Fused quinoline heterocycles I. First example of the 2,4-diazidoquinoline-3-carbonitrile and 1-aryl-1,5-dihydro-1,2,3,4,5,6-hexaazaacephenanthrylenes ring systems

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4-Alkylamino-2-chloroquinoline-3-carbonitriles **2a**–**f** react with hydrazine hydrate to give, in each case, the corresponding 3-amino-4-hydrazino-1*H*-pyrazolo[3,4-*b*]quinoline **7**. Diazotization of **7** leads to the formation of 2,4-diazidoquinoline-3-carbonitrile **8**, a new heterocyclic ring system. The azidoquinoline **8** can be converted to the corresponding aminoquinolines **14**, and **15** and **16**, by reaction with morpholine and sodium dithionite, respectively. On the other hand, 3-amino-4-arylamino-1*H*-pyrazolo[3,4-*b*]quinolines **4g**–**j** were prepared by reaction of 4-arylamino-2-chloroquinoline-3-carbonitriles **2g**–**j** with hydrazine hydrate at 50–60 °C. Diazotization of **4g**–**j** afforded the novel tetracyclic ring system 1-aryl-1,5-dihydro-1,2,3,4,5,6-hexaazaacephenanthrylenes **5g**–**j**.

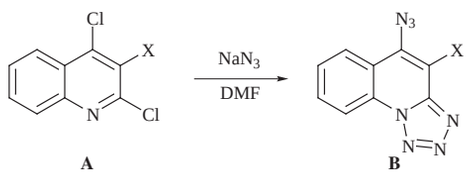
Introduction

Tetracyclic systems containing the quinoline moiety are expected to have wide-spectrum biological activity. We are exploring methods to construct the tetracyclic pyrazolotriazinoquinoline system **5**. In previous work we prepared novel heterocyclic ring systems, containing the quinoline skeleton, with potential pharmaceutical activity.[1–5] Pyrazoloquinoline derivatives have useful biological properties as antitumor reagents[6,7] and are active agents for the treatment of herpes virus infections.[8] Pyrazolotriazines also have considerable biological and medicinal activities as antitumor,[9] antiinflammatory,[10] and antiviral agents.[11] We therefore wanted to develop an efficient procedure for the synthesis of new heterocyclic systems containing both pyrazole and triazine moieties condensed with a quinoline nucleus, with the expectation that they would be of potential biological interest. A literature search revealed that pyrazolotriazinoquinolines have been largely ignored. We envisaged that the reaction of 4-amino-2-chloroquinoline-3-carbonitriles **2a**–**f** with hydrazine hydrate might afford the corresponding pyrazolo[3,4-*b*]quinolines **4** and subsequent reaction with sodium nitrite in a solution of H_2SO_4 (70%) at −5 °C would lead to the formation of the hitherto unknown tetracyclic system **5**. Interestingly, however, a new compound, 2,4-diazidoquinoline-3-carbonitrile **8**, was obtained. To the best of our knowledge, there are no reports on the synthesis of 2,4-diazidoquinolines. Steinschifter and Stadlbauer[12] showed that the reaction of 2,4-dichloroquinolines **A** with sodium azide in DMF gave the azidotetrazolo[1,5-*a*]quinoline structure **B** (Fig. 1). The presence of the tetrazolo moiety in structure **B** was demonstrated by chemical and spectroscopic methods.[12] Their attempts to obtain diazidoquinolines, with electron-donor substituents in the 3-position, by raising the temperature and using a larger excess of sodium azide or catalysts such as Cryptofix 5 failed.

The present investigation describes the synthesis of the first number of a novel heterosystem, 2,4-diazidoquinoline-3-carbonitrile **8**, and 1-aryl-1,5-dihydro-1,2,3,4,5,6-hexaazaacephenanthrylenes **5**.

Results and discussion

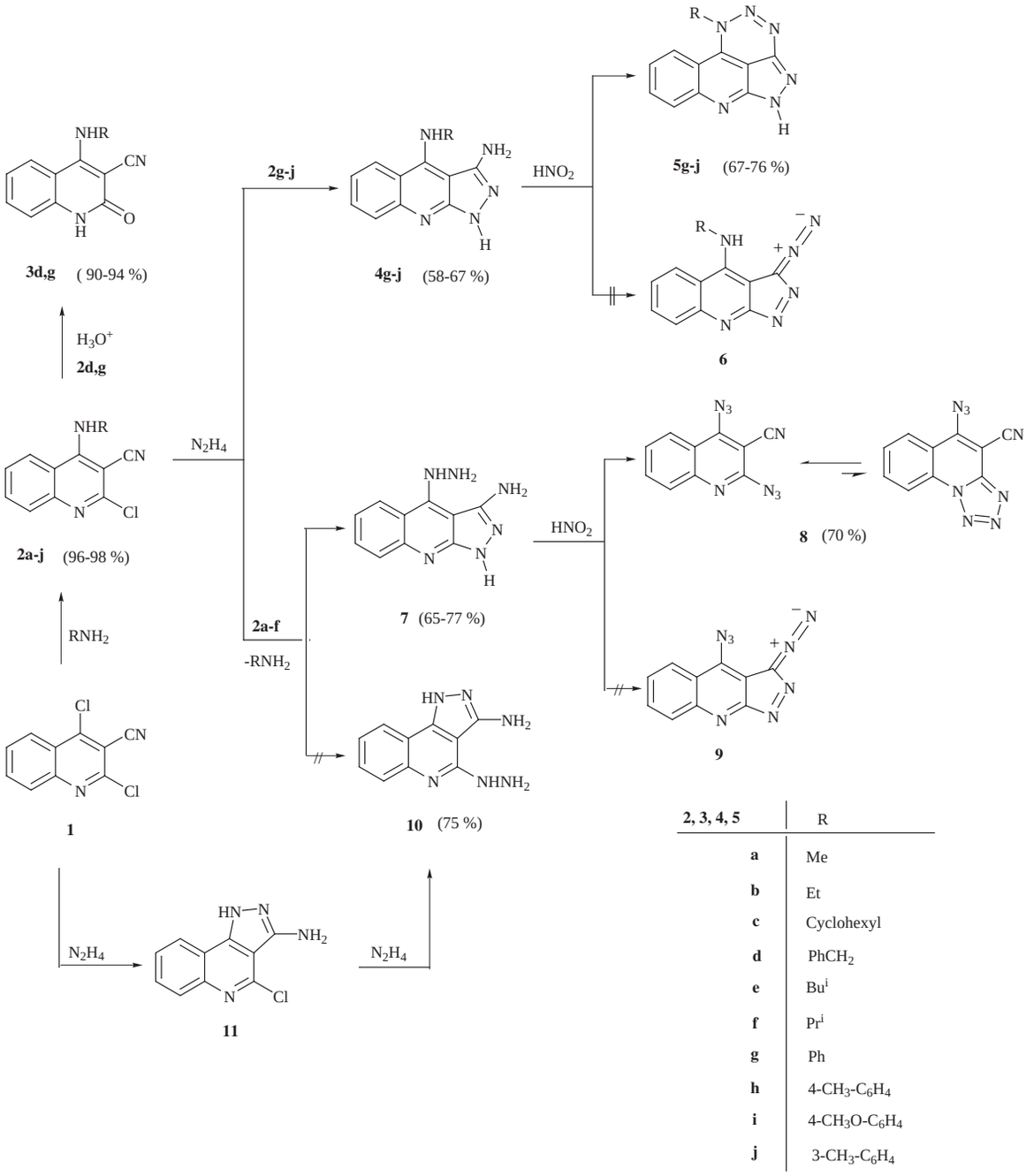
2,4-Diazidoquinoline-3-carbonitrile **8** was obtained in three steps starting from 2,4-dichloroquinoline-3-carbonitrile **1**.[2] Reaction of **1** with an excess of the appropriate alkylamine in DMF solution at room temperature gave the corresponding



A **B**

Fig. 1

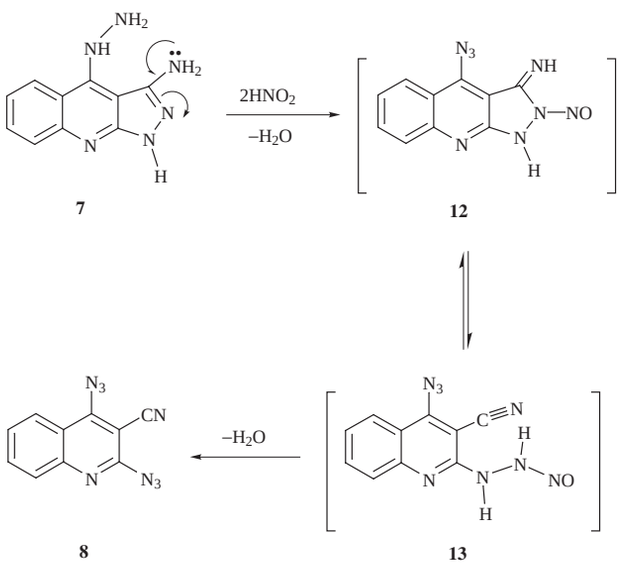
4-alkylamino-2-chloroquinoline-3-carbonitrile **2a**–**f**, where the nucleophilic substitution first takes place at position 4. This was confirmed chemically by acid hydrolysis of **2a**–**f** with a mixture of acetic acid and water, resulting in the formation of the corresponding quinolin-2-ones. For example, acid hydrolysis of **2d** produced, in one step, 4-benzylamino-3-cyanoquinolin-2(1*H*)-one **3d**. The structure of the isomeric quinolin-4-one for compound **3d** could be excluded because the IR spectrum showed significantly an amide carbonyl function at 1650 cm^{-1},[13,14] whereas 4-quinolinones are known to have carbonyl absorptions below 1600 cm^{-1}.[15–17] Refluxing these amines with excess of hydrazine hydrate (80%) did not afford the 4-alkylamino-3-amino-1*H*-pyrazolo[3,4-*b*]quinoline derivatives **4a**–**f**, but rather gave one of the two unexpected isomeric structures **7** or **10**. Spectral data could not unequivocally differentiate these isomers. Therefore, 3-amino-4-hydrazine-1*H*-pyrazolo[4,3-*c*]quinoline **10** was prepared separately to chemically verify the structure of its isomer **7**. The reaction of **1** with hydrazine hydrate according to ref. 2 gave **11** and reaction of **11** with excess of hydrazine hydrate in DMF at reflux yielded **10**. The structural assignment for **7** was established on the basis of consistent elemental and spectral data. The IR spectrum showed no cyano absorption at 2200 cm^{-1}, but absorption bands at 3400, 3330, 3300 and 3150 cm^{-1} were assigned as NH and NH_2 amino functions. Moreover, the ^1H NMR spectrum revealed the absence of alkyl protons and the presence of signals for hydrazino protons at C-4, two amino protons at C-3, and a pyrazole NH proton in addition to aromatic protons in their expected positions. The mass spectrum showed a molecular ion at *m*/*z* 214 (100%). Formation of the pyrazoloquinoline **7** can be rationalized as follows: both the alkylamino group at position 4 and the chloro atom at position 2 of 4-alkylamino-2-chloroquinoline-3-carbonitriles **2a**–**f** undergo a nucleophilic substitution reaction with two molecules of hydrazine. Subsequent intramolecular cyclization *via* the attack of the NH_2 of the hydrazino group at position 2 on the nitrile carbon yields the pyrazolo-fused compound **7**. Reaction of compound **7** with



Scheme 1

sodium nitrite in a 70% solution of H_2SO_4 at −5 °C gave a solid product for which the two possible isomeric structures **8** and **9** can be written (see Scheme 1). Between these two possible structures, the previously unreported 2,4-diazidoquinoline structure **8** was assigned to the product isolated on the basis of its elemental analysis and spectral data. The IR spectra showed no absorption for amino and diazo groups but absorption bands for the N_3 and CN groups were observed at 2140 and 2190 cm^{-1}, respectively. The ^1H NMR spectrum showed no amino protons and the presence of only four aromatic protons at δ 7.70–8.28. Furthermore, ^{13}C NMR gave strong evidence for the formation of compound **8**, which confirmed the presence of a CN carbon at δ 118.54. If the reaction product was the isomer **9**, it would be difficult to assign this signal and consequently the other possible structure **9** was eliminated. Other signals have also been found at the expected field for compound **8** (see Experimental section). The reaction mechanism of formation of **8** is assumed to proceed *via* the reaction of **7** with nitrous acid to give the *N*-nitroso intermediate **12**. A proton shift to afford intermediate **13** was followed by ring opening and elimination of water to give the final product **8** (Scheme 2). The presence of the two azide groups at C-2 and C-4 was confirmed by conversion to the corresponding aminoquinolines **15** and **16**. Reduction of the two azido groups at positions 2 and 4 of **8**, utilizing sodium dithionite as reducing agent, gave the corresponding 2,4-diaminoquinoline-3-carbonitrile **16**.[18] On the other hand, reaction of compound **8** with excess of morpholine in DMF solution at room temperature yielded 2-azido-4-morpholinoquinoline-3-carbonitrile **14**, *via* nucleophilic attack at position 4. Reduction of the azido group at position 2 of **14** with sodium dithionite afforded the corresponding amino compound **15,** in high yield (Scheme 3). Acid hydrolysis of **15** yielded the aminoquinolines **18**, presumably *via* nucleophilic attack of water at C-4 followed by elimination of a morpholine molecule to give **18**. Overnight hydrolysis of **18** in 48% hydrobromic acid followed by basification yielded **17**.[19] The latter compound **17** was synthesized to emphasize chemically that the nucleophilic substitution, *i.e.* the replacement of the azido group with a morpholine moiety in **8**, first takes place at position 4. On the basis of these results, it may be concluded that

isolation of 2,4-diazidoquinolines **8** is attributed to the acidic medium. An azido–tetrazolo isomerization shifted the equilibrium towards the azido form, *i.e.*, in this case the azido form is more stable in the acidic medium. Our interest in developing synthetic approaches to the interesting heterocyclic pyrazolotriazinoquinoline ring system **5** led us to investigate the reaction of 4-arylamino-2-chloroquinoline-3-carbonitriles **2g–j** with hydrazine hydrate, which gave pyrazoloquinolines **4g–j**, good precursors for the preparation of tetracycles **5**. Thus, the required starting material 3-amino-4-arylamino-1*H*-pyrazoloquinoline derivatives **4g–j** were prepared from **1**. Replacement of the chloro atom at position 4 in **1** by aromatic amines was achieved when the reaction was performed in DMF solution at 50–60 °C, giving the corresponding amines **2g–j**. Beside the analytical and spectroscopic confirmation of the structure of compounds **2g–j** (see Experimental section), it was confirmed chemically by their conversion into the corresponding quinolin-2-ones, *via* hydrolysis with aq. acetic acid. For example, acid hydrolysis of **2g** yielded the corresponding quinolin-2-one **3g** (Scheme 1). Refluxing of amines **2g–j** with excess of hydrazine hydrate (80%) gave 3-amino-4-arylamino-1*H*-pyrazoloquinolines **4g–j.** The IR spectrum showed the absence of a cyano absorption. The ^{1}H NMR spectrum revealed the presence of signals for an amino group at C-3 and C-4 and there was a pyrazole NH as well as aromatic protons in their expected positions. When compounds **4g–j** reacted with sodium nitrite in a 70% solution of H_2SO_4 at −5 °C they yielded a solid product which was identified as a 1-aryl-1,5-dihydro-1,2,3,4,5,6-hexaazaacephenanthrylenes **5** (Scheme 1). The other possible structure **6** was readily ruled out for the reaction products on the basis of spectral data. Thus, the lack of a diazo absorption at 2160 cm^{-1} [20] in the IR spectrum of the reaction product supported the assigned structure **5** and allowed us to discard the other possible structure **6**. Moreover, the structure of **5** has been established by its ^{1}H NMR-spectrum which displayed the absence of an amino group (NH) signal for the quinoline C-4 at δ 10.64–10.83, present in the spectra of **4g–j**, and the presence of singlets at about $\delta \approx 14.2$, assignable to the pyrazole NH. It would be difficult to rationalize for this absorption if the reaction product was **6**, or to rationalize signals due to aryl protons. Several attempts were made to confirm the structures of **4g–j** and **5g–j** by mass spectrometry. However, the compounds decomposed under both electron-impact-ionization and fast-atom bombardment.



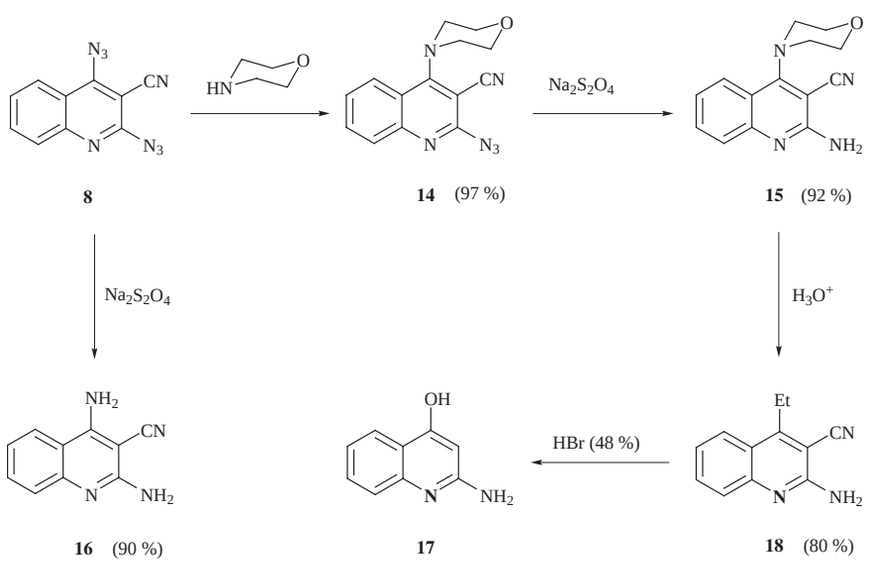
Scheme 2

Conclusions

The work described in this paper shows for the first time a novel and general route to pyrazoloquinolines **7**, *via* nucleophilic substitution of the alkylamino group at C-4 in quinolines **2a–f** by hydrazine hydrate as a nucleophile, and also to 1-aryl-1,5-dihydro-1,2,3,4,5,6-hexaazaacephenanthrylenes **5**. This method utilizes diazide compounds, which provide an excellent synthesis of the sensitive 2,4-diazidoquinolines. Currently we are working on an extension of this approach to prepare new tetracyclic ring systems from pyrazolo[4,3-*c*]quinolines.

Experimental

Mps (uncorrected) were obtained on a Gallenkamp melting point apparatus. Microanalyses were performed by the Microanalytical Data Unit at Cairo University. Mass spectra were recorded on GCMS-QP 1000EX or Finnigan Mat 8430 (ionization energy 70 eV). IR spectra (KBr) were recorded on a Shimadzu 470 spectrophotometer. ^{1}H NMR spectra were recorded on a Varian Gemini 200, a Bruker AC270 or a Bruker AM400 spectrometer at 200, 270 or 400 MHz, respectively, using [$^2H_6$]dimethyl sulfoxide as solvent with tetramethylsilane as internal standard. *J*-Values are given in Hz. ^{13}C NMR spectra were measured on Bruker AM 400 (400 MHz) spectrometer. Analytical TLC was performed with silica gel plates using silica gel 60 PF_{254} (Merck). 2-Amino-4-hydroxyquinoline **17** was prepared from 2-amino-4-hydroxyquinoline-3-carbonitrile **18** according to ref. 19.



Scheme 3

WARNING: Compound **8** is an explosive. A detonation occurred at its mp.

General procedure for the synthesis of 4-alkyl (or 4-aryl)amino-2-chloroquinoline-3-carbonitriles 2a–j

For 2a–f. The appropriate alkylamine (5.4 mmol) was added to a solution of **1** (0.2 g, 0.9 mmol) in DMF (3 mL). The reaction mixture was stirred for 10 min at room temperature and was than poured into water (10 mL). The precipitated solid product was isolated by suction and recrystallized from EtOH.

For 2g–j. The appropriate aromatic amine (13.44 mmol) was added to a solution of **1** (6.73 mmol) in DMF (15 mL). The reaction mixture was stirred at 50–60 °C for 4 h, during which time yellow crystals separated out. After cooling to room temperature the reaction mixture was worked up as described for **2a**–**f**. In the case of **2j**, the crude product was purified by preparative TLC using silica gel plates (toluene–acetone, 10 : 3 v/v), followed by recrystallization from EtOH.

2-Chloro-4-(methylamino)quinoline-3-carbonitrile 2a. Yield 0.190 g (97%) as *colorless needles*, mp 220–222 °C (Found: C, 60.74; H, 3.76; Cl, 16.20; N, 19.33. $C_{11}H_8ClN_3$ requires C, 60.69; H, 3.70; Cl, 16.31; N, 19.30%); ν_{max}/cm^{-1} 3350 (NH), 3050 (arom CH), 2930 (aliph CH) and 2200 (CN); δ 3.33 (d, *J* 4, 3H, NCH_3), 7.55–7.83 (m, 3H, 2 × ArH and NH), 8.27 (d, *J* 8, 1H, ArH) and 8.48 (d, *J* 8, 1H, ArH).

2-Chloro-4-(ethylamino)quinoline-3-carbonitrile 2b. Yield 0.202 g (97%) as *colorless needles*, mp 202–203 °C (Found: C, 62.18; H, 4.31; Cl, 15.53; N, 18.22. $C_{12}H_{10}ClN_3$ requires C, 62.20; H, 4.35; Cl, 15.32; N, 18.13%); ν_{max}/cm^{-1} 3330 (NH), 3050 (arom CH), 2980, 2920 (aliph CH) and 2220 (CN); δ 1.33 (t, *J* 6, 3H, CH_3), 3.87 (q, *J* 6, 2H, CH_2), 7.56–7.85 (m, 3H, 2 × ArH and NH) and 8.34–8.41 (m, 2H, ArH).

2-Chloro-4-(cyclohexylamino)quinoline-3-carbonitrile 2c. Yield 0.245 g (96%) as *colorless needles*, mp 137–138 °C (Found: C, 67.19; H, 5.79; Cl, 12.58; N, 14.62. $C_{16}H_{16}ClN_3$ requires C, 67.23; H, 5.64; Cl, 12.42; N, 14.70%); ν_{max}/cm^{-1} 3350 (NH), 3050 (arom CH), 2900 and 2850 (aliph CH) and 2200 (CN); δ 1.13–2.05 (m, 11H, aliph H), 7.55–7.80 (m, 3H, 2 × ArH and NH), 8.25 (d, *J* 8, 1H, ArH) and 8.45 (d, *J* 8, 1H, ArH).

4-Benzylamino-2-chloroquinoline-3-carbonitrile 2d. Yield 0.257 g (97%) as *colorless needles*, mp 205–207 °C (Found: C, 69.36; H, 4.29; Cl, 12.19; N, 14.23. $C_{17}H_{12}ClN_3$ requires C, 69.50; H, 4.12; Cl, 12.08; N, 14.30%); ν_{max}/cm^{-1} 3380 (NH), 3050 (arom CH), 2950 (aliph CH) and 2200 (CN); δ 5.10 (d, *J* 6, 2H, CH_2), 7.28–7.38 (m, 5H, ArH); 7.61–8.48 (m, 4H, ArH) and 8.99 (br s, 1H, NH).

2-Chloro-4-(isobutylamino)quinoline-3-carbonitrile 2e. Yield 0.280 g (96%) as *colorless needles*, mp 149–150 °C (Found: C, 64.89; H, 5.58; Cl, 13.53; N, 16.29. $C_{14}H_{14}ClN_3$ requires C, 64.73; H, 5.43; Cl, 13.67; N, 16.18%); ν_{max}/cm^{-1} 3350 (NH), 3050 (arom CH), 2950 (aliph CH) and 2200 (CN); δ 0.96 (d, *J* 6, 6H, 2 × CH_3), 2.10 (m, 1H, CH), 3.59 (t, *J* 6, 2H, CH_2), 7.56–7.84 (m, 3H, 2 × ArH and NH), 8.32 (d, *J* 8, 1H, ArH) and 8.51 (d, *J* 8, 1H, ArH).

2-Chloro-4-(isopropylamino)quinoline-3-carbonitrile 2f. Yield 0.212 g (96%) as *colorless needles*, mp 224–225 °C (Found: C, 63.76; H, 5.08; Cl, 14.29; N, 16.93. $C_{13}H_{12}ClN_3$ requires C, 63.53; H, 4.92; Cl, 14.45; N, 17.10%); ν_{max}/cm^{-1} 3350 (NH), 3080 (arom CH), 2980 (aliph CH) and 2200 (CN); δ 1.37 (d, *J* 6, 6H, 2 × CH_3), 4.74 (m, 1H, CH), 7.55–8.26 (m, 4H, 3 × ArH and NH) and 8.46 (d, *J* 8, 1H, NH).

4-Anilino-2-chloroquinoline-3-carbonitrile 2g. Yield 1.8 g (98%) as *yellowish needles*, mp 199–201 °C (Found: C, 68.59; H, 3.47; Cl, 12.52; N, 15.19. $C_{16}H_{10}ClN_3$ requires C, 68.69; H, 3.60; Cl , 12.69; N, 15.02%); ν_{max}/cm^{-1} 3400 (NH), 3050 (arom CH) and 2200 (CN); δ 7.28 (m, 5 H, ArH), 7.80 (m, 3 H, ArH), 8.45 (d, *J* 8, 1H, ArH) and 10.15 (s, 1H, NH).

2-Chloro-4-[(4-methylphenyl)amino]quinoline-3-carbonitrile 2h. Yield 1.94 g (98%) as *yellowish needles*, mp 207–209 °C (Found: C, 69.56; H, 4.17; Cl, 11.97; N, 14.33. $C_{17}H_{12}ClN_3$ requires C, 69.50; H, 4.12; Cl, 12.08; N, 14.30%); ν_{max}/cm^{-1} 3400 (NH), 3050 (arom CH), 2900 (aliph CH) and 2200 (CN); δ 2.36 (s, 3H, CH_3), 7.26 (m, 4H, ArH), 7.68 (m, 1H, ArH), 7.87 (m, 2 H, ArH), 8.50 (d, *J* 8, 1H, ArH) and 10.09 (s, 1H, NH).

2-Chloro-4-[(4-methoxyphenyl)amino]quinoline-3-carbonitrile 2i. Yield 2 g (96%) as *yellowish needles*, mp 216–218 °C (Found: C, 65.83; H, 4.0; Cl, 11.66; N, 13.50. $C_{17}H_{12}ClN_3O$ requires C, 65.91; H, 3.90; Cl, 11.46; N, 13.56%); ν_{max}/cm^{-1} 3320 (NH), 3050 (arom CH), 2950 and 2850 (aliph CH) and 2200 (CN); δ 3.81 (s, 3H, OCH_3), 7.01 (d, *J* 8, 2H, ArH), 7.33 (d, *J* 8, 2H, ArH), 7.65 (m, 1H, ArH), 7.84 (m, 2H, ArH), 8.51 (d, *J* 8, 1H, ArH) and 10.06 (s, 1H, NH).

2-Chloro-4-[(3-methylphenyl)amino]quinoline-3-carbonitrile 2j. Yield 1.909 g (96%) as *yellowish needles*, mp 165–166 °C (Found: C, 69.39; H, 4.16; Cl, 12.27; N, 14.38. $C_{17}H_{12}ClN_3$ requires C, 69.50; H, 4.12; Cl , 12.08; N, 14.30%); ν_{max}/cm^{-1} 3250 (NH), 3050 (arom CH), 2800 (aliph CH) and 2200 (CN); δ 2.35 (s, 3H, CH_3), 7.14 (m, 3H, ArH), 7.33 (m, 1H, ArH), 7.69 (m, 1H, ArH), 7.85 (m, 2H, ArH), 8.50 (d, *J* 8, 1H, ArH) and 10.11 (s, 1H, NH).

General procedure for the synthesis of 4-benzyl (or phenyl)amino-2-oxo-1,2-dihydroquinoline-3-carbonitrile 3d, g

A solution of **2d** or **2g** (1.7 mmol) in a mixture of acetic acid (10 mL) and water (2 mL) was refluxed for 6 h. The solvent was then removed under reduced pressure and the resulting solid product was collected by filtration, dried and recrystallized from DMF.

4-Benzylamino-2-oxo-1,2-dihydroquinoline-3-carbonitrile 3d. Yield 0.440 g (94%) as *colorless needles*, mp 252–253 °C (Found: C, 74.01; H, 4.95; N, 15.18. $C_{17}H_{13}N_3O$ requires C, 74.17; H, 4.76; N, 15.26%); ν_{max}/cm^{-1} 3300 and 3200 (NH), 2200 (CN) and 1650 (CO); δ 5.20 (d, *J* 6, 2H, CH_2), 7.30–7.40 (m, 5H, ArH), 7.62–8.49 (m, 4H, ArH), 9.01 (br s, 1H, NH) and 11.62 (s, 1H, quinoline NH).

4-Anilino-2-oxo-1,2-dihydroquinoline-3-carbonitrile 3g. Yield 0.40 g (90%) as *yellowish needles*, mp 332–334 °C (Found: C, 73.68; H, 4.35; N, 16.02. $C_{16}H_{11}N_3O$ requires C, 73.55; H, 4.24; N, 16.08%); ν_{max}/cm^{-1} 3300 and 3200 (NH), 2200 (CN) and 1650 (CO); δ 7.30 (m, 5H, ArH), 7.83 (m, 3H, ArH), 8.48 (d, *J* 8, 1H, ArH), 10.19 (s, 1H, NH) and 11.67 (s, 1H, quinoline NH).

Reaction of 2a–j and 8 with hydrazine hydrate

Synthesis of 3-amino-4-arylamino-1*H*-pyrazolo[3,4-*b*]quinolines 4g–j. A mixture of an arylamine **2g**–**j** (1.36 mmol) and hydrazine hydrate (5 ml; 80%) was refluxed for 3 h, until TLC showed the disappearance of the starting compounds. After cooling, the mixture was evaporated to dryness *in vacuo*. Methanol (3 mL) was added to the remaining oily residue with stirring. The solution was neutralized with acetic acid and the precipitated solid product was collected by filtration, washed with methanol, dried and recrystallized from DMF–EtOH.

3-Amino-4-anilino-1H-pyrazolo[3,4-b]quinoline ***4g***. Yield 0.251 g (67%) as *orange needles*, mp 290–292 °C (decomp.) (Found: C, 69.74; H, 4.92; N, 25.38. $C_{16}H_{13}N_5$ requires C, 69.80; H, 4.76; N, 25.44%); ν_{max}/cm^{-1} 3400–2700 (NH, NH_2) and 1640

(C=N); δ 5.69 (br s, 2H, NH_2), 7.19–8.71 (m, 9H, ArH), 10.83 (s, 1H, NH) and 12.52 (s, 1H, pyrazole NH).

3-Amino-4-[(4-methylphenyl)amino]-1H-pyrazolo[3,4-b]-quinoline ***4h***. Yield 0.237g (60%) as *orange needles*, mp 248–250 °C (decomp.) (Found: C, 70.46; H, 5.26; N, 24.14. $C_{17}H_{15}N_5$ requires C, 70.57; H, 5.23; N, 24.21%); ν_{max}/cm^{-1} 3400–2700 (NH, NH_2) and 1640 (C=N); δ 2.37 (s, 3H, CH_3), 6.04 (br s, 2H, NH_2), 7.11–8.66 (m, 8H, ArH), 10.65 (s, 1H, NH) and 12.45 (s, 1H, pyrazole NH).

3-Amino-4-[(4-methoxyphenyl)amino]-1H-pyrazolo[3,4-b]-quinoline ***4i***. Yield 0.266 g (60%) as *orange needles*, mp 276–278 °C (decomp.) (Found: C, 66.67; H, 5.02; N, 22.89. $C_{17}H_{15}N_5O$ requires C, 66.87; H, 4.95; N, 22.94%); ν_{max}/cm^{-1} 3400–2700 (NH, NH_2) and 1640 (C=N); δ 3.83 (s, 3H, OCH_3), 5.72 (br s, 2H, NH_2), 7.16–8.63 (m, 8H, ArH), 10.64 (s, 1H, NH) and 12.44 (s, 1H, pyrazole NH).

3-Amino-4-[(3-methylphenyl)amino]-1H-pyrazolo[3,4-b]-quinoline ***4j***. Yield 0.230 g (58%) as *orange needles*, mp 308–310 °C (decomp.) (Found: C, 70.41; H, 5.40; N, 24.12 $C_{17}H_{15}N_5$ requires C, 70.57; H, 5.23; N, 24.21%); ν_{max}/cm^{-1} 3400–2700 (NH, NH_2) and 1640 (C=N); δ 2.36 (s, 3H, CH_3), 5.71 (br s, 2H, NH_2), 7.18–8.68 (m, 8H, ArH), 10.81 (s, 1H, NH) and 12.50 (s, 1H, pyrazole NH).

Synthesis of 3-amino-4-hydrazino-1*H*-pyrazolo[3,4-*b*]quinoline 7. A mixture of an alkylamine **2a**–**f** (4.6 mmol) and hydrazine hydrate (80%; 8 mL) was heated under reflux for 15 min and then left to cool to room temperature, whereupon the product crystallized as orange needles. The resulting product was isolated by suction and washed with EtOH. The product was obtained in 65–77% yield as *orange needles*, mp 292–294 °C (decomp.) (from EtOH) (Found: C, 55.89; H, 4.79; N, 39.08. $C_{10}H_{10}N_6$ requires C, 56.06; H, 4.71; N, 39.23%); ν_{max}/cm^{-1} 3400, 3330, 3300 and 3150 (NH, NH_2), 1650 (δ NH) and 1610 (C=N); δ 5.42 (br s, 2H, NH_2), 6.04 (br s, 2H, NH_2), 7.59–8.41 (m, 4H, ArH), 8.91 (br s, 1H, NH) and 11.17 (s, 1H, pyrazole NH); *m/z* 214 (M^+, 100%), 184 (52), 169 (39), 155 (22), 143 (38), 129 (69) and 102 (41).

Synthesis of 3-amino-4-hydrazino-1*H*-pyrazolo[4,3-*c*]quinoline 10

A mixture of **11**[2] (0.6 g, 2.74 mmol) and hydrazine hydrate (99%; 0.28 g, 5.6 mmol) in DMF (5 mL) was refluxed for 15 min, during which time yellow crystals separated out. After cooling to room temperature, the resulting solid title product was filtered off, dried, and recrystallized from DMF to give *yellowish crystals* (0.440 g, 75%), mp 352–353 °C (Found: C, 56.14; H, 4.83; N, 39.15. $C_{10}H_{10}N_6$ requires C, 56.06; H, 4.71; N, 39.23%); ν_{max}/cm^{-1} 3300, 3250 and 3200 (NH, NH_2) and 1620 (C=N); δ 5.41 (br s, 2H, NH_2), 6.07 (br s, 2H, NH_2), 7.65 (m, 2H, ArH), 8.24 (d, *J* 8, 1H, ArH), 8.40 (d, *J* 8, 1H, ArH), 9.79 (br s, 1H, NH) and 13.13 (s, 1H, pyrazole NH).

Reaction of 4g–j and 7 with nitrous acid

General procedure for the 1-aryl-1,5-dihydro-1,2,3,4,5,6-hexaazaacephenanthrylenes 5g–j and 2,4-diazidoquinoline-3-carbonitrile 8. *For* ***5g–j***. Aq $NaNO_2$ (5.46 mmol in 3 mL) was added dropwise to a solution of an arylamine **4g–j** (1.82 mmol) in H_2SO_4 (10 mL, 70%) cooled in ice–salt to −10 °C, while the temperature of the reaction mixture was maintained at −10 to −5 °C. The reaction mixture was kept at −5 °C for 1 h and then was poured into ice–water. The precipitated solid product was collected by filtration, washed well with water, dried, and recrystallized from DMF to give the corresponding tetracycle **5g–j**.

For ***8***. Aq. $NaNO_2$ (0.967 g, 14 mmol in 3 mL) was added dropwise to a solution of **7** (1 g, 4.7 mmol) in H_2SO_4 (10 mL; 70%) and then the reaction mixture was worked up as described for **5g–j**.

1,5-Dihydro-1-phenyl-1,2,3,4,5,6-hexaazaacephenanthrylene ***5g***. Yield 0.380 g (73%), as *brownish needles*, mp 312–314 °C (decomp.) (Found: C, 66.94; H, 3.70; N, 29.22. $C_{16}H_{10}N_6$ requires C, 67.12; H, 3.52; N, 29.36%); ν_{max}/cm^{-1} 3400 (NH), 1670 (N=N) and 1640 (C=N); δ 7.69–8.85 (m, 9H, ArH) and 14.18 (s, 1H, NH).

1,5-Dihydro-1-(4-methylphenyl)-1,2,3,4,5,6-hexaazaacephenanthrylene ***5h***. Yield 0.388 g (71%) as *brownish needles*, mp > 360 °C (Found: C, 67.89; H, 4.14; N, 27.85. $C_{17}H_{12}N_6$ requires C, 67.99; H, 4.03; N, 27.98%); ν_{max}/cm^{-1} 3200 (NH), 2800 (aliph CH), 1670 (N=N) and 1630 (C=N); δ 2.38 (s, 3H, CH_3), 7.64–8.81 (m, 8H, ArH) and 14.16 (s, 1H, NH).

1,5-Dihydro-1-(4-methoxyphenyl)-1,2,3,4,5,6-hexaaza-acephenanthrylene ***5i***. Yield 0.437 g (76%) as *brownish needles*, mp > 360 °C (Found: C, 64.38; H, 3.79; N, 26.39. $C_{17}H_{12}N_6O$ requires C, 64.55; H, 3.83; N, 26.57%); ν_{max}/cm^{-1} 3200 (NH), 2850 (aliph CH), 1670 (N=N) and 1630 (C=N); δ 3.82 (s, 3H, OCH_3), 7.66–8.80 (m, 8H, ArH) and 14.15 (s, 1H, NH).

1,5-Dihydro-1-(3-methylphenyl)-1,2,3,4,5,6-hexaazaacephenanthrylene ***5j***. Yield 0.366 g (67%) as *brownish needles*, mp > 360 °C (Found: C, 67.78; H, 4.21; N, 28.15. $C_{17}H_{12}N_6$ requires C, 67.99; H, 4.03; N, 27.98%); ν_{max}/cm^{-1} 3200 (NH), 2800 (aliph CH), 1670 (N=N) and 1630 (C=N); δ 2.39 (s, 3H, CH_3), 7.65–8.84 (m, 8H, ArH) and 14.17 (s, 1H, NH).

2,4-Diazidoquinoline-3-carbonitrile ***8***. Yield 0.768 g (70%) as *brownish needles*, mp 130 °C [decomp. (with explosion)] (Found: C, 51.02; H, 1.59; N, 47.56. $C_{10}H_4N_8$ requires C, 50.85; H, 1.71; N, 47.44%); ν_{max}/cm^{-1} 2190 (CN) and 2140 (N_3); δ 7.70 (t, *J* 8, 1H, ArH), 7.90 (t, *J* 8, 1H, ArH), 8.14 (d, *J* 8, 1H, ArH) and 8.28 (d, *J* 8, 1H, ArH), δ_C 104.37 (C-3), 109.33 (C-4a), 118.54 (CN), 122.30 (C-6), 127.16 (C-5), 129.52 (C-7), 130.92 (C-8), 137.91 (C-8a), 147.47 (C-4), 160.94 (C-2); *m/z* 236 (M^+, 27%), 152 (68), 125 (11), 100 (40), 87 (100).

2-Azido-4-morpholinoquinoline-3-carbonitrile 14

Morpholine (0.295 g, 3.4 mmol) was added to a solution of **8** (0.2 g, 0.85 mmol) in DMF (3 mL). The mixture was stirred for 10 min at room temperature and then poured into water (10 mL). The precipitated solid product was collected by filtration and recrystallized from EtOH to give compound **14** as greenish microcrystals (0.230 g, 97%), mp 230–231 °C (decomp.) (Found: C, 59.87; H, 4.38; N, 29.79. $C_{14}H_{12}N_6O$ requires C, 59.99; H, 4.32; N, 29.98%); ν_{max}/cm^{-1} 3100 (arom CH), 2970 and 2850 (aliph CH), 2190 (CN), 2140 (N_3) and 1610 (C=N); δ 3.84 (br s, 4H, 2 × NCH_2), 3.93 (br s, 4H, 2 × OCH_2), 7.44 (t, *J* 8, 1H, ArH), 7.77 (t, *J* 8, 1H, ArH), 7.90 (d, *J* 8, 1H, ArH) and 8.26 (d, *J* 8, 1H, ArH).

General procedure for the 2,4-diaminoquinoline-3-carbonitriles 15, 16

Sodium dithionite (0.6 g, 3.45 mmol) was added portionwise to a stirred suspension of **14** (0.3 g, 1.07 mmol) in a methanol (20 mL)–water (10 mL) mixture. Stirring was maintained at 50–60 °C for 3 h. After cooling, water was added and the resulting solid product was collected by filtration, washed well with water, dried, and recrystallized from MeOH to give **15**. In the case of **16**, sodium dithionite (1.2 g, 6.90 mmol) was added to a stirred suspension of **8** (0.3 g, 1.3 mmol) in a methanol (30 mL)–water (15 mL) mixture. Stirring was maintained at 50–60 °C for 5 h. Then, the reaction mixture was worked up as described for **15**.

2-Amino-4-morpholinoquinoline-3-carbonitrile 15. Yield 0.250 g (92%) as *orange crystals*, mp 214–215 °C (decomp.) (Found: C, 66.33; H, 5.52; N, 21.89. $C_{14}H_{14}N_4O$ requires C , 66.23; H, 5.55; N, 22.03%); ν_{max}/cm^{-1} 3400, 3300 and 3200 (NH_2), 2950 and 2850 (aliph CH), 2200 (CN) and 1640 (C=N); δ 3.87 (br s, 4H, 2 × NCH_2), 3.91 (br s, 4H, 2 × OCH_2), 7.30 (t, *J* 8, 1H,

ArH), 7.67 (m, 2H, ArH), 8.37 (d, *J* 8, 1H, ArH) and 8.52 (br s, 2H, NH_2).

2,4-Diaminoquinoline-3-carbonitrile 16. Yield 0.210 g (90%) as yellowish crystals, mp 302–304 °C (lit.,[18] 303–305 °C).

2-Amino-4-hydroxyquinoline-3-carbonitrile 18

A mixture of **15** (0.5 g, 2.7 mmol), acetic acid (7 mL) and water (2 mL) was refluxed for 4 h. The solvent was removed *in vacuo* and the resulting solid product was collected by filtration, washed with water, dried, and recrystallized from DMF to afford *compound* **18** as colorless crystals (0.290 g, 80%), mp > 360 °C (Found: C, 64.76; H, 3.69; N, 22.82. $C_{10}H_7N_3O$ requires C, 64.86; H, 3.81; N, 22.69%); ν_{max}/cm^{-1} 3400, 3300, 3200 and 3100 (NH) and 2200 (CN); δ 7.15 (s, 2H, NH_2), 7.20–8.0 (m, 4H, ArH) and 11.18 (br s, 1H); *m*/*z* 185 (M^+, 100%), 157 (16), 129 (7), 120 (49), 92 (18).

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