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Synthesis, characterization and pharmacological investigations of some novel heterocyclic derivatives incorporating pyrene and sugar moieties

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Abstract A series of substituted pyrene derivatives **2–15** incorporated heterocyclic and sugar moieties were synthesized and evaluated as antiviral activities using 1-acetylpyrene as a starting material. The structure assignment of the new compounds was based on chemical and spectroscopic evidence. The detailed synthesis, spectroscopic data and pharmacological activities of the synthesized compounds were reported.

Keywords Pyrene derivatives · Nucleoside analogues · Anti-HIV-1 activities

Introduction

The development of synthetic molecules that bind to, modify or cleave DNA, and ultimately result in cell death has been under intense research for the last couple of decades [1]. DNA binding affinity and orientation affect the biological activities of

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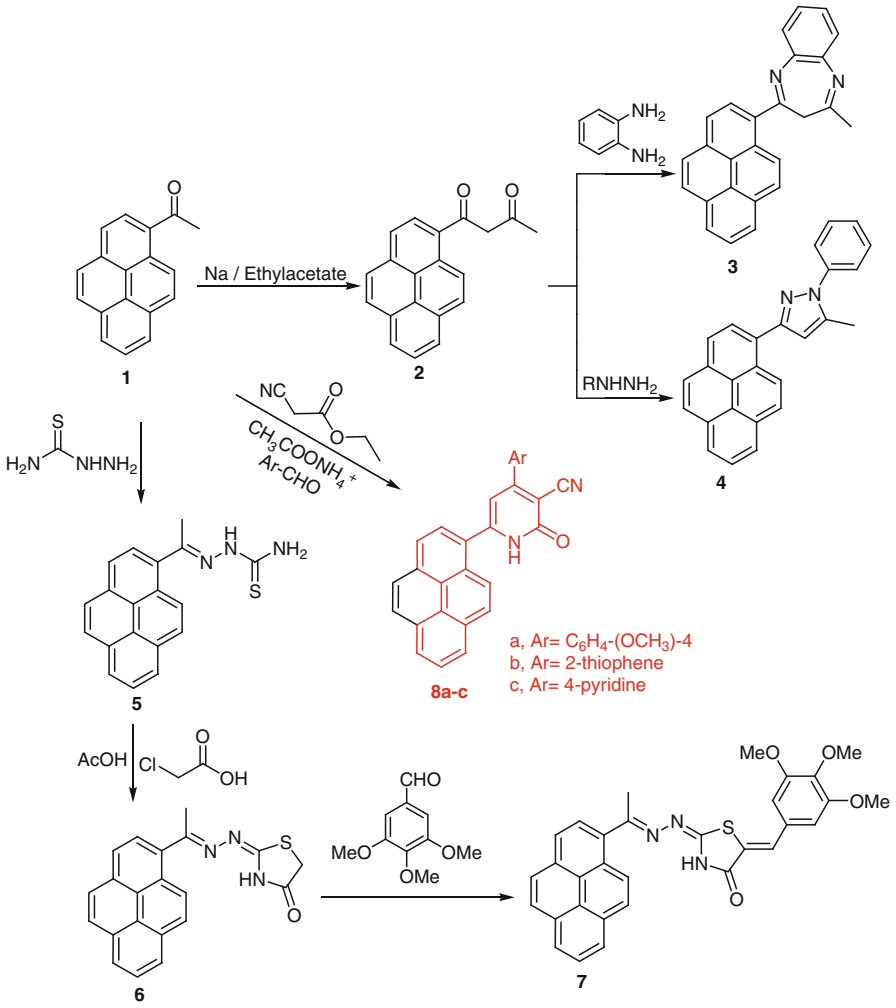
the molecules [2]. The interaction of DNA with drug molecules involve four types of binding modes: (1) electrostatic binding, (2) external binding, (3) groove binding (groove binder), and (4) intercalative binding (intercalator), which is the most effective for drugs targeted to DNA [3]. Pyrene is considered one of the most promising candidates for the intercalating moiety [4], because it has almost the same surface area as a regular Watson–Crick base pair, which makes a large stabilization through base stacking with neighboring base pairs. The fluorescence properties of pyrene have made its derivatives suitable to be used as biological probes for the investigation of structural properties of proteins and peptides [5], DNA recognition [6, 7], DNA oligomers, and duplexes in terms of their distances [8, 9], fluorescence probes [10–15], surfactant micelles, and vesicles properties [16]. Moreover, several glycosides have exhibited good biological inhibitions [17–21], inducers, and ligands [22]. Having the above aspects in mind, and as a continuation of our work on the synthesis of glycosides and nucleosides having biological activity [23–26], glycosylatives have been planned to target a group of pyridine compounds functionalized with cyano and pyrene ring. The anti-HIV activities of the newly synthesized compounds have been established.

Results and discussion

Chemistry

The reaction of 1-acetylpyrene (**1**) with an excess of ethyl acetate in the presence of sodium metal afforded the corresponding 1,3-dicarbonyl compound 1-(pyren-3-yl)butane-1,3-dione (**2**), which was reacted with *o*-phenylenediamine in ethanol to afford (1*Z*,4*E*)-2-methyl-4-(pyren-3-yl)-3H-benzo[b][1,4]diazepine (**3**). Also, compound **2** was condensed with phenyl hydrazine to afford 5-methyl-1-phenyl-3-(pyren-3-yl)-1H-pyrazole (**4**). Compound **1** was treated with thiosemicarbazide in ethanol to afford (*E*)-1-[1-(pyren-1-yl)ethylidene]thiosemicarbazide **5**, which was condensed with chloroacetic acid to give 4-thiazolidinones derivative **6**. The latter compound **6** was condensed with 3,4,5-trimethoxybenzaldehyde in glacial acetic acid in the presence of anhydrous sodium acetate afforded 5-arylidene-4-thiazolidinones derivative **7** (Scheme 1).

Additionally, compound **1** was condensed with aromatic and heterocyclic aldehydes and ethyl cyanoacetate in the presence of ammonium acetate to afford the corresponding cyanopyridone derivatives **8a–c**, respectively. Compound **8a** was reacted with 2-deoxy-3,5-di-*O*-(*p*-toluyl)-α-D-erythropentafuranosyl chloride in DMF in the presence of triethylamine at room temperature to afford the corresponding N-ribosyl pyridine derivative **9**. Deprotection of the acetoxy groups in the nucleoside **9** with ammonia in methanol afforded the product **10**. Compound **8a** was reacted with some alkyl halides, namely chloromethylmethylsulfide, chloromethylethylether or 3-bromo-1-propanol in dry DMF in the presence of anhydrous potassium carbonate at room temperature afforded the corresponding S-alkylated derivatives **11a–c**, respectively. Also, reaction of the pyridine-2-(1H)one **8a** with cycloalkyl halides, namely cyclopentyl bromide or cyclohexyl bromide in the presence of sodium hydride as a

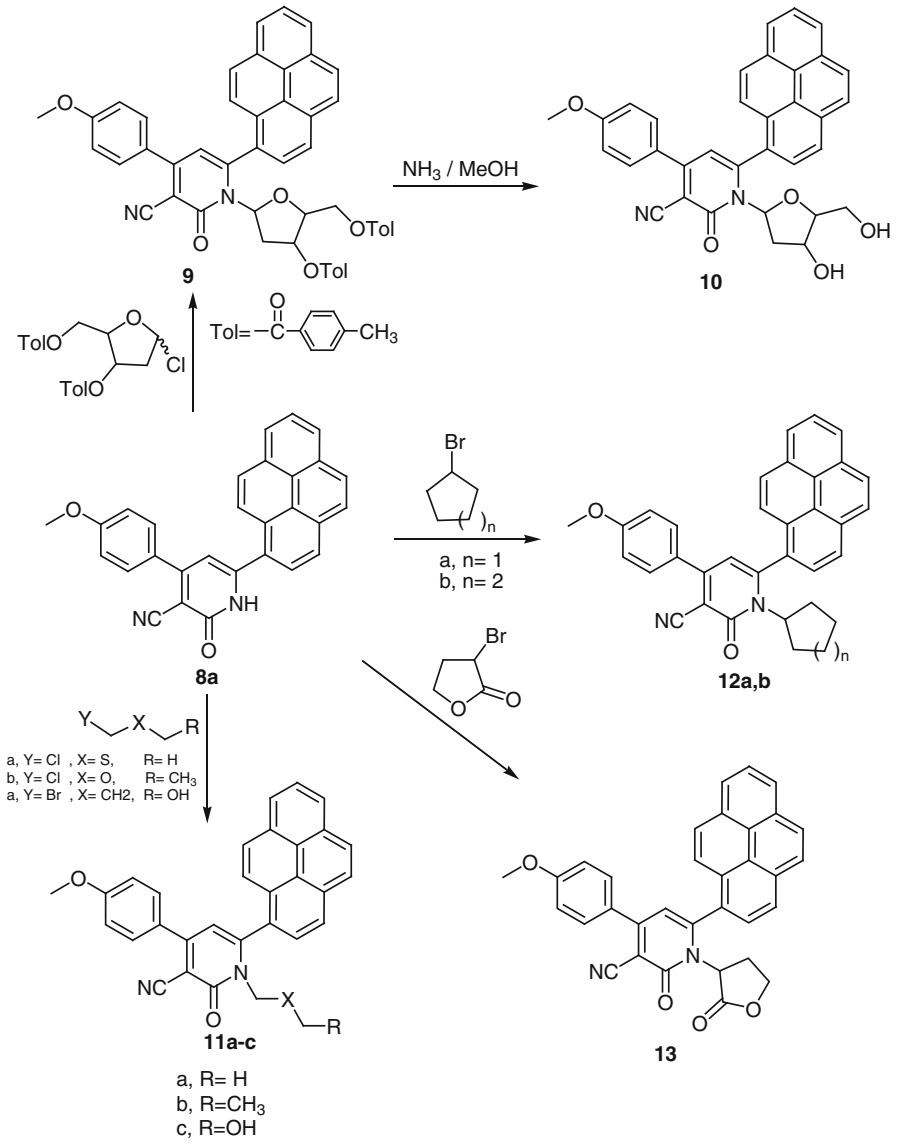


Scheme 1 Synthesis of compounds 2–7

base afforded the N-substituted derivatives **12a, b**, respectively. On the other hand, the interaction of compound **8a** with α-bromo-γ-butyrolactone caused the formation of N-lactone derivative **13** (Scheme 2).

Pharmacological screening

Compounds **7**, **8a**, **8b**, **9**, **11c**, and **12b** were evaluated for their antiviral activity against wild-type HIV-1 in MT-4 cells. Expression of HIV in culture medium was quantified by HIV antigen detection ELISA, and the results were compared with the antiviral activity of Emivirine (MKC-442), a well-examined HEPT analogue. All tested compounds were inactive against human immunodeficiency virus HIV-1 at the highest tested concentration of 100 μM.



Scheme 2 Synthesis of compounds 8–13

Inhibition of HIV-1 replication

Compounds were examined for possible antiviral activity against both strains of HIV-1 using MT-4 cells as target cells. For screening studies, MT-4 cells were incubated with the virus for 2 h, washed, and thereafter added in a proportion of 1:10 to uninfected cells which had been preincubated in growth medium containing the test compound for 2 h. Cultures were maintained with the test compound for 7 days in

parallel with virus-infected control cultures without addition of the compound. Expression of HIV-1 in the culture medium was quantitated by HIV antigen detection ELISA [27]. Compounds mediating less than 30 % reduction of antigen expression were considered to be without biological activity. Compounds mediating a reduction of 30 % or more were examined for cytotoxic potential using concentration-dependent inhibition of MT-4 cells proliferation as a measure of cytotoxicity. A 30 % inhibition of cell growth relative to control cultures was considered significant.

Experimental

Chemistry

All melting points were uncorrected and were taken on a Boetius melting point microscope. The infrared (IR) spectra were recorded on a Mattson 5000 FIR spectrometer, using KBr discs, at Cairo University. ^{1}HNMR and ^{13}CNMR spectra were performed on a Varian EMNMR spectrometer at the Microanalytical Center, Cairo University, Egypt, and on a Varian EM-360 270 MHz NMR Spectrophotometer at the University of Southern Denmark, Denmark, using tetramethylsilane (TMS) as internal standard. All chemical shifts are quoted in δ values using parts per million (ppm) scale downfield from TMS. Mass Spectra were recorded on a Finnigan SSQ 700 mass spectrometer at the University of Southern Denmark. Elemental analysis were performed by the micro-analytical unit at Cairo University and the results were within ± 0.3 of the theoretical values. All reactions were monitored by TLC using precoated aluminum sheet silica gel $60F_{254}$ plates (Merck) and detection of the components was made by short and long UV light. The silica gel (0.004–0.063 mm) used for column chromatography was purchased from Merck. The antiviral screening in vitro through the Retrovirus Laboratory, Department of Virology, State Serum Institute, Copenhagen, Denmark.

2-Methyl-4-pyren-1-yl-3H-benzo[b][1,4]diazepine (**3**)

A mixture of *o*-phenylenediamine (0.01 mol) and 1-pyren-1-yl-butan-1,3-dione (**2**) (0.01 mol) was heated under reflux in ethanol (40 mL) for 4 h. The reaction mixture was allowed to cool to room temperature and the separated precipitate was filtered off, washed with ethanol and crystallized from aqueous DMF to give **3** in yield of 67 %; m.p. >300 °C; ^{1}HNMR (DMSO-d_6) δ: 1.70 (s, 3H, CH_3), 2.80 (s, 2H, CH_2), 6.8–8.5 (m, 13H, ArH).

5-Methyl-1-phenyl-3-(pyren-3-yl)-1H-pyrazole (**4**)

A mixture of 1-pyren-1-yl-butan-1,3-dione (**2**) (0.005 mol) and phenyl hydrazine (0.02 mol) in acetic acid (10 mL) was refluxed for 5 h. The reaction mixture was concentrated under reduced pressure. The obtained precipitate was filtered off and crystallized from ethanol to afford compound **4** in yield of 65 %; m.p. >300 °C; ^{1}H NMR (DMSO-d_6) δ: 1.6 (s, 3H, CH_3), 6.3 (s, 1H, CH), 6.8–8.6 (m, 14H, ArH).

(*E*)-1-[1-(pyren-1-yl)ethylidene] thiosemicarbazide (**5**)

A mixture of compound **1** (0.01 mol) and thiosemicarbazide (0.01 mol) in absolute ethanol (25 mL) was refluxed for 8 h. After cooling, the obtained product was filtered off, dried and then crystallized from ethanol to give **5** in 73 % yield; m.p. 200 °C; ^{1}H NMR (DMSO-d_6) δ: 2.6 (s, 3H, CH_3), 4.5 (s, 2H, NH_2 exchangeable with D_2O), 8.20–8.75 (m, 9H, ArH), 10.36 (s, 1H, NH exchangeable with D_2O); ^{13}CNMR (DMSO-d_6) δ: 14.3, 123.81, 124.12, 124.21, 124.75, 125.10, 125.14, 126.23, 126.95, 127.28, 127.30, 127.51, 128.74, 130.09, 130.49, 130.91, 134.28, 168.27 and 181.93; MS: *m*/*z* 317 (M^+) consistent with the molecular formula ($C_{19}H_{15}N_3S$).

(*E*)-2[(1-(pyren-1-yl)ethylidene)hydrazono]thiazolidin-4-one (**6**)

A mixture of **5** (0.01 mol), chloroacetic acid (0.01 mol) and anhydrous sodium acetate (0.5 g) in ethanol (30 mL) was heated under reflux for 3 h. The solvent was evaporated and the reaction mixture was poured onto water. The formed product was filtered off and crystallized from ethanol to afford a pale yellow needles of **6** in 59 % yield; m.p. 243 °C; ^{1}HNMR (DMSO-d_6) δ: 2.55 (s, 3H, CH_3), 3.91 (s, 2H, CH_2), 7.90–8.47 (m, 9H, ArH), 12.11 (s, 1H, NH exchangeable with D_2O); ^{13}CNMR (DMSO-d_6) δ: 14.7, 33.4, 123.65, 124.23, 124.48, 124.82, 125.12, 125.19, 126.36, 126.89, 127.29, 127.41, 127.57, 128.86, 130.12, 130.56, 130.98, 134.39, 160.59, 163.76 and 173.25; MS: *m*/*z* 357 (M^+) consistent with the molecular formula ($C_{21}H_{15}N_3OS$).

(*E*)-2-{[1-pyren-1-yl)ethylidene]-hydrazono}-5-[1-(3,4,5-trimethoxyphenyl)-meth-(Z)-ylidene]-thiazolidin-4-one (**7**)

A mixture of **6** (0.01 mol), 3,4,5-trimethoxybenzaldehyde (0.01 mol) and anhydrous sodium acetate (0.5 g) was refluxed for 5 h in glacial acetic acid (15 mL). The reaction mixture was cooled and poured onto crushed ice. The obtained orange solid was filtered off, washed with water and crystallized from glacial acetic acid to afford **7** in a 80 % yield; m.p. >300 °C; ^{1}H NMR (DMSO-d_6) δ: 2.6 (s, 3H, CH_3), 3.7 (s, 3H, OCH_3), 3.8 (s, 6H, 2 OCH_3), 6.8 (s, 1H, CH), 8.0–8.8 (m, 11H, ArH), 12.1 (s, 1H, NH exchangeable with D_2O); ^{13}CNMR (DMSO-d_6) δ: 14.61, 55.32, 55.60, 104.11, 116.53, 123.51, 124.34, 124.45, 124.89, 125.08, 125.26, 126.42, 126.92, 127.26, 127.38, 127.73, 128.91, 129.44, 130.22, 130.49, 130.90, 134.41, 138.49, 143.06, 151.13, 162.79, 164.21, and 169.01; MS: *m*/*z* 535 (M^+) consistent with the molecular formula ($C_{31}H_{25}N_3O_4S$).

1,2-Dihydro-4-(substituted-aryl)-2-oxo-6-(pyren-8-yl)pyridin-3-carbonitrile **8a–c**

General method: a mixture of 1-(pyren-3-yl)ethanone (**1**) (0.01 mol), appropriate aromatic or heterocyclic aldehydes namely, *p*-methoxy benzaldehyde, 2-thiophene aldehyde and 4-pyridine aldehyde (0.01 mol), ethylcyanoacetate (0.01 mol) and ammonium acetate (0.08 mol) in ethanol (50 mL) was heated under reflux for

4–6 h. The formed precipitate was filtered off, washed successively with water and finally with ether, and crystallized from glacial acetic acid to afford the corresponding pyridones (**8a–c**), respectively.

*1,2-Dihydro-4-(4-methoxyphenyl)-2-oxo-6-(pyren-8-yl)pyridin-3-carbonitrile (**8a**)*

Yield 90 %; m.p. >300 °C; IR (KBr, cm^{-1}) ν_{max}: 3,415 (NH), 2,219 (C≡N), 1,678 (C=O); ^{1}HNMR (DMSO-d_6) δ: 3.89 (s, 3H, OCH_3), 6.19 (s, 1H, CH), 6.72–8.13 (m, 13 H, ArH), 12.90 (s, 1H, NH exchangeable with D_2O); ^{13}CNMR (DMSO-d_6) δ: 56.11, 103.23, 114.26, 115.38, 115.59, 123.72, 124.25, 124.37, 124.80, 124.95, 125.06, 125.38, 126.28, 126.92, 127.24, 127.32, 127.43, 127.65, 128.69, 130.15, 130.55, 130.98, 134.46, 156.57, 160.21, 162.34, 166.58; MS: *m/z* 426 (M^+) consistent with the molecular formula ($C_{29}H_{18}N_2O_2$).

*1,2-Dihydro-2-oxo-6-(pyren-8-yl)-4-(thiophen-2-yl)pyridin-3-carbonitrile (**8b**)*

Yield 79 %; m.p. >300 °C; IR (KBr, cm^{-1}) ν_{max}: 3,446 (NH), 2,223 (C≡N), 1,665 (C=O); ^{1}HNMR (DMSO-d_6) δ: 6.37 (s, 1H, CH), 7.21–8.12 (m, 12 H, ArH), 12.36 (s, 1H, NH exchangeable with D_2O); ^{13}CNMR (DMSO-d_6) δ: 105.21, 116.07, 121.34, 123.70, 124.05, 124.29, 124.81, 125.12, 125.18, 126.33, 126.89, 127.11, 127.26, 127.39, 127.57, 128.24, 128.68, 130.14, 130.45, 130.59, 130.99, 134.19, 137.15, 156.42, 161.86, 169.64; MS: *m/z* 402 (M^+) consistent with the molecular formula ($C_{26}H_{14}N_2OS$).

*1,2-Dihydro-2-oxo-6-(pyren-8-yl)-4-(pyridin-4-yl)pyridin-3-carbonitrile (**8c**)*

Yield 80 %; m.p. >300 °C; IR (KBr, cm^{-1}) ν_{max}: 3,450 (NH), 2,213 (C≡N), 1,680 (C=O); ^{1}HNMR (DMSO-d_6) δ: 6.81 (s, 1H, CH), 7.50–8.82 (m, 13 H, ArH), 13.40 (s, 1H, NH exchangeable with D_2O); ^{13}CNMR (DMSO-d_6) δ: 104.91, 116.36, 120.83, 122.01, 123.66, 124.17, 124.35, 124.80, 125.03, 125.29, 126.38, 126.87, 127.23, 127.34, 127.62, 128.77, 130.21, 130.45, 130.91, 134.43, 149.38, 149.85, 157.04, 161.71, 166.90; MS: *m/z* 397 (M^+) consistent with the molecular formula ($C_{27}H_{15}N_3O$).

1-[2-Deoxy-3,5-di-*O*-(4-methylbenzoyl)-D-erythropentafuranosyl]-3-cyano-6-pyren-1-yl-4-(4-methoxyphenyl)pyridine-2(1H)one (**9**)

A mixture of **8a** (0.01 mol) and 2-deoxy-3,5-di-(4-methylbenzoyl)-α-D-erythropentafuranosyl chloride (0.01 mol) in dry DMF (15 mL) and triethylamine (1 mL) was stirred at room temperature overnight and then evaporated to dryness under reduced pressure. After dilution with water (20 mL), the solution was extracted with dichloromethane (3 × 50 mL). The combined extracts were removed in vacuo to give the crude product which was purified by column chromatography on silica gel (eluent: ethylacetate/pet. Ether 60/80 30 %) to give **9** in 55 % yield as a yellowish foam; m.p. 127 °C; ^{1}HNMR ($CDCl_3$) δ: 2.44 (s, 6H, 2 CH_3), 3.17 (m, 2H, 2′-H), 3.76 (s, 3H, OCH_3), 4.60 (m, 2H, 5′-H), 4.69 (m, 1H, 4′-H), 5.73 (m, 1H, 3′-H), 6.89

(s, 1H, CH pyridine ring), 7.11 (m, 1H, 1′-H), 7.30–8.20 (m, 21 H, Ar–H); ^{13}CNMR ($CDCl_3$) δ: 21.79, 37.56, 55.39, 63.11, 74.67, 84.17, 96.17, 103.98, 114.25, 115.53, 116.19, 123.67, 124.05, 124.30, 124.78, 124.97, 125.02, 125.19, 126.47, 126.86, 127.20, 127.23, 127.35, 127.42, 127.59, 128.68, 129.06, 129.85, 130.12, 130.55, 130.94, 134.37, 135.11, 142.79, 157.31, 159.86, 166.34, 167.95; MS, FAB: *m/z* 778 (M^+) consistent with the molecular formula ($C_{50}H_{38}N_2O_7$).

1-(β-D-ribofuranos-2-yl)-4-(4-methoxy-phenyl)-2-oxo-6-pyrene-1yl-1,2-dihydro-pyridin-3-carbonitrile (**10**)

Compound **9** (0.0014 mol) was dissolved in absolute methanol (20 mL) and freshly prepared sodium methoxide (0.0014 mol) was added and the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was neutralized with NH_4Cl (0.014 mol) and stirring was continued for half an hour. The product was then purified by column chromatography on silica gel (eluent: 0–50 % Methanol/CH_2Cl_2) to afford **10** in 40 % yield; m.p. 269 °C; ^{1}HNMR (DMSO-d_6) δ: 2.19 (m, 2H, 2′ H), 3.50–3.85 (m, 3H, 4′ H and 5′ H), 4.17 (m, 1H, 3′ H), 4.6 (s, 1H, 5′ OH), 4.9 (s, 1H, 3′ OH), 6.23 (t, 1H, 1′ H), 6.59 (s, 1H, CH), 7.35–8.40 (m, 13 H, ArH).

1-[(Alkylthio)methyl]-4-(4-methoxyphenyl)-2-oxo-6-(pyren-1-yl)-1,2-dihydro-pyridin-3-carbonitrile **11a–c**

General method: a mixture of **8a** (0.001 mol), alkyl halides namely, chloromethylmethyl sulfide, chloromethylethylether and 3-bromo-1-propanol (0.001 mol) in dry DMF (15 mL) in the presence of anhydrous potassium carbonate (0.001 mol) was stirred at room temperature overnight and then evaporated to dryness under reduced pressure. After dilution with water (20 mL), the solution was extracted with dichloromethane (3 × 50 mL). The combined extracts were removed in vacuo to give the crude product which was purified by column chromatography (pet. Ether/ethylacetate 20 %) to give **11a–c**, respectively.

*1-[(Methylthio)methyl]-4-(4-methoxyphenyl)-2-oxo-6-(pyren-1-yl)-1,2-dihydro-pyridin-3-carbonitrile (**11a**)*

Yield 43 %; m.p. 197–199 °C; ^{1}HNMR (DMSO-d_6) δ: 2.23 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 4.34 (s, 2H, CH_2), 6.65 (s, 1H, CH), 6.80–8.13 (m, 13H, ArH); MS: *m/z* 486 (M^+) consistent with the molecular formula ($C_{31}H_{22}N_2O_2S$).

*1-[(Ethoxymethyl]-4-(4-methoxyphenyl)-2-oxo-6-(pyren-1-yl)-1,2-dihydro pyridin-3-carbonitrile (**11b**)*

Yield 49 %; m.p. 161–163 °C; ^{1}HNMR (DMSO-d_6) δ: 1.1 (t, 3H, CH_3), 3.45 (q, 2H, OCH_2), 3.79 (s, 3H, OCH_3), 5.3 (s, 2H, NCH_2), 6.87 (s, 1H, CH), 7.04–8.50 (m, 13H, ArH); MS: *m/z* 484 (M^+) consistent with the molecular formula ($C_{32}H_{24}N_2O_3$).

*1[-(3-Hydroxypropyl)]-4-(4-methoxyphenyl)-2-oxo-6-(pyren-1-yl)-1,2-dihydro-pyridin-3-carbonitrile (**11c**)*

Yield 57 %; m.p. 211–212 °C; ^{1}HNMR (DMSO-d_6) δ: 2.0 (m, 2H, CH_2-$\underline{CH_2}$-CH_2), 3.47 (s, 1H, OH), 3.66 (t, 2H, NCH_2), 3.79 (s, 3H, OCH_3), 4,71 (t, 2H, CH_2OH), 6.87 (s, 1H, CH), 7.04–8.50 (m, 13H, ArH); ^{13}CNMR (DMSO-d_6) δ: 31.03, 39.26, 55.49, 62.34, 105.08, 114.32, 115.62, 116.17, 123.81, 124.12, 124.21, 124.75, 124.93, 125.10, 125.14, 126.23, 126.95, 127.28, 127.30, 127.42, 127.51, 128.74, 130.09, 130.49, 130.91, 134.28, 135.21, 157.23, 160.09, 167.18; MS: *m*/*z* 484 (M^+) consistent with the molecular formula ($C_{32}H_{24}N_2O_3$).

1-Cycloalkyl-4-(4-methoxyphenyl)-2-oxo-6-pyren-1-yl-1,2-dihydropyridine-3-carbonitrile **12a, b**

General method: compound **8a** (0.002 mol) and sodium hydride (0.002 mol) were dissolved in anhydrous DMF (15 mL). After approximately 1 h of stirring, the appropriate cyclo alkyl halides, namely cyclopentyl bromide and cyclohexyl bromide (0.002 mol), were added, and the stirring was continued at room temperature overnight. The mixture was evaporated to dryness under reduced pressure. After dilution with water, the solution was extracted with dichloromethane (3 × 100 mL). The combined extracts were evaporated to dryness in vacuo to give the crude products which upon purification by column chromatography (pet. Ether/methanol 9:1) afforded compounds **12a, b**, respectively.

*1-Cyclopentyl-4-(4-methoxyphenyl)-2-oxo-6-pyren-1-yl-1,2-dihydropyridin-3-carbonitrile (**12a**)*

Yield 65 %; m.p. >300 °C; ^{1}HNMR (DMSO-d_6) δ: 1.20–1.84 (m, 8H, 4 CH_2), 3.76 (m, 1H, CH), 3.89 (s, 3H, OCH_3), 6.70 (s, 1H, CH), 6.73–8.12 (m, 13H, ArH); MS: *m*/*z* 494 (M^+) consistent with the molecular formula ($C_{34}H_{26}N_2O_2$).

*1-Cyclohexyl-4-(4-methoxyphenyl)-2-oxo-6-pyren-1-yl-1,2-dihydropyridin-3-carbonitrile (**12b**)*

Yield 49 %; m.p. >300 °C; ^{1}HNMR (DMSO-d_6) δ: 1.32–1.82 (m, 10H, 5 CH_2), 3.61 (m, 1H, CH), 3.86 (s, 3H, OCH_3), 6.34 (s, 1H, CH), 6.68–8.13 (m, 13H, ArH); ^{13}CNMR (DMSO-d_6) δ: 24.0, 27.98, 32.04, 56.19, 57.24, 105.02, 114.62, 115.38, 116.49, 123.81, 124.12, 124.21, 124.75, 125.10, 125.14, 125.39, 126.23, 126.95, 127.28, 127.30, 127.43, 127.51, 128.74, 130.09, 130.49, 130.91, 134.28, 135.41, 157.12, 161.37, 166.89; MS: *m*/*z* 508 (M^+) consistent with the molecular formula ($C_{35}H_{28}N_2O_2$).

1,2-Dihydro-1-(tetrahydro-2-oxofuran-3-yl)-4-(4-methoxyphenyl)-2-oxo-6-(pyren-8-yl)pyridine-3-carbonitrile (**13**)

To a stirred solution of **8a** (0.001 mol) in dry dimethylformamide (10 mL), (0.001 mol) of α-bromo-γ-butyrolactone and (0.001 mol) of anh. K_2CO_3 were

added. The reaction mixture was stirred at room temperature overnight and then evaporated to dryness in vacuo. The residue was purified by silica gel column chromatography (CH_2Cl_2/CH_3OH) to afford the desired derivative **13** in yield 73 %; m.p. 253–255 °C; ^{1}HNMR (DMSO-d_6) δ: 2.29 (m, 2H, CH_2), 3.86 (s, 3H, OCH_3), 4.52 (t, 2H, CH_2), 4.63(t, 1H, CH); 6.65 (s, 1H, CH), 6.72–8.12 (m, 13H, ArH); MS: *m*/*z* 510 (M^+) consistent with the molecular formula ($C_{33}H_{22}N_2O_4$).

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