Synthesis of New Heterocyclic Ring Systems *via* [1,3,5]Triazino[1,2-*a*]benzimidazole Derivatives§

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§ The Authors dedicate this article to the memory of Professor Antonio Da Settimo, who was an example of excellence in science and in life for them.

Three new heterocyclic ring systems were synthesized from [1,3,5]triazino[1,2-*a*]benzimidazole derivatives, which in turn were obtained by condensation of 2-guanidinobenzimidazole with *o*-substituted benzaldehydes.

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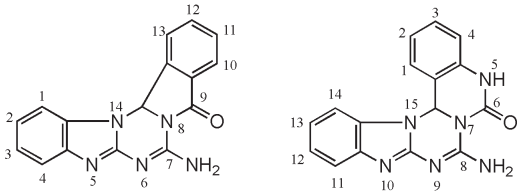
Introduction.

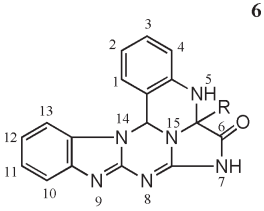
DNA replication constitutes the necessary condition for cell division and, consequently, it has become one of the preferred targets for the development of new drugs that are able to interrupt the proliferation of neoplastic cells. Among the DNA-binding agents, the intercalators represent one of the most important classes. Generally, they are characterized by the presence of a planar or pseudo-planar, aromatic or heteroaromatic chromophore, to which flexible basic side chains may be bound to improve DNA-intercalating properties [1-2].

On the basis of these considerations, in carrying out a program to prepare new potential DNA-intercalating agents, in recent papers we described some tetracyclic derivatives containing the purine, benzimidazole or indole nucleus [3-5]. The benzimidazole derivatives functionalized with dialkylaminoalkyl side chains have a cytotoxic activity mainly through an intercalative mode of binding to DNA. Moreover, the structure-activity relationships showed that both the length and the steric hindrance of the side chains are crucial for cytotoxicity [5].

Pursuing our interest in nitrogen chromophores containing the benzimidazole nucleus, in this paper we describe the easy preparation of some fused benzimidazoles representing three new heterocyclic ring systems: the isoindolo-[2',1':5,6][1,3,5]triazino[1,2-*a*]benzimidazole **3**, the benzimidazo[1',2':3,4][1,3,5]triazino[1,2-*c*]quinazoline **6** and the benzimidazo[1,2-*a*][1,3,3a^1,4,6]pentaazaacephenanthrylenes **7a,b** and **9** (Figure 1).



3 **6**

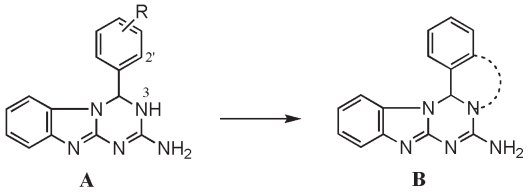


7a: R=H
7b: R=CH_3
9: R=C_2H_5

Figure 1

Results and Discussion.

The synthetic procedures utilized in the preparation of the new compounds described in this paper were based on the review of a paper where it was reported that [1,3,5]triazino[1,2-*a*]benzimidazole derivatives **A** (Figure 2) are readily available from a condensation of 2-guanidinobenzimidazole with benzaldehydes in refluxing ethanol or *N,N*-dimethylformamide [6].

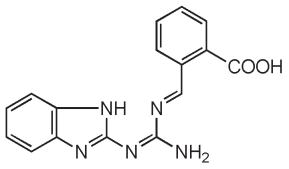


A **B**

Figure 2

We realized that compounds **A** could be useful precursors in the synthesis of new nitrogen-bearing chromophores if an appropriate R group were introduced in the 2' position by reacting 2-guanidinobenzimidazole with an *o*-substituted benzaldehyde. The R group, as such or after conversion into a reactive moiety, could form a new ring derivative **B** by reaction with 3-NH in the presence of a coupling agent (Figure 2).

As a first example of the potential of compounds **A**, we now describe the synthetic route to the isoindolotriazinobenzimidazole derivative **3** (Scheme 1), which represents a new heterocyclic ring system. The new triazinobenzimidazole intermediate **2** was obtained through the reaction of 2-guanidinobenzimidazole **1** with *o*-carboxybenzaldehyde in refluxing ethanol. The structure of **2** was confirmed by analytical and spectral data and, in particular, the ^{1}H nmr spectrum of **2** exhibited a singlet (7.22 ppm) relative to the 4-H proton. The ^{13}C nmr spectrum showed a peak at 170.90 ppm due to the carboxyl moiety and a peak at 63.60 ppm, which was assigned to the C-4 carbon, the only sp^3 hybridized carbon of the molecule. The presence of a signal due to a saturated carbon let us discard the isomeric azomethine structure **2a** for the carboxylic acid derivative (Figure 3).



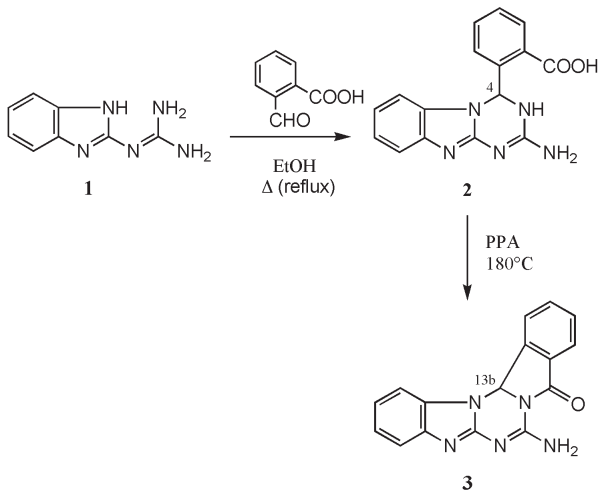
2a

Figure 3

Cyclization of **2** to the desired lactam **3** was effected by heating the former with an excess of polyphosphoric acid (Scheme 1). The most interesting features of the nmr spectra of compound **3** were the signals of the atoms in the 13b position of the nucleus: the proton absorbed at 7.00 ppm as a singlet and the sp^3 hybridized carbon resonated at 69.68 ppm.

To further explore the reactivity of derivatives **A** for the obtainment of new polyheterocyclic compounds, we synthesized the new key intermediate **5** (Scheme 2), which was characterized by the presence of an amino group in the 2' position. The diamino derivative **5** was obtained by catalytic hydrogenation of the nitro compound **4** [7], which, in turn, was prepared by reacting **1** and *o*-nitrobenzaldehyde in refluxing *N,N*-dimethylformamide. The structure of **4** and **5** was confirmed by analytical and spectral data. The ^{1}H nmr spectra of both compounds revealed the presence of the 4-H proton's singlet (7.34 ppm for **4** and 6.75 ppm for **5**), and their ^{13}C nmr spectra showed a peak in the saturated carbon range due to the C-4 carbon (62.36 ppm for **4** and 63.22 ppm for **5**).

Scheme 1



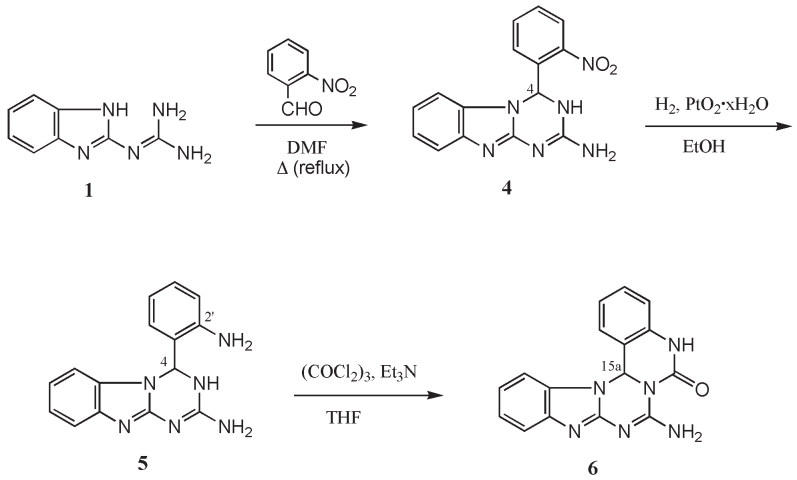
The condensation of the diamino compound **5** with triphosgene in tetrahydrofuran led to the formation of the quinazoline derivative **6**, which represents a new heterocyclic ring system (Scheme 2). The structure of **6** agreed with analytical and spectral data. In particular, in the ^{1}H nmr spectrum the presence was observed of a singlet at 6.82 ppm, which was assigned to the 15a-H proton, and the ^{13}C nmr spectrum showed a diagnostic signal at 66.90 ppm due to the C-15a carbon, the only saturated carbon of the molecule.

The reaction between the diamino derivative **5** and 2-ketoacids seemed to be interesting from a synthetic point of view because, in principle, the double functionality of the latter could be exploited to assemble new polyheterocyclic scaffolds. Therefore, we made **5** react with 2-ketoacids and examined the outcome of those condensations as shown in Scheme 3.

When compound **5** was reacted with glyoxylic acid or pyruvic acid in refluxing ethanol for 24 and 2 hours, the products were the pentaazaacephenanthrylene derivatives **7a** or **7b**, respectively, which represent a new heterocyclic ring system. Their structure was confirmed by analytical and spectral data, especially by their nmr spectra, which showed important similarities, as expected. The ^{1}H nmr spectrum of **7a** was characterized by two singlets at 5.35 ppm and 7.07 ppm, which were assigned to the 5a-H and 14a-H proton, respectively. The proton nmr spectrum of **7b** exhibited the 14a-H proton's singlet at 7.17 ppm and another singlet integrating for three protons at 1.67 ppm due to the methyl group linked to the 5a position. In the ^{13}C nmr spectrum of **7a** there were two peaks in the sp^3 hybridized carbon range at 62.62 ppm and 67.92 ppm, which were assigned to the C-14a and C-5a carbon, respectively. Compound **7b** had three saturated carbon atoms resonating at 23.31 ppm (CH_3), 61.73 ppm (C-14a) and 72.98 ppm (C-5a).

Based on the fact that the scaffolds of compounds **7a,b** had two saturated carbon atoms, we supposed that they formed through the mechanistic pathway illustrated in Scheme 4, according to which the imino intermediates **10a,b** cyclized to the quinazoline derivatives **11a,b** by the addition of 3-NH to the imino double bond. Finally, the carboxylic acids **11a,b** looses water intramolecularly to afford the hexacyclic ring systems

Scheme 2

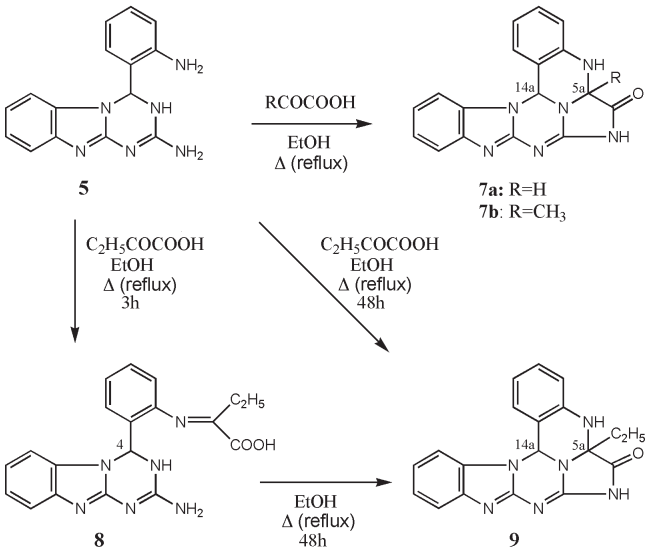


1 4 5 6

7a,b. Incidentally, we isolated none of the aforementioned intermediates because shorter reaction times only resulted in recovering mixtures of unreacted **5** and either compound **7a** or compound **7b**.

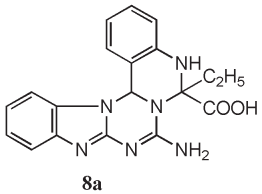
When the diamino derivative **5** and 2-ketobutyric acid were refluxed in absolute ethanol, we obtained either the iminobutyric acid **8** or the pentaazaacephenanthrylene derivative **9** (Scheme 3), depending on the reaction time (3 hours or 48 hours, respectively). The structure of product **9**, which is the same ring system as **7a,b**, was supported by analytical and spectral data. In its ^{1}H nmr spectrum we noted that the ethyl group showed a triplet at 0.91 ppm and a multiplet at 1.90-2.19 ppm because the CH_2 protons, being linked to the chiral carbon 5a, were diastereotopic and coupled to each other besides the CH_3 protons. Also, there was a singlet at 7.10 ppm due to the 14a-H proton. For what regards the ^{13}C nmr spectrum of **9**, apart from the ethyl signals at 8.03 ppm and 29.13 ppm, it revealed the presence of two more sp^3 hybridized carbon atoms resonating at 61.98 ppm (C-14a) and 76.55 ppm (C-5a) in accordance with the carbon nmr spectra of **7a,b**. There was also a chemical confirmation of the structure of **9** as this compound formed when the intermediate **8** was refluxed in absolute ethanol for 48 hours (Scheme 3).

Scheme 3



5 8 9

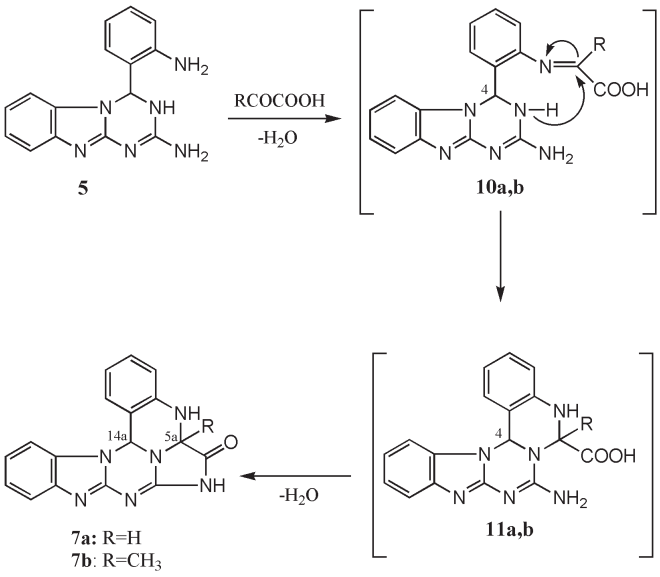
On the base of the reaction mechanism outlined above, the intermediate that we isolated and then cyclized to **9** could be the carboxylic acid **8a** (Figure 4) in alternative to the **8** reported in Scheme 3. The low solubility of the intermediate prevented us from taking the ^{13}C nmr spectrum, which could help us to assign either the imino structure **8** or the quinazoline scaffold **8a** to the compound because the latter has one saturated carbon more than the former. Therefore, lacking the carbon nmr data and based on the ^{1}H nmr spectrum, we ruled out the formation of the quinazoline derivative **8a** because the CH_2 protons of the ethyl group didn't couple to each other and showed a quartet at 2.54 ppm: if the structure were **8a**, the CH_2 protons would be diastereotopic due to their proximity to a chiral center and could exhibit a multiplet like the CH_2 protons of compound **9**. Another feature of the ^{1}H nmr spectrum of compound **8** was the presence of a singlet at 6.66 ppm due to the 4-H proton.



8a

Figure 4

Scheme 4



The isolation of compound **8a** was not possible because refluxing **8** in absolute ethanol for 48 hours led to **9** together with a small amount of unreacted **8**, while shorter reaction times only resulted in major amounts of recovered starting material.

Conclusions.

The easily available triazinobenzimidazole derivatives **A** proved to be a useful tool for the preparation of new polyheterocyclic ring systems containing the benzimidazole nucleus and their synthetic potential can be further developed by reacting them with a number of types of coupling agents.

The fused benzimidazoles obtained can function as intermediates in the synthesis of potential antitumor agents, since they bear NH_2 or NH groups to which dialkylaminoalkyl side chains can be linked.

EXPERIMENTAL

General.

Melting points were determined using a Reichert Köfler hot-stage apparatus and are uncorrected. Infrared spectra were recorded with a NICOLET/AVATAR 360 FT-IR spectrophotometer as nujol mulls. ^{1}H nmr spectra (200 MHz) and ^{13}C nmr spectra (50 MHz) were recorded in dimethylsulfoxide-d_6 solution, unless otherwise stated, on a Varian Gemini 200 spectrometer. Mass spectra were obtained on a FINNIGAN POLARIS/GCQ PLUS spectrometer using a direct exposure probe and an electron beam energy of 70 eV. Evaporations were performed *in vacuo* (rotary evaporator). Analytical tlc was carried out on Merck 0.2 mm precoated silica gel aluminium sheets (60 F_{254}). Elemental analyses were performed by our Analytical Laboratory and agreed with theoretical values to within ± 0.4%.

2-Amino-4-(2-carboxyphenyl)-3,4-dihydro-1,3,5-triazino[1,2-*a*]-benzimidazole (**2**).

o-Carboxybenzaldehyde (2.55 g, 17.0 mmol) was added to a stirred suspension of 2-guanidinobenzimidazole **1** (2.80 g, 16 mmol) in ethanol (50 mL) and the mixture was refluxed for 4 hours. After cooling, the solid that precipitated from the resulting solution was collected, washed with ethanol and recrystallized from *N*,*N*-dimethylformamide to give 4.22 g (84% yield) of pure **2**, white solid, mp 266-268 °C dec; ir (cm^{-1}): ν_{MAX} 3398, 3150, 1660, 1625, 1602, 1580, 1567, 1514; ^{1}H nmr: δ 6.49 (d, 1H), 6.84 (d, 1H), 7.03 (dd, 1H), 7.14-7.41 (m, 4H, ArH + 4-H at 7.22), 7.89-7.94 (m, 2H), 10.50 (s, 1H, exchangeable with deuterium oxide); ^{13}C nmr: δ 63.60 (C-4), 110.40, 112.90, 123.00, 124.00, 124.80, 129.10, 129.30, 130.70, 131.80, 132.10, 137.60, 138.00, 152.80, 157.30, 170.90 (COOH); ms (*m/z*, %): 307 (M$^+$, 2), 158 (100).

Anal. Calcd. for $C_{16}H_{13}N_5O_2$: C, 62.53; H, 4.26; N, 22.79. Found: C, 62.28; H, 4.26; N, 22.39.

7-Aminoisoindolo[2',1':5,6][1,3,5]triazino[1,2-*a*]benzimidazole-9(13b*H*)-one (**3**).

A stirred mixture of compound **2** (1.00 g, 3.26 mmol) and polyphosphoric acid (10.00 g) was heated at 180 °C for 2 hours. The hot mixture was poured into ice and neutralized (pH 6-7) with 30% ammonium hydroxide solution. The precipitate was collected, washed with water and recrystallized from *N*,*N*-dimethylformamide to give 0.90 g (97% yield) of pure **3**, pale yellow solid, mp 210-212 °C; ir (cm^{-1}): ν_{MAX} 3375, 1720, 1600, 1520, 1280, 735; ^{1}H nmr: δ 7.00-7.13 (m, 3H, ArH + 13b-H at 7.00), 7.40 (d, 1H), 7.57 (d, 1H), 7.75 (br s, 1H, exchangeable with deuterium oxide), 7.81-7.88 (m, 1H), 8.01-8.08 (m, 2H), 8.45 (br s, 1H, exchangeable with deuterium oxide), 8.53 (d, 1H); ^{13}C nmr: δ 69.68 (C-13b), 110.99, 118.14, 121.09, 122.16, 125.73, 128.48, 131.28, 132.19, 132.34, 134.89, 138.16, 144.17, 150.67, 155.04, 165.40; ms (*m/z*, %): 289 (M$^+$, 12), 73 (100).

Anal. Calcd. for $C_{16}H_{11}N_5O$: C, 66.43; H, 3.81; N, 24.22. Found: C, 66.72; H, 3.92; N, 24.60.

2-Amino-4-(2-nitrophenyl)-3,4-dihydro-1,3,5-triazino[1,2-*a*]-benzimidazole (**4**).

A stirred solution of 2-guanidinobenzimidazole **1** (2.80 g, 16 mmol) and *o*-nitrobenzaldehyde (2.44 g, 16 mmol) in *N*,*N*-dimethylformamide (30 mL) was refluxed for 1 hour. After cooling, the solid that precipitated was collected, washed with ethanol and recrystallized from ethanol to give 2.156 g (43% yield) of pure **4**, orange solid, mp 247-248 °C; ir (cm^{-1}): ν_{MAX} 3392, 3317, 3057, 1652, 1611, 1583, 1344, 1241, 811, 740; ^{1}H nmr: δ 6.52 (br s, 2H, 2-NH_2, exchangeable with deuterium oxide), 6.58-6.62 (m, 1H), 6.74-6.82 (m, 1H), 6.90-7.00 (m, 2H), 7.29 (d, 1H), 7.34 (s, 1H, 4-H), 7.60-7.65 (m, 2H), 7.84 (br s, 1H, 3-H, exchangeable with deuterium oxide), 8.18-8.23 (m, 1H); ^{13}C nmr (methanol-d_4): δ 62.36 (C-4), 108.34, 116.15, 120.70, 122.27, 125.55, 127.22, 130.59, 130.88, 133.90, 134.71, 141.90, 147.67, 153.86, 156.01; ms (*m/z*, %): 308 (M$^+$, 100).

Anal. Calcd. for $C_{15}H_{12}N_6O_2$: C, 58.44; H, 3.90; N, 27.27. Found: C, 58.04; H, 3.70; N, 26.96.

2-Amino-4-(2-aminophenyl)-3,4-dihydro-1,3,5-triazino[1,2-*a*]-benzimidazole (**5**).

To a solution of compound **4** (0.90 g, 2.92 mmol) in ethanol (300 mL) was added $PtO_2 \cdot xH_2O$ (0.07 g) and the mixture was

stirred under hydrogen at atmospheric pressure until the theoretical uptake of hydrogen was achieved (5 hours). The catalyst was removed by filtration and the filtrate was concentrated to a small volume to afford 0.523 g (64 % yield) of pure **5**, white solid, mp 225-226 °C; ir (cm^{-1}): ν_{MAX} 3304, 3221, 3147, 1651, 1607, 1577, 1522, 1504, 1395, 1238, 757, 740; ^1H nmr: δ 5.40 (br s, 2H, 2'-NH_2, exchangeable with deuterium oxide), 6.42 (br s, 2H, 2-NH_2, exchangeable with deuterium oxide), 6.50 (t, 1H), 6.60 (d, 1H), 6.70-6.79 (m, 3H, ArH + 4-H at 6.75), 6.88-6.95 (m, 2H), 7.05 (t, 1H), 7.21 (d, 1H), 7.82 (br s, 1H, 3-H, exchangeable with deuterium oxide); ^{13}C nmr: δ 63.22 (C-4), 108.89, 116.57, 116.89, 117.24, 119.50, 121.36, 122.49, 127.99, 130.43, 132.14, 144.05, 146.65, 154.68, 156.43; ms (*m/z*, %): 278 (M^+, 48), 261 (100).

Anal. Calcd. for $C_{15}H_{14}N_6$: C, 64.75; H, 5.04; N, 30.22. Found: C, 64.97; H, 5.27; N, 30.59.

8-Aminobenzimidazo[1',2':3,4][1,3,5]triazino[1,2-*c*]quinazoline-6(5*H*,15a*H*)-one (**6**).

A stirred suspension of compound **5** (0.20 g, 0.72 mmol) in anhydrous tetrahydrofuran (40 mL) was cooled to about –25 °C and triphosgene (0.086 g, 0.29 mmol) was added, followed by the dropwise addition of a solution of triethylamine (0.24 mL, 1.74 mmol) in anhydrous tetrahydrofuran (10 mL). The mixture was then stirred at –20 to –10 °C for 5 hours. The solid was collected, washed with water and recrystallized from ethanol to give 0.056 g (26% yield) of pure **6**, white solid, mp 237-238 °C; ir (cm^{-1}): ν_{MAX} 3345, 3276, 1699, 1641, 1604, 1539, 1334, 1310, 1255, 1078, 770, 730, 712; ^1H nmr: δ 5.97 (d, 1H), 6.73 (t, 1H), 6.82 (s, 1H, 15a-H), 6.95 (t, 1H), 7.02 (d, 1H), 7.20-7.35 (m, 2H), 7.54 (t, 1H), 7.77 (d, 1H), 7.94 (br s, 1H, exchangeable with deuterium oxide), 8.36 (br s, 1H, exchangeable with deuterium oxide), 10.62 (s, 1H, exchangeable with deuterium oxide); ^{13}C nmr: δ 66.90 (C-15a), 109.41, 112.31, 115.60, 118.30, 120.74, 121.45, 123.07, 130.44, 131.76, 132.61, 137.87, 143.61, 149.98, 154.39, 154.68; ms (*m/z*, %): 304 (M^+, 15), 146 (100).

Anal. Calcd. for $C_{16}H_{12}N_6O$: C, 63.16; H, 3.95; N, 27.36. Found: C, 62.89; H, 4.34; N, 27.05.

5,5a-Dihydrobenzimidazo[1,2-*a*][1,3,3a^1,4,6]pentaazaacephenanthrylene-6(7*H*,14a*H*)-one (**7a**).

A stirred suspension of compound **5** (0.30 g, 1.08 mmol) and glyoxylic acid monohydrate (0.085 g, 0.92 mmol) in ethanol (50 mL) was refluxed for 24 hours. The hot suspension was filtered and the solid was collected and washed with ethanol to afford 0.183 g (63% yield) of pure **7a**, white solid, mp >300 °C; ir (cm^{-1}): ν_{MAX} 3314, 3267, 1694, 1610, 1558, 1317, 1279, 1245, 1211, 1156, 907, 883, 859, 757, 733; ^1H nmr: δ 5.35 (s, 1H, 5a-H), 6.24 (d, 1H), 6.50 (t, 1H), 6.83-6.94 (m, 2H), 7.07 (s, 1H, 14a-H), 7.09-7.25 (m, 3H, 1H exchangeable with deuterium oxide), 7.50-7.60 (m, 2H); ^{13}C nmr: δ 62.62 (C-14a), 67.92 (C-5a), 109.43, 112.11, 115.97, 118.37, 120.70, 122.67, 123.80, 130.39, 133.08, 141.57, 142.19, 150.22, 154.70, 162.44, 176.77; ms (*m/z*, %): 316 (M^+, 89), 131 (100).

Anal. Calcd. for $C_{17}H_{12}N_6O$: C, 64.55; H, 3.80; N, 26.58. Found: C, 64.21; H, 4.20; N, 26.88.

5a-Methyl-5,5a-dihydrobenzimidazo[1,2-*a*][1,3,3a^1,4,6]pentaazaacephenanthrylene-6(7*H*,14a*H*)-one (**7b**).

A stirred solution of compound **5** (0.30 g, 1.08 mmol) and pyruvic acid (0.08 mL, 1.13 mmol) in absolute ethanol (30 mL) was refluxed for 2 hours. After cooling, the solid precipitate was collected, washed with ethanol and recrystallized from *N*,*N*-dimethylformamide-water to give 0.184 g (52% yield) of pure **7b**, white solid, mp 286-288 °C dec; ir (cm^{-1}): ν_{MAX} 3297, 1669, 1614, 1590, 1388, 1300, 1221, 1187, 1150, 740, 631; ^1H nmr: δ 1.67 (s, 3H, CH_3), 6.24 (d, 1H), 6.46-6.54 (m, 1H), 6.78-6.82 (m, 1H), 7.05-7.13 (m, 1H), 7.17 (s, 1H, 14a-H), 7.22-7.31 (m, 2H), 7.42 (br s, 1H, exchangeable with deuterium oxide), 7.52-7.63 (m, 2H), 12.27 (br s, 1H, exchangeable with deuterium oxide); ^{13}C nmr: δ 23.31 (CH_3), 61.73 (C-14a), 72.98 (C-5a), 109.61, 115.48, 118.34 (2C), 120.59, 122.78 (2C), 123.83, 130.41, 133.07, 141.60, 141.81, 149.78, 160.00, 176.00; ms (*m/z*, %): 330 (M^+, 12), 145 (100).

Anal. Calcd. for $C_{18}H_{14}N_6O$: C, 65.45; H, 4.24; N, 25.45. Found: C, 65.27; H, 4.43; N, 25.85.

2-[2-(2-Amino-3,4-dihydro-1,3,5-triazino[1,2-*a*]benzimidazol-4-yl)phenylimino]butyric acid (**8**).

A stirred suspension of compound **5** (0.20 g, 0.72 mmol) and 2-ketobutyric acid (0.074 g, 0.72 mmol) in absolute ethanol (30 mL) was refluxed for 3 hours. After cooling, the solid was collected and washed with ethanol to give 0.191 g (70% yield) of pure **8**, white solid, mp 263-266 °C dec.; ir (cm^{-1}): ν_{MAX} 3372, 3188, 1689, 1624, 1600, 1518, 1290, 1238, 1081, 1047, 887, 866, 846, 818, 740; ^1H nmr: δ 1.31 (t, 3H, CH_3), 2.49-2.59 (q, 2H, CH_2), 6.62-6.72 (m, 3H, Ar-H + 4-H at 6.66), 6.95-7.36 (m, 9H), 10.64 (br s, 1H, exchangeable with deuterium oxide); ^{13}C nmr: too insoluble to take the spectrum; ms (*m/z*, %): 344 (M^+-H_2O, 39), 159 (100).

Anal. Calcd. for $C_{19}H_{18}N_6O_2 \cdot H_2O$: C, 60.00; H, 5.26; N, 22.11. Found: C, 59.97; H, 5.23; N, 21.50.

5a-Ethyl-5,5a-dihydrobenzimidazo[1,2-*a*][1,3,3a^1,4,6]pentaazaacephenanthrylene-6(7*H*,14a*H*)-one (**9**).

A) From 2-amino-4-(2-aminophenyl)-3,4-dihydro-1,3,5-triazino-[1,2-*a*]benzimidazole (**5**).

A stirred suspension of compound **5** (0.30 g, 1.08 mmol) and 2-ketobutyric acid (0.111 g, 1.08 mmol) in absolute ethanol (30 mL) was refluxed for 48 hours. After cooling, the solid was collected, washed with chloroform and recrystallized from *N*,*N*-dimethylformamide to give 0.141 g (38% yield) of pure **9**, white solid, mp 279-281 °C dec; ir (cm^{-1}): ν_{MAX} 3283, 1710, 1620, 1518, 1293, 1201, 1174, 999, 740, 651; ^1H nmr: δ 0.91 (t, 3H, CH_3), 1.90-2.19 (m, 2H, CH_2), 6.24 (d, 1H), 6.49 (t, 1H), 6.82 (d, 1H), 7.06-7.13 (m, 2H, Ar-H + 4-H at 7.10), 7.19-7.30 (m, 2H), 7.40 (br s, 1H, exchangeable with deuterium oxide), 7.50-7.57 (m, 1H), 7.60-7.65 (m, 1H), 12.34 (br s, 1H, exchangeable with deuterium oxide); ^{13}C nmr: δ 8.03 (CH_3CH_2), 29.13 (CH_3CH_2), 61.98 (C-14a), 76.55 (C-5a), 109.76, 115.51, 118.35 (2C), 120.61, 122.82 (2C), 123.85, 130.44, 133.08, 141.53, 141.90, 149.69, 159.43, 176.13; ms (*m/z*, %): 344 (M^+, 46), 159 (100).

Anal. Calcd. for $C_{19}H_{16}N_6O$: C, 66.28; H, 4.65; N, 24.42. Found: C, 66.67; H, 4.59; N, 24.81.

B) From [2-(2-Amino-3,4-dihydro-1,3,5-triazino[1,2-*a*]benzimidazol-4-yl)phenylimino]butyric acid (**8**).

A stirred suspension of compound **8** (0.07 g, 0.18 mmol) in absolute ethanol (30 mL) was refluxed for 48 hours. The warm suspension was filtered to remove some unreacted **8** and the filtrate was concentrated to a small volume under vacuum. The solid that precipitated was collected and washed with chloroform to give 0.037 g (59% yield) of pure **9**.

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