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Synthesis of a Series of Novel 3,9-Disubstituted Phenanthrenes as Analogues of Known *N*-Methyl-D-aspartate Receptor Allosteric Modulators

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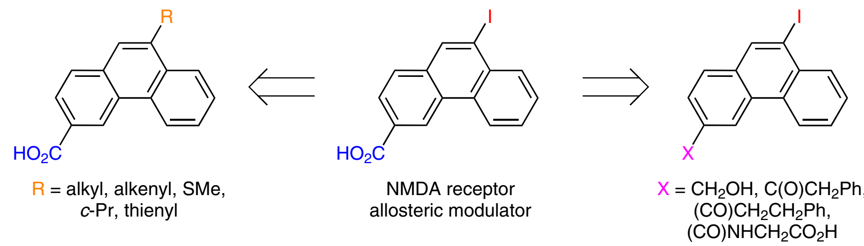

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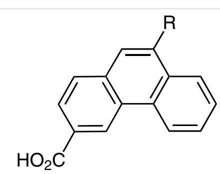
Abstract 9-Substituted phenanthrene-3-carboxylic acids have been reported to have allosteric modulatory activity at the *N*-methyl-D-aspartate (NMDA) receptor. This receptor is activated by the excitatory neurotransmitter L-glutamate and has been implicated in a range of neurological disorders such as schizophrenia, epilepsy and chronic pain, and in neurodegenerative disorders such as Alzheimer's disease. Herein, the convenient synthesis of a wide range of novel 3,9-disubstituted phenanthrene derivatives starting from a few common intermediates is described. These new phenanthrene derivatives will help to clarify the structural requirements for allosteric modulation of the NMDA receptor.

Key words phenanthrenes, NMDA receptor, allosteric modulators, palladium coupling, Wittig reaction

Phenanthrene is a naturally occurring polycyclic aromatic ring system that is found in a number of biologically active compounds.[2] Recently, we reported that phenanthrene derivatives such as **1**, **2** and **3** (Figure 1) are allosteric modulators of the *N*-methyl-D-aspartate (NMDA) family of ionotropic glutamate receptors (*i*-GluRs).[3] NMDA receptors are tetrameric ligand-gated ion channels comprised of GluN1 and GluN2A-D subunits.[3] NMDA receptors have been implicated in a range of neurological disorders such as epilepsy, schizophrenia and chronic pain, and neurodegenerative disorders such as ischaemia, Alzheimer's disease and Parkinson's disease.[3] Allosteric modulators have the potential to be used in the treatment of these disorders because they are less likely to interfere with the physiological roles of NMDA receptors compared with competitive antagonists or channel blockers.[3] A convenient synthetic route to 3-carboxy-phenanthrenes with a wide range of hydrophobic and hydrophilic substituents at the 9-position was required to conduct a structure-activity relationship (SAR) study on allosteric modulators **1**–**3**.



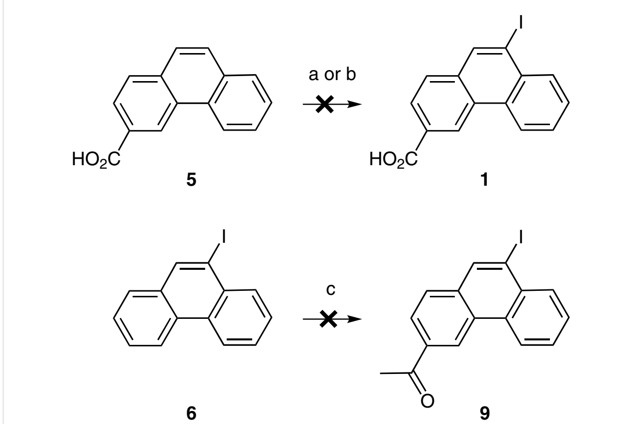
1 R = I
2 R = *c*-Pr
3 R = $(CH_2)_3$*i*-Pr

Figure 1 NMDA receptor allosteric modulators

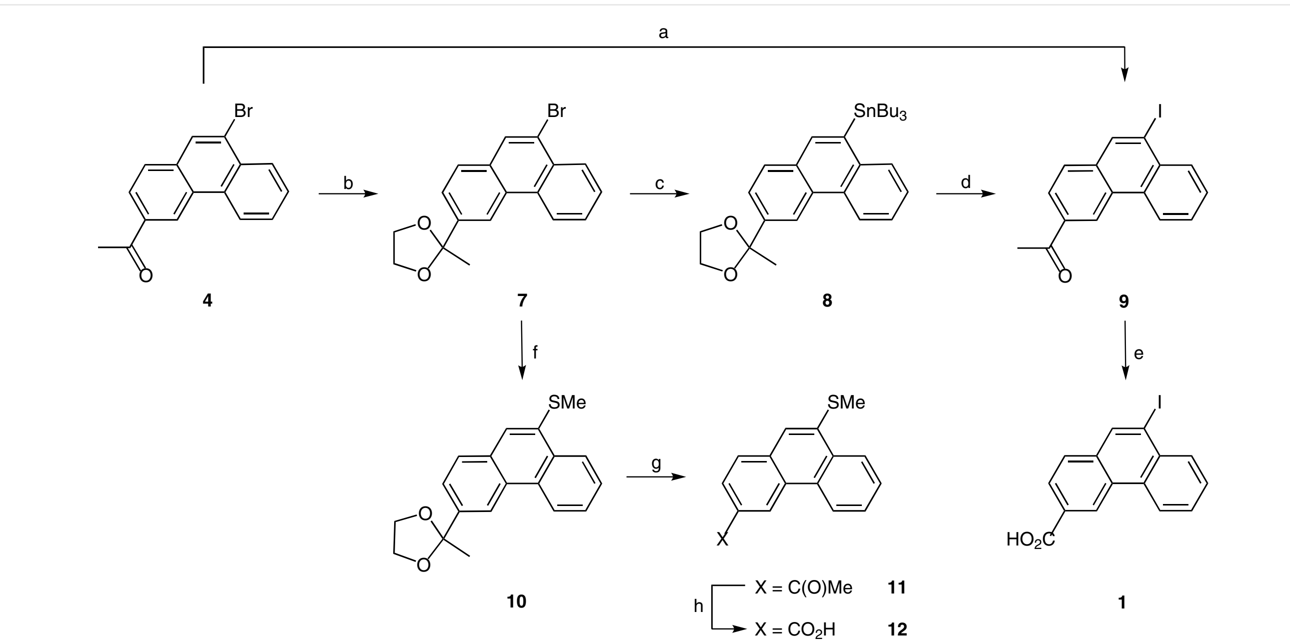
With the exception of the 9-bromo, 9-chloro and 9-carboxy derivatives, no 9-substituted 3-carboxyphenanthrenes have previously been reported.[4,5] Herein, we report the synthesis of **1**–**3** and a novel series of their derivatives starting from a few common intermediates.

Initial studies suggested that 9-iodophenanthrene-3-carboxylic acid (**1**) had an interesting pharmacological profile[3] and so we investigated suitable methods for larger scale production of this compound. We recently reported a two-step route to **1** in which an aromatic Finkelstein reaction[6] was utilised to convert 3-acetyl-9-bromophenanthrene (**4**) into its corresponding 9-iodo analogue **9** (Scheme 1).[7] A haloform reaction was then employed to oxidise the acetyl group and give the desired acid. However, although our initial experiments led to complete conversion, subsequent attempts to synthesise **9** led only to inseparable mixtures of **4** and **9**. Despite extensive investigation (e.g., different amine ligands, alternative solvents, purification of copper (I) iodide catalyst), no satisfactory reason for the non-reproducibility of the aromatic Finkelstein reaction could be established. With the halogen conversion route proving unreliable, an alternative and more robust pathway to **1** was sought. Unfortunately, attempts to iodinate the 9-position of phenanthrene-3-carboxylic acid (**5**) directly using either iodine monochloride or sodium iodide and sodium hypochlorite (Scheme 2) led only to the recovery of unreacted starting material. As a consequence, we decided to focus on developing an alternative route to ketone **9**. The most obvious route to this compound is through Friedel–Crafts acylation. However, whilst Friedel–Crafts acylation can be used to synthesise the 3-acetyl derivatives of both 9-bromo and 9-chlorophenanthrene, we found that employing the same reaction conditions on 9-iodophenanthrene (**6**) led only to the isolation of a black tar (Scheme 2).[4,5] Attempts to modify the reaction conditions by using aluminium iodide instead of aluminium chloride, or acetic anhydride instead of acetyl chloride, led to the same outcome. With all previous routes proving unsuccessful, we investigated the use of lithiation as a possible way of introducing the iodo substituent (Scheme 1). After protecting ketone **4** as the acetal **7**, lithiation at the 9-position followed by quenching with (n-Bu)$_3$SnCl afforded stannane **8**.

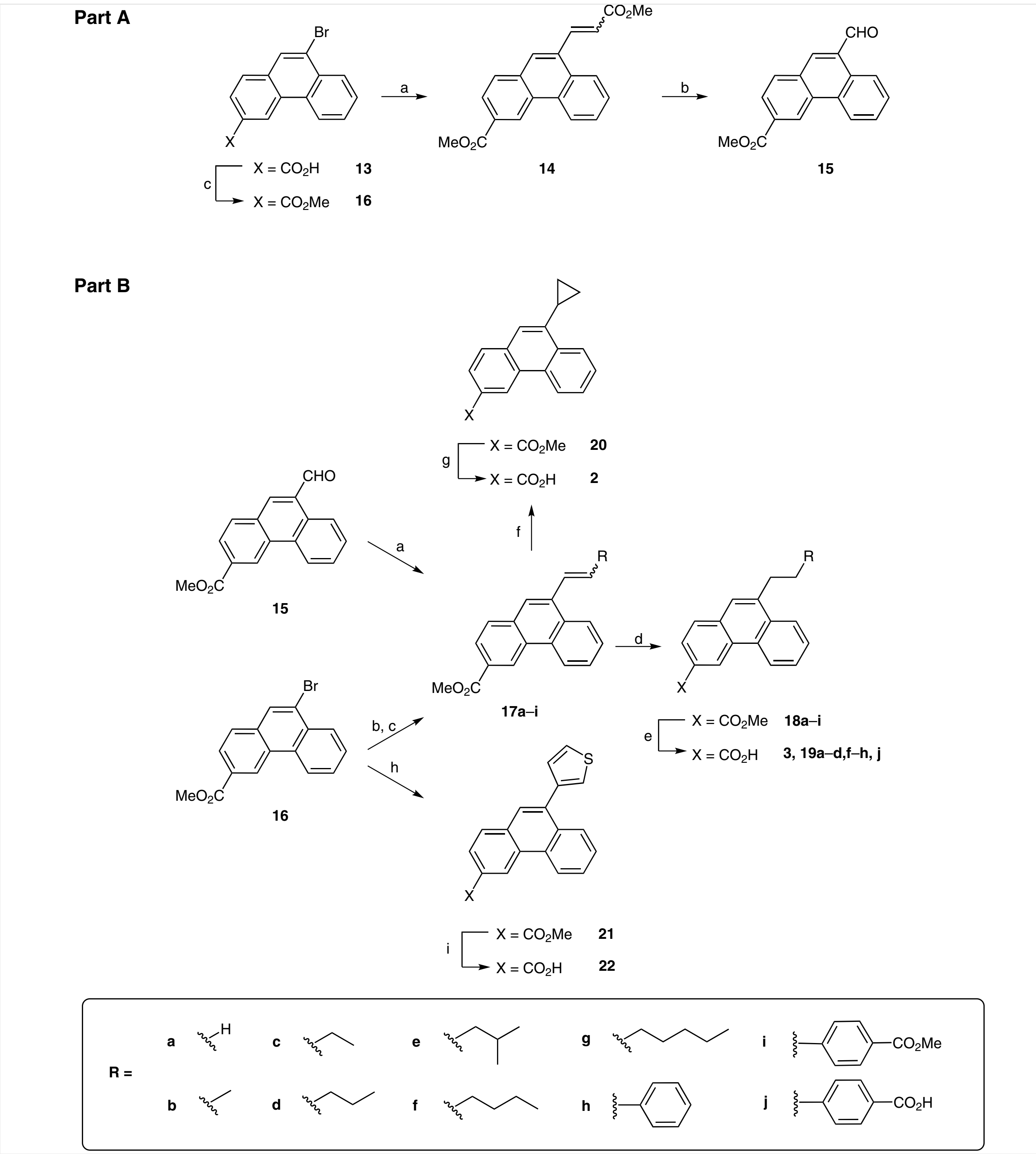
The 9-iodo group was then readily introduced by stirring with a saturated solution of iodine in dichloromethane at 0 °C. Subsequent deprotection gave ketone **9**, which was then easily converted into **1** by using the haloform reaction described previously. In theory, the iodo group could have been introduced by quenching the lithiated species with iodine. However, we were concerned that employing this route would lead to the formation of side products that could not be easily separated from the desired product. Although it added an additional step, utilising stannane **8** allowed **1** to be synthesised both cleanly and in high yield.



Scheme 2 *Reagents and conditions*: (a) ICl, AcOH, 118 °C, 18 h; (b) NaI, NaClO, NaOH, MeOH, 0 °C then r.t., 1 h; (c) AcCl, $AlCl_3$, CS_2, 5 °C then r.t., 18 h.



Scheme 1 *Reagents and conditions*: (a) NaI, CuI, *N*,*N*′-dimethylethylenediamine, dioxane, 110 °C, 65 h; (b) ethylene glycol, TsOH, toluene, 110 °C, 18 h; (c) i. *n*-BuLi, THF, –78 °C, 1 h, ii. (n-Bu)$_3$SnCl, –78 °C; (d) i. I_2, CH_2Cl_2, 0 °C, ii. 2 M HCl (aq), acetone, 0.5 h; (e) i. Br_2, NaOH (aq), dioxane, 70 °C, 1 h; ii. concd HCl (aq); (f) i. *n*-BuLi, THF, –78°C, 1 h; ii. MeSSMe, –78 °C then r.t.; (g) HCl–acetone, 1 h, r.t.; (h) i. Br_2, NaOH, dioxane, 40 °C, 1 h; ii. concd HCl.



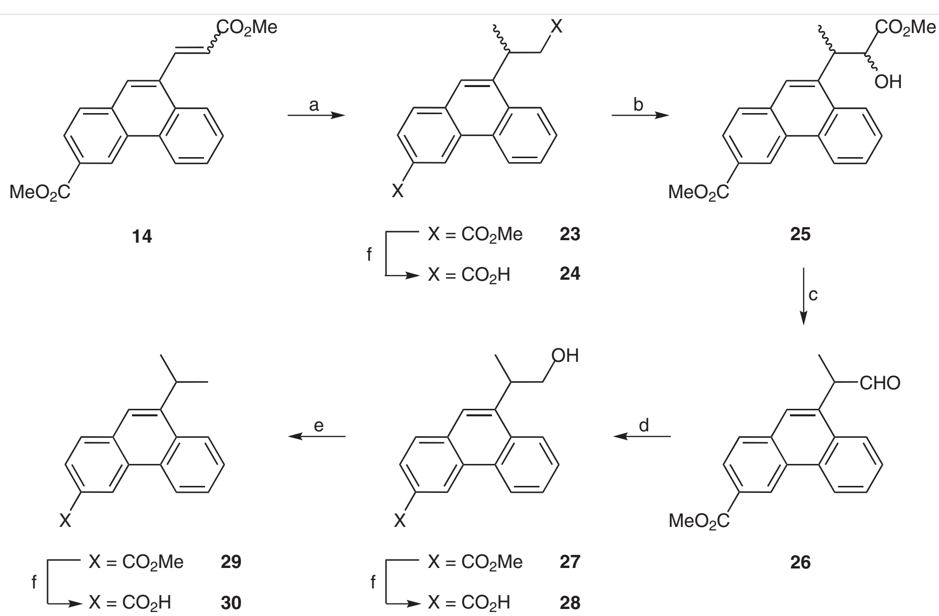
Scheme 3 *Reagents and conditions*: **Part A** (a) i. Methyl acrylate, (*o*-tolyl)$_3$P, Et_3N, Pd(OAc)$_2$, DMF, 100 °C, 18 h, ii. MeI, K_2CO_3, DMF, r.t., 18 h; (b) i. OsO_4, TMAO, *t*-BuOH/H_2O, r.t., 2 d; ii. $NaIO_4$; (c) MeOH, H_2SO_4, reflux, 48 h. **Part B** (a) RCH_2PPh_3X, KHMDS, THF, 4 h, r.t.; (b) alkene, (*o*-tolyl)$_3$P, Et_3N, Pd(OAc)$_2$, DMF, 100 °C, 18 h; (c) (*n*-Bu)$_3$SnCH=CH_2, Pd(PPh_3)$_4$, toluene, reflux, 4 h; (d) H_2, 10% Pd/C, EtOAc, r.t., 18 h; (e) i. NaOH or KOH (aq), THF, reflux or dioxane, 75 °C; ii. 1 M HCl (aq); (f) **17a**, CH_2I_2, Et_2Zn, CH_2Cl_2, 0 °C, 18 h; (g) i. LiOH (aq), dioxane, r.t., 18 h; ii. 1 M HCl (aq); (h) 3-thienylboronic acid, K_2CO_3, Pd(dppf)Cl_2·CH_2Cl_2, DME, 80 °C, 24 h; (i) i. NaOH (aq), dioxane, 75 °C; ii. 1 M HCl (aq); iii. crystallisation (AcOH).

Our attention then turned to the synthesis of a structurally diverse series of 3-carboxyphenanthrenes bearing hydrophobic substituents at the 9-position as analogues of compounds **1**–**3**. Amongst the initial group of compounds generated was thioether **12**, which was synthesised by using an identical strategy to that described for **1** with the exception that after being lithiated, acetal **7** was quenched with dimethyl disulfide (Scheme 1). Deprotection subsequently afforded acetyl **11**, which was then readily converted into carboxylic acid **12** by using the haloform reaction.

In addition to thioethers, compounds bearing alkyl substituents at the 9-position were synthesised. Initial attempts to generate these derivatives by reacting alkyl aldehydes with lithiated acetal **7** gave only a complex mixture of products. Consequently, an alternative route was devised to allow a range of alkyl chains to be introduced using common intermediates, which could be prepared both quickly and in high yield. With this in mind, the 9-formyl (**15**) and 9-bromo (**16**) substituted phenanthrenes were chosen because both functional groups could be easily manipulated by using either Wittig or palladium coupling chemistry to afford a large variety of 9-alkylphenanthrenes from commercially available reagents. Both **15** and **16** were conveniently prepared from 9-bromo acid **13** (Scheme 3, A).[7] Heck coupling of **13** with methyl acrylate followed by esterification with methyl iodide afforded diester **14**. Oxidation of alkene **14** with osmium tetroxide and cleavage of the resultant 1,2-diol with sodium periodate afforded 9-formyl derivative **15**. Methyl ester **16** was generated in good yield by Fisher esterification of acid **13**.[4]

Conducting either Wittig or Heck chemistry on **15** and **16** proceeded smoothly and led to the synthesis of alkene intermediates **17a**–**i**, which, in the majority of cases, were hydrogenated immediately to their corresponding alkyl counterparts **18a**–**i** (Scheme 3, B). Base-mediated hydrolysis subsequently afforded the desired 9-alkyl-3-carboxyphenanthrenes (**3**, **19a**–**d**, **19f**–**h**, and **19j**). The 9-cyclopropyl derivative **2** was synthesised from vinyl **17a** in two steps. First, the cyclopropyl ring was formed through a Simmons–Smith reaction to give **20**. Base-mediated hydrolysis of the ester subsequently afforded the desired acid **2**. Initially, alkene **17a** was prepared from **15** through Wittig chemistry. Although this route proved to be successful, we found that the compound was more conveniently prepared through Stille coupling between **16** and (tri-*n*-butyl)vinyl tin (Scheme 3, B).

To investigate the introduction of a heteroaromatic moiety, Suzuki coupling was employed to react **16** and 3-thienyl boronic acid (Scheme 3, B). Unfortunately, this reaction did not go to completion and led to the isolation of a mixture of product **21** and starting material **16** (ca. 75:25 ratio based on ^{1}H NMR spectroscopic analysis). Despite an investigation of different solvent systems, it was not possible to separate the individual esters by silica gel chromatography. Consequently, the mixture was taken forward and hydrolysed by using a base. By conducting multiple recrystallisations from glacial acetic acid, we were able to separate the mixture of acids and obtain a pure sample of **22** (Scheme 3, B).



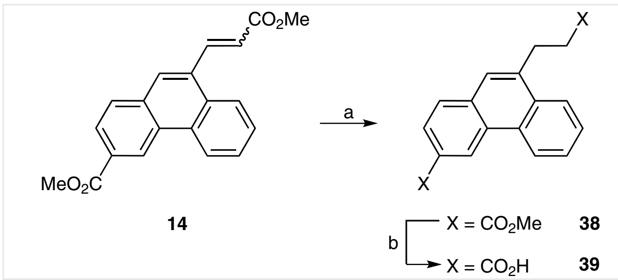
Scheme 4 *Reagents and conditions*: (a) CuI, NaI, MeMgCl, TMSCl, CH_2Cl_2/Me_2S, –78 °C then r.t., 3 h; (b) KHMDS, THF, 2-tosyl-3-phenyloxaziridine, –78 °C then r.t., 2 h; (c) i. $LiBH_4$, THF, 0 °C, 30 min then r.t., 4 h; ii. *t*-BuOH–H_2O (4:1), $NaIO_4$, r.t., 30 min; (d) $NaBH_4$, THF, r.t., 4 h; (e) i. MsCl, Et_3N, 0 °C, 1 h then r.t., 3 h; ii. NaI, acetone, reflux, 24 h; iii. H_2, Et_3N, 10% Pd/C, r.t., 18 h; (f) i. NaOH (aq), dioxane, 75 °C; ii. 1 M HCl (aq).

Synthesis of the branched 9-isopropyl derivative **30** required a different strategy to that described above (Scheme 4). This strategy had the added advantage of generating two intermediates (**24** and **28**) that could be pharmacologically characterised. Starting from diester **14**, 1,4-conjugate addition of methyl magnesium chloride afforded **23** in reasonable yield. Whilst a small amount of this compound was hydrolysed with base to diacid **24**, the majority was reacted with 2-tosyl-3-phenyloxaziridine[8] to generate alcohol **25** (Scheme 4). Reduction of the alkyl ester with lithium borohydride and cleavage of the resultant 1,2-diol with sodium periodate, led to the synthesis of aldehyde **26**.

Reduction of the aldehyde with sodium borohydride gave alcohol **27** in good yield. A small amount of this ester was hydrolysed to the corresponding acid **28** by using a base (Scheme 4). Alcohol **27** was then converted into the corresponding mesylate by reaction with methanesulfonyl chloride. The mesylate was, in turn, converted into the corresponding iodo derivative through a Finkelstein reaction. Subsequent hydrogenation led to dehalogenation and yielded the 9-isopropyl derivative **29**, which was readily hydrolysed to the desired acid **30** (Scheme 4).

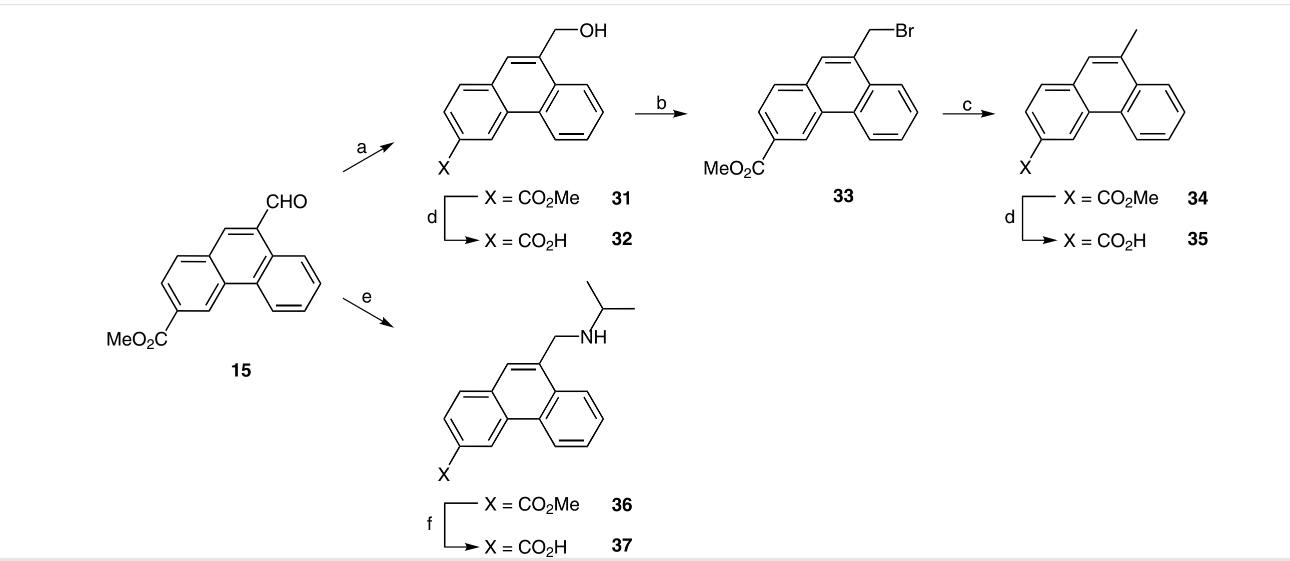
In addition to its use in the previously described Wittig chemistry, aldehyde **15** was utilised as a starting point for the synthesis of 9-methyl derivative **35** (Scheme 5). Reduction of the aldehyde by using sodium borohydride afforded 9-hydroxymethyl derivative **31**. A small portion of this compound was hydrolysed to yield acid **32** for pharmacological characterisation, whereas the majority was taken forward and reacted with phosphorus tribromide to afford 9-bromomethyl **33**. Hydrogenation subsequently afforded 9-methyl derivative **34**, which was readily hydrolysed to the corresponding acid **35** (Scheme 5).

Although the introduction of hydrophobic substituents was our primary focus, we wanted to synthesise some compounds with more polar groups at the 9-position to gather additional data on the requirements for biological activity. For example, aldehyde **15** was reacted with isopropylamine through reductive amination to afford ester **36**, which was subsequently hydrolysed to acid **37** (Scheme 5). Similarly, alkene **14** was hydrogenated to afford alkyl diester **38**, which was then hydrolysed to diacid **39** (Scheme 6).



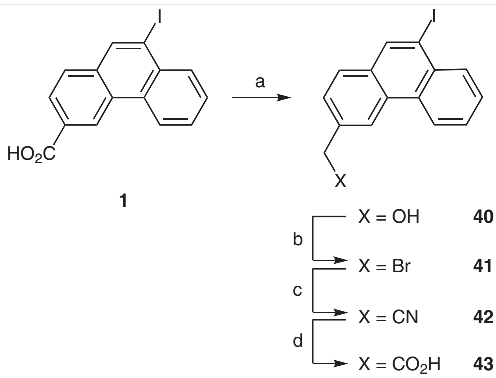
Scheme 6 *Reagents and conditions*: (a) H_2, 10% Pd/C, EtOAc, r.t., 18 h; (b) i. NaOH (aq), THF, reflux, 4 h; ii. 1 M HCl (aq).

To identify the optimal 3-position substituent for biological activity, the 3-carboxy group in **1** was subjected to chemical modification (Scheme 7). Interestingly, attempts to reduce this moiety by using lithium aluminium hydride led not only to reduction of the desired group but also to dehalogenation. Consequently, a pathway was devised in which the acid chloride of **1** was generated through reac-



Scheme 5 *Reagents and conditions*: (a) $NaBH_4$, THF, r.t., 4 h; (b) Br_3P, CH_2Cl_2, 0 °C then r.t., 2 h; (c) H_2, 10% Pd/C, r.t., 18 h; (d) i. NaOH (aq), dioxane, 75 °C, ii. 1 M HCl (aq); (e) *i*-$PrNH_2$, $NaBH(OAc)_3$, DCE, r.t., 40 h; (f) i. NaOH (aq), dioxane, 75 °C, 4 h; ii. 1 M HCl (aq); iii. ion-exchange chromatography.

tion with thionyl chloride and then reduced under mild conditions using sodium borohydride (Scheme 7). This route was successful and led to the synthesis of 3-hydroxymethyl **40** in good yield. Reaction of **40** with phosphorus tribromide afforded 3-bromomethyl **41**, which was, in turn, converted into the corresponding nitrile **42** by reaction with sodium cyanide under phase-transfer conditions. Hydrolysis of the nitrile under acidic conditions gave 3-acetic acid derivative **43** (Scheme 7).[9]



Scheme 7 *Reagents and conditions*: (a) i. $SOCl_2$, dioxane, reflux, 12 h; ii. $NaBH_4$, THF, 0 °C, 0.5 h, then r.t., 12 h; (b) Br_3P, CH_2Cl_2, 0 °C then r.t., 1 h; (c) NaCN, TBAB, H_2O/CH_2Cl_2 (1:1), r.t., 5 d; (d) AcOH, H_2SO_4, H_2O, 118 °C, 3 h.

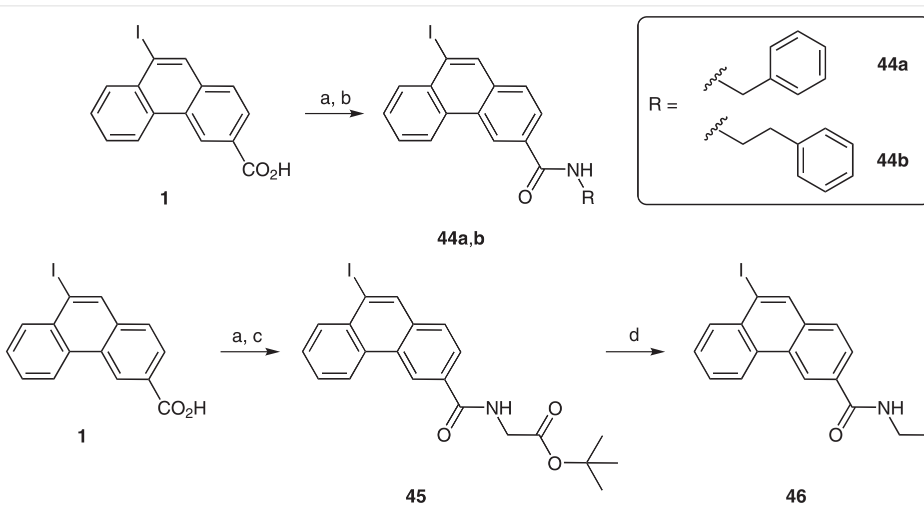
In a further modification to the 3-position, the acid chloride of **1** was reacted with benzylamine, phenethylamine and the *tert*-butyl ester of glycine to afford amides **44a**, **44b** and **45** (Scheme 8). Deprotection of the *tert*-butyl ester to afford acid **46** was achieved readily and in good yield by reaction with TFA (Scheme 8).

Table 1 Activity of Selected 3,9-Disubstituted Phenanthrene Derivatives at Recombinant NMDA Receptor Subtypes[a]

Compound[c]	NMDAR (n≥4)[b] GluN2A	GluN2B	GluN2C	GluN2D
1	8.6 ± 4.8	0.9 ± 0.1	–34.1 ± 8.3	–52.3 ± 3.0
2	36.0 ± 7.4	51.2 ± 13.2	–7.3 ± 0.4	5.6 ± 4.7
3	31.5 ± 10.0	34.0 ± 8.5	21.8 ± 8.1	24.3 ± 3.6
35	–4.8 ± 4.6	–3.2 ± 0.3	–15.1 ± 0.3	–4.1 ± 0.9
19b	6.6 ± 1.2	30.0 ± 1.8	5.2 ± 4.0	7.8 ± 1.8
19d	42.6 ± 9.6	42.1 ± 14.3	26.4 ± 5.4[d]	20.3 ± 5.3
19f	28.2 ± 11.4	20.5 ± 7.5	19.6 ± 3.0	24.6 ± 7.3
22	10.7 ± 6.4	3.9 ± 12.6	–52.7 ± 9.1	–45.2 ± 8.7
37	–21.9 ± 9.2	–0.3 ± 1.8	–13.0 ± 2.5	–2.6 ± 0.8
39	–48.1 ± 6.5	–51.1 ± 3.4	–17.8 ± 2.7	–15.1 ± 0.7
43	–23.5 ± 3.9	–30.9 ± 3.8	–46.7 ± 4.3	–66.6 ± 4.1

[a] All compounds tested at a concentration of 100 μM.
[b] Percent inhibition (negative number) or potentiation (positive number) of the responses of recombinant rat NMDA receptors (GluN1 expressed with the indicated GluN2 subunit) expressed in *Xenopus* oocytes (mean ± s.e.m.).
[c] All of the compounds were made up as stocks solutions in DMSO and were soluble up to a concentration of 100 μM in the buffer used in these assays.
[d] **19d** inhibited 22% in one experiment; this value was not included in the average shown.

A previously described electrophysiological assay on GluN1 and GluN2A-D subunits individually expressed in Xenopus oocytes[3] was used to pharmacologically characterise a selection of the synthesised phenanthrenes. The compounds were tested at a concentration of 100 μM for their effects on GluN1/GluN2A-D receptor responses and percentage antagonism or potentiation of responses to glutamate (10 μM) and glycine (10 μM) was determined (Table 1). Although only preliminary, these data suggest that:



Scheme 8 *Reagents and conditions*: (a) $SOCl_2$, benzene, 80 °C, 12 h; (b) RNH_2, Et_3N, dioxane, r.t., 3 h; (c) H-Gly-O*t*Bu·HCl, Et_3N, dioxane, r.t., 3 h; (d) TFA, CH_2Cl_2, r.t., 18 h.

(a) an alkyl substituent at the 9-position promotes NMDA receptor potentiating activity; (b) as the length and/or size of the alkyl chain increases so does NMDA receptor potentiation (compare activity of **35** vs. **2**, **3**, **19b**, **19d** and **19f**); (c) introduction of a polar group into the alkyl side chain promotes NMDA receptor antagonism over potentiation (**37** and **39**); (d) the 9-iodo group can be replaced by a 3-thienyl ring without adversely affecting activity (compare activity of **1** vs. **22**), and (e) moving the carboxyl group away from the phenanthrene ring is beneficial for NMDA receptor antagonism (compare activity of **1** vs. **43**).

In conclusion, we have developed an alternative and robust synthetic pathway to 9-iodophenanthrene-3-carboxylic acid (**1**), a novel allosteric NMDA receptor modulator. Starting from a few common intermediates, we have synthesised a series of novel phenanthrene derivatives with a variety of substituents at the 3- and 9-positions of the phenanthrene ring. It is hoped that these compounds will lead to a better understanding of the structural requirements for allosteric modulation of the NMDA receptor. The preliminary pharmacological data described here suggests that the new compounds have interesting profiles of activity on NMDA receptor subtypes. Further pharmacological characterisation of these newly synthesised compounds is ongoing and will be reported in due course.

Reagents were purchased from commercial suppliers and purified by standard techniques when necessary. All anhydrous solvents were obtained from either Acros or Sigma–Aldrich and used without further drying. All anhydrous reactions were conducted under an inert atmosphere. Melting points were determined with an Electrothermal IA9100 capillary apparatus and are uncorrected. ^{1}H NMR spectra were measured with either a Jeol spectrometer at 270.18 MHz, a Jeol JNM-LA300 spectrometer at 300.53 MHz, a Jeol JNM-ECP400 spectrometer at 400.18 MHz, or a Varian 400MR spectrometer at 399.77 MHz. ^{13}C NMR spectra were recorded with either a Jeol JNM-LA300 spectrometer at 75.57 MHz, a Jeol JNM-ECP400 spectrometer at 100.63 MHz, or a Varian 400MR spectrometer at 100.52 MHz. Chemical shifts (δ) are reported in parts per million (ppm) with 3-(trimethylsilyl)propionic-2,2,3,3-d_4 acid sodium salt in D_2O, or tetramethylsilane in $CDCl_3$ or DMSO-d_6 used as internal standards. Mass spectrometry was performed in the mass spectroscopy laboratories of the Department of Chemistry, University of Bristol, UK. Elemental analyses were performed in the microanalytical laboratories of the Department of Chemistry, University of Bristol, UK. The purity of all novel compounds was determined by combustion analysis, which confirmed that they were ≥95% pure. Thin-layer chromatography was performed on Merck silica gel 60 F_{254} plastic sheets. Flash chromatography was performed on Merck silica gel 60 (220–440 mesh) from Fisher.

2-(9-Bromophenanthren-3-yl)-2-methyl[1,3]dioxolane (7)

A stirred solution of **4**[4] (20.9 g, 70 mmol), ethylene glycol (8.68 g, 0.14 mol) and TsOH·H_2O (0.67 g, 3.5 mmol) in toluene (200 mL) was heated at reflux with a Dean–Stark trap in place overnight. After cooling to r.t., the reaction mixture was washed with sat. aq $NaHCO_3$ (50 mL) and H_2O (50 mL). The organic layer was isolated, dried over $MgSO_4$ and concentrated in vacuo to approximately 50 mL. At this point, the product precipitated out of solution as a white solid and was filtered off. Further concentration of the mother liquor to approximately 10 mL led to the precipitation of a second crop of product, which was again collected by filtration. The mother liquor was then concentrated in vacuo and the remaining residue was purified by flash chromatography (EtOAc–hexane, 2%) to give **7**.

Yield: 23.4 g (97%); white solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.79 (s, 3 H), 3.79–3.90 (m, 2 H), 4.07–4.18 (m, 2 H), 7.64–7.86 (m, 4 H), 8.10–8.23 (m, 1 H), 8.34–8.43 (m, 1 H), 8.69–8.79 (m, 2 H).

HRMS (CI): m/z $[M + H]^+$ calcd for $C_{18}H_{15}O_2Br$: 343.0334; found: 343.0338.

Tributyl-[3-(2-methyl[1,3]dioxolan-2-yl)phenanthren-9-yl]stannane (8)

To a solution of **7** (22.2 g, 65 mmol) in anhydrous THF (350 mL) at −78 °C was added carefully and dropwise a solution of *n*-BuLi (2.5 M in hexane, 31 mL, 78 mmol). The resultant mixture was stirred for 1 h at −78 °C, then the reaction was quenched with *n*-Bu_3SnCl (23 mL, 84.5 mmol). After complete addition, the solution was warmed to r.t., the reaction mixture was diluted with Et_2O (500 mL) and the organic layer was isolated, washed with H_2O (150 mL), dried over $MgSO_4$ and concentrated in vacuo. The resultant residue was purified by flash chromatography (EtOAc–hexane, 2%) to afford **8** (31.9 g, 89%), which was utilised in the next step without further analysis.

3-Acetyl-9-iodophenanthrene (9)

Compound **8** (31.9 g, 57.7 mmol) was dissolved in CH_2Cl_2 (150 mL) and a saturated iodine solution in CH_2Cl_2 was added slowly at 0 °C until the colour of the last drop of iodine did not disappear within 30 s. The organic solution was then washed with sat. $NaHSO_3$ (50 mL), H_2O (50 mL), dried over $MgSO_4$, and concentrated in vacuo. The resultant residue was dissolved in acetone (200 mL) and aq 2 M HCl (4 mL) was added dropwise. The ketone precipitated out of solution almost immediately and, after stirring for 30 min, **9** was collected by filtration.

Yield: 17.0 g (85%); white solid; mp 149–151 °C (Lit.[7] 148–150 °C).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.78 (s, 3 H), 7.67–7.75 (m, 2 H), 7.78 (d, J = 8.4 Hz, 1 H), 8.10 (dd, J = 8.4, 1.8 Hz, 1 H), 8.20–8.24 (m, 1 H), 8.44 (s, 1 H), 8.66–8.71 (m, 1 H), 9.24 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.7, 102.4, 122.7, 123.8, 126.1, 127.9, 128.1, 128.4, 129.8, 130.7, 132.4, 133.5, 135.1, 135.3, 137.9, 197.8.

9-Iodophenanthrene-3-carboxylic Acid (1)

Synthesised from **9** as described previously.[7]

2-Methyl-2-(9-methylsulfanylphenanthren-3-yl)-[1,3]dioxolane (10)

To a stirring solution of **7** (1.72 g, 5.00 mmol) in anhydrous THF (50 mL) at −78 °C was added dropwise a solution of *n*-BuLi (2.5 M in hexane, 2.4 mL, 6.00 mmol). After complete addition, the solution was stirred for 1 h, then the reaction was quenched by the dropwise addition of dimethyl disulfide (0.59 mL, 6.50 mmol). The mixture was then warmed to r.t. before being diluted with Et_2O (50 mL). The organic layer was isolated, washed with H_2O (50 mL), dried over $MgSO_4$ and concentrated in vacuo. The resulting residue was purified by flash chromatography (EtOAc–hexane, 2%) to afford **10**, which was utilised in the next step without further analysis.

1-[9-(Methylsulfanyl)phenanthren-3-yl]ethanone (11)

Concentrated HCl (0.4 mL) was added dropwise to a stirred solution of **10** in acetone (100 mL). The resultant solution was stirred for 1 h, during which a precipitate formed. This solid was filtered off and washed with cold acetone (20 mL). Recrystallisation from acetone afforded **11**.

Yield: 954 mg (72%); off-white solid; mp 135–137 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = (s, 3 H), 2.78 (s, 3 H), 7.50 (s, 1 H), 7.67–7.78 (m, 2 H), 7.83 (d, *J* = 8.4 Hz, 1 H), 8.12 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.31–8.35 (m, 1 H), 8.77–8.81 (m, 1 H), 9.25 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.3, 26.9, 120.8, 123.2, 124.0, 124.8, 126.1, 127.4, 127.7, 127.7, 127.7, 128.1, 130.5, 134.1, 134.9, 138.7, 198.0.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{17}H_{14}OS$: 266.0765; found: 266.0766.

Anal. Calcd for $C_{17}H_{14}OS$: C, 76.66; H, 5.30. Found: C, 76.60; H, 5.51.

(9-Methylsulfanyl)phenanthrene-3-carboxylic Acid (12)

A stirred suspension of **11** (400 mg, 1.50 mmol) in dioxane (50 mL) was heated at 40 °C until complete dissolution of the solid. At the same time, a solution of sodium hypobromite was prepared by the dropwise addition of bromine (0.38 mL, 7.50 mmol) to an ice-cooled solution of sodium hydroxide (1.05 g, 26.3 mmol) dissolved in H_2O (50 mL). The sodium hypobromite solution was then added dropwise to the dioxane solution (complete addition took around 10 min) and stirring was continued until TLC analysis indicated complete conversion. The mixture was then cooled to r.t. and a saturated sodium sulfite solution (10 mL) was added to quench excess hypobromite. The dioxane was removed in vacuo and the resultant suspension was topped up with H_2O and acidified to pH 1 by using concd HCl. Subsequent filtration gave a yellow solid, which was washed copiously with water (100 mL) and then dried over P_2O_5. Recrystallisation from a mixture of toluene and EtOH afforded **12**.

Yield: 104 mg (26%); light-yellow solid; mp 242–246 °C.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ = 2.72 (s, 3 H), 7.72–7.83 (m, 3 H), 8.02 (d, *J* = 8.0 Hz, 1 H), 8.12 (dd, *J* = 8.0, 1.2 Hz, 1 H), 8.19–8.25 (m, 1 H), 8.88 (d, *J* = 8.0 Hz, 1 H), 9.29 (s, 1 H), 13.09 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ = 14.1, 120.3, 123.4, 123.9, 124.4, 127.0, 127.0, 127.6, 127.6, 127.9, 129.4, 129.4, 134.1, 137.4, 167.4.

HRMS (ESI): *m*/*z* $[M - H]^-$ calcd for $C_{16}H_{12}O_2S$: 267.0485; found: 267.0489.

Anal. Calcd for $C_{16}H_{12}O_2S{\cdot}0.25\ H_2O$: C, 70.44; H, 4.62. Found: C, 70.43; H, 4.53.

Methyl 9-(3-Methoxy-3-oxoprop-1-en-1-yl)phenanthrene-3-carboxylate (14)

A flask was charged with **13** (30.1 g, 0.1 mol), palladium acetate (0.24 g, 0.1 mmol) and tri-*o*-tolylphosphine (1.28 g, 0.4 mmol). The flask was then briefly evacuated and backfilled with argon three times. A degassed solution of Et_3N (40 mL, 0.26 mol) and methyl acrylate (12 mL, 0.13 mol) in DMF (300 mL) was then added to the flask by using a cannula and the resultant mixture was heated at 100 °C for 18 h. After cooling to r.t., any remaining volatile compounds were removed in vacuo. Na_2CO_3 (10.6 g, 0.1 mol) was then added followed by methyl iodide (12.5 mL, 0.2 mol), and the reaction mixture was stirred at r.t. overnight. The mixture was then diluted with Et_2O (500 mL) and the organic layer was isolated, washed with H_2O (2 × 200 mL) and dried over $MgSO_4$. Concentration in vacuo gave **14** as a 1:1 mixture of *cis* and *trans* isomers.

Yield: 29.5 g (92%); pale-yellow solid; mp 186–188 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3 H), 3.88 (s, 3 H), 3.94 (s, 3 H), 4.02 (s, 3 H), 4.17 (d, *J* = 6.0 Hz, 1 H), 5.45 (d, *J* = 6.0 Hz, 1 H), 6.59 (d, *J* = 15.0 Hz, 1 H), 7.38–7.51 (m, 4 H), 7.65–7.75 (m, 2 H), 7.84–7.89 (m, 2 H), 7.99 (d, *J* = 7.8 Hz, 1 H), 8.06 (d, *J* = 7.8 Hz, 1 H), 8.14–8.17 (m, 2 H), 8.46 (d, *J* = 15.0 Hz, 1 H), 8.52 (d, *J* = 9.3 Hz, 1 H), 8.74–8.78 (m, 1 H), 9.12 (s, 1 H), 9.33 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.0, 52.3, 52.5, 52.6, 122.1, 123.3, 123.5, 124.0, 124.3, 124.6, 124.9, 125.1, 125.7, 126.6, 127.0, 127.6, 127.8, 128.4, 128.7, 129.0, 129.3, 130.2, 130.5, 130.7, 130.8, 133.4, 133.7, 133.9, 135.9, 142.2, 167.1, 167.2, 167.3, 172.7.

HRMS (CI): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{16}O_4$: 321.1127; found: 321.1125.

Methyl 9-Formylphenanthrene-3-carboxylate (15)

A solution of **14** (6.4 g, 20 mmol) in CH_2Cl_2 (30 mL) was diluted with *t*-BuOH (150 mL) and H_2O (50 mL) with vigorous stirring. TMAO (2.45 g, 22 mmol), OsO_4 (0.5 g, 0.2 mmol) and tartaric acid (4.2 g, 20 mmol) were added and the reaction was monitored by TLC analysis. When all the starting material had been consumed, $NaIO_4$ (21.3 g, 0.1 mol) was added. The aldehyde precipitated out of solution almost immediately. After stirring for an additional 20 min, the solvent (mainly *t*-BuOH) was removed in vacuo, and **15** was collected by filtration.

Yield: 5.17 g (98%); pale-yellow solid; mp 180–182 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.04 (s, 3 H), 7.71–7.80 (m, 2 H), 8.03 (d, *J* = 8.8 Hz, 1 H), 8.20–8.24 (m, 2 H), 8.74–8.77 (m, 1 H), 9.29–9.34 (m, 2 H), 10.38 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.7, 123.0, 125.2, 126.1, 127.2, 128.2, 128.4, 128.8, 130.5, 130.5, 132.2, 132.4, 132.8, 139.7, 166.9, 193.5.

MS (CI^+): *m*/*z* (%) = 265 (100) $[M + H]^+$.

Anal. Calcd for $C_{17}H_{12}O_3$: C, 77.26; H, 4.58. Found: C, 77.22; H, 4.49.

Methyl 9-Bromophenanthrene-3-carboxylate (16)

A flask containing **13**[7] (10.0 g, 33.2 mmol) was briefly evacuated and backfilled with argon. Anhydrous MeOH (300 mL) was then added to the flask by using a cannula followed by a catalytic amount of concentrated H_2SO_4 (3 mL). The resultant mixture was heated to reflux for 48 h, then cooled to r.t. before being concentrated in vacuo. The resultant dark-orange solid was dissolved in CH_2Cl_2 (250 mL) and washed with sat. aq $NaHCO_3$ (3 × 50 mL), H_2O (50 mL) and brine (50 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo to afford **16**.

Yield: 9.06 g (87%); orange solid; mp 151–153 °C (Lit.[4] 155–155.5 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.03 (s, 3 H), 7.69–7.77 (m, 2 H), 7.78 (d, *J* = 8.4 Hz, 1 H), 8.07 (s, 1 H), 8.17 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.33–8.37 (m, 1 H), 8.71–8.75 (m, 1 H), 9.32 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.4, 123.0, 124.6, 125.2, 127.1, 127.8, 128.0, 128.0, 128.2, 128.2, 129.1, 129.9, 130.5, 131.3, 134.7, 167.0.

General Procedure A; Wittig Reaction

To a stirred suspension of the appropriate triphenylphosphonium salt (3.6 mmol) in THF (20 mL) was added dropwise potassium bis(trimethylsilyl)amide (0.5 M in toluene, 7.2 mL, 3.6 mmol). The resultant mixture was stirred for 30 min before being added dropwise to a stirred solution of **15** (793 mg, 3 mmol) in THF (20 mL). After complete addition, the mixture was stirred at r.t. for approximately 4 h, then the reaction was quenched with sat. aq NH_4Cl (10 mL). The mixture was diluted with Et_2O (25 mL) and the organic layer was isolated and dried over $MgSO_4$. Concentration in vacuo gave the crude product, which was redissolved in Et_2O (30 mL) and passed through a short silica plug. Concentration in vacuo subsequently afforded the alkene phenanthrenes **17a**–**c**, which were utilised immediately in the next step.

Methyl 9-Vinylphenanthrene-3-carboxylate (17a)

By following General Procedure A, methyltriphenylphosphonium iodide (1.46 g) afforded **17a** as a light-yellow oil (677 mg, 86%).

Methyl 9-Prop-1-en-1-ylphenanthrene-3-carboxylate (17b)

By following General Procedure A, ethyltriphenylphosphonium bromide (1.34 g) afforded **17b** as a light-yellow oil (729 mg, 88%).

Methyl 9-But-1-en-1-ylphenanthrene-3-carboxylate (17c)

By following General Procedure A, propyltriphenylphosphonium bromide (1.38 g) afforded **17c** as a light-yellow oil (793 mg, 91%).

General Procedure B; Heck Reaction

A flask was charged with **16** (1.00 g, 3.17 mmol), palladium acetate (7.2 mg, 1 mol%), tri-*o*-tolylphosphine (39 mg, 4 mol%), and (if a solid) the appropriate alkene (3.96 mmol). The flask was then briefly evacuated and backfilled with argon three times. Degassed anhydrous DMF (25 mL) was then added followed by (if a liquid) the appropriate alkene (3.96 mmol) and Et_3N (1.11 mL, 7.93 mmol). The resultant mixture was heated at 100 °C overnight. After cooling to r.t., the reaction mixture was filtered through a Celite pad to remove any precipitated Pd(0) and then poured into a stirred solution of EtOAc (100 mL), H_2O (100 mL) and aqueous 1 M HCl (10 mL). The organic layer was subsequently isolated and the aqueous phase was further extracted with EtOAc (2 × 30 mL). The organic extracts were pooled, washed with H_2O (5 × 100 mL) and brine (100 mL), and dried over $MgSO_4$. Concentration in vacuo afforded the crude alkene phenanthrenes (**17d**–**i**), which were utilised immediately in the next step.

Methyl 9-Pent-1-en-1-ylphenanthrene-3-carboxylate (17d)

By following General Procedure B, 1-pentene (0.43 mL) afforded **17d** (850 mg, 88%) as a dark-orange oil.

Methyl 9-(4-Methylpent-1-en-1-yl)phenanthrene-3-carboxylate (17e)

By following General Procedure B, 4-methyl-1-pentene (0.50 mL) afforded **17e** (924 mg, 91%) as a dark-orange oil.

Methyl 9-Hex-1-en-1-ylphenanthrene-3-carboxylate (17f)

By following General Procedure B, 1-hexene (0.49 mL) afforded **17f** (950 mg, 94%) as a dark-orange oil.

Methyl 9-Hept-1-en-1-ylphenanthrene-3-carboxylate (17g)

By following General Procedure B, 1-heptene (0.56 mL) afforded **17g** (760 mg, 72%) as a dark-orange oil.

Methyl 9-(2-Phenylethenyl)phenanthrene-3-carboxylate (17h)

By following General Procedure B, styrene (0.45 mL) afforded **17h** (911 mg, 85%) as a yellow/brown solid.

Methyl 9-[2-(4-Methoxycarbonyl)phenylethenyl]phenanthrene-3-carboxylate (17i)

By following General Procedure B, methyl 4-vinylbenzoate (642 mg) afforded **17i** (1.02 g, 81%) as a yellow solid.

General Procedure C; Hydrogenation

The appropriate alkene phenanthrene was dissolved in EtOAc (100 mL) and the resultant solution was hydrogenated under 3 bar of hydrogen in the presence of 10 wt% palladium on activated carbon (50 mg) for 18 h. The reaction mixture was then filtered through a Celite pad before being concentrated in vacuo. Purification of the resultant residue by flash chromatography (EtOAc–hexane, 5 → 10%) afforded the individual alkyl phenanthrenes.

Methyl 9-Ethylphenanthrene-3-carboxylate (18a)

By following General Procedure C, **17a** (677 mg, 2.58 mmol) afforded **18a**.

Yield: 613 mg (90%); white solid; mp 82–83 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 (t, *J* = 7.6 Hz, 3 H), 3.17 (q, *J* = 7.6 Hz, 2 H), 4.02 (s, 3 H), 7.61 (s, 1 H), 7.64–7.73 (m, 2 H), 7.85 (d, *J* = 8.4 Hz, 1 H), 8.11–8.15 (m, 1 H), 8.17 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.81–8.85 (m, 1 H), 9.39 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 26.3, 52.2, 123.4, 124.4, 124.4, 125.0, 126.5, 126.7, 127.0, 127.1, 128.1, 129.0, 130.8, 131.4, 134.9, 141.2, 167.5.

HRMS (CI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{16}O_2$: 265.1229; found: 265.1223.

Methyl 9-*n*-Propylphenanthrene-3-carboxylate (18b)

By following General Procedure C, **17b** (729 mg, 2.62 mmol) afforded **18b**.

Yield: 685 mg (94%); clear oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (t, *J* = 7.8 Hz, 3 H), 1.81 (m, *J* = 7.8 Hz, 2 H), 2.98 (t, *J* = 7.8 Hz, 2 H), 3.23 (s, 3 H), 7.43 (s, 1 H), 7.57–7.66 (m, 2 H), 7.71 (d, *J* = 9.0 Hz, 1 H), 8.01–8.05 (m, 1 H), 8.14 (d, *J* = 9.0 Hz, 1 H), 8.72–8.75 (m, 1 H), 9.32 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4, 22.9, 31.8, 52.2, 123.4, 124.5, 125.0, 125.4, 126.5, 126.7, 127.0, 127.1, 128.1, 129.0, 130.9, 131.5, 134.8, 139.6, 167.5.

HRMS (CI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{18}O_2$: 279.1380; found: 279.1373.

Methyl 9-*n*-Butylphenanthrene-3-carboxylate (18c)

By following General Procedure C, **17c** (793 mg, 2.71 mmol) afforded **18c**.

Yield: 729 mg (92%); clear oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (t, *J* = 7.8 Hz, 3 H), 1.50–1.59 (m, 2 H), 1.79–1.87 (m, 2 H), 3.12 (t, *J* = 7.8 Hz, 2 H), 4.05 (s, 3 H), 7.58–7.59 (m, 1 H), 7.67–7.74 (m, 2 H), 7.82–7.86 (m, 1 H), 8.12–8.15 (m, 1 H), 8.20 (d, *J* = 8.0 Hz, 1 H), 8.82–8.85 (m, 1 H), 9.41 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 23.1, 32.4, 33.4, 52.3, 123.5, 124.7, 125.1, 125.5, 126.6, 126.8, 127.1, 127.2, 128.2, 129.1, 131.0, 131.6, 135.0, 140.1, 167.6.

HRMS (CI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{20}O_2$: 293.1542; found: 293.1553.

Methyl 9-*n*-Pentylphenanthrene-3-carboxylate (18d)

By following General Procedure C, **17d** (850 mg, 2.79 mmol) afforded **18d**.

Yield: 815 mg (95%); viscous yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 6.8 Hz, 3 H), 1.36–1.53 (m, 4 H), 1.77–1.88 (m, 2 H), 3.13 (t, *J* = 8.0 Hz, 2 H), 4.02 (s, 3 H), 7.61 (s, 1 H), 7.64–7.75 (m, 2 H), 7.86 (d, *J* = 8.0 Hz, 1 H), 8.12–8.15 (m, 1 H), 8.18 (dd, *J* = 8.0, 1.6 Hz, 1 H), 8.82–8.86 (m, 1 H), 9.41 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.6, 29.9, 32.1, 33.6, 52.2, 123.4, 124.6, 125.1, 125.4, 126.5, 126.7, 127.0, 127.0, 128.1, 129.0, 130.9, 131.4, 134.8, 140.0, 167.5.

HRMS (CI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{22}O_2$: 307.1698; found: 307.1696.

Methyl 9-(4-Methylpent-1-yl)phenanthrene-3-carboxylate (18e)

By following General Procedure C, **17e** (924 mg, 2.90 mmol) afforded **18e**.

Yield: 886 mg (95%); viscous yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (d, *J* = 6.4 Hz, 6 H), 1.36–1.44 (m, 2 H), 1.58–1.70 (m, 1 H), 1.78–1.87 (m, 2 H), 3.11 (t, *J* = 7.6 Hz, 2 H), 4.02 (s, 3 H), 7.61 (s, 1 H), 7.65–7.74 (m, 2 H), 7.88–7.84 (d, *J* = 8.4 Hz, 1 H), 8.11–8.15 (m, 1 H), 8.18 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.82–8.86 (m, 1 H), 9.41 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.6, 28.0, 28.1, 33.9, 39.2, 52.5, 123.4, 124.6, 125.1, 125.4, 126.5, 126.7, 127.0, 127.1, 128.1, 129.0, 130.9, 131.4, 134.9, 140.1, 167.5.

HRMS (CI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{24}O_2$: 321.1855; found: 321.1855.

Methyl 9-*n*-Hexylphenanthrene-3-carboxylate (18f)

By following General Procedure C, **17f** (950 mg, 2.98 mmol) afforded **18f**.

Yield: 899 mg (94%); viscous yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.2 Hz, 3 H), 1.30–1.42 (m, 4 H), 1.43–1.55 (m, 2 H), 1.77–1.87 (m, 2 H), 3.12 (t, *J* = 7.6 Hz, 2 H), 4.02 (s, 3 H), 7.61 (s, 1 H), 7.65–7.74 (m, 2 H), 7.86 (d, *J* = 8.4 Hz, 1 H), 8.11–8.15 (m, 1 H), 8.18 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.82–8.86 (m, 1 H), 9.40 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.7, 29.6, 30.2, 31.8, 33.6, 52.2, 123.4, 124.6, 125.1, 125.4, 126.5, 126.7, 127.0, 127.0, 128.1, 129.0, 130.9, 131.4, 134.9, 140.1, 167.5.

HRMS (CI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{24}O_2$: 321.1855; found: 321.1849.

Methyl 9-*n*-Heptylphenanthrene-3-carboxylate (18g)

By following General Procedure C, **17g** (760 mg, 2.29 mmol) afforded **18g**.

Yield: 500 mg (65%); viscous pale-yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.2 Hz, 3 H), 1.24–1.54 (m, 8 H), 1.83 (quint, *J* = 7.6 Hz, 2 H), 3.13 (t, *J* = 7.6 Hz, 2 H), 4.02 (s, 3 H), 7.61 (s, 1 H), 7.65–7.74 (m, 2 H), 7.86 (d, *J* = 8.4 Hz, 1 H), 8.11–8.15 (m, 1 H), 8.18 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.82–8.86 (m, 1 H), 9.41 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.7, 29.2, 29.8, 30.2, 31.9, 33.6, 52.2, 123.4, 124.6, 125.1, 125.4, 126.5, 126.7, 127.0, 127.1, 128.1, 129.0, 131.0, 131.4, 134.9, 140.1, 167.5.

HRMS (CI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{26}O_2$: 357.1831; found: 357.1822.

Methyl 9-Phenethylphenanthrene-3-carboxylate (18h)

By following General Procedure C, **17h** (911 mg, 2.69 mmol) afforded **18h**.

Yield: 599 mg (64%); viscous clear oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.11–3.18 (m, 2 H), 3.42–3.48 (m, 2 H), 4.03 (s, 3 H), 7.21–7.26 (m, 1 H), 7.27–7.38 (m, 4 H), 7.60 (s, 1 H), 7.68–7.77 (m, 2 H), 7.84 (d, *J* = 8.8 Hz, 1 H), 8.18–8.22 (m, 1 H), 8.19 (dd, *J* = 8.8, 1.6 Hz, 1 H), 8.85–8.89 (m, 1 H), 9.42 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.5, 36.4, 52.3, 123.5, 124.4, 125.1, 125.7, 126.2, 126.6, 126.8, 127.2, 127.3, 128.2, 128.4, 128.5, 129.1, 130.9, 131.2, 134.7, 138.8, 141.7, 167.5.

HRMS (CI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{20}O_2$: 341.1542; found: 341.1543.

Methyl 9-[2-(4-Methoxycarbonylphenyl)ethyl]phenanthrene-3-carboxylate (18i)

By following General Procedure C, **17i** (1.02 g, 2.57 mmol) afforded **18i**.

Yield: 625 mg (61%); viscous clear oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.15–3.21 (m, 2 H), 3.40–3.47 (m, 2 H), 3.91 (s, 3 H), 4.02 (s, 3 H), 7.31 (d, *J* = 8.4 Hz, 2 H), 7.53 (s, 1 H), 7.67–7.76 (m, 2 H), 7.80 (d, *J* = 8.0 Hz, 1 H), 7.98 (d, *J* = 8.4 Hz, 2 H), 8.13–8.19 (m, 2 H), 8.83–8.88 (m, 1 H), 9.40 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.0, 36.4, 52.0, 52.3, 123.6, 124.2, 125.1, 125.8, 126.7, 126.9, 127.3, 127.4, 128.2, 128.5, 129.2, 129.9, 131.0, 131.1, 134.6, 138.2, 147.1, 167.1, 167.4.

HRMS (CI): *m*/*z* [M]$^+$ calcd for $C_{26}H_{22}O_4$: 398.1518; found: 398.1511.

General Procedure D; Ester Hydrolysis

The appropriate ester was dissolved in a mixture of either THF or dioxane (100 mL) and H_2O (20 mL). A NaOH or KOH solution (3 equiv.) dissolved in H_2O (20 mL) was then added dropwise and the resulting solution was heated either to reflux (THF) or to 75 °C (dioxane) until TLC analysis indicated complete hydrolysis. The reaction mixture was then cooled to r.t. and the organic solvent was removed in vacuo. The resulting aqueous suspension was topped up with H_2O, extracted with Et_2O (30 mL) and acidified to pH 1 by using aq 1 M HCl. The solid that precipitated out of solution at this stage was filtered off, washed copiously with H_2O and then dried over P_2O_5 to afford the desired acid. Several compounds required purification and were recrystallised from an appropriate solvent.

9-Ethylphenanthrene-3-carboxylic Acid (19a)

By following General Procedure D, **18a** (550 mg, 2.08 mmol), NaOH (250 mg, 6.24 mmol) and dioxane afforded **19a**.

Yield: 495 mg (95%); white solid; mp 245–249 °C (dec).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.39 (t, *J* = 7.6 Hz, 3 H), 3.15 (q, *J* = 7.6 Hz, 2 H), 7.72–7.79 (m, 3 H), 8.02 (d, *J* = 8.4 Hz, 1 H), 8.12 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.17–8.22 (m, 1 H), 8.86–8.91 (m, 1 H), 9.33 (s, 1 H), 13.10 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 14.8, 26.0, 123.8, 124.7, 124.8, 124.9, 127.0, 127.6, 127.9, 128.6, 128.8, 130.5, 131.2, 134.7, 141.2, 168.0.

HRMS (ESI): m/z [M – H]⁻ calcd for $C_{17}H_{14}O_2$: 249.0921; found: 249.0929.

Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.75; H, 5.91.

9-*n*-Propylphenanthrene-3-carboxylic Acid (19b)

By following General Procedure D, **18b** (525 mg, 1.89 mmol), NaOH (227 mg, 5.67 mmol) and dioxane afforded **19b**.

Yield: 465 mg (93%); white solid; mp 234–238 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.02 (t, J = 7.6 Hz, 3 H), 1.77 (m, J = 7.6 Hz, 2 H), 3.09 (t, J = 7.6 Hz, 2 H), 7.71–7.78 (m, 3 H), 8.00 (d, J = 8.4 Hz, 1 H), 8.11 (dd, J = 8.4, 1.6 Hz, 1 H), 8.16–8.21 (m, 1 H), 8.85–8.90 (m, 1 H), 9.32 (s, 1 H), 13.12 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 14.0, 22.9, 34.6, 123.3, 124.3, 124.6, 125.3, 126.5, 127.1, 127.3, 128.1, 128.2, 128.3, 130.1, 130.8, 134.1, 139.2, 167.5.

HRMS (ESI): m/z [M – H]⁻ calcd for $C_{18}H_{16}O_2$: 263.1078; found 263.1085.

Anal. Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 82.05; H, 6.39.

9-*n*-Butylphenanthrene-3-carboxylic acid (19c)

By following General Procedure D, **18c** (650 mg, 2.22 mmol), NaOH (266 mg, 6.66 mmol) and dioxane afforded **19c** as a white solid which was recrystallised from a mixture of toluene and EtOH.

Yield: 248 mg (40%); white solid; mp 208–211 °C;

^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.95 (t, J = 7.6 Hz, 3 H), 1.45 (m, J = 7.6 Hz, 2 H), 1.73 (quint, J = 7.6 Hz, 2 H), 3.12 (t, J = 7.2 Hz, 2 H), 7.71–7.79 (m, 3 H), 8.01 (d, J = 8.0 Hz, 1 H), 8.11 (dd, J = 8.0, 1.2 Hz, 1 H), 8.16–8.21 (m, 1 H), 8.85–8.90 (m, 1 H), 9.32 (s, 1 H), 13.08 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 13.8, 22.2, 31.9, 32.3, 123.3, 124.3, 124.6, 125.2, 126.5, 127.1, 127.3, 128.0, 128.2, 128.3, 130.1, 130.8, 134.1, 139.4, 167.5.

HRMS (ESI): m/z [M – H]⁻ calcd for $C_{19}H_{18}O_2$: 277.1234; found 277.1232.

Anal. Calcd for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52. Found: C, 81.85; H, 6.41.

9-*n*-Pentylphenanthrene-3-carboxylic Acid (19d)

By following General Procedure D, **18d** (573 mg, 1.88 mmol), NaOH (226 mg, 5.64 mmol) and dioxane afforded **19d** as a white solid, which was recrystallised from toluene.

Yield: 141 mg (26%); white solid; mp 194–197 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.87 (t, J = 7.2 Hz, 3 H), 1.29–1.47 (m, 4 H), 1.74 (quint, J = 7.2 Hz, 2 H), 3.10 (t, J = 7.2 Hz, 2 H), 7.70–7.79 (m, 3 H), 8.00 (d, J = 8.4 Hz, 1 H), 8.11 (dd, J = 8.4, 1.6 Hz, 1 H), 8.15–8.20 (m, 1 H), 8.84–8.92 (m, 1 H), 9.33 (s, 1 H), 13.13 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 14.5, 22.6, 30.0, 31.9, 33.2, 123.9, 124.9, 125.1, 125.8, 127.2, 127.6, 127.9, 128.6, 128.8, 128.9, 130.7, 131.4, 134.7, 140.0, 168.2.

MS (ESI⁻): m/z (%) = 291 (100) [M – H]⁻, 247 (46).

Anal. Calcd for $C_{20}H_{20}O_2$: C, 82.16; H, 6.89. Found: C, 82.00; H, 6.82.

9-(4-Methylpent-1-yl)phenanthrene-3-carboxylic Acid (3)

By following General Procedure D, **18e** (675 mg, 2.11 mmol), NaOH (253 mg, 6.33 mmol) and dioxane afforded **3** as a white solid, which was recrystallised from toluene.

Yield: 264 mg (41%); white solid; mp 193–196 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.82 (d, J = 6.4 Hz, 6 H), 1.24–1.33 (m, 2 H), 1.48–1.60 (m, 1 H), 1.64–1.74 (m, 2 H), 3.03 (t, J = 8.0 Hz, 2 H), 7.66–7.77 (m, 3 H), 7.97 (d, J = 8.4 Hz, 1 H), 8.09–8.16 (m, 2 H), 8.82–8.89 (m, 1 H), 9.32 (s, 1 H), 13.13 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 22.4, 27.3, 27.6, 32.8, 38.4, 123.2, 124.3, 124.5, 125.1, 126.5, 127.0, 127.3, 128.0, 128.2, 128.3, 130.1, 130.7, 134.1, 139.4, 167.5.

MS (ESI⁻): m/z (%) = 305 (100) [M – H]⁻, 261 (25).

Anal. Calcd for $C_{21}H_{22}O_2$: C, 82.32; H, 7.24. Found: C, 82.30; H, 7.17.

9-*n*-Hexylphenanthrene-3-carboxylic Acid (19f)

By following General Procedure D, **18f** (679 mg, 2.12 mmol), NaOH (254 mg, 6.36 mmol) and dioxane afforded **19f** as a white solid, which was recrystallised from toluene.

Yield: 221 mg (34%); white solid; mp 196–199 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.85 (t, J = 7.2 Hz, 3 H), 1.22–1.37 (m, 4 H), 1.43 (quint, J = 7.2 Hz, 2 H), 1.73 (quint, J = 7.2 Hz, 2 H), 3.10 (t, J = 7.2 Hz, 2 H), 7.71–7.79 (m, 3 H), 8.00 (d, J = 8.4 Hz, 1 H), 8.11 (dd, J = 8.4, 1.6 Hz, 1 H), 8.14–8.20 (m, 1 H), 8.84–8.91 (m, 1 H), 9.32 (s, 1 H), 13.12 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 13.9, 22.1, 28.8, 29.7, 31.1, 32.7, 123.3, 124.3, 124.6, 125.2, 126.6, 127.1, 127.3, 128.1, 128.2, 128.3, 130.1, 130.8, 134.1, 139.4, 167.6.

MS (ESI⁻): m/z (%) = 305 (100) [M – H]⁻, 261 (20).

Anal. Calcd for $C_{21}H_{22}O_2$: C, 82.32; H, 7.24. Found: C, 82.01; H, 7.08.

9-*n*-Heptylphenanthrene-3-carboxylic Acid (19g)

By following General Procedure D, **18g** (450 mg, 1.35 mmol), NaOH (162 mg, 4.05 mmol) and dioxane afforded **19g** as a white solid, which was recrystallised from toluene.

Yield: 317 mg (73%); white solid; mp 185–188 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.83 (t, J = 7.2 Hz, 3 H), 1.18–1.45 (m, 8 H), 1.72 (quint, J = 7.6 Hz, 2 H), 3.08 (t, J = 7.6 Hz, 2 H), 7.70–7.78 (m, 3 H), 7.99 (d, J = 8.0 Hz, 1 H), 8.11 (dd, J = 8.0, 1.2 Hz, 1 H), 8.14–8.19 (m, 1 H), 8.85–8.90 (m, 1 H), 9.32 (s, 1 H), 13.09 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 13.9, 22.0, 28.5, 29.1, 29.8, 31.2, 32.6, 123.3, 124.2, 124.6, 125.2, 126.6, 127.0, 127.3, 128.2, 128.3, 130.1, 130.8, 134.1, 139.4, 167.6.

HRMS (ESI): m/z [M – H]⁻ calcd for $C_{22}H_{24}O_2$: 319.1704; found: 319.1707.

Anal. Calcd for $C_{22}H_{24}O_2$: C, 82.46; H, 7.55. Found: C, 82.12; H, 7.50.

9-Phenethylphenanthrene-3-carboxylic Acid (19h)

By following General Procedure D, **18h** (512 mg, 1.50 mmol), NaOH (180 mg, 4.50 mmol) and dioxane afforded **19h** as a white solid, which was recrystallised from a mixture of toluene and EtOH.

Yield: 105 mg (22%); white solid; mp 236–237 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.07 (t, J = 8.0 Hz, 2 H), 3.41 (t, J = 8.0 Hz, 2 H), 7.18–7.24 (m, 1 H), 7.27–7.37 (m, 4 H), 7.73–7.81 (m, 3 H), 7.98 (d, J = 8.4 Hz, 1 H), 8.11 (dd, J = 8.4, 1.6 Hz, 1 H), 8.26–8.32 (m, 1 H), 8.86–8.93 (m, 1 H), 9.34 (s, 1 H), 13.10 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 34.6, 35.7, 123.3, 124.3, 124.5, 125.4, 125.9, 126.6, 127.1, 127.5, 128.0, 128.1, 128.2, 128.3, 128.3, 130.1, 130.7, 134.0, 138.5, 141.4, 167.5.

MS (ESI⁻): m/z (%) = 325 (100) [M – H]⁻.

Anal. Calcd for $C_{23}H_{18}O_2$: C, 84.64; H, 5.56. Found: C, 84.53; H, 5.58.

9-[2-(4-Carboxyphenyl)ethyl]phenanthrene-3-carboxylic Acid (19j)

By following General Procedure D, **18i** (400 mg, 1.00 mmol), KOH (337 mg, 6.00 mmol) and THF afforded **19j**.

Yield: 216 mg (58%); off-white solid; mp >250 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.15 (t, *J* = 8.0 Hz, 2 H), 3.45 (t, *J* = 8.0 Hz, 2 H), 7.47 (d, *J* = 8.4 Hz, 2 H), 7.75–7.81 (m, 3 H), 7.88 (d, *J* = 8.4 Hz, 2 H), 7.98 (d, *J* = 8.0 Hz, 1 H), 8.11 (dd, *J* = 8.0, 1.6 Hz, 1 H), 8.27–8.32 (m, 1 H), 8.87–8.93 (m, 1 H), 9.34 (s, 1 H), 12.97 (br s, 1 H), 13.15 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 34.1, 35.6, 123.3, 124.3, 124.6, 125.5, 126.6, 127.2, 127.5, 128.2, 128.3, 128.4, 128.5, 128.6, 129.4, 130.1, 130.6, 134.0, 138.2, 146.7, 167.2, 167.5.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{24}H_{18}O_4$: 369.1132; found: 369.1142.

Anal. Calcd for $C_{24}H_{18}O_4 \cdot 0.63\ H_2O$: C, 75.51; H, 5.09. Found: C, 75.82; H, 5.48.

Methyl 9-Vinylphenanthrene-3-carboxylate (17a)

A flask containing **16** (1.00 g, 3.17 mmol) was evacuated and backfilled with argon three times. Anhydrous toluene (50 mL) was added to the flask by using a cannula and the resultant solution was degassed with argon for approximately 30 min. $Pd(PPh_3)_4$ (109.9 mg, 3 mol%) was then added and the mixture was degassed for a further 10 min before vinyl(tri-*n*-butyl)tin (1.12 mL, 3.80 mmol) was added. The resultant mixture was heated at reflux for 4 h before cooling to r.t. and filtered through Celite to remove any precipitated Pd(0). The filtrate was then poured into a stirring mixture of EtOAc (50 mL) and sat. aq NH_4Cl (50 mL). The organic layer was isolated and washed with aq 1 M KF (2 × 50 mL) to remove any tin by-products. The white solid (Bu_3SnF), which precipitated from solution after the first wash, was removed by filtration through Celite. The organic layer was then isolated, washed with H_2O (50 mL), brine (50 mL), dried over $MgSO_4$ and concentrated in vacuo to afford a dark-orange oil. Purification by flash chromatography (EtOAc–hexane, 5%) afforded **17a**.

Yield: 550 mg (66%); pale-yellow oil that partially solidified on standing.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.03 (s, 3 H), 5.59 (dd, *J* = 10.8, 1.6 Hz, 1 H), 5.91 (dd, *J* = 17.2, 1.6 Hz, 1 H), 7.48 (ddd, *J* = 17.2, 10.8, 0.8 Hz, 1 H), 7.65–7.77 (m, 2 H), 7.86 (s, 1 H), 7.93 (d, *J* = 8.4 Hz, 1 H), 8.16–8.22 (m, 2 H), 8.81–8.86 (m, 1 H), 9.41 (d, *J* = 0.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.3, 118.7, 123.4, 124.1, 124.9, 125.2, 126.8, 127.3, 127.3, 127.8, 128.9, 129.8, 130.7, 130.8, 134.8, 134.9, 137.4, 167.5.

HRMS (ES): *m*/*z* [M]$^+$ calcd for $C_{18}H_{14}O_2$: 262.0994; found: 262.0999.

Methyl 9-Cyclopropylphenanthrene-3-carboxylate (20)

Diiodomethane (1.82 g, 6.8 mmol) was dissolved in anhydrous CH_2Cl_2 (10 mL) and $ZnEt_2$ (1.0 M in hexane, 3.4 mL, 3.4 mmol) was added to this solution at 0 °C, followed by a solution of **17a** (450 mg, 1.7 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred vigorously overnight then the reaction was quenched with aq 1 M HCl. The mixture was extracted with Et_2O (50 mL) and the organic layer was isolated, dried over $MgSO_4$ and concentrated in vacuo. The resultant residue was purified by flash chromatography (EtOAc–hexane, 5%) to afford **20**.

Yield: 400 mg (85%); viscous clear oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83–0.89 (m, 2 H), 1.10–1.16 (m, 2 H), 2.31–2.40 (m, 1 H), 4.02 (s, 3 H), 7.53 (s, 1 H), 7.67–7.76 (m, 2 H), 7.82 (d, *J* = 9.0 Hz, 1 H), 8.16 (d, *J* = 9.0 Hz, 1 H), 8.49–8.53 (m, 1 H), 8.79–8.82 (m, 1 H), 9.38 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 6.5, 6.5, 14.1, 52.3, 123.2, 123.9, 125.1, 125.3, 126.6, 127.0, 127.1, 127.3, 128.3, 129.1, 130.7, 132.9, 135.0, 140.4, 167.6.

HRMS (CI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{16}O_2$: 277.1229; found: 277.1231.

9-Cyclopropylphenanthrene-3-carboxylic Acid (2)

Compound **20** (350 mg, 1.27 mmol) was dissolved in dioxane (10 mL) and sat. aq LiOH was added dropwise until the reaction mixture became a slurry (ca. 1 mL). The mixture was stirred at r.t. overnight, then extracted with Et_2O (20 mL) before being acidified to pH 1 with aq 1 M HCl. The acid precipitated out of solution and was subsequently collected by filtration, washed with H_2O and dried over P_2O_5 to afford **2**.

Yield: 310 mg (93%); white solid; mp >250 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.81–0.85 (m, 2 H), 1.10–1.15 (m, 2 H), 2.41–2.49 (m, 1 H), 7.69 (s, 1 H), 7.77–7.80 (m, 2 H), 8.02 (d, *J* = 8.8 Hz, 1 H), 8.10 (d, *J* = 8.8 Hz, 1 H), 8.52–8.54 (m, 1 H), 8.85–8.88 (m, 1 H), 9.31 (s, 1 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 7.0, 7.0, 13.9, 123.4, 123.5, 124.7, 125.5, 127.0, 127.8, 127.9, 128.6, 128.7, 129.0, 130.3, 132.6, 134.7, 140.4, 168.0.

MS (ESI$^-$): *m*/*z* (%) = 261 (100) [M – H]$^-$.

Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.84; H, 5.47.

Methyl 9-(Thiophen-3-yl)phenanthrene-3-carboxylate (21)

A flame-dried flask was successively charged with **16** (1.00 g, 3.17 mmol), 3-thienylboronic acid (573 mg, 4.48 mmol), K_2CO_3 (1.31 g, 9.51 mmol) and $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (261 mg, 0.32 mmol). After each addition, the flask was briefly evacuated and backfilled with argon. Degassed anhydrous DME (75 mL) was then added into the flask by using a cannula and the resultant mixture was stirred at 80 °C for 24 h. After cooling to r.t., the reaction mixture was diluted with EtOAc (100 mL) and H_2O (20 mL). The organic layer was isolated and washed with H_2O (2 × 25 mL) and then brine (2 × 25 mL). After drying over $MgSO_4$, concentration in vacuo afforded a dark-brown/black residue, which was partially purified by flash chromatography (EtOAc–hexane, 10%) to give a pale-yellow solid (618 mg, 61%), which ^{1}H NMR analysis showed was a mixture of **21** and **16** (ca. 75:25). The mixture was taken forward to the next step without further purification.

Compound 21: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.04 (s, 3 H), 7.35 (dd, *J* = 4.8, 1.6 Hz, 1 H), 7.49 (dd, *J* = 2.8, 1.6 Hz, 1 H), 7.51 (dd, *J* = 4.8, 2.8 Hz, 1 H), 7.59–7.64 (m, 1 H), 7.71–7.76 (m, 1 H), 7.77 (s, 1 H), 7.91 (d, *J* = 8.4 Hz, 1 H), 8.08 (dd, *J* = 8.4, 1.2, 1 H), 8.21 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.87 (d, *J* = 8.4 Hz, 1 H), 9.45 (s, 1 H).

9-(Thiophen-3-yl)phenanthrene-3-carboxylic Acid (22)

By following General Procedure D, **21** (541 mg, 1.70 mmol), NaOH (204 mg, 5.10 mmol) and dioxane afforded a pale-yellow solid, which was recrystallised four times from glacial acetic acid to give **22**.

Yield: 117 mg (23%); mp >250 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.42 (dd, *J* = 4.8, 1.6 Hz, 1 H), 7.68–7.73 (m, 1 H), 7.77–7.83 (m, 3 H), 7.94 (s, 1 H), 8.04 (dd, *J* = 8.4, 1.2 Hz, 1 H), 8.11 (d, *J* = 8.4 Hz, 1 H), 8.16 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.95 (d, *J* = 8.4 Hz, 1 H), 9.39 (s, 1 H), 13.15 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 123.7, 124.8, 125.3, 126.8, 127.0, 127.3, 128.0, 128.0, 129.1, 129.3, 129.4, 129.8, 130.7, 131.0, 134.2, 135.8, 140.3, 168.0.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{19}H_{12}O_2S$: 303.0485; found: 303.0495.

Anal. Calcd for $C_{19}H_{12}O_2S·0.55\ H_2O$: C, 72.61; H, 4.20. Found: C, 72.61; H, 4.02.

Methyl 9-(4-Methoxy-4-oxobutan-2-yl)phenanthrene-3-carboxylate (23)

To a cold (–78 °C) stirring mixture of CuI (25.2 g, 0.13 mol) and NaI (36 g, 0.24 mol) in Me_2S (79 mL) and CH_2Cl_2 (72 mL), was added methylmagnesium chloride (3.0 M in THF, 41 mL, 0.12 mol) and TMSCl (31 mL, 0.24 mol). The mixture was then stirred for 30 min at –78 °C and a solution of **14** (7.7 g, 24 mmol) in CH_2Cl_2 (72 mL) was added. The resultant mixture was stirred at –78 °C for 10 min and then slowly warmed to r.t. After stirring for 3 h, the reaction was quenched with sat. aq NH_4Cl. The organic layer was isolated and the aqueous phase was extracted with Et_2O (100 mL). The organic layers were pooled, dried over $MgSO_4$, and concentrated in vacuo. Purification of the resultant residue by flash column chromatography (EtOAc–hexane, 5%) afforded **23**.

Yield: 4.83 g (60%); light coloured oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (d, *J* = 7.8 Hz, 3 H), 2.69 (dd, *J* = 7.8, 12.0 Hz, 1 H), 2.89 (dd, *J* = 7.8, 12.0 Hz, 1 H), 3.87 (s, 3 H), 3.93 (s, 3 H), 4.06 (m, *J* = 7.8 Hz, 1 H), 7.75–7.78 (m, 2 H), 7.84 (s, 1 H), 7.92 (d, *J* = 8.7 Hz, 1 H), 7.94 (d, *J* = 8.7 Hz, 1 H), 8.00–8.10 (m, 1 H), 8.92–8.95 (m, 1 H), 9.33 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7, 31.0, 41.6, 54.3, 56.7, 122.8, 124.0, 124.3, 124.7, 127.0, 127.6, 128.0, 128.7, 128.8, 129.1, 130.6, 130.7, 134.1, 143.4, 168.0, 173.8.

HRMS (CI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{20}O_4$: 337.1440; found: 337.1442.

9-(4-Methoxy-4-oxobutan-2-yl)phenanthrene-3-carboxylic Acid (24)

By following General Procedure D, **23** (508 mg, 1.51 mmol), NaOH (362.4 mg, 9.06 mmol) and dioxane afforded **24**.

Yield: 377 mg (81%); white solid; mp >250 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.42 (d, *J* = 7.8 Hz, 3 H), 2.68 (dd, *J* = 7.8, 12.0 Hz, 1 H), 2.87 (dd, *J* = 7.8, 12.0 Hz, 1 H), 4.07 (m, *J* = 7.8 Hz, 1 H), 7.77–7.80 (m, 2 H), 7.86 (s, 1 H), 8.06 (d, *J* = 8.7 Hz, 1 H), 8.13 (d, *J* = 8.7 Hz, 1 H), 8.27–8.30 (m, 1 H), 8.90–8.93 (m, 1 H), 9.33 (s, 1 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 21.7, 31.0, 41.6, 122.8, 124.0, 124.3, 124.7, 127.0, 127.6, 128.0, 128.7, 128.8, 129.1, 130.6, 130.7, 134.5, 143.4, 168.0, 173.8.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{19}H_{16}O_4$: 307.0976; found: 307.0969.

Anal. Calcd for $C_{19}H_{16}O_4$: C, 74.01; H, 5.23. Found: C, 74.07; H, 5.18.

Methyl 9-(3-Hydroxy-2-methoxy-4-oxobutan-2-yl)phenanthrene-3-carboxylate (25)

To a stirring solution of **23** (2.74 g, 8.15 mmol) in anhydrous THF (40 mL) at –78 °C, was added dropwise KHMDS (0.5 M in toluene, 17.3 mL, 8.65 mmol) followed by a solution of 2-tosyl-3-phenyloxaziridine[8] (3.2 g, 12.25 mmol) in THF (20 mL). After complete addition, the mixture was warmed to r.t. and stirred for approximately 2 h. H_2O (30 mL) and Et_2O (60 mL) were then added and the organic layer was isolated and washed with sat. sodium sulfite solution (20 mL), aq 1 M HCl (20 mL), and brine (20 mL). Concentration in vacuo afforded **25** as an oil, which was utilised in the next step without further purification or analysis.

Methyl 9-(1-Oxopropan-2-yl)phenanthrene-3-carboxylate (26)

A stirred solution of **25** in anhydrous THF (20 mL) was cooled to 0 °C and $LiBH_4$ (227 mg, 12.3 mmol) was added portionwise over a period of 10 min. After complete addition, the mixture was stirred for 30 min at 0 °C and then at r.t. until TLC analysis indicated complete conversion. The reaction was then quenched by the addition of aq 1 M HCl (5 mL) and extracted with Et_2O (2 × 30 mL). The organic layers were pooled, dried over $MgSO_4$ and concentrated in vacuo to obtain the crude 1,2-diol as an orange oil. This intermediate was dissolved in a mixture of *t*-BuOH and H_2O (30 mL, 4:1), and $NaIO_4$ (5.13 g, 24 mmol) was added to the solution. The resultant mixture was stirred at r.t. for 30 min before the reaction was quenched by the addition of H_2O (20 mL). The aqueous mixture was then extracted with Et_2O (2 × 30 mL) and the organic layers were pooled, dried over $MgSO_4$, and concentrated in vacuo. Purification of the resultant residue by flash chromatography (EtOAc–hexane, 5%) afforded **26**.

Yield: 1.55 g (65%); viscous light-orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.67 (d, *J* = 7.2 Hz, 3 H), 4.03 (s, 3 H), 4.42 (q, *J* = 7.2 Hz, 1 H), 7.57 (s, 1 H), 7.68–7.79 (m, 2 H), 7.89 (d, *J* = 8.4 Hz, 1 H), 8.06–8.10 (m, 1 H), 8.21 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.85–8.89 (m, 1 H), 9.41 (s, 1 H), 9.82 (d, *J* = 1.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 49.0, 52.3, 123.8, 123.9, 125.0, 126.0, 126.9, 127.3, 127.6, 128.1, 128.6, 129.5, 130.7, 131.2, 134.2, 135.3, 167.2, 200.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{16}O_3$: 315.0997; found: 315.0992.

Methyl 9-(1-Hydroxypropan-2-yl)phenanthrene-3-carboxylate (27)

To a stirred solution of **26** (1.0 g, 3.42 mmol) in anhydrous THF (100 mL) was added portionwise $NaBH_4$ (388 mg, 10.26 mmol). *i*-PrOH (2 mL) was then added and the resultant suspension was stirred at r.t. until TLC analysis indicated complete reduction. Excess $NaBH_4$ was then destroyed by the dropwise addition of H_2O. The solvent was then removed in vacuo and the resultant residue was dissolved in a mixture of EtOAc (50 mL) and H_2O (50 mL). The organic layer was isolated and the aqueous layer was further extracted with EtOAc (2 × 25 mL). The organic layers were pooled, washed with H_2O (25 mL), brine (25 mL), dried over $MgSO_4$ and concentrated in vacuo. Purification of the resultant residue by flash column chromatography (EtOAc–hexane, 10%) afforded **27**.

Yield: 985 mg (98%); viscous pale-yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.51 (d, *J* = 6.7 Hz, 3 H), 3.85–3.91 (m, 2 H), 4.00 (s, 3 H), 4.05 (m, 1 H), 7.64–7.73 (m, 3 H), 7.87 (d, *J* = 8.8 Hz, 1 H), 8.15–8.22 (m, 2 H), 8.83 (d, *J* = 8.8 Hz, 1 H), 9.37 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.8, 21.1, 52.4, 67.7, 123.4, 123.7, 125.1, 126.7, 127.0, 127.3, 127.6, 128.6, 129.1, 131.1, 131.3, 134.5, 140.8, 167.5.

HRMS (CI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{18}O_3$: 295.1329; found: 295.1320.

9-(1-Hydroxypropan-2-yl)phenanthrene-3-carboxylic Acid (28)

By following General Procedure D, **27** (301 mg, 1.02 mmol), NaOH (122 mg, 3.06 mmol), and dioxane afforded **28**.

Yield: 213 mg (75%); white solid; mp >250 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.44 (d, *J* = 8.0 Hz, 3 H), 3.54–3.64 (m, 1 H), 3.69–3.78 (m, 1 H), 3.79–3.87 (m, 1 H), 4.82 (s, 1 H), 8.05 (d, *J* = 8.0 Hz, 1 H), 8.12 (d, *J* = 8.0 Hz, 1 H), 8.27–8.34 (m, 1 H), 8.86–8.93 (m, 1 H), 9.33 (s, 1 H), 13.14 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 17.8, 36.5, 66.3, 123.2, 123.4, 124.1, 124.3, 126.5, 127.0, 127.4, 128.1, 128.6, 130.1, 130.9, 134.1, 141.6, 167.6.

HRMS-ESI: *m*/*z* [M – H]$^-$ calcd for $C_{18}H_{16}O_3$: 279.1027; found 279.1019.

Anal. Calcd for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 77.37; H, 5.89.

Methyl 9-(Propan-2-yl)phenanthrene-3-carboxylate (29)

To a stirred solution of **27** (505 mg, 1.72 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added Et_3N (0.25 mL, 1.80 mmol) followed by methanesulfonyl chloride (0.14 mL, 1.80 mmol). The resultant mixture was stirred at 0 °C for 1 h and then at r.t. for 3 h. After this time, the reaction was diluted with CH_2Cl_2 (20 mL) and H_2O (20 mL) and the organic layer was isolated, washed with aq 1 M HCl (10 mL), brine (10 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude mesylate thus obtained was dissolved in acetone (75 mL) and sodium iodide (645 mg, 4.3 mmol) was added to the solution. The resultant mixture was heated at reflux for 24 h before cooling to r.t. Filtration then removed any solids, with the filter cake being rinsed with acetone. The filtrate and washes were combined and concentrated in vacuo. The resultant residue was dissolved in Et_2O (40 mL) and washed with H_2O (20 mL), sat. sodium sulfite solution (15 mL), H_2O (20 mL), and dried over $MgSO_4$. Concentration in vacuo afforded the crude iodo compound, which was then dissolved in dioxane (100 mL). Et_3N (0.25 mL, 1.80 mmol) was added and the resultant solution was hydrogenated under 3 bar of hydrogen in the presence of 10 wt% palladium on activated carbon (50 mg) for 18 h. The reaction mixture was then filtered through a Celite pad before being concentrated in vacuo. The resultant residue was taken up in CH_2Cl_2 (50 mL) and washed successively with aq 1 M HCl, H_2O, and brine (25 mL each). Drying over $MgSO_4$ followed by concentration in vacuo gave a residue, which was purified by flash column chromatography (EtOAc–hexane, 10%) to afford **29**.

Yield: 349 mg (73%); pale-yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49 (d, *J* = 7.2 Hz, 6 H), 3.74 (sept, *J* = 7.2 Hz, 1 H), 3.85 (s, 3 H), 7.66–7.72 (m, 3 H), 7.86 (d, *J* = 8.7 Hz, 1 H), 8.18–8.20 (m, 2 H), 8.82–8.86 (m, 1 H), 9.40 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.2, 28.8, 52.2, 121.7, 123.5, 124.1, 124.9, 126.5, 126.6, 127.0, 127.1, 128.3, 128.8, 131.0, 134.9, 145.5, 167.5.

HRMS (CI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{18}O_2$: 279.1380; found: 279.1371.

9-(Propan-2-yl)phenanthrene-3-carboxylic Acid (30)

By following General Procedure D, **29** (205 mg, 0.74 mmol), NaOH (89 mg, 2.22 mmol) and dioxane afforded **30**.

Yield: 166 mg (85%); white solid; mp 226–230 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.42 (d, *J* = 6.8 Hz, 6 H), 3.78 (sept, *J* = 6.8 Hz, 1 H), 7.72–7.79 (m, 2 H), 7.83 (s, 1 H), 8.06 (d, *J* = 8.4 Hz, 1 H), 8.12 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.24–8.31 (m, 1 H), 8.86–8.92 (m, 1 H), 9.33 (s, 1 H), 13.06 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 23.0, 28.1, 121.6, 123.4, 124.1, 124.2, 126.5, 127.0, 127.3, 128.1, 128.1, 128.5, 130.1, 130.3, 134.1, 145.0, 167.5.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{18}H_{16}O_2$: 263.1078; found: 263.1070.

Anal. Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.65; H, 6.01.

Methyl 9-(Hydroxymethyl)phenanthrene-3-carboxylate (31)

To a stirred solution of **15** (1.10 g, 4.16 mmol) in anhydrous THF (150 mL) was added slowly and portionwise $NaBH_4$ (472 mg, 12.48 mmol). *i*-PrOH (2 mL) was then added and the resultant suspension was stirred at r.t. until TLC analysis indicated complete reduction. Excess $NaBH_4$ was destroyed by the dropwise addition of H_2O. Concentration in vacuo afforded a solid, which was dissolved in a mixture of EtOAc (50 mL) and H_2O (50 mL). The organic layer was isolated and the aqueous layer was further extracted with EtOAc (2 × 25 mL). The organic layers were pooled, washed with H_2O (25 mL) and brine (25 mL), dried over $MgSO_4$ and concentrated in vacuo to afford **31**.

Yield: 1.05 g (95%); pale-yellow solid; mp 179–182 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.96 (s, 3 H), 5.05 (d, *J* = 5.6 Hz, 2 H), 5.52 (t, *J* = 5.6 Hz, 1 H), 7.69–7.81 (m, 2 H), 7.96 (s, 1 H), 8.07–8.18 (m, 3 H), 8.85–8.91 (m, 1 H), 9.34 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 52.2, 61.2, 123.2, 123.3, 124.3, 124.3, 126.3, 127.2, 127.2, 127.4, 128.7, 128.9, 129.7, 129.8, 134.2, 139.1, 166.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{14}O_3$: 289.0835; found: 289.0832.

Anal. Calcd for $C_{17}H_{14}O_3$: C, 76.68; H, 5.30. Found: C, 76.35; H, 5.31.

9-(Hydroxymethyl)phenanthrene-3-carboxylic Acid (32)

By following General Procedure D, **31** (500 mg, 1.88 mmol), NaOH (226 mg, 5.64 mmol) and dioxane afforded **32** as a light-yellow solid which was recrystallised from a mixture of toluene and EtOH.

Yield: 180 mg (38%); mp >250 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 5.04 (s, 2 H), 7.67–7.78 (m, 2 H), 7.93 (s, 1 H), 8.06 (d, *J* = 8.4 Hz, 1 H), 8.13 (dd, *J* = 8.4, 0.8 Hz, 2 H), 8.85 (d, *J* = 8.0 Hz, 1 H), 9.32 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 61.4, 123.2, 123.6, 124.5, 126.8, 127.4, 127.5, 128.5, 128.8, 128.9, 130.0, 134.1, 138.9, 167.7.

MS (ESI$^-$): *m*/*z* (%) = 251 (100) [M – H]$^-$.

Anal. Calcd for $C_{16}H_{12}O_3 \cdot 0.25\ H_2O$: C, 74.84; H, 4.91. Found: C, 74.82; H, 4.83.

Methyl 9-(Bromomethyl)phenanthrene-3-carboxylate (33)

A flask containing **31** (1.17 g, 4.39 mmol) was briefly evacuated and backfilled with argon. Anhydrous CH_2Cl_2 (100 mL) was added to the flask by using a cannula and the resulting solution was cooled to 0 °C. Phosphorus tribromide (1.65 mL, 17.56 mmol) was then added dropwise to the stirring solution. After complete addition, the reaction mixture was stirred at 0 °C for 30 min and then at r.t. until TLC analysis confirmed complete conversion. After approximately 2 h, the reaction mixture was again cooled to 0 °C and excess PBr_3 was destroyed by the dropwise addition of saturated $NaHCO_3$ solution. The organic layer was isolated, dried over $MgSO_4$ and concentrated in vacuo to afford an off-white solid, which was dissolved in Et_2O (100 mL) and washed successively with H_2O (40 mL) and brine (40 mL). Drying over $MgSO_4$ followed by concentration in vacuo yielded **33**.

Yield: 994 mg (69%); off-white solid; mp 135–139 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.03 (s, 3 H), 5.00 (s, 2 H), 7.73–7.78 (m, 2 H), 7.86 (s, 1 H), 7.90 (d, *J* = 8.4 Hz, 1 H), 8.20 (dd, *J* = 8.4, 1.8 Hz, 1 H), 8.22–8.27 (m, 1 H), 8.80–8.87 (m, 1 H), 9.39 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.8, 52.4, 123.5, 124.7, 125.1, 126.9, 127.4, 127.5, 128.1, 128.6, 128.8, 129.6, 130.3, 131.2, 134.0, 134.3, 167.2.

MS (CI$^+$): *m*/*z* (%) = 328/330 (69/67) [M$^+$], 249 (100).

Anal. Calcd for $C_{17}H_{13}O_2Br$: C, 62.03; H, 3.98; Found: C, 62.31; H, 4.31.

Methyl 9-Methylphenanthrene-3-carboxylate (34)

Compound **33** (500 mg, 1.52 mmol) and Et_3N (0.21 mL, 1.52 mmol) were dissolved in dioxane (100 mL) and the resultant solution was hydrogenated under 3 bar of hydrogen in the presence of 10 wt% palladium on activated carbon (50 mg) for 18 h. The reaction mixture was then filtered through a Celite pad before being concentrated in vacuo. The resultant solid was taken up in CH_2Cl_2 (50 mL) and washed successively with aq 1 M HCl, H_2O, and brine (25 mL each). Drying over $MgSO_4$ followed by concentration in vacuo afforded **34**.

Yield: 344 mg (91%); off-white solid; mp 152–156 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.74 (s, 3 H), 4.02 (s, 3 H), 7.58 (s, 1 H), 7.65–7.75 (m, 2 H), 7.81 (d, *J* = 8.4 Hz, 1 H), 8.04–8.09 (m, 1 H), 8.43 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.78–8.83 (m, 1 H), 9.38 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.2, 52.2, 123.2, 124.7, 125.0, 126.2, 126.5, 126.8, 127.0, 127.0, 127.8, 129.0, 130.5, 132.1, 134.8, 135.5, 167.5.

HRMS (CI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{14}O_2$: 251.1067; found: 251.1059.

9-Methylphenanthrene-3-carboxylic Acid (35)

By following General Procedure D, **34** (310 mg, 1.24 mmol), NaOH (149 mg, 3.72 mmol) and dioxane afforded **35**.

Yield: 199 mg (68%); off-white solid; mp >250 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.70 (s, 3 H), 7.69–7.78 (m, 3 H), 7.95 (d, *J* = 8.0 Hz, 1 H), 8.09 (dd, *J* = 8.0, 1.2 Hz, 1 H), 8.09–8.12 (m, 1 H), 8.82–8.86 (m, 1 H), 9.33 (s, 1 H), 13.01 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 19.7, 123.1, 124.3, 124.9, 125.9, 126.6, 127.2, 127.4, 128.0, 128.0, 128.3, 130.0, 131.5, 134.2, 135.2, 167.5.

MS (ESI$^-$): *m*/*z* (%) = 235 (100) [M – H]$^-$.

Anal. Calcd for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12. Found: C, 81.08; H, 5.40.

Methyl 9-(Isopropylaminomethyl)phenanthrene-3-carboxylate (36)

To a stirred mixture of **15** (750 mg, 2.84 mmol) and isopropylamine (0.41 mL, 4.97 mmol) in anhydrous DCE (100 mL) was added sodium triacetoxyborohydride (843 mg, 3.98 mmol). The resultant suspension was stirred at r.t. for 24 h. At this point TLC analysis indicated incomplete conversion, so 12 drops of glacial acetic acid were added to help catalyse the reaction. Stirring was continued for another 24 h, then excess sodium triacetoxyborohydride was destroyed through the dropwise addition of sat. aq $NaHCO_3$ solution. EtOAc (40 mL) was added and the organic phase was isolated, washed with brine (40 mL), dried over $MgSO_4$ and concentrated in vacuo to give an orange oil. Purification by flash chromatography (EtOAc then MeOH–EtOAc, 20%) afforded **36**.

Yield: 779 mg (89%); golden coloured oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21 (d, *J* = 6.4 Hz, 6 H), 2.98–3.09 (m, 1 H), 4.02 (s, 3 H), 4.27 (s, 2 H), 7.65–7.74 (m, 2 H), 7.77 (s, 1 H), 7.88 (d, *J* = 8.4 Hz, 1 H), 8.18 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.80–8.84 (m, 1 H), 9.38 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.1, 49.1, 49.6, 52.3, 123.4, 124.3, 125.0, 125.5, 126.6, 126.9, 127.2, 127.5, 128.4, 129.4, 130.9, 130.9, 134.5, 137.3, 167.4.

HRMS (ESI): *m*/*z* [M]$^+$ calcd for $C_{20}H_{21}NO_2$: 305.1572; found: 305.1598.

9-(Isopropylaminomethyl)phenanthrene-3-carboxylic Acid (37)

To a stirring solution of **36** (740 mg, 2.41 mmol) in a mixture of dioxane (80 mL) and H_2O (20 mL) was added dropwise a solution of NaOH (289 mg, 7.23 mmol) dissolved in H_2O (20 mL). The resultant mixture was stirred at 75 °C until TLC analysis indicated complete hydrolysis. After 4 h, the reaction mixture was cooled to r.t. and the dioxane was removed in vacuo. The resultant aqueous solution was topped up with H_2O and acidified to pH 3 by using aq 1 M HCl. No product precipitated from solution, so the pH was readjusted to pH 7 by using aq 1 M NaOH and the solution was concentrated in vacuo to afford a white solid. The crude product was dissolved in a minimum volume of H_2O and then absorbed onto AG-50 resin. The column was first eluted with H_2O until the pH of the aqueous fractions was neutral. The product was then eluted with aq 1 M pyridine. Concentration of the aqueous pyridine fractions in vacuo afforded **37** as a white solid, which was azeotroped with water to remove any remaining pyridine and then dried over P_2O_5.

Yield: 496 mg (70%); mp >250 °C.

^{1}H NMR (400 MHz, D_2O/NaOD, pH 11): δ = 0.99 (d, *J* = 6.4 Hz, 6 H), 2.61–2.72 (m, 1 H), 3.46 (s, 2 H), 6.99 (s, 1 H), 7.33–7.39 (m, 1 H), 7.42–7.52 (m, 3 H), 7.91 (dd, *J* = 8.0, 1.2 Hz, 1 H), 8.42 (d, *J* = 8.0 Hz, 1 H), 8.88 (s, 1 H).

^{13}C NMR (125 MHz, D_2O/NaOD, pH 11): δ = 21.2, 47.1, 47.9, 122.8, 123.1, 123.5, 124.5, 126.5, 126.6, 126.7, 127.8, 128.4, 129.5, 129.8, 132.4, 133.6, 134.1, 175.1.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{19}H_{19}NO_2$: 292.1343; found: 292.1352.

Anal. Calcd for $C_{19}H_{19}NO_2 \cdot 0.55\ H_2O$: C, 73.93; H, 6.76; N, 4.54. Found: C, 73.90; H, 6.41; N, 4.45.

Methyl 9-(3-Methoxy-3-oxopropyl)phenanthrene-3-carboxylate (38)

Compound **14** (1.00 g, 3.12 mmol) was dissolved in EtOAc (150 mL) with the aid of stirring and heating. The resultant solution was hydrogenated under 3 bar of hydrogen in the presence of 10 wt% palladium on activated carbon (100 mg) for 18 h. The reaction mixture was then filtered through a Celite pad before being concentrated in vacuo to afford a viscous pale-yellow oil. Purification by flash column chromatography (EtOAc–hexane, 5 → 30%) afforded **38**.

Yield: 536 mg (53%); light-coloured oil that solidified on standing; mp 88–92 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.84 (t, *J* = 8.0 Hz, 2 H), 3.48 (t, *J* = 8.0 Hz, 2 H), 3.72 (s, 3 H), 4.02 (s, 3 H), 7.63 (s, 1 H), 7.66–7.76 (m, 2 H), 7.85 (d, *J* = 8.0 Hz, 1 H), 8.10 (dd, *J* = 8.0, 1.6 Hz, 1 H), 8.15–8.21 (m, 1 H), 8.80–8.87 (m, 1 H), 9.39 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.5, 34.3, 51.8, 52.3, 123.6, 124.1, 125.0, 125.7, 126.6, 127.0, 127.3, 127.5, 128.2, 129.2, 130.9, 130.9, 134.6, 137.5, 167.4, 173.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{18}O_4$: 345.1097; found: 345.1095.

Anal. Calcd for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63; found: C, 74.34; H, 6.04.

9-(2-Carboxyethyl)phenanthrene-3-carboxylic Acid (39)

By following General Procedure D, **38** (350 mg, 1.09 mmol), NaOH (262 mg, 6.54 mmol) and THF afforded **39**.

Yield: 156 mg (49%); off-white solid; mp >250 °C.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.75 (t, *J* = 7.5 Hz, 2 H), 3.39 (t, *J* = 7.5 Hz, 2 H), 7.73–7.81 (m, 3 H), 8.01 (d, *J* = 8.0 Hz, 1 H), 8.12 (dd, *J* = 8.0, 1.5 Hz, 1 H), 8.17–8.22 (m, 1 H), 8.87–8.92 (m, 1 H), 9.33 (s, 1 H), 12.60 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 28.3, 34.4, 123.9, 124.8, 124.8, 125.7, 127.1, 127.7, 128.0, 128.8, 128.9, 128.9, 130.6, 131.0, 134.4, 138.2, 168.0, 174.2.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{18}H_{14}O_4$: 293.0819; found: 293.0821.

Anal. Calcd for $C_{18}H_{14}O_4 \cdot 0.25\ H_2O$: C, 72.35; H, 4.89; found: C, 72.36; H, 5.02.

(9-Iodophenanthren-3-yl)methanol (40)

A stirred suspension of **1** (3.00 g, 8.62 mmol) and thionyl chloride (10 mL) in anhydrous dioxane (150 mL) was heated to reflux for 12 h. The solution was then cooled to r.t. and the solvent was removed in vacuo. The product was then dissolved in anhydrous THF and again concentrated in vacuo to remove any traces of thionyl chloride. The crude acid chloride was then dissolved in anhydrous THF (100 mL) and the resulting solution was cooled to 0 °C by using an ice-water bath. $NaBH_4$ (571 mg, 15.09 mmol) was then added portionwise over a period of 10 min. After complete addition, the suspension was stirred at 0 °C for 30 min and then at r.t. for 12 h. Excess $NaBH_4$ was destroyed through the dropwise addition of H_2O. The solvent was then removed in vacuo and the resultant solid was suspended between EtOAc (100 mL) and H_2O (100 mL). The aqueous layer was further extracted with EtOAc (2 × 50 mL) and the organic layers were pooled, washed with H_2O (50 mL), brine (50 mL), and dried over $MgSO_4$. Concentration in vacuo gave a yellow solid. Purification by flash chromatography (EtOAc–hexane, 10 → 40%) afforded **40**.

Yield: 2.45 g (85%); yellow solid; mp 164–168 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.77 (s, 2 H), 5.44 (s, 1 H), 7.64 (d, *J* = 8.0 Hz, 1 H), 7.72–7.81 (m, 2 H), 7.92 (d, *J* = 8.0 Hz, 1 H), 8.10–8.17 (m, 1 H), 8.59 (s, 1 H), 8.75 (s, 1 H), 8.78–8.83 (m, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 63.1, 97.9, 120.0, 123.2, 126.3, 127.5, 127.7, 128.1, 129.4, 130.1, 131.4, 131.5, 132.4, 138.0, 142.1.

HRMS (CI): *m*/*z* [M$^+$] calcd for $C_{15}H_{11}OI$: 333.9855; found: 333.9862.

Anal. Calcd for $C_{15}H_{11}OI$: C, 53.92; H, 3.32. Found: C, 53.63; H, 3.54.

3-(Bromomethyl)-9-iodophenanthrene (41)

A flask containing **40** (2.43 g, 7.27 mmol) was briefly evacuated and backfilled with argon. Anhydrous CH_2Cl_2 (200 mL) was added to the flask by using a cannula and the resulting suspension was cooled to 0 °C. Phosphorus tribromide (2.73 mL, 29.08 mmol) was then added dropwise to the stirred suspension. After complete addition, the solution was stirred at 0 °C for 30 min and then at r.t. until TLC analysis confirmed complete conversion. After 1 h, the reaction mixture was again cooled to 0 °C and excess PBr_3 was destroyed by the dropwise addition of saturated $NaHCO_3$ solution. The organic layer was isolated, dried over $MgSO_4$ and concentrated in vacuo to afford a light-yellow solid, which was dissolved in Et_2O (100 mL) and washed successively with H_2O (40 mL) and brine (40 mL). Drying over $MgSO_4$ followed by concentration in vacuo gave **41**.

Yield: 1.87 g (65%); pale-yellow solid; mp 124–128 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.75 (s, 2 H), 7.61 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.66–7.72 (m, 2 H), 7.74 (d, *J* = 8.0 Hz, 1 H), 8.20–8.23 (m, 1 H), 8.41 (s, 1 H), 8.59–8.62 (m, 1 H), 8.63 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.1, 99.7, 122.9, 123.3, 127.8, 128.1, 128.3, 128.4, 130.4, 130.5, 132.4, 132.8, 133.5, 136.7, 138.2.

HRMS (CI): *m*/*z* [M$^+$] cald for $C_{15}H_{10}BrI$: 395.9011; found: 395.9012.

(9-Iodophenanthren-3-yl)acetonitrile (42)

Compound **41** (1.00 g, 2.52 mmol) was dissolved in anhydrous CH_2Cl_2 (75 mL) and stirred vigorously with a solution of NaCN (136 mg, 2.77 mmol) and tetra-*n*-butylammonium bromide (TBAB; 89 mg, 0.28 mmol) in H_2O (75 mL). After 5 d, TLC analysis indicated complete conversion. The organic layer was subsequently isolated and the aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated in vacuo to afford a brown oil. Purification by flash chromatography (EtOAc–hexane, 10 → 20%) gave **42**.

Yield: 492 mg (57%); yellow solid; mp 141–145 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.00 (s, 2 H), 7.50 (dd, *J* = 8.5, 2.0 Hz, 1 H), 7.68–7.74 (m, 2 H), 7.77 (d, *J* = 8.5 Hz, 1 H), 8.20–8.25 (m, 1 H), 8.41 (s, 1 H), 8.59–8.63 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.2, 99.5, 122.1, 122.8, 126.6, 127.8, 128.3, 128.5, 128.7, 130.0, 130.6, 132.4, 132.4, 133.4, 137.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ cald for $C_{16}H_{10}NI$: 365.9743; found: 365.9750.

(9-Iodophenanthren-3-yl)acetic Acid (43)

A stirred mixture of **42** (471 mg, 1.37 mmol), glacial acetic acid (15 mL), conc H_2SO_4 (3 mL) and H_2O (3 mL) was heated to reflux until TLC analysis indicated complete consumption of the starting material. After 3 h, the mixture was cooled to r.t. and then diluted with H_2O (100 mL). The aqueous mixture was extracted with Et_2O (100 mL then 2 × 50 mL) and the organic layers were pooled and extracted with aq 1 M NaOH (3 × 50 mL). The alkaline phases were combined and acidified to pH 1 by using aq 2 M HCl. The aqueous solution was then extracted with Et_2O (100 mL then 2 × 50 mL) and the organic layers were pooled, dried over Na_2SO_4 and concentrated in vacuo to give **43**.

Yield: 355 mg (72%); straw-coloured solid; mp 218–222 °C (dec).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.87 (s, 2 H), 7.58 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.73–7.80 (m, 2 H), 7.91 (d, *J* = 8.0 Hz, 1 H), 8.11–8.16 (m, 1 H), 8.59 (s, 1 H), 8.73 (s, 1 H), 8.78–8.83 (m, 1 H), 12.48 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 40.9, 98.1, 123.3, 123.6, 127.4, 127.7, 128.2, 129.1, 129.5, 129.9, 131.2, 131.4, 132.4, 134.6, 137.9, 172.5.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{16}H_{11}O_2I$: 360.9735; found: 360.9731.

Anal. Calcd for $C_{16}H_{11}O_2I$: C, 53.06; H, 3.06; Found: C, 52.85; H, 3.17.

9-Iodophenanthrene-3-carboxylic Acid Benzylamide (44a)

A stirred suspension of **1** (1.00 g, 2.87 mmol) and thionyl chloride (5 mL) in anhydrous benzene (45 mL) was heated to reflux for 12 h. The solution was then cooled to r.t. and the solvent was removed in vacuo. The product was dissolved in a second aliquot of anhydrous benzene and again concentrated in vacuo to remove traces of thionyl chloride. The crude acid chloride was then dissolved in anhydrous dioxane (20 mL) and added dropwise to a rapidly stirring solution of benzylamine (0.31 mL, 2.87 mmol) and Et_3N (0.40 mL, 2.87 mmol) in anhydrous dioxane (30 mL). After complete addition, the solution was stirred for 3 h at r.t. The solvent was then removed in vacuo and the resultant solid was dissolved in a mixture of CH_2Cl_2 (100 mL) and H_2O (40 mL). The organic layer was isolated and washed successively with aq 1 M HCl (2 × 30 mL), aq 1 M NaOH (2 × 30 mL), and H_2O (40 mL). Drying over $MgSO_4$ followed by concentration in vacuo afforded **44a**.

Yield: 459.2 mg (37%); off-white solid; mp 208–212 °C (dec).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.61 (d, *J* = 6.0 Hz, 2 H), 7.23–7.24 (m, 1 H), 7.33–7.38 (m, 2 H), 7.38–7.43 (m, 2 H), 7.78–7.87 (m, 2 H), 8.05 (d, *J* = 8.4 Hz, 1 H), 8.16–8.20 (m, 1 H), 8.17 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.68 (s, 1 H), 8.91–8.95 (m, 1 H), 9.38 (s, 1 H), 9.42 (t, *J* = 6.0 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 42.8, 101.0, 122.0, 123.6, 126.1, 126.8, 127.3, 127.7, 128.1, 128.3, 128.6, 129.1, 130.2, 131.6, 132.6, 132.7, 134.0, 137.7, 139.5, 165.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{16}NOI$: 460.0169; found: 460.0164.

Anal. Calcd for $C_{22}H_{16}NOI$: C, 60.43; H, 3.69; N, 3.20. Found: C, 60.14; H, 3.81; N, 2.85.

9-Iodophenanthrene-3-carboxylic Acid 2-Phenethyl Amide (44b)

The procedure was identical to that described for **44a** with the exception that phenethylamine (0.36 mL, 2.87 mmol) was used.

Yield: 430.8 mg (33%); light-brown solid; mp 194–197 °C (dec).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.94 (t, *J* = 7.6 Hz, 2 H), 3.56–3.63 (m, 2 H), 7.19–7.24 (m, 1 H), 7.28–7.34 (m, 4 H), 7.79–7.88 (m, 2 H), 8.03 (d, *J* = 8.4 Hz, 1 H), 8.09 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.16–8.20 (m, 1 H), 8.67 (s, 1 H), 8.88–8.92 (m, 1 H), 8.95 (t, *J* = 6.0 Hz, 1 H), 9.26 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 35.1, 41.0, 100.7, 121.8, 123.3, 125.9, 127.5, 128.0, 128.2, 128.4, 128.5, 129.0, 130.2, 131.6, 132.5, 132.9, 133.8, 137.7, 139.4, 165.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{18}NOI$: 474.0325; found: 474.0318.

Anal. Calcd for $C_{23}H_{18}NOI \cdot 0.39\ H_2O$: C, 60.27; H, 4.13; N, 3.06. Found: C, 60.27; H, 4.40; N, 2.96.

***tert*-Butyl [(9-Iodophenanthrene-3-carbonyl)amino]acetate (45)**

Initial synthesis and purification of the acid chloride was as described for **44a** with the exception that **1** (600 mg, 1.72 mmol), thionyl chloride (3 mL) and anhydrous benzene (45 mL) were used. The crude acid chloride was then dissolved in anhydrous dioxane (20 mL) and added dropwise to a rapidly stirring suspension of glycine *tert*-butyl ester hydrochloride (301.7 mg, 1.80 mmol) and Et_3N (0.48 mL, 3.44 mmol) in anhydrous dioxane (30 mL), which had been prestirred for 30 min. After complete addition, the mixture was stirred at r.t. for 3 h. The dioxane was then removed in vacuo and the resulting solid was dissolved in a mixture of CH_2Cl_2 (100 mL) and H_2O (30 mL). The organic layer was isolated and washed successively with aq 1 M HCl (2 × 30 mL), aq 1 M NaOH (2 × 30 mL), H_2O (30 mL) and brine (30 mL). Subsequent drying over $MgSO_4$ followed by concentration in vacuo afforded **45**.

Yield: 576.3 mg (73%); orange/yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55 (s, 9 H), 4.24 (d, *J* = 4.8 Hz, 2 H), 7.05 (t, *J* = 4.8 Hz, 1 H), 7.66–7.74 (m, 3 H), 7.89 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.14–8.20 (m, 1 H), 8.36 (s, 1 H), 8.58–8.64 (m, 1 H), 9.08 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.1, 42.7, 82.7, 101.4, 122.6, 123.0, 124.6, 127.8, 128.0, 128.3, 129.9, 130.4, 131.9, 132.2, 133.3, 134.5, 137.8, 167.1, 169.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{20}NO_3I$: 484.0380; found: 484.0371.

[(9-Iodophenanthrene-3-carbonyl)amino]acetic Acid (46)

To a stirred solution of **45** (565.9 mg, 1.23 mmol) and *m*-dimethoxybenzene (0.81 mL, 6.15 mmol) in CH_2Cl_2 (30 mL) was added dropwise TFA (4.57 mL, 61.5 mmol). The resulting mixture was stirred at r.t. until TLC analysis confirmed complete deprotection. The solvent was then removed in vacuo and the resulting solid was azeotroped with toluene (3 × 30 mL) to remove traces of TFA. The solid was then suspended in Et_2O (30 mL) and stirred for 10 min before being filtered off and washed thoroughly with Et_2O. Air-drying subsequently afforded **46**.

Yield: 346.4 mg (70%); light-yellow solid; mp 241–244 °C (dec).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.06 (d, *J* = 5.6 Hz, 2 H), 7.79–7.88 (m, 2 H), 8.05 (d, *J* = 8.4 Hz, 1 H), 8.14 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.16–8.20 (m, 1 H), 8.69 (s, 1 H), 8.90–8.94 (m, 1 H), 9.26 (t, *J* = 5.6 Hz, 1 H), 9.36 (s, 1 H), 12.71 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 41.3, 101.2, 122.1, 123.5, 126.0, 127.8, 128.2, 128.7, 129.1, 130.2, 131.7, 132.1, 132.6, 134.1, 137.7, 166.1, 171.3.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{17}H_{12}NO_3I$: 403.9789; found: 403.9803.

Anal. Calcd for $C_{17}H_{12}NO_3I$: C, 50.39; H, 2.99; N, 3.46. Found: C, 50.73; H, 2.93; N, 3.11.

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Supporting Information

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