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Synthesis of annelated [*a*]aza-anthracenones and thieno[3,2-*g*]aza-naphthalenones through ring transformation of 2*H*-pyran-2-one followed by photocyclization☆

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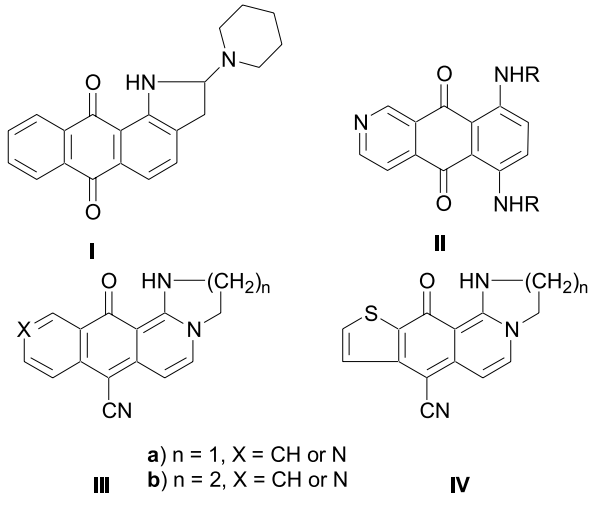
Abstract—A concise synthesis of some new classes of heterocycles (4-aryl-11-oxo-1,2,3,11-tetrahydro-1,3a-diaza-cyclopenta[*a*]anthracen-6-carbonitriles and 5-aryl-12-oxo-1,3,4,12-tetrahydro-2*H*-1,4a-diazabenzo[*a*]anthracene-7-carbonitriles) has been developed by the ring transformation of suitably functionalized 2*H*-pyran-2-one with α-oxoketene cyclic aminals to intermediates (8-aroyl-5-aryl-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyridine-7-ylidene)-acetonitriles and (9-aroyl-6-aryl-1,2,3,4-tetrahydropyrido[1,2-*a*]pyrimidin-8-ylidene)-acetonitriles) followed by their photocyclization either in $CHCl_3$ or acetonitrile. This reaction was further explored for the synthesis of methyl 4-aryl-11-oxo-1,2,3,11-tetrahydro-1,3a,9-triaza-cyclopenta[*a*]anthracene-6-carboxylate, 4-aryl-11-oxo-1,2,3,11-tetrahydro-1,3a,9-triaza-cyclopenta[*a*]anthracene-6-carbonitriles, 5-aryl-12-oxo-1,3,4,12-tetrahydro-2*H*-1,4a,10-triazabenzo[*a*]anthracene-7-carbonitriles, 4-aryl-10-oxo-1,2,3,10-tetrahydro-9-thia-1,3a-diazadicyclopenta[*a*,*g*]naphthalene-6-carbonitriles and 5-aryl-11-oxo-1,3,4,11-tetrahydro-2*H*-10-thia-1,4a-diazacyclopenta[*b*]phenanthrene-7-carbonitriles from the similar reactions.

1. Introduction

Protein tyrosine kinases including Src[1] are key elements that regulate numerous cell functions such as cell growth and differentiation through signal transduction. Over activation and expression of Src is responsible for various diseases including cancer.[2] 4-Anilino-1-azaanthracene-3-carbonitrile and aza analogs of quinoline have been found highly effective as Src kinase inhibitors in the treatment of cancer and other diseases.[3] Various compounds with anthracene (**I**) and azaanthracene (**II**) basic skeletons have been used in the clinical management of leukemia, breast and ovarian cancer.[4] The development of resistance against clinically used anticancer drugs, necessitated the design and synthesis of a new class of heterocycles, which could not only improve the therapeutic efficacy against multiple drug resistance but were also less toxic.[5] The therapeutic significance of 9,10-anthraquinone highlightened our interest in the synthesis of annelated [*a*]aza-anthracenone (**III**), and thieno[3,2-*g*]aza-naphthalenone (**IV**) not previously reported in the literature.



Non-annelated azaanthraquinones have been synthesized either by Diels–Alder reaction of azanaphthoquinone with an appropriate diene,[6] classical Friedel–Crafts[7] reactions or oxidation of 9,10-dihydroazaanthracene.[8] Considering the electronic aspects of prototype structures **I** and **II**, annelated [*a*] azaanthracenone (**III**) and thieno [3,2-*g*]

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Keywords: Azaanthracenones; Thieno[3,2-*g*]azanaphthalenone; Ring transformation; Photocyclization.
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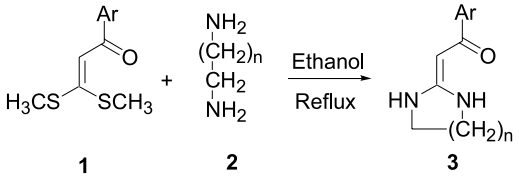
aza-naphthalenone (**IV**) were designed and by replacing the carbonyl oxygen with an electron withdrawing cyano substituent to retain an almost similar electronic status of the molecules.

The ubiquitous presence of 2*H*-pyran-2-one (**4**) in various natural products and its unique electronic topography led us to consider its suitability for ring transformation reactions to generate molecular diversity.[9] Herein, we report a concise and efficient synthesis of anneleted [*a*]aza-anthracenones (**6**), triaza-cyclopenta[*a*]anthracenones (**8**) and thieno[3,2-*g*]aza-naphthalenones (**9**) through ring transformation reaction of suitably functionalized 2*H*-pyran-2-one **4** with α-oxoketene cyclic aminals **3a–h** followed by photocyclization.

2. Results and discussion

Our strategy to synthesize 4-aryl-11-oxo-1,2,3,11-tetrahydro-1,3a-diazacyclopenta[*a*]anthracene-6-carbonitriles (**6a–e**) and 5-aryl-12-oxo-1,3,4,12-tetrahydro-2*H*-1,4a-diazabenzo[*a*]anthracene-7-carbonitriles (**6f,g**) was based on the ring transformation of 2*H*-pyran-2-ones[10] (**4**) with α-oxoketene cyclic aminals[11] (**3**), obtained from the reaction of α-oxoketene dithioacetal (**1**) with 1,2 or 1,3-diaminoalkanes (**2**) in alcohol at reflux temperature (Scheme 1).



1 **2** **3**

3	n	Ar	Yield (%)
a	1	C_6H_5	90
b	1	4-Cl.C_6H_4	85
c	1	4-Br.C_6H_4	88
d	1	2-thienyl	83
e	1	3-Pyridyl	83
f	2	4-Br.C_6H_4	80
g	2	2-thienyl	91
h	2	3-Pyridyl	79

Scheme 1. Preparation of α-oxoketene cyclic aminals (**3**).

Thus, stirring an equimolar mixture of **3** and **4** in the presence of powdered KOH in dry DMF for 24 h at ambient temperature in normal light provided **6** directly in poor yield (8%) after usual workup. Thus, attempts were made to trap the intermediate to understand the course of the reaction as well as to improve the yield of the final product.

The intermediate **5** was synthesized from the usual ring transformation of 2*H*-pyran-2-one (**4**) by **3** in the dark and purified by Si-gel column chromatography to isolate **5** as a pure product. The structure of intermediate (**5**) was confirmed by ^{1}H NMR spectroscopy and mass spectrometry. A solution of intermediate (**5**) was photochemically cyclized to **6** in 50% yield by irradiating its solution in chloroform with a 200 W electric bulb. The progress of the reaction was also monitored by recording the UV spectrum of **5** in DMSO. The initial absorption band at 435 nm disappeared after irradiation for 2 h with a hypsochromic shift and the appearance of a new absorption maxima at 385 nm (Fig. 1, Scheme 2).

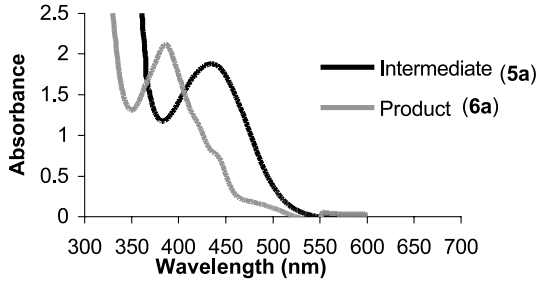


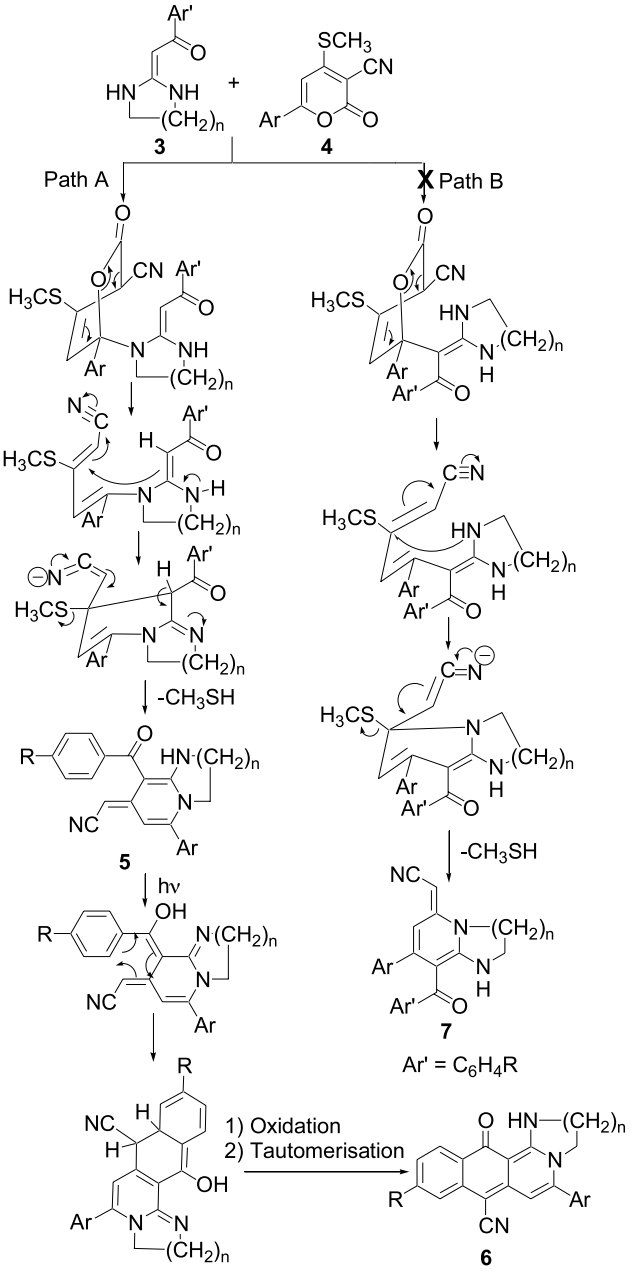
Figure 1. Absorption maxima of intermediate **5a** (435 nm) and product **6a** (385 nm) after irradiation (200 W electric bulb) for 2 h.

To generate molecular diversity, a reaction of **4** with different α-oxoketene cyclic aminals (**3e**,**h**) derived from 3,3-bis-methylsulfanyl-1-pyridin-3-yl-propanone was carried out analogously to obtain **8** as the major product (Scheme 3).

The ring transformation and photocyclization reactions were also achieved in a single step by simply irradiating a solution of a mixture of **3** and **4** in the presence of NaH in THF for 10–15 h.

In this reaction, there are two possible modes of photocyclization of the intermediate involving positions 2 and 4 of the pyridine ring and the α-vinylic carbon adjacent to the nitrile functionality. Isolation of only one product from this reaction, indicated the involvment of either C2 or C4 of the pyridine ring in the photocyclization. The proton NMR of **8f** showed one singlet for the C2 proton at δ 9.54 and confirmed the cyclization involving C4 of the pyridine ring. The downfield shift of the C2 proton was probably due to strong intramolecular H-bonding with the neighboring carbonyl oxygen. The two doublets for the C5 and C6 protons at δ 7.58 and 8.57, respectively, with 5.7 Hz coupling constant further supported cyclization involving C4. The scope of the reaction was further explored by synthesizing thieno[3,2-*g*]azanaphthalenones (**9**) directly by irradiating a solution of 2*H*-pyran-2-one (**4**) and α-oxoketene cyclic aminals **3** in the presence of NaH in THF for 15 h in moderate yield and produced a new class of heterocycle (Scheme 4).

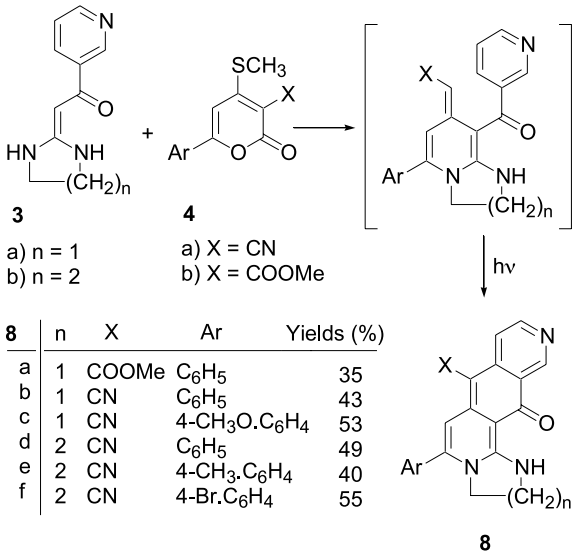
The nature of the substitutents present at positions 3 and 4 of the pyran ring greatly influence the ring transformation reactions. An electron withdrawing substituent, especially at position 3, is an essential requirement to enhance the electrophilicity of C6 of the pyran ring which facilitates the nucleophile induced ring transformation reactions. 2*H*-Pyran-2-ones (**4**) can be considered as a cyclic ketene hemithioacetal, prone to nucleophilic attack at C6 due to extended conjugation. α-Oxoketene cyclic aminals (**3**) are endowed with three nucleophilic centers, two of them due to the presence of two secondary amino groups and other due to the vinylic carbon, adjacent to the cyano function.



5/6	Ar	R	n	Yield (%) 5	6
a	C_6H_5	Cl	1	52	39
b	4-$CH_3OC_6H_4$	Cl	1	62	51
c	4-FC_6H_4	Cl	1	60	53
d	1-naphthyl	Cl	1	62	54
e	4-BrC_6H_4	Cl	1	62	62
f	4-BrC_6H_4	Br	2	64	52
g	4-$CH_3C_6H_4$	Br	2	65	55

Scheme 2. Proposed mechanism for the formation of aza-anthracenones.

Thus, the possibility for the formation of two products existed depending upon the initial involvement of either of the two secondary amino groups or vinylic carbon of the ring transformed product. The progress of the reaction through intermediate **7** (Scheme 2) was ruled out on the basis of the structure of the photochemically cyclized product **6** which can only be obtained from intermediate



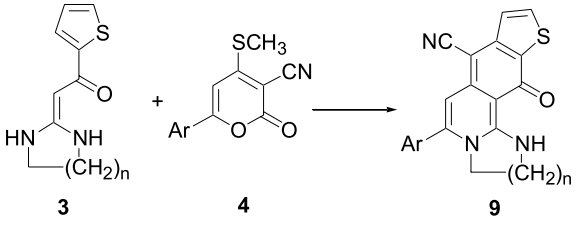
8	n	X	Ar	Yields (%)
a	1	COOMe	C_6H_5	35
b	1	CN	C_6H_5	43
c	1	CN	4-$CH_3O.C_6H_4$	53
d	2	CN	C_6H_5	49
e	2	CN	4-$CH_3.C_6H_4$	40
f	2	CN	4-$Br.C_6H_4$	55

Scheme 3. Preparation of triaza-cyclopenta[*a*]anthracene-6-carbonitriles **8**.

5.The structure was further confirmed by spectroscopy and also by single crystal X-ray diffraction analysis of **6f** (Fig. 2).[12] The presence of chloroform in the asymmetric unit of the crystal structure may be due to the presence of strong intermolecular H-bond between hydrogen atom of chloroform and N20 of the cyano group [C28–H28···N20A: H···A=2.36 Å, D···A=3.15(2) Å and ∠(DHA)=136.8°].

The possibility of a free radical mechanism for photocyclized product **6** was ruled out on the basis of formation of the same product in the presence of TEMPO. Thus, the reaction possibly proceeds through a photochemically allowed conrotatory cyclization[13] followed by aerial oxidation of dihydro intermediate to yield **6**.A plausible mechanism of this reaction is depicted in Scheme 2, where the nitrogen nucleophile attacks at C6 of the pyran ring with ring opening followed by decarboxylation and recyclization involving the vinylic carbon and C4 of the pyran ring with elimination of methyl mercaptan to yield **5** (Scheme 2, Fig. 3).

The stereoselectivity in the formation of intermediate **5** has possibly arised from strong intramolecular hydrogen bonding between the NH and CO functionalities or steric hindrance which plays a crucial role in restricting the



9	n	Ar	Yields(%)
a	1	C_6H_5	35
b	1	4-$CH_3O.C_6H_4$	51
c	2	4-$Br.C_6H_4$	48
d	2	4-$CH_3.C_6H_4$	52

Scheme 4. Preparation of thieno[3,2-*g*]azanaphthalenones (**10**).

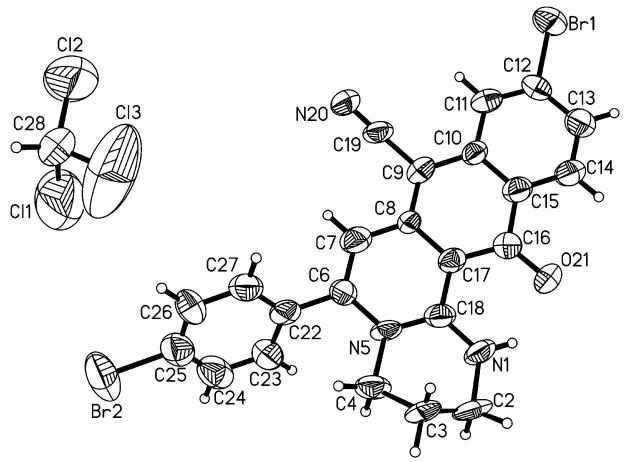


Figure 2. ORTEP diagram of **6f** showing the X-ray molecular structure in 50% probability level, solvent of crystallization 'chloroform' has been shown in the crystal structure.

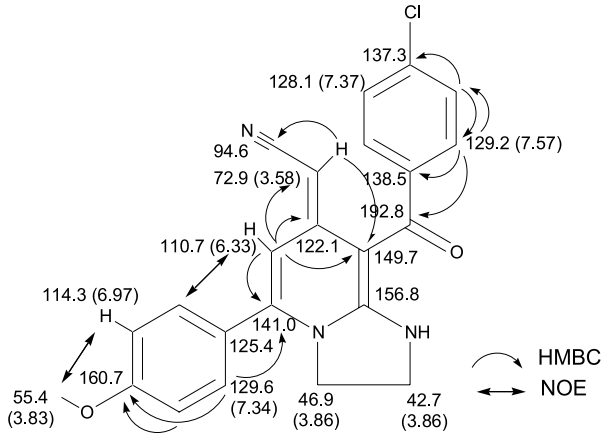


Figure 3. Chemical structure of **5b** showing HMBC and NOE.

rotation of the aroyl group, to attain *E*-geometry. The intermediates **5** isolated from the reaction were characterized by IR and NMR spectroscopy and mass spectrometry as (*E*)-2-(8-aroyl-5-aryl-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyridine-7-ylidene)acetonitrile (**5**, $n=1$) and pyrido[1,2-*a*]-pyrimidin-8-ylidene)acetonitrile (**5**, $n=2$). The proton NMR spectrum of **5b** showed two CH proton singlets at 6.33 and 3.59 ppm, a methyl singlet at 3.83 ppm and a set of aliphatic methylene protons as multiplet centered at 3.86 ppm, two sets of *ortho* coupled doublets at 7.34 and 7.57 and a broad singlet at 8.49 ppm for the NH proton. The ^{13}C NMR spectrum provided two methylene carbons at 42.7 and 46.9 ppm, one methyl carbon at 55.4 ppm, two methylene carbons at 72.9 and 110.7 ppm as shown in Figure 3. Three aromatic methyne carbons at 114.3, 129.0 and 129.6 ppm and the presence of two carbons at 129.6 ppm was corroborated in the HSQC experiment. Moreover, the ^{13}C assignments were carried out by the combined use of NOE difference, HSQC and HMBC experiments. The high field shift of the olefinic CH in the ^{1}H NMR spectrum at 3.59 ppm and at 72.7 ppm in the ^{13}C NMR was attributed to the shielding effect of the carbonyl and nitrile functionalities of **5b**.

In summary, our methodology provides a concerted approach to the synthesis of fused heterocyclic systems, using readily available starting materials under mild conditions. It opens as an efficient diversity-orientated synthetic route for the synthesis of complex nitrogen bridgehead aza-heterocycles.

3. Experimental

3.1. General

All reactions were conducted in flame dried glassware under nitrogen atmosphere. Pre-coated Merck TLC plates were used for monitoring reactions. Column chromatographic separations were performed on silica gel (60–120 mesh). IR spectra were taken on a Shimadzu 8201 PC FTIR Spectrophotometers. ^{1}H and ^{13}C NMR spectra were recorded, on Bruker DRX 300 or DPX 200 spectrometers. ^{13}C NMR assignments were obtained from DEPT and inverse H–C one bond and multiple bond correlation experiments. Mass spectra were recorded on JEOL SX-102 (FAB) spectrometers. Combustion analyses were performed on Elementar Vario EL III Carlo Erba 1108 analyzers.

3.2. General procedure for the synthesis of imidazo[1,2-*a*]-pyridines (5a–e) and pyrido[1,2-*a*]pyrimidine (5f,g)

A mixture of 2*H*-pyran-2-ones **4** (1 mmol), α-oxoketene cyclic aminal **3** (1 mmol) and NaH (60% suspension, 2.5 mmol) in dry THF (20 mL) was stirred for 2 h at 5–10 °C. After additional stirring for another 10 h at 20–25 °C, the reaction mixture was poured into ice-water (50 mL) and neutralized with 10% HCl. The separated solid was filtered, washed with water (50 mL) and dried. The entire reaction was carried out in the dark to prevent photocyclization. The crude solid obtained was further purified by column chromatography using 50% hexane–$CHCl_3$ as eluent in the dark.

3.2.1. [8-(4-Chlorobenzoyl)-5-phenyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyridin-7-ylidene]-acetonitrile (5a). Yields 52%; brown-red solid; mp 185–190 °C dec.; IR (neat): $\nu_{max}=3352$, 2923, 2855, 2168, 1638, 1595, 1517, 1287, 1085, 1010 cm^{-1}; ^{1}H NMR (200 MHz, DMSO): δ 3.53 (s, 1H, CH), 3.62–3.67 (m, 2H, NCH_2), 3.83–3.87 (m, 2H, NCH_2), 6.01 (s, 1H, CH), 7.49–7.62 (m, 9H, ArH), 8.40 (bs, 1H, NH); FAB (MS) 374 ($M^+ +1$); $C_{22}H_{16}ClN_3O_2$ (373.10) calcd: C, 70.68; H, 4.31; N, 11.24; found: C, 70.51; H, 4.41; N, 11.39.

3.2.2. [8-(4-Chlorobenzoyl)-5-(4-methoxyphenyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyridin-7-ylidene]-acetonitrile (5b). Yields 62%; brown-red solid; mp 175–180 °C dec.; IR (neat) ν_{max} 3353, 3019, 2927, 2856, 2175, 1640, 1597, 1529, 1295, 1216, 1091, 1013 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.58 (s, 1H, CH), 3.83–3.89 (m, 7H, OCH_3 and $2NCH_2$), 6.32 (s, 1H, CH), 6.96 (d, $J=8.7$ Hz, 2H, ArH), 7.32–7.39 (m, 4H, ArH), 7.57 (d, $J=8.7$ Hz, 2H, ArH), 8.49 (bs, 1H, NH); ^{13}C NMR (75 MHz in ppm) δ 42.7, 46.9, 55.4, 72.9, 110.7, 114.3, 122.1, 125.4, 129.6, 138.5, 149.7, 156.8, 160.7, 192.8; FAB (MS) 404 ($M^+ +1$);

$C_{23}H_{18}ClN_3O$ (403.11) calcd: C, 68.40; H, 4.49; N, 10.40; found: C, 68.61; H, 4.38; N, 10.59.

3.2.3. [8-(4-Chlorobenzoyl)-5-(4-fluorophenyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyridin-7-ylidene]-acetonitrile (5c). Yields 60%; brown-red solid; mp 165–170 °C dec.; IR (neat) ν_{max} 3367, 3019, 2926, 2177, 1641, 1596, 1527, 1292, 1216, 1091, 1011 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 3.62 (s, 1H, CH), 3.84 (m, 4H, $2NCH_2$), 6.33 (s, 1H, CH), 7.11–7.72 (m, 8H, ArH), 8.51 (bs, 1H, NH); FAB (MS) 453 ($M^+ + 1$); $C_{22}H_{15}ClFN_3O$ (391.01) calcd: C, 67.44; H, 3.86; N, 10.72; found: C, 67.61; H, 3.78; N, 10.69.

3.2.4. [8-(4-Chlorobenzoyl)-5-naphthalen-1-yl-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyridin-7-ylidene]-acetonitrile (5d). Yields 62%; brown-red solid; mp 135–139 °C dec.; IR (neat) ν_{max} 3431, 3019, 2927, 2177, 1643, 1599, 1528, 1216, 1092, 1011 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.56–3.78 (m, 5H, $2NCH_2$ and CH), 6.49 (s, 1H, CH), 7.28–7.66 (m, 7H, ArH), 7.81–7.99 (m, 4H, ArH), 8.48 (bs, 1H, NH); FAB (MS) 424 ($M^+ + 1$); $C_{26}H_{18}ClN_3O$ (423.89) calcd: C 73.67; H, 4.28 N, 9.91; found: C, 73.49; H, 4.36; N, 10.01.

3.2.5. [5-(4-Bromophenyl)-8-(4-chlorobenzoyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyridin-7-ylidene]-acetonitrile (5e). Yields 62%; brown-red solid; mp 123–128 °C dec.; IR (neat) ν_{max} 3368, 3017, 2925, 2176, 1641, 1599, 1527, 1293, 1216, 1092, 1011 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.60 (s, 1H, CH), 3.83 (m, 4H, $2NCH_2$), 6.31 (s, 1H, CH), 7.11–7.59 (m, 8H, ArH), 8.50 (bs, 1H, NH); FAB (MS) 453 ($M^+ + 1$) $C_{22}H_{15}BrClN_3O$ (452.73) calcd: C, 58.36; H, 3.34; N, 9.28; found: C, 58.49; H, 3.50; N, 9.11.

3.2.6. [9-(4-Bromobenzoyl)-6-(4-bromophenyl)-1,2,3,4-tetrahydro-pyrido[1,2-*a*]pyrimidin-8-ylidene]-acetonitrile (5f). Yields 64%; brown-red solid; mp 157–162 °C dec.; IR (neat) ν_{max} 3430, 3016, 2926, 2177, 1644, 1591, 1528, 1216, 1073, 1010 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.98–2.08 (m, 2H, CH_2), 3.45–3.54 (m, 5H, $2NCH_2$ and CH), 6.32 (s, 1H, CH), 7.23–7.26 (m, 2H, ArH), 7.42–7.49 (m, 4H, ArH), 7.58–7.63 (m, 2H, ArH), 10.94 (bs, 1H, NH); FAB (MS) 512 ($M^+ + 1$) $C_{23}H_{17}Br_2N_3O$ (511.21) calcd: C, 54.04; H, 3.35; N, 8.22; found: C, 54.21; H, 3.50; N, 8.01.

3.2.7. [9-(4-Bromobenzoyl)-6-(4-methylphenyl)-1,2,3,4-tetrahydro-pyrido[1,2-*a*]pyrimidin-8-ylidene]-acetonitrile (5g). Yields 65%; brown-red solid; mp 195–200 °C dec.; IR (neat) ν_{max} 3018, 2927, 2177, 1645, 1590, 1530, 1216, 1072, 1010 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.97–2.02 (m, 2H, CH_2), 2.41 (s, 3H, CH_3), 3.43–3.56 (m, 5H, $2NCH_2$ and CH), 6.32 (s, 1H, CH), 7.24–7.60 (m, 8H, ArH), 10.90 (bs, 1H, NH); FAB (MS) 447 ($M^+ + 1$); $C_{24}H_{20}BrN_3O$ (446.34) calcd: C, 64.58; H, 3.34; N, 9.28; found: C, 64.39; H, 3.49; N, 9.11.

3.3. General procedure for the synthesis of aza-[*a*]anthracenones (6)

A solution of **5** (0.05 mmol) in acetonitrile (10 mL) was irradiated under stirring for 10 h by 200 W electric bulb. A yellow solid separated, was filtered and washed with methanol. The crude product was further purified by column chromatography using 1% methanol in chloroform as eluent.

3.3.1. 8-Chloro-11-oxo-4-phenyl-1,2,3,11-tetrahydro-1,3*a*-diaza-cyclopenta[*a*]anthracene-6-carbonitrile (6a). Yields 39%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 3434, 2925, 2859, 2174, 1598, 1515 cm^{-1}; ^1H NMR (200 MHz, DMSO) δ 3.84–3.87 (m, 2H, NCH_2), 4.07–4.10 (m, 2H, NCH_2), 6.41 (s, 1H, CH), 7.21–7.59 (m, 7H, ArH), 8.17 (d, J=8.0 Hz, 1H, ArH), 10.00 (bs, 1H, NH); FAB (MS) 372 ($M^+ + 1$); $C_{22}H_{14}ClN_3O$ (371.08) calcd: C, 71.07; H, 3.80; N, 11.30; found: C 71.16; H, 3.71; N, 11.39.

3.3.2. 8-Chloro-4-(4-methoxyphenyl)-11-oxo-1,2,3,11-tetrahydro-1,3*a*-diaza-cyclopenta[*a*]anthracene-6-carbonitrile (6b). Yields 51%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 3447, 3255, 2910, 2194, 1646, 1595, 1524, 1435, 1303, 1258, 1025 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 3.89 (s, 3H, OCH_3), 4.03–4.06 (m, 2H, NCH_2), 4.14–4.17 (m, 2H, NCH_2), 6.79 (s, 1H, CH), 7.01 (d, J=8.0 Hz, 2H, ArH), 7.33–7.42 (m, 3H, ArH), 7.89 (s, 1H, ArH), 8.35 (d, J=8.0 Hz, 2H, ArH), 10.11 (bs, 1H, NH); FAB (MS) 402 ($M^+ + 1$); $C_{23}H_{16}ClN_3O_2$ (401.84) calcd: C, 68.74; H, 4.01; N, 10.46; found: C, 68.91; H, 3.91; N, 10.45.

3.3.3. 8-Chloro-4-(4-fluorophenyl)-11-oxo-1,2,3,11-tetrahydro-1,3*a*-diaza-cyclopenta[*a*]anthracene-6-carbonitrile (6c). Yields 53%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 3431, 3000, 2190, 1645, 1597, 1524, 1442, 1227, 1085 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.06–4.24 (m, 4H, $2NCH_2$), 6.74 (s, 1H, CH), 7.21–7.53 (m, 5H, ArH), 7.85 (s, 1H, ArH), 8.28 (d, J=8.7 Hz, 1H, ArH), 10.01 (bs, 1H, NH); FAB (MS) 390 ($M^+ + 1$); $C_{22}H_{13}ClFN_3O$ (389.81) calcd: C, 67.79; H, 3.36; N, 10.78; found: C, 67.81; H, 3.46; N, 10.92.

3.3.4. 8-Chloro-4-naphthalen-1-yl-11-oxo-1,2,3,11-tetrahydro-1,3*a*-diaza-cyclopenta[*a*]anthracene-6-carbonitrile (6d). Yield 54%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 3433, 3055, 2193, 1645, 1591, 1523, 1430, 1310, 1256, 1084 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.83–4.09 (m, 4H, $2NCH_2$), 7.02 (s, 1H, CH), 7.31–7.36 (m, 1H, ArH), 7.57–7.72 (m, 5H, ArH), 7.93–8.01 (m, 3H, ArH), 8.38 (d, J=8.7 Hz, 1H, ArH), 10.01 (bs, 1H, NH); FAB (MS) 422 ($M^+ + 1$); $C_{26}H_{16}ClN_3O$ (421.88) calcd: C, 74.02; H, 3.82; N, 9.96; found: C, 74.12; H, 3.92; N, 9.11.

3.3.5. 4-(4-Bromophenyl)-8-chloro-11-oxo-1,2,3,11-tetrahydro-1,3*a*-diaza-cyclopenta[*a*]anthracene-6-carbonitrile (6e). Yield 62%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 3330, 2183, 1642, 1593, 1516, 1219 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.06–4.23 (m, 4H, $2NCH_2$), 6.84 (s, 1H, CH), 7.28–7.40 (m, 4H, ArH), 7.67–7.71 (m, 3H, ArH); FAB (MS) 451 ($M^+ + 1$); $C_{22}H_{13}BrClN_3O$ (450.71) calcd: C, 58.63; H, 2.91; N, 9.32; found: C, 58.71; H, 3.05; N, 9.62.

3.3.6. 9-Bromo-5-(4-bromophenyl)-12-oxo-1,3,4,12-tetrahydro-2*H*-1,4*a*-diaza-benzo[*a*]anthracene-7-carbonitrile (6f). Yield 52%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 3435, 2179, 1646, 1600, 1514, 1326, 1207 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.08–2.16 (m, 2H, CH_2),

3.65 (t, $J=6.0$ Hz, 2H, NCH_2), 3.80 (t, $J=6.0$ Hz, 2H, NCH_2), 6.84 (s, 1H, CH), 7.41–7.54 (m, 5H, ArH), 8.09 (s, 1H, ArH), 8.31 (d, $J=9.0$ Hz, 1H, ArH), 14.04 (bs, 1H, NH); FAB (MS) 510 ($M^+ +1$); $C_{23}H_{15}Br_2N_3O$ (509.19) calcd: C, 54.25; H, 2.97; N, 8.25; found: C, 54.35; H, 2.92; N, 8.32.

3.3.7. 9-Bromo-12-oxo-5-(4-methylphenyl)-1,3,4,12-tetrahydro-2*H*-1,4*a*-diaza-benzo[*a*]anthracene-7-carbonitrile (6g). Yield 55%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 3430, 2193, 1738, 1641, 1598, 1515, 1325, 1208 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.07–2.13 (m, 2H, CH_2), 2.45 (s, 3H, CH_3), 3.63 (t, $J=5.5$ Hz, 2H, NCH_2), 3.79 (t, $J=5.5$ Hz, 2H, NCH_2), 6.80 (s, 1H, CH), 7.30–7.46 (m, 5H, ArH), 8.07 (s, 1H, ArH), 8.30 (d, $J=8.74$ Hz, 1H, ArH), 13.81 (bs, 1H, NH); FAB (MS) 445 ($M^+ +1$); $C_{24}H_{18}BrN_3O$ (444.32) calcd: C, 64.88; H, 4.08; N, 9.46; found: C, 65.06; H, 4.22; N, 9.41.

3.4. General procedure for the synthesis of triaza-cyclopenta[*a*]anthracene-6-carbonitriles (8) and thieno[3,2-*g*]-aza-naphthalenones (9)

A mixture of 2*H*-pyran-2-one (**4**, 1 mmol), α-oxoketene cyclic aminal (**3**, 1 mmol) and NaH (60% suspension, 2.5 mmol) in dry THF (15 mL) was stirred for 15 h under light irradiation by 200 W electric bulb. The reaction mixture was poured onto ice water (50 mL), neutralized with 10% HCl. The precipitate obtained was filtered, washed with water (50 mL) and dried. The crude solid was finally purified on Si-gel column chromatography using 4% methanol in chloroform as eluent.

3.4.1. 11-Oxo-4-phenyl-1,2,3,11-tetrahydro-1,3a,9-triaza-cyclopenta[*a*]anthracene-6-carboxylic acid methyl ester (8a). Yield 35%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 3398, 2926, 2370, 1851, 1705, 1657, 1597, 1441 cm^{-1}; ^1H NMR (200 MHz, 2 drop CD_3OD in $CDCl_3$) δ 3.95 (s, 3H, $COOCH_3$), 4.16 (t, $J=5.6$ Hz, 2H, NCH_2), 4.35 (t, $J=5.6$ Hz, 2H, NCH_2), 7.28 (s,1H, CH), 7.51–7.56 (m, 5H, ArH), 8.07 (d, $J=6.0$ Hz, 1H, ArH), 8.2 (d, $J=6.0$ Hz, 1H, ArH), 9.24 (s, 1H, ArH); FAB (MS) 372 ($M^+ +1$); $C_{22}H_{17}N_3O_3$ (371.13) calcd: C, 71.15; H, 4.61; N, 11.31; found: C, 71.22; H, 4.73; N, 11.33.

3.4.2. 11-Oxo-4-phenyl-1,2,3,11-tetrahydro-1,3a,9-triaza-cyclopenta[*a*]anthracene-6-carbonitrile (8b). Yield 43%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 3277, 2831, 2367, 2211, 1630, 1596, 1527, 1363 cm^{-1}; ^1H NMR (200 MHz, 2 drops CD_3OD in $CDCl_3$) δ 4.16–4.26 (m, 2H, NCH_2), 4.69–4.82 (m, 2H, NCH_2), 6.93 (s, 1H, CH), 7.52–7.61 (m, 5H, ArH), 7.91 (d, $J=6.2$ Hz, 1H, ArH), 8.32 (d, $J=6.2$ Hz, 1H, ArH), 9.26 (s, 1H, ArH); FAB (MS) 339 ($M^+ +1$); $C_{21}H_{14}N_4O$ (338.12) calcd: C, 74.54; H, 4.17; N, 16.56; found: C, 74.67; H, 4.23; N, 16.65.

3.4.3. 4-(4-Methoxyphenyl)-11-oxo-1,2,3,11-tetrahydro-1,3a,9-triaza-cyclopenta[*a*]anthracene-6-carbonitrile (8c). Yield 53%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 3377, 2926, 2833, 2368, 2186, 1632, 1589, 1362 cm^{-1}; ^1H NMR (200 MHz, 2 drops CD_3OD in $CDCl_3$) δ 3.76 (s, 3H, OCH_3), 4.09–4.18 (m, 2H, NCH_2), 4.26–4.30 (m, 2H, NCH_2), 6.83 (s, 1H, CH), 7.07 (d, $J=8.5$ Hz, 2H, ArH), 7.45 (d, $J=8.5$ Hz, 2H, ArH), 7.67 (d, $J=5.1$ Hz, 1H, ArH), 8.49 (d, $J=5.2$ Hz, 1H, ArH), 9.42 (s, 1H, ArH); FAB (MS) 369 ($M^+ +1$); $C_{22}H_{16}N_4O_2$ (368.13) calcd: C, 71.73; H, 4.38; N, 15.21; found: C, 71.81; H, 4.42; N, 15.27.

3.4.4. 12-Oxo-5-phenyl-1,3,4,12-tetrahydro-2*H*-1,4a,10-triaza-benzo[*a*]anthracene-7-carbonitrile (8d). Yield 49%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 3377, 2926, 2854, 2363, 2184, 1742, 1646, 1507, 1448, 1362 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.07–2.18 (m, 2H, CH_2), 3.64–3.66 (m, 2H, NCH_2), 3.78–3.84 (m, 2H, NCH_2), 6.84 (s,1H, CH), 7.40–7.45 (m, 2H, ArH), 7.52–7.56 (m, 3H, ArH), 7.65 (d, $J=5.8$ Hz, 1H, ArH), 8.57 (s, 1H, ArH), 9.62 (s, 1H, ArH); FAB (MS) 353 ($M^+ +1$); $C_{22}H_{16}N_4O$ (352.13) calcd: C, 74.98; H, 4.58; N, 15.90; found: C, 74.91; H, 4.62; N, 15.83.

3.4.5. 12-Oxo-5-(4-methylphenyl)-1,3,4,12-tetrahydro-2*H*-1,4a,10-triaza-benzo[*a*]anthracene-7-carbonitrile (8e). Yield 40%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 3404, 2832, 2368, 2188, 1635, 1605, 1514, 1362 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.12–2.17 (m, 2H, CH_2), 2.47 (s, 3H, CH_3), 3.68 (t, $J=5.7$ Hz, 2H, NCH_2), 3.87 (t, $J=5.7$ Hz, 2H, NCH_2), 6.82 (s, 1H, CH), 7.35–7.41 (m, 4H, ArH), 7.67 (d, $J=5.7$ Hz, 1H, ArH), 8.48–8.49 (m, 1H, ArH), 9.51 (s, 1H, ArH); FAB (MS) 367 ($M^+ +1$); $C_{23}H_{18}N_4O$ (366.15) calcd: C, 75.39; H, 4.95; N, 15.29; found: C, 75.48; H, 5.08; N, 15.34.

3.4.6. 5-(4-Bromophenyl)-12-oxo-1,3,4,12-tetrahydro-2*H*-1,4a,10-triaza-benzo[*a*]anthracene-7-carbonitrile (8f). Yield 55%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 3404, 2930, 2832, 2368, 2191, 1630, 1590, 1510, 1362 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.09–2.14 (m, 2H, CH_2), 3.61–3.63 (m, 2H, NCH_2), 3.75–3.80 (m, 2H, NCH_2), 6.69 (s, 1H, CH), 7.32 (d, $J=8.3$ Hz, 2H, ArH), 7.58 (d, $J=5.8$ Hz, 1H, ArH), 7.67 (d, $J=8.3$ Hz, 2H, ArH), 8.57 (d, $J=5.8$ Hz, 1H, ArH), 9.53 (s, 1H, ArH); FAB (MS) 432 ($M^+ +1$); $C_{22}H_{15}BrN_4O$ (430.04) calcd: C, 61.27; H, 3.51; N, 12.99; found: C, 61.39; H, 3.74; N, 13.11.

3.4.7. 10-Oxo-4-phenyl-1,2,3,10-tetrahydro-9-thia-1,3a-diaza-dicyclopenta[*a*,*g*]naphthalene-6-carbonitrile (9a). Yield 35%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 2929, 2832, 2717, 2191, 1628, 1593, 1364 cm^{-1}; ^1H NMR (200 MHz, 2 drops CD_3OD in $CDCl_3$) δ 4.10–4.26 (m, 4H, $2NCH_2$), 6.93 (s, 1H, CH), 7.34 (s, 1H, ArH), 7.44–7.57 (m, 5H, ArH), 7.78 (d, $J=5.3$ Hz, 1H, ArH); FAB (MS) 344 ($M^+ +1$); $C_{20}H_{13}N_3OS$ (343.08) calcd: C, 69.95; H, 3.82; N, 12.24; found: C, 69.86; H, 3.91; N, 12.32.

3.4.8. 4-(4-Methoxyphenyl)-10-oxo-1,2,3,10-tetrahydro-9-thia-1,3a-diaza-dicyclopenta[*a*,*g*]naphthalene-6-carbonitrile (9b). Yield 51%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 2936, 2832, 2717, 2363, 2210, 1705, 1648, 1592, 1364 cm^{-1}; ^1H NMR (200 MHz, 2 drops CD_3OD in $CDCl_3$) δ 3.9 (s, 3H, OCH_3), 4.10–4.28 (m, 4H, $2NCH_2$), 6.90 (s, 1H, CH), 7.05 (d, $J=8.5$ Hz, 2H, ArH), 7.42–7.46 (m, 3H, ArH), 7.79 (d, $J=5.3$ Hz, 1H, ArH); FAB (MS) 374 ($M^+ +1$); $C_{21}H_{15}N_3O_2S$ (373.08) calcd: C, 67.54; H, 4.05; N, 11.25; found: C, 67.69; H, 4.25; N, 11.32.

3.4.9. 5-(4-Bromophenyl)-11-oxo-1,3,4,11-tetrahydro-2*H*-10-thia-1,4a-diaza-cyclopenta[*b*]phenanthrene-7-carbonitrile (9c). Yield 48%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 3424, 2365, 2197, 1635, 1593, 1528, 1351 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.07–2.13 (m, 2H, CH_2), 3.62 (t, J=5.8 Hz, 2H, NCH_2), 3.77 (t, J=5.9 Hz, 2H, NCH_2), 6.86 (s, 1H, CH), 7.31 (d, J=8.3 Hz, 2H, ArH), 7.43 (d, J=5.3 Hz, 1H, ArH), 7.67 (d, J=8.3 Hz, 2H, ArH), 7.71 (d, J=5.3 Hz, 1H, ArH); FAB (MS) 437 (M^++2); $C_{21}H_{14}BrN_3OS$ (435.00) calcd: C, 57.81; H, 3.23; N, 9.63; found: C, 57.89; H, 3.33; N, 9.82.

3.4.10. 11-Oxo-5-(4-methylphenyl)-1,3,4,11-tetrahydro-2*H*−10-thia-1,4a-diaza-cyclopenta[*b*]phenanthrene-7-carbonitrile (9d). Yield 52%; yellow powder; mp >250 °C; IR (KBr) ν_{max} 2832, 2379, 2192, 1634, 1586, 1526, 1361 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.05–2.14 (m, 2H, CH_2), 2.46 (s, 3H, CH_3), 3.82–3.87 (m, 4H, $2NCH_2$), 6.84 (s, 1H, CH), 7.20–7.38 (m, 4H, ArH), 7.41 (d, J=5.3 Hz, 1H, ArH), 7.46 (d, J=5.3 Hz, 1H, ArH); FAB (MS) 372 (M^++1); $C_{22}H_{17}N_3OS$ (371.11) calcd: C, 71.14; H, 4.61; N, 11.31; found: C, 71.16; H, 4.72; N, 11.45.

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