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# Synthetic approaches towards benzo[*h*]quinoline-3-carbonitriles

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2-Alkoxybenzo[*h*]quinoline-3-carbonitriles **2** were readily synthesized *via* Dimroth rearrangement of 2-amino-4-aryl-5,6-dihydro-4*H*-naphtho[1,2-*b*]pyran-3-carbonitriles **5** induced by ethanolic and methanolic KOH. Compounds **2** were also obtained by the reaction of 2-arylmethylidene-3,4-dihydro-1(2*H*)-naphthalenones **1** with malononitrile or of ylidenemalononitriles **4** with 1,2,3,4-tetrahydro-1-naphthalenone in ethanolic and methanolic KOH. The molluscicidal activity of the products towards *Biomphalaria alexandrina* snails was screened.

## 1. Introduction

Considerable interest has been directed towards the reaction of α,β-unsaturated Michael acceptors with many active methylene compounds as a general route for carbon carbon bond formation. For example, the reaction of α,β-unsaturated ketones with malononitrile or ethyl cyanoacetate in the presence of ammonium acetate led to the formation of 3-cyanopyridines [1–8]. However, addition of malononitrile to α,β-unsaturated ketones in the presence of organic [9–11] or inorganic [12, 13] basic catalysts yielded open-chain Michael adducts. Otherwise, reaction of malononitrile with 1,2,3-triaryl-2-propen-1-ones gave the 2-amino-3-cyano-4,5,6-triaryl-4*H*-pyrans [14, 15]. It was assumed that the introduction of an aryl group at the α-position of the Michael acceptor is essential for this cyclization process [14, 15]. On the other hand, reaction of 1,3-diaryl-2-propen-1-ones with malononitrile in the presence of a sufficient amount of alkoxide anion led to the formation of 2-alkoxy-3-cyanopyridines [15–17].

In the present work, we investigated the reaction of malononitrile with arylidenes derived from 1,2,3,4-tetrahydro-1-naphthalenone under different reaction conditions, aiming not only to isolate the corresponding benzoquinolines but also to study the route of their formation. The fact that many benzoquinolines have been reported to exhibit interesting biological activity such as antibacterial [18–22], antifungal [23–25], antimalarial [26, 27] antiinflammatory [28], and antihypertensive [29] in addition to herbicidal [25, 30] and insecticidal [25] properties also prompted the present investigation.

## 2. Investigations, results and discussion

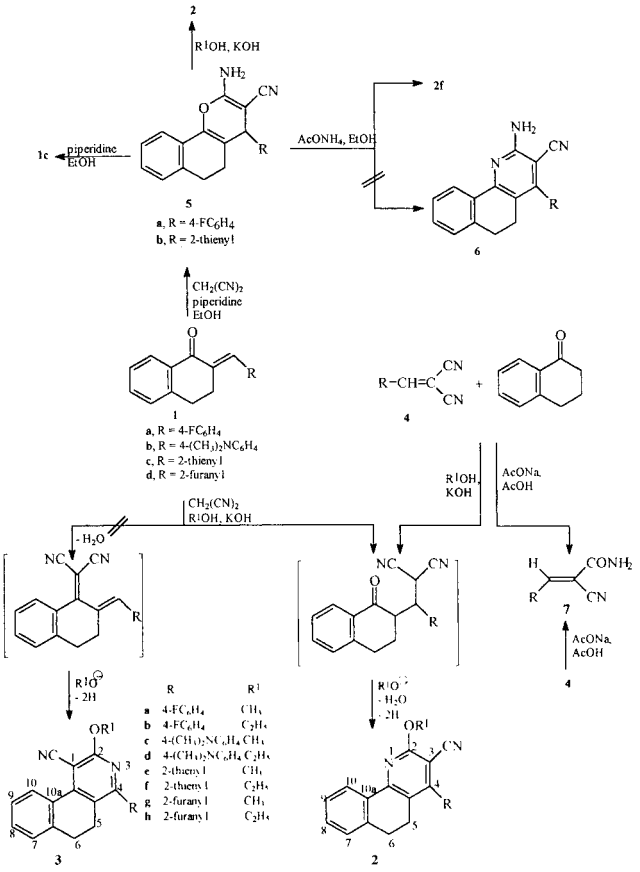
### *2.1. Synthesis of the compounds*

Reaction of 2-arylmethylidene-3,4-dihydro-1(2*H*)-naphthalenones **1a–d** with malononitrile in alcoholic KOH solution gave products, the structure of which could be assigned as either benzo[*h*]quinolines **2** or their isomeric benzo[*f*]isoquinolines **3** based on analytical and spectral data. The formation of **2** was presumably initiated *via* Michael addition of malononitrile at the β-carbon of unsaturated system of **1**. Then, nucleophilic alkoxide anion attack at one of the nitrile groups followed by dehydration and subsequent dehydrogenation finally gave **2**. On the other hand, the formation of **3** probably took place by Knoevenagel condensation of the active methylene compound with the ketonic residue of **1**. Then, through the alkoxide anion attack at the nitrile group followed by dehydrogenation, the condensed isoquinolines 3 were eventually formed. The products isolated were established to be **2** rather than **3** based on their independent synthesis from the reaction of the corresponding ylidenemalononitriles **4** with 1,2,3,4-tetrahydro-1-naphthalenone in alcoholic KOH solution. (Scheme 1).

The structure of **2** was inferred from their IR spectra, which exhibit a nitrile stretching vibration band (2221 to 2214 $cm^{-1}$) and lack of any carbonyl stretching vibration band. Also, $^1H$ NMR spectra reveal the presence of the corresponding alkoxide proton signals confirming the involvement of the alkoxide anion used in the cyclization process and hence the formation of the cyclic product.

On the other hand, reaction of naphthalenones **1a, c** with malononitrile in the presence of piperidine (as a basic catalyst) afforded the corresponding 2-amino-4-aryl-5,6-dihydro-4*H*-naphtho[1,2-*b*]pyran-3-carbonitriles **5a, b**. The structure of **5** was established from analytical and spectral data. Thus, the IR spectra of **5** reveal the amino absorption band at 3476–3171 $cm^{-1}$ and a nitrile stretching vibration band at 2192–2191 $cm^{-1}$. The $^1H$ NMR spectra also exhibit the H-4 pyran singlet signal (δ = 4.09–4.43) in addition to the $D_2O$-exchangeable amino absorption signal (δ = 4.63–4.64).

**Scheme 1**



Treatment of **5a, b** with alcoholic KOH solution led to the formation of the corresponding 2-alkoxybenzo[*h*]quinolines **2**. The reaction presumably took place through Dimroth rearrangement due to the alkoxide nucleophilic attack at the condensed pyran heterocycle.

However, reaction of **5b** with excess ammonium acetate in boiling ethanol yielded the corresponding **2f** instead of the expected 2-amino-4-aryl-5,6-dihydrobenzo[*h*]quinoline-3-carbonitrile **6**. This could either be attributed to the availability of the alkoxide anion in the reaction medium rather than the ammonium anion (where the alkoxide anion largely generated to a large extent in the reaction derived from the ionization of the ethanolic reaction solvent) or may be explained in terms of the nucleophilic strength.

In an attempt to investigate the role of secondary amine on the Dimroth reaction, **5b** was allowed to react with excess piperidine in boiling alcohol, where the corresponding naphthalenone **1c** was isolated. The reaction probably proceeded *via* ring opening of the condensed pyran **5b** due to the effect of the base used, followed by retro-Michael reaction finally giving **1c**.

Alternatively, arylmethylidenemalononitriles **4** were allowed to react with 1,2,3,4-tetrahydro-1-naphthalenone in the presence of excess sodium acetate in boiling acetic acid aiming to isolate the corresponding naphthopyrans **5**. However, the corresponding 3-aryl-2-cyano-2-propenamides **7** were formed exclusively without involving the cycloalkanone used in the reaction. So, the reaction adopted was to boil the ylidenes **4** with sodium acetate in glacial acetic acid.

The present investigation was extended to study the reaction of 3,4-dihydro-2-(2-hydroxyaryl)methylidene-1(2*H*)-naphthalenones **8a**–**c** with malononitrile in alcoholic KOH solution. Thus, whereas **8a** yielded the benzopyran **10** in methanolic KOH solution; **8a**–**c** gave the corresponding benzo[*h*]quinolines **9** in either ethanolic or methanolic KOH. This could be attributed to the effect of the hydroxyl group as a good nucleophilic centre that may attack one of the nitrile groups in the Michael adduct intermediate yielding **10** (Scheme 2). The structure of **10** was established from IR, $^1$H and $^{13}$C NMR spectra in addition to elemental analysis data. $^{13}$C NMR (decoupled and DEPT) exhibit two $CH_2$ signals at δ 23.2, 28.1; two CH signals at δ 34.7, 54.9 and the benzopyran C-3 at δ 52.5 in addition to the other skeletal carbons.

### *2.2. Molluscicidal activity*

Schistosomiasis is the most important trematode disease in man. The intermediate host of *Schistosoma mansoni* which affects the intestinal system and is widespread in Egypt, is called the *Biomphalaria alexandrina* snails. The snails were collected from irrigation canals that were not being treated with molluscicides [31, 32]. The tests were carried out by dissolving 0.1 g of the test compound in 10 ml of acetone and adding the appropriate volume of that solution to 1 l of water to get the required concentration. Ten snails were used in each experiment. Reference experiments were carried out using the same volume of acetone added in 1 l of water. Exposure and recovery periods are 24 h each.

From the results obtained (Table), it is obvious that most of the compounds show mild activity. However, some products exhibit recognizable molluscicidal activity, particularly the 2-arylidene-1-naphthalenones **1**, **8** and condensed 4*H*-pyrans **5**, **10**. These compounds may suggest possible agents with better molluscicidal activity.

**Table: Molluscicidal activity of the compounds**

| Compd. | Number of snails out of 10 killed at a concentration of | | |
|---|---|---|---|
| | 20 ppm | 10 ppm | 5 ppm |
| **1a** | 10 | 9 | 6 |
| **1b** | 10 | 7 | – |
| **1c** | 10 | 7 | 3 |
| **1d** | 10 | 10 | 7 |
| **2a** | – | – | – |
| **2b** | – | – | – |
| **2c** | 2 | 1 | – |
| **2d** | 2 | 2 | – |
| **2e** | 2 | 2 | – |
| **2f** | – | – | – |
| **2g** | 8 | 1 | – |
| **2h** | 2 | 2 | – |
| **5a** | 10 | 10 | 2 |
| **5b** | 10 | 10 | 5 |
| **7a** | 1 | – | – |
| **7b** | 1 | 1 | 1 |
| **7c** | 1 | 1 | 1 |
| **7d** | 1 | – | – |
| **8a** | 10 | 10 | 6 |
| **8b** | 10 | 3 | 3 |
| **8c** | 10 | 10 | 7 |
| **9a** | 6 | 1 | 1 |
| **9b** | 7 | 7 | 7 |
| **9c** | 10 | 7 | 3 |
| **10** | 10 | 10 | 9 |

## 3. Experimental

Melting points are uncorrected. IR spectra were recorded (KBr) on a Perkin Elmer 1650 spectrophotometer. $^1$H NMR spectra were recorded on a Varian GEMINI spectrometer 200 (200 MHz). $^{13}$C NMR (decoupled and DEPT) spectra were recorded on a JEOL EX spectrometer 270 (67.5 MHz). The starting compounds **1a**–**d** [33–36], **4a**–**d** [37–40] and **8a** [41] were prepared according to previously reported procedures. All the results of elemental analyses were as expected within acceptable limits.

#### *3.1. 2-Alkoxy-4-aryl-5,6-dihydrobenzo[h]quinoline-3-carbonitriles* **2a**–**h**

Method A: A mixture of equimolecular amounts of the appropriate **1a**–**d** and malononitrile (5 mmol) in alcoholic KOH solution (25 ml; 4%) was stirred at room temperature (20–25 °C) for 24 h. The solid separated was collected and crystallized from a suitable solvent yielding the corresponding compounds **2a**–**h**.

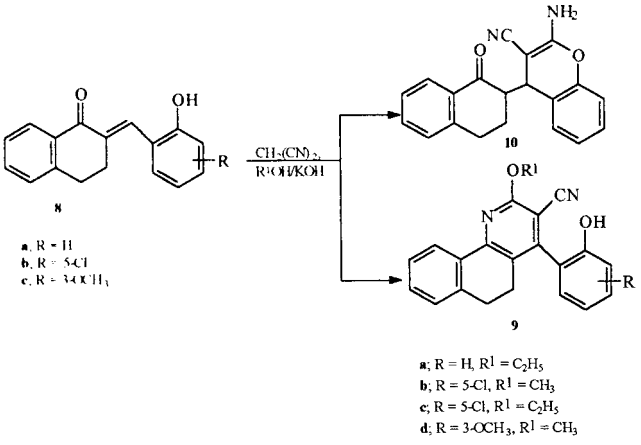
Method B: A mixture of equimolecular amounts of the appropriate **4a**–**d** and 1,2,3,4-tetrahydro-1-naphthalenone (5 mmol) in alcoholic KOH solution (25 ml; 4%) was stirred at room temperature (20–25 °C) for 24 h. The solid separated was collected and crystallized from a suitable solvent yielding the corresponding compounds **2a**–**h**.

*3.1.1. 5,6-Dihydro-4-(4-fluorophenyl)-2-methoxybenzo[h]quinoline-3-carbonitrile* (**2a**)

Crystallized from *n*-butanol (colourless crystals); m.p. 189–190 °C; yield 55, 42% (method A and B, respectively). IR: ν 2218 cm$^{-1}$ (CN); 1603, 1556 (C=N, C=C). $^1$H NMR ($CDCl_3$): δ 2.64-2.87 (m, 4H, 2 $CH_2$); 4.20 (s, 3 H, $OCH_3$); 7.17–8.37 (m, 8 H, arom. H).

$C_{21}H_{15}FN_2O$ (330.4).

**Scheme 2**



*3.1.2. 5,6-Dihydro-2-ethoxy-4-(4-fluorophenyl)benzo[h]quinoline-3-carbonitrile* (**2b**)

Crystallized from ethanol (colourless crystals); m.p. 178–180 °C; yield 47, 38% (method A and B, respectively). IR: ν 2216 $cm^{-1}$ (CN); 1603, 1556 (C=N, C=C). $^1H$ NMR ($CDCl_3$): δ 1.52 (t, 3H, $CH_3$, J = 7 Hz); 2.63–2.87 (m, 4 H, 2 $CH_2$); 4.66 (q, 2 H, $OCH_2$ J = 7 Hz); 7.17–8.35 (m, 8 H, arom. H).
$C_{22}H_{17}FN_2O$ (344.4)

*3.1.3. 5,6-Dihydro-4-(4-dimethylaminophenyl)-2-methoxybenzo[h]-quinoline-3-carbonitrile* (**2c**)

Crystallized from *n*-butanol (yellow crystals); m.p. 224–226 °C; yield 51, 48% (method A and B, respectively). IR: ν 2220 $cm^{-1}$ (CN); 1609, 1560 (C=N, C=C). $^1H$ NMR ($CDCl_3$): δ 2.80 (s, 4 H, 2 $CH_2$); 3.03 [s, 6 H, $N(CH_3)_2$]; 4.17 (s, 3 H, $OCH_3$); 6.78–8.36 (m, 8 H, arom. H).
$C_{23}H_{21}N_3O$ (355.4)

*3.1.4. 5,6-Dihydro-4-(4-dimethylaminophenyl)-2-ethoxybenzo[h]quinoline-3-carbonitrile* (**2d**)

Crystallized from ethanol (yellow crystals); m.p. 215–217 °C; yield 38% (methods A and B). IR: ν 2216 $cm^{-1}$ (CN); 1607, 1546 (C=N, C=C). $^1H$ NMR ($CDCl_3$): δ 1.51 (t, 3H, $CH_2\underline{CH_3}$, J = 7 Hz); 2.79 (s, 4 H, 2 $CH_2$); 3.03 [s, 6 H, $N(CH_3)_2$]; 4.65 (q, 2 H, $\overline{OCH_2}$, J = 7 Hz); 6.78-8.32 (m, 8 H, arom. H).
$C_{24}H_{23}N_3O$ (369.4)

*3.1.5. 5,6-Dihydro-2-methoxy-4-(2-thienyl)benzo[h]quinoline-3-carbonitrile* (**2e**)

Crystallized from *n*-butanol (colourless crystals); m.p. 179–181 °C; yield 44, 50% (method A and B, respectively). IR: ν 2214 $cm^{-1}$ (CN); 1602, 1553 (C=N, C=C). $^1H$ NMR ($CDCl_3$): δ 2.86 (s, 4 H, 2 $CH_2$); 4.18 (s, 3 H, $OCH_3$); 7.17–8.35 (m, 7 H, arom. H).
$C_{19}H_{14}N_2OS$ (318.4)

*3.1.6. 5,6-Dihydro-2-ethoxy-4-(2-thienyl)benzo[h]quinoline-3-carbonitrile* (**2f**)

Crystallized from methanol (colourless crystals); m.p. 131–133° C; yield 42% (methods A and B). IR: ν 2221 $cm^{-1}$ (CN); 1602, 1557 (C=N, C=C). $^1H$ NMR ($CDCl_3$): δ 1.51 (t, 3 H, $CH_3$, J = 7 Hz); 2.85 (s, 4 H, 2 $CH_2$); 4.65 (q, 2 H, $OCH_2$, J = 7 Hz); 7.17–8.32 (m, 7 H, arom. H).
$C_{20}H_{16}N_2OS$ (332.4)

*3.1.7. 5,6-Dihydro-4-(2-furanyl)-2-methoxybenzo[h]quinoline-3-carbonitrile* (**2g**)

Crystallized from a benzene-light petroleum (60–80 °C) mixture as 1 : 20 v/v (colourless crystals); m.p. 155–157 °C; yield 46, 40% (method A and B respectively). IR: ν 2219 $cm^{-1}$ (CN); 1597, 1551 (C=N, C=C). $^1H$ NMR ($CDCl_3$): δ 2.84–2.99 (m, 4 H, 2 $CH_2$); 4.16 (s, 3 H, $OCH_3$); 6.61 to 8.32 (m, 7 H, arom. H).
$C_{19}H_{14}N_2O_2$ (302.3)

*3.1.8. 5,6-Dihydro-2-ethoxy-4-(2-furanyl)benzo[h]quinoline-3-carbonitrile* (**2h**)

Crystallized from methanol (colourless crystals); m.p. 143–144 °C; yield 44, 38% (method A and B, respectively). IR: ν 2217 $cm^{-1}$ (CN); 1587, 1548 (C=N, C=C). $^1H$ NMR ($CDCl_3$): δ 1.51 (t, 3 H, $CH_3$, J = 7 Hz); 2.83–3.03 (m, 4 H, 2 $CH_2$); 4.64 (q, 2 H, $OCH_2$, J = 7.2 Hz); 6.60–8.29 (m, 7 H, arom. H).
$C_{20}H_{16}N_2O_2$ (316.4)

### *3.2. 2-Amino-4-aryl-5,6-dihydro-4H-naphtho[1,2-b]pyran-3-carbonitriles* **5a, b**

A mixture of equimolecular amounts of the appropriate **1a, c** and malononitrile (5 mmol) in absolute ethanol (20 ml) containing piperidine (0.5 ml) was stirred at room temperature (20–25 °C) for 24 h. The solid formed was collected and crystallized from a suitable solvent yielding the corresponding **5a**, **b**.

*3.2.1. 2-Amino-5,6-dihydro-4-(4-fluorophenyl)-4H-naphtho[1,2-b]pyran-3-carbonitrile* (**5a**)

Crystallized from methanol (90%) (colourless crystals); m.p. 190–192 °C; yield 63%. IR: ν 3461, 3316, 3258, 3210 $cm^{-1}$ ($NH_2$); 2192 (CN); 1692, 1651 (C=C). $^1H$ NMR ($CDCl_3$): δ 1.98–2.86 (m, 4 H, 2 $CH_2$); 4.09 (s, 1 H, hetero. H-4); 4.63 (s, 2 H, $NH_2$); 6.98-7.50 (m, 8 H, arom. H).
$C_{20}H_{15}FN_2O$ (318.3)

*3.2.2. 2-Amino-5,6-dihydro-4-(2-thienyl)-4H-naphtho[1,2-b]pyran-3-carbonitrile* (**5b**)

Crystallized from methanol (pale yellow crystals); m.p. 179–181 °C; yield 65%. IR: ν 3476, 3292, 3171 $cm^{-1}$ ($NH_2$); 2191 (CN); 1687, 1633 (C=C). $^1H$ NMR ($CDCl_3$): δ 2.25 (t, 2 H, $CH_2$, J = 8.2 Hz); 2.80 (t, 2 H, $CH_2$, J = 8.6 Hz); 4.43 (s, 1 H, hetero. H-4); 4.65 (s, 2 H, $NH_2$); 6.92–7.49 (m, 7 H, arom. H).
$C_{18}H_{14}N_2OS$ (306.4).

### *3.3. Action of alcoholic KOH on* **5a, b**

A solution of the appropriate **5a**, **b** (3 mmol) in alcoholic KOH solution (25 ml; 4%) was stirred at room temperature (20–25 °C) for 24 h. The solid formed was collected, crystallized from a suitable solvent and identified as the corresponding **2a**, **b**; **e**, **f** (mixed m.p. and IR spectra); yield 51, 49, 52, 50% for **2a**, **2b**, **2e** and **2f**, respectively.

### *3.4. Action of ammonium acetate on* **5b**

A mixture of **5b** (3 mmol) and ammonium acetate (15 mmol) in absolute ethanol (25 ml) was boiled under reflux for 30 h. The solid separated upon cooling the reaction mixture (5 °C) was collected, crystallized from methanol and identified as **2f** (mixed m.p. and IR spectra); yield 60%.

### *3.5. Action of piperidine on* **5b**

A mixture of **5b** (3 mmol) and piperidine (9 mmol) in absolute ethanol (20 ml) was boiled under reflux for 25 h. The solid separated upon cooling the reaction mixture (5 °C) was collected, crystallized from methanol and identified as **1c** (mixed m.p. and IR spectra); yield 69%.

### *3.6. 3-Aryl-2-cyano-2-propenamides* **7a–d**

A mixture of the appropriate **4a–d** (5 mmol) and anhydrous sodium acetate (1 g) in glacial acetic acid (20 ml) was refluxed for the appropriate time. The solid formed was collected and crystallized from a suitable solvent yielding the corresponding **7a–d**.

*3.6.1. 2-Cyano-3-(4-fluorophenyl)-2-propenamide* (**7a**)

Reaction time 24 h; crystallized from benzene (pale yellow crystals); m.p. 152–153 °C; yield 65%. IR: ν 3300, 3162 $cm^{-1}$ ($NH_2$); 2213 (CN); 1701 (CO); 1587 (C=C). $^1H$ NMR ($CDCl_3$): δ 6.10-6.40 (br. s, 2 H, $NH_2$); 7.15 to 8.02 (m, 4 H, arom. H); 8.31 (s, 1 H, olefinic H).
$C_{10}H_7FN_2O$ (190.2)

*3.6.2. 2-Cyano-3-(4-dimethylaminophenyl)-2-propenamide* (**7b**)

Reaction time 50 h; crystallized from toluene (orange yellow crystals); m.p. 191–193 °C; yield 47%. IR: ν 3399, 3155 $cm^{-1}$ ($NH_2$); 2200 (CN); 1679 (CO); 1610 (C=C). $^1H$ NMR ($CDCl_3$): δ 3.11 [s, 6 H, $N(CH_3)_2$]; 5.80–6.20 (br. s, 2 H, $NH_2$); 6.70 (d, 2 H, arom. H, J = 9.2 Hz); 7.90 (d, 2 H, arom. H, J = 9 Hz); 8.16 (s, 1 H, olefinic H).
$C_{12}H_{13}N_3O$ (215.2)

*3.6.3. 2-Cyano-3-(2-thienyl)-2-propenamide* (**7c**)

Reaction time 15 h; crystallized from benzene (pale yellow crystals); m.p. 155–157 °C; yield 62%. IR: ν 3467, 3135 $cm^{-1}$ ($NH_2$); 2205 (CN); 1701 (CO); 1584 (C=C). $^1H$ NMR ($CDCl_3$): δ 6.11–6.27 (br. s, 2 H, $NH_2$); 7.20–7.79 (m, 3 H, arom. H); 8.44 (s, 1 H, olefinic H).
$C_8H_6N_2OS$ (178.2)

*3.6.4. 2-Cyano-3-(2-furanyl)-2-propenamide* (**7d**)

Reaction time 20 h; crystallized from benzene (pale yellow crystals); m.p. 153–155 °C; yield 62%. IR: ν 3410, 3202, 3144 $cm^{-1}$ ($NH_2$); 2211 (CN); 1697 (CO); 1595 (C=C). $^1H$ NMR ($CDCl_3$): δ 6.10–6.40 (br. s, 2 H, $NH_2$); 6.62–7.74 (m, 3 H, arom. H); 8.07 (s, 1 H, olefinic H).
$C_8H_6N_2O_2$ (162.1)

### *3.7. 3,4-Dihydro-2-[(2-hydroxyaryl)methylidene]-1(2H)-naphthalenones* **8b, c**

A solution of ethanolic KOH (20 ml; 10%) was added to a mixture of equimolecular amounts of the appropriate aldehyde and 1,2,3,4-tetrahydro-1-naphthalenone (10 mmol) in ethanol (15 ml). The reaction mixture was boiled under reflux for 5 h. Upon cooling the reaction mixture, water (100 ml) was added, then acidified with acetic acid (10 ml) a solid separated which was collected and crystallized from a suitable solvent yielding the corresponding **8b, c**.

*3.7.1. 2-[(5-Chloro-2-hydroxyphenyl)methylidene]-3,4-dihydro-1(2H)-naphthalenone* (**8b**)

Crystallized from methanol (pale yellow crystals); m.p. 154–155 °C; yield 85%. IR: ν 3206 $cm^{-1}$ (OH); 1646 (CO); 1597, 1567 (C=C); 961 (*trans* C=C). $^1H$ NMR ($CDCl_3$): δ 2.86–2.98 (m, 4 H, 2 $CH_2$); 6.91–8.12 (m, 9 H, 7 arom. H + olefinic H + $D_2O$ exchangeable OH).
$C_{17}H_{13}ClO_2$ (284.7)

*3.7.2. 3,4-Dihydro-2-[(2-hydroxy-3-methoxyphenyl)methylidene]-1(2H)-naphthalenone* (**8c**)

Crystallized from methanol (pale yellow crystals); m.p. 147–149 °C; yield 80%. IR: ν 3334 $cm^{-1}$ (OH); 1654 (CO); 1603, 1581 (C=C); 963 (*trans* C=C). $^1H$ NMR ($CDCl_3$): δ 2.91–3.08 (m, 4 H, 2 $CH_2$); 3.92 (s, 3 H, $OCH_3$); 6.04 (s, 1 H, $D_2O$ exchangeable OH); 6.86-8.18 (m, 8 H, 7 arom. H + olefinic H).
$C_{18}H_{16}O_3$ (280.3)

### *3.8. Reaction of* 8a–c *with malononitrile*

A mixture of equimolecular amounts of the appropriate **8a–c** and malononitrile (5 mmol) in alcoholic KOH solution (25 ml; 4%) was stirred at room temperature (20–25 °C) for the appropriate time. The solid separated was collected and crystallized from a suitable solvent yielding the corresponding compound **9d**. In case of **9a–c**, the reaction mixture was acidified with dil. HCl (20 ml; 5%) then diluted with water until the total volume reached 70 ml. The solid separated was collected yielding **9a, c**. However, in the case of **9b**, after acidification and dilution with water, the oily mass formed was extracted with chloroform (3 times, each with 20 ml). The chloroform layer was dried over anh. sodium sulfate and evaporated to dryness under reduced pressure. The separated residue was triturated with methanol (5 ml) yielding the corresponding **9b**. Applying the same reaction with **8a** in methanolic KOH solution, the corresponding **10** was obtained directly.

*3.8.1. 5,6-Dihydro-2-ethoxy-4-(2-hydroxyphenyl)benzo[h]quinoline-3-carbonitrile* (**9a**)

Reaction time 96 h; crystallized from methanol (80%) (colourless crystals); m.p. 96–98 °C; yield 35%. IR: ν 3358 $cm^{-1}$ (OH); 2223 (CN); 1605, 1587 (C=N, C=C). $^1H$ NMR ($CDCl_3$): δ 1.51 (t, 3 H, $CH_3$, J = 7.2 Hz); 2.59–2.86 (m, 4 H, 2 $CH_2$); 4.65 (q, 2 H, $OCH_2$, J = 7 Hz); 5.50 (br. s, 1 H, OH); 6.89–8.33 (m, 8 H, arom. H).
$C_{22}H_{18}N_2O_2$ (342.4)

*3.8.2. 4-(5-Chloro-2-hydroxyphenyl)-5,6-dihydro-2-methoxybenzo[h]-quinoline-3-carbonitrile* (**9b**)

Reaction time 48 h; crystallized from methanol (colourless crystals); m.p. 244–246 °C; yield 33%. IR: ν 3283 $cm^{-1}$ (OH); 2223 (CN); 1583, 1554 (C=N, C=C). $^1H$ NMR ([D6]DMSO): δ 2.51–2.87 (m, 4 H, 2 $CH_2$); 4.14 (s, 3 H, $OCH_3$); 7.03–8.32 (m, 7 H, arom. H); 10.25 (s, 1 H, OH).
$C_{21}H_{15}ClN_2O_2$ (362.8)

*3.8.3. 4-(5-Chloro-2-hydroxyphenyl)-5,6-dihydro-2-ethoxybenzo[h]-quinoline-3-carbonitrile* (**9c**)

Reaction time 96 h; crystallized from methanol (90%) (colourless crystals); m.p. 197–199 °C; yield 53%. IR: ν 3245 $cm^{-1}$ (OH); 2239 (CN); 1553, 1500 (C=N, C=C). $^1H$ NMR ($CDCl_3$): δ 1.50 (t, 3 H, $CH_3$, J = 7.2 Hz); 2.60–2.87 (m, 4 H, 2 $CH_2$); 4.64 (q, 2 H, $OCH_2$, J = 7 Hz); 6.17 (s, 1 H, $D_2O$ exchangeable OH); 6.80–8.32 (m, 7 H, arom. H).
$C_{22}H_{17}ClN_2O_2$ (376.8)

*3.8.4. 5,6-Dihydro-4-(2-hydroxy-3-methoxyphenyl)-2-methoxybenzo[h]-quinoline-3-carbonitrile* (**9d**)

Reaction time 48 h; crystallized from methanol (90%) (colourless crystals); m.p. 242–244 °C; yield 34%. IR: ν 3413 $cm^{-1}$ (OH); 2224 (CN); 1557, 1444 (C=N, C=C). $^1H$ NMR ([D6]DMSO): δ 2.51–2.84 (m, 4 H, 2 $CH_2$); 3.89 (s, 3 H, $OCH_3$); 4.14 (s, 3 H, $OCH_3$); 6.76–8.31 (m, 7 H, arom. H); 9.18 (s, 1 H, OH).
$C_{22}H_{18}N_2O_3$ (358.4)

*3.8.5 2-Amino-4-[(1,2,3,4-tetrahydro-1-naphthalenone)-2-yl]-4H-[1]benzopyran-3-carbonitrile* (**10**)

Reaction time 1.5 h; crystallized from ethanol (colourless crystals); m.p. 215–217 °C; yield 63%. IR: ν 3469, 3317 $cm^{-1}$ ($NH_2$); 2178 (CN); 1670 (CO); 1648, 1596 (C=N, C=C). $^1H$ NMR ([D6]DMSO): δ 1.26–3.11 (m, 5 H, 2 $CH_2$ + COCH); 4.54 (d, 1 H, hetero. H-4, J = 2.2 Hz); 6.98–7.95 (m, 10 H, 8 arom. H + $NH_2$). $^{13}C$ NMR ([D6]DMSO): δ 23.2, 28.1 (2 $CH_2$); 34.7, 54.9 (2 CH); 52.5 (hetero. C-3); 115.9, 126.6, 126.8, 128.2, 128.3, 133.7, 144.3, 150.2 (8 arom. CH); 120.7, 121.7, 124.5, 128.8, 132.2, 162.4 (5 arom. quaternary C + CN); 197.6 (CO).
$C_{20}H_{16}N_2O_2$ (316.4)

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