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Synthesis and Structure of 2-Phenyl-4-aryl-3,4,5,6-tetrahydrobenzo[h]quinazolines

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Summary. The reaction of 2-arylidene-1-tetralones **1** with benzamidine gave 2-phenyl-4-aryl-3,4,5,6-tetrahydrobenzo[h]quinazolines **2**. Investigations on the tautomeric equilibria of **2** by IR, ^{1}H- and ^{13}C-NMR showed the compounds to exist predominantly in the tautomeric form **2A** both in the solid state and in solution. Acetylation and oxidation of the heterocyclic ring of **2** provided further evidence for the structural assignment of the title compounds.

Keywords. Synthesis; Benzo[h]quinazolines; ^{1}H- and ^{13}C-NMR spectroscopy; Tautomerism.

Synthese und Struktur von 2-Phenyl-4-aryl-3,4,5,6-tetrahydrobenzo[h]chinazolinen

Zusammenfassung. Die Reaktion von 2-Aryliden-1-tetralonen **1** mit Benzamidin ergab 2-Phenyl-4-aryl-3,4,5,6-tetrahydrobenzo[h]chinazoline **2**. Untersuchungen über das tautomere Gleichgewicht von **2** mittels IR, ^{1}H-NMR, und ^{13}C-NMR Spektroskopie zeigten, daß für die Verbindungen das Tautomere **2A** dominierte (sowohl in fester Phase als auch in Lösung). Acetylierung und Oxidation des heterocyclischen Ringes von **2** ergab weitere Beweise für die Struktur der Titelverbindungen.

Introduction

The most common procedure for synthesis of benzo[h]quinazolines involves condensation of an appropriately substituted α-tetralone and some small nitrogen containing substrate [1]. Thus, reaction of α-tetralones with amidines [2], (thio)-urea [3, 4], or guanidines [5, 6] proved to be an attractive approach to the synthesis of these compounds. As a continuation of our synthetic work with 2-benzylidene-cyclanones [7, 8], we studied the reaction of some 2-arylidene-1-tetralones with benzamidines. In these reactions formation of 2-phenyl-4-aryl-tetrahydrobenzo[h]-quinazolines was expected [2], whose dihydropyrimidine moiety is of great interest from both biological [9] and structural (tautomeric) [10–12] aspects.

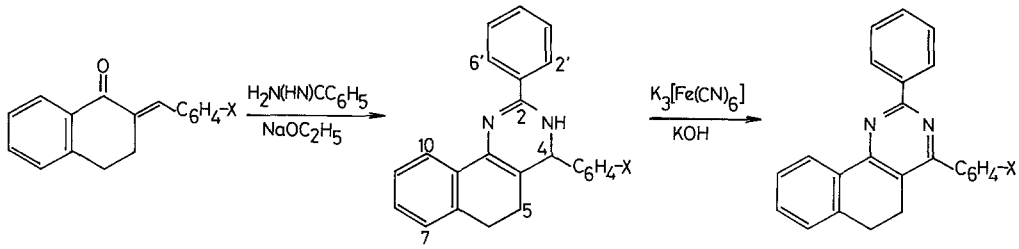
Results and Discussion

2-Arylidene-1-tetralones **1a–g** were reacted with benzamidine in boiling ethanol to form 2-phenyl-4-aryl-3,4,5,6-tetrahydrobenzo[h]quinazolines **2a–g** (Scheme 1).

Table 1. ^{1}H-NMR (80 MHz, $CDCl_3$) spectra of compounds **2** and **5**

Compounds	H-10 (1H, m)	H-2′,6′ (2H, m)	*Ar*H(m)	H-4 (1H, s)	H-6 (2H, m)	H-5 (2H, m)	NH (1H, bs)	Others
2a	8.2–8.1	8.0–7.8	7.6–6.9[a]	5.29	3.0–2.7	2.3–2.0	5.75	
2a[b,c]	8.2–7.8[d]		7.7–6.9[a]	5.23	2.9–2.4	2.3–1.7	8.2–7.8[d]	
2b	8.1–8.0	7.9–7.6	7.5–6.8[e]	5.19	2.9–2.6	2.2–1.9	5.60	3.75[f]
2c	8.2–8.1	7.9–7.7	7.5–6.7[e]	5.18	2.9–2.6	2.2–1.9	5.62	3.71[f]
2d	8.2–8.0	7.9–7.7	7.5–7.0[e]	5.16	2.9–2.6	2.2–1.9	5.55	2.30[g]
2e	8.1–8.0	7.9–7.8	7.6–7.1[e]	5.19	2.9–2.6	2.2–1.9	5.40	
2f	8.2–8.1	7.9–7.7	7.5–7.0[e]	5.14	2.9–2.6	2.1–1.9	5.66	
2g	8.2–8.1	7.9–7.7	7.6–7.1[e]	5.64	3.0–2.7	2.3–2.0	5.75	
5a	8.1–8.0	7.6–7.1[h]		6.28	3.1–2.8	2.6–2.3	–	1.77[i]
5b	8.1–8.0	7.6–6.7[j]		6.22	3.1–2.8	2.6–2.3	–	3.70[f], 1.75[i]
5d	8.1–8.0	7.7–7.0[j]		6.24	3.0–2.8	2.6–2.3	–	2.26[g], 1.76[i]
5e	8.1–8.0	7.6–7.1[j]		6.23	3.1–2.8	2.6–2.3	–	1.77[i]

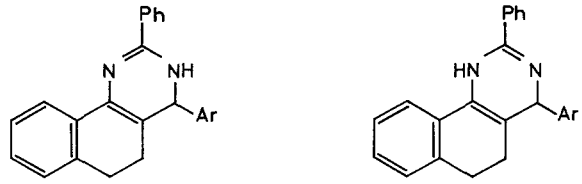
[a] 11H; [b] *DMSO-d_6*; [c] 60 MHz; [d] 4H(m); [e] 10H; [f] 3H(s, CH_3O); [g] 3H(s, CH_3); [h] 13H; [i] 3H (s, CH_3CO); [j] 12H



1 2 3

	a	b	c	d	e	f	g
X	H	4-OCH_3	3-OCH_3	4-CH_3	4-Cl	3-Cl	2-Cl

Scheme 1



2A 2B

Scheme 2

The structures of the compounds obtained were verified by IR and NMR studies. In the IR spectra (see Exp. Part) appearance of ν(NH) and the ν(C=N) bands gave unambiguous proof of the progress of the reactions, which was evidenced by the ^{1}H-NMR spectra as well (see Table 1). Since the compounds can exist in two tautomeric forms **2A** and **2B** (Scheme 2) having very similar IR and ^{1}H-NMR characteristics [10], further studies were carried out to elucidate the position of the possible tautomeric equilibrium.

The IR spectra of **2a–g** using solid samples (KBr) or solutions ($CHCl_3$) show ν(C=N) bands only at about 1630 cm^{-1}, which are in good agreement with values reported for the **A** tautomeric form of 6-methyl-2,4-diphenyldihydropyrimidine [11], suggesting existence of the same **2A** tautomer of **2a–g** both in the solid state and in solution.

The single sets of signals observed in the ^{1}H- and ^{13}C-NMR spectra of **2a–g** indicate that, if the **2A**$\rightleftharpoons$**2B** interconversion exists, it has to be fast in the NMR time scale. It was shown in an earlier tautomeric study on the related 2-methylmercapto-4-phenyl-3,4,5,6-tetrahydrobenzo[h]quinazoline **4a** and its 3-methyl derivative **4b** (Scheme 3) of fixed tautomeric structure **2A**, that the ^{13}C-NMR chemical shift

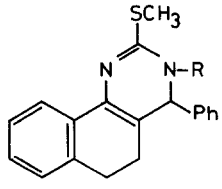
Table 2. Relevant ^{13}C-NMR (20.1 MHz, $CDCl_3$) data of compounds **2** and **5**

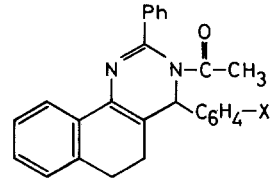
Compounds	C-1a	C-2	C-4	C-4a	C-5	C-6	C-6a	C-10a	Others
2a	133.6	152.4	59.7	113.5	24.8	27.7	135.4	126.6	
2a[a]	134.4	152.3	58.0	113.6	25.0	27.4	135.2	126.2	
2b	135.5	152.0	59.0	113.9	25.0	27.8	135.4	126.8	55.1[b]
2c	134.1	152.2	59.3	113.4	24.8	27.7	135.3	126.2	55.0[b]
2d	134.2	152.0	59.0	113.8	24.9	27.7	135.5	126.7	20.9[c]
2e	133.8	152.0	59.3	112.8	24.8	27.7	135.4	126.3	
2f	133.9	152.1	58.9	112.9	24.9	27.6	135.2	126.8	
2g	135.3[d]	152.4	54.5	112.1	25.2	27.8	135.5[d]	126.9	
5a	136.6[d]	150.6	55.8	122.4	25.6	27.4	135.2[d]	126.5	25.4[e], 170.8[f]
5b	132.3	150.5	54.9	122.8	25.4	27.4	135.1	126.5	55.3[b], 25.5[e], 170.7[f]
5d	134.4	150.6	55.6	122.7	25.5	27.4	135.1	126.5	20.9[c], 25.4[e], 170.7[f]
5e	132.1	150.5	55.1	121.7	25.5	27.3	135.1	126.6	25.4[e], 170.9[f]

[a] *DMSO-d_6*; [b] CH_3O; [c] CH_3; [d] Interchangeable assignments; [e] $CH_3(CO)$; [f] $CH_3(CO)$

of the C-1a carbon atom is strongly influenced by the presence of a conjugated C=N double bond in the adjacent 1,2 position [13]. Comparison of the ^{13}C-NMR chemical shift of the C-1a atom of the above mentioned **4a** and **4b** ($\delta = 133.8$ and 133.9, respectively) [13] with those of **2a–g**, (Table 2) suggests a similar tautomeric structure **2A** of compounds **2** and **4**. This is also supported by the large downfield shift of the C-1a signals of **2a–g**, **4a**, and **4b** (about $\delta = 134$ ppm) compared to that of 4-phenyl-3,4,5,6-tetrahydrobenzo[h]quinazoline-2(1*H*)-thione ($\delta = 126.6$ ppm) [13], which indicates the presence of a C=N double bond in the 1,2 position, i.e. a pronounced shift of the tautomeric equilibrium towards the **2A** form for compounds **2** and **4**.

In the ^{1}H-NMR spectra of **2a–g** the well separated H-4 signal provides evidence





4a R = H
4b R = CH_3

5a X=H
5b X=4–OCH_3
5d X=4–CH_3
5e X=4–Cl

Scheme 3

for the unsaturated dihydropyrimidin moiety of the compounds. In the aromatic region of the spectra a multiplet integrated up to one proton appears separately at about $\delta = 8.2–8.0$ ppm in each case (Table 1). Since such a signal does not appear in the ^{1}H-NMR spectra of **4a** and **4b** [13], these low field signals can be assigned to the H-10 protons, whose large downfield shift can be explained by the magnetic anisotropy and conjugation effect of the coplanar C=N double bond in 1,2 position [14]. This observation is in accordance not only with the results of the ^{1}H-NMR investigation of **4a** and **4b** [13] but also with those of some condensed pyrazole derivatives [15]. In a recent paper reporting on the synthesis of 2-methyl-4-phenyl-3,4,5,6-tetrahydrobenzo[h]quinazoline with **2B** tautomeric structure, this low field multiplet was absent in the ^{1}H-NMR spectrum [16].

Thus, all IR, ^{1}H- and ^{13}C-NMR investigations support the **2A** tautomeric form of **2a–g**. These results are in contrary to the conclusion of El-Rayyes et al., who characterized some 2,4-diaryl-3,4,5,6-tetrahydrobenzo[h]quinazolines with the **2B** tautomeric form on the basis of their IR and ^{1}H-NMR spectra [2]. The authors, however, did not mention any detailed basis for their structure determination. In this respect it is worth mentioning that repetition of their slightly different synthetic procedure starting from **1a** and benzamidine gave a compound with the same physical and spectroscopic characteristics as those of **2a**.

In order to get a more complete structural characterization of **2a–g**, we performed acetylation and aromatization of the compounds. Dihydropyrimidines **2a**, **2b**, **2d**, and **2e** were treated with acetic anhydride in absolute pyridine to give the corresponding N-acetyl derivatives **5** (Scheme 3). Appearance of the amide I bands in their IR spectra as well as the H–C**H**$_3$(CO) and C–C**H**$_3$(CO) signals in their ^{1}H- and ^{13}C-NMR spectra gave unambiguous evidence of progress of the reactions. The electron ionization mass spectra of **5b** and **5d** exhibited significant peaks of molecular ions at $m/z = 408.184$ and 392.189, respectively, corresponding to chemical formulae $C_{27}H_{24}N_2O_2$ (**5b**) and $C_{27}H_{24}N_2O$ (**5d**). The main fragments in the spectra are due to the loss of a $CH_3CO^{\cdot}$ radical followed by elimination of XC_6H_4–H. In the metastable ion spectra a reverse sequence of eliminations: primary loss of a $XC_6H_4^{\cdot}$ radical and, subsequently, CH_2CO elimination were also observable. The high similarity of the spectra indicates a common acetylation site for the compounds. The large (about 1 ppm) downfield shift of H-4 signals of **5** compared to those of **2** gives support for introduction of the acetyl group into the N-3 position of **5** [17]. The chemical shifts of H-10 and C-1a atoms of **5** are very close to those of **2** (Table 1), supporting the same tautomeric structure of the compounds.

Using the $KOH/K_3[Fe(CN)_6]$ method applied to the aromatization of 4-aryl-dihydroquinazolines by Girke [18], **2a–g** underwent oxidation to yield the coresponding **3a–g** (Scheme 1). In their IR spectra there is no ν(C=N) band and a strong $\nu(C{=}C_{Ar})$ skeletal vibration characteristic for aromatic quinazolines [19] appears. In the ^{1}H-NMR spectra the H-4 signal is absent. The H-10 signal appears separately from the other aromatic signals (see Exp. Part), which can be attributed to the ring current of the heteroaromatic ring. This observation is in agreement with the results of ^{1}H-NMR investigation of the closely related 2-amino-4-aryl-5,6-dihydrobenzo[h]quinazolines [6], and provides further support for the **2A** tautomeric structure of **2a–g**.

Experimental Part

Melting points were determined on a Boetius apparatus and are uncorrected. IR spectra were taken with a Specord 75 IR spectrophotometer. ^{1}H-NMR spectra were recorded with a Perkin-Elmer R-12 (60 MHz) and a Bruker WP 80 SY (80 MHz) spectrophotometer. ^{13}C-NMR measurements were carried out on a Bruker WP 80 SY (20.1 MHz) instrument. In all the NMR measurements tetramethylsilane (*TMS*) was used as internal standard. Mass spectra were taken and exact mass measurements were carried out using an AEI MS-902 type spectrometer. Operating conditions: 70 eV, 100 μA, 8 kV, direct inlet, 160 °C source temperature. Elemental analyses were performed at the Central Research Laboratory, University Medical School, Pécs, and at the Department of Organic Chemistry, Eötvös Loránd University, Budapest.

The 2-benzylidene-1-tetralones **1a–g** were prepared by base-catalyzed condensation of 1-tetralone with aromatic aldehydes [20]. Their (*E*)-configuration was based on IR [21] and ^{1}H-NMR [22] investigations.

The progress of the reactions, as well as the purity of the compounds synthesized, was checked by TLC performed on Kieselgel GF 254 plates (Merck) using benzene and/or benzene:ethanol (4:1 *v/v*) as eluant.

General Procedure for Preparation of Tetrahydrobenzo[h]quinazolines **2a–g**

Metallic sodium (0.04 mol) was dissolved in 100 ml of anhydrous ethanol and benzamidine hydrochloride (0.035 mol) was added. After standing at room temperature for 0.5 h, the precipitate formed was filtered off, and the filtrate was mixed with a solution of 2-arylidene-1-tetralone **1a–g** (0.02 mol) in 100 ml of anhydrous ethanol. The reaction mixture was refluxed with the exclusion of atmospheric moisture for 4 h. Then the mixture was evaporated to appr. half of its original volume and was kept in the refrigerator overnight. The product formed was filtered off and purified by crystallization from methanol to give pale yellow crystals.

2,4-Diphenyl-3,4,5,6-tetrahydrobenzo[h]quinazoline (**2a**)

Yield: 86%, m.p. 155–158 °C. IR (KBr) $\nu = 3410\,cm^{-1}$ (NH), $1630\,cm^{-1}$ (C=N), $1590\,cm^{-1}$ ($C=C_{Ar}$). IR ($CHCl_3$) $\nu = 1630\,cm^{-1}$ (C=N). $C_{24}H_{20}N_2$ (336.44). Calcd. C 85.68, H 5.99, N 8.33; found C 85.55, H 6.31, N 8.16.

2-Phenyl-4-(4-methoxyphenyl)-3,4,5,6-tetrahydrobenzo[h]quinazoline (**2b**)

Yield: 89%, m.p. 204–207 °C. IR (KBr) $\nu = 3405\,cm^{-1}$ (NH), $1640\,cm^{-1}$ (C=N), 1605, $1585\,cm^{-1}$ ($C=C_{Ar}$). IR ($CHCl_3$) $\nu = 1630\,cm^{-1}$ (C=N). $C_{25}H_{22}N_2O$ (366.47). Calcd. C 81.94, H 6.05, N 7.64; found C 82.03, H 6.11, N 7.55.

2-Phenyl-4-(3-methoxyphenyl)-3,4,5,6-tetrahydrobenzo[h]quinazoline (**2c**)

Yield: 78%, m.p. 155–158 °C. IR (KBr) $\nu = 3430\,cm^{-1}$ (NH), $1640\,cm^{-1}$ (C=N), 1605, $1595\,cm^{-1}$ ($C=C_{Ar}$). IR ($CHCl_3$) $\nu = 1635\,cm^{-1}$ (C=N). $C_{25}H_{22}N_2O$ (366.47). Calcd. C 81.94, H 6.05, N 7.64; found C 81.82, H 6.27, N 7.38.

2-Phenyl-4-(4-methylphenyl)-3,4,5,6-tetrahydrobenzo[h]quinazoline (**2d**)

Yield: 87%, m.p. 196–199 °C. IR (KBr) $\nu = 3430\,cm^{-1}$ (NH), $1635\,cm^{-1}$ (C=N), $1595\,cm^{-1}$ ($C=C_{Ar}$). IR ($CHCl_3$) $\nu = 1635\,cm^{-1}$ (C=N). $C_{25}H_{22}N_2$ (350.47). Calcd. C 85.68, H 6.33, N 7.99; found C 85.50, H 6.60, N 8.00.

2-Phenyl-4-(4-chlorophenyl)-3,4,5,6-tetrahydrobenzo[h]quinazoline (**2e**)

Yield: 92%, m.p. 182–185 °C. IR (KBr) $\nu = 3420\,cm^{-1}$ (NH), $1640\,cm^{-1}$ (C=N), $1585\,cm^{-1}$ (C=C_{Ar}). IR ($CHCl_3$) $\nu = 1635\,cm^{-1}$ (C=N). $C_{24}H_{19}ClN_2$ (370.89). Calcd. C 77.72, H 5.16, N 7.55; found C 77.49, H 4.93, N 7.36.

2-Phenyl-4-(3-chlorophenyl)-3,4,5,6-tetrahydrobenzo[h]quinazoline (**2f**)

Yield: 85%, m.p. 152–155 °C. IR (KBr) $\nu = 3415\,cm^{-1}$ (NH), $1635\,cm^{-1}$ (C=N), $1595\,cm^{-1}$ (C=C_{Ar}). IR ($CHCl_3$) $\nu = 1635\,cm^{-1}$ (C=N). $C_{24}H_{19}ClN_2$ (370.89). Calcd. C 77.72, H 5.16, N 7.55; found C 77.61, H 5.27, N 7.81.

2-Phenyl-4-(2-chlorophenyl)-3,4,5,6-tetrahydrobenzo[h]quinazoline (**2g**)

Yield: 78%, m.p. 185–188 °C. IR (KBr) $\nu = 3430\,cm^{-1}$ (NH), $1630\,cm^{-1}$ (C=N), $1585\,cm^{-1}$ (C=C_{Ar}). IR ($CHCl_3$) $\nu = 1630\,cm^{-1}$ (C=N). $C_{24}H_{19}ClN_2$ (370.89). Calcd. C 77.72, H 5.16, N 7.55; found C 77.75, H 5.38, N 7.27.

General Procedure for Aromatization of Tetrahydrobenzo[h]quinazolines **2a–g** to **3a–g**

Potassium hydroxide (0.1 mol) and $K_3[Fe(CN)_6]$ (0.02 mol) was dissolved in 200 ml of distilled water and the solution obtained was mixed with a solution of tetrahydrobenzo[h]quinazoline **2a–g** (0.01 mol) in 100 ml of benzene. The mixture was stirred at room temperature until TLC analysis of the organic phase did not show presence of starting material (8–10 days). Then the organic phase was separated, washed with water (3 × 50 ml), dried (Na_2SO_4), and evaporated. The product obtained was subjected to column chromatography (Merck, Kieselgel 60, 0.063–0.2 mm; benzene) and crystallized from methanol to give colourless crystals, of **3a–g**. The characteristic IR band at 1530–1540 cm^{-1} (see data below) is due to a heteroaromatic skeletal vibration.

2,4-Diphenyl-5,6-dihydrobenzo[h]quinazoline (**3a**)

Yield: 78%, m.p. 172–175 °C. IR (KBr) $\nu = 1605$, $1585\,cm^{-1}$ (C=C_{Ar}), $1540\,cm^{-1}$ (C=C_{Ar}). $C_{24}H_{18}N_2$ (334.42). Calcd. C 86.20, H 5.43, N 8.38; found C 86.15, H 5.34, N 8.32. ^{1}H-NMR (60 MHz, $CDCl_3$) $\delta = 8.8$–8.4 (3H, m, H-10, H-2′, H-6′), 7.8–7.0 (11H, m, *Ar*H), 3.2–2.6 (4H, m, H-5, H-6).

2-Phenyl-4-(4-methoxyphenyl)-5,6-dihydrobenzo[h]quinazoline (**3b**)

Yield: 75%, m.p. 146–147 °C. IR (KBr) $\nu = 1610$, $1580\,cm^{-1}$ (C=C_{Ar}), $1535\,cm^{-1}$ (C=C_{Ar}). $C_{25}H_{20}N_2O$ (364.45). Calcd. C 82.39, H 5.53, N 7.69; found C 82.19, H 5.50, N 7.69. ^{1}H-NMR (60 MHz, $CDCl_3$) $\delta = 8.8$–8.4 (3H, m, H-10, H-2′, H-6′), 7.7–6.7 (10H, m, *Ar*H), 3.70 (3H, s, OCH_3), 3.1–2.4 (4H, m, H-5, H-6).

2-Phenyl-4-(3-methoxyphenyl)-5,6-dihydrobenzo[h]quinazoline (**3c**)

Yield: 71%, m.p. 128–130 °C. IR (KBr) $\nu = 1600$, $1590\,cm^{-1}$ (C=C_{Ar}), $1540\,cm^{-1}$ (C=C_{Ar}). $C_{25}H_{20}N_2O$ (364.45). Calcd. C 82.39, H 5.53, N 7.69; found C 82.00, H 5.44, N 7.63. ^{1}H-NMR (60 MHz, $CDCl_3$) $\delta = 8.8$–8.4 (3H, m, H-10, H-2′, H-6′), 7.6–6.7 (10H, m, *Ar*H), 3.70 (3H, s, OCH_3), 3.1–2.4 (4H, m, H-5, H-6).

2-Phenyl-4-(4-methylphenyl)-5,6-dihydrobenzo[h]quinazoline (**3d**)

Yield: 73%, m.p. 159–162 °C. IR (KBr) $\nu = 1605$, $1585\,cm^{-1}$ (C=C_{Ar}), $1535\,cm^{-1}$ (C=C_{Ar}). $C_{25}H_{20}N_2$ (348.45). Calcd. C 86.18, H 5.79, N 8.04; found C 86.42, H 5.68, N 8.09. ^{1}H-NMR (60 MHz, $CDCl_3$)

$\delta = 8.7–8.2$ (3H, m, H-10, H-2′, H-6′), 7.6–6.8 (10H, m, *Ar*H), 3.1–2.4 (4H, m, H-5, H-6), 2.31 (3H, s, CH_3).

2-Phenyl-4-(4-chlorophenyl)-5,6-dihydrobenzo[h]quinazoline (**3e**)

Yield: 82%, m.p. 171–173 °C. IR (KBr) $\nu = 1600\,cm^{-1}$ ($C{=}C_{Ar}$), $1540\,cm^{-1}$ ($C{=}C_{Ar}$). $C_{24}H_{17}ClN_2$ (368.87). Calcd. C 78.15, H 4.65, N 7.59; found C 78.20, H 4.60, N 7.60. ^{1}H-NMR (60 MHz, $CDCl_3$) $\delta = 8.7–8.3$ (3H, m, H-10, H-2′, H-6′), 7.7–6.9 (10H, m, *Ar*H), 3.1–2.5 (4H, m, H-5, H-6).

2-Phenyl-4-(3-chlorophenyl)-5,6-dihydrobenzo[h]quinazoline (**3f**)

Yield: 68%, m.p. 123–126 °C. IR (KBr) $\nu = 1610, 1590\,cm^{-1}$ ($C{=}C_{Ar}$), $1540\,cm^{-1}$ ($C{=}C_{Ar}$). $C_{24}H_{17}ClN_2$ (368.87). Calcd. C 78.15, H 4.65, N 7.59; found C 77.91, H 4.76, N 7.45. ^{1}H-NMR (60 MHz, $CDCl_3$) $\delta = 8.7–8.3$ (3H, m, H-10, H-2′, H-6′), 7.7–6.9 (10H, m, *Ar*H), 3.0–2.5 (4H, m, H-5, H-10).

2-Phenyl-4-(2-chlorophenyl)-5,6-dihydrobenzo[h]quinazoline (**3g**)

Yield: 65%, m.p. 136–139 °C. IR (KBr) $\nu = 1595\,cm^{-1}$ ($C{=}C_{Ar}$), $1530\,cm^{-1}$ ($C{=}C_{Ar}$). $C_{24}H_{17}ClN_2$ (368.87). Calcd. C 78.15, H 4.65, N 7.59; found C 77.91, H 4.76, N 7.45. ^{1}H-NMR (60 MHz, $CDCl_3$) $\delta = 8.7–8.3$ (3H, m, H-10, H-2′, H-6′), 7.6–6.9 (10H, m, *Ar*H), 3.0–2.4 (4H, m, H-5, H-6).

General Procedure for Preparation of N-Acetyl-tetrahydrobenzo[h]quinazolines **5**

Tetrahydrobenzo[h]quinazoline **2** (0.008mol) was dissolved in 100 ml of anhydrous pyridine and acetic acid anhydride (0.024 mol) was added. The reaction mixture was refluxed with exclusion of atmospheric moisture for 6 h, then it was poured into crushed ice. After standing overnight, the precipitate formed was filtered off, washed free of acid with water, dried, and chromatographed (Merck, Kieselgel 60, 0.063–0.2 mm; benzene). The product was recrystallized from methanol to yield yellow crystals.

3-Acetyl-2,4-diphenyl-3,4,5,6-tetrahydrobenzo[h]quinazoline (**5a**)

Yield: 73%, m.p. 163–165 °C. IR (KBr) $\nu = 1675\,cm^{-1}$ (amide I). $C_{26}H_{22}N_2O$ (378.47). Calcd. C 82.51, H 5.86, N 7.40; found C 82.27, H 5.75, N 7.24.

3-Acetyl-2-phenyl-4-(4-methoxyphenyl)-3,4,5,6-tetrahydrobenzo[h]quinazoline (**5b**)

Yield: 77%, m.p. 175–178 °C. IR (KBr) $\nu = 1680\,cm^{-1}$ (amide I). $C_{27}H_{24}N_2O_2$ (408.50). Calcd. C 79.39, H 5.92, N 6.86; found C 79.17, H 5.74, N 6.83. Ms (70 eV) m/z (I%) = 408(14), M; 407(6); 366(27); 365(100); 338(1); 321(2); 259(36); 232(5); 230(4); 129(4); 128(8); 127(7); 77(6); 43(18).

3-Acetyl-2-phenyl-4-(4-methylphenyl)-3,4,5,6-tetrahydrobenzo[h]quinazoline (**5d**)

Yield: 75%, m.p. 123–126 °C. IR (KBr) $\nu = 1680\,cm^{-1}$ (amide I). $C_{27}N_{24}N_2O$ (392.50). Calcd. C 82.62, H 6.16, N 7.14; found C 82.50, H 6.35, N 7.02. Ms (70 eV) m/z (I%) = 392(13), M; 391(6); 350(28); 349(100); 333(0.9); 322(1); 260(9); 259(47); 246(5); 232(4); 230(5); 129(6); 128(9); 127(8); 115(5); 77(3); 43(14).

3-Acetyl-2-phenyl-4-(4-chlorophenyl)-3,4,5,6-tetrahydrobenzo[h]quinazoline (**5e**)

Yield: 81%, m.p. 167–170 °C. IR (KBr) $\nu = 1680\,cm^{-1}$ (amide I). $C_{26}H_{21}ClN_2O$ (412.92). Calcd. C 75.63, H 5.13, N 6.78; found C 75.55, H 5.09, N 6.81.

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