Palladium-Catalysed Synthesis of Dibenzo[*de,g*]quinolines. A Novel Approach to the B-Ring System of Aporphine-Related Heterocycles

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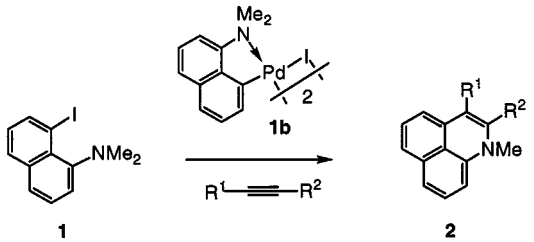
Dibenzo[*de,g*]quinolines **5** were formed by the palladium-catalysed heteroannulation of disubstituted alkynes and 1-iodo-10-(dimethylamino)phenanthrene (**3c**). Symmetric alkynes led to high levels of regioselectivity. These reactions constitute a new synthesis of the B-ring system of aporphine heterocycles.

Introduction

The metallation of aromatic tertiary amines has been the subject of intensive investigation, notably in palladium(II) chemistry[1] and synthetic applications of the resulting cyclopalladated complexes have been explored. In particular, reactions of these complexes with disubstituted alkynes have been developed into attractive and powerful methods for heterocycle synthesis.[2] Whereas intensive studies have been directed towards the palladium-mediated synthesis of five- and six-membered N-heterocycles starting from primary or secondary amines containing an *ortho* iodo substituent,[3] only a few examples involving tertiary amine substrates have been reported.

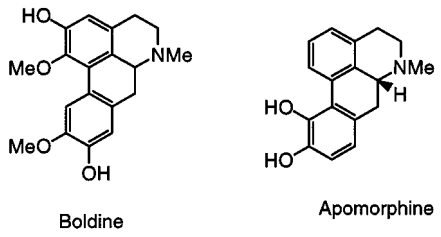
Recently, we embarked on a study aimed at extending the synthetic potential of the reaction of cyclopalladated aromatic tertiary amines with alkynes with a view to preparing heterocyclic compounds with potential biological activity. We showed that the heteroannulation of 8-iodo-1-(dimethylamino)naphthalene (**1**) with a number of disubstituted alkynes catalysed by the palladium complex **1b** led to the benzo[*d,e*]quinolines **2** (Scheme 1).[4]



Scheme 1

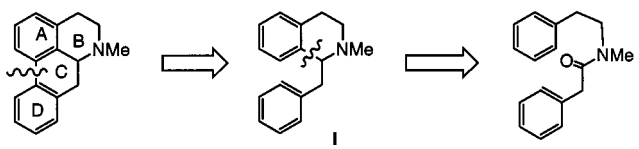
Key features of this protocol, which involves the formation of both a C−C and a C−N bond, include the favourable yields obtained for alkynes containing aryl or electron-withdrawing groups, the high level of regioselectivity observed in the insertion of disymmetric alkynes and the in situ *N*-demethylation leading to the neutral six-membered heterocycles **2**.

Aporphines are isoquinoline-related alkaloids with diverse therapeutic or physiological properties and occur in numerous plants. For example, Boldine (*Peumus boldus*) has choleretic and cholagogue properties;[5a] apomorphine, a nonnatural aporphine, is used as an antiparkinsonism agent,[5b] while several others have potential uses in cancer treatment[5c] (Scheme 2).



Scheme 2

These alkaloids are usually prepared according to a multistep protocol employing a Bischler−Napieralski condensation followed by a Pschorr cyclisation[6a] or a non-phenolic oxidative coupling[6b] of the intermediate benzylisoquinoline **I** (Scheme 3).



Scheme 3

The benzo[*d*,*e*]quinolines, **2** depicted above effectively constitute the ABC fragment of aporphines.[6c] Therefore the route presented in Scheme 1, which involves the construction of the B fragment, merited further investigation as a potential synthetic strategy for the preparation of closely related analogues of these alkaloids by the heteroannulation

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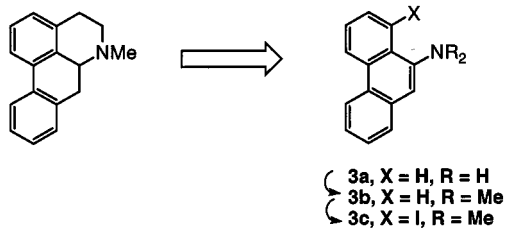
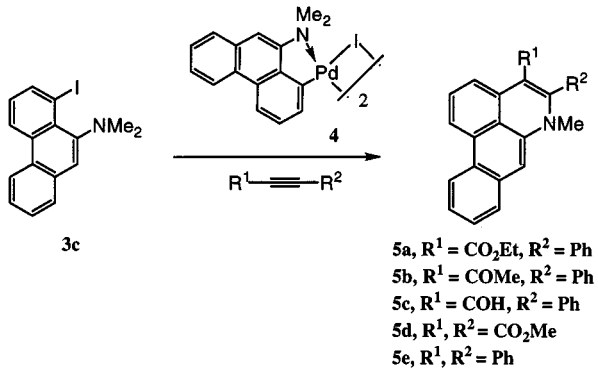
of 1-iodo-10-(dimethylamino)phenanthrene (**3c**) (Scheme 4).



Scheme 4

In this paper we report the reaction between **3c** and alkynes in the presence of a palladium catalyst **4** (Scheme 5). We chose this system based upon our previous observations made with the related system **1**.[4]



Scheme 5

Results and Discussion

The starting material, 9-phenanthrylamine **3a**, which is both commercially available and accessible by a multistep synthesis,[7] was obtained in 80% yield by lithiation of 9-bromophenanthrene followed by treatment with trimethylsilylmethyl azide (TMSMA)[8] and subsequent hydrolysis. Dimethylation gave the known **3b**,[9] which was converted into the iodo-bridged cyclopalladated complex **4**[9] by a C−H activation process, or into **3c** by a chelation controlled lithiation followed by the addition of iodine.

Our initial attempts at catalysis focused on directly applying the conditions developed earlier for the synthesis of **2** (see Scheme 1) in which the best palladium catalyst was found to be the iodo-bridged cyclopalladated (dimethylamino)naphthalene compound **1b** in refluxing PhCl. The use of other conventional palladium catalysts were (in general) unsuccessful, although in the case of PhC≡CCOOEt the corresponding heterocycle **2a** could be synthesised in 70% yield using the $Pd(OAc)_2/PPh_3$ catalytic system.[10]

In the present case, the dimer **4** abbreviated as $\{(dmpa)Pd(\mu\text{-}I)\}_2$, was also found to be the best catalyst for the reaction depicted in Scheme 5, although the precise reaction conditions had to be modified in order to achieve the best results. Thus we found that **4** had to be added to a solution of the alkyne in PhCl at reflux temperature. The reaction medium turned black, most likely because of the partial formation of metallic palladium, then became apparently more homogeneous as the black precipitate appeared to redissolve after 0.1 h with the formation of a clear yellow solution. Addition of **3c** to this solution did not alter its appearance and the catalytic formation of the heterocycle took place without any visible change in the solution. However, a decrease in temperature led to the irreversible deposition of palladium black with a consequent loss of catalytic activity. This observation is in marked contrast to previous observations[4] where the formation of **2** occurred in the presence of palladium black.

This behaviour seems to indicate that the novel heterocycle **5** obtained may interact with the palladium(0) formed, thus preventing its precipitation as palladium metal. However, every attempt to characterise such species failed. Note that the role of **3c** is obviously to regenerate **4** from this latter soluble Pd^0 species, as we have shown that in the absence of **4**, no heterocyclisation occurs (see below, Table 2, entry 5).

The catalytic heterocyclisation of **1** could be achieved with alkynes bearing either electron-releasing or electron-withdrawing substituents. No reaction was observed when **3c** was treated with electron-rich alkynes such as 2,2-dimethyl-4-pentyne or 3-hexyne. Even with diphenylacetylene, good yields of the expected heterocycle **5e** could only be obtained when **4** was treated with one equivalent of alkyne per palladium atom in a stoichiometric reaction. In this case, carrying out the reaction as depicted in Scheme 5, i.e. with 10% of **4** did not lead to reproducible results: we found in one case only a 50% conversion of **3c** to **5e** after 21 h. However, this result was achieved on one occasion only and thus the stoichiometric route for the preparation of **5e** was preferred.

Previously, we have noted that "electron-poor" alkynes afford the best yields in the heterocyclisation of **1**, this was also the case in our current study; dimethylacetylene dicarboxylate yielded 32% of **5d** starting with **3c** in the presence of **4** (10%).

The best yields of compounds **5** were obtained with non-symmetrical internal alkynes in which one substituent is electron-withdrawing. The comparison of three alkynes, ethyl phenylpropynoate, 4-phenyl-3-butyn-2-one, and phenylpropynal (Table 1) showed that the best conversion was attained when the alkyne was substituted by the most electron-withdrawing group of the series (i.e. −CHO).

Table 1. Results for the heterocyclisation of **3c** and alkynes substituted with different electron-withdrawing groups on use of 5% palladium

Entry	R^1	R^2	Product	Reflux (h)	Conversion (%)[a]
1	COOEt	Ph	**5a**	100	81
2	COMe	Ph	**5b**	100	100
3	CHO	Ph	**5c**	58	100

[a] Measured by ^1H NMR vs. Ph_3CH as the internal reference − see Experimental Section.

High levels of regioselectivity were observed when symmetric alkynes were employed. In accord with previous results, we conclude from ^{1}H NMR that the phenyl group in **5a**, **5b**, and **5c** is on the carbon adjacent to the nitrogen atom[11] i.e. C-5. In *N*-methyl-2,3-diphenyldibenzo[*de,g*]quinoline **5e** an important shielding of the H-3 proton was observed due to the adjacent Ph group, whereas in **5a**, **5b**, and **5c** such a high-field shift was absent. Therefore we concluded that the phenyl group was not attached to C-4 but to C-5. Analysing the reaction between **3c** and ethyl phenylpropynoate in closer detail allowed us to obtain interesting information about both the likely reaction pathway and the optimisation of the reaction conditions. For a given catalyst concentration, the concentration of **5a** increases linearly as a function of time, over a given period the duration of which is a function of the concentration of **4**. The resulting rate constant enabled us to calculate the corresponding TOF; the concentration of **5a** attained (at the end of this period) is evidently related to the maximum conversion of **3c** to **5a**.

Table 2. Catalytic heterocyclisation of **3c** and PhC≡CCOOEt to **5a**

Entry	**4** (mmol-%)	Reaction time (h)	Max conversion (%)	TOF (h^{-1})
1	10	100	95	0.07
2	5	100	81	0.10
3	1	50	55	1.10
4	0.6	60	34	0.95
5	0	127	0	0

TOF and maximum conversion are reported vs. the amount of palladium used (mmol-%) and Figure 1 indicates that maximum catalytic activity should be observed for ca. 2.5% of **4** leading to an optimum yield of 70% of the heterocycle **5a**. Conversely, with higher amounts of **4** a lower activity was observed, although an almost quantitative yield of **5a** resulted. This suggests that when higher concentrations of **4** are employed, a small amount of catalyst is required for the reaction, but it may be replaced by the "stock" of **4** present in solution thus leading to higher conversions.

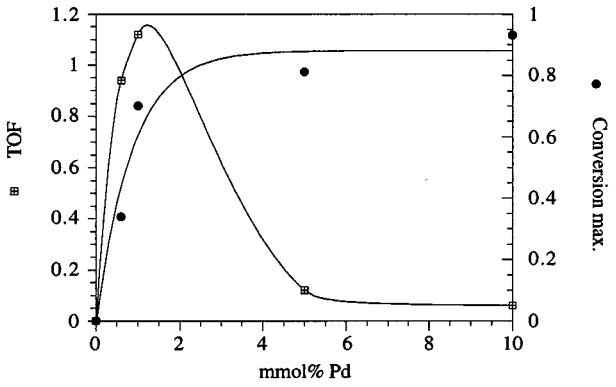
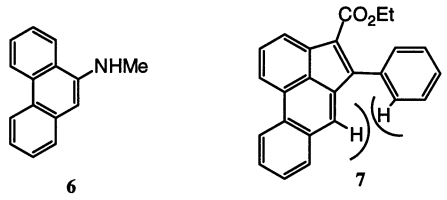


Figure 1

The reaction conditions proved to be crucial in the case of PhC≡CCOOEt, since a totally different reaction course was noted and different products observed when **4** was added to a reaction mixture containing the alkyne and **3c**. In this instance the reaction mixture darkened and remained so throughout the reaction, and in addition to **5a** (22%), two other products were characterised (Scheme 6). The first of them was easily identified as the *N*-methylated derivative **6** (20%), and the second displayed a ^{1}H-NMR spectrum very similar to that of **5a** with the exception that no N−Me group was observed. This product was deduced to be the carbocyclic derivative **7** (23%) on the basis of both a High-Resolution FAB mass spectrum and a ROESY NMR experiment, which allowed us to conclude that the phenyl unit was indeed at the carbon atom adjacent to C-6.



6 **7**

Scheme 6

Conclusion

A palladium-catalysed route towards aporphine-related dibenzo[*de,g*]quinolines has been developed. Although this reaction is closely related to the protocol employed for the synthesis of **2** (see Scheme 1), it is clearly not a simple extension of this work. The reaction is thought to proceed by an initial stoichiometric-like insertion of the alkyne in the Pd−C bond of **4**, followed by reductive elimination with C−N bond formation to afford **5** and palladium(0). The latter undergoes oxidative addition to **3c** with the regeneration of **4** and continuation of the catalytic cycle. The demethylation reaction that occurs synchronously to the insertion of the alkynes is a very important feature of this heterocyclisation process. In the related reaction involving **1** (Scheme 1) we were able to show that MeI was produced, whereas when the corresponding *N*,*N*-diethyl derivative of **1** was used, EtI was formed.[9] Since the alkyl halides formed in both cases are primary alkyl iodides, we favour an S_N2 like mechanism for the dealkylation process.

The total synthesis of true aporphines with this methodology as a key step would necessitate (i) the preliminary synthesis of phenanthrylamines in which the phenanthrene unit has a closer structural analogy to those found in the natural alkaloids,[12] and (ii) to establish the conditions for the removal of the substituents at C-4 and C-5. From this latter point of view, the diester **5d** is an ideal candidate.

Experimental Section

General: Reactions were carried out under a dry nitrogen atmosphere. All solvents were purified by conventional distillation techniques with the exception of commercial grade chlorobenzene (PhCl) which was used as received. Palladium reagents were prepared from $PdCl_2$ according to the literature.[13] − NMR experi-

ments were performed on Bruker SY 200, AC 300, AM 400, and DRX 500 spectrometers. For the ^{13}C-NMR spectra, the nature of the different carbon atoms was specified using a Dept 135 experiment when possible. The spectra were measured in $CDCl_3$ and chemical shifts are given in ppm relative to TMS. − Mass spectra and microanalysis were performed by the Service Commun de Microanalyse and the Laboratoire de Spectrométrie de Masse de Strasbourg. − The chromatographic separations were performed on Merck silica gel Si 60 (40−63 μm) unless otherwise specified. − Ph_3CH (used as internal reference) and *n*-butyllithium (*n*BuLi, 1.6 M in hexanes) were commercial products. Alkynes were obtained from commercial sources, trimethylsilylmethylazide (TMSMA),[8] **3b**[9] and **4**[9] were synthesised according to known procedures.

9-Phenanthrylamine (3a) (*CAUTION*: Aromatic amines are known to be mutagenic and carcinogenic agents. Therefore the following synthesis should only be undertaken in well-ventilated room with appropriate safety clothes): *n*BuLi (31.3 mmol, 19.5 mL) was added dropwise to a solution of 9-bromophenanthrene (6.7 g, 26.1 mmol) in a 1:9 Et_2O/*n*-hexane mixture (50 mL) in a 500 mL round-bottomed Schlenk flask equipped with *a large magnetic stirrer*. After 1.5 h, the white precipitate was collected by filtration, washed with *n*-hexane (2 × 10 mL), dried in vacuo, and suspended in Et_2O. TMSMA (1.2 equiv.) was added, and after 1.5 h, treated with 6 N HCl (100 mL). The sticky pale pink precipitate formed was rapidly collected (light-sensitive), and ether (200 mL) and a saturated solution of KOH (50 mL) was added. The mixture was stirred vigorously, the organic phase separated, and the aqueous phase re-extracted with several 50 mL portions of ether until the orange amine colouration disappeared. The original acidic aqueous layer was neutralised and extracted with ether as described above. The combined organic phases were concentrated in vacuo, redissolved in CH_2Cl_2, dried with $CaCl_2$, and treated with activated charcoal. Filtration through Celite and concentration of the filtrate afforded 4.0 g of **3a** (80%), yellowish pink solid. Spectral data (^{1}H and ^{13}C NMR) were consistent with those from a commercial sample (Aldrich).

10-(Dimethylamino)-1-iodophenanthrene (3c): *n*BuLi (15.5 mL, 25 mmol) was added to 1:1 Et_2O/*n*-hexane (20 mL) solution of **3b** (3.6 g, 16.4 mmol) and stirred for 4 days at room temperature. The off-white precipitate was collected by filtration, washed with *n*-pentane (2 × 10 mL) then suspended in ether (20 mL). An ethereal solution (40 mL) of iodine (4.5 g, 17.7 mmol) was slowly added and the reaction mixture stirred for one hour. After washing with a saturated $Na_2S_2O_3$ solution (2 × 50 mL), the organic phase was dried with $MgSO_4$ then treated with activated charcoal. Filtration and concentration of the filtrate afforded 3.45 g of **3c** (61%) as a brown oil. Yellow needles were obtained from CH_2Cl_2/*n*-hexane (99:1). − ^{1}H NMR (300 MHz): δ = 8.72−8.69 (m, 1 H), 8.55−8.52 (m, 1 H), 8.36−8.34 (m, 1 H), 7.80−7.78 (m, 1 H), 7.57−7.52 (m, 2 H), 7.47 (s, 1 H), 7.24−7.19 (m, 1 H), 2.74 (s, 6 H). − ^{13}C NMR (75 MHz): δ = 148.0, 141.9, 133.6, 132.4, 128.2, 127.5, 127.3, 127.1, 125.2, 123.6, 122.6, 115.7, 89.5, 44.5. − $C_{16}H_{14}IN$ (315.11): C 55.35, H 4.06, N 4.03; found C 55.91, H 4.20, N 3.86.

Catalysis: The amount of **3c** indicated was calculated to take into account the corresponding tertiary amine present in the catalyst **4**. The data reported in Table 2 were obtained by taking several samples (2 mL) of the reaction mixture during the reaction time. Each sample was dried in vacuo and dissolved in $CDCl_3$ prior to NMR analysis. The concentration of the various species was calculated from their normalised integrals (for **3c**, δ = 2.74, 6 H, NMe_2; for **5**, δ ≈ 3, 3 H, NMe and δ ≈ 6.5, 1 H, H_7) vs. the integral of the methine proton of Ph_3CH (δ = 5.50) employed as internal standard. − "Standard conditions" refer to a Schlenk tube equipped with a magnetic stirrer and a condenser in a thermostated oil bath at 150°C.

Ethyl *N*-Methyl-2-phenyldibenzo[*de*,*g*]quinoline-3-carboxylate (5a): Ethyl phenylpropynoate (124 mg, 0.71 mmol) in PhCl (20 mL) was heated to reflux under the standard conditions (see above). At reflux, a solution of **4** (27 mg) in PhCl (20 mL) was rapidly added, causing the colour of the reaction mixture to turn from light yellow to black. The iodo compound **3c** (204 mg, 0.59 mmol) in PhCl (20 mL) was then added. A few minutes later, the colour of the reaction mixture became bright yellow and remained so for the remainder of the reaction (7.5 h). Removal of the solvent in vacuo, followed by chromatography of the resulting black oily residue (Et_2O:hexane, 10:90) gave bands of unchanged **3c** followed by the heterocycle **5a** (Et_2O/hexane, 30:70), as golden flakes (115 mg, 47%) and ^{1}H-NMR data in accord with previous observations[9]. − ^{13}C NMR (125 MHz): δ = 167.7, 146.0, 139.9, 135.8, 133.8, 132.0, 130.8, 129.1, 125.2, 110.2 (quaternary carbons), 129.1 (2C), 129.0, 128.7 (2C), 128.2, 127.1, 126.9, 123.3, 122.6, 118.3, 116.8, 100.0 (CH), 60.3 (CH_2), 37.3, 13.5 (CH_3).

3-Acetyl-*N*-methyl-2-phenyldibenzo[*de*,*g*]quinoline (5b): Same conditions as for **5a**. 24% yield (28 mg) from 4-phenyl-3-butyn-2-one (49 mg, 0.34 mmol), **4** (13 mg), and **3c** (101 mg, 0.29 mmol), reaction time 6 h. **5b** was obtained as yellow crystals from CH_2Cl_2/*n*-hexane (99:1) at −20°C. − ^{1}H NMR (500 MHz): δ = 8.36 (d, 1 H, *J* = 8.2 Hz), 8.19 (d, 1 H, *J* = 8.2 Hz), 7.62 (d, 1 H, *J* = 8.0 Hz), 7.50−7.34 (m, 8 H), 7.17 (d, 1 H, *J* = 7.7 Hz), 6.53 (s, H_7), 3.06 (s, 3 H, NMe), 1.77 (s, 3 H, COMe). − ^{13}C NMR (125 MHz): δ = 203.2, 143.5, 140.2, 135.0, 133.8, 132.3, 130.6, 129.9 (2C), 129.8, 129.2 (2C), 128.3, 127.2, 126.9, 125.4, 125.1, 123.4, 122.7, 119.4, 118.5, 116.6, 100.1, 37.6, 31.6. − $C_{25}H_{19}NO$ (349.15): C 85.93, H 5.48, N 4.01; found C 85.81, H 5.50, N 3.97.

Dimethyl *N*-Methyldibenzo[*de*,*g*]quinoline-2,3-dicarboxylate (5d): Same conditions as for **5a**. 32% yield (35 mg) from dimethyl acetylenedicarboxylate (66 mg, 0.47 mmol), **4** (13 mg), and **3c** (101 mg, 0.29 mmol), reaction time 3.5 h. **5d** was obtained as orange crystals from CH_2Cl_2/*n*-hexane (99:1) at −20 °C overnight, in with ^{1}H-NMR data in accord with those previously reported[9]. − ^{13}C NMR (50 MHz): δ = 166.2, 165.1, 144.4, 138.0, 133.0, 131.8, 129.1, 128.3, 127.4, 127.1, 125.9, 125.4, 124.3, 122.6, 119.5, 119.5, 104.9, 101.3, 53.1, 51.9, 37.3.

***N*-Methyl-2,3-diphenyldibenzo[*de*,*g*]quinoline (5e):** Compound **5e** was obtained from diphenylacetylene (83 mg, 0.46 mmol) by treatment with an approximately stoichiometric amount of **4** (200 mg, 0.44 mmol) in PhCl (30 mL) at reflux for 3 h. **5e** was obtained as greenish yellow crystals from hot CH_2Cl_2 (261 mg, 77%). − ^{1}H NMR (400 MHz): δ = 8.37 (d, 1 H, *J* = 8.3 Hz), 8.14 (d, 1 H, *J* = 7.8 Hz), 7.65 (d, 1 H, *J* = 8.1 Hz), 7.47−7.43 (m, 1 H), 7.36−7.32 (m, 1 H), 7.26−7.07 (m, 11 H), 6.61 (d, 1 H, *J* = 7.5 Hz), 6.50 (s, 1 H), 3.03 (s, 3 H). − ^{13}C NMR (100 MHz): δ = 142.3, 141.0, 138.0, 136.2, 135.6, 134.5, 132.2, 131.8, 130.2 (2C), 128.3 (2C), 128.2 (3C), 127.9, 127.8, 127.0, 126.7, 126.3, 125.6, 124.7, 122.7, 122.5, 117.8, 117.7, 116.9, 98.1, 37.4. − $C_{29}H_{21}N$ (383.17): C 90.83, H 5.52, N 3.65; found C 90.23, H 5.51, N 3.58.

2-Formyl-*N*-methyl-3-phenyldibenzo[*de*,*g*]quinoline (5c): Phenylpropynal (33.2 mg, 0.3 mmol) was added to a 0.04 M solution of Ph_3CH in PhCl (25 mL) and it was heated to reflux in the standard conditions. The volume was adjusted to 40 mL with PhCl, 2.5 mL of a 0.0018 M solution of **4** in PhCl and 5 mL of a 0.03 M solution of **3c** in PhCl. After 58 h at reflux, the same isolation procedure as

before gave the pure heterocycle **5c** (45 mg, 81%) as red crystals from CH_2Cl_2 after storage at −20°C overnight. − ^{1}H NMR (500 MHz): δ = 9.15 (s, 1 H), 9.02 (d, 1 H, *J* = 7.8 Hz), 8.44 (d, 1 H, *J* = 7.9 Hz), 8.33 (d, 1 H, *J* = 8.3 Hz), 7.68−7.39 (m, 9 H), 6.79 (s, 1 H), 3.11 (s, 3 H). − ^{13}C NMR (125 MHz): δ = 190.0, 161.1, 137.9, 133.0, 132.6, 131.2, 129.9, 129.5 (2C), 129.5, 129.4, 129.3, 128.7, 127.5, 127.2, 126.5, 124.8, 124.7, 122.6, 119.6, 119.3, 112.9, 103.5, 37.5. − $C_{24}H_{17}NO$ (335.13): C 85.95, H 5.11, N 4.18; found C 85.55, H 5.07, N 4.10.

Ethyl 5-Phenylacephenanthrylene-4-carboxylate (7): The same procedure as for **5c** was applied with ethyl phenylpropynoate (60 mg, 0.3 mmol) except that **3c** (85.4 mg, 0.25 mmol) was added prior to **4** [1 mL of a 11.5 mg solution in PhCl (10 mL)]. After 124 h reflux, the solvent was removed in vacuo and the residue chromatographed (200 mL Et_2O/*n*-hexane, 10:90 then 200 mL Et_2O/*n*-hexane, 15:85) to afford **7** (R_f = 0.43, yellow solid, 20 mg, 23%) and **6** (R_f = 0.32, brown wax, 10 mg, 20%) and finally **5a** (R_f = 0.32, 21 mg, 22%). − ^{1}H NMR (500 MHz): δ = 8.70 (d, 1 H, *J* = 8.1 Hz), 8.47 (d, 1 H, *J* = 8.1 Hz), 8.27 (d, 1 H, *J* = 6.9 Hz), 8.03 (s, 1 H), 8.00 (ddd, 1 H, *J* = 8.0, 0.6, 0.6 Hz), 7.80−7.74 (m, 2 H), 7.66−7.62 (m, 3 H), 7.56−7.49 (m, 3 H), 4.33 (q, 2 H), 1.27 (t, 3 H). − HRMS (FAB); *m/z*: 350.1312. − $C_{25}H_{18}O_2$ (350.4170).

***N*-Methylphenanthrylamine (6):** − ^{1}H NMR (300 MHz): δ = 8.71 (d, 1 H, *J* = 7.7 Hz), 8.54 (d, 1 H, *J* = 8.2 Hz), 7.89 (d, 1 H, *J* = 8.5 Hz), 7.74−7.61 (m, 3 H), 7.52−7.37 (m, 2 H), 6.78 (s, 1 H), 4.43 (br s, 1 H), 3.11 (s, 3 H). − HRMS (FAB); *m/z*: 207.1049. − $C_{15}H_{13}N$ (207.1048).

Alternative Synthesis of Ethyl *N*-Methyl-2-phenylbenzo[*d,e*]quinoline-3-carboxylate (2a): An NMP suspension (40 mL) of **1** (320 mg, 1.1 mmol), $Pd(OAc)_2$ (13.4 mg, 0.06 mmol), ethyl phenylpropynoate (222 mg, 1.3 mmol), Na_2CO_3 (552 mg, 5.2 mmol), LiCl (44 mg, 1.0 mmol), and PPh_3 (14 mg, 0.05 mmol) was heated for 21 h at 130°C. After cooling to room temperature, water was added (50 mL) and the product extracted with ether (5 × 25 mL). The combined organic phases were washed with water (5 × 25 mL), dried with $MgSO_4$, filtered, and concentrated to yield a brown oil. Purification by column chromatography (alumina: CH_2Cl_2/*n*-hexane, 30:70).gave yellow crystals (257 mg, 71%) on concentration. ^{1}H-NMR data were in agreement with those previously reported.[4]

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