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Expeditious Green Synthesis of Novel 4-Methyl-1,2,5,6-tetraazafluoranthen-3(2*H*)-one Analogue from Ninhydrin: N/S-Alkylation and Aza-Michael Addition

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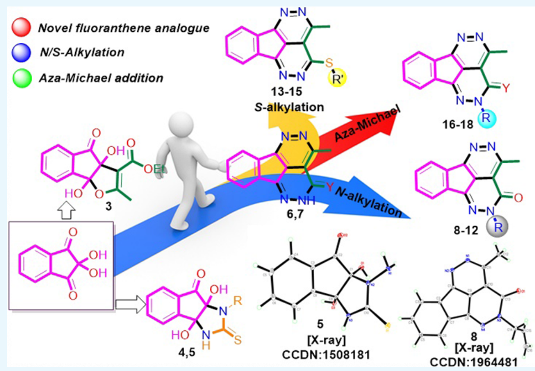
ABSTRACT: A straightforward green synthesis of 4-methyl-1,2,5,6-tetraazafluoranthen-3(2*H*)-one **6** is reported from ninhydrin **1** via condensation with ethyl acetoacetate, followed by cyclization with hydrazine hydrate in water as a benign solvent. Tetraazafluoranthen-3-thione **7** was obtained using Lawesson's reagent. N-alkylated tetraazafluoranthen-3-one **8−12** and S-alkylated analogues **13−15** were synthesized via alkylation. The investigation of the unique reactivity of 4-methyl-1,2,5,6-tetraazafluoranthen-3(2*H*)-one/thione toward the alkylation and aza-Michael additions was explored.



■ INTRODUCTION

Fluoranthenes represent an intriguing class of polycyclic aromatic compounds with remarkable and interesting applications.[1−3] Considerable research has focused on their sensing as well as organic electronics applications[4] and related natural products. Many fungal natural products contain a fluoranthene in their structures, for example, hortein[5] and daldinone E.[6] Moreover, FLUN-550 was introduced as a fluoranthene-based fluorescent probe for selective staining of intracellular lipid droplets.[6] Synthesis and derivatization of fluoranthenes have received much attention in the recent years. Diels−Alder reaction[7−10] and transition metal-catalyzed reactions are the most commonly used methods for their synthesis.[11−22]

The vast majority of reported fluoranthenes were synthesized from 1,8-dichloronaphthalenes and arylboronic acids in the presence of Pd catalyst under the conditions of high catalyst loading [20 mol % $Pd_2(dba)_3$] and high reaction temperatures (155−175 °C).[23] Synthesis of fluoranthenes was accomplished via inter- and intramolecular C−H arylation in three steps in the presence of Pd catalyst.[24] Substituted fluoranthenes were obtained selectively via Suzuki−Miyaura reaction using tetrakis-(triphenylphosphine)palladium(0) ($Pd(PPh_3)_4$) and Pd(dppf)-Cl_2 catalysts starting from 1,8-diiodonaphthalene.[25]

Fluoranthenes aza analogues were also synthesized by Koutentis and co-workers via an oxidative and nonoxidative cyclization protocol.[26]

Herein, we report a novel, straightforward, simple, effective, and catalyst free method for the synthesis of tetraazafluoranthen-3-one in a short time. In addition, to the best of our knowledge, there are no literature reports for the construction of tetraazafluoranthen-3(2*H*)-one so far (Figure 1).

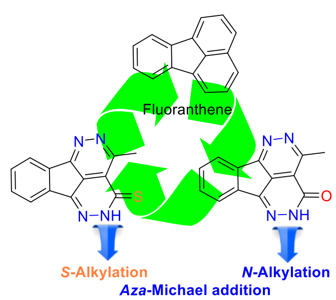


Figure 1.

■ RESULTS AND DISCUSSION

As part of our current studies on the development of new routes in heterocyclic synthesis,[28−35] here we focused on the synthesis of new heterocyclic systems from ninhydrin. Stirring ninhydrin **1** with ethyl acetoacetate **2** in water for 15 min afforded ethyl indeno[1,2-*b*]furan-3-carboxylate **3** in excellent yield.[33] Reac-

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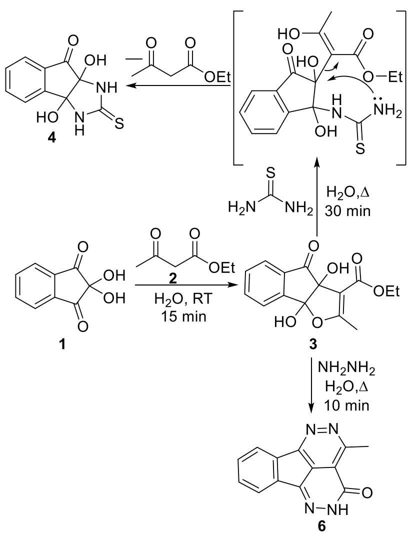
tion of **3** with hydrazine hydrate in water or ethanol and reflux for 10 min, interestingly, afforded tetraazafluoranthen-3(2*H*)-one **6** in good yield. Heating of **3** with thiourea, surprisingly, gave indeno-imidazole **4** (Scheme 1). The plausible reaction mechanism of the formation of **4** by nucleophilic ring opening/ring closer via the intermediate was followed by removal of ethyl acetoacetate, as shown in Scheme 1.

Scheme 1. Synthesis of Indeno-Imidazole 4 and Tetraazafluoranthen-3(2*H*)-one 6



The suggested mechanism for the formation of tetraazafluoranthen-3(2*H*)-one **6** involves, at first, condensation of ethyl acetoacetate with ninhydrin to give ethyl indeno[1,2-*b*]furan-3-carboxylate **3**, which was attacked by two hydrazine molecules at the carbonyl carbon (C4) and the carbon (C8b), leading to cleavage of the furan ring with the loss of four water molecules and EtOH. During this process, recyclization occurs to form tetraazafluoranthen-3-one (Scheme 2). The structure of 4-methyl-1,2,5,6-tetraazafluoranthen-3(2*H*)-one **6** was deduced from its nuclear magnetic resonance (NMR) spectra, which showed the methyl protons at 2.99 ppm and four aromatic protons between 7.96 and 8.19 ppm, in addition to one deshielded signal at 13.29 ppm, which was assigned for NH. The methyl carbon appeared at 21.26 ppm in addition to 12 aromatic carbons including C=O, which appeared between 119.10 and 158.94 ppm.

Reaction of ninhydrin with thiourea and thiosemicarbazide in water and reflux for 10 min were performed to afford the crystalline compounds indeno-imidazole **4** and 1-amino-indeno-imidazole **5**, respectively, in good yield (Scheme 3).

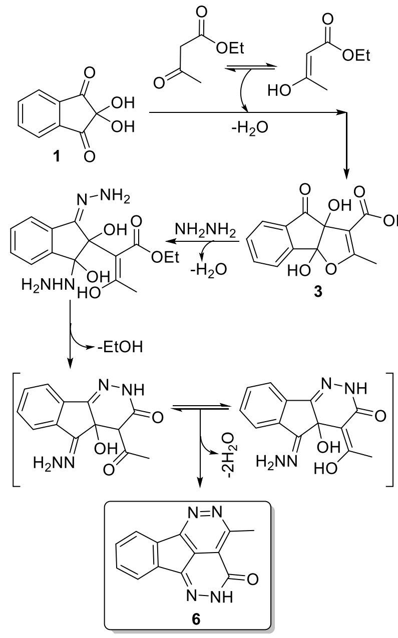
Thionation of tetraazafluoranthen-3-one **6** was achieved using Lawesson's reagent in dry toluene to produce tetraazafluoranthen-3-thione **7** in good yield (Scheme 4). The desired thione **7** did not form utilizing P_2S_5 and pyridine. 4-Methyl-tetraazafluoranthene-3-thione **7** structure was confirmed from the NMR spectra, which showed the NH proton at 14.76 ppm and the thiocarbonyl carbon at 181.43 ppm.

Given the uniqueness of tetraazafluoranthen-3-one **6** and **7**, we have also explored their reactivity in further synthetic transformations including N/S-alkylation and aza-Michael additions.

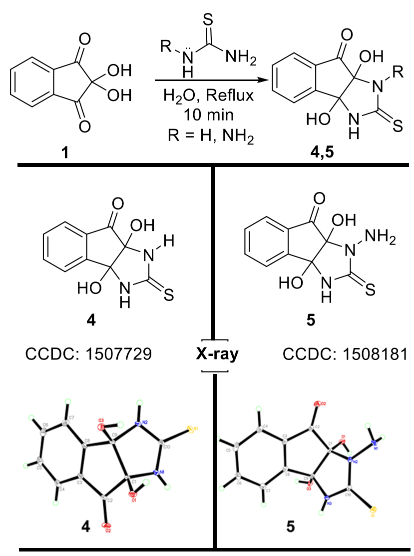
Coupling of tetraazafluoranthen-3-one **6** with allyl bromide, ethyl chloroacetate, benzyl bromide, amyl bromide, and phenacyl bromide in the presence of K_2CO_3 in acetone and dimethyl formamide (DMF) afforded the N-alkylated products **8−12** in good yields (Scheme 5).

N-alkylation products **8−12** were confirmed from the loss of the NH signal. Further, aza- not or oxa-alkylation of tetraazafluoranthen-3-one was confirmed by single-crystal X-ray diffraction analysis for **8**.

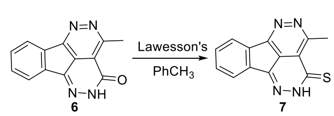
Scheme 2. Proposed Mechanism for the Formation of Tetraazafluoranthen-3-one 6



Scheme 3. Synthesis of 2-Thioxo-tetrahydroindeno[2,1-*d*]imidazol-ones 4 and 5



Scheme 4. Thionation of 6 to Afford Tetraazafluoranthen-3-thione 7



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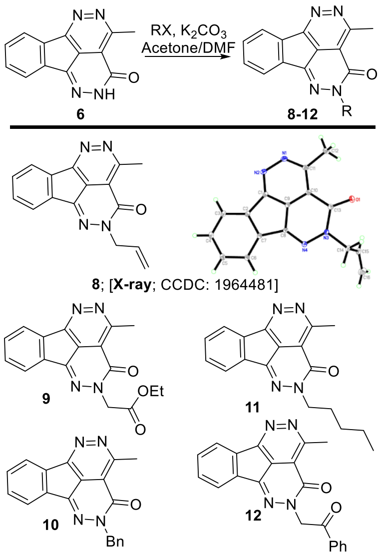
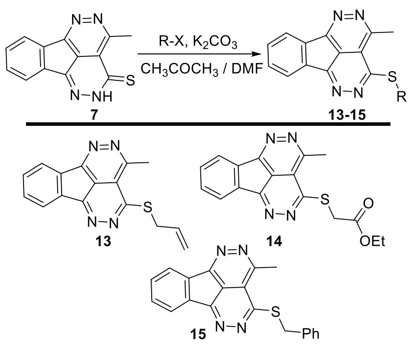
Scheme 5. Synthesis of N-Alkylated Tetraazafluoranthen-3-one 8−12



From the above-mentioned experiment, other analogues of S-alkylated tetraazafluoranthen-3-one **13−15** were explored. Coupling of **7** with allyl bromide, ethyl chloroacetate, and benzyl bromide afforded the S-alkylated products **13−15**, respectively (Scheme 6). S-alkylation of **7** was confirmed from the S−CH_2−carbon signals around 33.00 ppm to yield **13−15**.

Scheme 6. Synthesis of S-Alkylated Tetraazafluoranthen-3-one 13−15



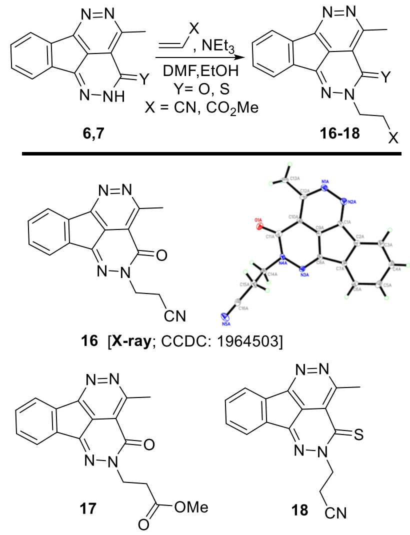
Aza-Michael addition of **6** or **7** as Michael donor to acrylonitrile and methyl acrylate as Michael acceptors in DMF/EtOH containing Et_3N leads to aza-Michael adduct **16−18** (Scheme 7).

Aza- not thia-Michael addition was deduced from the methylene signal 54.22 ppm and thiocarbonyl carbon (C═S) at 180.08 ppm. Additionally, single-crystal X-ray analysis of compound **16** was performed.

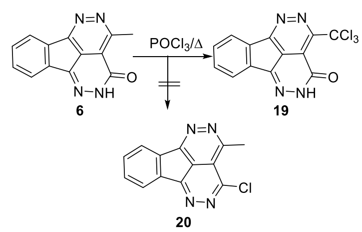
Interestingly, chlorination of **6** by reflux in $POCl_3$ led to chlorination of methyl branch to provide the halogenated compound **19,** whereas compound **20** was not obtained (Scheme 8).

Chlorination of the methyl group in **19** was deduced from the disappearance of the proton and carbon methyl signals; on the other hand, a new carbon signal appeared at 95.46 ppm corresponding to the highly deshielded $-CCl_3$. The NH proton signal was found at 13.44 ppm. The plausible mechanism for the formation of compound **19** proceeds via typical free radical substitution reaction (Scheme 9).[36,37]

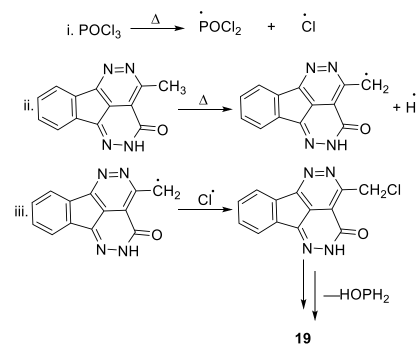
Scheme 7. Aza-Michael Addition and Synthesis of Tetraazafluoranthen-3-one Scaffold 16−18



Scheme 8. Chlorination of 6 Using $POCl_3$



Scheme 9. Proposed Mechanism for Compound 19



■ CONCLUSIONS

In conclusion, green syntheses of indeno-imidazole, 1-amino-indeno-imidazole, and tetraazafluoranthen-3-one were achieved in water, starting from ninhydrin. Compound **4** was formed via nucleophile ring opening and closer. Tetraazafluoranthen-3-one **6** was converted to tetraazafluoranthen-3-thione **7** using Lawesson's reagent. In addition, a set of N/S-alkylations of tetraazafluoranthen-3-one analogue were performed. Aza-Michael addition was also investigated. Further studies are underway in our laboratory.

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■ EXPERIMENTAL SECTION

General Information. All reactions were monitored by thin-layer chromatography (TLC) using aluminum-backed plates precoated with silica gel (60 Å, F_{254}). Visualization of spots was detected using ultraviolet light. NMR spectra were measured on a Bruker spectrometer at 400 MHz for ^{1}H NMR spectra and at 100 MHz for ^{13}C NMR spectra calibrated with (tetramethylsilane, 0 ppm) as the internal standard.

Synthesis of 3. Ethyl 3a,8b-dihydroxy-2-methyl-4-oxo-3a,8b-dihydro-4*H*-indeno[1,2-*b*]furan-3-carboxylate **3** was synthesized according to a known procedure.[27]

Synthesis of Indeno[2,1-*d*]imidazolones 4 and 5. *Method A: General Method for the Synthesis of **4** and **5**.* A mixture of ninhydrin (1.0 mmol) and the appropriate thioamide (thiourea and thiosemicarbazide) (1.1 mmol) was refluxed in 5.0 mL of water for 10 min until the reaction was completed (monitored by TLC). The crystals formed were hot; they were left to cool and then collected by filtration and recrystallized from ethanol.

*Method B: For the Synthesis of **4**.* A mixture of ninhydrin (1.0 mmol) and ethyl acetoacetate (1.5 mmol) in 10 mL of water was stirred at room temperature for 15 min. A white solid was formed, which was collected by filtration and dried to give **3** in 98% yield, mp 89−90 °C. Compound **3** (1.0 mmol) was refluxed with thiourea (1.0 mmol) in 5.0 mL of water for 30 min and left to cool. The white precipitate formed was collected by filtration, dried, and recrystallized from ethanol.

*3a,8a-Dihydroxy-2-thioxo-1,2,3,3a-tetrahydroindeno[2,1-d]imidazol-8(8aH)-one **4**.* Yield: 96%$_{\text{method A}}$, 71%$_{\text{method B}}$ as colorless crystals, mp 221−222 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 6.87 (s, 1H, OH), 6.95 (s, 1H, OH), 7.63−7.66 (m, 1H, arom), 7.78 (d, 1H, *J* 7.5 Hz, arom), 7.82 (d, 1 H, *J* 7.5 Hz, arom), 7.89−7.91 (m, 1H, arom), 9.51 (s, 1H, NH), 9.80 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 90.10, 90.62 (2C, aliph), 124.08, 125.86, 130.99, 132.89, 137.42, 151.32 (6C, arom), 178.74 (C═S), 196.8 (C═O); CHN analysis calcd for [$C_{10}H_8N_2O_3S$]: C, 50.84; H, 3.41; N, 11.86; S, 13.57. Found: C, 50.64; H, 3.31; N, 11.76; S, 13.61.

*1-Amino-3a,8a-dihydroxy-2-thioxo-1,2,3,3a-tetrahydroindeno[2,1-d]imidazol-8(8aH)-one **5**.* Yield: 85%$_{\text{method A}}$ as colorless crystals, mp 201−202 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ 4.48 (s, 2H, NH_2), 6.93 (s, 1H, OH), 7.35 (s, 1H, OH), 7.64−7.66 (m, 1H, arom), 7.77 (d, 1H, *J* 7.5 Hz, arom), 7.83 (d, 1H, *J* 7.5 Hz, arom), 7.88−7.90 (m, 1H, arom), 9.97 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 87.97, 90.86 (2C, aliph), 123.93, 125.68, 131.03, 132.76, 137.19, 150.70 (6C, arom), 179.20 (C═S), 194.49 (C═O). CHN analysis calcd for [$C_{10}H_9N_3O_3S$]: C, 47.80; H, 3.61; N, 16.72; S, 12.76. Found: 47.92; H, 3.81; N, 16.65; S, 12.93.

*Synthesis of 4-Methyl-1,2,5,6-tetraazafluoranthen-3(2H)-one **6**.* A mixture of **3** [3.0 g] and hydrazine hydrate [5.0 mL] was refluxed in water or ethanol [5.0 mL] for 15 min. A gray precipitate appeared. Then, the reaction mixture was left to cool, and the precipitate was collected by filtration, dried, and recrystallized from DMF.

Yield: 54%, mp 315−316 °C; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 2.99 (s, 3H, CH_3), 7.66 (m, 2H, aromatic), 7.96 (d, 1H, *J* 6.3 Hz, aromatic), 8.17 (d, 1H, *J* 6.1 Hz, aromatic), 13.29 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 21.26 (CH_3), 119.10, 123.11, 123.62, 126.53, 131.67, 132.59, 135.55, 137.82, 145.17, 156.77, 158.06, 158.94 (12C$_{\text{aromatic}}$); CHN analysis calcd for $C_{13}H_8N_4O$ [236.0698]: C, 66.10; H, 3.41; N, 23.72. Found: C, 66.06; H, 3.66; N, 23.66.

*4-Methyl-1,2,5,6-tetraazafluoranthene-3(2H)-thione **7**.* A mixture of **6** (1.0 mmol) and Lawesson's reagent (1.1 mmol) was refluxed in toluene for 4 h. A brownish precipitate formed, which was filtered while hot and recrystallized from DMF/EtOH.

Yield: 43%, mp 280−281 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.16 (s, 3H, CH_3), 7.70 (m, 24H, aromatic), 8.03 (m, 1H, aromatic), 8.19 (m, 1H, aromatic), 14.76 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 23.64 (CH_3), 120.99, 123.53, 123.76, 125.13, 132.49, 132.60, 135.06, 137.66, 149.79, 157.68, 159.41 (11C$_{\text{aromatic}}$), 181.43 (C═S); CHNS analysis calcd for C_{13}H8N_4S [252.0470]: C, 61.71; H, 3.45; N, 22.21; S, 12.71. Found: C, 61.89; H, 3.20; N, 21.87; S, 12.41.

General Procedures for the N/S-Alkylation of 8−12 and 13−15. A mixture of the selected nucleophile **6** or **7** (1.0 mmol) and K_2CO_3 (1.1 mmol) in dry acetone/DMF (10:2 mL) was stirred for 1 h. Then, the appropriate alkyl halide (1.1 mmol) was added portion wise, and stirring was continued overnight. The solvent was removed under vacuum; water was added; the solid was filtered, dried, and recrystallized from EtOH or DMF/EtOH.

*2-Allyl-4-methyl-1,2,5,6-tetraazafluoranthen-3(2H)-one **8**.* Yield: 85%$_{\text{EtOH}}$, mp 208−209 °C; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 3.02 (s, 3H, CH_3), 4.85 (d, 2H, *J* 5.3 Hz, NC$\underline{H_2}$−CH═CH_2), 5.24 (d, 1H, *J* 10.4 Hz, NCH_2−CH═C$\underline{H}^{cis}$H^{trans}), 5.28 (d, 1H, *J* 17.2 Hz, NCH_2−CH═CH$^{cis}\underline{H}^{trans}$), 6.02−6.08 (ddt, 1H, *J* 17.2, 10.4, 5.3 Hz, NCH_2−C$\underline{H}$═CH_2), 7.67−7.70 (m, 2H, aromatic), 7.99−8.00 (m, 1H, aromatic), 8.21−8.22 (m, 1H, aromatic); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 20.33 (CH_3), 54.67 (NCH_2), 118.21, 118.51, 123.29, 123.74, 126.24, 131.93, 132.66, 133.09, 135.45, 137.85, 144.77, 156.87, 157.40, 158.17 (14C$_{\text{12aromatic+2vinylic}}$); CHN analysis calcd for $C_{16}H_{12}N_4O$ [276.1011]: C, 69.55; H, 4.38; N, 20.28. Found: C, 69.15; H, 4.25; N, 20.27.

*2-Ethoxycarbonylmethyl-4-methyl-1,2,5,6-tetraazafluoranthen-3(2H)-one **10**.* Yield: 74%$_{\text{DMF/EtOH}}$, mp 230−231 °C; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 1.25 (t, 3H, CH_3), 3.01 (s, 3H, CH_3), 4.21 (q, 2H, CH$_{\text{2ester}}$), 5.05 (s, 2H, NCH_2), 7.69−7.71 (m, 2H, aromatic), 7.99−8.00 (m, 1H, aromatic), 8.22−8.24 (m, 1H, aromatic); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 14.47 (CH_3), 21.26 (CH_3), 54.52 (NCH_2), 61.74 (OCH_2), 118.26, 123.47, 123.86, 126.51, 132.27, 132.79, 135.12, 138.02, 145.09, 156.74, 157.72, 258.20 (12C$_{\text{aromatic}}$), 168.05 (C═O$_{\text{ester}}$); CHN analysis calcd for $C_{17}H_{14}N_4O_3$ [322.1066]: C, 63.35; H, 4.38; N, 17.38. Found: C, 63.21; H, 4.55; N, 17.25.

*2-Benzyl-4-methyl-1,2,5,6-tetraazafluoranthen-3(2H)-one **10**.* Yield: 71%$_{\text{DMF/EtOH}}$, mp 217−218 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.01 (s, 3H, CH_3), 5.44 (s, 2H, NCH_2), 7.29−7.43 (m, 5H, Phenyl), 7.67−7.69 (m, 2H, aromatic), 7.98−8.00 (m, 1H, aromatic), 8.19−8.22 (m, 1H, aromatic); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 21.28 (CH_3), 55.72 (NCH_2), 118.58, 123.30, 123.67, 126.24, 128.00, 128.23, 128.95, 131.94, 132.58, 135.39, 137.19, 137.91, 144.93, 156.86, 157.65, 158.14 (18C$_{\text{aromatic}}$); CHN analysis calcd for $C_{20}H_{14}N_4O$ [326.1168]: C, 73.61; H, 4.32; N, 17.17. Found: C, 73.90; H, 4.53; N, 17.18.

*4-Methyl-2-pentyl-1,2,5,6-tetraazafluoranthen-3(2H)-one **11**.* Yield: 65%$_{\text{DMF/EtOH}}$, mp 145−146 °C; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 0.90 (s, 3H, CH_3), 1.36−1.37 (m, 4H, 2CH_2), 1.81−1.83 (m, 2H, CH_2), 3.03 (s, 3H, CH_3), 4.23 (t, 2H, NCH_2), 7.68−7.69 (m, 2H, aromatic), 8.00−8.02 (m, 1H, aromatic), 8.21−8.22 (m, 1H, aromatic); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 14.21 (CH_3), 21.30 (CH_3), 22.22, 28.28, 28.65 (3CH_2), 52.35 (NCH_2), 118.27, 123.12, 123.66, 125.90, 131.78, 132.58, 135.49, 137.72, 144.26, 156.84, 157.74, 158.09 (12$C_{aromatic}$); CHN analysis calcd for $C_{18}H_{18}N_4O$ [306.1481]: C, 70.57; H, 5.92; N, 18.29. Found: C, 70.52; H, 5.88; N, 18.14.

4-Methyl-2-phenacyl-1,2,5,6-tetraazafluoranthen-3(2H)-one ***12***. Yield: 75%$_{DMF}$, mp 222−223 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.99 (s, 3H, CH_3), 5.84 (s, 2H, NCH_2), 7.60−7.76 (m, 5H, aromatic), 7.90−7.91 (m, 1H, aromatic), 8.11−8.16 (m, 3H, aromatic); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 21.26 (CH_3), 59.52 (NCH_2), 118.23, 123.42, 123.88, 128.61, 129.49, 132.17, 132.80, 134.64, 135.25, 137.94, 145.0, 156.83, 157.72, 158.13 (18$C_{aromatic}$), 193.24 (C=O); CHN analysis calcd for $C_{21}H_{14}N_4O_2$ [354.1117]: C, 71.18; H, 3.98; N, 15.81. Found: C, 70.93; H, 4.18; N, 16.06.

3-(Allylsulfanyl)-4-methyl-1,2,5,6-tetraazafluoranthene ***13***. Yield: 84%$_{EtOH}$, mp 151−152 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.05 (s, 3H, CH_3), 4.21 (d, 2H, *J* 6.9 Hz, SCH_2CH=CH^{cis}H^{trans}), 5.25 (d, 1H, *J* 10.0 Hz, SCH$_2$CH=C*H*^{cis}H^{trans}), 5.50 (dd, 1H, *J* 17.0 Hz, J_{gem} 1.4 Hz, SCH$_2$CH=CH^{cis}*H*^{trans}), 6.05−6.15 (ddt, 1H, *J* 17.0, 10.0, 6.9 Hz, SCH$_2$−C<u>H</u>=CH$_2$), 7.69−7.71 (m, 2H, aromatic), 8.13−8.19 (m, 2H, aromatic); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 24.02 (CH_3), 33.62 (SCH_2), 117.78, 119.86, 120.50, 124.10, 124.28, 132.84, 132.98, 137.42, 154.72, 157.65, 157.74, 159.01 (14$C_{aromatic+vinyl}$); CHNS analysis calcd for $C_{16}H_{12}N_4S$ [292.0783]: C, 65.73; H, 4.14; N, 19.16; S, 10.97. Found: C, 65.53; H, 4.43; N, 19.03; S, 10.79.

3-(Ethoxycarbonylmethyl)-4-methyl-1,2,5,6-tetraazafluoranthene ***14***. Yield: 79%$_{EtOH}$, mp 200 °C; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 1.24 (t, 3H, CH_3), 3.10 (s, 3H, CH_3), 4.19 (q, 2H, CH_{2ester}), 4.39 (s, 2H, SCH_2), 7.71−7.72 (m, 2H, aromatic), 8.18−8.21 (m, 2H, aromatic); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 14.54 (CH_3), 23.81 (CH_3), 33.68 (SCH_2), 61.71 (OCH_2), 117.66, 120.55, 124.31, 133.01, 137.41, 137.56, 154.55, 156.95, 158.02, 159.05 (13$C_{aromatic}$), 168.31 (C=O); CHNS analysis calcd for $C_{17}H_{14}N_4O_2S$ [338.0837]: C, 60.34; H, 4.17; N, 16.56; O, 9.46; S, 9.48. Found: C, 60.26; H, 4.2; N, 16.66; S, 9.52.

3-(Benzylsulfanyl)-4-methyl-1,2,5,6-tetraazafluoranthene ***15***. Yield: 90%$_{EtOH}$, mp 198−199 °C; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 3.05 (s, 3H, CH_3), 4.82 (s, 2H, SCH_2Ph), 7.31 (t, 1H, Phenyl), 7.38 (t, 2H, phenyl), 7.59 (d, 2H, *J* 7.7 Hz, phenyl), 7.71−7.72 (m, 2H, aromatic), 8.18−8.21 (m, 2H, aromatic); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 23.92 (CH_3), 35.17 (SCH_2), 117.58, 120.46, 124.07, 127.95, 132.76, 136.87, 137.44, 154.60, 157.92, 158.89 (18$C_{aromatic+phenyl}$); CHNS analysis calcd for $C_{20}H_{14}N_4S$ [342.0939]: C, 70.15; H, 4.12; N, 16.36; S, 9.36. Found: C, 69.93; H, 4.18; N, 16.15; S, 9.18.

General Procedures for Michael Addition of 16−18. A mixture of the selected Michael donor **6** or **7** (1.0 mmol) and the appropriate Michael acceptor (1.0 mmol) was refluxed in ethanol/DMF 10:1 mL containing Et_3N (2.0 mmol) for 6 h, cooled, and filtered. The precipitates were dried and recrystallized from ethanol.

2-Cyanoethyl-4-methyl-1,2,5,6-tetraazafluoranthen-3(2H)-one ***16***. Yield: 60%, mp 243−244 °C; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 3.01 (s, 3H, CH_3), 3.09 (t, 2H, −NCH$_2$C*H*$_2$CN), 4.47 (t, 2H, −NC*H*$_2$CH$_2$CN), 7.66−7.68 (m, 2H, aromatic), 7.92−7.93 (m, 1H, aromatic), 8.14−8.16 (m, 1H, aromatic); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 16.93 (NCH_2CH_2CN), 21.28 (CH_3), 47.91 (NCH_2CH_2CN), 118.21, 118.97, 123.39, 123.81, 126.02, 132.18, 132.76, 135.10, 137.71, 144.76, 156.66, 157.38, 157.96 (13$C_{(aromatic+CN)}$); CHN analysis calcd for $C_{16}H_{11}N_5O$ [289.0964]: C, 66.43; H, 3.83; N, 24.21. Found: C, 66.77; H, 4.03; N, 24.02.

2-Methoxycarbonylethyl-4-methyl-1,2,5,6-tetraazafluoranthen-3(2H)-one ***17***. Yield: 60%, mp 139−140 °C; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 2.88 (t, 2H, −NCH$_2$C*H*$_2$COOCH$_3$), 2.99 (s, 3H, CH_3), 3.64 (S, 3H, −NCH$_2$CH$_2$COOC*H*$_3$), 4.45 (t, 2H, −NC*H*$_2$CH$_2$COOCH$_3$), 7.65−7.67 (m, 2H, aromatic), 7.90−7.92 (m, 1H, aromatic), 8.14−8.16 (m, 1H, aromatic); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 21.37 (CH_3), 32.95 (NCH$_2$*C*H$_2$COOCH$_3$), 48.12 ($NCH_2CH_2COOCH_3$), 52.10 ($NCH_2CH_2COOCH_3$), 118.30, 123.19, 123.77, 125.94, 131.98, 132.72, 135.25, 137.66, 144.39, 156.80, 157.48, 158.06 (12$C_{aromatic}$), 171.60 (C=O); CHN analysis calcd for $C_{17}H_{14}N_4O_3$ [322.1066]: C, 63.35; H, 4.38; N, 17.38. Found: C, 63.34; H, 4.62; N, 17.25.

2-Cyanoethyl-4-methyl-1,2,5,6-tetraazafluoranthen-3(2H)-thione ***18***. Yield: 69%$_{DMF/EtOH}$, mp 249−250 °C; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 3.20 (s, 3H, CH_3), 3.24 (t, 2H, −NCH$_2$C*H*$_2$CN), 5.03 (t, 2H, −NC*H*$_2$CH$_2$CN), 7.74−7.76 (m, 2H, aromatic), 8.08 (*d*, 1H, *J* 6.8 Hz, aromatic), 8.24 (d, 1H, *J* 7.0 Hz, aromatic); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 15.68 (NCH_2CH_2CN), 24.61 (CH_3), 54.22 (NCH_2CH_2CN), 118.67, 119.71, 123.79, 124.14, 125.76, 132.82, 133.17, 134.63, 137.82, 149.14, 158.01, 159.56 (12$C_{(aromatic+CN)}$) 180.08 (C=S); CHN analysis calcd for $C_{16}H_{11}N_5S$ [305.0735]: C, 62.93; H, 3.63; N, 22.93; S, 10.50. Found: C, 62.83; H, 3.95; N, 22.71; S, 10.30.

4-(Trichloromethyl)-1,2,5,6-tetraazafluoranthen-3(2H)-one ***19***. Tetraazafluoranthen-3(2*H*)-one **6** (1.0 mmol) was refluxed in $POCl_3$ (10 mL) for 3 h, left to cool, and added to ice water. The formed precipitate was collected, dried, and recrystallized from DMF/EtOH.

Yield: 84%$_{DMF}$, mp 316−318 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.65 (t, 1H, aromatic), 7.72 (t, 1H, aromatic), 7.95 (d, 1H, *J* 7.4 Hz, aromatic), 8.21 (d, 1H, *J* 7.2 Hz, aromatic) 13.44 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 95.46 (CCl_3), 118.06, 123.07, 124.45, 129.77, 131.77, 133.96, 135.92, 136.84, 144.05, 153.04, 154.97 (11$C_{aromatic}$), 162.09 (C=O); CHN analysis calcd for $C_{13}H_5Cl_3N_4O$ [337.9529]: C, 45.98; H, 1.48; Cl, 31.32; N, 16.50. Found: C, 45.78; H, 1.51; Cl, 31.62; N, 16.59.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.0c00045.

Copies of ^{1}H and ^{13}C NMR spectra and X-ray data (PDF)

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Notes

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