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Straightforward and simple synthesis of novel pyranodipyrimidine derivatives *via* reaction of aromatic aldehydes and heterocyclic-1,3-dicarbonyl compound

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ABSTRACT

An efficient and simple procedure has been described for the synthesis of a novel series of polycyclic compounds containing pyranodipyrimidine core *via* cyclocondensation reaction of 2,3-dihydro-thiazolo[3,2-*a*]pyrimidine-5,7-dione and aromatic aldehyde derivatives in the presence of diisopropylethylamine as an organo-base catalyst. This procedure gave the desired products in high yields.

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Knoevenagel; DIPEA;
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GRAPHICAL ABSTRACT



Introduction

It is well known that systems containing a pyrimidine ring exhibit biological properties such as antimicrobial, antiviral and anticancer activities.^[1–5] On the other hand, pyran derivatives also show excellent pharmaceutical and biological applications like antimicrobial, antitumor and antibacterial activities.^[6–11] Meanwhile, high activity was also observed at annulated derivatives of pyrimidine and pyran, for example, pyrano[2,3-*d*]pyrimidine derivatives have attracted widespread attention over the recent years due to their vast range of different pharmacological actions such as antitumor,^[12,13] cardiotoxic,^[14,15] activity, and human immunodeficiency virus type 1 (HIV-1) integrase inhibitor,^[16,17] (Figure 1, molecule A). Besides, thiazolo[3,2-*a*]pyrimidine framework as biologically active molecules,^[18–20] have been used as anti-HIV-1 and anti-cancer drugs (Figure 1, molecules B and C).^[21,22]

The synthetic procedures of various polycyclic compounds have been extremely studied.^[23] Spite the extensive developments in the synthesis of pyrimidine derivatives,^[24–26] small attentions have been attracted for the chemistry and synthesis and pyranopyrimidine molecules.^[27–29] The usual strategy for the synthesis of pyrano[2,3-*d*]pyrimidines normally include the reaction of barbituric acid, malononitrile and aromatic aldehydes in the presence of the base.^[30–33] Thus, due to the significant importance of pyranopyrimidine derivatives in

biological and pharmaceutical fields, there is a pressing need for the synthesis of new derivatives of pyranopyrimidine *via* the reaction of different cyclic 1,3-dicarbonyl compounds.

As part of our attempts to development of new approaches for the synthesis of heterocyclic molecules from readily available starting materials,^[34–41] in this study, we employed the heterocyclic 1,3-dicarbonyl compound named 2,3-dihydro-thiazolo[3,2-*a*]pyrimidine-5,7-dione for the synthesis of a novel series of polycyclic compounds containing pyranodipyrimidine core through the one-pot addition process in the presence of an organo-base. Therefore, a simple and straightforward approach has been developed *via* one-pot condensation reaction of 2,3-dihydro-thiazolo[3,2-*a*]pyrimidine-5,7-dione (1), aromatic aldehyde derivatives (2a-1), and diisopropylethylamine (DIPEA) in ethanol at reflux condition to produce the corresponding 5-aryl-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[*b,i*]anthracene-4,6-diones derivatives (3a-1) in high yields (Scheme 1).

Result and discussion

First, the reaction conditions were optimized and the observations have been summarized in Table 1. It is noteworthy that the base and its amount, solvent and temperature have a huge influence on the reaction. In our initial investigation, the

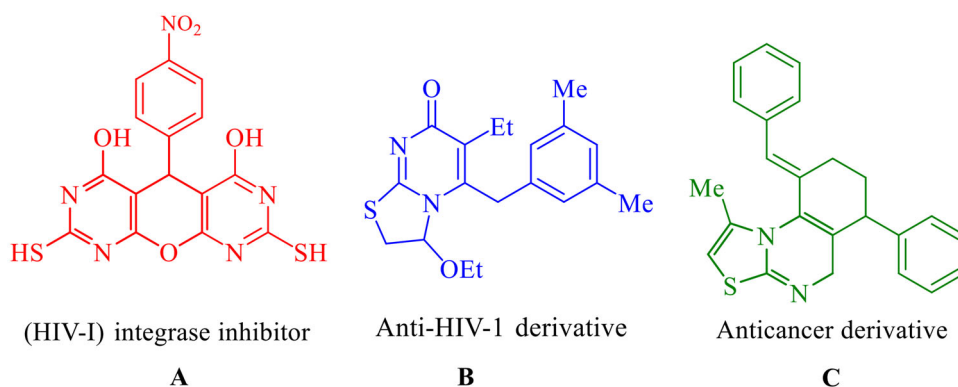
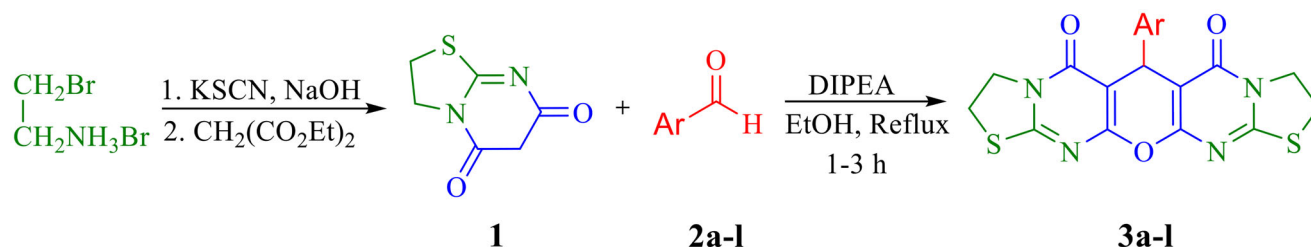
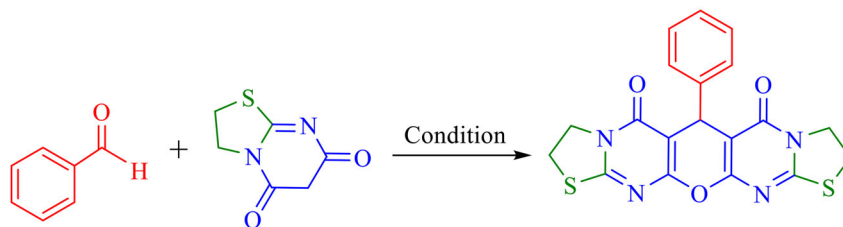


Figure 1. Examples of biologically active pyrano[2,3-*d*]pyrimidine and thiazolo[3,2-*a*]pyrimidines.



Scheme 1. Synthesis of 5-aryl-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclo-pentab,1]anthracene-4,6-diones derivatives.

Table 1. Optimization of the reaction conditions.^a



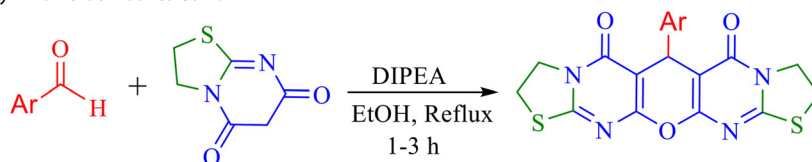
Entry	Acid or base (mol%)	Solvent	Temp. (°C)	Time (h)	Yield (%) ^b
1	–	EtOH	Reflux	4.0	70
2	Acetic acid (5.0)	EtOH	Reflux	3.0	60
3	Lactic acid (5.0)	EtOH	Reflux	3.0	66
4	PTSA (5.0)	EtOH	Reflux	6.0	–
5	DABCO (5.0)	EtOH	Reflux	3.0	79
6	K ₂ CO ₃ (5.0)	EtOH	Reflux	3.0	70
7	DBU (5.0)	EtOH	Reflux	2.0	60
8	TEA (5.0)	EtOH	Reflux	2.0	80
9	DIPEA (5.0)	EtOH	Reflux	1.0	91
10	DIPEA (3.0)	EtOH	Reflux	5.0	85
11	DIPEA (10)	EtOH	Reflux	5.0	91
12	DIPEA (5.0)	CH ₃ CN	Reflux	3.0	50
13	DIPEA (5.0)	THF	Reflux	3.0	55
14	DIPEA (5.0)	CH ₂ Cl ₂	Reflux	5.0	45
15	DIPEA (5.0)	DMF	80	3.0	40
16	DIPEA (5.0)	EtOH	r.t	6.0	84
17	DIPEA (5.0)	EtOH	50	5.0	82

^aAll reactions were carried out using **1a** (0.25 mmol), and **2** (0.5 mmol) in 3 mL of solvent.

^bIsolated yields.

reaction of 2,3-dihydro-thiazolo[3,2-*a*]pyrimidine-5,7-dione (**1**), benzaldehyde (**2a**) and a base has been selected as a model reaction in ethanol at boiling temperature (Scheme 1). At first, the reaction has been performed in the absence of a base and the yield of the reaction was only 70% after 4 h running the reaction (Table 1, entry 1). Then, we screened the ability of various acids and bases such as acetic acid, lactic acid, *p*-toluenesulfonic acid (PTSA), K₂CO₃, DABCO,

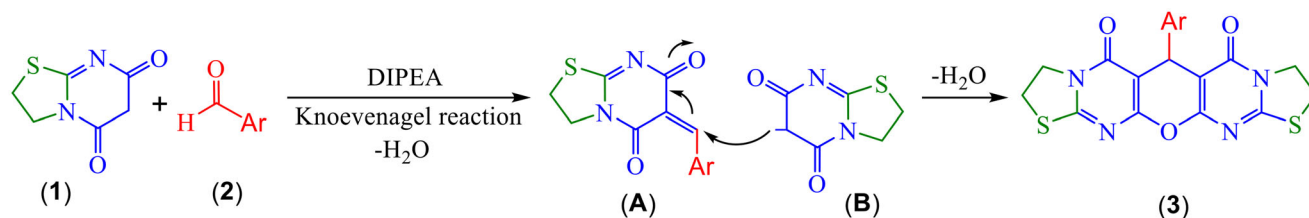
NEt₃, DBU, and DIPEA, to catalyze the condensation reaction of benzaldehyde and 2,3-dihydro-thiazolo[3,2-*a*]pyrimidine-5,7-dione (**2**) (Table 1, entries 2–9). Among the acidic catalysts, acetic acid and lactic acid carried out better the model reaction (entries 2 and 3) compared to PTSA and PTSA could not perform the reaction properly (entry 4). Among the bases, DIPEA was the most efficient organo-base for the synthesis of **3a** (Table 1, entry 9). In the second step,

Table 2. Synthesis of pyranodipyrimidine derivatives **3a–l**.

Entry	Ar	Product	Yield (%) ^b
1	C ₆ H ₅	3a	91
2	2-ClC ₆ H ₄	3b	93
3	4-ClC ₆ H ₄	3c	90
4	4-BrC ₆ H ₄	3d	90
5	2-NO ₂ C ₆ H ₄	3e	93
6	4-NO ₂ C ₆ H ₄	3f	90
7	4-MeC ₆ H ₄	3g	92
8	3-MeC ₆ H ₄	3h	91
9	4-OMeC ₆ H ₄	3i	93
10	2-Thienyl	3j	91
11	1-Naphthyl	3k	90
12	2-Naphthyl	3l	91

^aAll reactions were carried out in presence of and 2,3-dihydro-thiazolo[3,2-*a*]pyrimidine-5,7-dione **1** (0.5 mmol) and aromatic aldehydes **1a–l** (0.25 mmol) in 3.0 mL of ethanol at reflux condition.

^bIsolated yields.



Scheme 2. Proposed mechanism for synthesis of 5-aryl-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[*b,i*]anthracene-4,6-diones derivatives.

the amount of the base has been optimized (Table 1, entries 9–11). We found that the highest yield of **3a** was formed in 5.0 mol% of DIPEA/aldehyde (Table 1, entry 9). In the next step, the effects of different solvents like acetonitrile, tetrahydrofuran, dichloromethane, dimethylformamide and ethanol have been investigated on the synthesis of pyranodipyrimidine **3a** (Table 1, entries 12–15). After optimization, EtOH was the best solvent for this reaction. Finally, the temperature was studied (Table 1, entries 16 and 17) and reflux condition was the best and yield of the reaction at room temperature and 50 °C was about 80%. The best conditions were therefore 5.0 mol% of DIPEA in ethanol under reflux conditions (Table 1, entry 9).

Subsequently, the scope and generality of the procedure was also checked for the synthesis of various pyranodipyrimidine derivatives under optimized reaction conditions (Table 2). By examination of different substituted aldehydes, interestingly, we observed that both aromatic aldehydes carrying electron-donating and electron-withdrawing groups gave the desirable products in excellent yields and all the products has been obtained in more than 90% isolated yields (Table 2, entries 1–12).

The structures of the products **3a–l**, have been characterized by various techniques like FT-IR, proton NMR, carbon NMR and mass spectra and CHN analysis. For instance, the IR spectrum of **3a** showed absorption peaks at 1510 and 1650 cm⁻¹ attributed to C=N and C=O groups respectively. The

¹H NMR spectrum of **3a** exhibited a multiplet signal for the CH₂-S (δ = 3.49 ppm, 4H), a triplet signal for CH₂-N (δ = 4.28 ppm, 4H), a singlet signal for benzylic CH (δ = 6.06 ppm, 1H) and a multiplet signal for aromatic ring (δ = 7.00–7.20 ppm, 5H). The ¹³C NMR spectrum of **3a** also showed characteristic ¹³C NMR signals due to the CH₂-S (δ = 26.55 ppm), methine (δ = 32.57 ppm), CH₂-N (δ = 49.03 ppm), C=N (δ = 162.35) and C=O (δ = 163.11). The ¹H NMR and ¹³C NMR spectra of **3b–l** are comparable with the spectrum of **3a** except for substituted groups on the aromatic moiety, which showed characteristic signals with appropriate chemical shifts (see Supplemental Materials).

The plausible reaction mechanism has been proposed as shown in Scheme 2.^[42] The first step involves the formation of intermediate (A) by Knoevenagel condensation reaction between 2,3-dihydro-thiazolo[3,2-*a*]pyrimidine-5,7-dione (1) and aromatic aldehyde (2). In the second step, from the Michael addition of carbanion (B) to intermediate (A) and followed by cyclization reaction and eventually water elimination, the corresponding pyranodipyrimidine (3) was produced (Scheme 2).

Conclusion

In summary, we have introduced a novel method for the synthesis of polycyclic compounds that contain pyranodipyrimidine core through the one-pot Knoevenagel condensation

Michael addition and cyclo-dehydration of 2,3-dihydro-thiazolo[3,2-*a*]pyrimidine-5,7-dione with aryl aldehydes in the presence of DIPEA as a base in the ethanol as a green solvent and mild condition with high yields.

Experimental

General

All materials were purchased from Sigma-Aldrich and Merck companies and 2,3-dihydro-thiazolo[3,2-*a*]pyrimidine-5,7-dione was synthesized according to the literature.^[43,44] Melting points were recorded on an Electrothermal-type 9100 melting point apparatus and are uncorrected. The IR spectra were obtained on an Avatar 370 FT-IR Thermo-Nicolet spectrometer. ¹H and ¹³C NMR spectra were run on BRUKER DRX-300 AVANCE spectrometer at 300 MHz for ¹H NMR, and 75 MHz for ¹³C NMR and DMSO-*d*₆ was used as solvent. The mass spectra were recorded on a Varian Mat CH-7 at 70 eV. Elemental analysis was performed on a Thermo Finnigan Flash EA microanalyser. The Supplemental Materials contains sample ¹H and ¹³C NMR and mass and IR spectra for the products 3 (Figures S1–S48).

Spectral analysis for 2,3-dihydro-thiazolo[3,2-*a*]pyrimidine-5,7-dione (1)

144 mg, (85%); white powder, mp: 244–245 °C, IR (KBr, cm⁻¹): ν = 2500–3423 (broad OH), 3088 (CH), 2949 (CH), 1648 (C=O), 1616 (C=N); ¹H NMR (300 MHz, CDCl₃): δ 3.51 (2H, *t*, *J* = 7.67 Hz, CH₂-S), 4.27 (2H, *t*, *J* = 7.67 Hz, CH₂-N), 5.09 (1H, *s*, CH), 11.34 (1H, *s*_{br}, OH) ppm; ¹³C NMR (75.46 MHz, CDCl₃): δ 26.26 (CH₂-S), 48.38 (CH₂-N), 84.88 (CH), 161.74 (C=N), 165.34 and 169.38 (2C=O) ppm; MS (*m/z*, %): 170 (72), 169 (100), 141 (72), 128 (92), 102 (42), 85 (68), 28 (74); Anal. Calcd for C₆H₆N₂O₂S (%): C, 42.34; H, 3.55; N, 16.46%. Found: C, 42.54; H, 3.59; N, 16.63%.

General procedure for synthesis of pyranodipyrimidine derivatives 3a–l

To a stirred solution of aromatic aldehyde **1a–l** (0.25 mmol) and heterocyclic-1,3-dicarbonyl **2** (0.5 mmol) in EtOH (3.0 mL), 5.0 mol% of DIPEA/aldehyde was added and the solution was refluxed in oil bath. After the reaction was completed (1–3 h) that it was controlled by TLC, the desired product was filtered and the precipitate was washed with cold ethanol. The 5-aryl-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[*b,i*]anthracene-4,6-diones derivatives have been achieved in high yields.

5-Phenyl-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[*b,i*]anthracene-4,6-dione (3a)

White powder; 0.186 g, yield 91%; mp: 264–267 °C, IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1650 (C=O), 1510 (C=N); ¹H NMR (300 MHz, DMSO-*d*₆): δ = 3.42–3.54 (m, 4H, CH₂-S), 4.28 (*t*, 4H, *J* = 7.24 Hz, CH₂-N), 6.06 (*s*, 1H, CH), 7.00–7.20 (m,

5H, H_{Ar}); ¹³C NMR (75 MHz, DMSO-*d*₆): δ = 26.55 (CH₂-S), 32.57 (CH), 49.03 (CH₂-N), 98.76 (C-C=O), 125.25, 126.73, 127.80, 129.18, 129.52 140.87 (C_{Ar}), 162.35 (C=N), 163.11 (C=O), 167.98 (CO-C=C-O); MS, *m/z* (%): 410 (M⁺, 9), 279 (100), 256 (92), 213 (90), 185 (90), 179 (47); Anal. Calcd for C₁₉H₁₄N₄O₃S₂ (410.05): C, 55.60; H, 3.44; N, 13.65%. Found: C, 55.41; H, 3.30; N, 13.55%.

5-(2-Chloro-phenyl)-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[*b,i*]anthracene-4,6-dione (3b)

White powder; 0.21 g, yield 93%; mp: 300 °C, IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1678 (C=O), 1558 (C=N); ¹H NMR (300 MHz, DMSO-*d*₆): δ = 3.35–3.52 (m, 4H, CH₂-S), 4.25 (*t*, 4H, *J* = 7.51 Hz, CH₂-N), 5.82 (*s*, 1H, CH), 7.11–7.26 (m, 4H, H_{Ar}); ¹³C NMR (75 MHz, DMSO-*d*₆): δ = 26.45 (CH₂-S), 33.23 (CH), 48.85 (CH₂-N), 97.71 (C-C=O), 126.03, 127.12, 128.83, 130.50, 132.72, 139.87 (C_{Ar}), 161.78 (C=N), 162.06 (C=O), 166.91 (CO-C=C-O); MS, *m/z* (%): 445 (M⁺, 26), 382 (42), 353 (100), 339 (60), 264 (57); Anal. Calcd for C₁₉H₁₃ClN₄O₃S₂ (444.91): C, 51.29; H, 2.95; N, 12.59%. Found: C, 51.19; H, 2.80; N, 12.45%.

5-(4-Chloro-phenyl)-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[*b,i*]anthracene-4,6-dione (3c)

White powder; 0.19 g, yield 90%; mp: 250 °C, IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1662 (C=O), 1565 (C=N); ¹H NMR (300 MHz, DMSO-*d*₆): δ = 3.33–3.41 (m, 4H, CH₂-S), 4.17–4.20 (m, 4H, CH₂-N), 6.05 (*s*, 1H, CH), 6.96 (*d*, 2H, *J* = 9.00 Hz, H_{Ar}), 7.15 (*d*, 2H, *J* = 9.00 Hz, H_{Ar}); ¹³C NMR (75 MHz, DMSO-*d*₆): δ = 26.05 (CH₂-S), 31.88 (CH), 48.74 (CH₂-N), 98.34 (C-C=O), 127.23, 128.70, 128.93, 142.32 (C_{Ar}), 160.73 (C=N), 162.75 (C=O), 170.85 (CO-C=C-O); MS, *m/z* (%): 445 (M⁺, 26), 387 (55), 293 (100), 262 (97), 246 (75); Anal. Calcd for C₁₉H₁₃N₄O₃S₂ (444.91): C, 51.29; H, 2.95; N, 12.59%. Found: C, 51.20; H, 2.89; N, 12.55%.

5-(4-Bromo-phenyl)-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[*b,i*]anthracene-4,6-dione (3d)

White powder; 0.21 g, yield 90%; mp: 288 °C, IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1675 (C=O), 1580 (C=N); ¹H NMR (300 MHz, DMSO-*d*₆): δ = 3.34–3.41 (m, 4H, CH₂-S), 4.18–4.20 (m, 4H, CH₂-N), 6.03 (*s*, 1H, CH), 6.90 (*d*, 2H, *J* = 7.3 Hz, H_{Ar}), 7.28 (*d*, 2H, *J* = 7.5 Hz, H_{Ar}); ¹³C NMR (75 MHz, DMSO-*d*₆): δ = 26.06 (CH₂-S), 31.94 (CH), 48.73 (CH₂-N), 98.32 (C-C=O), 117.38, 129.18, 130.14, 142.80 (C_{Ar}), 160.74 (C=N), 16.75 (C=O), 170.87 (CO-C=C-O); MS, *m/z* (%): 489 (M⁺, 17), 369 (52), 337 (100), 309 (98), 257 (92); Anal. Calcd for C₁₉H₁₃BrN₄O₃S₂ (489.37): C, 46.63; H, 2.68; N, 11.45%. Found: C, 46.35; H, 2.60; N, 11.41%.

5-(2-Nitro-phenyl)-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[b,i]anthracene-4,6-dione (3e)

White powder; 0.21 g, yield 93%; mp: 269–270 °C, IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1659 (C=O), 1535 (C=N), 1522, 1337 (NO₂); ¹H NMR (300 MHz, DMSO-*d*₆): δ = 3.51 (t, 4H, *J* = 7.3 Hz, CH₂-S), 4.24 (t, 4H, *J* = 7.4 Hz, CH₂-N), 6.08 (s, 1H, CH), 7.28–7.68 (m, 4H, H_{Ar}); ¹³C NMR (75 MHz, DMSO-*d*₆): δ = 26.50 (CH₂-S), 31.64 (CH), 48.84 (CH₂-N), 97.04 (C–C=O), 123.56, 126.80, 130.52, 131.79, 135.71, 149.38 (C_{Ar}), 161.71 (C=N), 162.31 (C=O), 166.25 (CO–C=C–O), MS, *m/z* (%): 455 (M⁺, 7), 420 (40), 311 (100), 287 (90), 271 (91), Anal. Calcd for C₁₉H₁₃N₅O₅S₂ (455.47): C, 50.10; H, 2.88; N, 15.38%. Found: C, 50.03; H, 2.79; N, 15.22%.

5-(4-Nitro-phenyl)-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[b,i]anthracene-4,6-dione (3f)

White powder; 0.19 g, yield 90%; mp: 250 °C, IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1680 (C=O), 1669 (C=N), 1531, 1347 (NO₂); ¹H NMR (300 MHz, DMSO-*d*₆): δ = 3.35–3.45 (m, 4H, CH₂-S), 4.15–4.30 (m, 4H, CH₂-N), 6.20 (s, 1H, CH), 7.22 (d, 2H, *J* = 8.3 Hz, H_{Ar}), 8.03 (d, 2H, *J* = 8.50, H_{Ar}); ¹³C NMR (75 MHz, DMSO-*d*₆): δ = 26.10 (CH₂-S), 33.04 (CH), 48.75 (CH₂-N), 98.06 (C–C=O), 122.78, 127.98, 145.01, 152.97 (C_{Ar}), 161.09 (C=N), 162.58 (C=O), 170.88 (CO–C=C–O); MS, *m/z* (%): 455 (M⁺, 22), 368 (100), 353 (68), 313 (98), 299 (66), 295 (45); Anal. Calcd for C₁₉H₁₃N₅O₅S₂ (455.47): C, 50.10; H, 2.88; N, 15.38%. Found: C, 50.01; H, 2.75; N, 15.28%.

5-(4-Methylphenyl)-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[b,i]anthracene-4,6-dione (3g)

White powder; 0.20 g, yield 92%; mp: 263 °C, IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1657 (C=O), 1545 (C=N); ¹H NMR (300 MHz, DMSO-*d*₆): δ = 2.19 (s, 3H, CH₃), 3.35–3.40 (m, 4H, CH₂-S), 4.17–4.34 (m, 4H, CH₂-N), 6.02 (s, 1H, CH), 6.84–6.92 (m, 4H, H_{Ar}); ¹³C NMR (75 MHz, DMSO-*d*₆): δ = 20.51 (CH₃), 25.99 (CH₂-S), 31.73 (CH), 48.69 (CH₂-N), 98.80 (C–C=O), 126.72, 127.94 (1 CH), 133.04, 139.72 (2C_{Ar}), 160.45 (C=N), 162.98 (C=O), 170.99 (CO–C=C–O); MS, *m/z* (%): 397 (M⁺, 16), 258 (45), 170 (100), 86 (82), 77 (62), 63 (64); Anal. Calcd for C₂₀H₁₆N₄O₃S₂ (424.5): C, 56.59; H, 3.80; N, 13.20%. Found: C, 56.50; H, 3.72; N, 13.16%.

5-(3-Methylphenyl)-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[b,i]anthracene-4,6-dione (3h)

Yellow powder; 0.19 g, yield 90%; mp: 258–259 °C, IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1660 (C=O), 1642 (C=N); ¹H NMR (300 MHz, DMSO-*d*₆): δ = 2.18 (s, 3H, CH₃), 3.42–3.44 (m, 4H, CH₂-S), 4.14–4.29 (m, 4H, CH₂-N), 6.04 (s, 1H, CH), 6.80–6.85 (m, 3H, H_{Ar}), 6.98–7.06 (m, 1H, H_{Ar}); ¹³C NMR

(75 MHz, DMSO-*d*₆): δ = 21.35 (CH₃), 26.13 (CH₂-S), 32.14 (CH₂-N), 48.81 (CH), 98.78 (C–C=O), 124.06, 125.34, 127.32, 136.06, 142.73 (C_{Ar}), 160.78 (C=N), 162.96 (C=O), 170.66 (CO–C=C–O); MS, *m/z* (%): 397 (M⁺, 16), 258 (55), 170 (100), 86 (82), 77 (68), 63 (50); Anal. Calcd for C₂₀H₁₆N₄O₃S₂ (424.5): C, 56.59; H, 3.80; N, 13.20%. Found: C, 56.50; H, 3.72; N, 13.16%.

5-(4-Methoxyphenyl)-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[b,i]anthracene-4,6-dione (3i)

White powder; 0.22 g, yield 93%; mp: 226–229 °C, IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1662 (C=O), 1580 (C=N); ¹H NMR (300 MHz, DMSO-*d*₆): δ = 3.47–3.48 (m, 4H, CH₂-S), 3.67 (s, 3H, OCH₃), 4.21–4.29 (m, 4H, CH₂-N), 5.99 (s, 1H, CH), 6.71 (d, 2H, *J* = 8.5 Hz, H_{Ar}), 6.88 (m, 2H, *J* = 8.3 Hz, H_{Ar}); ¹³C NMR (75 MHz, DMSO-*d*₆): δ = 26.29 (CH₂-S), 31.59 (CH), 48.90 (CH₂-N), 54.92 (OCH₃), 98.95 (C–C=O), 112.99 (2 CH), 127.71 (2 CH), 156.82, 161.27 (2C_{Ar}), 163.03 (C=N, C=O), 169.35 (CO–C=C–O); MS, *m/z* (%): 440 (M⁺, 22), 290 (100), 275 (98), 259 (95), 255 (64); Anal. Calcd for C₂₀H₁₆N₄O₄S₂ (440.5): C, 54.53; H, 3.66; N, 12.72%. Found: C, 54.48; H, 3.39; N, 12.70%.

5-Thiophen-2-yl-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[b,i]anthracene-4,6-dione (3j)

White powder; 0.20 g, yield 91%; mp: 252–253 °C, IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1691 (C=O), 1619 (C=N); ¹H NMR (300 MHz, DMSO-*d*₆): δ = 3.49–3.54 (m, 4H, CH₂-S), 4.22–4.34 (m, 4H, CH₂-N), 6.20 (s, 1H, CH), 6.60 (s, 1H, H_{Ar}), 6.81 (t, 1H, *J* = 4.6, H_{Ar}), 7.20 (d, 1H, *J* = 4.8, H_{Ar}); ¹³C NMR (75 MHz, DMSO-*d*₆): δ = 26.57 (CH₂-S), 30.73 (CH), 49.06 (CH₂-N), 99.15 (C–C=O), 121.34, 123.73, 126.28 (3 CH), 138.05 (C_{Ti}), 162.69 (C=N), 162.85 (C=O), 167.69 (CO–C=C–O); MS, *m/z* (%): 416 (M⁺, 16), 264 (100), 257 (100), 236 (92), 229 (78), 208 (82); Anal. Calcd for C₁₇H₁₂N₄O₃S₃ (416.5): C, 49.02; H, 2.90; N, 13.45%. Found: C, 18.85; H, 2.88; N, 13.39%.

5-Naphthalen-1-yl-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[b,i]anthracene-4,6-dione (3k)

White powder; 0.23 g, yield 94%; mp: 268 °C, IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1679 (C=O), 1559 (C=N); ¹H NMR (300 MHz, DMSO-*d*₆): δ = 3.49–3.53 (m, 4H, CH₂-S), 4.27–4.32 (m, 4H, CH₂-N), 6.36 (s, 1H, CH), 7.26–7.42 (m, 4H, H_{Ar}), 7.69–7.86 (m, 3H, H_{Ar}); ¹³C NMR (75 MHz, DMSO-*d*₆): δ = 26.55 (CH₂-S), 31.99 (CH), 49.01 (CH₂-N), 99.16 (C–C=O), 123.36, 125.05, 125.12, 125.55, 125.68, 126.38, 128.63, 131.47, 133.42, 137.37 (C_{Ar}), 162.17 (C=N), 162.45 (C=O), 166.62 (CO–C=C–O); MS, *m/z* (%): 460 (M⁺, 8), 307 (100), 280 (100), 247 (96), 238 (90), 222 (96), 207 (90); Anal. Calcd for C₂₃H₁₆N₄O₃S₂ (460.53): C, 59.98; H, 3.50; N, 12.17%. Found: C, 59.90; H, 3.40; N, 12.02%.

5-Naphthalen-2-yl-2,3,7,8-tetrahydro-5H-11-oxa-1,9-dithia-3a,6a,10,12-tetraaza-dicyclopenta[b,i]anthracene-4,6-dione (3I)

White powder; 0.20 g, yield 91%; mp: 278–281 °C, IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1671 (C=O), 1565 (C=N); ^1H NMR (300 MHz, DMSO- d_6): δ = 3.50–3.52 (m, 4H, CH₂-S), 4.28–4.30 (m, 4H, CH₂-N), 6.21 (s, 1H, CH), 7.18–7.21 (m, 1H, H_{Ar}), 7.39–7.47 (m, 3H, H_{Ar}), 7.69–7.78 (m, 3H, H_{Ar}); ^{13}C NMR (75 MHz, DMSO- d_6): δ = 26.42 (CH₂-S), 32.93 (CH), 48.97 (CH₂-N), 98.71 (C-C=O), 124.33, 124.87, 125.61, 126.43, 127.07, 127.20, 127.41, 131.43, 132.99 (C_{Ar}), 161.90 (C=N), 162.10 (C=O), 168.90 (CO-C=C-O); MS, m/z (%): 480 (M⁺, 8), 310 (100), 152 (96), 129 (64), 86 (42), 60 (60); Anal. Calcd for C₂₃H₁₆N₄O₃S₂ (460.53): C, 59.98; H, 3.50; N, 12.17%. Found: C, 59.90; H, 3.40; N, 12.02%.

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