Synthesis of Novel Fluoranthene-Based Conformationally Constrained α-Amino Acid Derivatives and Polycyclic Aromatics via the Diels–Alder Reaction

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Received: 02.01.2014; Accepted after revision: 25.02.2014

Abstract: Conformationally constrained cyclic α-amino acid moieties have been fused to the fluoranthene system. Aminoindanecarboxylic acid (Aic) and 1,2,3,4-tetrahydroisoquinolinecarboxylic acid (Tic) derivatives were synthesized by an alkylation sequence, whereas a aminotetralincarboxylic acid (Atc) derivative was assembled using the Diels–Alder reaction as a key step. These α-amino acid derivatives are considered as constrained analogues of phenylalanine (Phe) and play an important role in the design and synthesis of bioactive peptides and some fluorescence chemosensor molecules. Moreover, this strategy has been extended to polycyclic aromatics via the Diels–Alder reaction and subsequent aromatization with DDQ.

Key words: amino acids, alkylation, bioorganic chemistry, fused-ring systems, Diels–Alder reaction

Various polycyclic aromatic hydrocarbons (e.g., fluoranthene derivatives) play significant roles in optoelectronics, fluorescent chemosensors, and self assembly. They can act as critical building blocks in the design of organic light-emitting diodes (OLEDs) and organic field-effect transistors (OFETs).[1] In this regard, fluoranthene-fused sulfones such as **1** act as a light-emitting compound.[2] Moreover, fluoranthene derivatives (Figure 1), such as **2** and **3**,[3a] and **4** and **5**,[3b,c] exhibit interesting photophysical and electrochemical properties, and compounds such as **6** act as fluorescent chemosensors for the detection of explosives such as 2,4,6-trinitrotoluene and picric acid.[3d]

In view of the interesting photophysical and electrochemical properties of various fluoranthene-fused derivatives, strategies for their syntheses are of great interest.[2–4] To this end, Fabrizio et al. reported the synthesis of fluoranthene-fused sulfone derivatives such as 9,10-dimethylsulfone-7,12-diphenylbenzo[*k*]fluoranthene **1** (DSDPBF)[2] employing the Diels–Alder reaction. On the other hand, Pei and co-workers reported the synthesis of fluoranthene-fused imide derivatives[3b,c] using the Diels–Alder reaction and decarbonylation as key steps. Similarly, Patil and co-workers demonstrated the synthesis of fluoranthene-fused derivatives, such as fluorescent chemosensor **6**,[3d] by the Diels–Alder reaction.

As a part of our major program for the design of unusual α-amino acid derivatives and polycyclic aromatics, we chose to incorporate the fluoranthene ring as a core structural unit and thus α-amino acid derivatives **7**–**9** and polycyclic aromatics such as **10**–**12** became our synthetic targets. Due to various interesting properties of fluoranthene-fused derivatives,[2–4] we designed a simple route to these α-amino acid derivatives and polycyclic compounds using the Diels–Alder reaction[5] and alkylation as key steps. Here, we report a simple route to fluoranthene-

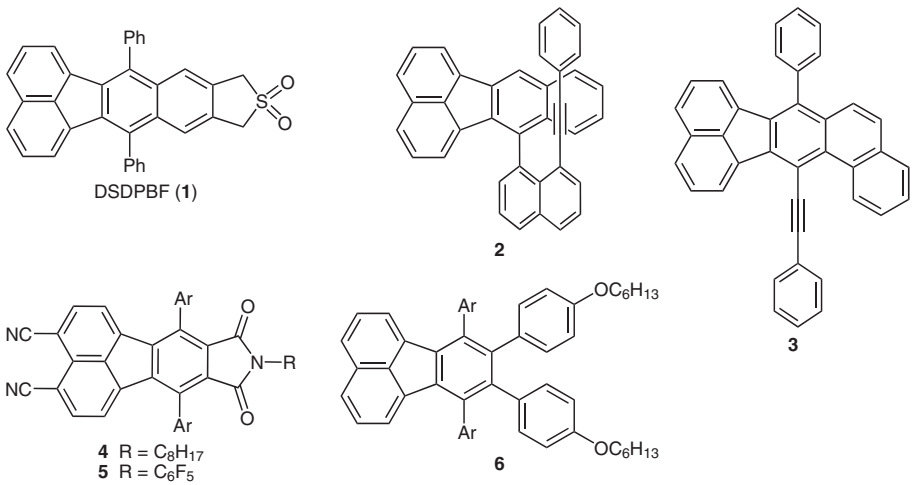


Figure 1 Various fluoranthene-fused polycyclic aromatic hydrocarbons[2,3]

SYNTHESIS 2014, 46, 1525–1531
Advanced online publication: 31.03.2014
DOI: 10.1055/s-0033-1341042; Art ID: SS-2014-Z0002-OP

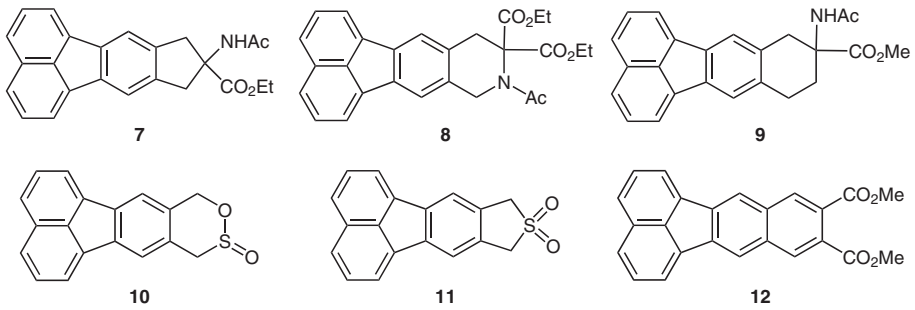
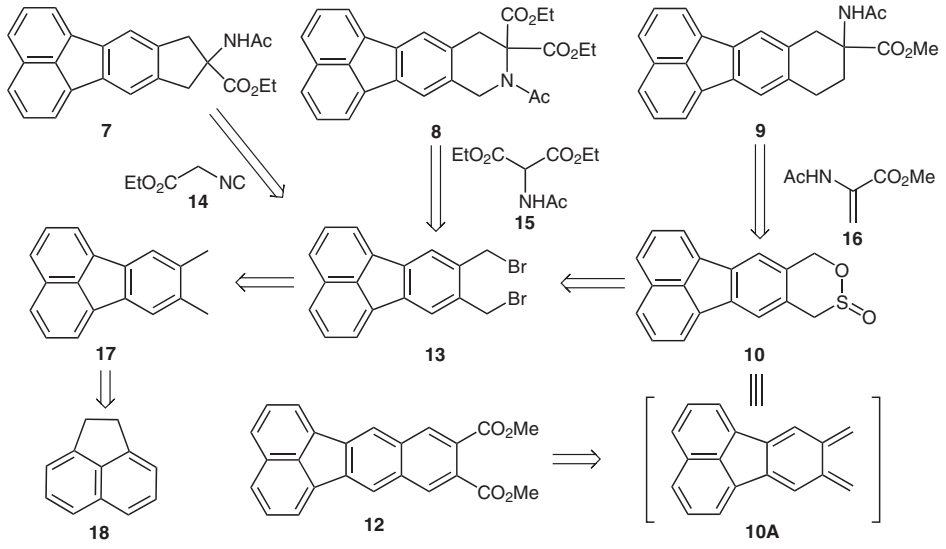


Figure 2 Fluoranthene-fused α-amino acid derivatives **7–9** and polycyclic aromatics **10–12**

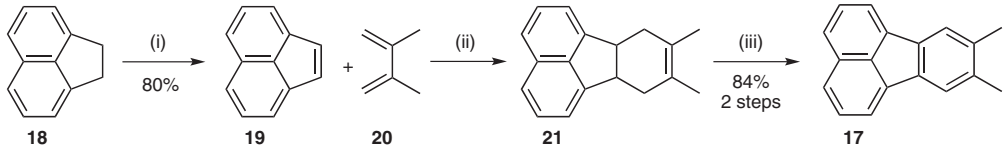
fused conformationally constrained cyclic α-amino acid derivatives involving aminoindanecarboxylic acid **7** (Aic), 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid **8** (Tic), and aminotetralincarboxylic acid **9** (Atc) derivatives, and polycyclic compounds such as **10–12** (Figure 2).

In the design of conformationally constrained α-amino acid derivatives,[6–13] fluoranthene-fused derivatives **7–9** and polycyclic aromatic compound **12** are considered worthwhile targets. To this end, 8,9-bis(bromomethyl)fluoranthene (**13**) was identified as a key building block. A possible route to α-amino acid derivatives **7** and **8** was envisioned involving ethyl isocyanoacetate (**14**)[14] and diethyl acetamidomalonate (**15**). Alternatively, α-amino acid derivative **9** could be derived by Diels–Alder reaction of fluoranthene-fused sultine **10** and methyl 2-acetamidoacrylate (**16**) involving the transient diene intermediate **10A**. Our strategy may be extended toward the synthesis of fluoranthene-fused polycyclic compound **12** by a Diels–Alder reaction involving sultine intermediate **10**, which can act as a latent diene equivalent **10A** (Scheme 1).

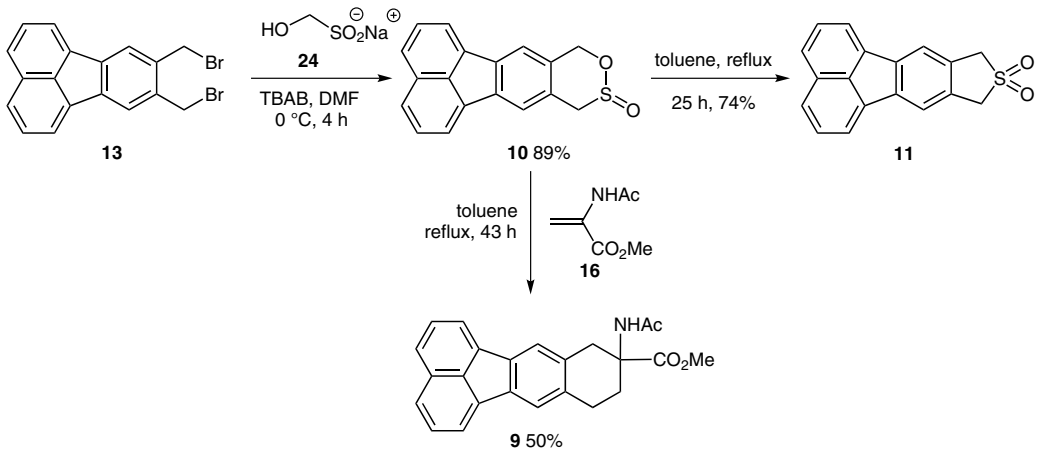
The required 8,9-dimethylfluoranthene (**17**) was prepared by following the literature procedure.[15,16] Although, Clar and Stephen[17a] reported the synthesis of 8,9-bis(bromomethyl)fluoranthene (**13**) by a different route[17] with limited data (melting point and CHN analysis only), we prepared 8,9-bis(bromomethyl)fluoranthene (**13**) by following a slightly modified route with the aid of *N*-bromosuccinimide by adopting the radical bromination of an aromatic methyl group.



Scheme 1 Retrosynthetic pathway to α-amino acid derivatives and polycyclic aromatics



Scheme 2 Preparation of 8,9-dimethylfluoranthene (**17**). *Reagents and conditions*: (i) DDQ, toluene, reflux, 24 h; (ii) toluene, sealed tube, 150 °C, 48 h; (iii) chloranil, *o*-xylene, reflux, 7 h.



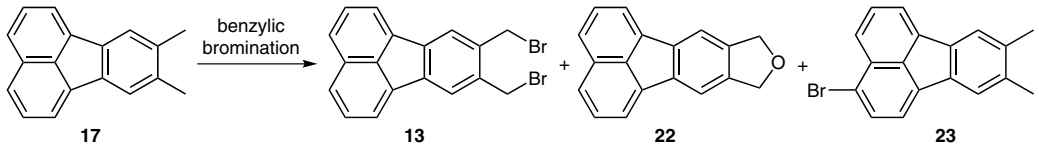
Scheme 3 Synthesis of tetralin-based α-amino acid **9** derivative via sultine building block **10**

In this regard, we started from readily available 1,2-dihydroacenaphthene (**18**), which was oxidized with 2,2-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in toluene at reflux to give acenaphthylene (**19**) as a yellow crystalline solid in 80% yield, which was subjected to a [4+2]-cycloaddition reaction with 2,3-dimethylbuta-1,3-diene (**20**) (toluene, sealed tube, 150 °C, 48 h) to deliver the cycloadduct **21**. Treatment of the cycloadduct **21** with chloranil in refluxing *o*-xylene for seven hours gave 8,9-dimethylfluoranthene (**17**) as a pale-yellow crystalline solid in 84% yield (Scheme 2).

Toward the synthesis of α-amino acid derivatives, such as **7**–**9**, and polycyclic derivatives, the synthesis of the key building block 8,9-bis(bromomethyl)fluoranthene (**13**) seems to be a non-trivial task. In this regard, 8,9-dimethylfluoranthene (**17**) was subjected to radical bromination to deliver 8,9-bis(bromomethyl)fluoranthene (**13**).[17a] The results are summarized in Table 1.

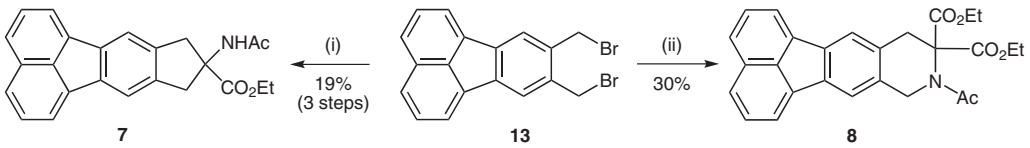
Treatment of 8,9-dimethylfluoranthene (**17**) with *N*-bromosuccinimide in the presence of catalytic amounts of radical initiator such as benzoyl peroxide in various solvent systems under reflux conditions gave two products, dibromide **13** and ether **22**, in low yields (entries 1–3). In an attempt to improve the yield, 8,9-dimethylfluoranthene (**17**) was treated with benzyltrimethylammonium tribromide[18] in the presence of benzoyl peroxide in dichloromethane–methanol (1:1) at 65 °C, but this gave ring-substituted product **23** in 84% yield (entry 4). The dibromide **13** was obtained in 40% yield by treating compound **17** with *N*-bromosuccinimide in carbon tetrachloride in the presence of a catalytic amount of benzoyl peroxide at room temperature for two hours by irradiation with a 200-W lamp (entry 6). The product was purified by silica gel column chromatography. Elution of the column with 10% dichloromethane in petroleum ether gave the product and further crystallization from benzene furnished the crystalline product. 8,9-Bis(bromomethyl)fluoranthene (**13**) was characterized by ^{1}H and ^{13}C

Table 1 Reaction Conditions for the Preparation of 8,9-Bis(bromomethyl)fluoranthene (**13**)

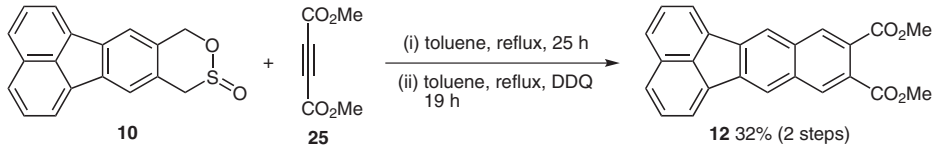


Entry	Reagent	Initiator	Solvent	Temp (°C)	Time (h)	Yield[a] (%)		
						13	**22**	**23**
1	NBS	Bz_2O_2	CCl_4	75–80	15	15	10	–
2	NBS	Bz_2O_2	CCl_4	75–80	6	4	13	–
3	NBS	Bz_2O_2	$PhCF_3$	100	4	10	24	–
4	$BnMe_3NBr_3$	Bz_2O_2	CH_2Cl_2–MeOH (1:1)	65	3	–	–	84
5	NBS	AIBN	CCl_4	75–80	51	12	15	–
6	NBS	Bz_2O_2	CCl_4	r.t.[b]	2	40	–	–

[a] Yields refers isolated yields of various products as characterized by ^{1}H and ^{13}C NMR spectroscopic data.
[b] Conducted using *hν* (200 W lamp).



Scheme 4 Synthesis of indane- and Tic-based α-amino acid derivatives. *Reagents and conditions*: (i) (a) ethyl isocyanoacetate (**14**), Bu_4NHSO_4, K_2CO_3, MeCN, 75 °C, 21 h; (b) EtOH, concd HCl, CH_2Cl_2, r.t., 3 h; (c) Ac_2O, MeCN, r.t., 42 h; (ii) diethyl acetamidomalonate (**15**), K_2CO_3, MeCN, reflux, 15 h.



Scheme 5 Synthesis of polycyclic aromatic **12**

NMR spectroscopic data and further supported by mass spectral data where fragment ion corresponds to the [M – Br] fragment.

The dibromo compound **13** was treated with sodium hydroxymethanesulfinate (rongalite) (**24**) in *N*,*N*-dimethylformamide in the presence of tetrabutylammonium bromide as a phase-transfer catalyst at 0 °C for four hours to afford the sultine **10** in 89% yield. However, NMR data indicate that the sultine product was contaminated with a small amount of sulfone **11** and it was difficult to remove the sulfone by column chromatography. Further, sultine **10** was heated at 100 °C to deliver the corresponding sulfone **11** in 74% yield. Later, the sultine **10** was treated with methyl 2-acetamidoacrylate (**16**) in toluene at reflux for 43 hours to furnish the desired product, aminotetralincarboxylic acid **9** (Atc) derivative in 50% yield (Scheme 3).

Next, the 8,9-bis(bromomethyl)fluoranthene (**13**) was reacted with ethyl isocyanoacetate (**14**) in the presence of potassium carbonate in refluxing acetonitrile under phase-transfer conditions to give the alkylated product, which was directly treated with concentrated hydrochloric acid in absolute ethanol to generate the desired amino ester. Subsequent acetylation of the amino ester with acetic anhydride in acetonitrile at room temperature gave the desired acetylated product **7** as an off-white solid in 19% yield (3 steps; overall yield). Similarly, the dibromide **13** reacted with diethyl acetamidomalonate (**15**) in the presence of potassium carbonate as the base in acetonitrile at reflux for 15 hours to furnish the required 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (Tic) **8** derivative as a white solid in 30% yield (Scheme 4).

To expand this strategy to fluoranthene-fused polycyclic aromatics, sultine derivative **10** was treated with dimethyl acetylenedicarboxylate (**25**) in refluxing toluene for 25 hours to afford the cycloadduct, which was directly subjected to an aromatization sequence in the presence of DDQ in refluxing toluene to give the desired aromatized product **12** in 32% (Scheme 5).

The steady state absorption spectra were recorded on a Jasco V530 spectrophotometer, and steady state PL spectra were recorded on a Varian Cary Eclipse fluorescence spectrophotometer bandwidth of 5 nm. Fluoranthene is known to exhibit strong fluorescence owing to its rigid and highly conjugated structure. The quantum yield (QY) of fluoranthene is 0.30 in dilute cyclohexane solution.[19] The fluoranthene-based α-amino acid derivatives were studied, and are found to be considerably fluorescent. All the fluorescence measurements were performed using dry acetonitrile as the solvent. The fluorescent QY calculated[20] for the three derivatives were between 0.1 to 0.3. Furthermore, it has been shown that Tic derivative **2** has similar value of QY (0.28), indane- **1** and tetralin-based **3** α-amino acid derivatives have QY (0.10) and (0.14) respectively nearly half that compared to the fluoranthene chromophore. The time resolved fluorescent measurements were performed using a time-correlated single photon counting (TCSPC) system, from IBH (UK), with λ_{ex} = 294 nm. The fluorescence decay profile of the compounds showed a fast fluorescence decay component of around 500 ps in addition to a slow component. Due to the different functional groups and various ring substituents in the fluoranthene unit, there is slight difference in the fluorescence lifetime. The data for the fluorescence study can be found in the supporting information.

We have demonstrated a simple strategy for the synthesis of novel fluoranthene-fused conformationally constrained cyclic α-amino acid derivatives via the Diels–Alder reaction as a key step. This strategy has been extended to polycyclic aromatics. Moreover, the methodology developed here is useful for the design the biologically active compounds and is likely to play a significant role in the preparation of optoelectronics and fluorescent chemosensors molecules.

Melting points were recorded on a Labhosp or Veego melting point apparatus and are uncorrected. ^{1}H NMR spectra were generally recorded on Varian VXR (400 MHz) or Bruker (400 MHz) spectrometers. ^{13}C NMR spectra were recorded on Varian VXR (75 MHz) or Bruker (100 MHz) spectrometers. NMR spectra were generally per-

formed in $CDCl_3$ soln with TMS as the internal standard. Analytical TLC was performed on glass plates coated with silica gel G or GF 254 (Acme, 13% $CaSO_4$ as a binder).

All reactions were monitored by TLC using an appropriate solvent system for development. The transfer of moisture-sensitive materials was carried out using standard syringe-septum techniques and reactions were maintained under a N_2 atmosphere until workup. Anhyd CCl_4 and CH_2Cl_2 were obtained by distillation over P_2O_5. $MgSO_4$ and Na_2SO_4 were dried in an oven at 130 °C for 1 d. All solvent extracts were washed successively with H_2O and brine, dried (anhyd $MgSO_4$ or Na_2SO_4), and concentrated at reduced pressure on a Buchi R-114 rotary evaporator. Petroleum ether = PE. Yields reported are isolated, chromatographically pure, yields. Ethyl isocyanoacetate was prepared by following the literature procedure.[14] Methyl 2-acetamidoacrylate and diethyl acetamidomalonate were purchased from Aldrich. All the commercial grade reagents were used without further purification.

8,9-Bis(bromomethyl)fluoranthene (13)[17a] (Table 1, Entry 6)
To a 50-mL round-bottomed flask was added 8,9-dimethylfluoranthene (**17**, 200 mg, 0.09 mmol) in CCl_4 (15 mL). Then, NBS (321 mg, 1.80 mmol) and Bz_2O_2 (0.25 equiv) were added. The resulting mixture was stirred at r.t. under irradiation (200-W lamp) for 2 h (TLC monitoring). At the conclusion of the reaction, the mixture was extracted with CH_2Cl_2 (2 × 15 mL). The organic layer was washed with H_2O (2 × 15 mL), dried (anhyd Na_2SO_4), and filtered. Evaporation of the solvent gave the crude product, which was purified by column chromatography (10% CH_2Cl_2–PE) to afford **13** (136.5 mg, 40%) as a pale-yellow solid, which on further crystallization (benzene) afforded needle-shaped crystals; mp 195–196 °C. (Note: Since, benzene is known to be carcinogenic, extra care should be taken while handling benzene and the experiment was carried out in well-ventilated hood.)

IR (neat): 3054, 2987, 1559, 1422, 1351, 1047, 740 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 6.7 Hz, 2 H, H_{Ar}), 7.88 (s, 2 H, H_{Ar}), 7.86 (s, 2 H, H_{Ar}), 7.66–7.62 (m, 2 H, H_{Ar}), 4.81 (s, 4 H, 2 CH_2Br).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.5, 135.8, 133.0, 130.1, 128.2, 127.6, 124.3, 121.0, 31.1.

HRMS (Q-ToF MS ES$^+$): *m/z* [M – Br] calcd for $C_{18}H_{12}Br$: 307.0121; found: 307.0122.

8,9-Bis(bromomethyl)fluoranthene (13) and 1,3-Dihydroacenaphtho[1,2-*f*]isobenzofuran (22) (Table 1, Entry 1)
To a 50-mL round-bottomed flask was added 8,9-dimethylfluoranthene (**17**, 60 mg, 0.26 mmol) in CCl_4 (12 mL). Then, NBS (98 mg, 0.54 mmol) and Bz_2O_2 (31 mg, 0.5 equiv) were added. The resulting mixture was stirred at 75 °C for 15 h (TLC monitoring). At the conclusion of the reaction, the mixture was extracted with CH_2Cl_2 (2 × 15 mL). The organic layer was washed with H_2O (2 × 15 mL), dried (anhyd $MgSO_4$), and filtered. Evaporation of the solvent gave the crude product, which was purified by column chromatography (10% EtOAc–PE) to afford dibromide **13** (15 mg, 15%) as a pale-yellow solid and the ether **22** (6 mg, 10%) as an off-white solid.

Ether 22
Mp 222–224 °C.

IR (neat): 2956, 2917, 1559, 1454, 1421, 1041, 772 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 6.7 Hz, 2 H, H_{Ar}), 7.84 (d, *J* = 8.3 Hz, 2 H, H_{Ar}), 7.71 (s, 2 H, H_{Ar}), 7.64 (s, *J* = 8.0 Hz, 2 H, H_{Ar}), 5.20 (s, 4 H, 2 CH_2O).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.6, 138.8, 136.6, 132.9, 130.1, 128.1, 126.8, 120.0, 114.2, 73.7.

HRMS (Q-ToF MS ES$^+$): *m/z* [M + H]$^+$ calcd for $C_{18}H_{13}O$: 245.0966; found: 245.0962.

3-Bromo-8,9-dimethylfluoranthene (23) (Table 1, Entry 4)
To a 50-mL round-bottomed flask were added 8,9-dimethylfluoranthene (**17**, 30 mg, 0.13 mmol) and Bz_2O_2 (15 mg, 0.5 equiv) in CH_2Cl_2–MeOH (1:1, 15 mL). Then $BnMe_3NBr_3$ (146 mg, 0.39 mmol) was added, and the mixture was refluxed under N_2 for 3 h (TLC monitoring). The mixture was extracted with CH_2Cl_2 (2 × 15 mL). The organic layer was washed with H_2O (2 × 15 mL), dried (anhyd Na_2SO_4), and filtered. Evaporation of the solvent gave the crude product, which was purified by column chromatography (10% EtOAc–PE) to afford **23** (33.9 mg, 84%) as a pale-yellow solid; mp 165–167 °C.

IR (neat): 3054, 2987, 1559, 1422, 1362, 1052, 739 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 8.4 Hz, 1 H, H_{Ar}), 7.83 (d, *J* = 6.7 Hz, 1 H, H_{Ar}), 7.77 (d, *J* = 7.6 Hz, 1 H, H_{Ar}), 7.65–7.59 (m, 4 H, H_{Ar}), 2.37 (s, 6 H, 2 CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.8, 137.3, 137.2, 136.8, 136.5, 133.9, 131.2, 130.0, 129.2, 125.5, 123.1, 123.0, 121.3, 120.2, 120.2, 20.5, 20.5.

HRMS (Q-ToF MS ES$^+$): *m/z* [M + H]$^+$ calcd for $C_{18}H_{14}Br$: 309.0276; found: 309.0279.

1,4-Dihydrofluorantheno[8,9-*d*][1,2]oxathiin-3-one (10)
To a suspension of rongalite **24** (240 mg, 1.5 mmol) in DMF (4 mL) was added **13** (60 mg, 0.15 mmol) and TBAB (48 mg, 0.15 mmol). The resulting suspension was stirred at 0 °C for 4 h (TLC monitoring). The mixture was diluted with H_2O (10 mL) and extracted with CH_2Cl_2. The organic layer was washed with H_2O (2 × 10 mL) and dried (anhyd Na_2SO_4). Evaporation of the organic layer under reduced pressure gave crude product, which was purified by column chromatography (20% EtOAc–PE) to afford **10** (40.8 mg, 89%) as an off-white solid; mp 267–268 °C.

IR (neat): 2983, 2934, 1508, 1353, 1275, 1053, 747 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.90 (m, 4 H, H_{Ar}), 7.72 (s, 2 H, H_{Ar}), 7.69 (m, 2 H, H_{Ar}), 5.38 (0.5 ABq, *J* = 3.5 Hz, 1 H), 5.06 (0.5 ABq, *J* = 3.4 Hz, 1 H), 4.56 (0.5 ABq, *J* = 15.3 Hz, 1 H), 3.65 (0.5 ABq, *J* = 15.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.9, 139.2, 136.0, 133.6, 132.7, 130.1, 128.2, 128.2, 127.5, 127.3, 125.9, 122.6, 120.7, 120.6, 119.2, 119.0, 64.4, 58.6.

HRMS (Q-ToF MS ES$^+$): *m/z* [M + H]$^+$ calcd for $C_{18}H_{13}O_2S$: 293.0636; found: 293.0629.

1,3-Dihydroacenaphtho[1,2-*f*]isobenzothiophene-2,2-dione (11)
To a 25-mL round-bottomed flask was added sultine **10** (15 mg) in toluene (3 mL) the mixture was heated at 100 °C for 25 h (TLC monitoring). Evaporation of the solvent gave the crude product, which was further purified by column chromatography (20% EtOAc–PE) to afford **11** (11 mg, 74%) as a yellow solid; mp 272–274 °C.

IR (neat): 2989, 2928, 1542, 1418, 1296, 1119, 741 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.89 (m, 4 H, H_{Ar}), 7.77 (br s, 2 H, H_{Ar}), 7.68 (m, 2 H, H_{Ar}), 4.48 (s, 4 H, $ArCH_2$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.1, 135.8, 130.1, 130.1, 128.3, 127.6, 120.8, 119.1, 57.4.

HRMS (ESI): *m/z* [M + Na] calcd for $C_{18}H_{12}O_2SNa$: 315.0458; found: 315.0450.

Methyl 9-Acetamido-8,9,10,11-tetrahydrobenzo[*k*]fluoranthene-9-carboxylate (9)
To a solution of **10** (10 mg, 0.03 mmol) in toluene (3 mL) was added methyl 2-acetamidoacrylate (**16**, 11 mg, 0.07 mmol). The resulting mixture was refluxed for 43 h (TLC monitoring). Evaporation of the solvent gave the crude product, which was further purified by column chromatography (50% EtOAc–PE) to afford **9** (6 mg, 50%) as a white solid; mp 243–245 °C.

IR (neat): 3053, 2987, 1724, 1541, 1422, 1049, 739 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.87 (m, 2 H, H_{Ar}), 7.84 (s, 1 H, H_{Ar}), 7.82 (s, 1 H, H_{Ar}), 7.66–7.60 (m, 4 H, H_{Ar}), 5.73 (br s, 1 H, NH), 3.80 (s, 3 H, OCH_3), 3.42 (d, *J* = 6.7 Hz, 1 H), 3.16 and 3.12 (d, *J* = 6.7, 6.8 Hz, 1 H), 3.06–2.88 (m, 2 H, CH_2), 2.67–2.61 (m, 1 H, CH), 2.29–2.20 (m, 1 H, CH), 1.95 (s, 3 H, $COCH_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.1, 170.3, 138.4, 138.0, 136.8, 136.8, 134.6, 133.0, 131.4, 130.2, 128.1, 126.7, 126.7, 122.6, 122.0, 119.9, 119.8, 58.2, 52.8, 38.7, 28.2, 26.0, 23.3.

HRMS (Q-ToF MS ES$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{22}NO_3$: 372.1600; found: 372.1596.

Ethyl 9-Acetamido-9,10-dihydro-8*H*-cyclopenta[*k*]fluoranthene-9-carboxylate (7)

To a suspension of **13** (84 mg, 0.21 mmol), Bu_4NHSO_4 (28 mg, 0.08 mmol), and K_2CO_3 (580 mg, 4.2 mmol) in MeCN (15 mL) was added ethyl isocyanoacetate (**14**, 10 equiv). The mixture was stirred under N_2 at 75–80 °C for 21 h, then cooled to r.t., and filtered through sintered glass. The solid obtained was washed with CH_2Cl_2 and the filtrate was evaporated under reduced pressure. The crude product obtained was hydrolyzed directly without further purification. The crude product in CH_2Cl_2 (10 mL), was reacted with dry EtOH (20 mL) in the presence of concd HCl (1 mL). The mixture was stirred at r.t. for 3 h and then diluted with CH_2Cl_2 (100 mL) and H_2O (150 mL), and the mixture was made alkaline by slow addition of $NaHCO_3$ with stirring. The separated CH_2Cl_2 layer was washed with H_2O (2 × 30 mL), dried (anhyd Na_2SO_4), and then filtered. Evaporation of the solvent gave the crude product, which was acetylated directly. The crude product obtained was reacted in anhyd MeCN (10 mL) with Ac_2O (1.5 mL) at r.t. for 42 h. Evaporation of the solvent gave the crude product, which was purified by column chromatography (50% EtOAc–PE) to give pure **7** (15 mg, 19% over 3 steps) as an off-white solid; mp 225–227 °C.

IR (neat): 3274, 2988, 2944, 1688, 1574, 1420, 1362, 1047, 742 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 6.7 Hz, 2 H, H_{Ar}), 7.83 (d, *J* = 8.0 Hz, 2 H, H_{Ar}), 7.72 (s, 2 H, H_{Ar}), 7.63 (t, *J* = 6.7 Hz, 2 H, H_{Ar}), 6.1 (s, NH), 4.27 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 3.76 and 3.36 (d, *J* = 16.3 Hz, 2 H, $ArCH_2$ and d, *J* = 16.6 Hz, 2 H, $ArCH_2$), 1.96 (s, 3 H, $COCH_3$), 1.29 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.0, 170.3, 139.5, 139.2, 136.9, 132.7, 130.1, 128.1, 126.6, 119.9, 118.0, 66.4, 61.9, 43.6, 23.3, 14.3.

HRMS (Q-ToF MS ES$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{22}NO_3$: 372.1611; found: 372.1600.

Diethyl 2-Acetyl-1,2,3,4-tetrahydroacenaphtho[1,2-*g*]isoquinoline-2,2-dicarboxylate (8)

To a suspension of **13** (30 mg, 0.07 mmol) and K_2CO_3 (48 mg, 0.35 mmol) in anhyd MeCN (10 mL) was added diethyl acetamidomalonate (**15**, 21 mg, 0.09 mmol). The mixture was stirred under N_2 at 75–80 °C for 15 h, then cooled to r.t., and filtered through sintered glass. The solid was washed with CH_2Cl_2 and the filtrate was evaporated under reduced pressure. The crude product obtained was purified by column chromatography (50% EtOAc–PE) to afford pure **8** (10 mg, 30%) as a white solid; mp 172–174 °C.

IR (neat): 3053, 2985, 1741, 1677, 1499, 1421, 1060, 739 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.94–7.85 (m, 4 H, H_{Ar}), 7.71 (s, 1 H, H_{Ar}), 7.70 (s, 1 H, H_{Ar}), 7.66–7.62 (m, 2 H, H_{Ar}), 4.82 (s, 2 H, NCH_2), 4.17 (q, *J* = 7.1 Hz, 4 H, 2 × OCH_2CH_3), 3.56 (s, 2 H, CCH_2), 2.34 (s, 3 H, $COCH_3$), 1.18 (t, *J* = 7.1 Hz, 6 H, 2 × OCH_2CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 168.1 (C=O ester), 139.3, 138.9, 136.4, 132.8, 132.1, 131.9, 130.2, 128.2, 127.1, 127.1, 121.1, 120.4, 120.2, 119.4, 68.3, 62.1, 48.6, 38.2, 22.6, 14.1.

HRMS (Q-ToF MS ES$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{26}NO_5$: 444.1811; found: 444.1817.

Dimethyl Benzo[*k*]fluoranthene-9,10-dicarboxylate (12)

To a solution of **10** (37 mg, 0.12 mmol) in anhyd toluene (6 mL) was added DMAD (**25**, 0.06 mL, 0.51 mmol); the mixture was refluxed for 25 h under N_2. At the conclusion of the reaction (TLC monitoring), the solvent was removed at reduced pressure to deliver the crude product, which was directly subjected to the aromatization reaction without further purification.

To a solution of the crude Diels–Alder adduct in toluene (10 mL) was added DDQ (1.2 equiv), and the mixture was refluxed for 19 h. At the conclusion of the reaction (TLC monitoring), the mixture was quenched with H_2O and extracted with CH_2Cl_2 (3 × 10 mL). The organic layer was washed with H_2O, and dried (anhyd Na_2SO_4), filtered. Evaporation of the solvent under reduced pressure gave the crude product, which was purified by column chromatography (silica gel, 10% EtOAc–PE) to give **12** (32 mg, 32% over 2 steps) as a pale-yellow solid; mp 151–153 °C.

IR (neat): 3055, 2986, 1723, 1446, 1127, 1053, 739 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.37 (s, 2 H, H_{Ar}), 8.34 (s, 2 H, H_{Ar}), 8.09 (d, *J* = 6.9 Hz, 2 H, H_{Ar}), 7.93 (d, *J* = 8.0 Hz, 2 H, H_{Ar}), 7.73 (dd, J_1 = 7.0 Hz, J_2 = 7.0 Hz, 2 H), 3.99 (s, 6 H, 2 OCH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4, 140.5, 136.0, 135.4, 133.6, 130.8, 130.6, 128.5, 127.3, 120.8, 120.3, 52.9.

HRMS (Q-ToF MS ES$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{17}O_4$: 369.1113; found: 369.1127.

Acknowledgement

We thank Department of Science and Technology (DST) and CSIR, New Delhi for the financial support. S.K. thanks DST for the award of a J. C. Bose fellowship. Milind Meshram thanks CSIR for the award of a research fellowship. We also thank to Prof. Anindya Datta, and Mr. Avinash Singh for their help in collecting fluorescence data.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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