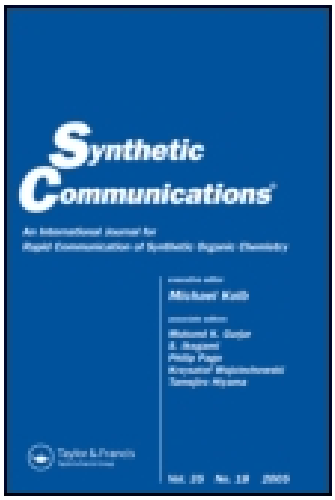

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FUSED QUINOLINE HETEROCYCLES. II. FIRST SYNTHESIS OF 1,2,3,4,5,6-HEXAAZAACEANTHRYLENES AND 5,7,8,10a,11-PENTAAZABENZO[a]-FLUORENES

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ABSTRACT

The new tetracyclic ring systems 5-alkyl-1,5-dihydro-1,2,3,4,5,6-hexaazaaceanthrylenes **5a–d** were synthesized by diazotization of 4-alkylamino-3-amino-1*H*-pyrazolo[4,3-c]quinolines **4a–d**. The 4-arylamino-3-diazo-1*H*-pyrazolo-[4,3-c]-quinolines **6e–h**, which were prepared by diazotisation of the corresponding amines **4e–h**, readily formed the novel tetracyclic ring system ethyl 6-arylamino-10-methyl-5,7,8,10a,11-pentaazabenzo[a]fluorene-9-carboxylates **8e–h**, when treated with ethyl acetoacetate.

Recent years have witnessed a significant interest in the synthesis of new heterocyclic rings stimulated by reports that a wide range of polyheterocyclic compounds isolated from marine organisms show anti-tumor activity.[1–4] Tetracyclic ring systems, such as 2-dimethylamino[1]

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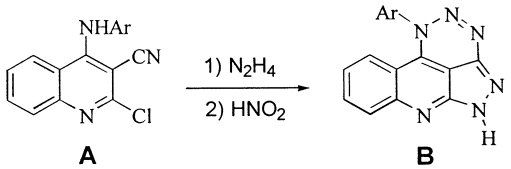
benzothiopyrano[4,3,2-de]-quinoline,[5] 1-amino-6-methyl[1]benzothiopyrano-[4,3,2-de]quinoline-2(3*H*)-one[6] and pyrido [3$^-$, 2$^-$: 6,5]thiopyrano[4,3,2-de]-quinoline[7] have already been synthesized and reported to have promising antitumor activity or analgesic and psychopharmacological properties. These valuable properties prompted us to prepare new tetracyclic systems containing a quinoline nucleus with potential biological activity in our search for novel heterocyclic compounds of pharmacological interest.



A **B**

In a previous paper,[8] we have shown that the reaction of 4-arylamino-2-chloroquinoline-3-carbonitriles **A** with hydrazine hydrate gave 3-amino-4-arylamino-1*H*-pyrazolo[3,4-b]quinolines which by diazotization yielded 1-aryl-1,5-dihydro-1,2,3,4,5,6-hexaazaacephenanthrylenes **B**, as new tetracyclic ring systems. Interestingly, when 4-alkylamino-2-chloroquinoline-3-carbonitriles underwent the same sequence of reactions, the reaction took a different course. In all cases, the unexpected 2,4-diazidoquinoline-3-carbonitrile was the isolated product instead of the tetracyclic system (**B**).[8] In order to obtain better understanding of this kind of reaction and to extend the scope of this reaction to other heterocyclic systems, we examined this reaction sequence in 3-amino-4-chloro-1*H*-pyrazolo[4,3-c]quinoline **2**, as another model system for pyrazoloquinolines. In this paper and as a further extension of our previous work,[8–14] aimed to prepare new heterocyclic systems containing the quinoline moiety. We would like to report on a novel and convenient procedure for new 5-alkyl-1,5-dihydro-1,2,3,4,5,6-hexaazaaceanthrylenes **5a–d** and 5,7,8,10a,11-pentaazabenzo[a]fluorenes **8e–h**, containing both the pyrazole and triazine moieties condensed with a quinoline nucleus, otherwise accessible only with difficulty, commencing with 3-amino-4-chloro-1*H*-pyrazolo-[4,3-c]quinoline (**2**). In a search of the literature it is surprising that these ring systems have been largely ignored.

The key 3-amino-4-chloro-1*H*-pyrazolo[4,3-c]quinoline **2** was easily prepared by reacting 2,4-dichloroquinoline-3-carbonitrile (**1**)[9] with hydrazine hydrate in DMF at room temperature. Replacement of the chlorine atom at position 4 was achieved when compound **2** was heated in an excess of the alkylamines **3a–d** at reflux temperature, giving the corresponding 4-alkylamino-3-amino-1*H*-pyrazolo[4,3-c]quinolines **4a–d**, in yields higher than 80%. Analytical and spectroscopic data fully support the structural

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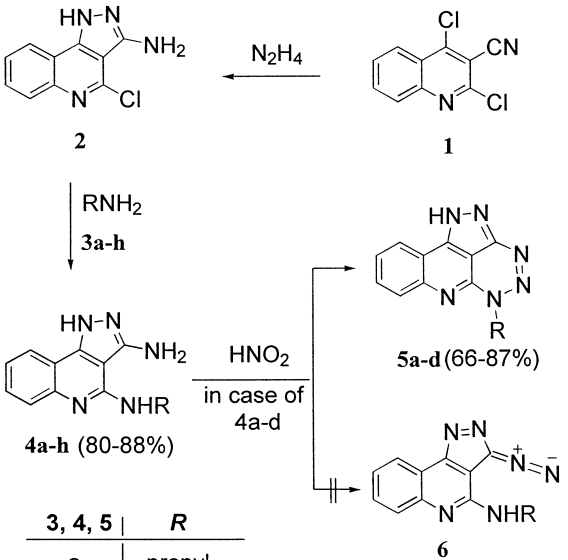
assignment for compounds **4a–d**. The ^{1}H NMR spectra showed the presence of signals corresponding to the protons of the amino groups at C-3, C-4 and a singlet in the region δ 12.63–12.68 ppm due to the pyrazole NH as well as aliphatic protons in their expected positions. Reaction of compounds **4a–d** with sodium nitrite in a 70% solution of H_2SO_4 at -5°C gave the previously unreported 5-alkyl-1,5-dihydro-1,2,3,4,5,6-hexaazaaceanthrylenes **5a–d** (Scheme 1), in good yield. The other possible structure **6** was readily ruled out for the reaction product on the basis of spectral data. The absence of a diazo absorption at 2160 cm^{-1} [15] in IR spectrum of the reaction product confirmed the assigned structure **5** and allowed us to discard the other possible structure **6**. Furthermore, the structures of **5a–d** were established from their ^{1}H NMR spectra, correct elemental analyses as well as mass spectra. The data used to characterize these prepared compounds are given in the Experimental.



3, 4, 5	*R*
a	propyl
b	isobutyl
c	butyl
d	cyclohexyl
e	Ph
f	3-F-C_6H_4
g	4-CH_3-C_6H_4
h	4-OCH_3-C_6H_4

Scheme 1.

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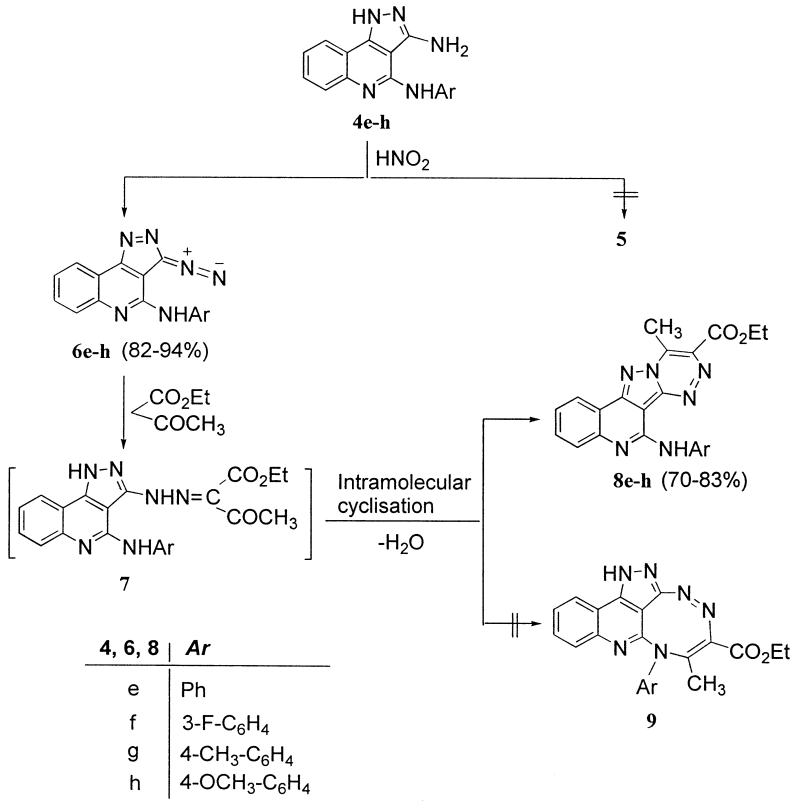
Our interest to synthesize the interesting novel heterocyclic pyrazolo-triazino-quinoline ring system **5**, led us to investigate the reaction of **2** with arylamines **3e–h**, which gave pyrazoloquinolines **4e–h**, a good precursor for the synthesis of **5**. When compound **2** was reacted with **3e–h** in DMF at reflux for 3 hours the corresponding 4-arylamino-pyrazoloquinolines **4e–h** were isolated. Structural elucidation of compounds **4e–h** was accomplished from their elemental analyses and spectroscopic data. The ^{1}H NMR spectra were in accord with the proposed structures which revealed the presence of signals at δ 5.62–5.72 and δ 8.16–8.44 ppm assignable to amino group at C-3, C-4, respectively, and there was a pyrazole NH at δ 12.88–12.99 ppm, besides signals due to aromatic protons in their expected positions. We expected that the reaction of **4e–h** 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**, since a similar reaction had readily been achieved with



4, 6, 8	*Ar*
e	Ph
f	3-F-C_6H_4
g	4-CH_3-C_6H_4
h	4-OCH_3-C_6H_4

Scheme 2.

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the analogous compound, 3-amino-4-arylamino-1*H*-pyrazolo[3,4-b]quinolines.[8] Surprisingly, we found that the new 4-arylamino-3-diazo-1*H*-pyrazolo-[4,3-c]quinolines **6e–h** were obtained by diazotisation of the amines **4e–h** under ordinary condition, when it separated from the reaction mixture, in high yields, without the need for basification. The structural constitutions of compounds **6** were inferred from their elemental analyses and spectral data. The IR spectra exhibited absorption bands at 3350 and 2150 cm^{-1} due to the NH and (diazo) groups, respectively. The ^1H NMR spectra gave strong evidence for the formation of the diazo compound **6**, which revealed the presence of an absorption band at about $\delta \approx 8.70$ ppm, assigned for NH group at quinoline C-2 and the absence of pyrazole NH (ca. 14.34 ppm).

In view of the work already described we aimed first to prepare the new tetracyclic ring system of type **5**. We treated the 3-diazo compound **6e–h** with ethyl acetoacetate in the expectation that the respective hydrazones **7** would be formed,[16] and that they could subsequently be cyclised. In practice, the hydrazones **7** cyclised spontaneously, to afford directly the target tetracyclic ring system **8** for which the alternative isomeric structure **9** is theoretically possible. The latter structure could be eliminated on account of the ^1H NMR spectra, which revealed the presence of NH group at quinoline C-2; and the absence of pyrazole NH in their expected positions. It should be noted that compound **8** had been formed by intramolecular cyclisation, *via* elimination of water, involving the acetyl group of the hydrazone **7**, rather than the ethoxycarbonyl group, this is perhaps surprising since cyclisation *via* the latter would have preserved the aromaticity of quinoline ring.

We conclude that this second-generation version of our annulation strategy shows for the first time a new general route to 5-alkyl-1,5-dihydro-1,2,3,4,5,6-hexaazaaceanthrylenes **5a–d** and ethyl 6-arylamino-10-methyl-5,7,8,10a,11-pentaazabenzo[a]fluorene-9-carboxylates **8e–h** bearring various substituents at the triazine ring. This synthetic approach, for the preparation of **5a–d** and **8e–h**, may be useful in view of the pharmacological interest in this compound class. Further studies are under way in our laboratory aimed at the application of this methodology to the preparation of new tetracyclic systems starting from pyrrolo[3,2-c]quinolines.

EXPERIMENTAL

M.P.'s were measured on a Gallenkamp melting point apparatus and are uncorrected. IR spectra were recorded on a Shimadzu 470 spectrophotometer (KBr pellets). ^1H NMR spectra were recorded on a Bruker AC270 or a Bruker AM400 spectrometer at 270 or 400 MHz, respectively, in (DMSO-d_6) using TMS as internal standard and Chemical shifts are

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expressed as δ values (ppm). Microanalyses were performed by the microanalytical Data Unit at Cairo University. Mass spectra were recorded on GCMS-QP 1000EX spectrometer (ionization energy 70 eV). Analytical TLC was performed with silica gel plates using silica gel 60 PF_{254} (Merck). 3-Amino-4-cyclohexylamino-1*H*-pyrazolo[4,3-c]quinoline (**4d**) was prepared according to the procedure described in reference 9.

General Procedure for the Synthesis of 3-Amino-4-amino-substituted-1*H*-pyrazolo[4,3-c]quinolines 4a–h

For **4a–d**: A solution of **2** (0.5 g, 2.29 mmol) in excess of alkylamines **3a–c** (15 mL) was heated at reflux. After 96 hours all the starting **2** was consumed (tlc). After cooling, the mixture was evaporated to dryness in vacuo. Crushed ice was added to the remaining oil residue with stirring. The solution was neutralized with conc. HCl, the precipitated solid product was collected by filtration, dried and recrystallized from methanol. For **4e–h**, the appropriate aromatic amine (4.58 mmol) was added to a solution of **2** (0.5 g, 2.29 mmol) in DMF (10 mL). The reaction mixture was heated at reflux for 3 hours. The mixture was then evaporated to dryness under reduced pressure. The residue was triturated with cold water and the resulting solid product was collected, dried and recrystallized from methanol.

3-Amino-4-propylamino-1*H*-pyrazolo[4,3-c]quinoline, **4a**

Colorless prisms, Yield 82%, mp 247–248°C; ^{1}H NMR (DMSO-d_6): δ 0.97 (t, 3H), 1.68 (m, 2H), 3.50 (q, 2H), 5.49 (s br, 2H), 6.42 (t, 1H), 7.13 (t, 1H), 7.40 (t, 1H), 7.50 (d, 1H), 7.95 (dd, 1H) and 12.64 (s, 1H) ppm; Infrared (KBr): 3400, 3300, 3200 (NH, NH_2), 2950, 2900 (aliph CH) and 1625 (C = N) cm^{-1}; Anal. Calcd. for $C_{13}H_{15}N_5$: C, 64.71; H, 6.26; N, 29.02. Found: C, 64.89; H, 6.37; N, 29.07.

3-Amino-4-isobutylamino-1*H*-pyrazolo[4,3-c]quinoline, **4b**

Colorless prisms, Yield 86%, mp 307–308°C; ^{1}H NMR (DMSO-d_6): δ 0.97 (d, 6H), 2.08 (m, 1H), 3.56 (t, 2H), 5.54 (s br, 2H), 6.35 (t, 1H), 7.14 (t, 1H), 7.46 (t, 1H), 7.58 (d, 1H), 8.00 (d, 1H) and 12.68 (s, 1H) ppm; Infrared (KBr): 3400, 3150 (NH, NH_2), 2950, 2900 (aliph CH) and 1620 (C = N) cm^{-1}; Mass Spectrum (m/z): 255 (15) (M^+); Anal. Calcd. for $C_{14}H_{17}N_5$: C, 65.86; H, 6.71; N, 27.43. Found: C, 65.70; H, 6.85; N, 27.50.

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3-Amino-4-butylamino-1*H*-pyrazolo[4,3-c]quinoline, **4c**

Colorless crystals, Yield 83%, mp 224–225°C; ^{1}H NMR (DMSO-d_6): δ 0.95 (t, 3H), 1.42 (m, 2H), 1.65 (m, 2H), 3.54 (q, 2H), 5.47 (s br, 2H), 6.38 (t, 1H), 7.13 (t, 1H), 7.40 (t, 1H), 7.52 (d, 1H), 7.95 (d, 1H) and 12.63 (s, 1H) ppm; Infrared (KBr): 3400, 3150 (NH, NH_2), 2950, 2900, 2850 (aliph CH) and 1625 (C = N) cm^{-1}; Anal. Calcd. for $C_{14}H_{17}N_5$: C, 65.86; H, 6.71; N, 27.43. Found: C, 65.96; H, 6.77; N, 27.41.

3-Amino-4-anilino-1*H*-pyrazolo[4,3-c]quinoline, **4e**

Colorless crystals, Yield 87%, mp 258–259°C; ^{1}H NMR (DMSO-d_6): δ 5.64 (s, 2H), 7.00–7.64 (m, 5H), 7.96–8.07 (m, 4H), 8.24 (s, 1H) and 12.92 (s, 1H) ppm; Infrared (KBr): 3350, 3200 (NH, NH_2), 3050 (ArCH) and 1625 (C = N) cm^{-1}; Mass Spectrum (m/z): 275 (86) (M^+); Anal. Calcd. for $C_{16}H_{13}N_5$: C, 69.80; H, 4.76; N, 25.44. Found: C, 69.68; H, 4.57; N, 25.30.

3-Amino-4-(3-fluorophenylamino)-1*H*-pyrazolo[4,3-c]quinoline, **4f**

Buff crystals; Yield 84%, mp 235–237°C; ^{1}H NMR (DMSO-d_6): δ 5.70 (s, 2H), 7.33–7.71 (m, 5H), 8.08–8.21 (m, 3H), 8.44 (s, 1H) and 12.99 (s, 1H) ppm; Infrared (KBr): 3350, 3200 (NH, NH_2), 3050 (ArCH) and 1620 (C = N) cm^{-1}; Mass Spectrum (m/z): 293 (98) (M^+); Anal. Calcd. for $C_{16}H_{12}FN_5$: C, 65.52; H, 4.13; N, 23.88. Found: C, 65.67; H, 3.95; N, 24.02.

3-Amino-4-(4-methylphenylamino)-1*H*-pyrazolo[4,3-c]quinoline, **4g**

Colorless crystals, Yield 88%, mp 296–298°C; ^{1}H NMR (DMSO-d_6): δ 2.32 (s, 3H), 5.62 (s, 2H), 7.03–7.42 (m, 4H), 7.64–8.05 (m, 4H), 8.20 (s, 1H) and 12.89 (s, 1H) ppm; Infrared (KBr): 3350, 3300, 3200 (NH, NH_2) and 1640 (C = N) cm^{-1}; Anal. Calcd. for $C_{17}H_{15}N_5$: C, 70.57; H, 5.23; N, 24.20. Found: C, 70.39; H, 5.26; N, 24.11.

3-Amino-4-(4-methoxyphenylamino)-1*H*-pyrazolo[4,3-c]quinoline, **4h**

Colorless crystals, Yield 80%, mp 235–237°C; ^{1}H NMR (DMSO-d_6): δ 3.77 (s, 3H), 5.72 (s, 2H), 6.95 (d, 2H), 7.26 (t, 1H), 7.47 (t, 1H), 7.58 (d, 1H), 7.81 (d, 2H), 8.04 (d, 1H), 8.16 (s, 1H) and 12.88 (s, 1H) ppm;

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Infrared (KBr): 3350, 3200 (NH, NH_2) and 1630 (C = N) cm^{-1}; Anal. Calcd. for $C_{17}H_{15}N_5O$: C, 66.87; H, 4.95; N, 22.94. Found: C, 66.95; H, 4.97; N, 22.88.

General Procedure for the Synthesis of 5-Alkyl-1,5-dihydro-1,2,3,4,5,6-hexaazaaceanthrylenes 5a–d and 4-Arylamino-3-diazo-1*H*-pyrazolo[4,3-c]quinolines 6e–h

A solution of $NaNO_2$ (4.5 mmol) in H_2O (2 mL) was added dropwise to a solution of **4a–h** (1.5 mmol) in H_2SO_4 (5 mL, 70%) cooled to −10°C, whilst maintaining the temperature at (−10°C) to (−5°C). The reaction mixture was kept at −5°C for 1 hour and then poured into ice water. The resulting solid product was filtered, washed well with water, dried and recrystallized from methanol to give **5a–d** and **6e–h**.

1,5-Dihydro-5-propyl-1,2,3,4,5,6-hexaazaaceanthrylene, **5a**

Yellow crystals, Yield 68%, mp 216–218°C (decp.); ^{1}H NMR (DMSO-d_6): δ 0.99 (t, 3H), 1.93 (m, 2H), 4.37 (t, 2H), 7.42 (t, 1H), 7.59 (t, 1H), 7.80 (d, 1H), 7.99 (d, 1H) and 14.33 (s, 1H) ppm; Infrared (KBr): 3350 (NH), 3050 (ArCH), 2950, 2900, 2800 (aliph CH), 1685 (N = N) and 1630 (C = N) cm^{-1}; Mass Spectrum (m/z): 252 (8) (M^+); Anal. Calcd. for $C_{13}H_{12}N_6$: C, 61.89; H, 4.80; N, 33.31. Found: C, 61.98; H, 4.77; N, 33.38.

1,5-Dihydro-5-isobutyl-1,2,3,4,5,6-hexaazaaceanthrylene, **5b**

Yellow crystals, Yield 70%, mp 240°C (decp.); ^{1}H NMR (DMSO-d_6): δ 0.99 (d, 6H), 2.10 (m, 1H), 4.24 (d, 2H), 7.44 (t, 1H), 7.59 (t, 1H), 7.81 (d, 1H), 8.00 (d, 1H) and 14.35 (s, 1H) ppm; Infrared (KBr): 3350 (NH), 3050 (ArCH), 2950, 2900 (aliph CH), 1685 (N = N) and 1630 (C = N) cm^{-1}; Mass Spectrum (m/z): 266 (12) (M^+); Anal. Calcd. for $C_{14}H_{14}N_6$: C, 63.14; H, 5.30; N, 31.56. Found: C, 62.95; H, 5.26; N, 31.42.

5-Butyl-1,5-dihydro-1,2,3,4,5,6-hexaazaaceanthrylene, **5c**

Yellow crystals, Yield 66%, mp 202–204°C; ^{1}H NMR (DMSO-d_6): δ 0.96 (t, 3H), 1.43 (m, 2H), 1.89 (m, 2H), 4.40 (t, 2H), 7.42 (t, 1H), 7.59 (t, 1H),

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7.80 (d, 1H), 7.99 (d, 1H) and 14.34 (s, 1H) ppm; Infrared (KBr): 3400 (NH), 3050 (ArCH), 2950, 2900, 2850 (aliph CH), 1685 (N = N) and 1630 (C = N) cm^{-1}; Anal. Calcd. for $C_{14}H_{14}N_6$: C, 63.14; H, 5.30; N, 31.56. Found: C, 63.21; H, 5.36; N, 31.69.

5-Cyclohexyl-1,5-dihydro-1,2,3,4,5,6-hexaazaaceanthrylene, **5d**

Orange crystals, Yield 87%, mp 220–222°C (decp.); ^1H NMR (DMSO-d_6): δ 1.32–2.05 (m, 10H), 4.87 (m, 1H), 7.43 (t, 1H), 7.60 (t, 1H), 7.83 (d, 1H), 8.01 (d, 1H) and 14.34 (s, 1H) ppm; Infrared (KBr): 3350 (NH), 3050 (ArCH), 2950, 2850 (aliph CH), 1685 (N = N) and 1630 (C = N) cm^{-1}; Mass Spectrum (m/z): 292 (18) (M^+); Anal. Calcd. for $C_{16}H_{16}N_6$: C, 65.73; H, 5.52; N, 28.75. Found: C, 65.54; H, 5.57; N, 28.58.

4-Anilino-3-diazo-1*H*-pyrazolo[4,3-c]quinoline, **6e**

Off-brown crystals, Yield 85%, mp 315–316°C (decp.); ^1H NMR (DMSO-d_6): δ 7.28–8.06 (m, 9H) and 8.74 (s, 1H) ppm; Infrared (KBr): 3350 (NH), 3050 (ArCH), 2150 (diazo) and 1620 (C = N) cm^{-1}; Mass Spectrum (m/z): 286 (5) (M^+); Anal. Calcd. for $C_{16}H_{10}N_6$: C, 67.12; H, 3.52; N, 29.36. Found: C, 67.23; H, 3.48; N, 29.31.

3-Diazo-4-(3-fluorophenylamino)-1*H*-pyrazolo[4,3-c]quinoline, **6f**

Orange crystals, Yield 92%, mp 302–304°C (decp.); ^1H NMR (DMSO-d_6): δ 7.18–8.25 (m, 8H) and 8.80 (s, 1H) ppm; Infrared (KBr): 3350 (NH), 3050 (ArCH), 2150 (diazo) and 1620 (C = N) cm^{-1}; Anal. Calcd. for $C_{16}H_9FN_6$: C, 63.15; H, 2.98; N, 27.62. Found: C, 63.09; H, 3.05; N, 27.76.

3-Diazo-4-(4-methylphenylamino)-1*H*-pyrazolo[4,3-c]quinoline, **6g**

Orange crystals, Yield 94%, mp 310–311°C (decp.); ^1H NMR (DMSO-d_6): δ 2.37 (s, 3H), 7.19–7.52 (m, 3H), 7.62–8.04 (m, 5H) and 8.57 (s, 1H) ppm; Infrared (KBr): 3400 (NH), 3050 (ArCH), 2950 (aliph CH), 2150 (diazo) and 1620 (C = N) cm^{-1}; Mass Spectrum (m/z): 272 (54) M^+ -N_2); Anal. Calcd. for $C_{17}H_{12}N_6$: C, 67.99; H, 4.03; N, 27.98. Found: C, 67.87; H, 4.01; N, 27.83.

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3-Diazo-4-(4-methoxyphenylamino)-1*H*-pyrazolo[4,3-c]quinoline, **6h**

Off-brown crystals, Yield 82%, mp > 360°C (decp.); ^{1}H NMR (DMSO-d_6): δ 3.75 (s, 3H), 7.20–7.61 (m, 4H), 7.73–8.05 (m, 4H) and 8.70 (s, 1H) ppm; Infrared (KBr): 3350 (NH), 2800 (aliph CH), 2150 (diazo) and 1620 (C = N) cm^{-1}; Anal. Calcd. for $C_{17}H_{12}N_6O$: 64.55; H, 3.82; N, 26.57. Found: C, 64.39; H, 3.76; N, 26.46.

General Procedure for the Synthesis of Ethyl 6-Arylamino-10-methyl-5,7,8,10a,11-pentaazabenzo-[a]fluorene-9-carboxylates 8e-h

A stirred mixture of the 3-diazo compound **6e–h** (1 mmol), ethyl acetoacetate (0.156 g, 1.2 mmol) and absolute ethanol (10 mL) was kept at room temperature for 20 h. The resulting pink precipitate was collected, dried and purified by preparative TLC (toluene:acetone, 10:3), followed by recrystallization from acetone to afford **8e–h**.

Ethyl 6-Anilino-10-methyl-5,7,8,10a,11-pentaazabenzo[a]fluorene-9-carboxylate, **8e**

Yellow crystals, Yield 70%, mp 209–210°C (decp.); ^{1}H NMR (DMSO-d_6): δ 1.45 (t, 3H), 3.16 (s, 3H), 4.53 (q, 2H) and 7.08–8.71 (m, 10H) ppm; Infrared (KBr): 3400 (NH), 3050 (ArCH), 2950 (aliph CH), 1730 (ester C = O) and 1620 (C = N) cm^{-1}; Mass Spectrum (m/z): 398 (89) (M^+); Anal. Calcd. for $C_{22}H_{18}N_6O_2$: C, 66.32; H, 4.55; N, 21.09. Found: C, 66.43; H, 4.68; N, 20.99.

Ethyl 6-(3-Fluorophenylamino)-10-methyl-5,7,8,10a,11-pentaazabenzo-[a]fluorene-9-carboxylate, **8f**

Orange crystals, Yield 79%, mp 206–208°C (decp.); ^{1}H NMR (DMSO-d_6): δ 1.46 (t, 3H); 3.18 (s, 3H), 4.53 (q, 2H) and 6.88–8.80 (m, 9H) ppm; Infrared (KBr): 3400 (NH), 3050 (ArCH), 2950, 2900 (aliph CH), 1720 (ester C = O) and 1620 (C = N) cm^{-1}; Mass Spectrum (m/z): 416 (100) (M^+); Anal. Calcd. for $C_{22}H_{17}FN_6O_2$: C, 63.45; H, 4.12; N, 20.18. Found: C, 63.66; H, 4.02; N, 20.36.

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Ethyl 6-(4-Methylphenylamino)-10-methyl-5,7,8,10a,11-pentaazabenzo-[a]-fluorene-9-carboxylate, **8g**

Orange crystals, Yield 73%, mp 270–271°C (decp.); ^{1}H NMR (DMSO-d_6): δ 1.44 (t, 3H); 2.33 (s, 3H), 3.28 (s, 3H), 4.54 (q, 2H), 7.24 (d, 2H), 7.49 (t, 1H), 7.76 (t, 1H), 7.85 (d, 1H), 8.02 (d, 2H), 8.45 (d, 1H) and 8.82 (s, 1H) ppm; Infrared (KBr): 3380 (NH), 2900, 2850 (aliph CH), 1710 (ester C = O) and 1620 (C = N) cm^{-1}; Mass Spectrum (m/z): 412 (100) (M^+); Anal. Calcd. for $C_{23}H_{20}N_6O_2$: C, 66.97; H, 4.89; N, 20.38. Found: C, 67.14; H, 4.95; N, 20.29.

Ethyl 6-(4-Methoxyphenylamino)-10-methyl-5,7,8,10a,11-pentaazabenzo-[a]-fluorene-9-carboxylate, **8h**

Orange crystals, Yield 83%, mp 220–221°C (decp.); ^{1}H NMR (DMSO-d_6): δ 1.46 (t, 3H), 3.23 (s, 3H), 3.79 (s, 3H), 4.53 (q, 2H), 6.99 (d, 2H), 7.44 (t, 1H), 7.70 (t, 1H), 7.74 (d, 1H), 7.99 (d, 2H), 8.36 (d, 1H) and 8.66 (s, 1H) ppm; Infrared (KBr): 3400 (NH), 2900 (aliph CH), 1710 (ester C = O) and 1620 (C = N) cm^{-1}; Mass Spectrum (m/z): 428 (100) (M^+); Anal. Calcd. for $C_{23}H_{20}N_6O_3$: C, 64.47; H, 4.71; N, 19.62. Found: C, 64.28; H, 4.56; N, 19.46.

REFERENCES

1. Molinski, T.F. Chem. Rev. **1993**, *93*, 1825.
2. Carroll, A.R. and Scheuer, P.J. J. Org. Chem. **1990**, *55*, 4426; Charyulu, G.A.; McKee, T.Z. and Ireland, C.M. Tetrahedron Lett. **1989**, *30*, 4201.
3. Kobayashi, J.; Cheng, J.F.; Walchli, M.R.; Nakamura, H.; Hirata, Y.; Sasaki, T. and Ohizumi, Y. J. Org. Chem. **1988**, *53*, 1800; Rudi, A. and Kashman, Y. J. Org. Chem. **1989**, *54*, 5331; Carroll, A.R.; Cooray, N.M.; Poiner, A. and Scheuer, J.P. J. Org. Chem. **1989**, *54*, 4231.
4. Cinfolini, M.A. and Byrne, N.E. J. Am. Chem. Soc. **1991**, *113*, 8016; Schmitz, F.J.; DeGuzman, F.S.; Hossain, M.B. and Van der Helm, D. J. Org. Chem. **1991**, *56*, 804; Kobayashi, J.; Cheng, J.F.; Nakamura, H.; Ohizuma, Y.; Hirata, Y.; Sasaki, T.; Ohta, T. and Nozoe, S. Tetrahedron Lett. **1988**, *29*, 1177.
5. Eiden, F. and Berndl, K. Arch. Pharm. **1986**, *319*, 347.
6. Eiden, F. and Dusemund, J. Arch. Pharm. Ber. Dent. Pharm. Ges. **1972**, *305*, 324.

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7. Fujiwara, H. and Okabayashi, I. Heterocycles **1993**, *36*, 1105.
8. Mekheimer, R. J. Chem. Soc., Perkin Trans. 1 **1999**, 2183 is considered to be part 1.
9. Mekheimer, R. Pharmazie **1994**, *49*, 486.
10. Mekheimer, R. Bull. Soc. Chim. Fr. **1994**, *131*, 279.
11. Mekheimer, R. J. Chem. Res. (S) **1994**, 304.
12. Hassan, A.A.; Mekheimer, R. and Mohamed, N.K. Pharmazie **1997**, *52*, 589.
13. Mekheimer, R. and Kappe, T. Heterocyclic Commun. **1998**, *4*, 131.
14. Mekheimer, R. Synth. Commun. **1998**, *28*, 3665.
15. Golec, J.M.C.; Scrowston, R.M. and Dunleavy, M. J. Chem. Soc., Perkin Trans. 1 **1992**, 239.
16. Kocevar, M.; Stanovnik, B. and Tisler, M. J. Heterocycl. Chem. **1978**, *15*, 1175.

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