

Full Paper

Facile Synthesis of 5, 6, 7, 8-Tetrahydropyrimido [4, 5-b]-quinoline Derivatives

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Abstract: 2-Amino-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile (**3**) was synthesized by treating cyclohexanone (**1**) with 2-benzylidenemalononitrile (**2**) in the presence of ammonium acetate. The reactivity of compound **3** towards dimethylformamide dimethyl acetal (DMF-DMA), carbon disulfide, urea, thiourea, formamide, formic acid, acetyl chloride and isothiocyanate were studied. In addition, the antimicrobial activity of some selected derivatives is reported.

Keywords: Tetrahydroquinoline; pyrimidine; thiourea; pyrimidoquinoline; X-ray crystal structure.

Introduction

Pyrimidoquinolines are important compounds because of their biological properties, which are known to depend mainly on the nature and position of substituents, and include antimalarial [1], anticancer [2], antimicrobial [3, 4], and anti-inflammatory activities [5, 6]. Recently there has also been considerable interest in the synthesis and chemistry of tetrahydroquinolines and their fused derivatives [7-11]. Our aim in the work presented herein was to synthesize pyrimido[4,5-b]quinolines using tetrahydroquinoline carbonitriles as building blocks. Such a synthesis of condensed azines is of biological interest due to the formal isoelectronic relationship that exists between the pyrimidine ring and tetrahydroquinoline [12-23].

Results and Discussion

Treatment of cyclohexanone (**1**) with the α,β -unsaturated nitrile derivative **2** in the presence of ammonium acetate afforded the tetrahydroquinoline derivative **3**. The structure of **3** was unambiguously confirmed by X-ray crystallography (cf. Figure 1 and Table 1). On the other hand, compounds **4a,b** could be obtained upon reaction of **1** with **2** in absolute ethanol in the presence of *p*-chloroaniline or *p*-hydroxyaniline (Scheme 1).

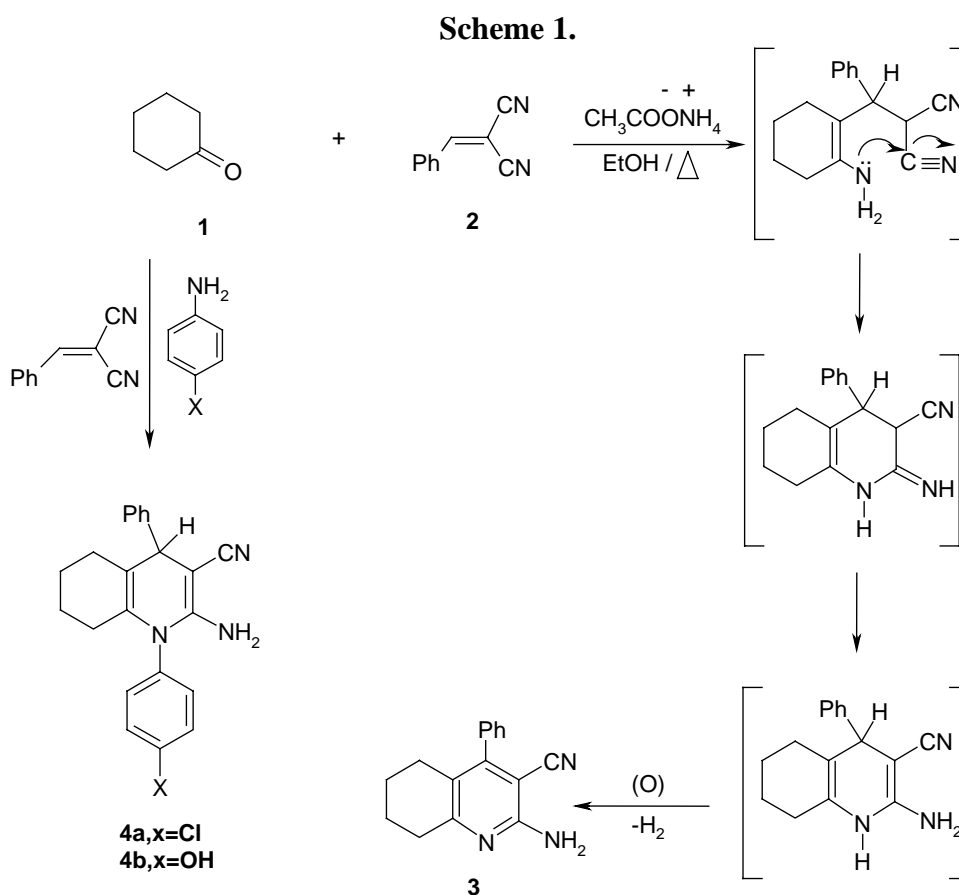


Figure 1. ORTEP diagram of compound **3**.

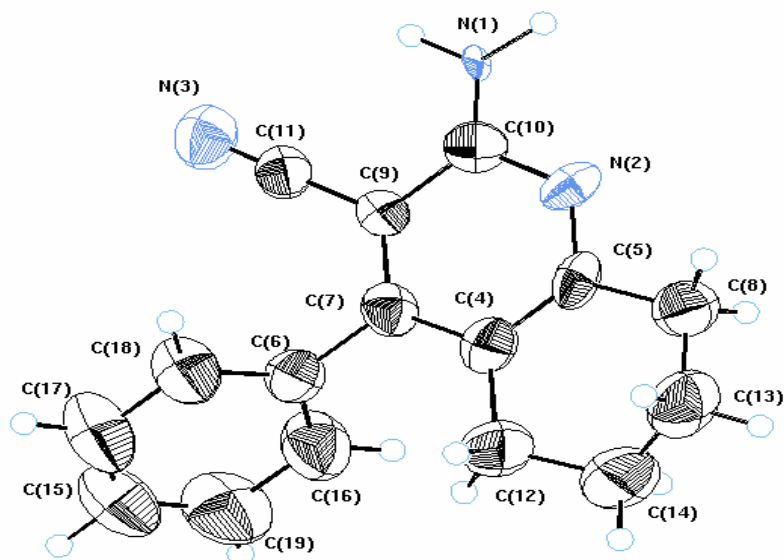


Table 1. Crystal data and structure refinement for compound **3**.

Empirical formula	C ₁₆ H ₁₅ N ₃
Formula weight	249.317
Temperature	289 K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2 ₁ /c
Unit cell dimensions	a = 12.7076 (11) Å b = 5.8985 (5) Å c = 18.227 (2) Å α = 90.00° β = 101.395 (3)°
Volume	1339.3(7) Å ³
Z, Calculated density	4, 1.237 Mg/m ³
Absorption coefficient	0.08 mm ⁻¹
F(000)	236
Crystal size	1.00 x 0.22 x 0.16 mm
Diffract meter	Kappa CCD
θ Rang (°)	2.910—19.211 °
Limiting indices	-11 ≤ h ≤ 11, -5 ≤ k ≤ 5, -16 ≤ l ≤ 16
Reflections collected / unique	2106 / 1242 [R(int) = 0.044]
Absorption correction	None
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	1242 / 0 / 172
Goodness-of-fit on F ²	2.291
Final R indices [I > 3σ(I)]	R ₁ = 0.055, wR ₂ = 0.103
R indices (all data)	R ₁ = 0.1261, wR ₂ = 0.117
Extinction coefficient	0.047(2)
Largest diff. peak and hole	0.37 and -0.30 e. Å ⁻³

Compound **3** reacted with DMF-DMA in dioxane to afford compound **5**, whose structure was also unambiguously confirmed by X-ray crystallography (Figure 2 and Table 2). When compound **5** was refluxed with hydrazine hydrate in absolute ethanol it yielded the corresponding 3-amino-4(3H) imino-5-phenyl-6,7,8,9-tetrahydropyrimido[4, 5-b]quinoline (**7**) through the intermediate **6** (Scheme 2).

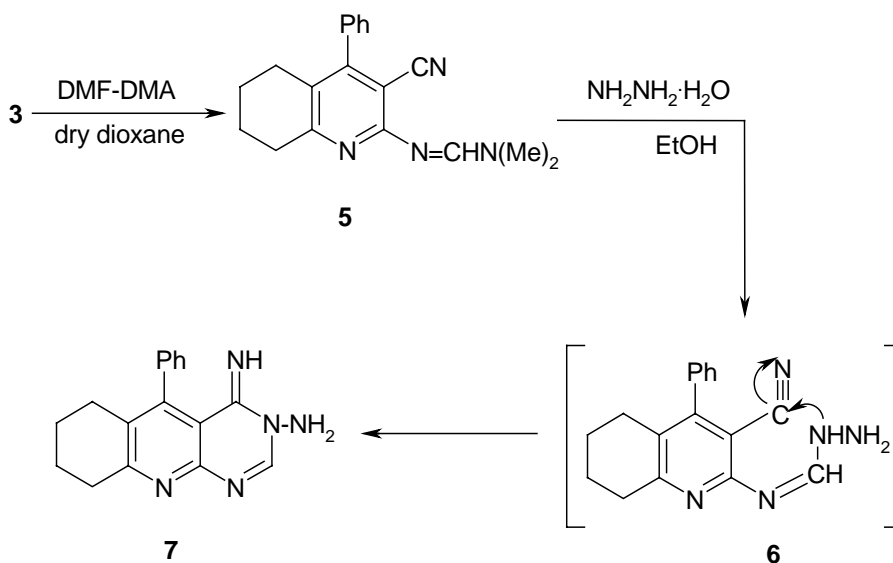
Scheme 2.

Figure 2. ORTEP diagram of Compound 5.

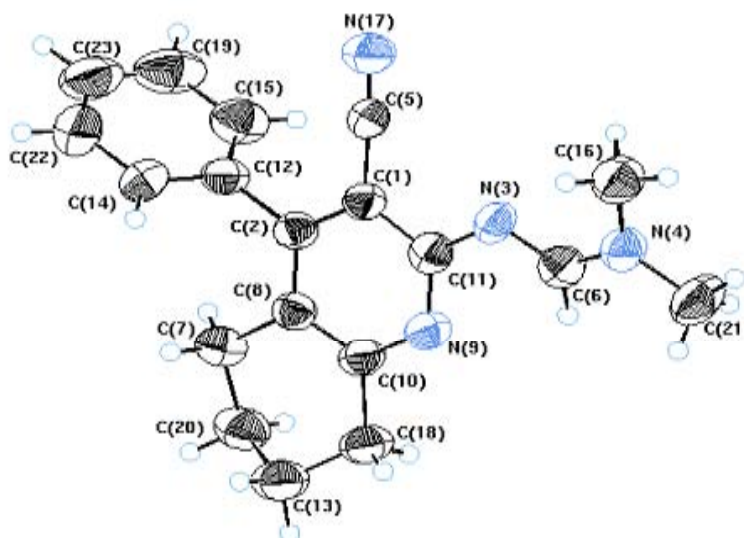


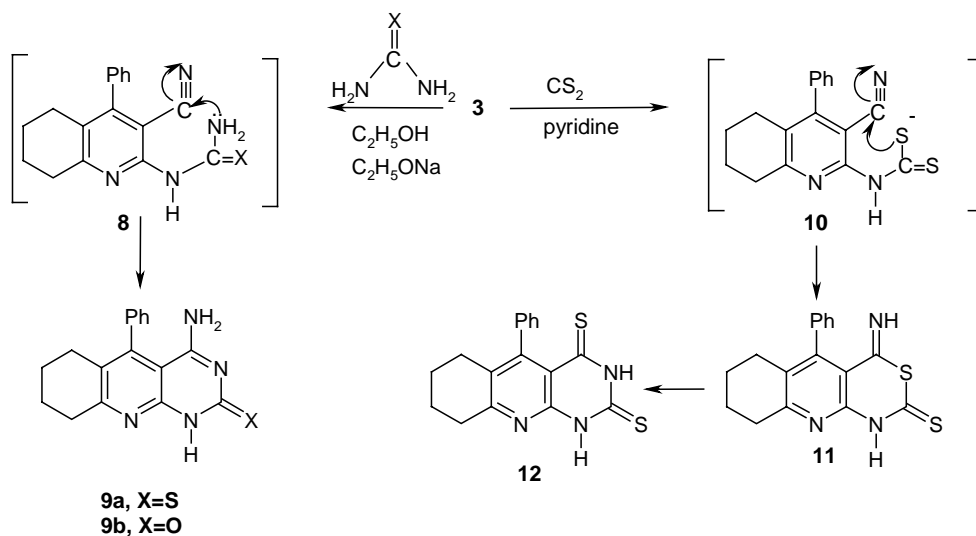
Table 2. Crystallographic and experimental data of compound 5.

Empirical formula	$C_{19}H_{20}N_4$
Formula weight	304.359
Temperature	298 K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, $P2_1/c$
Unit cell dimensions	$a = 7.3256 (4) \text{ \AA}$ $b = 11.4319 (6) \text{ \AA}$ $c = 20.2817 (11) \text{ \AA}$ $\alpha = 90.00^\circ$ $\beta = 98.810 (3)^\circ$
Volume	$1678.5 (2) \text{ \AA}^3$
Z, Calculated density	4, 1.493 Mg/m^3
Absorption coefficient	0.10 mm^{-1}
F(000)	236
Crystal size	$1.00 \times 0.22 \times 0.16 \text{ mm}$
Diffract meter	Kappa CCD
θ Rang ($^\circ$)	$2.910\text{--}26.733^\circ$
Limiting indices	$-9 \leq h \leq 9, -13 \leq k \leq 14, -25 \leq l \leq 24$
Reflections collected / unique	5914 / 4177 [R(int) = 0.048]
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1395 / 0 / 208
Goodness-of-fit on F^2	2.768
Final R indices [$I > 3\sigma(I)$]	$R_1 = 0.093, wR_2 = 0.223$
R indices (all data)	$R_1 = 0.381, wR_2 = 0.218$
Extinction coefficient	$0.030(2)$
Largest diff. peak and hole	0.68 and $-0.67 \text{ e. \AA}^{-3}$

Compound **3** reacted with thiourea or urea in an ethanol/sodium ethoxide mixture for 6 h to afford the 4-amino-10-phenyl-6, 7, 8, 9-tetrahydropyrimido[4,5-b]quinoline-2(1H)-thione/one derivatives **9a** and **9b** (Scheme 3). The reaction products **9** were formed via the intermediate **8** by loss of an ammonia molecule, followed by an intramolecular addition to the cyano function to give the final isolated products **9a,b**.

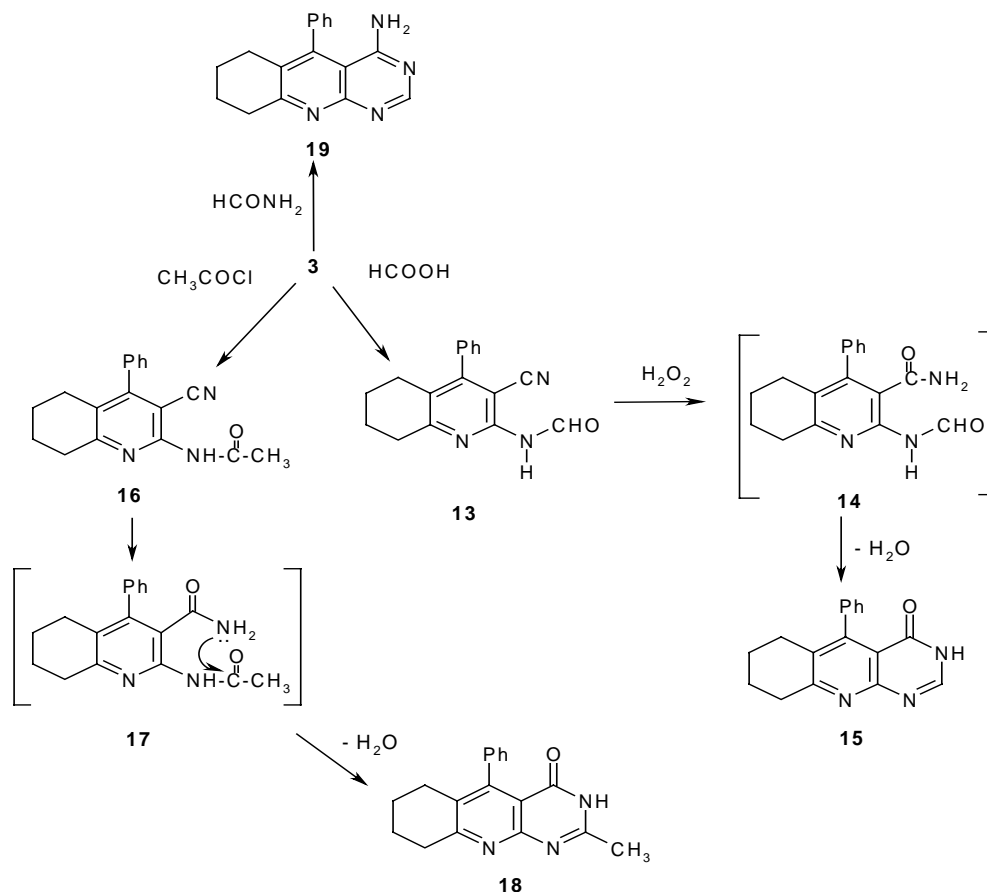
The target ring system **12** was synthesized by reaction of **3** with carbon disulfide through the intermediates **10** and **11**, whose subsequent rearrangement leads to the fused pyrimidinedithione **12**.

Scheme 3.



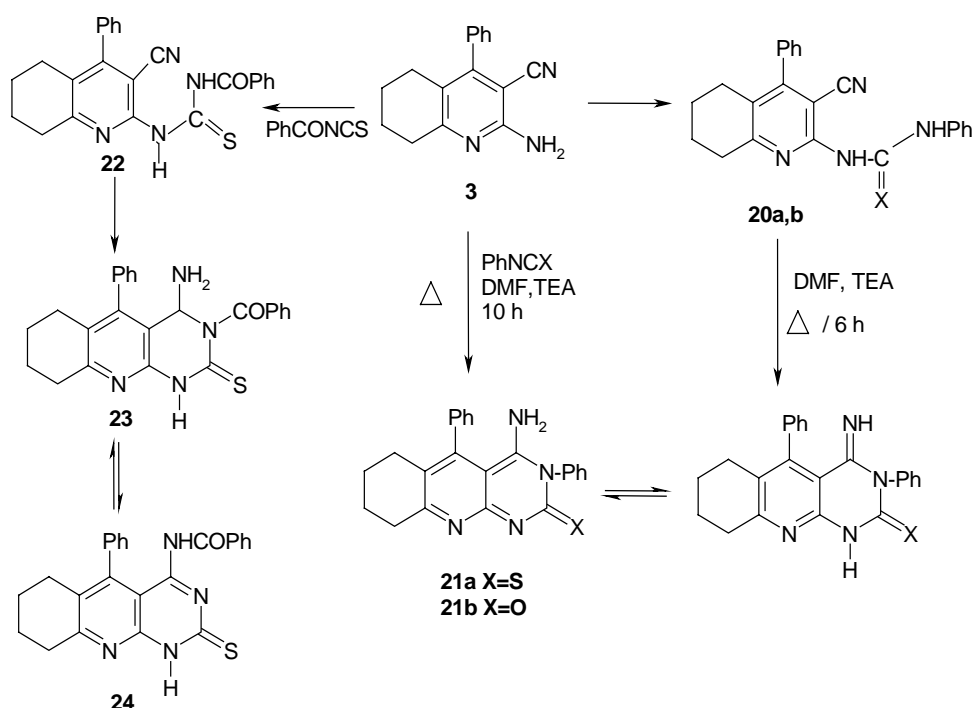
Compound **3** reacted with formic acid to yield **13**, which was treated with alkaline hydrogen peroxide to give the corresponding cyclized pyrimidoquinoline derivative **15** via the intermediate **14**. The reaction proceeds by initial hydration of the nitrile group to give a carboxamide, which then undergoes cyclization in the alkaline medium. The structures of both **13** and **15** were confirmed by elemental and spectral analyses. Meanwhile, acylation of **3** with acid chloride gave 2-methyl-5-phenyl-6,7,8,9-tetrahydropyrimido[4,5-b]quinolin-4-(3H)one (**18**) through the intermediates **16** and **17** (Scheme 4).

Scheme 4.



In addition, compound **3** was refluxed with excess formamide to afford 4-amino-5-phenyl-6,7,8,9-tetrahydropyrimido[4,5-b]quinoline (**19**) (Scheme 4). The structure of the reaction product was established based on its elemental analysis and spectra data. Both isocyanates and isothiocyanates reacted with **3** to give initially the corresponding substituted ureido or thioureido derivatives **20a,b**, which readily cyclized to give the corresponding fused heterocyclic systems **21a,b** (Scheme 5). The same reaction products **21a,b** could be obtained in a one step reaction through prolonged heating of **3** with phenylisocyanate or phenyl isothiocyanate in DMF containing a catalytic amount of TEA. Finally, compound **3** reacted with benzoylisothiocyanate to yield **22**, which then cyclized into **23** which undergoes a Dimroth rearrangement to give **24** (Scheme 5).

Scheme 5.



Biological Activity

Screening of antimicrobial activity was performed at the Microbiology Lab of the National Research Center. Representative derivatives **3**, **4a**, **4b**, **7**, **9a**, **12**, **13**, **15**, **18**, **20**, **22** and **24** were selected and tested for their antimicrobial activity against three yeasts (*Candida albicans*, *Aspergillus niger* and *Saccharomyces cerevisiae*) and two bacteria (*Staphylococcus aureus* and *Escherichia coli*) using the modified agar diffusion cylinder method [24]. The results are given in Table 3.

Table 3. The antimicrobial activity of select derivatives at 1000 ppm concentration.

Compd.	Species tested				
	<i>C. albicans</i>	<i>A. niger</i>	<i>S. cerevisiae</i>	<i>S. aureus</i> Gram (+ve)	<i>E. coli</i> Gram (-ve)
3	-	+	-	+	+
4a	-	++	++	++	-
4b	+	-	++	-	+
7	+	-	-	++	-
9a	+	+++	+	-	-

Table 3. Cont.

Compd.	Species tested				
	<i>C. albicans</i>	<i>A. niger</i>	<i>S. cerevisiae</i>	<i>S. aureus</i> Gram (+ve)	<i>E. coli</i> Gram (- ve)
12	++	-	+	+	-
13	-	+	+++	-	+
15	+	++	-	+	-
18	-	++	+	+	-
20a	++	+	+	-	+
22	++	+	++	-	+
24	++	+	++	-	+

+++ : Strong activity, ++ : Moderate activity, + : Weak activity, - : No activity

Conclusions

The varied biological activities of tetrahydropyrimidoquinoline derivatives prompted us to synthesize some new compounds and study their antimicrobial activities. The antifungal activity assays showed that compounds **12**, **20a**, **22** and **24** display moderate activity against *C. albicans*, while compound **9a** shows strong activity against *A. niger* and compound **13** shows strong activity against *S. cerevisiae*. The bactericidal activity studies revealed that compounds **4a** and **7** show moderate activities against *S. aureus*.

Experimental

General

All melting points are uncorrected. Elemental analyses were carried out in the Microanalytical Center, Cairo University, Giza, Egypt. IR spectra (KBr) were recorded on Pye Unicam SP 1200 Spectrophotometer. ¹H-NMR spectra were recorded in CDCl₃ or DMSO- d₆ on a 90 MHz Varian NMR Spectrometer using TMS as an internal standard and chemical shifts are expressed as δ ppm units. The mass spectra were determined with HP model MS-5988 at electron energy 70 eV. The homogeneity of all compounds synthesized was checked by TLC on 2.0cm x 6.0cm aluminum sheets recoated with silica gel 60 containing a fluorescent indicator, to a thickness of 0.25. Characterization data of the various compounds prepared are given in Tables 4 and 5.

X-ray crystallography [25]

X-ray quality crystals of the title compounds **3** and **5** were obtained by slow crystallization from dimethyl sulfoxide. Experimental data is summarized in Tables 1 and 2. The data were collected with the maXus computer programs on a Bruker Nonius instrument [26-30].

2-Amino-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile (3).

A solution of cyclohexanone (**1**, 0.01 mol) in absolute ethanol (30 mL) containing excess ammonium acetate and the arylidene derivative **2** (0.01 mol) was heated under reflux for 3-5 h. The solid material which separated during heating was collected by filtration and recrystallized from ethanol to yield the tetrahydroquinoline derivative **3**.

2-Amino-3-cyano-1,4-diphenyl-1,4,5,6,7,8-hexahydroquinoline derivatives 4a,b.

A solution of **2** (0.01 mol) and absolute ethanol (100 mL) was placed in a conical flask, cyclohexanone (**1**, 0.01 mol) and *p*-chloroaniline or *p*-hydroxylaniline (0.01 mol) were added and the reaction mixture was refluxed for 10-12 h. and then left to cool to room temperature overnight. The solids obtained were recrystallized from ethanol to give the title compounds **4a,b**.

2-Dimethylaminomethelenimino-3-cyano-4-phenyl-5,6,7,8-tetrahydroquinoline (5)

A solution of **3** (0.005 mol) in dry dioxane (20 mL) and DMF-DMA (0.005 mol) was refluxed for 4 hr. and the reaction mixture was then cooled to room temperature and poured into ice/cold water to complete precipitation. The solid was filtered off and recrystallized from ethanol to give compound **5**.

3-Amino-4-(3H)imino-5-phenyl-6,7,8,9-tetrahydropyrimido[4,5-b]quinoline (7).

A mixture of **5** (0.005 mol) and hydrazine hydrate (0.005 mol) in absolute ethanol (30 mL) was refluxed for 4 hr. and the reaction mixture was left at room temperature overnight and then poured into ice/cold water to complete precipitation. The product was filtered off and recrystallized from dry benzene to give compound **7**.

4-Amino-5-phenyl-6,7,8,9-tetrahydropyrimido[4,5-b]quinoline-2(1H)-thione/one derivatives 9a,b.

A mixture of **3** (0.005 mol) and thiourea (0.005 mol) or urea (0.005 mol) in absolute ethanol (20 mL) containing sodium ethoxide (0.005 mol) was refluxed for 6 hr. The reaction mixture was left to cool to room temperature, then poured into ice cold water (50 mL) and neutralized with dilute hydrochloric acid; the separated material was filtered off and recrystallized from ethanol to give compounds **9a,b**.

5-Phenyl-1,3,6,7,8,9-hexahydropyrimido[4,5-b]quinolin-2,4-dithione (12).

To a solution of **3** (0.005 mol) in dry pyridine (30 mL) carbon disulphide (0.005 mol) was added and the reaction mixture was refluxed on a water bath for 6 hr., then left to cool to room temperature, poured into cold water and neutralized with diluted hydrochloric acid to complete precipitation. The solid obtained was filtered off, washed with water, dried well and recrystallized from methanol to give compound **12**.

2-Formylamino-3-cyano-4-phenyl-5,6,7,8-tetrahydroquinoline (13).

An equimolar amount of **3** (0.005 mol) and formic acid (0.005 mol) in absolute ethanol (30 mL) was refluxed for 2 hr. The reaction mixture was then concentrated and left to cool overnight to room temperature for complete precipitation. The precipitated solid was filtered off, dried well and recrystallized from aqueous ethanol to give compound **13**.

5-Phenyl-6,7,8,9-tetrahydropyrimido[4,5-b]quinolin-4(3H)-one (15).

A solution of **13** (0.002 mol) in potassium carbonate (10 %, 10 mL) and hydrogen peroxide (30 %, 5 mL) was refluxed for 1 hr. The reaction mixture was left to cool at room temperature for complete precipitation. The precipitated solid was collected by filtration and recrystallized from aqueous ethanol to give compound **15**.

2-Methyl-5-phenyl-6,7,8,9-tetrahydropyrimido[4,5-b]quinolin-4(3H)-one (18).

Acetyl chloride (0.005 mol) was added to a solution of **3** (0.005 mol) in dry pyridine (30 mL) and the mixture was refluxed on a water bath for 3 hr., then left to cool to room temperature and poured into ice cold water and neutralized by diluted hydrochloric acid for complete precipitation. The separated material was collected by filtration, washed with water, dried well and recrystallized from acetic acid to yield compound **18**.

4-Amino-5-phenyl-6,7,8,9-tetrahydropyrimido[4,5-b]quinoline (19).

Compound **3** (0.005 mol) and an excess of formamide was placed in a conical flask and the reaction mixture was refluxed for 4 hr., then left to cool for complete precipitation. The separated solid product was filtered and recrystallized from ethanol to give compound **19**.

2-(Phenylthioureido)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile (20a,b).

A mixture of **3** (0.005 mol) and phenylisothiocyanate (0.005 mol) or phenylisocyanate (0.005 mol) in dimethylformamide containing a catalytic amount of triethylamine (4 drops) was refluxed for 6 hr. and then left to cool to room temperature. The reaction mixture was poured into cold water for complete precipitation, then filtered off washed with water dried well and recrystallized from aqueous methanol to give compounds **20a,b**

4-Amino-5-phenyl-6,7,8,9-tetrahydropyrimido[4,5-b]quinoline-2(3H) thione/one derivatives (21a,b).

Method A: A few drops of triethylamine were added to a solution of **20a,b** (0.005 mol) in dimethylformamide and the reaction mixture was refluxed for 6 hr., then left to cool. The product was filtered off, washed with water, dried well and recrystallized from ethanol to give compounds **21a,b**.

Method B: An equimolar mixture of **3** (0.005 mol) and phenylisocyanate (0.005 mol) or phenylisothiocyanate (0.005 mol) in dimethylformamide (30 mL) in the presence of a few drops of triethylamine (4 drops) was refluxed for 10 hr. The reaction mixture was left to cool and poured into cold water for complete precipitation. The separated solid was filtered off, washed with water, dried well and recrystallized from ethanol to give compounds **21a, b**.

2-(Phenylthioureido)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile (22).

A mixture of **3** (0.005 mol) and benzoylisothiocyanate (0.005 mol) in dimethylformamide (30 mL) containing a catalytic amount of triethylamine (4 drops) was refluxed for 6 hr. and left to cool to room temperature. The reaction mixture was poured into cold water for complete precipitation, and then filtered off, washed with water dried well and recrystallized from aqueous methanol to give compound **22**.

3-Benzoylamino-5-phenyl-6,7,8,9-tetrahydropyrimido[4,5-b]quinolin-2-(1H)thione (24).

Method A: To a solution of **22** (0.005 mol) in dimethylformamide was added few drops of triethylamine. The reaction mixture was refluxed 6 hr., then left to cool, the solids filtered off, washed with water, dried well and recrystallized from ethanol to give compound **24**.

Method B: An equimolar mixture of **3** (0.005 mol) and benzoylisothiocyanate (0.005 mol) was refluxed for 10 hr. in dimethylformamide (30 mL) containing four drops of triethylamine. The reaction mixture was left to cool and poured into cold water for complete precipitation. The separated solid was filtered off, washed with water, dried well and recrystallized from ethanol to give compound **24**.

Table 4. Physical properties and elemental analyses of the new compounds.

Compd.	M.P. °C	Formula (mw)	Analysis % Calcd. (Found)				
			C	H	N	S	Cl
3	240	C ₁₆ H ₁₅ N ₃ (249.326)	77.08 (77.02)	6.06 (6.01)	16.86 (16.86)	–	–
4a	270	C ₂₂ H ₂₀ N ₃ Cl (361.87)	73.02 (73.00)	5.57 (5.46)	11.61 (11.49)	–	9.8 (9.74)
4b	260	C ₂₂ H ₂₁ N ₃ O (343.43)	76.94 (76.89)	6.16 (6.04)	12.24 (12.15)	–	–
5	184	C ₁₉ H ₂₀ N ₄ (304.373)	74.98 (74.89)	6.62 (6.56)	18.14 (18.20)		
7	210	C ₁₇ H ₁₇ N ₅ (291.323)	70.33 (70.24)	5.55 (5.47)	24.12 (24.04)	–	–
9a	290	C ₁₇ H ₁₆ N ₄ S (308.413)	66.21 (66.07)	5.22 (5.09)	18.17 (18.07)	10.4 (10.34)	–
9b	213	C ₁₇ H ₁₆ N ₄ O (292.342)	69.85 (69.74)	5.51 (5.43)	19.17 (19.11)	–	–

Table 4. Cont.

Compd.	M.P. °C	Formula (mw)	Analysis % Calcd. (Found)				
			C	H	N	S	Cl
12	207~209	C ₁₇ H ₁₅ N ₃ S ₂ (325.464)	62.74 (62.79)	4.64 (4.62)	12.91 (12.94)	19.70 (19.79)	–
13	195~196	C ₁₇ H ₁₅ N ₃ O (277.332)	73.63 (73.74)	5.45 (5.40)	15.15 (15.21)	–	–
15	187~188	C ₁₇ H ₁₅ N ₃ O (277.332)	73.63 (73.83)	5.45 (5.14)	15.15 (15.27)	–	–
18	187~188	C ₁₈ H ₁₇ N ₃ O (291.364)	74.21 (74.03)	5.88 (5.73)	14.42 (14.27)	–	–
19	205	C ₁₇ H ₁₆ N ₄ (276.343)	73.89 (73.84)	5.83 (5.78)	20.27 (20.18)	–	–
20a	172	C ₂₃ H ₂₀ N ₄ S (384.51)	71.84 (72.01)	5.24 (5.29)	14.57 (14.59)	8.34 (8.29)	–
20b	160	C ₂₃ H ₂₀ N ₄ O (368.444)	74.98 (74.67)	5.47 (5.63)	15.21 (15.04)	–	–
21a	218	C ₂₃ H ₂₀ N ₄ S (384.51)	71.84 (72.00)	5.24 (5.29)	14.57 (14.52)	8.34 (8.29)	–
21b	190	C ₂₃ H ₂₀ N ₄ O (368.444)	74.98 (74.71)	5.47 (5.67)	15.21 (15.11)	–	–
22	174	C ₂₄ H ₂₀ N ₄ OS (412.527)	69.88 (69.74)	4.88 (4.73)	13.58 (13.42)	7.77 (7.71)	–
24	225	C ₂₄ H ₂₀ N ₄ OS (412.527)	69.88 (69.79)	4.88 (4.81)	13.58 (13.52)	7.77 (7.71)	–

Table 5. IR, ¹H-NMR, and MS of the new compounds.

Compd.	IR (cm ⁻¹)	¹ H-NMR (δ, ppm) and/or MS
3	3420-3305 (NH ₂), 2212 (CN), 1645 (C=N).	1.6-2.8 (m, 8H, 4CH ₂); 5.3(s, 2H, NH ₂); 7.2-7.6 (m, 5H, Ar-H). MS: m/e = 249 (M ⁺ , 100%).
4a	3424-3345 (NH ₂), 2211 (CN), 1650 (C=N).	1.6-2.8 (m, 8H, 4CH ₂); 4.8 (s, 1H, quinoline H-4), 5.8 (s, 2H, NH ₂), 7.2-7.4 (m, 9H, Ar-H). MS: m/e = 361 (M ⁺ , 18%), 362 (M+1, 6%).
4b	3421 (OH), 3306 (NH ₂), 2215 (CN), 1622 (C=N).	1.6-2.8 (m, 8H, 4CH ₂); 4.8 (s, 1H, quinoline H-4); 5.3 (s, 2H, NH ₂); 7.2-7.6 (m, 9H, Ar-H); 9.2 (s, 1H, OH). MS: m/e = 343 (M ⁺ , 75 %).
5	2216 (CN), 1623 (C=N).	1.6-2.8 (m, 8H, 4CH ₂); 3.2 (s, 6H, 2CH ₃); 7.2-7.4 (m, 5H, Ar-H); 8.4 (s, 1H, vinyl H). MS: m/e = 304 (M ⁺ , 100%).
7	3421-3360 (NH ₂), 3148 (NH), 1645 (C=N).	1.6-2.8 (m, 8H, 4CH ₂); 5.4 (s, 2H, NH ₂); 7.2-7.4 (m, 5H, Ar-H); 7.50 (s, 1H, pyrimidine H); 8.01 (s, 1H, NH). MS: m/e = 291 (M ⁺ , 15%).

Table 5. Cont.

Compd.	IR (cm ⁻¹)	¹ H-NMR (δ, ppm) and/or MS
9a	3408-3320 (NH ₂), 3226 (NH), 1337 (C=S).	1.6-2.8 (m, 8H, 4CH ₂); 5.4 (s, 2H, NH ₂); 7.1-7.5 (m, 5H, Ar-H); 8.2 (s, 1H, NH). MS: m/e = 308 (M ⁺ , 15 %).
9b	3421 (NH ₂), 3426 (NH), 1717 (C=O), 1646 (C=N).	MS: m/e = 292 (M ⁺ , 50%).
12	3426 (NH), 1643 (C=N), 1344 (C=S).	1.62-2.88 (m, 8H, 4CH ₂); 5.8 (s, 1H exchangeable, NH); 7.12- 7.64 (m, 5H, Ar-H); 9.08 (bs, 1H, exchangeable, NH). MS: m/e = 325 (M ⁺ , 10%).
13	3228 (NH), 2211 (CN), 1692 (C=O), 1581 (C=N).	MS: m/e = 277 (M ⁺ , 30%).
15	3146 (NH), 1707 (C=O), 1645 (C=N).	1.34-1.98 (m, 8H, 4CH ₂); 7.13-7.35 (m, 5H, Ar-H); 7.50 (s, 1H, pyrimidine H); 8.01 (s, 1H, NH).
18	3146 (NH), 1707 (C=O), 1645 (C=N).	0.9 (s, 3H, CH ₃); 1.34-1.96 (m, 8H, 4CH ₂); 7.14-7.30 (m, 5H, Ar-H); 8.01 (s, 1H, NH). MS: m/e = 291 (M ⁺ , 15%).
19	3319-3322 (NH ₂), 1661 (C=N).	1.35-2.68 (m, 8H, 4CH ₂); 5.4 (s, 2H, NH ₂); 4.8 (s, 1H, pyrimidine H); 7.13-7.46 (m, 5H, Ar-H). MS: m/e = 276 (M ⁺ , 55 %).
20a	3148 (NH), 3059 (NH), 2211(CN), 645 (C=N), 1346 (C=S).	MS: m/e = 384 (M ⁺ , 10%).
20b	3179 (NH), 3149 (NH), 2228 (CN), 1707 (C=O), 1631 (C=N).	MS: m/e = 368(M ⁺ , 40%).
21a	3421 – 3307 (NH ₂), 1645 (C=N), 1346 (C=S).	MS: m/e = 384 (M ⁺ , 10%).
21b	3419-3303 (NH ₂), 1645 (C=N), 1707 (C=O).	MS: m/e = 368 (M ⁺ , 40%).
22	3148 (NH), 3059 (NH), 2211 (CN), 1677 (C=O), 1645(C=N), 1346 (C=S).	MS: m/e = 412 (M ⁺ , 10%).
24	3182 (NH), 3120 (NH), 1672 (C=O), 1605 (C=N), 1363 (C=S) .	MS: m/e = 412 (M ⁺ , 10%).

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