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Cyclisation reactions of *N*-cinnamoyl-9-aminoanthracenes.

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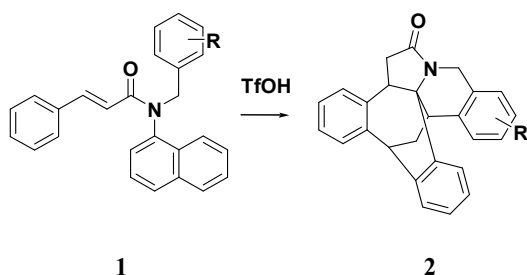
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N-cinnamoyl-9-aminoanthracenes cyclise with PPA or triflic acid to form novel 2-azahexacyclo[10.6.6.0^{1,5}.0^{6,11}.0^{13,18}.0^{19,24}]tetracos-6(11),7,9,13,15,17,19(24),20,22-nonaen-3-ones. In contrast, both *N*-cinnamoyl-*N*-methyl-9-(2-aminomethyl)anthracene and *N*-cinnamoyl-9-(2-aminoethyl)anthracene undergo an intramolecular Diels-Alder cycloaddition.

Introduction

An amine and one or more aryl groups are key structural features of many modulators of G-protein coupled receptors. We are therefore interested in approaches to the synthesis of structures which have a unique special disposition of these functional groups to identify more potent and selective modulators. We have recently reported that the triflic acid-mediated cyclisation of *N*-cinnamoyl-anilines¹ and *N*-cinnamoyl-naphthylamines² give novel azacycles. For example, *N*-benzyl-*N*-cinnamoyl-1-naphthylamines **1** cyclise to give the polycyclics **2** (Scheme 1).²



Scheme 1 TFOH-mediated cyclisation of *N*-benzyl-*N*-cinnamoyl-1-aminonaphthalenes

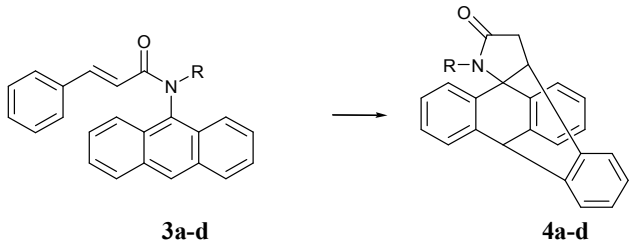
In this paper, we report the results obtained from an investigation into the cyclisation of *N*-cinnamoyl-9-aminoanthracenes and homologues. Anthracenes have a very reactive central ring. For example, 9-amidoanthracenes are known to act as dienes in Diels-Alder cycloadditions³ and nitration in HCl gives the 9-nitro-10-chloro addition product.⁴ Therefore, by analogy with the cinnamoyl-naphthylamines, we anticipated that we would get novel products from either Diels-Alder or carbocation addition to the central ring.

Results and discussion

The *N*-cinnamoyl-9-aminoanthracenes **3a**, **3e-m** were prepared from 9-aminoanthracene⁴ and the appropriate cinnamoyl chloride with *N,N*-dimethylaniline as base. The required products formed as precipitates, which

were collected and dried. Further product could be obtained from the mother liquors by column chromatography. The *N*-substituted analogues **3b-d** and **3f-n** were readily prepared by *N*-alkylation with the appropriate iodide or bromide with KOT-Bu as base.

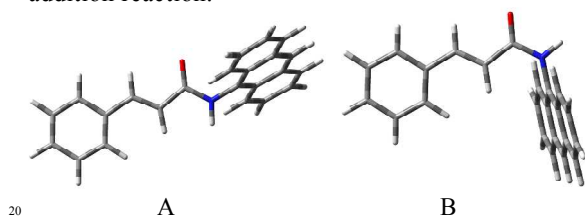
The amides **3a** and **3e-m** were found to be very insoluble in a wide range of solvents. However, recrystallisation was possible from DMSO/water. Considering the structure of these amides, the NMR of **3a** at room temperature showed a symmetry about the anthracene, with no evidence of rotamers in DMSO-*d*₆. In contrast, despite its low solubility in CDCl₃, two sets of peaks were observed in CDCl₃ solution with the ratio of 3:2. Exchange cross-peaks were observed in NOESY spectra, confirming that the observed two sets of peaks are due to two rotamers. The largest chemical shift difference was observed for the COCH=C proton resonating at 6.95 ppm in the major rotamer and at 5.91 ppm in the minor rotamer. Therefore, we concluded that the structure of the major rotamer has the expected *syn* relationship of the amide carbonyl⁵ (Figure 1, A), with the amide plane orthogonal to the plane of the anthracene. This conformation would minimise the steric interactions between the amide carbonyl and COCH=C proton, and the 1,8 protons of the anthracene. The upfield shift of the COCH=C proton in the minor conformer is due to the ring current effect⁶ and suggests that this proton is placed above the anthracene ring, in agreement with structure B in Figure 1. Ring current effects are relatively strong and are felt at relatively long distances of >4 Å.⁶ Therefore, the change in chemical shift of the *ortho*-Ph protons from 7.65 ppm in the major rotamer to 7.08 ppm in the minor rotamer is also in agreement with structures A (major) and B (minor) shown in Figure 1. The NMR spectra of the *N*-alkyl derivatives **3b-d** showed symmetry similar to that in **3a**, but with a large upfield shift of the COCH=C cinnamoyl proton to δ 5.82-5.87 ppm in **3b-d**. As discussed above for rotamer **3a-B**, this is consistent with a shielding ring current effect when the proton is placed above the the aromatic ring.⁶ For the *N*-benzyl **3d**, NOEs were observed between the COCH=C proton and the 1,8 protons of the anthracene, and the COCH=CH

Table 1 Acid-mediated cyclisation of *N*-cinnamoyl-9-aminoanthracenes **3a-d**


Entry	amide	R	solvent	Acid*	Temp. °C	Time h	product	R	Yield %
1	3a	H	CHCl ₃	TfOH	65	3	4a	H	69
2	3a	H	-	PPA	120	2	4a	H	78
3	3a	H	-	CSA	120	5	4a	H	0
4	3a	H	PhCl	AlCl ₃	25	24	4a	H	0
5	3b	Me	CHCl ₃	TfOH	65	2	4b	Me	92
6	3b	Me	-	PPA	120	2	4b	Me	89
7	3c	Et	-	PPA	120	2	4c	Et	90
8	3d	PhCH ₂	-	PPA	120	2	4d	PhCH ₂	88

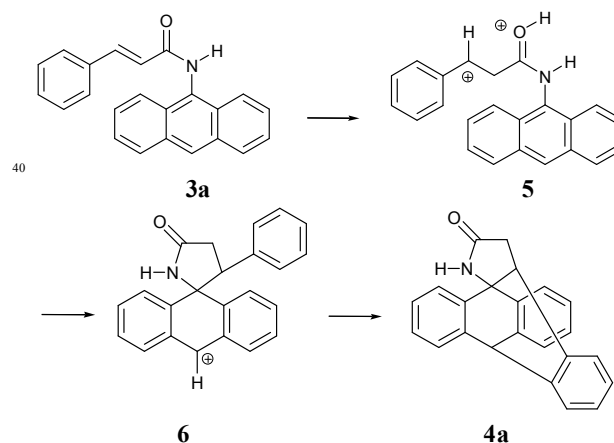
*TfOH: triflic acid; PPA: polyphosphoric acid; CSA: (+) 10-camphorsulfonic acid.

proton and the ortho protons of the cinnamoyl phenyl. No NOE was observed with the benzylic CH₂, which itself showed NOE's with the 1.8-protons of the anthracene and the ortho protons of the benzyl phenyl. Thus, we believe that the structure of the *N*-alkyl derivatives also have the amide group orthogonal to the plane of the anthracene, but with the anthracene *anti* to the carbonyl and the alkyl group *syn*. This would place the COCH=C proton over the top of the anthracenyl central ring (Figure 1, B). The conformation of the amide in rotamer B would be that required for a cyclo-addition reaction.

**Fig. 1** DFT-optimised geometries of two rotamers of **3a**

The results from the acid-mediated cyclisation reactions are shown in Table 1. From TLC, the initial reaction of **3a** with TfOH (10 equiv.) in CHCl₃ (Table 1, entry 1) gave a trace of a less polar product, which under uv light showed as a bright blue fluorescent spot, and a more polar product that was weak when viewed under uv light, but reacted strongly with KMnO₄. On purification by column chromatography on SiO₂, the small amount of the less polar product could not be obtained in pure form. However, the more polar major product (69% yield) was found to be the 9,10 addition product **4a** (Scheme 2).

The structure was assigned by ¹H and ¹³C NMR. In particular, in the ¹H NMR spectrum, there were four aliphatic protons, three mutually coupled doublet of doublets and a singlet at δ 4.96, and twelve aromatic

**Scheme 2** Proposed mechanism of formation of **4a**

protons. In the ¹³C NMR spectrum, four aliphatic C signals were observed, a CH₂, two CH and a C, consistent with the proposed structure, which was further verified using two- and three-bond ¹H-¹³C correlations in the HMBC spectrum.

Other acids were investigated and PPA was found to give a superior yield of **4a** (78% yield). However, neither (+) 10-camphorsulfonic acid nor AlCl₃ gave any **4a**. The former gave recovered starting material and the latter a black insoluble material. By analogy with the reaction with *N*-benzyl-*N*-cinnamoyl-1-amino-naphthalenes,² we believe that the acid doubly protonates the cinnamoyl group to form a benzylic carbocation, which adds to the 9 position to form a spiro intermediate, with the carbocation now located at the 10 position, close to the phenyl group, which facilitates ring closure (Scheme 2).

The *N*-methyl **3b** gave excellent yields of the 9,10 addition product **4b** with both TfOH (92% yield) and PPA (89% yield). The NMR of **4b** was similar to that of **4a** and the structure was confirmed by X-ray

We believe that the electron withdrawing nature of the chlorine reduces the rate of the final carbocation cyclisation $6 \rightarrow 4a$ (Scheme 2). This result is also consistent with the formation of the spiro carbocation **6** being reversible, in equilibrium with the carbocation **5**. This could then undergo the alternative, less favoured cyclisation to give **7**, analogous to that previously observed with the *N*-cinnamoyl-naphthylamines.² *N*-alkylation would be expected to inhibit this reaction due to a steric interaction with the 8-proton of the anthracene. In agreement with this, cyclisation of the *N*-benzyl derivative **3h** with TfOH gave a good yield of product **4h** (entry 8), better than with PPA (entry 7), with little formation of the *N*-benzyl analogue of **7**.

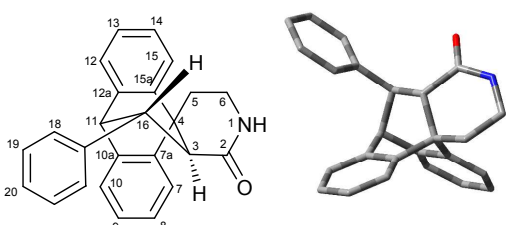
With the much more electron withdrawing CF₃ substituent (entries 9-12), no cyclisation was observed and starting material was recovered. With the 4-methoxy compound **3k**, only moderate yields of **4k** were obtained with both PPA (entry 13) and TfOH (entry 14) under the normal heated conditions. However, with TfOH at room temperature, **3k** rapidly reacted to give a slightly better yield of **4k** (entry 15). Similarly the *N*-benzyl derivative **3l** rapidly cyclised with TfOH at room temperature to give a good yield of **4l** (entry 16). For both **3m** (entry 17) and **3n** (entry 18), only single regioisomers, **4m** and **4n** respectively, were formed in good yields. NMR analysis showed that they were the products derived from cyclisation onto the less sterically hindered 6-position, para to the methyl. This result was surprising, as in a previous study on the TfOH-mediate iminium ion cyclisation onto a meta-methyl substituted phenyl, a mixture of isomers derived from cyclisation onto both the ortho and para positions was obtained.⁸ Similar electrophilic reactions, such as nitration, of meta-xylene give mixtures of products.⁹ However, on examination of molecular models, it appears that the product derived from cyclisation onto the ortho position of the meta-substituted phenyl would have a severe steric clash between the 10-methyl group and the 12-CH proton.

The cyclisation reaction to form the polycyclics could theoretically be reversible. If the reaction were reversible, heating the polycyclics with TfOH in benzene should re-form the initial carbocation **5** (Scheme 2), which would be trapped by the solvent to form the 3,3-diphenylpropionamide.¹⁰ However, on heating the polycyclics **4a** and **4d** with TfOH in benzene at reflux for 18h, no reaction was observed and starting material was recovered in both cases. Thus it would appear that the cyclisation reaction is essentially irreversible.

The investigation of homologated cinnamides was then undertaken to see if 6- and 7-membered spiro compounds could be formed. The aminoethyl analogue **8** was prepared in a 68% yield by a one-pot procedure via alane reduction of 9-(2-nitrovinyl)anthracene,¹¹ followed by acylation with cinnamoyl chloride. Previously, the use of LAH had been reported, but no yield of the amine was quoted.¹² Reaction of **8** with TfOH gave no identifiable products. However, with PPA the product obtained was the Diels-Alder adduct **9**

(96% yield). The same product was obtained in similar yield simply by heating **8** in chlorobenzene. However, the reaction in chlorobenzene was slower (4h vs. 30 min.). In both cases, the expected *trans* stereochemistry was obtained.¹⁵ The NMR assignments for **9** are included in Table 3. The NMR spectrum in the aliphatic region clearly showed a –CH₂–CH₂– and a separate –CH–CH– arrangement. In the carbon spectrum there was also an aliphatic, tetra-substituted C at δ 44.83, a mono-substituted phenyl and two 1,2-disubstituted phenyls. The bicyclo[2.2.2]octane unit, formed by carbons 15a, 12a, 11, 10a, 7a, 4, 3 and 16, is a rigid structure and the coupling between the 3-H and 16-H of 6.3 Hz is

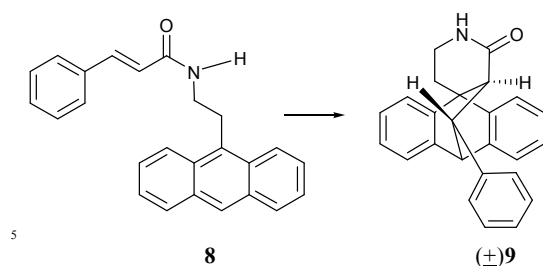
Table 3: ¹H and ¹³C NMR assignments for (\pm)**9**. The optimised geometry (below) and calculated *J* couplings (in brackets) are also shown



Proton	δ / ppm	Coupled protons	<i>J</i> / Hz
3	2.66	3,16	6.3 (5.1)
5a	2.88	5a,5e	-14.1 (-13.2)
5e	3.12	5a,6a	11.7 (11.2)
6e	3.72	5a,6e	7.9 (7.7)
16	3.85	5e,6a	6.1 (5.7)
6a	4.09	5e,6e	1.9 (0.9)
11	4.20	6a,6e	-12.4 (-11.6)
NH	5.84	11,16	2.3 (2.4)
18	6.76	12,13	7.3 (6.5)
12	7.04	12,14	1.4 (0.9)
13	7.08	13,14	7.3 (6.6)
8	7.12	13,15	1.2 (0.8)
9	7.13	14,15	7.6 (6.7)
20	7.13		
19	7.14		
14	7.22		
15	7.31		
10	7.33		
7	7.40		

Carbon	δ / ppm	Carbon	δ / ppm
5-CH ₂	23.89	14-CH	126.06
6-CH ₂	39.25	20-CH	126.47
3-CH	54.14	9-CH	126.52
4-C	44.83	12-CH	126.62
16-CH	48.51	18-CH	128.04
11-CH	51.82	19-CH	128.23
15-CH	119.79	7a-C	140.23
7-CH	122.04	12a-C	141.59
10-CH	124.02	17-C	144.29
8-CH	125.79	15a-C	145.98
13-CH	125.92	10a-C	146.31
		2-C=O	172.81

consistent with a *trans* orientation. There is also a strong NOE observed between the signals for the 3-H and the 18-H protons, consistent with them being *cis*.



Based upon the NMR studies and using a DFT geometry optimisation, the solution phase structure of **9** (A) is shown in Figure 3 together with the ORTEP (50% probability ellipsoids) diagram (B) from the X-ray crystal structure analysis.

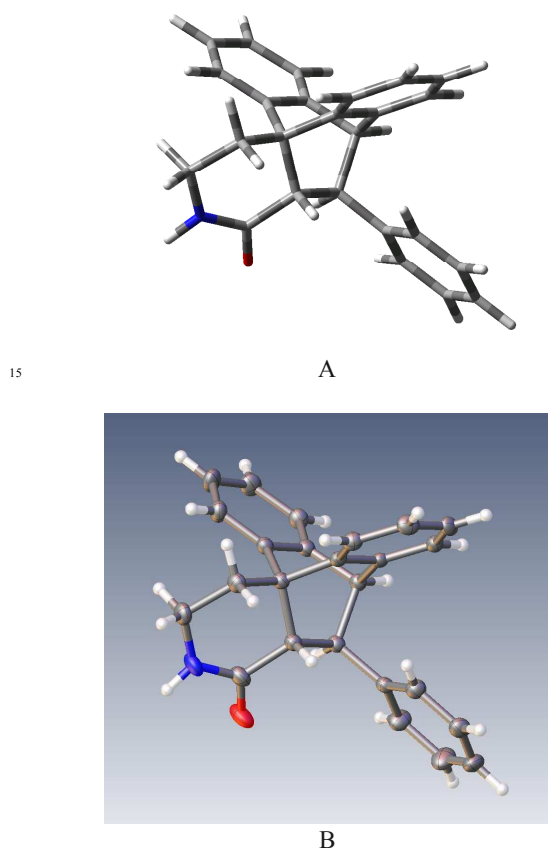
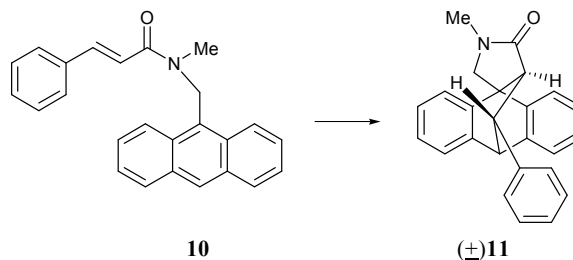


Fig. 3: Solution phase structure of (19S,20R) **9** from NMR studies (A) and (B), an ORTEP diagram of (19R,20S) **9** (50% probability ellipsoids) from X-ray structure crystallography. Cambridge Crystallographic Data Centre deposition number CDC 984577.

The anthracenylmethyl homologue **10**, prepared from the commercially available amine, gave no identifiable product with either TfOH or PPA, although the starting material rapidly disappeared. We believe that the anthracenylmethyl group is rapidly cleaved due to the high

stability of the 9-anthracenylmethyl carbocation.¹³ Indeed, 9-anthracenylmethyl has been used as an acid-cleavable protecting group for phenols.¹⁴ However, on heating in chlorobenzene, **10** gave an excellent yield of the Diels-Alder product **11**. The structure of **11** was assigned by NMR spectral comparison with **9**.



Summary and conclusion

We have shown that both *N*-cinnamoyl-9-aminomethyl- and *N*-cinnamoyl-9-aminoethyl-anthracenes give Diels-Alder cyclo-addition products on heating. However, *N*-cinnamoyl-9-aminoanthracenes cyclise with either PPA or TfOH to give the novel polycyclic 2-azahexacyclo[10.6.6.0^{1,5}.0^{6,11}.0^{13,18}.0^{19,24}]tetracos-6(11),7,9,13,15,17,19(24),20,22-nonaen-3-ones in moderate to good yields. We believe that protonation of the cinnamoyl group forms a benzylic carbocation, which adds to the 9-position of the anthracene to give a doubly benzylic-stabilised carbocation at the 10 position. This then undergoes an electrophilic ring closure onto the phenyl of the cinnamoyl group. The cyclisation reaction is facilitated by electron donating groups on the phenyl ring. In most cases, for NH cinnamamides, a small amount of by-product is formed *via* cyclisation onto the 1-position of the anthracene. *N*-alkylation inhibits this side reaction. Only with a mildly electron withdrawing group on the cinnamoyl moiety is this by-product formed in sufficient quantity to be isolated, purified and characterised. However, no cyclisation is observed with strongly electron withdrawing substituents. We believe that the 9-aminoanthracenes do not undergo the Diels-Alder cycloadditions because the resultant spiroazetidinones would be too strained to be thermodynamically favoured.

Experimental

All reagents were commercially available, unless otherwise specified, and used without purification. The chloroform used was stabilized with amylene. Petroleum ether was the 40–60°C fraction. Infrared spectra were run neat on a Perkin Elmer 100 FT IR spectrometer. Solution ¹H and ¹³C NMR spectra were recorded on a Bruker NMR spectrometer DRX500 or Avance III 600 equipped with z-gradient facilities. ¹H and ¹³C chemical shifts are given relative to TMS. Unless otherwise specified, spectra were recorded at 25°C. NMR *J*-couplings were predicted using calculations based on density functional theory (DFT), as described in detail previously.¹⁶ Geometry optimisations were carried using M06-2X/6-31+G(d) level of theory. Mass spectra were run on a Thermo Mat900XP. Melting

points were determined on a Sanyo-Gallenkamp capillary melting point apparatus and are uncorrected.

General procedure for the synthesis of *N*-cinnamoyl-9-aminoanthracenes

A suspension of the appropriate acid (2.5 g, 15 mmol), oxalyl chloride (1.4 mL, 16 mmol) and DMF (2 drops) in DCM (50 mL) was stirred at ambient temperatures until evolution of CO₂ had ceased (about 2h). CHCl₃ (50 mL) was added and the solvent removed by rotary evaporation. The residue was dissolved in EtOAc (20 mL) and added to a stirred solution of 9-aminoanthracene⁴ (2.9 g, 15 mmol) and *N,N*-diethylaniline (2.5 mL, 20 mmol) in EtOAc (100 mL), then heated to 60°C for 1h. On cooling to 0°C, the solid product was collected, washed with EtOAc (2 x 20 mL) and dried. The product was used for reactions without further purification, although a small amount was recrystallised from DMSO/EtOH for characterization purposes. Additional product was obtained by washing the EtOAc mother liquors with 1M HCl (2 x 50 mL), water (2 x 50 mL), 1M NaOH (1 x 50 mL), brine (50 mL), drying (MgSO₄), concentration *in vacuo* and purification by flash column chromatography on SiO₂, the product eluting with DCM to 2% MeOH/DCM, depending upon the polarity. Quoted yields are that of the combined quantities.

N-Cinnamoyl-9-aminoanthracene 3a

Isolated as a yellow solid (78% yield); mp >310 °C; ¹H NMR (600 MHz, CDCl₃), Rotamer **A**: δ 6.95 (1H, d, *J* = 15.6 Hz, COCH), 7.44 (1H, m, *p*-Ph), 7.45 (2H, m, *m*-Ph), 7.49 (2H, m, H-3,6), 7.54 (2H, m, H-2,7), 7.65 (2H, m, *o*-Ph), 7.91 (1H, d, *J* = 15.6 Hz, COCHCH), 8.04 (2H, d, *J* = 8.0 Hz, H-4,5), 8.09 (2H, d, *J* = 8.1 Hz, H-1,8), 8.48 (1H, s, H-10); Rotamer **B**: δ 5.91 (1H, d, *J* = 15.5 Hz, COCH), 7.08 (2H, m, *o*-Ph), 7.14 (2H, m, *m*-Ph), 7.20 (1H, m, *p*-Ph), 7.53 (2H, m, H-3,6), 7.58 (2H, m, H-2,7), 7.86 (1H, d, *J* = 15.5 Hz, COCHCH), 8.10 (2H, d, *J* = 8.6 Hz, H-4,5), 8.22 (2H, d, *J* = 8.7 Hz, H-1,8), 8.58 (1H, s, H-10); ¹H NMR (600 MHz, DMSO-*d*₆) 7.23 (1H, d, *J* = 15.9 Hz), 7.45 (1H, t, *J* = 7.5 Hz), 7.50 (2H, t, *J* = 7.5 Hz), 7.53 – 7.59 (4H, m), 7.69 (1H, d, *J* = 15.9 Hz), 7.73 (2H, d, *J* = 7.2 Hz), 8.08 (2H, m), 8.15 (2H, m), 8.63 (1H, s), 10.55 (1H, s); ¹³C NMR (150.1 MHz, DMSO-*d*₆) δ = 121.6 (CH), 124.0 (CH), 125.6 (CH), 125.9 (CH), 126.1 (CH), 127.9 (CH), 127.9 (C), 128.5 (CH), 129.1 (CH), 129.5 (C), 129.9 (CH), 131.3 (C), 134.9 (C), 140.4 (CH), 165.2 (C); FTIR (solid) ν = 3253, 1652, 1623, 1502, 1338, 1205, 963, 729, 695, 676 cm⁻¹; MS (EI) *m/z* (%) 323 (M⁺, 69), 193 (100), 131 (31); HMRS (EI): *m/z* calcd for C₂₃H₁₇NO [M⁺] 323.1310, found 323.1306.

N-(4-Methylcinnamoyl)-9-aminoanthracene 3e

Isolated as a yellow solid (82% yield); mp >310°C; ¹H NMR (600 MHz, DMSO-*d*₆) δ 2.36 (3H, s), 7.15 (1H, d, *J* = 15.6 Hz), 7.29 (2H, d, *J* = 7.8 Hz), 7.52 – 7.57 (4H, m), 7.60 (2H, d, *J* = 8.4 Hz), 7.63 (1H, d, *J* = 15.6 Hz), 8.03–8.06 (2H, m), 8.12–8.15 (2H, m), 8.61 (1H, s), 10.49 (1H, s); ¹³C NMR (150.1 MHz, DMSO-*d*₆) δ 21.1

(CH₃), 120.5 (CH), 123.9 (CH), 125.6 (CH), 125.9 (CH), 126.0 (CH), 126.8 (CH), 127.8 (CH), 127.9 (C), 128.4 (CH), 129.6 (CH), 129.7 (CH), 131.3 (C), 132.1 (C), 133.8 (C), 134.6 (CH), 139.7 (C), 140.4 (CH), 165.3 (C); FTIR (solid) ν = 3245, 1649, 1613, 1499, 1333, 1191, 975, 815, 731 cm⁻¹; MS (EI) *m/z* (%) 337 (M⁺, 57), 193 (94), 145 (60), 86 (69), 85 (100); HMRS (EI): *m/z* calcd for C₂₄H₁₉NO [M⁺] 337.1467, found 337.1460.

N-(4-Chlorocinnamoyl)-9-aminoanthracene 3g

Isolated as a yellow solid, (84% yield); mp >310 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.21 (1H, d, *J* = 15.8 Hz), 7.53 – 7.70 (7H, m), 7.67 (1H, d, *J* = 15.8 Hz), 7.76 (2H, d, *J* = 8.3 Hz), 8.05 – 8.08 (2H, m), 8.13 – 8.16 (2H, m), 8.63 (1H, s), 10.51 (1H, s); ¹³C NMR (150.1 MHz, DMSO-*d*₆) δ 122.4 (CH), 123.9 (CH), 125.6 (CH), 126.0 (CH), 126.1 (CH), 127.9 (C), 128.5 (CH), 129.1 (CH), 129.4 (C), 129.6 (CH), 131.3 (C), 133.8 (C), 134.3 (C), 139.0 (CH), 164.9 (C); FTIR (solid) ν = 3244, 1650, 1615, 1504, 1206, 1093, 973, 822, 730 cm⁻¹; MS (EI) *m/z* (%) 359 (M⁺, 10), 357 (M⁺, 31), 193 (100), 165 (47); HMRS (EI): *m/z* calcd for C₂₃H₁₆ClNO [M⁺] 357.0924, found 357.0934.

N-(4-Trifluoromethylcinnamoyl)-9-aminoanthracene 3i

Isolated as a yellow solid, (75% yield); mp 296 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.30 (1H, d, *J* = 15.9 Hz), 7.50 – 7.58 (4H, m), 7.71 (1H, d, *J* = 15.9 Hz), 7.82 (2H, d, *J* = 8.1 Hz), 7.93 (2H, d, *J* = 8.0 Hz), 8.02 (2H, d, *J* = 7.7 Hz), 8.13 (2H, dd, *J* = 1.8, 8.1 Hz), 8.61 (1H, s), 10.89 (1H, s); ¹³C NMR (150.1 MHz, DMSO-*d*₆) δ 124.0 (CH), 124.1 (CH), 124.5 (C, q, *J* = 272 Hz), 124.6 (C), 124.7 (CH), 126.1 (CH), 126.3 (CH), 126.7 (CH), 128.2 (C), 128.8 (CH), 128.9 (CH), 129.4 (CH), 129.9 (C, q, *J* = 32 Hz), 131.6 (C), 139.2 (CH), 139.3 (C), 165.3 (C); F NMR (376.4 MHz, DMSO-*d*₆) δ = -61.15; FTIR (solid) ν = 3245, 1653, 1614, 1504, 1324, 1169, 1116, 1067, 835, 734 cm⁻¹; MS (EI) *m/z* (%) 391 (M⁺, 92), 199 (32), 193 (100); HMRS (EI): *m/z* calcd for C₂₄H₁₆F₃NO [M⁺] 391.1184, found 391.1195.

N-(4-Methoxycinnamoyl)-9-aminoanthracene 3k

Isolated as a yellow solid (95% yield); mp >310 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ 3.80 (3H, s), 7.01 – 7.07 (3H, m), 7.50 – 7.56 (4H, m), 7.59 (1H, d, *J* = 15.8 Hz), 7.67 (2H, d, *J* = 8.3 Hz), 8.02 (2H, d, *J* = 8.2 Hz), 8.13 (2H, m), 8.61 (1H, s), 10.50 (1H, s); ¹³C NMR (150.1 MHz, DMSO-*d*₆) δ 55.3 (CH₃), 114.5 (CH), 118.8 (CH), 123.8 (CH), 125.6 (CH), 125.9 (CH), 126.2 (CH), 127.2 (C), 127.9 (C), 128.5 (CH), 129.4 (C), 129.6 (CH), 131.3 (C), 140.4 (CH), 160.7 (C), 165.7 (C); FTIR (solid) ν = 3266, 1646, 1601, 1512, 1254, 1176, 1036, 973, 830, 731 cm⁻¹; MS [EI] *m/z* (%) 353 (M⁺, 64), 193 (96), 161 (91), 84 (100), 71 (88); HMRS (EI): *m/z* calcd for C₂₄H₁₉NO₂ [M⁺] 353.1416, found 353.1410.

N-(3-Methylcinnamoyl)-9-aminoanthracene 3m

Isolated as a yellow solid (89% yield); mp >310 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ 2.38 (s, 3H), 6.98 (1H, d, *J*

= 6.9 Hz), 7.20 – 7.57 (7H, m), 8.06 (2H, d, $J = 8.9$ Hz), 8.14 (2H, d, $J = 7.0$ Hz), 8.28 (1H, d, $J = 8.8$ Hz); 8.62 (1H, s), 10.51 (1H, s); ^{13}C NMR (150.1 MHz, DMSO- d_6) δ 21.0 (CH₃), 121.5 (CH) 124.0 (CH), 125.1 (CH), 125.6 (CH), 125.9 (CH), 126.1 (CH), 127.9 (C), 128.4 (CH), 128.5 (CH), 129.0 (CH), 129.5 (C); 129.9 (C); 130.6 (CH), 131.3 (C); 134.8 (C); 138.3 (C); 140.4 (CH), 165.2 (C); FTIR (solid) $\nu = 3250, 1650, 1614, 1504, 1018, 972, 952, 758, 729\text{ cm}^{-1}$; MS (EI) m/z (%) 337 (M^+ , 17), 193 (58), 145 (32), 86 (62), 84 (100%); HMRS (EI): m/z calcd for C₂₄H₁₉NO [M^+], 337.1467, found 337.1471.

General procedure for the synthesis of *N*-alkyl-*N*-cinnamoyl-9-aminoanthracenes

The appropriate *N*-cinnamoyl-9-aminoanthracene (5.0 mmol), alkyl iodide or benzyl bromide (0.60 mL, 5.0 mmol) and K^tBuO (0.55 g, 5.0 mmol) in THF (100 mL) were stirred and heated under reflux for 2 h. On cooling, the THF was removed by rotary evaporation and the residue partitioned between H₂O (50 mL) and EtOAc (100 mL). The EtOAc was separated, washed with brine (50 mL) and dried (MgSO₄). Removal of the solvent gave the crude product, which was purified by column chromatography on SiO₂, the product eluting with 1:1 DCM/petrol to DCM depending upon the polarity of the product.

N-Methyl-*N*-cinnamoyl-9-aminoanthracene 3b

Product isolated from the SiO₂ column by elution with DCM + 5% Et₂O as a yellow solid (83% yield); mp 56-58 °C; ^1H NMR (500 MHz, CDCl₃) δ 3.58 (3H, s), 5.87 (1H, d, $J = 15.5$ Hz), 7.00 (2H, d, $J = 7.8$ Hz), 7.09 (2H, t, $J = 7.3$ Hz), 7.11 – 7.15 (1H, m), 7.50 – 7.59 (4H, m), 7.76 (1H, d, $J = 15.5$ Hz), 7.97 (2H, d, $J = 8.7$ Hz), 8.10 (2H, d, $J = 8.3$ Hz), 8.56 (1H, s); ^{13}C NMR (125.8 MHz, CDCl₃) δ 37.0 (CH₃), 118.1 (CH), 122.9 (CH), 126.0 (CH), 127.6 (CH), 127.9 (CH), 128.5 (CH), 128.9 (CH), 128.9 (C), 129.5 (CH), 132.0 (C), 134.5 (C), 135.0 (C), 142.7 (CH), 167.8 (C); FTIR (solid) $\nu = 1650, 1611, 1373, 1351, 1213, 1084, 762, 735\text{ cm}^{-1}$; MS (EI) m/z (%) 337 (M^+ , 20), 207 (38), 144 (100), 131 (41); HMRS (EI): m/z calcd for C₂₄H₁₉NO [M^+] 337.1467, found 337.1456.

N-Ethyl-*N*-cinnamoyl-9-aminoanthracene 3c

Product isolated from the SiO₂ column by elution with DCM + 5% Et₂O as a grey solid (78% yield); mp 141-142 °C; ^1H NMR (500 MHz, CDCl₃) δ 1.21 (3H, t, $J = 7.2$ Hz), 4.12 (2H, q, $J = 7.2$ Hz), 5.83 (1H, d, $J = 15.5$ Hz), 6.98 (2H, d, $J = 7.8$ Hz), 7.08 (2H, t, $J = 7.3$ Hz), 7.10 – 7.15 (1H, m), 7.50 – 7.57 (4H, m), 7.76 (1H, d, $J = 15.5$ Hz), 7.97 (2H, d, $J = 8.7$ Hz), 8.10-8.13 (1H, m), 8.07- 8.11 (1H, m), 8.56 (1H, s); ^{13}C NMR (125.8 MHz, CDCl₃) δ 13.8 (CH₃), 45.5 (CH₂), 118.6 (CH), 123.5 (CH), 125.9 (CH), 127.4 (CH), 127.8 (CH), 127.9 (CH), 128.5 (CH), 128.8 (CH), 129.4 (CH), 129.7 (C), 132.0 (C), 133.4 (C), 135.1 (C), 142.6 (CH), 167.4 (C); FTIR (solid) $\nu = 1649, 1613, 1393, 1341, 1241, 977, 886, 845, 764, 740\text{ cm}^{-1}$; MS (EI) m/z (%) 351 (M^+ , 11), 158 (100), 131 (31), 84 (43);

HMRS (EI): m/z calcd for C₂₅H₂₁NO [M^+] 351.1623, found 351.1618.

65 *N*-Benzyl-*N*-cinnamoyl-9-aminoanthracene 3d

Product isolated from the SiO₂ column by elution with DCM as a grey solid (75% yield); mp 138-140 °C; ^1H NMR (600 MHz, CDCl₃) δ 5.20 (2H, s), 5.82 (1H, d, $J = 15.6$ Hz), 6.98 (2H, d, $J = 7.8$ Hz), 7.05 – 7.18 (8H, m), 7.34 (2H, dd, $J = 7.8, 8.4$ Hz), 7.46 (2H, t, $J = 7.2$ Hz), 7.67 (2H, d, $J = 8.4$ Hz), 7.81 (1H, d, $J = 15.6$ Hz), 8.05 (2H, d, $J = 8.4$ Hz), 8.55 (1H, s); ^{13}C NMR (150.9 MHz, CDCl₃) δ 54.0 (CH₂), 118.3 (CH), 123.5 (CH), 125.8 (CH), 127.1 (CH), 127.7 (CH), 127.9 (CH), 128.1 (CH), 128.3 (CH), 128.5 (CH), 128.7 (CH), 129.5 (C), 129.6 (CH), 130.5 (CH), 131.9 (C), 133.2 (C), 135.0 (C), 137.1 (C), 143.2 (CH), 167.6 (C); FTIR (solid) $\nu = 1643, 1602, 1389, 1338, 1220, 997, 959, 740\text{ cm}^{-1}$; MS [EI] m/z (%) 413 (M^+ , 3), 322 (22), 220 (100), 131 (34), 91 (54); HMRS (EI): m/z calcd for C₃₀H₂₃NO [M^+] 413.1779, found 413.1761.

N-Benzyl-*N*-(4-methylcinnamoyl)-9-aminoanthracene 3f

Product isolated from the SiO₂ column by elution with DCM as a pale yellow solid (87% yield); mp 222-223 °C; ^1H NMR (600 MHz, CDCl₃) δ 2.18 (3H, s), 5.19 (2H, s), 5.75 (1H, d, $J = 15.6$ Hz), 6.88 (4H, s), 7.06 – 7.12 (4H, m), 7.13 – 7.17 (1H, m), 7.33 (2H, t, $J = 7.5$ Hz), 7.45 (2H, t, $J = 7.2$ Hz), 7.66 (2H, d, $J = 8.4$ Hz), 7.77 (1H, d, $J = 15.6$ Hz), 8.05 (2H, d, $J = 8.4$ Hz), 8.53 (1H, s); ^{13}C NMR (150.9 MHz, CDCl₃) δ = 21.4 (CH₃), 53.9 (CH₂), 117.3 (CH), 123.6 (CH), 125.8 (CH), 127.0 (CH), 127.7 (CH), 127.9 (CH), 128.0 (CH), 128.2 (CH), 128.6 (CH), 129.2 (CH), 129.5 (C), 130.5 (CH), 131.9 (C), 132.3 (C), 133.3 (C), 137.2 (C), 139.9 (C), 143.2 (CH), 167.8 (C); FTIR (solid) $\nu = 1648, 1614, 1604, 1381, 1331, 1221, 1207, 815, 740, 700\text{ cm}^{-1}$; MS [EI] m/z (%) 427 (M^+ , 37), 283 (32), 234 (100), 145 (76), 91 (58); HMRS (EI): m/z calcd for C₂₄H₁₉NO [M^+] 427.1936, found 427.1930.

N-Benzyl-*N*-(4-chlorocinnamoyl)-9-aminoanthracene 3h

Product isolated from the SiO₂ column by elution with 3:1 DCM:petrol as a pale yellow solid (82% yield); mp 210-211 °C; ^1H NMR (500 MHz, CDCl₃) δ 5.18 (2H, s), 5.77 (1H, d, $J = 15.5$ Hz), 6.88 (2H, d, $J = 8.6$ Hz), 7.13 – 7.16 (3H, m), 7.16 – 7.19 (1H, m), 7.31 – 7.38 (2H, m), 7.42 – 7.49 (2H, m), 7.64 (2H, d, $J = 8.8$ Hz), 7.73 (1H, d, $J = 15.5$ Hz), 8.05 (2H, d, $J = 8.3$ Hz), 8.70 (1H, s); ^{13}C NMR (125.8 MHz, CDCl₃) δ = 54.0 (CH₂), 118.9 (CH), 123.4 (CH), 125.8 (CH), 127.1 (CH), 127.7 (CH), 128.1 (CH), 128.2 (CH), 128.6 (CH), 128.7 (CH), 129.0 (CH), 129.4 (C), 130.4 (CH), 131.9 (C), 133.0 (C), 133.5 (C), 135.3 (C), 137.0 (C), 141.7 (CH), 167.2 (C); FTIR (solid) $\nu = 1648, 1614, 1381, 1213, 984, 822, 739, 701\text{ cm}^{-1}$; MS [EI] m/z (%) 447 (M^+ , 12), 356 (12), 283 (15), 254 (50), 91 (100); HMRS (EI): m/z calcd for C₃₀H₂₂ClNO [M^+] 447.1390, found 447.1391.

***N*-Benzyl-*N*-(4-trifluoromethylcinnamoyl)-9-aminoanthracene 3j**

Product isolated from the SiO₂ column by elution with 3:1 DCM:petrol as a white solid (73% yield); mp 164-165 °C; ¹H NMR (500 MHz, CDCl₃) δ 5.20 (2H, s), 5.88 (1H, d, *J* = 15.5 Hz), 6.98 – 7.21 (6H, m), 7.30 – 7.42 (4H, m), 7.45 (2H, t, *J* = 7.6 Hz), 7.65 (2H, d, *J* = 8.8 Hz), 7.80 (1H, d, *J* = 15.5 Hz), 8.06 (2H, d, *J* = 8.5 Hz), 8.56 (1H, s); ¹³C NMR (125.8 MHz, CDCl₃) δ 54.0 (CH₂), 120.9 (CH), 123.3 (CH), 123.8 (C, q, *J* = 270 Hz), 125.4 (CH, q, *J* = 3.8 Hz), 125.8 (CH), 127.2 (CH), 127.8 (CH), 127.9 (CH), 128.2 (CH), 128.7 (CH), 129.4 (CH), 130.4 (CH), 131.0 (C, q, *J* = 32 Hz), 131.9 (C), 132.8 (C), 136.8 (C), 138.4 (C), 141.3 (C), 141.4 (CH), 167.0 (C); FTIR (solid) ν = 1652, 1619, 1320, 1217, 1165, 1126, 1067, 833, 738, 702 cm⁻¹; MS [EI] *m/z* (%) 481 (M⁺, 75), 390 (76), 288 (95), 193 (33), 91 (96%), 84 (100); HMRS (EI): *m/z* calcd for C₂₄H₁₉NO [M⁺] 481.1654, found 481.1649.

***N*-Benzyl-*N*-(4-methoxycinnamoyl)-9-aminoanthracene 3l**

Product isolated from the SiO₂ column by elution with DCM + 5% Et₂O as a white solid (86% yield); mp 202-203 °C; ¹H NMR (500 MHz, CDCl₃) δ 3.66 (3H, s), 5.19 (2H, s), 5.68 (1H, d, *J* = 15.4 Hz), 6.59 (2H, d, *J* = 8.7 Hz), 6.92 (2H, d, *J* = 8.7 Hz), 7.07 – 7.20 (4H, m), 7.31 – 7.35 (2H, m), 7.43 – 7.50 (2H, m), 7.66 (2H, d, *J* = 8.8 Hz), 7.75 (1H, d, *J* = 15.4 Hz), 8.04 (2H, d, *J* = 8.5 Hz), 8.53 (1H, s); ¹³C NMR (125.8 MHz, CDCl₃) δ 53.9 (CH₂), 55.3 (CH₃), 113.9 (CH), 116.0 (CH), 123.6 (CH), 125.7 (CH), 126.9 (CH), 127.6 (CH), 127.8 (C), 127.9 (CH), 128.2 (CH), 128.6 (CH), 129.4 (CH), 129.5 (C), 130.4 (CH), 131.9 (C), 133.4 (C), 137.2 (C), 142.8 (C), 142.8 (CH), 160.8 (C), 167.8 (C); FTIR (solid) ν = 1647, 1616, 1594, 1509, 1257, 1214, 1167, 827, 738, 698 cm⁻¹; MS [EI] *m/z* (%) 443 (M⁺, 13), 283 (18), 250 (80), 161 (100), 91 (37); HMRS (EI): calcd for C₂₄H₁₉NO [M⁺] 443.1885, found 443.1878.

***N*-Benzyl-*N*-3-methyl-cinnamoyl-9-anthracene 3n**

Product isolated from the SiO₂ column by elution with 3:1 DCM:petrol as a pale grey solid (90% yield); mp 127-128 °C; ¹H NMR (600 MHz, CDCl₃) δ 2.12 (3H, s), 5.19 (2H, s), 5.79 (1H, d, *J* = 15.6 Hz), 6.76 (1H, d, *J* = 6.6 Hz), 6.80 (1H, s), 6.92 – 6.98 (2H, m), 7.06 – 7.12 (4H, m), 7.13 – 7.18 (1H, m), 7.34 (2H, dd, *J* = 6.6, 7.8 Hz), 7.46 (2H, t, *J* = 7.5 Hz), 7.66 (2H, d, *J* = 8.4 Hz), 7.77 (1H, d, *J* = 15.6 Hz), 8.05 (2H, d, *J* = 8.4 Hz), 8.54 (1H, s); ¹³C NMR (150.9 MHz, CDCl₃) δ 21.2 (CH₃), 54.0 (CH₂), 118.1 (CH), 123.6 (CH), 124.9 (CH), 125.8 (CH), 127.1 (CH), 127.7 (CH), 128.0 (CH), 128.2 (CH), 128.4 (CH), 128.7 (CH), 128.8 (CH), 129.5 (C), 130.4 (CH), 130.5 (CH), 131.9 (C), 133.2 (C), 134.9 (C), 137.1 (C), 138.2 (C), 143.5 (CH), 167.7 (C); FTIR (solid) ν = 1645, 1612, 1387, 1336, 1239, 961, 891, 849, 790, 740 702 cm⁻¹; MS [EI] *m/z* (%) 427 (M⁺, 82), 336 (28), 283 (28), 234 (100), 145 (21), 86 (35), 84 (57); HMRS (EI): calcd for C₂₄H₁₉NO [M⁺] 427.1936, found 427.1930.

General procedure for the PPA-mediated cyclisation.

A suspension of the *N*-cinnamoyl-9-aminoanthracene (1.0 mmol) in CHCl₃ (5 mL) and PPA (5 g) was heated to 120°C (block temperature), distilling off the CHCl₃. After heating for 2h, the reaction mixture was cooled and partitioned between ice/water (50 g) and DCM (100 mL). The organic layer was separated, dried (MgSO₄), filtered and concentrated *in vacuo*. The residue was purified by column chromatography on SiO₂.

General procedure for the TfOH-mediated cyclisation

Triflic acid (1 mL, 10 mmol) was added to a stirred solution of the amide (2.0 mmol) in CHCl₃ (20 mL) and the reaction mixture was heated under gentle reflux until no starting material was present by TLC. The reaction mixture was cooled to room temperature, water (20 mL) was added and the mixture basified with an excess of solid K₂CO₃ until CO₂ evolution ceased. The product was extracted into EtOAc (3 × 50 mL), dried (MgSO₄), concentrated *in vacuo* and the product purified by column chromatography on SiO₂.

2-azahexacyclo[10.6.6.0^{1,5}.0^{6,11}.0^{13,18}.0^{19,24}]tetracosan-6(11),7,9,13,15,17,19(24),20,22-nonaen-3-one 4a

a) With PPA. Following the general procedure, reaction of **3a** (0.32 g) with PPA and elution of the SiO₂ column with DCM + 5% Et₂O gave the title compound **4a** (0.25 g, 78% yield) as a buff solid; mp 234-236 °C; ¹H NMR (500 MHz, CDCl₃) δ 2.44 (H-4, dd, *J* = 12.9, 16.0 Hz), 2.95 (H-4, dd, *J* = 7.6, 16.0 Hz), 3.75 (H-5, dd, *J* = 7.6, 12.9 Hz), 4.94 (H-12, s), 6.88 (H-7, m), 6.88 (NH, brs), 7.11 (H-8, m), 7.13 (H-9, m), 7.21 (H-22, dt, *J* = 1.4, 2.3 Hz); 7.24 (H-21, dt, *J* = 1.4, 7.4 Hz), 7.25 (H-15, dt, *J* = 1.3, 7.4 Hz), 7.29 (H-16, dt, *J* = 1.4, 7.4 Hz), 7.36 (H-10, m), 7.37 (H-14, m), 7.46 (H-23, dd, *J* = 1.4, 7.2 Hz), 7.47 (H-20, dd, *J* = 1.4, 7.4 Hz), 7.51 (H-17, dd, *J* = 1.4, 7.5 Hz); ¹³C NMR (125.8 MHz, CDCl₃) δ 35.8 (C-13), 48.2 (C-5), 55.3 (C-12), 66.2 (C-1), 119.9 (C-17), 124.3 (C-20), 125.0 (C-10), 126.8 (C-23), 127.0 (C-21), 127.4 (C-9), 127.4 (C-16), 127.6 (C-8), 127.7 (C-15), 127.8 (C-14), 128.2 (C-22), 129.7 (C-7), 134.6 (C-6), 136.4 (C-13), 139.4 (C-11), 139.5 (C-19), 141.8 (C-18), 144.5 (C-24), 178.0 (C-3); FTIR (solid) ν = 1696, 747, 722, 613, 477 cm⁻¹; MS [EI] *m/z* (%) 323 (M⁺, 100), 294 (20), 280 (41), 265 (27); HMRS (EI): *m/z* calcd for C₂₃H₁₇NO [M⁺] 323.1310, found 323.1319.

b) With TfOH. Following the general procedure, reaction of **3a** (0.32 g) and purification as above gave the title product **4a** (0.22g, 69% yield).

(±) 2-methyl-2-azahexa-cyclo[10.6.6.0^{1,5}.0^{6,11}.0^{13,18}.0^{19,24}]tetracosan-6(11),7,9,13,15,17,19(24),20,22-nonaen-3-one 4b

Following the general procedure, reaction of **3b** (0.34 g) with PPA and elution of the SiO₂ column with DCM + 5%

Et₂O gave the title compound **4b** (0.31 g, 89% yield) as a white solid; mp 240-242 °C; ¹H NMR (500 MHz, CDCl₃) δ 2.40 (1H, dd, *J* = 13.1, 15.7 Hz), 3.00 (1H, dd, *J* = 7.7, 15.7 Hz), 3.23 (3H, s), 3.57 (1H, dd, *J* = 7.7, 13.1 Hz), 4.99 (1H, s), 6.86 – 6.89 (1H, m), 7.00 – 7.02 (1H, m), 7.08 – 7.11 (2H, m), 7.20 – 7.23 (2H, m), 7.27 (1H, dt, *J* = 1.4, 7.4 Hz), 7.29 – 7.34 (2H, m), 7.37 – 7.41 (2H, m), 7.48 (1H, dd, *J* = 1.1, 7.3 Hz); ¹³C NMR (125.8 MHz, CDCl₃) δ = 29.7 (CH₃), 35.3 (CH₂), 46.8 (CH), 55.2 (CH), 71.3 (C), 121.8 (CH), 125.1 (CH), 125.2 (CH), 126.7 (CH), 126.9 (CH), 127.3 (CH), 127.3 (CH), 127.4 (CH), 127.6 (CH), 127.6 (CH), 128.2 (CH), 129.8 (CH), 133.6 (C), 134.6 (C), 139.5 (C), 139.8 (C), 141.1 (C), 144.7 (C), 176.4 (C); (solid) *v* = 1691, 1367, 757, 747, cm⁻¹; MS [EI] *m/z* (%) 337 (M⁺, 100), 265 (33); HMRS (EI): *m/z* calcd for C₂₄H₁₉NO [M⁺] 337.1467, found 337.1471.

(±) 2-ethyl-2-azahexacyclo[10.6.6.0^{1,5}.0^{6,11}.0^{13,18}.0^{19,24}]tetracos-6(11),7,9,13,15,17,19(24),20,22-nonaen-3-one 4c

Following the general procedure, **3c** (0.36 g) was reacted with PPA and elution of the SiO₂ column with DCM + 5% Et₂O gave the title compound **4c** (0.33 g, 90% yield) as a white solid; mp 204-205 °C; ¹H NMR (500 MHz, CDCl₃) δ 1.73 (3H, t, *J* = 7.1 Hz), 2.36 (1H, dd, *J* = 12.8, 16.0 Hz), 3.00 (1H, dd, *J* = 7.8, 16.0 Hz), 3.09 (1H, dq, *J* = 7.1, 14.4 Hz), 3.57 (1H, dd, *J* = 7.8, 12.8 Hz), 3.93 (1H, dq, *J* = 7.1, 14.4 Hz), 4.93 (1H, s), 6.86 – 6.89 (1H, m), 7.07 – 7.13 (3H, m), 7.18 – 7.22 (2H, m), 7.28 (1H, dt, *J* = 1.2, 7.4 Hz), 7.30 – 7.35 (2H, m), 7.36 – 7.40 (1H, m), 7.48 (1H, dd, *J* = 1.2, 7.4 Hz), 7.56 (1H, dd, *J* = 0.8, 7.3 Hz); ¹³C NMR (125.8 MHz, CDCl₃) δ 14.6 (CH₃), 35.9 (CH₂), 39.6 (CH₂), 46.9 (CH), 55.2 (CH), 73.0 (C), 121.6 (CH), 125.1 (CH), 125.5 (CH), 126.7 (CH), 126.8 (CH), 127.3 (CH), 127.3 (CH), 127.4 (CH), 127.5 (CH), 128.1 (CH), 129.9 (CH), 134.7 (C), 139.6 (C), 140.9 (C), 144.3 (C), 177.4 (C); FTIR (solid) *v* = 1682, 1393, 1346, 1315, 753, 743, 732 cm⁻¹; MS [EI] *m/z* (%) 351 (M⁺, 100), 265 (34); *m/z* calcd for C₂₅H₂₁NO [M⁺] 351.1623, found 351.1619.

(±) 2-benzyl-2-azahexacyclo[10.6.6.0^{1,5}.0^{6,11}.0^{13,18}.0^{19,24}]tetracos-6(11),7,9,13,15,17,19(24),20,22-nonaen-3-one 4d

Following the general procedure, **3d** (0.41 g) was reacted with PPA and elution of the SiO₂ column with 2:1 DCM: petroleum ether gave the title compound **4d** (0.36 g, 88% yield) as a white solid; mp 230-231 °C; ¹H NMR (600 MHz, CDCl₃) δ 2.46 (1H, dd, *J* = 13.2, 16.2 Hz), 3.16 (1H, dd, *J* = 7.8, 16.2 Hz), 3.71 (1H, dd, *J* = 7.8, 13.2 Hz), 4.06 (1H, d, *J* = 16.2 Hz), 4.94 (1H, s), 5.39 (1H, d, *J* = 16.2 Hz), 6.90 – 6.95 (2H, m), 7.07 (1H, d, *J* = 7.8 Hz), 7.09 – 7.17 (4H, m), 7.23 – 7.28 (2H, m), 7.32 – 7.37 (2H, m), 7.40 – 7.45 (4H, m), 7.48 (2H, d, *J* = 7.2 Hz); ¹³C NMR (150.1 MHz, CDCl₃) δ 34.3 (CH₂), 46.7 (CH), 48.1 (CH₂), 55.2 (CH), 73.7 (C), 122.8 (CH), 125.4 (CH), 125.5 (CH), 126.4 (CH), 127.0 (CH), 127.1 (CH), 127.3 (CH), 127.4 (CH), 127.6 (CH), 127.7 (CH), 127.7 (CH), 128.3 (CH), 128.8 (CH), 130.0 (CH), 134.6 (C), 134.7 (C), 138.5 (C), 139.6 (C), 139.7 (C), 140.3 (C), 144.7 (C), 177.9 (C);

FTIR (solid) *v* = 1689, 1357, 754, 745, 712 cm⁻¹; MS [EI] *m/z* (%) 413 (M⁺, 100), 322 (19), 280 (45), 265 (55), 91 (42); *m/z* calcd for C₃₀H₂₃NO [M⁺] 413.1779, found 413.1780.

(±) 9-methyl-2-azahexacyclo[10.6.6.0^{1,5}.0^{6,11}.0^{13,18}.0^{19,24}]tetracos-6(11),7,9,13,15,17,19(24),20,22-nonaen-3-one 4e

Following the general procedure, **3e** (0.34 g) was reacted with PPA and elution of the SiO₂ column with DCM gave the title compound **4e** (0.28 g, 82% yield) as a light brown solid; mp >310 °C; ¹H NMR (500 MHz, CDCl₃) δ 2.29 (3H, s), 2.41 (1H, dd, *J* = 12.9, 16.0 Hz), 2.92 (1H, dd, *J* = 7.6, 16.0 Hz), 3.70 (1H, dd, *J* = 7.6, 12.9 Hz), 4.88 (1H, s), 6.68 (1H, s), 6.76 (1H, d, *J* = 7.8 Hz), 6.92 (1H, d, *J* = 7.8 Hz), 7.16 – 7.29 (5H, m), 7.37 (1H, dd, *J* = 1.4, 7.5 Hz), 7.42 – 7.46 (2H, m), 7.49 (1H, d, *J* = 7.4 Hz); ¹³C NMR (125.8 MHz, CDCl₃) δ 21.0 (CH₃), 35.8 (CH₂), 47.9 (CH), 55.3 (CH), 66.2 (C), 119.8 (CH), 124.2 (CH), 124.9 (CH), 126.6 (CH), 126.9 (CH), 127.3 (CH), 127.5 (CH), 128.1 (CH), 128.2 (CH), 128.5 (CH), 129.5 (CH), 131.4 (C), 136.4 (C), 137.1 (C), 139.0 (C), 141.8 (C), 144.6 (C), 177.6 (C); FTIR (solid) *v* = 1694, 1346, 818, 763, 731, cm⁻¹; MS [EI] *m/z* (%) 337 (M⁺, 100), 294 (28), 279 (22), 86 (29), 84 (47); *m/z* calcd for C₂₄H₁₉NO [M⁺] 337.1467, found 337.1467.

(±) 2-Benzyl-9-methyl-2-azahexacyclo[10.6.6.0^{1,5}.0^{6,11}.0^{13,18}.0^{19,24}]tetracos-6(11),7,9,13,15,17,19(24),20,22-nonaen-3-one 4f

Following the general procedure, **3f** (0.43 g) was reacted with PPA and elution of the SiO₂ column with DCM gave the title compound **4f** as a white solid (0.38 g, 88% yield); mp 288-289 °C; ¹H NMR (600 MHz, CDCl₃) δ 2.28 (3H, s), 2.42 (1H, dd, *J* = 12.6, 16.2 Hz), 3.13 (1H, dd, *J* = 7.8, 16.2 Hz), 3.66 (1H, dd, *J* = 7.8, 12.6 Hz), 4.04 (1H, d, *J* = 15.6 Hz), 4.89 (1H, s), 5.37 (1H, d, *J* = 15.6 Hz), 6.91 (1H, d, *J* = 7.8 Hz), 6.89 – 6.94 (2H, m), 7.06 (1H, d, *J* = 7.2 Hz), 7.12 – 7.17 (3H, m), 7.23 – 7.27 (2H, m), 7.34 (1H, t, *J* = 7.2 Hz), 7.39 – 7.43 (4H, m), 7.46 (2H, d, *J* = 7.2 Hz); ¹³C NMR (150.9 MHz, CDCl₃) δ 21.1 (CH₃), 35.8 (CH₂), 46.4 (CH), 48.1 (CH₂), 55.3 (CH), 73.7 (C), 122.8 (CH), 125.3 (CH), 125.5 (CH), 126.3 (CH), 127.0 (CH), 127.1 (CH), 127.2 (CH), 127.4 (CH), 127.7 (CH), 128.3 (CH), 128.3 (CH), 128.3 (CH), 128.8 (CH), 129.9 (CH), 131.5 (C), 134.6 (C), 137.1 (C), 138.6 (C), 139.4 (C), 139.6 (C), 140.3 (C), 144.7 (C), 178.0 (C); FTIR (solid) *v* = 1688, 1392, 1353, 810, 762, 749, 735, 709 cm⁻¹; MS [EI] *m/z* (%) 427 (M⁺, 100), 336 (15), 294 (21), 279 (27); HMRS (EI): *m/z* calcd for C₂₄H₁₉NO [M⁺] 427.1936, found 427.1939.

(±) 9-chloro-2-azahexacyclo[10.6.6.0^{1,5}.0^{6,11}.0^{13,18}.0^{19,24}]tetracos-6(11),7,9,13,15,17,19(24),20,22-nonaen-3-one 4g and 4-phenyl-3,4-dihydro-1H-1-azacyclohept[de]anthracen-2-one 7

Following the general procedure, **3g** (0.36 g) was reacted with PPA and elution of the SiO₂ column with 2:1 DCM/petroleum ether gave the title compound **7** (0.06 g, 16% yield) as an orange solid; mp >310 °C; ¹H NMR (600 MHz, CDCl₃) δ 3.31 – 3.41 (2H, m), 4.91 – 4.95 (1H, m), 7.06 (2H, d, *J* = 8.4 Hz), 7.22 (2H, d, *J* = 8.4 Hz), 7.25 – 7.30 (1H, m), 7.39 (1H, t, *J* = 7.8 Hz), 7.53 – 7.59 (2H, m), 7.99 (1H, d, *J* = 8.4 Hz), 8.03 (2H, d, *J* = 8.8 Hz), 8.10 (1H, d, *J* = 8.8 Hz), 8.36 (1H, s); ¹³C NMR (150.9 MHz, CDCl₃) δ 41.7 (CH₂), 47.7 (CH), 121.3 (CH), 122.4 (C), 123.8 (C), 124.9 (CH), 125.7 (CH), 126.2 (CH), 127.2 (CH), 128.2 (C), 128.7 (CH), 128.9 (CH), 129.2 (CH), 129.5 (CH), 129.7 (CH), 131.6 (C), 132.7 (C), 133.4 (C), 172.6 (C); MS [EI] *m/z* (%) 359 (M⁺, 35), 357 (M⁺, 100), 314 (85), 204 (23), 111 (24); *m/z* calcd for C₂₃H₁₆ClNO [M⁺] 357.0924, found 357.0925. Further elution with DCM gave the title compound **4g** (0.13 g, 36 % yield) as a light brown solid; mp >310 °C; ¹H NMR (500 MHz, CDCl₃) δ 2.40 (1H, dd, *J* = 12.9, 14.5 Hz), 2.91 (1H, dd, *J* = 7.6, 14.5 Hz), 3.68 (1H, dd, *J* = 7.6, 12.9 Hz), 4.89 (1H, s), 6.75–6.82 (2H, m), 7.08 (1H, dm, *J* = 6.4 Hz), 7.2 – 7.34 (4H, m), 7.35 – 7.39 (2H, m), 7.42 – 7.53 (3H, m); ¹³C NMR (125.8 MHz, CDCl₃) δ 35.6 (CH₂), 47.8 (CH), 54.9 (CH), 65.9 (C), 119.9 (CH), 124.3 (CH), 125.1 (CH), 126.8 (CH), 127.3 (CH), 127.6 (CH), 127.7 (CH), 127.7 (CH), 128.3 (CH), 131.1 (CH), 132.7 (C), 133.0 (C), 136.2 (C), 138.8 (C), 140.9 (C), 141.6 (C), 143.8 (C), 177.1 (C); FTIR (solid) *v* = 1702, 1346, 841, 815, 759, 748, 722 cm⁻¹; MS [EI] *m/z* (%) 359 (M⁺, 35), 357 (M⁺, 100), 314 (34), 299 (14), 279 (13), 165 (20), 84 (25); *m/z* calcd for C₂₃H₁₆ClNO [M⁺] 357.0924, found 357.0926.

(±) **2-Benzyl-9-chloro-2-azahexacyclo[10.6.6.0^{1,5}.0^{6,11}.0^{13,18}.0^{19,24}]tetracos-6(11),7,9,13,15,17,19(24),20,22-nonaen-3-one 4h**

Following the general procedure, **3h** (0.45 g) was reacted with PPA and elution of the SiO₂ column with DCM gave the title compound **4h** (0.2 g, 45% yield) as a white solid; mp 308–309 °C; ¹H NMR (600 MHz, CDCl₃) δ 2.41 (1H, dd, *J* = 13.2, 16.2 Hz), 3.12 (1H, dd, *J* = 7.8, 16.2 Hz), 3.64 (1H, dd, *J* = 7.8, 13.2 Hz), 4.03 (1H, d, *J* = 15.6 Hz), 4.89 (1H, s), 5.37 (1H, d, *J* = 15.6 Hz), 6.85 (1H, d, *J* = 8.4 Hz), 6.93 (1H, dt, *J* = 0.6, 7.5 Hz), 7.06 (1H, d, *J* = 7.8 Hz), 7.09 (1H, dt, *J* = 2.4, 8.4 Hz), 7.12 – 7.15 (1H, m), 7.17 (1H, dt, *J* = 0.6, 7.5 Hz), 7.26 – 7.30 (2H, m), 7.32 – 7.36 (2H, m), 7.39 – 7.47 (6H, m); ¹³C NMR (150.9 MHz, CDCl₃) δ 35.7 (CH₂), 46.3 (CH), 48.1 (CH₂), 54.8 (CH), 73.5 (C), 122.9 (CH), 126.5 (CH), 127.3 (CH), 127.3 (CH), 127.4 (CH), 127.5 (CH), 127.5 (CH), 127.6 (CH), 127.7 (CH), 128.4 (CH), 128.8 (CH), 131.5 (CH), 132.6 (C), 133.1 (C), 134.4 (C), 138.4 (C), 140.1 (C), 141.2 (C), 143.9 (C), 177.6 (C); FTIR (solid) *v* = 1693, 1475, 1394, 1356, 852, 812, 751, 716 cm⁻¹; MS [EI] *m/z* (%) 449 (M⁺, 35), 447 (M⁺, 100), 356 (15), 314 (26), 299 (17), 279 (17); *m/z* calcd for C₃₀H₂₂ClNO [M⁺] 447.1390, found 447.1379.

(±) **9-Methoxy-2-azahexacyclo[10.6.6.0^{1,5}.0^{6,11}.0^{13,18}.0^{19,24}]tetracos-6(11),7,9,13,15,17,19(24),20,22-nonaen-3-one 4k**

Following the general procedure, **3k** (0.35 g) was reacted with PPA and elution of the SiO₂ column with DCM gave the title compound **4k** as a light grey solid (0.11g, 31% yield); mp >310 °C; ¹H NMR (600 MHz, CDCl₃) δ 2.40 (1H, dd, *J* = 13.2, 16.2 Hz), 2.91 (1H, dd, *J* = 7.8, 16.2 Hz), 3.67 (1H, dd, *J* = 7.8, 13.2 Hz), 3.78 (3H, s), 6.65 (1H, dd, *J* = 3.0, 8.4 Hz), 6.75 (1H, brs), 6.79 (1H, d, *J* = 8.4 Hz), 6.93 (1H, d, *J* = 3.0 Hz), 7.19 – 7.27 (3H, m), 7.29 (1H, t, *J* = 6.9 Hz), 7.36 (1H, d, *J* = 6.6 Hz), 7.45 (2H, m), 7.50 (1H, d, *J* = 7.8 Hz); ¹³C NMR (150.9 MHz, CDCl₃) δ 36.0 (CH₂), 47.7 (CH), 55.4 (CH), 55.4 (CH₃), 66.2 (C), 112.2 (CH), 113.8 (CH), 119.9 (CH), 124.3 (CH), 125.0 (CH), 126.5 (C), 126.8 (CH), 127.0 (CH), 127.5 (CH), 127.6 (CH), 128.1 (CH), 130.8 (C), 136.5 (C), 139.2 (C), 140.4 (C), 141.8 (C), 144.2 (C), 158.5 (C), 177.7 (C); FTIR (solid) *v* = 1700, 1661, 1350, 1257, 981, 801, 731 cm⁻¹; MS [EI] *m/z* (%) 353 (M⁺, 100), 310 (16), 86 (20), 84 (30); HMRS (EI): *m/z* calcd for C₂₄H₁₉NO₂ [M⁺] 353.1416, found 353.1419.

(±) **2-Benzyl-9-methoxy-2-azahexacyclo[10.6.6.0^{1,5}.0^{6,11}.0^{13,18}.0^{19,24}]tetracos-6(11),7,9,13,15,17,19(24),20,22-nonaen-3-one 4l**

Following the general procedure, **3l** (0.44 g) was reacted with TfOH, but with stirring at room temperature for 1h and elution of the SiO₂ column with DCM gave the title compound **4l** as a white solid (0.34 g 77% yield); mp 268–269 °C; ¹H NMR (600 MHz, CDCl₃) δ 2.40 (1H, dd, *J* = 12.6, 16.2 Hz), 3.11 (1H, dd, *J* = 7.8, 16.2 Hz), 3.63 (1H, dd, *J* = 7.8, 12.6 Hz), 3.77 (3H, s), 4.04 (1H, d, *J* = 15.6 Hz), 4.87 (1H, s), 5.37 (1H, d, *J* = 15.6 Hz), 6.65 (1H, dd, *J* = 3.0, 8.4 Hz), 6.83 (1H, d, *J* = 8.4 Hz), 6.89 (1H, d, *J* = 3.0 Hz), 6.91 (1H, dt, *J* = 1.2, 7.8 Hz), 7.06 (1H, d, *J* = 7.2 Hz), 7.11 – 7.17 (2H, m), 7.23 – 7.27 (2H, m), 7.34 (1H, t, *J* = 7.2 Hz), 7.39 – 7.44 (4H, m), 7.46 (2H, d, *J* = 7.2 Hz); ¹³C NMR (150.9 MHz, CDCl₃) δ 36.0 (CH₂), 46.2 (CH), 48.1 (CH₂), 55.4 (CH), 55.4 (CH₃), 73.8 (C), 112.3 (CH), 113.6 (CH), 122.8 (CH), 125.4 (CH), 125.5 (CH), 126.4 (CH), 126.5 (C), 127.0 (CH), 127.2 (CH), 127.2 (CH), 127.4 (CH), 127.7 (CH), 128.3 (CH), 131.1 (CH), 134.6 (C), 138.5 (C), 139.2 (C), 140.3 (C), 140.7 (C), 144.3 (C), 158.4 (C), 178.0 (C); FTIR (solid) *v* = 1688, 1501, 1351, 1244, 1034, 842, 762, 732, 712 cm⁻¹; MS [EI] *m/z* (%) 443 (M⁺, 100), 352 (15), 310 (21), 295 (16), 91 (21); HMRS (EI): calcd for C₂₄H₁₉NO [M⁺] 443.1885, found 443.1890.

(±) **8-methyl-2-azahexacyclo[10.6.6.0^{1,5}.0^{6,11}.0^{13,18}.0^{19,24}]tetracos-6(11),7,9,13,15,17,19(24),20,22-nonaen-3-one 4m**

Following the general procedure, **3m** (0.34 g) was reacted with PPA and elution of the SiO₂ column with DCM gave the title compound **4m** (0.25 g, 73% yield) as a light brown solid; mp 304–306 °C; ¹H NMR (500 MHz, CDCl₃) δ 2.20 (3H, s), 2.44 (1H, dd, *J* = 12.9, 16.0 Hz), 2.94 (1H, dd, *J* = 7.6, 16.0 Hz), 3.71 (1H, dd, *J* = 7.6, 12.9 Hz), 4.91 (1H, s), 6.69 (1H, s), 6.95 (1H, d, *J* = 7.6 Hz), 7.17 – 7.30 (6H, m), 7.35 (1H, d, *J* = 7.1 Hz), 7.44 (1H, d, *J* = 7.2 Hz), 7.45–7.50 (2H, m), 7.53 (1H, d, *J* = 7.4 Hz); ¹³C NMR (125.8

MHz, CDCl₃) δ 21.0 (CH₃), 35.9 (CH₂), 48.2 (CH), 55.0 (CH), 66.4 (C), 119.9 (CH), 124.3 (CH), 124.8 (CH), 126.6 (CH), 126.8 (CH), 127.3 (CH), 127.5 (CH), 127.6 (CH), 128.0 (CH), 128.1 (CH), 130.3 (CH), 134.3 (C), 136.5 (C), 136.5 (C), 137.3 (C), 139.7 (C), 141.8 (C), 144.7 (C), 178.1 (C); FTIR (solid) ν = 3180, 1697, 1343, 812, 736 cm⁻¹; MS [EI] *m/z* (%) 337 (M⁺, 100), 294 (30), 279 (25), 86 (18), 84 (29); *m/z* calcd for C₂₄H₁₉NO [M⁺] 337.1467, found 337.1452.

(±) 2-Benzyl-8-methyl-2-azahexacyclo[10.6.6.0^{1,5}.0^{6,11}.0^{13,18}.0^{19,24}]tetracos-6(11),7,9,13,15,17,19(24),20,22-nonaen-3-one 4n.

Following the general procedure, **3n** (0.43 g) was reacted with PPA and elution of the SiO₂ column with DCM gave the title compound **4n** (0.37 g, 87% yield) as a pale yellow solid; mp 156-158°C; ¹H NMR (600 MHz, CDCl₃) δ 2.23 (3H, s), 2.49 (1H, dd, *J* = 12.6, 16.2 Hz), 3.18 (1H, dd, *J* = 7.8, 16.2 Hz), 3.70 (1H, dd, *J* = 7.8, 12.6 Hz), 4.08 (1H, d, *J* = 16.2 Hz), 4.95 (1H, s), 5.41 (1H, d, *J* = 16.2 Hz), 6.76 (1H, s), 6.90 – 6.97 (2H, m), 7.10 (1H, d, *J* = 7.2 Hz), 7.14 – 7.19 (2H, m), 7.24 – 7.30 (3H, m), 7.37 (1H, t, *J* = 7.2 Hz), 7.40 – 7.48 (4H, m), 7.50 (2H, d, *J* = 7.2 Hz); ¹³C NMR (150.9 MHz, CDCl₃) δ 21.3 (CH₃), 36.0 (CH₂), 46.8 (CH), 48.3 (CH₂), 54.7 (CH), 73.9 (C), 123.6 (CH), 126.3 (CH), 126.9 (CH), 127.1 (CH), 127.3 (CH), 127.4 (CH), 127.6 (CH), 127.8 (CH), 128.0 (CH), 128.3 (CH), 128.8 (CH), 130.9 (CH), 134.4 (C), 134.6 (C), 136.9 (C), 137.4 (C), 138.6 (C), 139.8 (C), 140.3 (C), 145.0 (C), 178.2 (C); FTIR (solid) ν = 1698, 1454, 1346, 1320, 744, 710 cm⁻¹; MS [EI] *m/z* (%) 427 (M⁺, 100), 336 (20), 294 (23), 279 (24), 86 (58), 84 (89); *m/z* calcd for C₃₁H₂₅NO [M⁺] 427.1936, found 427.1931.

***N*-(Anthracen-9-yl-ethyl)-3-phenylacryl-amide 8**

To a stirred solution of LAH (5 mL of a 2M solution) in dry THF (30 mL) under Ar at -78°C was added, in one portion, AlCl₃ (0.5 g, 3.7 mmol) and the solution warmed to 0°C over 10 min. On re-cooling to -78°C, 9-(2-nitrovinyl)anthracene (1.3 g, 5.2 mmol)¹¹ was added in one portion and the reaction mixture allowed to warm to room temperature, then heated to 40°C for 30 min. On cooling to 0°C, 50 mL of THF was added, followed by careful addition of 2M NaOH (3 mL). After stirring for 30 min, Et₃N (0.7 mL, 5 mmol) and cinnamoyl chloride (0.8 g, 4.8 mmol) were added, and the reaction stirred at room temperature for 1h. The reaction mixture was filtered through celite and the collected solids washed with DCM (3 x 50 mL). The combined organics were concentrated by rotary evaporation and the residue redissolved in 9:1 Et₂O/DCM. This solution was then washed with 2M HCl (30 mL), H₂O (3 x 30 mL) and 1M NaOH (30 mL) and dried (MgSO₄). Filtration and removal of the solvent by rotary evaporation gave an oil which, on trituration with ether gave the title compound (0.8g) as pale yellow solid. Purification of the concentrated mother liquors by column chromatography on SiO₂, eluting with 3:1 DCM/petrol – DCM gave a further 0.45 g of product, total yield 1.25g, (68% yield);

mp 189-190°C; ¹H NMR (600 MHz, CDCl₃) δ 3.83 (2H, m), 3.96 (2H, 7.3 Hz), 5.79 (1H, brs), 6.25 (1H, d, *J* = 15.6 Hz), 7.25 (1H, s), 7.32 – 7.38 (2H, m), 7.43 – 7.49 (3H, m), 7.53 (2H, ddd, *J* = 1.2, 6.4, 7.7 Hz), 7.62 (1H, d, *J* = 15.6 Hz), 8.02 (2H, d, *J* = 8.4 Hz), 3.70 (2H, d, *J* = 8.9 Hz), 8.39 (1H, s); ¹³C NMR (150.9 MHz, CDCl₃) δ 27.8 (CH₂), 40.9 (CH₂), 120.6 (CH), 124.4 (CH), 125.2 (CH), 126.2 (CH), 126.7 (CH), 127.9 (CH), 128.9 (CH), 129.3 (CH), 129.8 (CH), 130.3 (C), 131.0 (C), 131.7 (C), 134.9 (C), 141.2 (CH), 166.5 (C); FTIR (solid) ν = 3302, 1651, 1613, 1535, 1329, 1215, 1120, 969, 873, 834, 727, 714, 658 cm⁻¹; MS [EI] *m/z* (%) 351 (M⁺, 8), 204 (41), 191 (100), 189 (48), 131 (85), 103 (53), 69 (51); *m/z* calcd for C₂₅H₂₁NO [M⁺] 351.1623, found 351.1620.

(19S,20R)(19R,20S)-20-phenyl-17-azapentacyclo[6.-6.-6.-0^{1,19}.0^{2,7}.0^{9,14}]icosa-2,4,6,9(14),10,12-hexaen-18-one 9

Following the general procedure for the PPA cyclisation, **9** (0.70 g, 2 mmol) was heated for 30 min at 130°C (heating block temperature). The product was purified by column chromatography on SiO₂, eluting with 5% EtOAc/DCM, isolated as a cream solid from ether trituration (0.67g, 96% yield); mp 159-160°C; ¹H NMR (600 MHz, CDCl₃) δ 2.77 (3H, s), 5.80 (2H, s), 6.88 (1H, d, *J* = 15.6 Hz), 7.32 – 7.40 (3H, m), 7.50 (2H, t, *J* = 7.5 Hz), 7.52 – 7.59 (4H, m), 7.86 (1H, d, *J* = 15.6 Hz), 8.05 (2H, d, *J* = 8.4 Hz), 8.37 (2H, d, *J* = 8.4 Hz), 8.50 (1H, s); ¹³C NMR (150.9 MHz, CDCl₃) δ 33.2 (CH₃), 41.9 (CH₂), 117.8 (CH), 124.3 (CH), 125.3 (CH), 126.9 (CH), 127.8 (C), 128.0 (CH), 128.5 (CH), 128.9 (CH), 129.4 (CH), 129.8 (CH), 131.5 (C), 135.4 (C), 143.2 (C), 143.2 (CH), 166.7 (C); FTIR (solid) ν = 1647, 1593, 1408, 1242, 1115, 990, 885, 760, 733, 701, 518 cm⁻¹; MS [EI] *m/z* (%) 351 (M⁺, 64), 204 (100), 191 (83), 189 (29), 131 (47), 103 (19); *m/z* calcd for C₂₅H₂₁NO [M⁺] 351.1623, found 351.1627.

***N*-(Anthracen-9-yl-methyl)-*N*-methyl-3-phenylacryl-amide 10**

To a stirred solution of *N*-anthracen-9-yl-methyl-methylamine (1.0 g, 4.6 mmol) and Et₃N (0.7 mL, 5 mmol) in DCM (50 mL) was added cinnamoyl chloride (0.77 g, 4.6 mmol) in DCM (20 mL) and stirred at room temperature for 1h. Water (20 mL) was added and the solid collected, washed with water (20 mL), Et₂O (2 x 50 mL) and dried (1.5 g, 92% yield). A small sample was recrystallised from EtOAc/petroleum ether as a white solid, mp 211-212 °C; ¹H NMR (600 MHz, CDCl₃) δ 2.77 (3H, s), 5.80 (2H, s), 6.88 (1H, d, *J* = 15.6 Hz), 7.32 – 7.40 (3H, m), 7.50 (2H, t, *J* = 7.5 Hz), 7.52 – 7.59 (4H, m), 7.86 (1H, d, *J* = 15.6 Hz), 8.05 (2H, d, *J* = 8.4 Hz), 8.37 (2H, d, *J* = 8.4 Hz), 8.50 (1H, s); ¹³C NMR (150.9 MHz, CDCl₃) δ 33.2 (CH₃), 41.9 (CH₂), 117.8 (CH), 124.3 (CH), 125.3 (CH), 126.9 (CH), 127.8 (C), 128.0 (CH), 128.5 (CH), 128.9 (CH), 129.4 (CH), 129.8 (CH), 131.5 (C), 135.4 (C), 143.2 (C), 143.2 (CH), 166.7 (C); FTIR (solid) ν = 1686, 1398, 776, 765, 755, 731, 704, 591 cm⁻¹; MS [EI] *m/z* (%) 351 (M⁺, 100),

220 (58), 191 (49); MS [EI] m/z (%) 351 (M^+ , 100), 220 (19), 191 (17), 179 (26); m/z calcd for $C_{25}H_{21}NO$ [M^+] 351.1623, found 351.1611.

(±) 16-methyl-19-phenyl-16-azapentacyclo[6.6.5.0^{1,18}.0^{2,7}.0^{9,14}]nonadeca-2,4,6,9(14),10,12-hexaen-17-one **11**

A solution of **10** (0.35g, 1 mmol) in chlorobenzene (10 mL) was heated under gentle reflux for 2h. The reaction mixture was cooled and the product purified by column chromatography on silica, initially eluting with 3:1 petroleum ether/DCM to remove the chlorobenzene, then with DCM to give 0.30g of (±) 16-methyl-19-phenyl-16-azapentacyclo[6.6.5.0^{1,18}.0^{2,7}.0^{9,14}]nonadeca-2,4,6,9(14),10,12-hexaen-17-one **11** as a white solid (86% yield), crystallised from Et₂O/petroleum ether, mp 211-212°C; ¹H NMR (600 MHz, CDCl₃) δ 2.70 (1H, dd, J = 0.9, 7.6 Hz), 3.03 (3H, d, J = 0.9 Hz), 3.31 (1H, dd, J = 1.7, 7.66 Hz), 4.31 (1H, d, J = 10.5 Hz), 4.34 (1H, d, J = 10.5 Hz), 4.88 (1H, d, J = 1.7 Hz), 7.11 (2H, d, J = 7.2 Hz), 7.14 – 7.23 (6H, m), 7.25 – 7.27 (1H, m), 7.31 – 7.36 (2H, m); ¹³C NMR (150.9 MHz, CDCl₃) δ 30.41 (CH₃), 45.1 (CH), 48.8 (CH₂), 50.4 (CH), 51.1 (CH), 119.3 (CH), 121.7 (CH), 123.2 (CH), 126.1 (CH), 126.2 (CH), 126.3 (CH), 126.6 (CH), 126.8 (CH), 127.1 (CH), 127.7 (CH), 128.5 (CH), 138.4 (C), 140.8 (C), 143.6 (C), 143.8 (C), 146.7 (C), 173.6 (C); FTIR (solid) ν = 1686, 1398, 776, 765, 755, 731, 704, 591 cm⁻¹; MS [EI] m/z (%) 351 (M^+ , 100), 220 (58), 191 (49); m/z calcd for $C_{25}H_{21}NO$ [M^+] 351.1623, found 351.1620.

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References

- 1 F. D. King and S. Caddick, *Tetrahedron*, 2013, **69**, 8592.
- 2 F. D. King, A. E. Aliev, S. Caddick and D. A. Tocher, *J. Org. Chem.* 2013, **76**, 10938.
- 3 H. Adams, R. A. Bawa, K. G. McMillan and S. Jones, *Tetrahedron: Asymmetry*, 2007, **18** 1003.
- 4 O. Dimroth *Chem. Ber.*, 1901, **34**, 219.
- 5 M. Avalos, R. Babiano, J. L. Barneto, P. Cintas, F. R. Clemente, J. L. Jimenez and J. C. Palacios, *J. Org. Chem.*, 2003, **68**, 1834.
- 6 H. Günther, *NMR Spectroscopy: Basic Principles, Concepts and Applications in Chemistry*, 2nd ed, Wiley, 1995, (see Eq. 4.13b).
- 7 S. Ram and L. D. Spicer, *Tetrahedron Lett.*, 1987, **28**, 515.
- 8 F. D. King, A. E. Aliev, S. Caddick and R. C. B. Copley, *Org. Biomol. Chem.* 2009, **7**, 3561.
- 9 T. N. Parac-Vogt, N. Tatjana and K. Binnemans, *Tetrahedron Lett.*, 2004, **45**, 3137.
- 10 K.Y. Koltunov, S. Walspurger and J. Sommer, *Eur. J. Org. Chem.*, 2004, 4039.
- 11 N. Mase, K. Takabe and F. Tanaka, *Tetrahedron Lett.*, 2013, **54**, 4306.
- 12 R. A. Glennon, S. P. Runyon, M. Taroua, R. B. Westkaemper, B. L. Roth and J. E. Savage, *Bioorg. Med. Chem. Lett.*, 2001, **11**, 655; S. M. Bagale, A. S. Brown, T. L. Micotto, K. Saleesh J. N. Wilson, G. Carballos, M. Melissa, I. D. Hentall and A. Vitores, *Bioorg. Med. Chem. Lett.* 2011, **21**, 7387.

- 13 T. M. Krygowski, M. K. Cyrański, K. Nakata, M. Fujio and Y. Tsuno, *Tetrahedron*, 1997, **53**, 11383.
- 14 N. Kornblum and A. Scott, *J. Amer. Chem. Soc.*, 1974, **96**, 590.
- 15 C. S. Rondestved and C. D. ver Nooy, *J. Amer. Chem. Soc.*, 1955, **77**, 4878.
- 16 A. E. Aliev, Z. A. Mia, H. S. Khaneja and F. D. King, *J. Phys. Chem. A*, 2012, **116**, 1093.