Heteroatom Chemistry
Volume 14, Number 5, 2003

Syntheses of 3,4,7-Triazaacenaphthylene and Pyrido[3,4,5-*de*]cinnoline Derivatives

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Received 14 February 2003

ABSTRACT: *The title compounds were prepared by four different routes: (1) reaction of cycloalkanopyridazines* **3a–e** *with trichloroacetonitrile in basic medium; (2) reaction of* **3a–d** *with DMF DMA, followed by nucleophilic treatment with a primary amine; (3) reaction of 2-(dimethylamino)methylene-cycloalkylidene-malononitrile with arene diazonium salt, followed by amine treatment; (4) reaction of cycloalkylidenemalononitrile with phenyl or benzoyl isothiocyanate and heating the product with diazoaminobenzene.* © 2003 Wiley Periodicals, Inc. Heteroatom Chem 14:427–433, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10168

INTRODUCTION

Activated methylene nitriles are highly reactive reagents that have found extensive application in organic synthesis [1–3]. Condensed azines comprise a very interesting class of compounds because of their biological and medicinal activities [4–6]. In the last decade we reported several novel syntheses of azines, utilizing activated nitriles as starting material [7–9]. Herein we report the reactivity of ylidene derivatives **1a,b** toward different type of organic reagents with the aim of preparing 3,4,7-triazaacenaphthylene and cinnolineamine ring systems.

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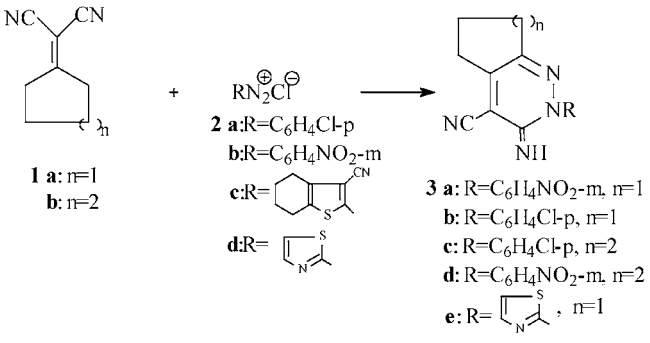
RESULTS AND DISCUSSION

Ylidene derivatives **1a,b** readily coupled with diazonium salts **2a–d** to give products, which were established as having structure **3a–e** (see Scheme 1). The mass spectrum of **3a** showed molecular ion peak at *m*/*z* 281 and its IR spectrum reveals the presence of NH and cyano groups at 3320 and 2212 cm^{-1}, respectively. Moreover, the ^1H NMR spectrum reveals the presence of aromatic protons at δ 7.98–7.53 ppm. In ^{13}C NMR the low field signal at δ 165.16 ppm indicates the imine carbon atom and the signal at δ 116.89 ppm indicates the presence of a cyano group. The signals of other skeletal carbon atoms appeared at expected positions. Similarly, the structures of **3b–e** were established.

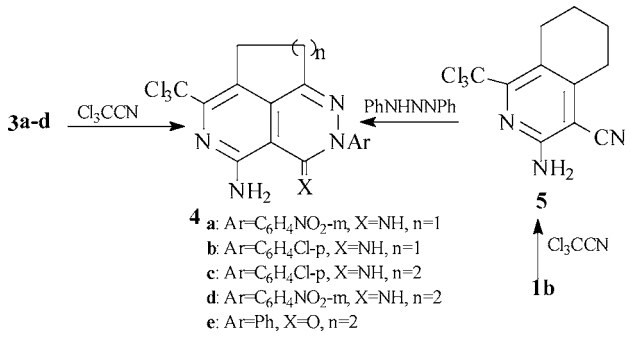
Cycloalkanopyridazine **3a–d** reacted readily under basic condition with trichloroacetonitrile to give 3,4,7-triazaacenaphthylene or cinnolineamine derivatives **4a–d** in good yield (see Scheme 2). The product **4c** could also be obtained in low yield by treating **1b** with trichloroacetonitrile to give **5,** followed by coupling with arene diazonium salt **2a**. The oxo derivative **4e** was obtained in good yield by treating the pyridine derivative **5** with diazoaminobenzene in refluxing aqueous acetic acid/hydrochloric acid mixture. The structures of **4a–e** were established on their elemental analysis and spectral data. For example, mass spectra of **4a** revealed molecular ion peaks at *m*/*z* 424 (65%, M); 426 (60%, M + 2); 428 (25%, M + 4); 430 (3%, M + 6).

Furthermore, *N*,*N*-dimethylformamide dimethyl acetal (DMF DMA) reacts with **3a–d** to give **6a–d** (Scheme 3). The structures of the isolated products were confirmed on the basis of elemental analysis

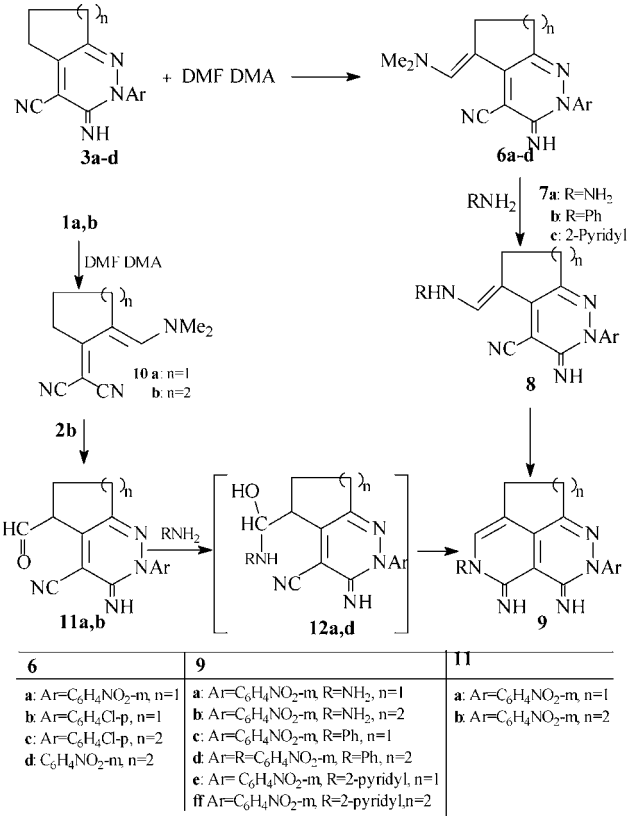


SCHEME 1

and spectral data. For example, ^{1}H NMR of compound **6a** revealed the presence of ethylenic proton at δ 6.98 ppm in addition to the NMe_2 protons at δ 2.95 ppm. The reactivity of compounds **6a,b** toward some nitrogen nucleophiles was investigated. Thus, enamine **6a,d** reacted with hydrazine hydrate **7a** or aromatic amines **7b,c** to give pyridopyridazine derivatives **9a–f**. The intermediates **8** are believed to form via addition of amino group to ethylenic double bond followed by loss of dimethylamine. Intramolecular cyclization gives the final isolated products **9** (Scheme 3). Alternatively, compounds **1a,b** were treated with DMF DMA in DMF and piperidine to give the condensation products **10a,b**. The latter coupled with arene diazonium salt **2b** to give the aldehydic derivatives **11a,b** (Scheme 3). We assume that the initially formed arylazo derivatives hydrolyze to aldehydic arylhydrazono derivatives followed by cyclization. Transformation of an imino to an aldehydic group has been reported under similar reaction condition [10]. Compounds **11a,b** reacted with hydrazine hydrate in ethanolic DMF mixture to give the final isolated products **9a,b**. It is assumed that the amino group adds to the electrophilic carbonyl carbon atom affording the nonisolated intermediate **12**, followed by intramolecular cyclization and loss of water molecule. The structure of **9a,b** was



SCHEME 2



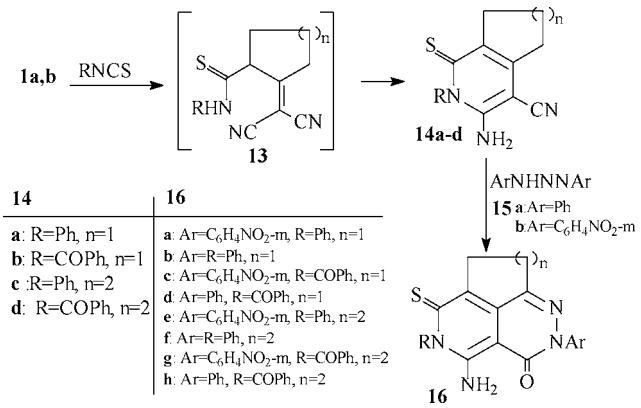
SCHEME 3

established by elemental analysis and spectral data. Thus, the IR spectrum of **9a** revealed the disappearance of the aldehydic carbonyl and cyano groups. The ^{1}H and ^{13}C NMR spectra agree with the proposed structure.

Moreover, the target ring system could be obtained by treating **1a,b** with phenylisothiocyanate or benzoylisothiocyanate to give **14a–d** through the nonisolated intermediate **13**, which was formed upon addition of cyclic active methylene group to isothiocyanate. The pyridazine ring could form by coupling with either a benzenediazonium salt or a diazoaminobenzene. With the latter high yields of the product were obtained. Thus, compounds **14a-d** reacted with diazoaminobenzene **15a,b** in aqueous acetic acid/hydrochloric acid mixture to afford the final isolated products **16a–h** (Scheme 4). These were established based on elemental analysis and spectral data.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded in KBr with a IR spectrophotometer Shimadzu 408. ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian EM-390 MHz spectrometer using



SCHEME 4

TMS as internal reference and chemical shifts δ are expressed as ppm. Mass spectra were measured on a Shimadzu GCMS-QP 1000 Ex mass spectrometer. Microanalytical data were obtained from the Microanalytical Data Unit at Cairo University, Egypt. Compounds **14a,c,d** were prepared as described in the previous publication [11,12].

General Method for the Preparation of **3a–e**

A solution of the diazonium salts (prepared from 0.01 mol of aromatic or heteroaromatic amine with the appropriate quantities of sodium nitrite and hydrochloric acid) was added to cycloalkylidenemalononitrile **1a** or **1b** (0.01 mol) in ethanol (50 ml) and sodium hydroxide (0.50 g). The reaction mixture was stirred at room temperature for 2 h. The solid product, so formed, was collected by filtration and recrystallized from ethanol.

*3-Imino-2-(3-nitrophenyl)-3,5,6,7-tetrahydro-2H-cyclopenta[c]pyridazine-4-carbonitrile (***3a***).* Brown crystals (78%) from ethanol; mp 147°C; IR: 3320 (NH), 3088 (CH-aromatic), 2993 (CH-aliphatic), 2212 (CN), 1650 cm^{-1} (C=NH); ^{1}H NMR: δ 7.98–7.53 (m, 4H, Ar), 6.25 (br, 1H, NH), 1.82–1.45 (m, 6H, $3CH_2$); ^{13}C NMR δ 165.16 (C-3), 157.12 (C-7a), 140.06, 139.12, 137.01, 135.11, 134.21, 129.61, 127.11, 124.10 (aromatic carbon atoms), 116.89 (CN), 28.66, 27.45, 25.98 ($3CH_2$); MS: *m/z* 281 (M^+). Anal. for $C_{14}H_{11}N_5O_2$ (281.3): C, 59.77; H, 3.94; N, 24.90. Found: C, 60.01; H, 4.00; N, 25.01.

*2-(4-Chlorophenyl)-3-imino-3,5,6,7-tetrahydro-2H-cyclopenta[c]pyridazine-4-carbonitrile (***3b***).* Yellow crystals (70%) from ethanol; mp 140°C; IR: 3324 (NH), 3081 (CH-aromatic), 2995 (CH-aliphatic), 2209 (CN); 1652 cm^{-1} (C=NH); ^{1}H NMR: δ 7.89–7.33 (m, 4H, Ar), 6.05 (br, 1H, NH), 1.81–1.45 (m, 6H, $3CH_2$). Anal. for $C_{14}H_{11}ClN_4$ (270.74): C, 62.10; H, 4.10; N, 20.69. Found: C, 62.32; H, 3.99; N, 20.65.

*2-(4-Chlorophenyl)-3-imino-2,3,5,6,7,8-hexahydrocinnoline-4-carbonitrile (***3c***).* Yellow crystals (72%) from ethanol; mp 165°C; IR: 3320 (NH), 3085 (CH-aromatic), 2998 (CH-aliphatic), 2212 (CN), 1650 cm^{-1} (C=NH); ^{1}H NMR: δ 7.78–7.21 (m, 4H, Ar), 6.30 (br, 1H, NH), 2.82–1.17 (m, 8H, $4CH_2$). Anal. for $C_{15}H_{13}ClN_4$ (284.77): C, 63.26;H, 4.61; N, 19.67. Found: C, 63.36; H, 4.50; N, 19.85.

*3-Imino-2-(3-nitrophenyl)-2,3,5,6,7,8-hexahydrocinnoline-4-carbonitrile (***3d***).* Yellow crystals (76%) from ethanol; mp 123°C; IR: 3330 (NH), 3092 (CH-aromatic), 2996 (CH-aliphatic), 2210 (CN), 1653 cm^{-1} (C=NH); ^{1}H NMR: δ 7.97–7.43 (m, 4H, Ar), 6.20 (br, 1H, NH), 2.84–1.18 (m, 8H, $4CH_2$). Anal. for $C_{15}H_{13}N_5O_2$ (295.33): C, 60.99; H, 4.44; N, 23.71. Found: C, 61.00; H, 4.32; N, 23.73.

*3-Imino-2-thiazol-2-yl-3,5,6,7-tetrahydro-2H-cyclopenta[c]pyridazine-4-carbonitrile (***3e***).* Pale brown crystals (66%) from ethanol; mp 200°C; IR: 3239 (NH), 3089 (CH-aromatic), 2986 (CH-aliphatic), 2211 (CN), 1654 cm^{-1} (C=NH); ^{1}H NMR: δ 8.98 (br, 1H, NH), 7.99–7.46 (m, 2H, thiazolyl-H), 1.85–1.07 (m, 6H, $3CH_2$). Anal. for $C_{11}H_9N_5S$ (243.32): C, 54.29; H, 3.73; N, 28.78; S, 13.18. Found: C, 54.32; H, 4.00; N, 28.58; S, 13.43.

General Method for the Preparation of **4a–e**

Method A (**4a–d**): To a solution of **3a** or **3b** or **3c** or **3d** (0.01 mol) in DMF, trichloroacetonitrile (0.01 mol) and few drops of piperidine were added. The reaction mixture was heated under reflux for 1 h. The reaction product was treated with ice-cold water and the solid product, so formed, was filtered and crystallized from proper solvent.

Method B (**4e**): A mixture of **5** (0.01 mol), diazoaminobenzene (0.01 mol), glacial acetic acid (15 ml), hydrochloric acid (15 ml, 36% wt/wt), and few drops of water was heated under reflux for 3 h and then allowed to cool. The reaction product was neutralized using sodium bicarbonate solution. The solid product so formed was collected by filtration, washed with ice-cold water several times, dried, and crystallized from a proper solvent.

*5-Imino-4-(3-nitrophenyl)-8-(trichloromethyl)-1,2,4,5-tetrahydro-3,4,7-triazaacenaphthylen-6-amine (***4a***).* Brown crystals (65%) from ethanol; mp >250°C; IR: 3401, 3358, 3325 (NH_2 & NH), 3100

(CH-aromatic), 2991 (CH-aliphatic), 1651 cm^{-1} (C=NH); ^1H NMR: δ 7.87–7.42 (m, 4H, Ar), 8.50, 6.25 (br, 3H, NH & NH_2), 1.72–1.45 (m, 4H, $2CH_2$); ^{13}C NMR: δ 158.93, 157.87, 155.59, 154.93, 153.32, 149.30, 148.33, 147.35, 145.72, 141.32, 139.39, 137.38, 134.36 (aromatic carbon atoms), 97.73 (CCl_3), 27.76, 26.33 ($2CH_2$); MS: *m/z* 424 (65%, M^+), 426 (60%, M + 2), 428 (25%, M + 4), 430 (3%, M + 6). Anal. for $C_{16}H_{11}Cl_3N_6O_2$ (425.68): C, 45.14; H, 2.61; N, 19.74. Found: C, 45.32; H, 2.60; N, 19.76.

*4-(4-Chlorophenyl)-5-imino-8-(trichloromethyl)-1,2,4,5-tetrahydro-3,4,7-triazaacenaphthylen-6-amine (***4b***).* Yellow crystals (63%) from ethanol; mp 242°C; IR: 3411, 3345, 3320 (NH_2 & NH), 3100 (CH-aromatic), 2993 (CH-aliphatic), 1650 cm^{-1} (C=NH); ^1H NMR: δ 7.98–7.32 (m, 4H, Ar), 8.40, 6.25 (br, 3H, NH & NH_2), 1.71–1.50 (m, 4H, $2CH_2$). Anal. for $C_{16}H_{11}Cl_4N_5$ (415.12): C, 46.29; H, 2.67; N, 16.87. Found: C, 46.53; H, 2.59; N, 16.59.

*2-(4-Chlorophenyl)-3-imino-6-(trichloromethyl)-2,7,8,9-tetrahydro-3H-pyrido[3,4,5-de]cinnolin-4-amine (***4c***).* Yellow crystals (63%) from ethanol; mp 284°C; IR: 3434, 3373, 3331 (NH_2 & NH), 3101 (CH-aromatic), 2997 (CH-aliphatic), 1651 cm^{-1} (C=NH); ^1H NMR: δ 7.76–7.01 (m, 4H, Ar), 8.40, 6.24 (br, 3H, NH & NH_2), 1.85–1.06 (m, 6H, $3CH_2$). Anal. for $C_{17}H_{13}Cl_4N_5$ (429.15): C, 47.57; H, 3.05; N, 16.32. Found: C, 47.58; H, 3.00; N, 16.36.

*3-Imino-2-(3-nitrophenyl)-6-(trichloromethyl)-2,7,8,9-tetrahydro-3H-pyrido[3,4,5-de]cinnolin-4-amine (***4d***).* Brown crystals (73%) from DMF; mp 124°C; IR: 3422, 3331, 3321 (NH_2 & NH), 3100 (CH-aromatic), 2996 (CH-aliphatic), 1653 cm^{-1} (C=NH); ^1H NMR: δ 7.88–7.24 (m, 4H, Ar), 8.42, 6.31 (br, 3H, NH & NH_2), 1.82–1.06 (m, 6H, $3CH_2$). Anal. for $C_{17}H_{13}Cl_3N_6O_2$ (439.71): C, 46.43; H, 2.98; N, 19.11. Found: C, 46.34; H, 3.01; N, 19.00.

*4-Amino-2-phenyl-6-(trichloromethyl)-2,7,8,9-tetrahydro-3H-pyrido[3,4,5-de]cinnolin-3-one (***4e***).* Brown crystals (70%) from DMF; mp 108°C; IR: 3418, 3321 (NH_2), 3095 (CH-aromatic), 2992 (CH-aliphatic), 1659 cm^{-1} (CO); ^1H NMR: δ 7.57–7.10 (m, 5H, Ar), 8.40 (br, 2H, NH_2), 1.80–1.07 (m, 6H, $3CH_2$). Anal. for $C_{17}H_{13}Cl_3N_4O$ (395.69): C, 51.59; H, 3.31; N, 14.16. Found: C, 51.22; H, 3.53; N, 14.00.

*3-Amino-1-(trichloromethyl)-5,6,7,8-tetrahydroiosquinoline-4-carbonitrile (***5***)*

A solution of ylidene **1b** (0.01 mol) in DMF (20 ml), trichloroacetonitrile (0.01 mol), and few drops of piperidene was refluxed for 2 h. The reaction mixture was evaporated under vacuum and the solid product so formed was collected by filtration and crystallized from ethanol.

Pale brown crystals (69%); mp 160°C; IR: 3422, 3328 (NH_2), 2989 (CH-aliphatic), 2213 cm^{-1} (CN); ^1H NMR: δ 8.05 (br, 2H, NH_2), 1.85–105 (m, 8H, $4CH_2$). Anal. for $C_{11}H_{10}Cl_3N_3$ (290.59): C, 45.46;H, 3.47; N, 14.46. Found: C, 45.66; H, 3.75; N, 14.36.

General Method for the Preparation of **6a–d**

A solution of pyridazines **3a** or **3b** or **3c** or **3d** (0.01 mol) in DMF (25 ml) was treated with DMF DMA (0.01 mol) and few drops of piperidene. The reaction mixture was heated under reflux for 2 h and then treated with cold water. The reaction product was collected by filtration and crystallized from proper solvent.

*(5E)-5-[(Dimethylamino)methylene]-3-imino-2-(3-nitrophenyl)-3,5,6,7-tetrahydro-2H-cyclopenta[c]-pyridazine-4-carbonitrile (***6a***).* Brown crystals (75%) from EtOH; mp 197°C; IR: 3323 (NH), 3100 (CH-aromatic), 2981 (CH-aliphatic), 2210 (CN), 1651 cm^{-1} (C=NH); ^1H NMR: δ 7.93–7.15 (m, 4H, Ar), 6.98 (s, 1H, CH), 5.89 (br, 1H, NH), 2.95 (s, 6H, 2Me), 1.71–1.51 (m, 4H, $2CH_2$). Anal. for $C_{17}H_{16}N_6O_2$ (336.39): C, 60.69; H, 4.80; N, 24.98. Found: C, 60.71; H,4.94; N, 24.76.

*(5E)-2-(4-Chlorophenyl)-5-[(dimethylamino)methylene]-3-imino-3,5,6,7-tetrahydro-2H-cyclopenta-[c]pyridazine-4-carbonitrile (***6b***).* Pale brown crystals (78%) from EtOH; mp 213°C; IR: 3329 (NH), 3099 (CH-aromatic), 2983 (CH-aliphatic), 2211 (CN), 1650 cm^{-1} (C=NH); ^1H NMR: δ 7.67–7.15 (m, 4H, Ar), 6.98 (s, 1H, CH), 5.87 (br, 1H, NH), 2.45 (s, 6H, 2Me), 1.70–1.51 (m, 4H, $2CH_2$). Anal. for $C_{17}H_{16}ClN_5$ (325.83): C, 62.66; H, 4.95; N, 21.49. Found: C, 62.41; H, 4.83; N, 21.43.

*(5E)-2-(4-Chlorophenyl)-5-[(dimethylamino)methylene]-3-imino-2,3,5,6,7,8-hexahydrocinnoline-4-carbonitrile (***6c***).* Yellow crystals (64%) from EtOH; mp 201°C; IR: 3331 (NH), 3100 (CH-aromatic), 2983 (CH-aliphatic), 2212 (CN), 1653 cm^{-1} (C=NH); ^1H NMR: δ 7.87–7.15 (m, 4H, Ar), 6.98 (s, 1H, CH), 5.89 (br, 1H, NH), 2.45 (s, 6H, 2Me), 1.83–1.08 (m, 6H, $3CH_2$). Anal. for $C_{18}H_{18}ClN_5$ (339.86): C, 63.60; H, 5.34; N, 20.61. Found: C, 63.93; H, 5.41; N, 20.41.

*(5E)-5-[(Dimethylamino)methylene]-3-imino-2-(3-nitrophenyl)-2,3,5,6,7,8-hexahydro-cinnoline-4-carbonitrile (***6d***).* Yellow crystals (66%) from EtOH;

mp 189°C; IR: 3331(NH), 3100 (CH-aromatic), 2985 (CH-aliphatic), 2212 (CN), 1651 cm^{-1} (C=NH); ^1H NMR: δ 7.98–7.13 (m, 4H, Ar), 6.97 (s, 1H, CH), 5.79 (br, 1H, NH), 2.46 (s, 6H, 2Me), 1.85–1.07 (m, 6H, $3CH_2$). Anal. for $C_{18}H_{18}N_6O_2$ (350.42): C, 61.69; H, 5.18; N, 23.98. Found: C, 61.39; H, 5.01; N, 23.74.

General Method for the Preparation of **9a–f**

Method A: To a solution of **6a** or **6b** or **6c** or **6d** (0.01 mol) in DMF (25 ml), hydrazine hydrate (0.01 mol) or aniline (0.01 mol) or 2-aminopyridine (0.01 mol) was added. The reaction mixture was heated under reflux for 2 h. Ice-cold water was added and the solid product so formed was collected by filtration and crystallized from proper solvent.

Method B: To a solution of **11a** or**11b** (0.01 mol), in ethanol/DMF mixture (1:1, 30 ml), hydrazine hydrate (0.01 mol) was added. The reaction mixture was heated under reflux for 2 h. Ice-cold water added and the solid product so formed was collected by filtration and crystallized from proper solvent.

*5,6-Diimino-4-(3-nitrophenyl)-1,2,4,6-tetrahydro-3,4,7-triazaacenaphthylen-7(5H)-amine (**9a**).* Yellow crystals (79%) from DMF/EtOH; mp 157°C; IR: 3412, 3334, 3226, 3215 (NH_2, 2NH), 3100 (CH-aromatic), 2993 (CH-aliphatic), 1651, 1656 cm^{-1} (2C=NH); ^1H NMR: δ 10.32 (br, 2H, NH_2), 8.03 (s, 1H, Pyridine-H), 7.89–7.10 (m, 4H, Ar), 6.95, 5.79 (br, 2H, 2NH), 1.85–1.07 (m, 4H, $2CH_2$); ^{13}C NMR: δ 159.13, 158.78, 158.33, 157.02, 153.21, 149.12, 148.25, 147.68, 143.21, 138.21, 137.25, 135.01, 132.35 (aromatic carbon atoms), 26.35, 27.60 ($2CH_2$); MS: *m/z*323 (73.03%, M^+). Anal. for $C_{15}H_{13}N_7O_2$ (323.35): C, 55.71; H, 4.06; N, 30.32. Found: C, 55.69; H, 4.31; N, 30.63.

*3,4-Diimino-2-(3-nitrophenyl)-2,7,8,9-tetrahydro-3H-pyrido[3,4,5-de]cinnolin-5(4H)-amine (**9b**).* Yellow crystals (72%) from DMF/EtOH; mp 168°C; IR: 3411, 3333, 3229, 3220 (NH_2, 2NH), 3099 (CH-aromatic), 2995 (CH-aliphatic), 1652, 1656 cm^{-1} (2C=NH). ^1H NMR: δ 10.02 (br, 2H, NH_2), 8.13 (s, 1H, Pyridine-H), 7.79–7.10 (m, 4H, Ar), 6.85, 5.77 (br, 2H, 2NH), 2.78–1.11 (m, 6H, $3CH_2$). Anal. for $C_{16}H_{15}N_7O_2$ (337.38): C, 56.95; H, 4.49; N, 29.06. Found: C, 57.01; H, 4.53; N, 29.01.

*4-(3-Nitrophenyl)-7-phenyl-1, 2, 4, 7-tetrahydro-3,4,7-triazaacenaphthylene-5,6-diimine (**9c**).* Brown crystals (74%) from DMF/EtOH; mp >250°C; IR: 3331, 3219 (2NH), 3100 (CH-aromatic), 2998 (CH-aliphatic), 1650, 1655 cm^{-1} (2C=NH); ^1H NMR: δ 8.69 (s, 1H, Pyridine-H), 7.89–7.01 (m, 9H, Ar), 6.85, 5.59 (br, 2H, 2NH), 1.85–1.07 (m, 4H, $2CH_2$). Anal. for $C_{21}H_{16}N_6O_2$ (384.43): C, 65.60; H, 4.20; N, 21.86. Found: C, 65.71; H, 4.20; N, 21.83.

*2-(3-Nitrophenyl)-5-phenyl-5,7,8,9-tetrahydro-3H-pyrido[3, 4, 5-de]cinnoline-3,4-(2H)-diimine (**9d**).* Brown crystals (76%) from DMF/EtOH; mp 165°C; IR: 3331, 3219 (2NH), 3101 (CH-aromatic), 2996 (CH-aliphatic), 1652, 1657 cm^{-1} (2C=NH); ^1H NMR: δ 8.57 (s, 1H, Pyridine-H), 7.91–7.11 (m, 9H, Ar), 6.85, 5.77 (br, 2H, 2NH), 2.79–1.23 (m, 6H, $3CH_2$). Anal. for $C_{22}H_{18}N_6O_2$ (398.46): C, 66.31; H, 4.56; N, 21.09. Found: C, 66.31; H, 4.81; N, 21.38.

*4-(3-Nitrophenyl)-7-pyridin-2-yl-1,2,4,7-tetrahydro-3,4,7-triazaacenaphthylene-5,6-diimine (**9e**).* Brown crystals (76%) from DMF/EtOH; mp 134°C; IR: 3345, 3219 (2NH), 3103 (CH-aromatic), 2993 (CH-aliphatic), 1653, 1657 cm^{-1} (2C=NH); ^1H NMR: δ 8.78 (s, 1H, Pyridine-H), 7.84–7.21 (m, 8H, pyridine & Ar), 6.75, 5.59 (br, 2H, 2NH), 1.85–1.17 (m, 4H, $2CH_2$). Anal. for $C_{20}H_{15}N_7O_2$ (385.42): C, 62.32; H, 3.93; N, 25.44. Found: C, 62.31; H, 4.01; N, 25.53.

*2-(3-Nitrophenyl)-5-pyridin-2-yl-5,7,8,9-tetrahydro-3H-pyrido[3,4,5-de]cinnoline-3,4(2H)-diimine (**9f**).* Brown crystals (73%) from DMF/EtOH; mp 176°C; IR: 3365, 3223 (2NH), 3100 (CH-aromatic), 2998 (CH-aliphatic), 1651, 1653 cm^{-1} (2C=NH); ^1H NMR: δ 8.35 (s, 1H, Pyridine-H), 7.91–7.12 (m, 8H, pyridine & Ar), 6.65, 6.09 (br, 2H, 2NH), 2.80–1.11 (m, 6H, $3CH_2$). Anal. for $C_{21}H_{17}N_7O_2$ (399.45): C, 63.13; H, 4.29; N, 24.55. Found: C, 63.31; H, 4.39; N, 24.63.

General Method for the Preparation of **10a,b**

A solution of ylidene derivatives **1a** or **1b** (0.01 mol) in DMF (25 ml) was treated with DMF DMA (0.01 mol) and few drops of piperidine. The reaction mixture was heated under reflux for 2 h and then treated with ice-cold water. The reaction product was collected by filtration and crystallized from proper solvent.

*{(2E)-2-[(Dimethylamino)methylene]cyclopentylidene}malononitrile (**10a**).* Yellow crystals (76%) from DMF/EtOH; mp 145°C; IR: 2998 (CH-aliphatic), 2220, 2221 (2CN), 1400 (C–N); ^1H NMR: δ 6.69 (s, 1H, CH), 2.46 (s, 6H, $2CH_3$), 1.83–1.44 (m, 6H, $3CH_2$). Anal. for $C_{11}H_{13}N_3$ (187.27): C, 70.54; H, 7.01; N, 22.44. Found: C, 70.31; H, 7.30; N, 22.62.

*{(2E)-2-[(Dimethylamino)methylene]cyclohexaylidene}malononitrile (***10b***).* Yellow crystals (74%) from DMF/EtOH; mp 153°C; IR: 2989 (CH-aliphatic), 2220, 2221 (2CN), 1401 (C—N); ^{1}H NMR: δ 6.94 (s, 1H, CH), 2.45 (s, 6H, 2Me), 2.81–1.17 (m, 8H, 4CH_2). Anal. for $C_{12}H_{15}N_3$ (201.30): C, 71.59; H, 7.52; N, 20.87. Found: C, 71.35; H, 7.31; N, 20.71.

General Method for the Preparation of **11a,b**

A solution of the diazonium salts, (prepared as described in the preparation of **3a–d**) was added dropwise with strong stirring for 2 h, to a solution of **10a** or **10b** (0.01 mol) in DMF and a solution of NaOH (0.1 g dissolved in 10 ml of water). The solid product so formed was collected by filtration and crystallized from proper solvent.

*5-Formyl-3-imino-2-(3-nitrophenyl)-3,5,6,7-tetrahydro-2,3,5,6,7-2H-cyclopenta[c]pyridazine-4-carbonitrile (***11a***).* Red crystals (69%) from acetone; mp 144°C; IR: 3323 (NH), 3100 (CH-aromatic), 2991 (CH-aliphatic), 2212 (CN), 1728 (CO), 1652 cm^{-1} (C=NH); ^{1}H NMR: δ 10.45 (s, 1H, CHO), 7.98–7.23 (m, 4H, Ar), 6.23 (br, 1H, NH), 2.84–1.53 (m, 5H, 1CH & 2CH_2); ^{13}C NMR: δ 204.70 (CHO), 165.01, 157.36, 151.71, 143.31, 139.01, 137.37, 135.30, 134.31, 125.20, 124.93 (aromatic carbon atoms), 116.31 (CN), 37.31, 29.36, 27.29 (3CH_2); MS: *m/z* 309 (65.30%, M^+). Anal. for $C_{15}H_{11}N_5O_3$ (309.31): C, 58.24; H, 3.59; N, 22.64. Found: C, 58.24; H, 3.52; N, 22.46.

*5-Formyl-3-imino-2-(3-nitrophenyl)-2,3,5,6,7,8-hexahydrocinnoline-4-carbonitrile (***11b***).* Red crystals (72%) from acetone; mp 158°C; IR: 3333 (NH), 3100 (CH-aromatic), 2992 (CH-aliphatic), 2210 (CN), 1727 (CO), 1653 cm^{-1} (C=NH); ^{1}H NMR: δ 10.50 (s, 1H, CHO), 7.97–7.20 (m, 4H, Ar), 6.05 (br, 1H, NH), 2.86–1.43 (m, 7H, 1CH & 3CH_2). Anal. for $C_{16}H_{13}N_5O_3$ (323.34): C, 59.42; H, 4.06; N, 21.66. Found: C, 59.38; H, 3.84; N, 21.77.

*3-Amino-2-benzoyl-1-thioxo-2,5,6,7-tetrahydro-1H-cyclopenta[c]pyridine-4-carbonitrile (***14b***)*

To a solution of **1a** (0.01 mol) in ethanol (25 ml), benzoyl isothiocyanate (0.01 mol) and few drops of piperidine were added. The reaction mixture was heated under reflux for 3 h. The solid product so formed, upon treating the reaction mixture with ice-cold water, was collected by filtration and crystallized from ethanol.

Brown crystals (64%); mp 173°C; IR: 3342, 3328 (NH_2), 3101 (CH-aromatic), 2993 (CH-aliphatic), 2210 (CN), 1661 cm^{-1} (CO); ^{1}H NMR: δ 7.54–7.01 (m, 5H, Ar), 6.52 (br, 2H, NH_2), 1.85–1.17 (m, 6H, 3CH_2). Anal. for $C_{16}H_{13}N_3OS$ (295.39): C, 65.05; H, 4.44; N, 14.22; S, 10.85. Found: C, 65.00; H, 4.34; N, 14.01; S, 11.00.

General Method for the Preparation of **16a–h**

A mixture of **14a** or **14b** or **14c** or **14d** (0.01 mol), diazoaminobenzene (0.01 mol), glacial acetic acid (15 ml), hydrochloric acid (15 ml, 36% wt/wt), and few drops of water was heated under reflux for 3 h and then allowed to cool. The reaction product was neutralized using sodium bicarbonate solution. The solid product so formed was collected by filtration, washed with ice-cold water several times, dried, and crystallized from a proper solvent.

*6-Amino-4-(3-nitrophenyl)-7-phenyl-8-thioxo-1,8-ethano-2,4,7,8-tetrahydro-3,4,7-triazaacenaphthylene-5(1H)-one (***16a***).* Deep yellow crystals (70%) from DMF; mp 188°C; IR: 3343, 3332 (NH_2), 3100 (CH-aromatic), 2992 (CH-aliphatic), 1658 cm^{-1} (CO); ^{1}H NMR: δ 7.82–7.23 (m, 9H, Ar), 6.51 (br, 2H, NH_2), 1.85–1.06 (m, 4H, 2CH_2); MS: *m/z*417 (M^+). Anal. for $C_{21}H_{15}N_5O_3S$ (417.48): C, 60.41; H, 3.62; N, 16.77; S, 7.68. Found: C, 65.51; H, 3.45; N, 16.98; S, 7.83.

*6-Amino-4,7-diphenyl-8-thioxo-1,8-ethano-2,4,7,8-tetrahydro-3,4,7-triazaacenaphthylene-5(1H)-one (***16b***).* Brown crystals (71%) from DMF; mp 218°C; IR: 3342, 3329 (NH_2), 3104 (CH-aromatic), 2994 (CH-aliphatic), 1559 cm^{-1} (CO); ^{1}H NMR: δ 7.72–7.23 (m, 10H, Ar), 6.53 (br, 2H, NH_2), 1.85–1.07 (m, 4H, 2CH_2). Anal. for $C_{21}H_{16}N_4OS$ (372.48): C, 67.71; H, 4.33; N, 15.04; S, 8.60. Found: C, 67.60; H, 4.05; N, 14.91; S, 8.31.

*6-Amino-7-benzoyl-4-(3-nitrophenyl)-8-thioxo-1,8-ethano-2,4,7,8-tetrahydro-3,4,7-triazaacenaphthylene-5(1H)-one (***16c***).* Yellow crystals (74%) from DMF; mp 243°C; IR: 3343, 3329 (NH_2), 3103 (CH-aromatic), 2997 (CH-aliphatic), 1651, 1659 cm^{-1} (2CO); ^{1}H NMR: δ 7.91–7.21 (m, 9H, Ar), 6.54 (br, 2H, NH_2), 1.85–1.07 (m, 4H, 2CH_2). Anal. for $C_{22}H_{15}N_5O_4S$ (445.49): C, 59.30; H, 3.40; N, 15.72; S, 7.19. Found: C, 59.37; H, 3.13; N, 16.01; S, 7.28.

*6-Amino-7-benzoyl-4-phenyl-8-thioxo-1,8-ethano-2,4,7,8-tetrahydro-3,4,7-triazaacenaphthylene-5(1H)-one (***16d***).* Brown crystals (73%) from DMF; mp >250°C; IR: 3343, 3328 (NH_2), 3100 (CH-aromatic), 2998 (CH-aliphatic), 1655, 1661 cm^{-1} (2CO); ^{1}H NMR: δ 7.85–7.31 (m, 10H, Ar), 6.53 (br, 2H, NH_2), 1.85–1.10 (m, 4H, 2CH_2). Anal. for $C_{22}H_{16}N_4O_2S$

(400.49): C, 65.97; H, 4.03; N, 13.99; S, 8.00. Found: C, 66.01; H, 3.98; N, 14.02; S, 8.34.

*4-Amino-2-(3-nitrophenyl)-5-phenyl-6-thioxo-2,5,6,7,8,9-hexahydro-3H-pyrido[3,4,5-de]cinnoline-3-one (***16e***).* Deep yellow crystals (74%) from DMF; mp 206°C; IR: 3348, 3335 (NH_2), 3100 (CH-aromatic), 2992 (CH-aliphatic), 1663 cm^{-1} (CO); ^1H NMR: δ 7.93–7.22 (m, 9H, Ar), 6.52 (br, 2H, NH_2), 2.85–1.37 (m, 6H, $3CH_2$). Anal. for $C_{22}H_{17}N_5O_3S$ (431.51): C, 61.23; H, 3.97; N, 16.23; S, 7.43. Found: C, 61.60; H, 3.61; N, 16.43; S, 7.34.

*4-Amino-2,5-diphenyl-6-thioxo-2,5,6,7,8,9-hexahydro-3H-pyrido[3,4,5-de]cinnoline-3-one (***16f***).* Brown crystals (73%) from DMF; mp 233°C; IR: 3342, 3329 (NH_2), 3099 (CH-aromatic), 2989 (CH-aliphatic), 1659 cm^{-1} (CO); ^1H NMR: δ 7.83–7.32 (m, 10H, Ar), 6.52 (br, 2H, NH_2), 2.85–1.36 (m, 6H, $3CH_2$). Anal. for $C_{22}H_{18}N_4OS$ (386.51): C, 68.36; H, 4.70; N, 14.49; S, 8.29. Found: C, 68.21; H, 4.57; N, 14.23; S, 8.29.

*4-Amino-5-benzoyl-2-(3-nitrophenyl)-6-thioxo-2,5,6,7,8,9-hexahydro-3H-pyrido[3,4,5-de]cinnoline-3-one (***16g***).* Yellow crystals (72%) from DMF; mp 195°C; IR: 3342, 3328 (NH_2), 3100 (CH-aromatic), 2997 (CH-aliphatic), 1663, 1659 cm^{-1} (2CO); ^1H NMR: 7.93–7.22 (m, 9H, Ar), 6.50 (br, 2H, NH_2), 2.85–1.35 (m, 6H, $3CH_2$). Anal. for $C_{23}H_{17}N_5O_4S$ (459.52): C, 60.11; H, 3.73; N, 15.24; S, 6.97. Found: C, 60.45; H, 3.51; N, 15.50; S, 6.90.

*4-Amino-5-benzoyl-2-phenyl-6-thioxo-2,5,6,7,8,9-hexahydro-3H-pyrido[3,4,5-de]cinnoline-3-one (***16h***).* Brown crystals (70%) from DMF; mp 212°C; IR: 3331, 3328 (NH_2), 3101 (CH-aromatic), 2989 (CH-aliphatic), 1660, 1658 cm^{-1} (2CO); ^1H NMR: 7.73–7.22 (m, 10H, Ar), 6.51 (br, 2H, NH_2), 2.85–1.37 (m, 6H, $3CH_2$). Anal. for $C_{23}H_{18}N_4O_2S$ (414.52): C, 66.63; H, 4.38; N, 13.51; S, 7.73. Found: C, 66.89; H, 4.00; N, 13.80; S, 7.82.

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