HMQC with gradient selection. Heteronuclear long-range correlation spectra were made using either carbon detected COLOC or proton detected HMBC sequence with gradient selection. One-bond coupling constant was 145 Hz in proton–carbon correlation spectra and 95 Hz in proton–nitrogen HMQC spectrum. In ^{1}H–^{13}C and ^{1}H–^{15}N HMBC spectra 8 Hz was used as a long-range coupling constant $^nJ_{CH}$ or $^nJ_{NH}$ (n=2 or 3) between proton and hetero nuclei. 2D homonuclear H,H-correlation experiments were acquired using phase-sensitive double quantum filtered COSY. The spectral widths of 2D spectra were in proton and carbon measurements optimised from 1D spectra. In ^{1}H–^{15}N HMBC and ^{1}H–^{15}N HMQC spectra, 512 points were used in f1 axis consisting of 500 ppm frequency range giving 1 ppm resolution. Thus the deviation in nitrogen shifts is ±0.5 ppm. However, the comparison with the results by refocused INEPT with 32k data points, showed very good (±0.1 ppm) correspondence between the 1D and 2D methods. All spectra were measured using standard pulse sequences.[23]

The purity of the synthesized compounds was checked by tlc (Silufol UV-254 plates).

4.2. General procedure for synthesis of compounds 1–3

Carbonyl compound (3 mmol) was added to a solution of 2-aminomethylaniline (3 mmol) in water-free benzene (10 mL), the mixture was kept for 24 h at room temperature, concentrated in vacuo, and the residue was recrystallized.

4.2.1. 2-Methyl-1,2,3,4-tetrahydroquinazoline (1a). Yield 79% (yellow crystals); mp 64–66°C (pentane); R_f 0.55 (acetonitrile–pyridine, 1:1). δ_H (DMSO-d_6): 1.19 (3H, d, J=6.0 Hz, CH_3), 3.72 (1H, d, J=16.5 Hz, H-4x), 3.88 (1H, d, J=16.5 Hz, H-4y), 4.08 (1H, q, J=6.0 Hz, H-2), 5.67 (1H, s, NH-1), 6.44 (1H, d, J=7.7 Hz, H-8), 6.45 (1H, t, J=7.2 Hz, H-6), 6.76 (1H, d, J=7.2 Hz, H-5), 6.85 (1H, dd, J=7.2, 7.7 Hz, H-7), NH-3 proton was not detected. δ_C (DMSO-d_6): 21.98 (CH_3), 45.78 (C-4), 62.12 (C-2), 113.75 (C-8), 115.62 (C-6), 120.47 (C-4a), 125.55 (C-5), 126.38 (C-7), 144.64 (C-8a). Anal calcd for $C_9H_{12}N_2$: C, 72.94; H, 8.16; N, 18.90. Found C, 72.92; H, 8.15; N, 18.88%.

4.2.2. 2-Propyl-1,2,3,4-tetrahydroquinazoline (1b). Yield 36% (yellow crystals); mp 64–66°C (pentane); R_f 0.52 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6): 0.90 (3H, t, J=6.9 Hz, CH_3), 1.45 (6H, m, $2CH_2$), 2.60 (1H, br. s, NH-3), 3.73 (1H, d, J=16.6 Hz, H-4x), 3.86 (1H, d, J=16.6 Hz, H-4y), 3.94 (1H, q, J=4.9 Hz, H-2), 5.57 (1H, s, NH-1), 6.44 (1H, t, J=7.4 Hz, H-6), 6.47 (1H, d, J=8.1 Hz, H-8), 6.75 (1H, d, J=7.4 Hz, H-5), 6.85 (1H, dd, J=7.4, 8.1 Hz, H-7). δ_C (DMSO-d_6): 14.05 (CH_3), 17.72 (CH_2-2′), 37.98 (CH_2-1′), 45.69 (C-4), 65.83 (C-2), 113.90 (C-8), 115.52 (C-6), 120.83 (C-4a), 125.49 (C-5), 126.35 (C-7), 144.63 (C-8a). Anal calcd for $C_{11}H_{16}N_2$: C, 74.96; H, 9.15; N, 15.89. Found C, 74.85; H, 9.15; N, 15.26%.

4.2.3. 2-*i*-Propyl-1,2,3,4-tetrahydroquinazoline (1c). Yield 36%; yellow oil; R_f 0.44 (ethanol). δ_H (DMSO-d_6): 0.94 (3H, d, J=7.0 Hz, CH_3), 0.96 (3H, d, J=6.8 Hz, CH_3'), 1.73 (1H, m, CH-1′), 3.74 (1H, d, J=16.4 Hz, H-4x), 3.76 (1H, q, J=5.6 Hz, H-2), 3.85 (1H, d, J=16.4 Hz, H-4y), 5.49 (1H, s, NH-1), 6.44 (1H, t, J=7.3 Hz, H-6), 6.53 (1H, d, J=7.9 Hz, H-8), 6.75 (1H, d, J=7.3 Hz, H-5), 6.85 (1H, dd, J=7.3, 7.9 Hz, H-7), NH-3 proton was not detected. δ_C (DMSO-d_6): 17.15 (CH_3), 18.10 (CH_3'), 32.07 (CH-1′), 45.87 (C-4), 70.78 (C-2), 114.04 (C-8), 115.45 (C-6), 120.95 (C-4a), 125.38 (C-5), 126.31 (C-7), 144.91 (C-8a). Anal calcd for $C_{11}H_{16}N_2$: C, 74.96; H, 9.15; N, 15.89. Found C, 74.89; H, 9.15; N, 15.18%.

4.2.4. 2,2-Dimethyl-1,2,3,4-tetrahydroquinazoline (1d). Yield 68%; colorless oil; R_f 0.50 (ethanol). δ_H (DMSO-d_6): 1.33 (6H, s, $2CH_3$), 3.95 (2H, s, H-4), 6.52 (1H, d, J=8.1 Hz, H-8), 6.55 (1H, t, J=7.4 Hz, H-6), 6.92 (1H, d, J=7.4 Hz, H-5), 6.95 (1H, dd, J=7.4, 8.1 Hz, H-7), NH-protons were not detected. δ_C (DMSO-d_6): 26.22 ($2CH_3$), 40.44 (C-4), 62.50 (C-2), 114.47 (C-8), 116.05 (C-4a), 116.27 (C-6), 126.20 (C-5), 127.22 (C-7), 142.04 (C-8a). Anal calcd for $C_{10}H_{14}N_2$: C, 74.03; H, 8.70; N, 17.27. Found C, 74.10; H, 8.68; N, 17.28%.

4.2.5. 3′,4′-Dihydro-1′*H*-spiro[cyclohexane-1,2′-quinazoline] (1e). Yield 61% (white crystals); mp 63–65°C (hexane–benzene); R_f 0.47 (ethyl acetate). δ_H (DMSO-d_6): 1.26–1.62 (10H, m, 4H-1′, 4H-2′, 2H-3′), 3.71 (2H, s, 2H-4), 5.60 (1H, s, NH-1), 6.40 (1H, t, J=7.3 Hz, H-6), 6.47 (1H, d, J=7.8 Hz, H-8), 6.76 (1H, d, J=7.3 Hz, H-5), 6.83 (1H, dd, J=7.3, 7.8 Hz, H-7), NH-3 proton was not detected. δ_C (DMSO-d_6): 21.47 (C-3′), 25.63 (2C-2′), 36.37 (2C-1′),

40.94 (C-4), 64.51 (C-2), 113.82 (C-8), 114.84 (C-6), 119.67 (C-4a), 125.34 (C-5), 126.34 (C-7), 143.60 (C-8a). Anal calcd for $C_{13}H_{18}N_2$: C, 77.18; H, 8.97; N, 13.85. Found C, 77.15; H, 8.85; N, 13.86%.

4.2.6. 2-Methyl-2-phenyl-1,2,3,4-tetrahydroquinazoline (2a). Yield 37% (white crystals); mp 95–97°C (hexane–benzene); R_f 0.46 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6): 1.46 (3H, s, CH_3), 2.96 (1H, br. s, NH-3), 3.33 (1H, d, J=16.8 Hz, H-4x), 3.61 (1H, d, J=16.8 Hz, H-4y), 6.39 (1H, dd, J=6.9, 7.3 Hz, H-6), 6.61 (1H, s, NH-1), 6.65 (1H, d, J=7.8 Hz, H-8), 6.66 (1H, d, J=6.9 Hz, H-5), 6.89 (1H, dd, J=7.3, 7.8 Hz, H-7), 7.16 (1H, t, J=7.2 Hz, H-4′), 7.27 (2H, t, J=7.2 Hz, 2H-3′), 7.54 (2H, d, J=7.2 Hz, 2H-2′). δ_C (DMSO-d_6): 32.25 (CH_3), 42.17 (C-4), 68.64 (C-2), 113.41 (C-8), 115.14 (C-6), 119.75 (C-4a), 125.37 (C-5), 126.38 (C-7), 126.46 (C-2′), 126.48 (C-4′), 127.95 (C-3′), 143.59 (C-8a), 147.33 (C-1′). Anal calcd for $C_{15}H_{16}N_2$: C, 80.32; H, 7.19; N, 12.49. Found C, 80.35; H, 7.22; N, 12.45%.

4.2.7. 2-Methyl-2-(4-methylphenyl)-1,2,3,4-tetrahydroquinazoline (2b). Yield 43% (white crystals); mp 87–89°C (hexane–benzene); R_f 0.65 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6): 1.43 (3H, s, 2-CH_3), 2.23 (3H, s, 4′-CH_3), 2.63 (1H, br. s, NH-3), 3.32 (1H, d, J=16.6 Hz, H-4x), 3.58 (1H, d, J=16.6 Hz, H-4y), 6.38 (1H, dd, J=6.8, 7.3 Hz, H-6), 6.56 (1H, s, NH-1), 6.63 (1H, d, J=7.9 Hz, H-8), 6.64 (1H, d, J=6.8 Hz, H-5), 6.88 (1H, dd, J=7.3, 7.9 Hz, H-7), 7.07 (2H, d, J=7.9 Hz, 2H-3′), 7.40 (2H, d, J=7.9 Hz, 2H-2′). δ_C (DMSO-d_6): 20.45 (4′-CH_3), 32.24 (2-CH_3), 42.12 (C-4), 68.44 (C-2), 113.37 (C-8), 115.05 (C-6), 119.75 (C-4a), 125.30 (C-5), 126.38 (2C-2′), 126.40 (C-7), 128.52 (2C-3′), 135.30 (C-4′), 143.65 (C-8a or C-1′), 144.28 (C-8a or C-1′). δ_N (DMSO-d_6): −297.8 (N-1), −331.7 (N-3). Anal calcd for $C_{16}H_{18}N_2$: C, 80.63; H, 7.61; N, 11.75. Found C, 80.53; H, 7.66; N, 11.74%.

4.2.8. 2-Methyl-2-(4-nitrophenyl)-1,2,3,4-tetrahydroquinazoline (2c). Yield 44% (orange crystals); mp 143–145°C (benzene); R_f 0.52 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6): 1.47 (3H, s, 2-CH_3), 2.96 (1H, br. s, NH-3), 3.25 (1H, d, J=16.7 Hz, H-4x), 3.64 (1H, d, J=16.7 Hz, H-4y), 6.41 (1H, dd, J=6.6, 7.3 Hz, H-6), 6.65 (1H, d, J=7.8 Hz, H-8), 6.67 (1H, d, J=6.6 Hz, H-5), 6.76 (1H, s, NH-1), 6.90 (1H, dd, J=7.3, 7.8 Hz, H-7), 7.78 (2H, d, J=8.7 Hz, 2H-2′), 8.15 (2H, d, J=8.7 Hz, 2H-3′). δ_C (DMSO-d_6): 31.68 (CH_3), 42.06 (C-4), 68.79 (C-2), 113.57 (C-8), 115.58 (C-6), 119.54 (C-4a), 123.34 (2C-3′), 125.49 (C-5), 126.66 (C-7), 128.00 (2C-2′), 142.98 (C-8a), 146.39 (C-4′), 155.66 (C-1′). Anal calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found C, 66.94; H, 5.66; N, 15.57%.

4.2.9. 2-(4-Methoxyphenyl)-2-methyl-1,2,3,4-tetrahydroquinazoline (2d). Yield 61% (yellow crystals); mp 86–88°C (hexane–benzene); R_f 0.54 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6): 1.44 (3H, s, 2-CH_3), 3.33 (1H, d, J=16.7 Hz, H-4x), 3.59 (1H, d, J=16.7 Hz, H-4y), 3.69 (3H, s, 4′-OCH_3), 6.39 (1H, t, J=7.2 Hz, H-6), 6.55 (1H, s, NH-1), 6.64 (1H, m, H-5 or H-8), 6.65 (1H, m, H-5 or H-8), 6.82 (2H, d, J=8.8 Hz, 2H-3′), 6.89 (1H, t, J=7.5 Hz, H-7), 7.43 (2H, d, J=8.8 Hz, 2H-2′), NH-3 proton was not detected. δ_C (DMSO-d_6): 32.34 (2-CH_3), 42.15 (C-4), 54.88 (4′-OCH_3), 68.31 (C-2), 113.33 (2C-3′), 113.44 (C-8), 115.12 (C-6), 119.83 (C-4a), 125.37 (C-5), 126.47 (C-7), 127.64 (2C-2′), 139.14 (C-1′), 143.69 (C-8a), 157.88 (C-4′). Anal calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.01. Found C, 75.46; H, 7.53; N, 11.27%.

4.2.10. 2-Methyl-2-naphthalen-2-yl-1,2,3,4-tetrahydroquinazoline (3). Yield 39% (yellow crystals); mp 113–115°C (hexane–benzene); R_f 0.64 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6): 1.53 (3H, s, CH_3), 2.89 (1H, br. s, NH-3), 3.32 (1H, d, J=16.7 Hz, H-4x), 3.64 (1H, d, J=16.7 Hz, H-4y), 6.39 (1H, dd, J=6.8, 7.1 Hz, H-6), 6.64 (1H, d, J=7.9 Hz, H-8), 6.71 (1H, d, J=7.1 Hz, H-5), 6.74 (1H, s, NH-1), 6.92 (1H, dd, J=6.8, 7.9 Hz, H-7), 7.46 (2H, m, H-6′ and H-7′), 7.74–7.76 (2H, m, H-3′ and H-8′), 7.83–7.84 (2H, m, H-4′ and H-5′), 7.94 (1H, s, H-1′). δ_C (DMSO-d_6): 32.02 (CH_3), 42.30 (C-4), 68.86 (C-2), 113.49 (C-8), 115.17 (C-6), 119.80 (C-4a), 125.12 (C-1′), 125.16 (C-3′), 125.39 (C-5), 125.54 (C-6′ or C-7′), 125.80 (C-6′ or C-7′), 126.58 (C-7), 127.26 (C-5′), 127.74 (C-8′), 127.78 (C-4′), 132.01 (C-4a′), 132.68 (C-8a′), 143.57 (C-8a) 144.94 (C-5). Anal calcd for $C_{19}H_{18}N_2$: C, 83.18; H, 6.61; N, 10.21. Found C, 82.97; H, 6.95; N, 10.27%.

4.3. General procedure for synthesis of compounds 4–7

Carbonyl compound (3 mmol) was added to a solution of 2-aminomethylaniline (3 mmol) in methanol (10 mL), the mixture was kept for 24 h at room temperature, concentrated in vacuo, and the residue was recrystallized.

4.3.1. 2-(4-Nitrophenyl)-1,2,3,4-tetrahydroquinazoline (4a). Yield 56% (orange crystals); mp 105–107°C (methanol, 100–102°C[11]); R_f 0.60 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6): 2.99 (1H, br. s, NH-3), 3.61 (1H, d, J=16.6 Hz, H-4x), 3.90 (1H, d, J=16.6 Hz, H-4y), 5.27 (1H, s, H-2), 6.32 (1H, s, NH-1), 6.52 (1H, t, J=7.3 Hz, H-6), 6.64 (1H, d, J=7.9 Hz, H-8), 6.82 (1H, d, J=7.3 Hz, H-5), 6.94 (1H, dd, J=7.3, 7.9 Hz, H-7), 7.76 (2H, d, J=8.7 Hz, 2H-2′), 8.22 (2H, d, J=8.7 Hz, 2H-3′). δ_C (DMSO-d_6): 43.98 (C-4), 66.89 (C-2), 114.31 (C-8), 116.16 (C-6), 120.78 (C-4a), 123.20 (2C-3′), 125.69 (C-5), 126.67 (C-7), 128.42 (2C-2′), 143.75 (C-8a), 146.86 (C-4′), 150.52 (C-1′). Anal calcd for $C_{14}H_{13}N_3O_2$: C, 65.87; H, 5.13; N, 16.46. Found C, 65.58; H, 5.17; N, 16.53%.

4.3.2. 2-(4-Chlorophenyl)-1,2,3,4-tetrahydroquinazoline (4b). Yield 70% (white crystals); mp 88–90°C (hexane–benzene); R_f 0.64 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6, ring): 2.84 (1H, br. s, NH-3), 3.66 (1H, d, J=16.3 Hz, H-4x), 3.92 (1H, d, J=16.3 Hz, H-4y), 5.11 (1H, s, H-2), 6.15 (1H, s, NH-1), 6.51 (1H, t, J=7.3 Hz, H-6), 6.60 (1H, d, J=7.9 Hz, H-8), 6.81 (1H, d, J=7.3 Hz, H-5), 6.91 (1H, dd, J=7.3, 7.9 Hz, H-7), 7.41 (2H, d, J=8.6 Hz, 2H-3′), 7.51 (2H, d, J=8.6 Hz, 2H-2′). δ_C (DMSO-d_6, ring): 44.52 (C-4), 67.18 (C-2), 114.20 (C-8), 115.97 (C-6), 120.69 (C-4a), 125.61 (C-5), 126.53 (C-7), 127.94 (2C-3′), 128.92 (2C-2′), 131.95 (C-4′), 141.83 (C-1′), 144.18 (C-8a). δ_N (DMSO-d_6, ring): −302.8 (N-1), −339.2 (N-3). δ_H (DMSO-d_6, chain): 4.64 (2H, s, H-4), 5.03 (2H, s, NH_2-1), 6.53 (1H, dd, J=6.5, 7.5 Hz, H-6), 6.68 (1H, d, J=7.9 Hz, H-8), 6.98 (1H, dd, J=6.5, 7.9 Hz, H-7), 7.01 (1H, d, J=7.5 Hz, H-5), 7.51 (2H, d, J=8.5 Hz, H-3′), 7.78 (2H, d, J=8.5 Hz, H-2′), 8.45 (1H, s, H-2). δ_C (DMSO-d_6, chain): 61.17 (C-4), 114.80 (C-8),

116.15 (C-6), 122.84 (C-4a), 127.67 (C-7), 128.67 (C-5), 128.72 (2C-3′), 129.50 (2C-2′), 134.84 (C-4′), 135.24 (C-1′), 146.34 (C-8a), 160.11 (C-2). δ_N (DMSO-d_6, chain): −50.5 (N-3), N-1 was not detected. Anal calcd for $C_{14}H_{13}ClN_2$: C, 68.71; H, 5.35; N, 11.45. Found C, 68.89; H, 5.47; N, 11.27%.

4.3.3. 2-Phenyl-1,2,3,4,-tetrahydroquinazoline (4c). Yield 61% (white crystals); mp 102–105°C (methanol, 102–103°C[10]); R_f 0.52 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6, ring): 2.70 (1H, br. s, NH-3), 3.71 (1H, d, J=16.5 Hz, H-4x), 3.96 (1H, d, J=16.5 Hz, H-4y), 5.10 (1H, s, H-2), 6.10 (1H, s, NH-1), 6.50 (1H, dd, J=6.6, 7.2 Hz, H-6), 6.60 (1H, d, J=8.0 Hz, H-8), 6.81 (1H, d, J=7.2 Hz, H-5), 6.91 (1H, dd, J=6.6, 8.0 Hz, H-7), 7.30 (H, t, J=7.1 Hz, H-4′), 7.36 (2H, t, J=7.1 Hz, 2H-3′), 7.50 (2H, d, J=7.1 Hz, 2H-2′). δ_C (DMSO-d_6, ring): 44.96 (C-4), 68.08 (C-2), 114.17 (C-8), 115.84 (C-6), 120.68 (C-4a), 125.60 (C-5), 126.48 (C-7), 126.98 (2C-2′), 127.47 (C-4′), 128.00 (2C-3′), 142.76 (C-8a or C-1′), 144.52 (C-8a or C-1′). δ_N (DMSO-d_6, ring): −302.3 (N-1), −337.5 (N-3). δ_H (DMSO-d_6, chain): 4.65 (2H, s, H-4), 5.05 (2H, s, NH_2-1), 6.54 (1H, dd, J=6.4, 7.5 Hz, H-6), 6.69 (1H, d, J=7.9 Hz, H-8), 6.98 (1H, t, J=6.4, 7.9 Hz, H-7), 7.02 (1H, d, J=7.5 Hz, H-5), 7.46 (3H, m, H-3′ and H-4′), 7.77 (2H, d, J=7.3 Hz, H-2′), 8.46 (1H, s, H-2). δ_C (DMSO-d_6, chain): 61.28 (C-4), 114.78 (C-8), 116.15 (C-6), 123.06 (C-4a), 127.63 (C-7), 127.86 (2C-2′), 128.62 (2C-3′), 128.64 (C-5), 130.65 (C-4′), 136.02 (C-1′), 146.37 (C-8a), 161.28 (C-2). δ_N (DMSO-d_6, chain): −322.1 (N-1), −52.4 (N-3). Anal calcd for $C_{14}H_{14}N_2$: C, 79.97; H, 6.71; N, 13.32. Found C, 79.71; H, 6.76; N, 13.52%.

4.3.4. 2-(4-Fluorophenyl)-1,2,3,4-tetrahydroquinazoline (4d). Yield 47% (white crystals); mp 95–97°C (hexane–benzene); R_f 0.62 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6, ring): 2.75 (1H, br. s, NH-3), 3.69 (1H, d, J=16.4 Hz, H-4x), 3.95 (1H, d, J=16.4 Hz, H-4y), 5.11 (1H, s, H-2), 6.12 (1H, s, NH-1), 6.52 (1H, t, J=7.3 Hz, H-6), 6.61 (1H, d, J=8.1 Hz, H-8), 6.82 (1H, d, J=7.3 Hz, H-5), 6.92 (1H, dd, J=7.3, 8.1 Hz, H-7), 7.17 (2H, t, J=8.8 Hz (J_H and J_F), 2H-3′), 7.54 (2H, dd, J=5.6 (J_F), 8.8 (J_H) Hz, 2H-2′). δ_C (DMSO-d_6, ring): 44.81 (C-4), 67.37 (C-2), 114.23 (C-8), 114.67 (2C-3′, J_F=21.5 Hz), 115.98 (C-6), 120.70 (C-4a), 125.63 (C-5), 126.52 (C-7), 128.98 (2C-2′, J_F=8.3 Hz), 139.04 (C-1′, J_F=2.8 Hz), 144.37 (C-8a), 161.58 (C-4′, J_F=242.8 Hz). δ_N (DMSO-d_6, ring): −302.8 (N-1), −337.5 (N-3). δ_H (DMSO-d_6, chain): 4.64 (2H, s, H-4), 5.05 (2H, s, NH_2-1), 6.54 (1H, t, J=7.3 Hz, H-6), 6.70 (1H, d, J=7.9 Hz, H-8), 6.99 (1H, dd, J=7.3, 7.9 Hz, H-7), 7.02 (1H, d, J=7.3 Hz, H-5), 7.27 (2H, t, J=8.8 Hz (J_H and J_F), H-3′), 7.83 (2H, dd, J=5.8 (J_F), 8.8 (J_H) Hz, H-2′), 8.45 (1H, s, H-2). δ_C (DMSO-d_6, chain): 61.19 (C-4), 114.82 (C-8), 115.63 (2C-3′, J_F=21.5 Hz), 116.18 (C-6), 123.03 (C-4a), 127.66 (C-7), 128.65 (C-5), 130.08 (2C-2′, J_F=8.7 Hz), 132.66 (C-1′, J_F=2.8 Hz), 146.36 (C-8a), 160.00 (C-2) 163.54 (C-4′, J_F=248.3 Hz). δ_N (DMSO-d_6, chain): −54.2 (N-3), N-1 was not detected. Anal calcd for $C_{14}H_{13}FN_2$: C, 73.66; H, 5.74; N, 12.27. Found C, 73.62; H, 5.46; N, 11.99%.

4.3.5. 2-(4-Methoxyphenyl)-1,2,3,4,-tetrahydroquinazoline (4e). Yield 58% (white crystals); mp 105–107°C (hexane, 108–109°C;[10] R_f 0.56 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6, ring): 3.70 (1H, d, J=16.4 Hz, H-4x), 3.74 (3H, s, OCH_3), 3.95 (1H, d, J=16.4 Hz, H-4y), 5.04 (1H, s, H-2), 6.02 (1H, s, NH-1), 6.49 (1H, t, J=7.3 Hz, H-6), 6.58 (1H, d, J=7.9 Hz, H-8), 6.80 (1H, d, J=7.3 Hz, H-5), 6.90 (1H, dd, J=7.3, 7.9 Hz, H-7), 6.91 (2H, d, J=8.4 Hz, 2H-3′), 7.41 (2H, d, J=8.4 Hz, 2H-2′), NH-3 proton was not detected. δ_C (DMSO-d_6, ring): 45.08 (C-4), 55.03 (OCH_3), 67.68 (C-2), 113.35 (2C-3′), 114.14 (C-8), 115.79 (C-6), 120.63 (C-4a), 125.57 (C-5), 126.44 (C-7), 128.08 (2C-2′), 134.88 (C-1′), 144.60 (C-8a), 158.70 (C-4′). δ_N (DMSO-d_6, ring): −301.9 (N-1), −337.3 (N-3).δ_H (DMSO-d_6, chain): 3.79 (3H, s, OCH_3), 4.59 (2H, s, H-4), 5.04 (2H, s, NH_2-1), 6.53 (1H, t, J=7.5 Hz, H-6), 6.67 (1H, d, J=7.7 Hz, H-8), 6.97 (1H, n.r., H-7), 6.99 (2H, n.r., H-3′), 7.00 (1H, n.r., H-5), 7.70 (2H, d, J=8.5 Hz, H-2′), 8.36 (1H, s, H-2). δ_C (DMSO-d_6, chain): 55.23 (OCH_3), 61.34 (C-4), 114.02 (2C-3′), 114.74 (C-8), 116.12 (C-6), 123.38 (C-4a), 127.54 (C-7), 128.56 (C-5), 128.87 (C-1′), 129.47 (2C-2′), 146.36 (C-8a), 160.50 (C-2), 161.22 (C-4′). δ_N (DMSO-d_6, chain): −61.1 (N-3), N-1 was not detected. Anal calcd for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66. Found C, 75.02; H, 6.78; N, 11.68%.

4.3.6. 2-(4-Ethoxyphenyl)-1,2,3,4-tetrahydroquinazoline (4f). Yield 42% (white crystals); mp 96–98°C (methanol); R_f 0.44 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6, ring): 1.31 (3H, t, J=7.0 Hz, CH_3), 2.62 (1H, br. s, NH-3), 3.69 (1H, d, J=16.4 Hz, H-4x), 3.94 (1H, d, J=16.4 Hz, H-4y), 4.01 (2H, q, J=7.0 Hz, OCH_2), 5.03 (1H, s, H-2), 6.01 (1H, s, NH-1), 6.48 (1H, t, J=7.3 Hz, H-6), 6.57 (1H, d, J=7.9 Hz, H-8), 6.80 (1H, d, J=7.3 Hz, H-5), 6.89 (3H, m, H-7 and 2H-3′), 7.38 (2H, d, J=8.8 Hz, 2H-2′). δ_C (DMSO-d_6, ring): 14.61 (CH_3), 45.07 (C-4), 62.92 (OCH_2), 67.67 (C-2), 113.85 (2C-3′), 114.11 (C-8), 115.76 (C-6), 120.62 (C-4a), 125.56 (C-5), 126.42 (C-7), 128.06 (2C-2′), 134.76 (C-1′), 144.61 (C-8a), 157.93 (C-4′). δ_N (DMSO-d_6, ring): −301.8 (N-1), −337.5 (N-3).δ_H (DMSO-d_6, chain): 1.33 (3H, t, J=6.8 Hz, CH_3), 4.06 (2H, q, J=6.8 Hz, OCH_2), 4.58 (2H, s, H-4), 5.03 (2H, s, NH_2-1), 6.52 (1H, t, J=7.3 Hz, H-6), 6.66 (1H, d, J=7.9 Hz, H-8), 6.96 (1H, n.r., H-7), 6.97 (2H, n.r., H-3′), 6.99 (1H, n.r., H-5), 7.68 (2H, d, J=8.7 Hz, H-2′), 8.35 (1H, s, H-2). δ_C (DMSO-d_6, chain): 14.50 (CH_3), 61.28 (C-4), 63.19 (OCH_2), 114.43 (2C-3′), 114.73 (C-8), 116.10 (C-6), 123.39 (C-4a), 127.52 (C-7), 128.53 (C-5), 128.71 (C-1′), 129.46 (2C-2′), 146.35 (C-8a), 160.50 (C-2 and C-4′). δ_N (DMSO-d_6, chain): −322.1 (N-1), −61.1 (N-3). Anal calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.01. Found C, 75.50; H, 7.13; N, 11.08%.

4.3.7. 4-(1,2,3,4-Tetrahydroquinazoline-2-yl)phenol (4g). Yield 71% (white crystals); mp 173–175°C (methanol); R_f 0.45 (ethyl acetate). δ_H (DMSO-d_6, ring): 2.51 (1H, br. s, NH-3), 3.71 (1H, d, J=16.2 Hz, H-4x), 3.95 (1H, d, J=16.2 Hz, H-4y), 4.98 (1H, s, H-2), 5.95 (1H, s, NH-1), 6.48 (1H, t, J=7.4 Hz, H-6), 6.57 (1H, d, J=8.1 Hz, H-8), 6.74 (2H, d, J=8.6 Hz, 2H-3′), 6.80 (1H, d, J=7.4 Hz, H-5), 6.89 (2H, dd, J=7.4, 8.1 Hz, H-7), 7.28 (2H, d, J=8.6 Hz, 2H-2′), 9.38 (1H, br. s, OH). δ_C (DMSO-d_6, ring): 45.29 (C-4), 67.94 (C-2), 114.13 (C-8), 114.71 (2C-3′), 115.76 (C-6), 120.61 (C-4a), 125.59 (C-5), 126.44 (C-7), 128.04 (2C-2′), 133.16 (C-1′), 144.73 (C-8a), 156.82 (C-4′). δ_N (DMSO-d_6, ring): −300.9 (N-1), −336.5 (N-3).δ_H (DMSO-d_6, chain): 4.57 (2H, s, H-4), 5.03 (2H, s, NH_2-1), 6.52 (1H, t,

J=7.5 Hz, H-6), 6.66 (1H, d, J=7.9 Hz, H-8), 6.82 (2H, d, J=8.5 Hz, H-3′), 6.97 (1H, dd, J=7.5, 7.9 Hz, H-7), 6.99 (1H, d, J=7.5 Hz, H-5), 7.59 (2H, d, J=8.5 Hz, H-2′), 8.30 (1H, s, H-2), 9.38 (1H, br. s, OH). δ_C (DMSO-d_6, chain): 61.35 (C-4), 114.75 (C-8), 115.44 (2C-3′), 116.15 (C-6), 123.57 (C-4a), 127.37 (C-1′), 127.53 (C-7), 128.56 (C-5), 129.64 (2C-2′), 146.36 (C-8a), 159.87 (C-4′), 160.67 (C-2). δ_N (DMSO-d_6, chain): −322.1 (N-1), −64.9 (N-3). Anal calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found C, 74.21; H, 6.24; N, 12.28%.

4.3.8. *N*-(2-Aminobenzyl)-*N*-{(1*E*)-[4-(dimethylamino)-phenyl]methylene}amine (4h). Yield 61% (yellow crystals); mp 96–98°C (hexane–benzene, 97–99°C[11]); R_f 0.35 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6, ring): 2.87 (6H, s, 2CH_3), 3.72 (1H, d, J=16.2 Hz, H-4x), 3.95 (1H, d, J=16.2 Hz, H-4y), 4.98 (1H, s, H-2), 5.92 (1H, s, NH-1), 6.48 (1H, dd, J=6.9, 7.3 Hz, H-6), 6.57 (1H, d, J=7.7 Hz, H-8), 6.70 (2H, d, J=8.8 Hz, 2H-3′), 6.79 (1H, d, J=6.9 Hz, H-5), 6.88 (1H, dd, J=7.3, 7.7 Hz, H-7), 7.29 (2H, d, J=8.8 Hz, 2H-2′), NH-3 proton was not detected. δ_C (DMSO-d_6, ring): 40.23 (2CH_3), 45.30 (C-4), 67.93 (C-2), 111.98 (2C-3′), 114.06 (C-8), 115.62 (C-6), 120.59 (C-4a), 125.53 (C-5), 126.37 (C-7), 127.50 (2C-2′), 130.46 (C-1′), 144.77 (C-8a), 150.07 (C-4′). δ_N (DMSO-d_6, ring): −300.8 (N-1), other nitrogens were not detected. δ_H (DMSO-d_6, chain): 2.95 (6H, s, 2CH_3), 4.55 (2H, s, H-4), 5.04 (2H, s, NH_2-1), 6.52 (1H, t, J=7.5 Hz, H-6), 6.66 (1H, d, J=7.7 Hz, H-8), 6.72 (2H, d, J=8.7 Hz, H-3′), 6.96 (1H, dd, J=7.5, 7.7 Hz, H-7), 6.99 (1H, d, J=7.5 Hz, H-5), 7.56 (2H, d, J=8.7 Hz, H-2′), 8.25 (1H, s, H-2). δ_C (DMSO-d_6, chain): 39.69 (2CH_3), 61.50 (C-4), 111.43 (2C-3′), 114.68 (C-8), 116.07 (C-6), 123.85 (C-4a or C-1′), 123.87 (C-4a or C-1′), 127.41 (C-7), 128.46 (C-5), 129.16 (2C-2′), 146.37 (C-8a), 151.83 (C-4′), 160.78 (C-2). δ_N (DMSO-d_6, chain): −70.5 (N-3), other nitrogens were not detected. Anal calcd for $C_{16}H_{19}N_3$: C, 75.85; H, 7.56; N, 16.59. Found C, 75.87; H, 7.58; N, 16.59%.

4.3.9. *N*-(2-Aminobenzyl)-*N*-{(1*E*)-[4-(diethylamino)phenyl]methylene}amine (4i). Yield 57% (brown crystals); mp 122–124°C (methanol); R_f 0.66 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6, ring): 1.07 (6H, t, J=7.0 Hz, 2CH_3), 3.31 (4H, q, J=7.0 Hz, 2CH_2), 3.72 (1H, d, J=16.2 Hz, H-4x), 3.95 (1H, d, J=16.2 Hz, H-4y), 4.95 (1H, s, H-2), 5.90 (1H, s, NH-1), 6.47 (1H, t, J=7.3 Hz, H-6), 6.56 (1H, d, J=7.8 Hz, H-8), 6.63 (2H, d, J=8.8 Hz, 2H-3′), 6.80 (1H, d, J=7.3 Hz, H-5), 6.88 (1H, dd, J=7.3, 7.7 Hz, H-7), 7.25 (2H, d, J=8.8 Hz, 2H-2′), NH-3 proton was not detected. δ_C (DMSO-d_6, ring): 12.34 (2CH_3), 43.66 (2CH_2), 45.45 (C-4), 68.06 (C-2), 111.14 (2C-3′), 114.03 (C-8), 115.58 (C-6), 120.53 (C-4a), 125.53 (C-5), 126.35 (C-7), 127.79 (2C-2′), 129.22 (C-1′), 144.84 (C-8a), 146.93 (C-4′). δ_N (DMSO-d_6, ring): −300.4 (N-1), −336.5 (N-3), −298.9 (N(Et)$_2$). δ_H (DMSO-d_6, chain): 1.09 (6H, t, J=7.1 Hz, 2CH_3), 3.35 (4H, q, J=7.1 Hz, 2CH_2), 4.54 (2H, s, H-4), 5.04 (2H, s, NH_2-1), 6.52 (1H, t, J=7.2 Hz, H-6), 6.66 (3H, m, H-8 and 2H-3′), 6.96 (1H, dd, J=7.2, 7.6 Hz, H-7), 6.99 (1H, d, J=7.2 Hz, H-5), 7.53 (2H, d, J=9.0 Hz, H-2′), 8.22 (1H, s, H-2). δ_C (DMSO-d_6, chain): 12.34 (2CH_3), 43.66 (2CH_2), 61.51 (C-4), 110.75 (2C-3′), 114.66 (C-8), 116.05 (C-6), 123.02 (C-1′), 123.38 (C-4a), 127.36 (C-7), 128.38 (C-5), 129.49 (2C-2′), 146.36 (C-8a), 149.15 (C-4′), 160.72 (C-2). δ_N (DMSO-d_6, chain): −72.6 (N-3), −307.6 (N(Et)$_2$), N-1 was not detected. Anal calcd for $C_{18}H_{23}N_3$: C, 76.83; H, 8.24; N, 14.93. Found C, 76.88; H, 8.24; N, 14.95%.

4.3.10. 2-(1,2,3,4-Tetrahydroquinazoline-2-yl)phenol (5a). Yield 70% (yellow crystals); mp 102–103°C (hexane–benzene, 109–111°C[11]); R_f 0.69 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6, ring): 3.65 (1H, d, J=16.3 Hz, H-4x), 3.90 (1H, d, J=16.3 Hz, H-4y), 5.35 (1H, d, J=2.1 Hz, H-2), 6.33 (1H, br. d, J=2.1 Hz, NH-1), 6.51 (1H, t, J=7.5 Hz, H-6), 6.67 (1H, d, J=7.9 Hz, H-8), 6.76 (1H, t, J=7.5 Hz, H-5′), 6.77 (1H, d, J=7.7 Hz, H-3′), 6.80 (1H, d, J=7.5 Hz, H-5), 6.94 (1H, dd, J=7.5, 7.9 Hz, H-7), 7.12 (1H, dd, J=7.5, 7.7 Hz, H-4′), 7.27 (1H, d, J=7.5 Hz, H-6′), 13.5 (1H, br.s, OH), NH-3 was not detected. δ_C (DMSO-d_6, ring): 42.84 (C-4), 64.24 (C-2), 114.33 (C-8), 115.66 (C-3′), 116.13 (C-6), 118.45 (C-6′), 119.35 (C-4a), 125.90 (C-5), 126.29 (C-1′), 126.80 (C-7), 127.87 (C-6′), 128.69 (C-4′), 143.26 (C-8a), 156.15 (C-2′). δ_N (DMSO-d_6, ring): −308.7 (N-1), −343.3 (N-3). δ_H (DMSO-d_6, chain): 4.67 (2H, s, H-4), 5.05 (2H, s, NH_2-1), 6.54 (1H, t, J=7.3 Hz, H-6), 6.69 (1H, d, J=7.7 Hz, H-8), 6.87 (1H, d, J=7.5 Hz, H-3′), 6.88 (1H, t, J=7.5 Hz, H-5′), 7.00 (1H, dd, J=7.3, 7.7 Hz, H-7), 7.01 (1H, d, J=7.3 Hz, H-5), 7.31 (1H, t, J=7.5 Hz, H-4′), 7.42 (1H, d, J=7.5 Hz, H-6′), 8.64 (1H, s, H-2), 13.5 (1H, br.s, OH). δ_C (DMSO-d_6, chain): 58.36 (C-4), 114.86 (C-8), 116.13 (C-6), 116.45 (C-3′), 118.39 (C-5′), 118.71 (C-1′), 121.40 (C-4a), 128.07 (C-7), 128.89 (C-5), 131.54 (C-6′), 132.21 (C-4′), 146.25 (C-8a), 160.63 (C-2′), 165.75 (C-2). δ_N (DMSO-d_6, chain): −321.8 (N-1), −86.2 (N-3). Anal calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found C, 74.28; H, 6.25; N, 12.40%.

4.3.11. 2-(3-Nitrophenyl)-1,2,3,4-tetrahydroquinazoline (5b). Yield 90% (orange crystals); mp 89–91°C (methanol, 91–93°C[11]); R_f 0.64 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6): 3.02 (1H, br. s, NH-3), 3.63 (1H, d, J=16.4 Hz, H-4x), 3.92 (1H, d, J=16.4 Hz, H-4y), 5.27 (1H, d, J=1.6 Hz, H-2), 6.34 (1H, d, J=1.6 Hz, NH-1), 6.53 (1H, t, J=7.4 Hz, H-6), 6.64 (1H, d, J=7.9 Hz, H-8), 6.82 (1H, d, J=7.4 Hz, H-5), 6.94 (1H, dd, J=7.4, 7.9 Hz, H-7), 7.66 (1H, t, J=7.9 Hz, H-5′), 7.96 (1H, d, J=7.9 Hz, H-6′), 8.16 (1H, d, J=7.9 Hz, H-4′), 8.36 (1H, s, H-2′). δ_C (DMSO-d_6): 44.13 (C-4), 66.75 (C-2), 114.36 (C-8), 116.23 (C-6), 120.82 (C-4a), 121.83 (C-2′), 122.42 (C-4′), 125.70 (C-5), 126.69 (C-7), 129.62 (C-5′), 134.05 (C-6′), 143.83 (C-8a), 145.35 (C-1′), 147.73 (C-3′). Anal calcd for $C_{14}H_{13}N_3O_2$: C, 65.87; H, 5.13; N, 16.46. Found C, 65.87; H, 5.74; N, 16.36%.

4.3.12. 2-(3-Iodophenyl)-1,2,3,4-tetrahydroquinazoline (5c). Yield 64% (white crystals); mp 79–81°C (hexane–benzene); R_f 0.65 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6): 2.82 (1H, br. s, NH-3), 3.64 (1H, d, J=16.0 Hz, H-4x), 3.91 (1H, d, J=16.5 Hz, H-4y), 5.07 (1H, s, H-2), 6.17 (1H, s, NH-1), 6.50 (1H, dd, J=7.0, 7.5 Hz, H-6), 6.58 (1H, d, J=8.1 Hz, H-8), 6.80 (1H, d, J=7.0 Hz, H-5), 6.91 (1H, dd, J=7.5, 8.1 Hz, H-7), 7.16 (1H, t, J=7.9 Hz, H-5′), 7.50 (1H, d, J=7.9 Hz, H-6′), 7.65 (1H, d, J=7.9 Hz, H-4′), 7.86 (1H, s, H-2′). δ_C (DMSO-d_6): 44.58 (C-4), 67.11 (C-2), 94.46 (C-3′), 114.18 (C-8), 115.98 (C-6), 120.67 (C-4a), 125.61 (C-5), 126.54 (C-7), 126.60 (C-6′), 130.27 (C-5′), 135.66 (C-2′), 136.12 (C-4′), 144.14 (C-8a), 145.46 (C-1′). Anal

calcd. for $C_{14}H_{13}IN_2$: C, 50.02; H, 3.90; N, 8.33. Found C, 50.22; H, 3.97; N, 8.39%.

4.3.13. 2-(2-Methoxy-5-nitrophenyl)-1,2,3,4-tetrahydroquinazoline (6a). Yield 91% (orange crystals); mp 93–95°C (methanol); R_f 0.57 (ethyl acetate–benzene, 1:1).δ_H (DMSO-d_6): 2.96 (1H, br. s, NH-3), 3.72 (1H, d, J=16.4 Hz, H-4x), 3.95 (1H, d, J=16.4 Hz, H-4y), 3.96 (3H, s, OCH_3), 5.42 (1H, br. s, H-2), 5.98 (1H, br. s, NH-1), 6.54 (1H, t, J=7.3 Hz, H-6), 6.59 (1H, d, J=7.7 Hz, H-8), 6.85 (1H, d, J=7.3 Hz, H-5), 6.93 (1H, dd, J=7.3, 7.7 Hz, H-7), 7.25 (1H, d, J=9.0 Hz, H-3′), 8.24 (1H, dd, J=2.8, 9.0 Hz, H-4′), 8.35 (1H, d, J=2.8 Hz, H-6′). δ_C (DMSO-d_6): 45.13 (C-4), 56.53 (OCH_3), 62.03 (C-2), 111.53 (C-3′), 114.27 (C-8), 116.24 (C-6), 120.72 (C-4a), 123.25 (C-6′), 125.15 (C-4′), 125.73 (C-5), 126.61 (C-7), 131.56 (C-1′), 140.47 (C-5′), 144.52 (C-8a), 161.81 (C-2′). Anal calcd for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73. Found C, 63.36; H, 5.12; N, 14.53%.

4.3.14. 2-(2,4-Dichlorophenyl)-1,2,3,4-tetrahydroquinazoline (6b). Yield 70% (white crystals); mp 90–92°C (methanol); R_f 0.72 (ethyl acetate). δ_H (DMSO-d_6, ring): 2.85 (1H, br. s, NH-3), 3.67 (1H, d, J=16.3 Hz, H-4x), 3.93 (1H, d, J=16.3 Hz, H-4y), 5.42 (1H, s, H-2), 6.10 (1H, s, NH-1), 6.53 (1H, t, J=7.3 Hz, H-6), 6.58 (1H, d, J=7.9 Hz, H-8), 6.84 (1H, d, J=7.3 Hz, H-5), 6.93 (1H, dd, J=7.3, 7.9 Hz, H-7), 7.44 (1H, dd, J=2.1, 8.5 Hz, H-5′), 7.59 (1H, d, J=2.1 Hz, H-3′), 7.61 (1H, d, J=8.5 Hz, H-6′). δ_C (DMSO-d_6, ring): 44.58 (C-4), 64.63 (C-2), 114.14 (C-8), 116.16 (C-6), 120.59 (C-4a), 125.69 (C-5), 126.65 (C-7), 127.07 (C-5′), 128.64 (C-3′), 130.00 (C-6′), 132.77 (C-2′ or C-4′), 133.05 (C-2′ or C-4′), 138.81 (C-1′), 144.24 (C-8a). δ_N (DMSO-d_6, ring): −304.8 (N-1), −340.5 (N-3). δ_H (DMSO-d_6, chain): 4.72 (2H, s, H-4), 5.03 (2H, s, NH_2-1), 6.53 (1H, n.r., H-6), 6.68 (1H, d, J=7.7 Hz, H-8), 6.98 (1H, n.r., H-7), 7.00 (1H, n.r., H-5), 7.48 (1H, n.r., H-5′), 7.69 (1H, d, J=1.9 Hz, H-3′), 8.00 (1H, d, J=8.6 Hz, H-6′), 8.74 (1H, s, H-2). δ_C (DMSO-d_6, chain): 61.21 (C-4), 114.84 (C-8), 116.16 (C-6), 122.41 (C-4a), 127.81 (C-7), 128.86 (C-5), 129.2–134.8 (5C, C-2′, C-3′, C-4′, C-5′ and C-6′), 135.91 (C-1′), 146.38 (C-8a), 156.44 (C-2). Anal calcd for $C_{14}H_{12}Cl_2N_2$: C, 60.23; H, 4.33; N, 10.03. Found C, 60.19; H, 4.27; N, 10.03%.

4.3.15. 2-(2-Chloro-6-nitrophenyl)-1,2,3,4-tetrahydroquinazoline (6c). Yield 72% (yellow crystals); mp 104–106°C (methanol); R_f 0.69 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6, ring): 2.87 (1H, m, NH-3), 3.86 (1H, dd, J=3.2, 16.4 Hz, H-4x), 4.01 (1H, dd, J=10.2, 16.4 Hz, H-4y), 5.68 (1H, d, J=11.3 Hz, H-2), 6.14 (1H, s, NH-1), 6.45 (1H, d, J=7.9 Hz, H-8), 6.59 (1H, t, J=7.4 Hz, H-6), 6.86 (1H, d, J=7.4 Hz, H-5), 6.93 (1H, dd, J=7.4, 7.9 Hz, H-7), 7.56 (1H, dd, J=7.5, 7.9 Hz, H-4′), 7.71 (1H, d, J=7.5 Hz, H-5′), 7.78 (1H, d, J=7.9 Hz, H-3′). δ_C (DMSO-d_6, ring): 45.90 (C-4), 65.70 (C-2), 115.20 (C-8), 117.24 (C-6), 121.80 (C-4a), 123.01 (C-5′), 125.63 (C-5), 126.68 (C-7), 130.30 (C-4′), 131.60 (C-1′), 133.03 (C-3′), 134.32 (C-2′), 143.99 (C-8a) 151.74 (C-6′). δ_N (DMSO-d_6, ring): −306.4 (N-1), −341.1 (N-3), −3.3 (NO_2). δ_H (DMSO-d_6, chain): 4.68 (2H, s, H-4), 4.92 (2H, s, NH_2-1), 6.55 (1H, t, J=7.3 Hz, H-6), 6.70 (1H, d, J=7.7 Hz, H-8), 6.98 (1H, n.r., H-7), 7.00 (1H, n.r., H-5), 7.66 (1H, t, J=7.9 Hz, H-4′), 7.84 (1H, d, J=7.9 Hz, H-3′), 7.88 (1H, d, J=7.9 Hz, H-5′). δ_C (DMSO-d_6, chain): 61.47 (C-4), 114.91 (C-8), 116.32 (C-6), 121.83 (C-4a), 122.89 (C-5′), 127.66 (C-1′), 127.86 (C-7), 128.66 (C-5), 131.71 (C-4′), 133.60 (C-3′), 134.13 (C-2′), 146.27 (C-8a), 149.61 (C-6′), 155.54 (C-2). Anal calcd for $C_{14}H_{12}ClN_3O_2$: C, 58.04; H, 4.17; N, 14.50. Found C, 58.02; H, 4.17; N, 14.55%.

4.3.16. 2-(3,4-Dimethoxyphenyl)-1,2,3,4-tetrahydroquinazoline (6d). Yield 91% (white crystals); mp 118–120°C (methanol); R_f 0.35 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6, ring): 3.73 (1H, d, J=16.5 Hz, H-4x), 3.73 (3H, s, 3′-OCH_3 or 4′-OCH_3), 3.75 (3H, s, 3′-OCH_3 or 4′-OCH_3), 3.97 (1H, d, J=16.5 Hz, H-4y), 5.02 (1H, s, H-2), 6.00 (1H, s, NH-1), 6.49 (1H, t, J=7.3 Hz, H-6), 6.58 (1H, d, J=8.0 Hz, H-8), 6.81 (1H, d, J=7.3 Hz, H-5), 6.90 (1H, dd, J=7.3, 8.0 Hz, H-7), 6.91 (1H, d, J=8.3 Hz, H-5′), 7.00 (1H, d, J=8.3 Hz, H-6′), 7.11 (1H, s, H-2′), NH-3 was not detected. δ_C (DMSO-d_6, ring): 45.28 (C-4), 55.45 (3′-OCH_3 or 4′-OCH_3), 55.58 (3′-OCH_3 or 4′-OCH_3), 68.03 (C-2), 110.79 (C-2′), 111.35 (C-5′), 114.20 (C-8), 115.88 (C-6), 119.08 (C-6′), 120.67 (C-4a), 125.61 (C-5), 126.47 (C-7), 135.31 (C-1′), 144.65 (C-8a), 148.32 (C-4′), 148.58 (C-3′). δ_H (DMSO-d_6, chain): 3.85 (3H, s, 3′-OCH_3 or 4′-OCH_3), 3.89 (3H, s, 3′-OCH_3 or 4′-OCH_3), 4.59 (2H, s, H-4), 5.02 (2H, s, NH_2-1), 6.53 (1H, t, J=7.5 Hz, H-6), 6.67 (1H, d, J=7.9 Hz, H-8), 6.97 (1H, n.r., H-7), 7.00 (2H, m, H-5 and H-5′), 7.24 (1H, d, J=8.3 Hz, H-6′), 7.38 (1H, s, H-2′), 8.33 (1H, s, H-2). δ_C (DMSO-d_6, chain): 55.36 (3′-OCH_3 or 4′-OCH_3), 55.54 (3′-OCH_3 or 4′-OCH_3), 61.09 (C-4), 109.22 (C-2′), 111.24 (C-5′), 114.80 (C-8), 116.18 (C-6), 122.51 (C-6′), 123.30 (C-4a), 127.61 (C-7), 128.75 (C-5), 129.05 (C-1′), 146.39 (C-8a), 148.94 (C-4′), 151.10 (C-3′), 160.80 (C-2). Anal calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found C, 71.39; H, 6.79; N, 10.46%.

4.3.17. 2,4-Dichloro-6-(1,2,3,4-tetrahydroquinazolin-2-yl)phenol (6e). Yield 74% (orange crystals); mp 200–202°C (methanol); R_f 0.69 (ethyl acetate-benzene, 1:1). δ_H (DMSO-d_6, ring): 3.57 (1H, d, J=16.4 Hz, H-4x), 3.87 (1H, d, J=16.4 Hz, H-4y), 5.46 (1H, s, H-2), 6.55 (1H, t, J=7.2 Hz, H-6), 6.7 (1H, br. s, NH-1), 6.73 (1H, d, J=8.1 Hz, H-8), 6.81 (1H, d, J=7.2 Hz, H-5), 6.99 (1H, dd, J=7.2, 8.1 Hz, H-7), 7.21 (1H, s, H-6′), 7.38 (1H, s, H-4′), NH-3 and OH were not detected. δ_C (DMSO-d_6, ring): 41.04 (C-4), 63.86 (C-2), 114.50 (C-8), 116.71 (C-6), 118.40 (C-4a), 120.53 (C-3′), 121.67 (C-5′), 126.16 (C-5), 126.57 (C-6′), 127.23 (C-7), 128.19 (C-4′), 128.87 (C-1′), 141.72 (C-8a), 152.00 (C-2′). δ_H (DMSO-d_6, chain): 4.73 (2H, s, H-4), 5.22 (2H, s, NH_2-1), 6.55 (1H, n.r., H-6), 6.70 (1H, n.r., H-8), 7.02 (1H, n.r., H-7), 7.05 (1H, d, J=7.1 Hz, H-5), 7.41 (1H, s, H-6′), 7.54 (1H, s, H-4′), 8.59 (1H, s, H-2). δ_C (DMSO-d_6, chain): 54.21 (C-4), 115.14 (C-8), 116.21 (C-6), 117.18 (C-1′), 117.46 (C-5′), 119.39 (C-4a), 124.19 (C-3′), 128.85 (C-7), 129.54 (C-5), 130.17 (C-6′), 132.62 (C-4′), 146.55 (C-8a), 162.56 (C-2′), 164.85 (C-2). Anal calcd for $C_{14}H_{12}Cl_2N_2O$: C, 56.97; H, 4.10; N, 9.49. Found C, 56.94; H, 4.17; N, 9.32%.

4.3.18. 2-{(*E*)-[(2-Aminobenzyl)imino]methyl}-4-methoxyphenol (6f). Yield 58% (yellow crystals); mp 116–118°C (methanol); R_f 0.53 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6, ring): 3.63 (3H. s, OCH_3), 3.65 (1H, d,

J=16.0 Hz, H-4x), 3.89 (1H, d, J=16.0 Hz, H-4y), 5.30 (1H, s, H-2), 6.29 (1H, s, NH-1), 6.51 (1H, t, J=7.4 Hz, H-6), 6.65 (1H, n.r., H-8), 6.69 (1H, n.r., H-3′), 6.71 (1H, n.r., H-4′), 6.79 (1H, d, J=7.4 Hz, H-5), 6.88 (1H, s, H-6′), 6.93 (1H, n.r., H-7), NH-3 and OH were not detected. δ_C (DMSO-d_6, ring): 43.03 (C-4), 55.34 (OCH_3), 64.13 (C-2), 113.44 (C-4′), 113.98 (C-6′), 114.37 (C-8), 116.07 (C-3′), 116.20 (C-6), 119.56 (C-4a), 125.91 (C-5), 126.83 (C-7), 127.22 (C-1′), 143.38 (C-8a), 149.66 (C-2′), 151.91 (C-5′). δ_H (DMSO-d_6, chain): 3.71 (3H. s, OCH_3), 4.66 (2H, s, H-4), 5.04 (2H, s, NH_2-1), 6.53 (1H, t, J=7.4 Hz, H-6), 6.67 (1H, n.r., H-8), 6.81 (1H, d, J=9.0 Hz, H-3′), 6.93 (1H, n.r., H-4′), 6.99 (2H, m, H-5 and H-7), 7.02 (1H, s, H-6′), 8.58 (1H, s, H-2). δ_C (DMSO-d_6, chain): 55.53 (OCH_3), 58.64 (C-4), 114.78 (C-6′), 114.89 (C-8), 116.16 (C-6), 117.17 (C-3′), 118.60 (C-1′), 119.24 (C-4′), 121.52 (C-4a), 128.09 (C-7), 128.92 (C-5), 146.29 (C-8a), 151.55 (C-5′), 154.37 (C-2′), 165.43 (C-2). Anal calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found C, 70.21; H, 6.29; N, 11.12%.

4.3.19. 1-(1,2,3,4-Tetrahydroquinazolin-2-yl)-naphthalen-2-ol (7). Yield 86% (yellow crystals); mp 176–178°C (hexane); R_f 0.51 (ethyl acetate). δ_H (DMSO-d_6): 4.74 (2H, s, H-4), 5.28 (2H, s, NH_2-1), 6.57 (1H, t, J=7.6 Hz, H-6), 6.71 (2H, m, H-8 and H-3′), 7.04 (1H, t, J=7.6 Hz, H-7), 7.16 (1H, d, J=7.6 Hz, H-5), 7.18 (1H, dd, J=7.4, 7.9 Hz, H-6′), 7.42 (1H, dd, J=7.4, 8.3 Hz, H-7′), 7.61 (1H, d, J=7.9 Hz, H-5′), 7.71 (1H, d, J=9.4 Hz, H-4′), 8.04 (1H, d, J=8.3 Hz, H-8′), 9.22 (1H, s, H-2), 14.1 (1H, br.s, OH). δ_C (DMSO-d_6): 51.14 (C-4), 105.71 (C-1′), 115.13 (C-8), 116.22 (C-6), 118.28 (C-8′), 120.19 (C-4a), 122.09 (C-6′), 125.17 (C-4a′), 125.49 (C-3′), 127.83 (C-7′), 128.82 (C-7), 128.86 (C-5′), 129.46 (C-5), 134.33 (C-8a′), 137.02 (C-4′), 146.52 (C-8a), 158.57 (C-2), 177.22 (C-2′). Anal calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84; N, 10.14. Found C, 78.35; H, 5.52; N, 10.34%.

4.4. Compounds 8–9

4.4.1. 2-Methyl-3,4-dihydroquinazoline (8). A solution of acetone (0.17 g, 3 mmol) with 2-aminomethylaniline (0.36 g, 3 mmol) in methanol (10 mL), was boiled for a week, concentrated in vacuo, and the residue was recrystallized. Yield 47% (white crystals); mp 204–205°C (ethanol, 204–205°C[24,25]); R_f 0.52 (acetic acid–ethanol, 1:1). δ_H (DMSO-d_6): 1.79 (3H, s, CH_3), 3.73 (2H, s, H-4), 6.52 (1H, t, J=7.4 Hz, H-6), 6.64 (1H, d, J=8.1 Hz, H-8), 6.98 (1H, t, J=7.4, 8.1 Hz, H-7), 7.05 (1H, d, J=7.4 Hz, H-5), NH-1 proton was not detected. δ_C (DMSO-d_6): 22.89 (CH_3), 40.93 (C-4), 114.91 (C-8), 115.87 (C-6), 122.37 (C-4a), 127.97 (C-5), 129.07 (C-7), 146.79 (C-8a), 173.47 (C-2). Anal calcd for $C_9H_{10}N_2$: C, 73.93; H, 6.89; N, 19.16. Found C, 73.97; H, 6.98; N, 19.11%.

4.4.2. 2-{(*E*)-[(2-{[(1*E*)-(2-Hydroxyphenyl)methylene]-amino}benzyl)imino]methyl}phenol (9a). A solution of salicylaldehyde (0.73 g, 6 mmol) with 2-aminomethylaniline (0.36 g, 3 mmol) in methanol (10 mL), was boiled for 48 h, concentrated in vacuo, and the residue was recrystallized. Yield 76% (yellow crystals); mp 108–109°C (ethanol); R_f 0.88 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6, a and b refer to aniline and benzylamino type linear moieties, respectively): 4.92 (2H, s, H-4), 6.83 (1H, d, J=7.9 Hz, H-b-3′), 6.86 (1H, t, J=7.5 Hz, H-b-5′), 6.98 (2H, m, H-a-3′ and H-a-5′), 7.29 (1H, dd, J=7.5, 7.9 Hz, H-b-4′), 7.31 (1H, t, J=7.4 Hz, H-7), 7.37 (2H, m, H-8 and H-b-6′), 7.42 (3H, m, H-5, H-6 and H-a-4′), 7.68 (1H, d, J=7.9 Hz, H-a-6′), 8.65 (1H, s, b-C═H), 8.89 (1H, s, a-C═H), 12.9 (1H, br.s, a-OH or b-OH), 13.3 (1H, br.s, a-OH or b-OH). δ_C (DMSO-d_6, a and b refer to aniline and benzylamino type linear moieties, respectively): 58.72 (C-4), 116.34 (C-b-3′), 116.54 (C-a-6′), 118.54 (C-b-5′), 118.56 (C-8), 118.63 (C-b-1′), 119.11 (C-a-5′), 119.46 (C-a-1′), 126.96 (C-7), 128.81 (C-6), 129.07 (C-5), 131.59 (C-b-6′), 132.07 (C-4a), 132.30 (C-b-4′), 132.46 (C-a-6′), 133.37 (C-a-4′), 147.03 (C-8a), 160.14 (C-a-2′), 160.32 (C-b-2′), 163.62 (C-a-C═N), 166.51 (C-b-C═N). δ_N (DMSO-d_6, a and b refer to aniline and benzylamino type linear moieties, respectively): −87.0 (a-N), −85.1 (b-N). Anal calcd for $C_{21}H_{18}N_2O_2$: C, 76.31; H, 5.49; N, 8.48. Found C, 76.28; H, 5.45; N, 8.40%.

4.4.3. 2-{(*E*)-[(2-{[(1*E*)-(2-Hydroxy-5-nitrophenyl)-methylene]amino}benzyl)imino]methyl}-4-nitrophenol (9b). Synthesized as compound (**Ia**) from 2-hydroxy-5-nitro-benzaldehyde and 2-aminomethylaniline. Yield 96% (yellow crystals); mp 248–250°C (ethanol); R_f 0.54 (ethyl acetate–benzene, 1:1). δ_H (DMSO-d_6, a and b refer to aniline and benzylamino type linear moieties, respectively): 5.05 (2H, s, H-4), 6.69 (1H, d, J=9.5 Hz, H-a-2′), 7.13 (1H, d, J=9.0 Hz, H-b-2′), 7.38 (2H, m, H-6 and H-8), 7.50 (2H, m, H-5 and H-7), 8.05 (1H, d, J=9.5 Hz, H-a-3′), 8.27 (H, d, J=9.0 Hz, H-b-3′), 8.34 (H, s, H-a-5′), 8.75 (1H, s, H-b-5′), 8.84 (1H, s, b-C═H), 9.00 (1H, s, a-C═H), OH protons were not detected. Anal calcd for $C_{21}H_{16}N_4O_6$: C, 60.00; H, 3.84; N, 13.33. Found C, 60.02; H, 3.78; N, 13.35%.

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