A New Synthetic Approach to Dioxoaporphines − Application to the Synthesis of *N*-Methylouregidione

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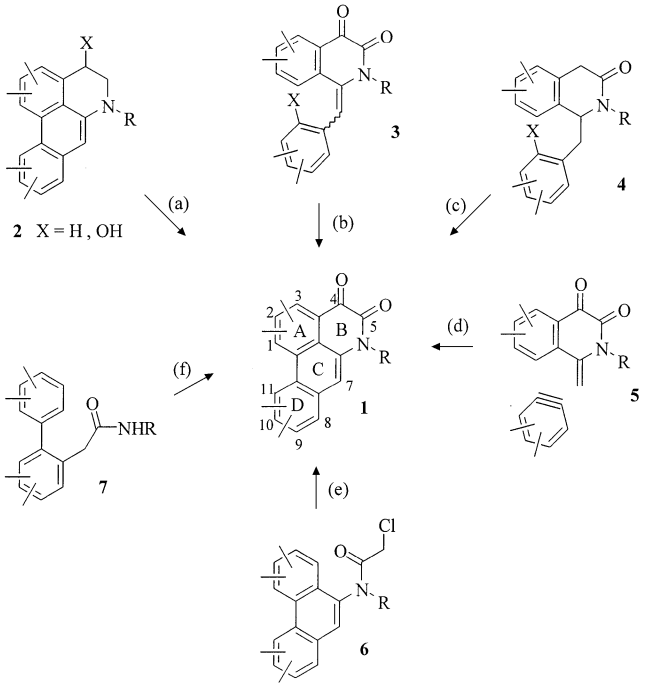
A convenient and versatile short-step synthesis of dioxoaporphines, illustrated by the first total synthesis of the alkaloid *N*-methylouregidione (**1c**), is described.

4,5-Dioxoaporphine alkaloids **1** constitute a small group of isoquinoline alkaloids of significant biological importance, but found only in very low proportions in natural sources.[1] They are most probably derived from aporphine by biological oxidation[2] and it has been suggested that these highly oxidized aporphinoids exhibit DNA-modifying bioactivity[3] and might act as post-infection phytoalexins, with the reduced aporphines as their immediate precursors.[4] Furthermore, they are structurally and biogenetically related to aristolactams and aristolochic acids, both of recognized antitumoral activity.[5] The total synthesis of these alkaloids has been achieved by several different approaches (Scheme 1). Historically, the first synthetic routes to these tetracyclic nitrogenous substances involved the sensitized photooxidation[6] or direct oxidation of the dehydroaporphines **2** (X = H)[7] or hydroxydehydroaporphines[2] **2** (X = OH), respectively (Scheme 1, route a). The conceptually different synthetic routes b and c share the feature that the strategic biaryl bond connecting the A and D rings is formed in the key final operation and assembly of the phenanthrene ring system is then achieved either by photochemical electrocyclization of 1-benzylideneisoquinoline-3,4-diones **3**[8] or by tributyltin hydride mediated intramolecular radical cyclization of 1-bromobenzylisoquinolin-3-ones **4.**[9] A more convergent synthetic route based on the formation of ring C by intermolecular benzyne cycloaddition (IBC) to 1-methylene-3,4-dioxoisoquinolines **5** generated in situ (route d) has also been reported.[10] The use of photochemistry also proved to be a method of choice for carrying out the final cyclization of the *N*-alkylchloroacetamides **6** (route e).[11] Finally, the most simple and versatile synthesis of the oxidized aporphine alkaloids **1** involves the cyclization of the biphenylacetamide **7**, induced by excess of oxalyl chloride/stannic chloride, to construct rings B and C sequentially in a single-step reaction (route f).[12]



Scheme 1. Different synthetic pathways to dioxoaporphines

However, all these elegant, skilful, and complementary synthetic approaches suffer from several drawbacks and limitations. For example, the semisynthetic precursor (hydroxy)aporphines **2** are found only in very low amounts in vegetable sources. The synthetic approaches b and c are of interest when substituents at positions 1, 2, 9, and 10 of the aporphine nucleus are the same, since the key step in the preparation of the starting isoquinolinones **3** and **4** is the self-condensation of the appropriately substituted phenylacetic acids. Additionally, the photocyclization of compounds **3** proceeds only in moderate yields. The IBC approach between 1-methyleneisoquinolines and arynes gives acceptable yields, but even though the reaction exhibits good regioselectivity it has to be used mainly for alkaloids unsubstituted in ring D. On the other hand, the chloroacetamides **6** involved in route e are obtained by acylation of the *N*-alkylaminophenanthrenes produced from the corresponding phenanthrols by Bucherer amination reaction. These air-sensitive phenols are obtained in nine steps from substituted fluorenones that are accessible only with

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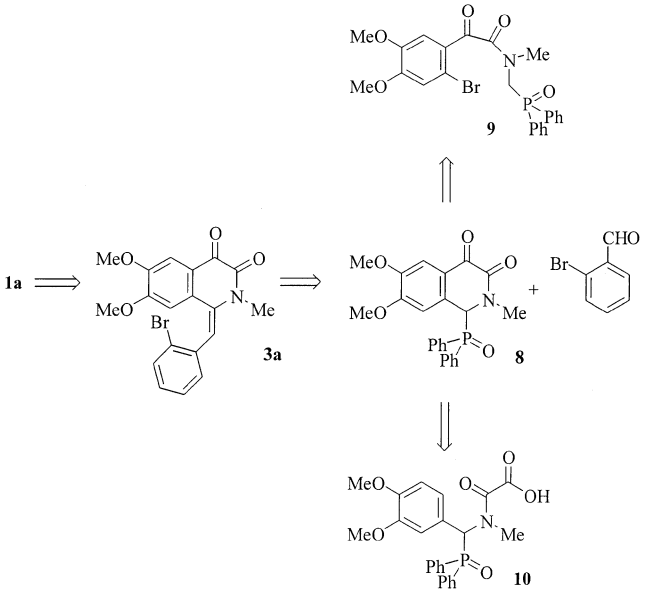
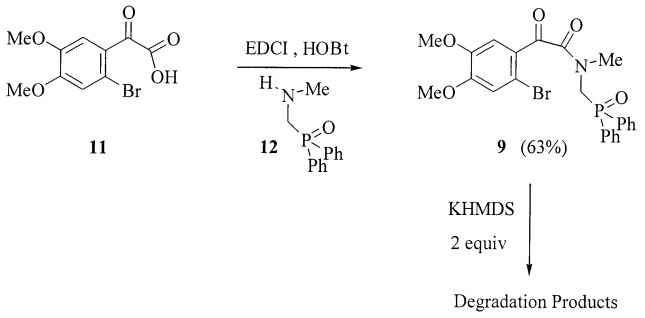
difficulty, and their formation involves the hydrolysis of the appropriate morpholinoamides in the last step. Moreover this simple approach is subject to steric hindrance, since an increase in the number of methoxy substituents in the phenanthrols slows down the Bucherer reaction, and hydrolysis of the parent morpholinoamides in this case results exclusively in oxidation to the phenanthrones.[12] Lastly, the biphenylacetamides **7** may be obtained from the Baeyer−Villiger oxidation of appropriate fluorenones followed by some conventional chemical transformations, but this synthetic pathway is rather limited in scope and does not allow for incorporation of diverse substituents on the compact framework of the dioxoaporphines **1**. In particular, all the models elaborated by the synthetic approaches depicted in routes e and f are invariably alkoxylated at position 1 in aromatic ring A. Even though some of the drawbacks associated with the synthesis of the starting materials may, a priori, be solved by the recently reported syntheses of a larger variety of fluorenones[13] and aminophenanthrenes,[14] these limitations, together with recent findings concerning the cytotoxicity of 4,5-dioxoaporphines[11] − including the *N*-methoxylated artabotrine[3] − prompted us to explore an alternative and complementary synthetic approach to this type of alkaloids.

Initially, we envisaged the construction of the arylmethylenedioxoisoquinoline **3a** by means of a Horner reaction[15] between the phosphorylated dioxoisoquinoline **8** and *o*-bromobenzaldehyde (Scheme 2). We assumed that it should be possible, by proper choice of the required base and solvent, to control the stereochemical outcome of the reaction[16] and force the reaction to produce the acylenamide **3a** exclusively in its (*E*) configuration, the essential candidate for the annulation reaction giving rise to **1a** (Scheme 2).



Scheme 2. Retrosynthetic scheme

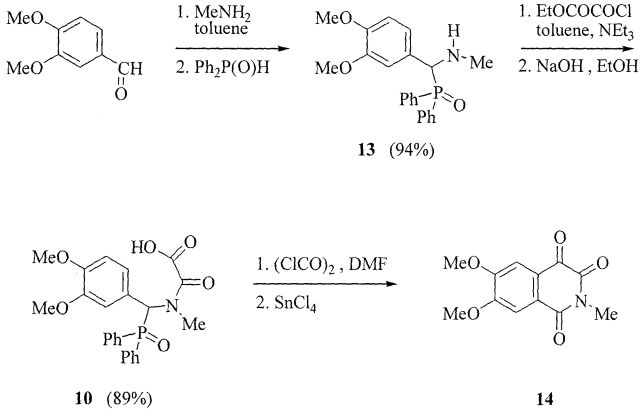
For the first part of this synthesis, the assembly of the phosphorylated dioxo compound **8**, we intended to take advantage of our newly developed aryne-mediated cyclization methodology, already successfully applied to halo-*N*-(diphenylphosphinoylmethyl)benzamide derivatives.[17] For this purpose, the phosphorylated α-(*o*-bromoaryl)-α-oxoacetamide **9** was chosen as a model. This dimethoxylated compound was readily synthesized by coupling the oxo acid **11**, easily obtained by oxidation of the corresponding *o*-bromoacetophenone derivative, with the phosphorylated *N*-methylamine **12** (Scheme 3). Unfortunately, exposure of the phosphorylated α-(*o*-bromoaryl)-α-oxoacetamide **9** to potassium bis(trimethylsilyl)azide (KHMDS, 2 equiv.) at −78 °C in THF − intended to induce the regioselective formation of the stabilized α-amino carbanion and concomitant formation of the aryne[18] − failed to furnish the desired annulated compound **8**. Instead, degradation products were obtained.



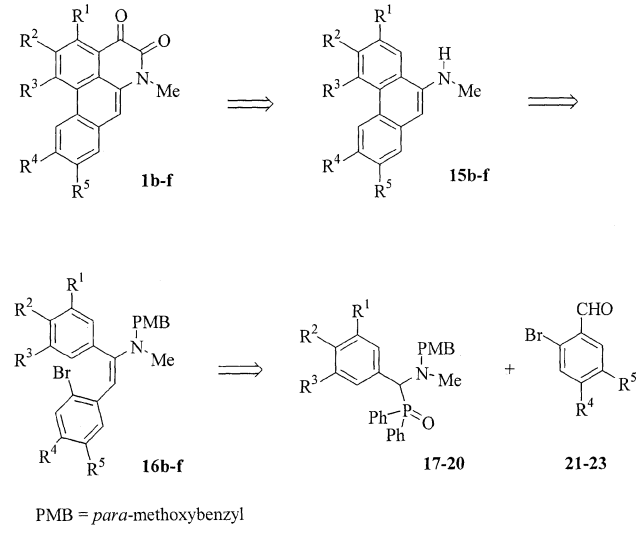
Scheme 3. Synthesis and reactivity of the α-(*o*-bromoaryl)-α-oxoacetamide **9**

We then opted for a strategy of constructing the phosphorylated dioxoisoquinoline **8** by means of carbocationic ring closure of the phosphorylated oxalamic acid **10** (Scheme 2), and so embarked on the synthesis of the dimethoxy derivative **10**, which appeared an excellent candidate for the Friedel−Crafts annulation process. The synthesis started with the elaboration of the phosphorylated amine **13**, readily obtained by treatment of the Schiff base derived from the condensation of veratraldehyde and methylamine with diphenylphosphane oxide (Scheme 4). Acylation of **13** with ethyl chlorooxoacetate, followed by saponification of the phosphorylated ethyl oxalamate, delivered the desired phosphorylated oxalamic acid **10** in excellent yield (84% over three steps). Once again, though, all attempts to obtain the phosphorylated dioxoisoquinoline **8** by cyclization of the open model **10** were unrewarding. Indeed even under the optimized reaction conditions defined by Suau and colleagues,[12a] the sole product was the trioxoisoquinoline **14**, obtained in excellent yield (74%, Scheme 4).

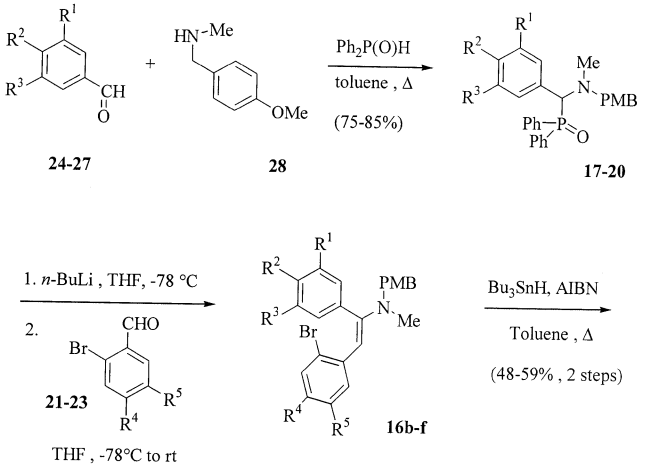
Considering then that the synthetic strategies for the elaboration of the highly sensitive model **8** would invariably be doomed to failure, we decided to switch our plans and to adopt different synthetic tactics. Our new approach to the synthesis of the representative dioxoaporphines **1b**−**f**, depicted in the retrosynthetic analysis shown in Scheme 5, involved three stages. Of central importance was the construction of the aminostilbenes **16b**−**f**, with the requisite (*E*) configurations. Once prepared, these diarylethylene intermediates might be used to generate the aminophenanthr-

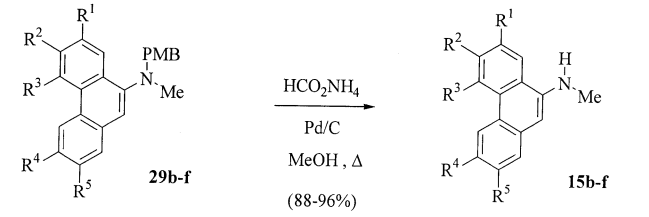


Scheme 4. Synthesis and reactivity of the phosphorylated oxalamic acid **10**



Scheme 5. Retrosynthetic scheme





Scheme 6. Synthesis of the polysubstituted (methylamino)phenanthrenes **15b−f**

Table 1. Synthesis of phosphorylated dibenzylamine derivatives **17−20**

Product	Starting aldehyde	R^1	R^2	R^3	Yield (%)
17	**24**	$O-CH_2-O$		H	78
18	**25**	OCH_3	OCH_3	OCH_3	85
19	**26**	H	H	H	75
20	**27**	H	OCH_3	H	77

enes **15b−f**, which could serve as a framework for the introduction of the dicarbonyl unit, thus completing the synthesis of the target compounds **1b−f**.

Firstly, the phosphorylated dibenzylamine derivatives **17−20** were readily and efficiently obtained by means of a reaction between diphenylphosphane oxide and the carbinolamines[19] obtained by condensation of 4-methoxy-*N*-methylbenzylamine (**28**) with the appropriate benzaldehydes **24−27** (Scheme 6, Table 1).

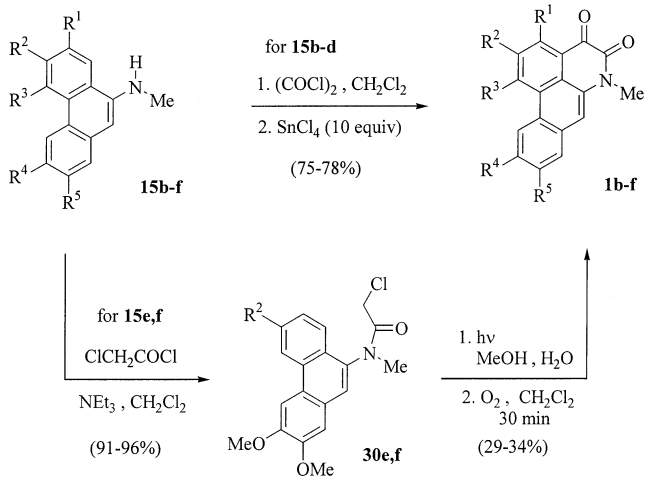
For the subsequent synthesis of the required (dialkylamino)stilbene derivatives **16b−f**, the Horner protocol − which has mainly been employed in related systems for homologation of a variety of carbonyl compounds[20] and for the generation of acyl anion equivalents[21] − was applied. Treatment of derivatives **17−20** with *n*BuLi (−78 °C, THF), followed by addition of the appropriate aromatic aldehydes **21−23** and warming to room temperature, resulted in direct completion of the Horner reaction and almost exclusive formation of the enamines **16b−f** in excellent yield (Scheme 6, Table 2). In contrast to the morpholino derivatives,[22] enamines **16b−f** were obtained almost exclusively as the desired (*E*) forms, the configuration of the double bond being established from the vinylic proton chemical shift values. Indeed, the olefinic proton chemical shifts in the (*E*) isomers (e.g., δ = 5.51 for **16c**) agree very well with those calculated from the substituent shielding constants[23] (calcd. for **16c**: δ = 5.40−5.60) and are slightly lower than those calculated for the (*Z*) isomers (calcd. for **16c**: δ = 5.90−6.10). The driving force arising from the high degree of conjugation of these stilbene models and the presence of the bulky bromine atom on the aromatic ring D and the *p*-methoxybenzylamino group account for the high yields and stereoselectivity of this synthesis of the (*E*) alkenes. Because the enamines partially hydrolyzed during chromatographic treatment, they were subjected directly to the well-documented oxidative radical cyclization conditions[24] (Scheme 6). The radical reaction was performed by slow, dropwise addition of a benzene solution of tributyltin hydride (1.5 equiv.) and AIBN (1 equiv.) to a refluxing benzene solution of **16b−f** under argon. This technique delivered the fused aminophenanthrenes **29b−f** in satisfactory

Table 2. Synthesis of phenanthrylamine derivatives **29b−f**, **15b−f**, and dioxoaporphines **1b−f**

	R^1	R^2	R^3	R^4	R^5	**16b−f** (starting materials)	**29b−f** yield (%)	**15b−f** yield (%)	Method A **1b−d** yield (%)	Method B **1e,f** yield (%)
b	O−CH_2−O		H	H	H	(**17** + **21**)	52	92	78	−
c	OCH_3	OCH_3	OCH_3	H	H	(**18** + **21**)	57	88	81	−
d	OCH_3	OCH_3	OCH_3	OCH_3	H	(**18** + **22**)	56	94	75	−
e	H	H	H	OCH_3	OCH_3	(**19** + **23**)	48	91	−	34
f	H	OCH_3	H	OCH_3	OCH_3	(**20** + **23**)	59	96	−	29

yields (Table 2). The benzyl protecting groups on the anilino functions of **29b−f** were readily removed ($HCOONH_4$, Pd on C, MeOH), providing almost quantitative yields of the stable aminophenanthrenes **15b−f** (Scheme 6, Table 2).

The last step of the synthesis, the formation of ring C, was strongly dependent on the nature of the substituents on the aromatic ring A. For electron-rich compounds such as **15b−d**, the creation of the CO−CO−N unit was readily accomplished by preliminary treatment with oxalyl chloride in dry dichloromethane and subsequent Friedel−Crafts acylation[12] in the presence of stannic chloride at 20 °C over 48 h (Scheme 7, Table 2, Method A).



Scheme 7. Syntheses of the target dioxoaporphines

This technique afforded the synthetic targets in excellent yields, and the potential of this synthetic methodology is illustrated by the first total synthesis of *N*-methylouregidione (**1c**), in an overall yield of 35% over the last five steps. Unfortunately, attempts to cyclize compounds **15e** and **15f**, unsubstituted or monomethoxylated on the aromatic ring A, met with no success. For these compounds, we opted to develop the alternative photochemical approach[11] depicted in Scheme 7. The phenanthrylamines **15e** and **15f** were first transformed into the corresponding chloroacetamides **30e** and **30f** under Schotten−Baumann conditions and solutions of these compounds in 30% aqueous methanol were subjected to irradiation (Rayonet RPR 3000 Å and 3500 Å, 4 h) under aerobic conditions to furnish the target compounds **1e** and **1f**, albeit in moderate yields (Table 2, Method B).

In conclusion, a synthesis of 4,5-dioxoaporphine alkaloids, based on the sequential formation of C and B rings of these tetracyclic compounds, is described. The reported methodology complements existing approaches and the total synthesis of the alkaloid *N*-methylouregidione emphasizes its synthetic potential. We also certainly believe that this synthetic route should be broadened to include other naturally occurring dioxoaporphine alkaloids and their biogenetically related congeners.

Experimental Section

General: Tetrahydrofuran (THF) and ether (Et_2O) were pre-dried with anhydrous Na_2SO_4 and distilled from sodium benzophenone ketyl under Ar before use. CH_2Cl_2, NEt_3, and toluene were distilled from CaH_2. Dry glassware was obtained by oven-drying and assembly under dry Ar. The glassware was fitted with rubber septa and reagent transfer was performed by syringe. For flash chromatography, Merck silica gel 60 (230−400 mesh ASTM) was used. − Melting points were taken with a Reichert-Thermopan apparatus and are not corrected. − NMR: Bruker AM 300 (300 MHz, 75 MHz and 121 MHz, for ^1H, ^{13}C and ^{31}P respectively). For ^1H NMR and ^{13}C NMR, $CDCl_3$ as solvent, TMS as internal standard; for ^{31}P NMR, $CDCl_3$ as solvent, H_3PO_4 as external standard. − Microanalyses were performed by the CNRS microanalysis center. − Bromobenzaldehyde derivatives **22**[25] and **23**[26] were prepared according to literature methods. The phosphorylated amine **12**[18b] and the benzylamine derivative **28**[27] were also synthesized according to reported procedures.

Preparation of the Phosphorylated Phenyloxoacetamide 9

2-(2-Bromo-4,5-dimethoxyphenyl)-2-oxoacetic Acid (11): Compound **11** was obtained by SeO_2/pyridine[28] oxidation of 1-(2-bromo-4,5-dimethoxyphenyl)ethanone[29] and was used directly in the next step without further purification (82%). − ^1H NMR (mixture of two rotational isomers A and B, 80:20): δ = 3.77 (s, 3 H, OCH_3, B), 3.79 (s, 3 H, OCH_3, A), 3.82 (s, 3 H, OCH_3, B), 3.87 (s, 3 H, OCH_3, A), 7.20 (s, 1 H, aromatic H, B), 7.27 (s, 1 H, aromatic H, A), 7.28 (s, 1 H, aromatic H, A), 7.36 (s, 1 H, aromatic H, B). − ^{13}C NMR (rotational isomer A): δ = 55.8, 56.4, 113.8, 116.6, 116.7, 126.0, 148.2, 153.3, 165.3 (s, COOH), 188.0 (s, C=O).

2-(2-Bromo-4,5-dimethoxyphenyl)-*N*-(diphenylphosphinoylmethyl)-*N*-methyl-2-oxoacetamide (9): A solution of compound **11** (290 mg, 1 mmol), 1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide (EDCI, 297 mg, 1 mmol), 1-hydroxy-1*H*-benzotriazole (HOBt, 135 mg, 1 mmol), and triethylamine (100 mg, 1 mmol) in anhydrous CH_2Cl_2 (20 mL) was vigorously stirred under argon at 0 °C for 1 h and was then treated with a solution of the phosphorylated amine **12**

(245 mg, 1 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred for an additional 2 h at room temperature and washed successively with aqueous HCl (10%, 3 × 30 mL), water, and brine, and finally dried with $MgSO_4$. The solvent was evaporated to dryness, and the residue was triturated with Et_2O and purified by recrystallization from hexane/toluene to afford **9** (325 mg, 63%), m.p. 173−174 °C. − IR (KBr): $\tilde{\nu}$ = 1723 cm^{-1} (C=O), 1659 (C=O), 1151 (P=O). − ^1H NMR: δ = 3.25 (s, 3 H, NCH_3), 3.79 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 4.44 (d, J = 5.6 Hz, 2 H, NCH_2P), 6.95 (s, 1 H, aromatic H), 7.29 (s, 1 H, aromatic H), 7.47−7.54 (m, 6 H, aromatic H), 7.83−7.90 (m, 4 H, aromatic H). − ^{13}C NMR: δ = 37.1, 46.5 (d, J_{CP} = 77 Hz, NCH_2P), 56.2, 56.5, 114.3, 115.2, 116.3, 126.4, 128.8 (d, J_{CP} = 12 Hz), 130.9 (d, J_{CP} = 99 Hz), 131.1 (d, J_{CP} = 10 Hz), 132.4, 148.6, 153.8, 167.2 (s, NCO), 189.0 (s, C=O). − ^{31}P NMR: δ = 29.5. − $C_{24}H_{23}NO_5P$ (516.3): calcd. C 55.83, H 4.49, N 2.71; found C 55.71, H 4.21, N 2.88.

Preparation of the Oxalamic Acid 10

***N*-[(3,4-Dimethoxyphenyl)(diphenylphosphinoyl)methyl]-*N*-methylamine (13):** The crude benzaldimine (1.0 g, 5.6 mmol) obtained quantitatively by condensation of veratraldehyde with methylamine in toluene at 0 °C in the presence of molecular sieves (4 Å) was treated with diphenylphosphane oxide (1.13 g, 5.6 mmol) in anhydrous toluene (50 mL). The mixture was refluxed for 1 h, the solvent was removed under vacuum, and the resulting white solid was triturated with Et_2O, filtered, and finally recrystallized from hexane/toluene (2.03 g, 95%), m.p. 143−144 °C. − IR (KBr): $\tilde{\nu}$ = 1177 cm^{-1} (P=O). − ^1H NMR: δ = 2.01 (s, 1 H, NH), 2.28 (s, 3 H, NCH_3), 3.58 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 4.28 (d, J = 10.5 Hz, 1 H, CHP), 6.56 (s, 1 H, aromatic H), 6.65 (s, 2 H, aromatic H), 7.25−7.30 (m, 2 H, aromatic H), 7.42−7.55 (m, 6 H, aromatic H), 7.76−7.79 (m, 2 H, aromatic H). − ^{13}C NMR: δ = 55.6, 55.7, 65.2 (d, J_{CP} = 80 Hz, NCHP), 110.5, 111.6 (d, J_{CP} = 6 Hz), 121.6 (d, J_{CP} = 6 Hz), 127.1, 128.0 (d, J_{CP} = 11.5 Hz), 128.4 (d, J_{CP} = 11.5 Hz), 130.7 (d, J_{CP} = 96 Hz), 130.9 (d, J_{CP} = 96 Hz), 131.6, 131.8 (d, J_{CP} = 9 Hz), 131.9, 132.1 (d, J_{CP} = 8.5 Hz), 148.5, 148.6. − ^{31}P NMR: δ = 31.3. − $C_{22}H_{24}NO_3P$ (381.4): calcd. C 69.28, H 6.34, N 3.67; found C 69.17, H 6.26, N 3.60.

Ethyl *N*-[(3,4-Dimethoxyphenyl)(diphenylphosphinoyl)methyl]-*N*-methyloxalamate: A solution of ethyl chlorooxoacetate (0.82 g, 6 mmol) in toluene (5 mL) was carefully added at 0 °C under argon to a solution of the phosphorylated amine **13** (1.5 g, 4 mmol) and triethylamine (0.6 g, 6 mmol) in toluene (20 mL). The mixture was stirred at this temperature for 1 h, water was then added, and the organic layer was successively washed with aqueous HCl (10%, 3 × 10 mL), water, and brine, and dried with $MgSO_4$. The crude product was finally purified by chromatography on silica gel, using acetone/hexanes (3:2) as eluent, and the desired amido ester was obtained as a colorless, viscous oil (1.81 g, 94%). − IR (KBr): $\tilde{\nu}$ = 1733 cm^{-1} (C=O), 1648 (C=O), 1188 (P=O). − ^1H NMR: δ = 1.20 (t, J = 6.8 Hz, 3 H, CH3), 3.10 (s, 3 H, NCH_3), 3.81 (s, 6 H, 2 × OCH_3), 4.15 (q, J = 6.8 Hz, 2 H, OCH_2), 6.51 (d, J = 7.8 Hz, 1 H, NCHP), 6.75 (d, J = 7.8 Hz, 1 H, aromatic H), 7.30−7.34 (m, 5 H, aromatic H), 7.48−7.52 (m, 3 H, aromatic H), 7.65−7.68 (m, 2 H, aromatic H), 7.85−7.89 (m, 2 H, aromatic H). − ^{13}C NMR: δ = 13.8, 32.8, 53.9 (d, J_{CP} = 73 Hz, NCHP), 55.7, 55.9, 62.0, 111.1, 113.7 (d, J_{CP} = 7.5 Hz), 123.9 (d, J_{CP} = 7.5 Hz), 124.6, 128.6 (d, J_{CP} = 11.5 Hz), 130.2 (d, J_{CP} = 90 Hz), 130.9 (d, J_{CP} = 9 Hz), 131.0 (d, J_{CP} = 9.5 Hz), 132.0, 132.3, 148.8, 149.3, 161.9 (s, C=O), 162.1 (s, C=O). − ^{31}P NMR: δ = 32.2. − $C_{26}H_{28}NO_6P$ (481.5): calcd. C 64.86, H 5.86, N 2.91; found C 65.01, H 5.75, N 2.87.

***N*-[(3,4-Dimethoxyphenyl)(diphenylphosphinoyl)methyl]-*N*-methyloxalamic Acid (10):** The title compound **10** was obtained by saponification of the above compound with ethanolic NaOH under standard conditions (95%), m.p. 105−106 °C. − IR (KBr): $\tilde{\nu}$ = 1727 cm^{-1} (C=O), 1646 (C=O), 1150 (P=O). − ^1H NMR: δ = 3.07 (s, 3 H, NCH_3), 3.65 (s, 3 H, OCH_3), 3.68 (s, 3 H, OCH_3), 6.57 (d, J = 7.8 Hz, 1 H, NCHP), 6.89 (d, J = 8.9 Hz, 1 H, aromatic H), 7.20 (d, J = 7.9 Hz, 1 H, aromatic H), 7.21 (s, 1 H, aromatic H), 7.42−7.59 (m, 6 H, aromatic H), 7.77−7.90 (m, 4 H, aromatic H), 14.15 (br.s, 1 H, COOH). − ^{13}C NMR: δ = 32.6, 52.7 (d, J_{CP} = 78 Hz, NCHP), 55.3, 55.4, 111.7, 113.8 (d, J_{CP} = 7 Hz), 123.1 (d, J_{CP} = 7 Hz), 124.8, 128.6 (d, J_{CP} = 11.5 Hz), 128.7 (d, J_{CP} = 11 Hz), 130.5 (d, J_{CP} = 8.5 Hz), 130.6 (d, J_{CP} = 8.5 Hz), 131.9, 132.2, 148.3, 148.9, 163.1 (s, C=O), 164.2 (s, C=O). − ^{31}P NMR: δ = 30.8. − $C_{24}H_{24}NO_6P$ (453.4): calcd. C 63.57, H 5.34, N 3.09; found C 63.66, H 5.24, N 3.21.

Attempted Preparation of the Phosphorylated Isoquinolinedione 8: Treatment of the oxalamic acid **10** with oxalyl chloride and subsequent cyclization with $SnCl_4$ according to a previously reported procedure[12a] exclusively furnished 6,7-dimethoxy-2-methylisoquinoline-1,3,4(2*H*)-trione (**14**)[30] and no trace of the phosphorylated isoquinolinedione **8** could be detected after chromatographic treatment of the reaction mixture.

General Procedure for the Synthesis of the Phosphorylated Dibenzylamine Derivatives 17−20: A solution of 4-methoxy-*N*-methylbenzylamine (**28**) (20 mmol) in toluene (10 mL) was slowly added at 0 °C under argon to a solution of the appropriate benzaldehyde derivative **21**−**23** (20 mmol) in the same solvent (20 mL). The mixture was then refluxed for 1 h, cooled to room temperature, and subsequently treated with diphenylphosphane oxide (4.04 g, 20 mmol). The mixture was then refluxed for 1 h in a Dean−Stark apparatus, with azeotropic removal of water. The crude product obtained after removal of the solvent under reduced pressure was triturated with Et_2O, filtered, purified by flash column chromatography on silica gel using an acetone/hexanes mixture (3:2) as eluent, and finally recrystallized from hexane/toluene.

***N*-[1,3-Benzodioxol-5-yl(diphenylphosphinoyl)methyl]-*N*-(4-methoxyphenylmethyl)-*N*-methylamine (17):** 78%, m.p. 129−130 °C. − IR (KBr): $\tilde{\nu}$ = 1171 cm^{-1} (P=O). − ^1H NMR: δ = 2.35 (s, 3 H, NCH_3), 3.25 (d, J = 13.2 Hz, 1 H, CH_2Ar), 3.65 (d, J = 13.2 Hz, 1 H, CH_2Ar), 3.70 (s, 3 H, OCH_3), 4.30 (d, J = 12.0 Hz, 1 H, NCHP), 5.92 (s, 2 H, OCH_2O), 6.70 (d, J = 9.6 Hz, 2 H, aromatic H), 6.71 (d, J = 9.1 Hz, 1 H, aromatic H), 6.80 (d, J = 9.6 Hz, 2 H, aromatic H), 6.92 (dd, J = 9.1, 2.0 Hz, 1 H, aromatic H), 7.20−7.60 (m, 9 H, aromatic H), 7.75−7.85 (m, 2 H, aromatic H). − ^{13}C NMR: δ = 39.9 (d, J_{CP} = 4.5 Hz, NCH_3), 55.2, 59.5 (d, J_{CP} = 11 Hz), 65.2 (d, J_{CP} = 89 Hz, NCHP), 100.0, 107.8, 111.7 (d, J_{CP} = 7 Hz), 113.5, 124.4 (d, J_{CP} = 4 Hz), 125.3 (d, J_{CP} = 8.5 Hz), 128.1 (d, J_{CP} = 10 Hz), 128.2 (d, J_{CP} = 10 Hz), 130.0, 130.8, 131.1 (d, J_{CP} = 8 Hz), 131.15 (d, J_{CP} = 2.5 Hz), 131.3 (d, J_{CP} = 2.5 Hz), 131.7 (d, J_{CP} = 9 Hz), 132.5 (d, J_{CP} = 102 Hz), 132.9 (d, J_{CP} = 100 Hz), 147.2, 147.4, 158.5. − ^{31}P NMR: δ = 32.2. − $C_{29}H_{28}NO_4P$ (485.5): calcd. C 71.74, H 5.81, N 2.88; found C 71.49, H 5.91, N 3.05.

***N*-[(Diphenylphosphinoyl)(3,4,5-trimethoxyphenyl)methyl)]-*N*-(4-methoxyphenylmethyl)-*N*-methylamine (18):** 85%, m.p. 132−133 °C. − IR (KBr): $\tilde{\nu}$ = 1168 cm^{-1} (P=O). − ^1H NMR: δ = 2.45 (s, 3 H, NCH_3), 3.29 (d, J = 13.2 Hz, 1 H, CH_2Ar), 3.70 (s, 3 H, OCH_3), 3.72 (d, J = 13.2 Hz, 1 H, CH_2Ar), 3.74 (s, 6 H, 2 × OCH_3), 3.77 (s, 3 H, OCH_3), 4.29 (d, J = 11.3 Hz, 1 H, NCHP), 6.66 (d, J = 8.6 Hz, 2 H, aromatic H), 6.72 (s, 2 H, aromatic H), 6.79 (d, J =

8.6 Hz, 2 H, aromatic H), 7.14−7.22 (m, 3 H, aromatic H), 7.42−7.51 (m, 5 H, aromatic H), 7.79−7.85 (m, 2 H, aromatic H). − ^{13}C NMR: δ = 40.0 (d, J_{CP} = 4 Hz, NCH_3), 55.1, 56.2, 59.6 (d, J_{CP} = 11 Hz), 60.8, 65.8 (d, J_{CP} = 87 Hz, NCHP), 108.9 (d, J_{CP} = 8 Hz), 113.5, 126.7 (d, J_{CP} = 3 Hz), 128.0 (d, J_{CP} = 11 Hz), 128.2 (d, J_{CP} = 11 Hz), 130.0, 130.7, 130.9 (d, J_{CP} = 8 Hz), 131.1 (d, J_{CP} = 3 Hz), 131.4 (d, J_{CP} = 3 Hz), 131.7 (d, J_{CP} = 8.5 Hz), 132.6 (d, J_{CP} = 95 Hz), 152.6, 158.6. − ^{31}P NMR: δ = 32.3. − $C_{31}H_{34}NO_5P$ (531.6): calcd. C 70.04, H 6.45, N 2.63; found C 69.88, H 6.49, N 2.71.

***N*-[(Diphenylphosphinoyl)phenylmethyl]-*N*-(4-methoxyphenylmethyl)-*N*-methylamine (19):** 75%, m.p. 149−150 °C. − IR (KBr): $\tilde{\nu}$ = 1175 cm^{-1} (P=O). − ^{1}H NMR: δ = 2.48 (s, 3 H, NCH_3), 3.27 (d, *J* = 12.1 Hz, 1 H, CH_2Ar), 3.75 (d, *J* = 12.1 Hz, 1 H, CH_2Ar), 3.80 (s, 3 H, OCH_3), 4.40 (d, *J* = 11.4 Hz, 1 H, NCHP), 6.71 (d, *J* = 8.6 Hz, 2 H, aromatic H), 6.84 (d, *J* = 8.6 Hz, 2 H, aromatic H), 7.11−7.69 (m, 13 H, aromatic H), 7.80−7.95 (m, 2 H, aromatic H). − ^{13}C NMR: δ = 40.0 (d, J_{CP} = 4 Hz, NCH_3), 56.2, 59.6 (d, J_{CP} = 11 Hz), 65.7 (d, J_{CP} = 87 Hz, NCHP), 113.5, 127.9 (d, J_{CP} = 9.5 Hz), 128.0, 128.2 (d, J_{CP} = 11 Hz), 130.1, 130.8, 130.9 (d, J_{CP} = 10 Hz), 131.1 (d, J_{CP} = 3 Hz), 131.3 (d, J_{CP} = 3 Hz), 131.6 (d, J_{CP} = 8.5 Hz), 131.8 (d, J_{CP} = 9 Hz), 132.5 (d, J_{CP} = 102 Hz), 132.8 (d, J_{CP} = 96 Hz), 144.6, 158.5. − ^{31}P NMR: δ = 32.2. − $C_{28}H_{28}NO_2P$ (441.5): calcd. C 76.17, H 6.39, N 3.17; found C 75.97, H 6.50, N 3.23.

***N*-[(Diphenylphosphinoyl)(4-methoxyphenyl)methyl]-*N*-(4-methoxyphenylmethyl)-*N*-methylamine (20):** 77%, m.p. 162−163 °C. − IR (KBr): $\tilde{\nu}$ = 1170 cm^{-1} (P=O). − ^{1}H NMR: δ = 2.45 (s, 3 H, NCH_3), 3.26 (d, *J* = 14.1 Hz, 1 H, CH_2Ar), 3.69 (s, 3 H, OCH_3), 3.73 (s, 3 H, OCH_3), 3.75 (d, *J* = 14.1 Hz, 1 H, CH_2Ar), 4.39 (d, *J* = 11.9 Hz, 1 H, NCHP), 6.69 (d, *J* = 8.6 Hz, 2 H, aromatic H), 6.80 (d, *J* = 8.6 Hz, 2 H, aromatic H), 6.81 (d, *J* = 8.6 Hz, 2 H, aromatic H), 7.10−7.26 (m, 3 H, aromatic H), 7.46−7.52 (m, 7 H, aromatic H), 7.83−7.89 (m, 2 H, aromatic H). − ^{13}C NMR: δ = 39.9 (d, J_{CP} = 4 Hz), 55.1, 55.2, 59.5 (d, J_{CP} = 11 Hz), 64.9 (d, J_{CP} = 88 Hz, NCHP), 113.4, 113.5, 122.8 (d, J_{CP} = 3 Hz), 128.1 (d, J_{CP} = 11 Hz), 128.2 (d, J_{CP} = 11 Hz), 130.0, 130.1 (d, J_{CP} = 8 Hz), 130.9, 131.1 (d, J_{CP} = 3 Hz), 131.3 (d, J_{CP} = 3 Hz), 131.7 (d, J_{CP} = 9 Hz), 131.9 (d, J_{CP} = 8 Hz), 132.7 (d, J_{CP} = 94 Hz), 133.0 (d, J_{CP} = 99 Hz), 158.6, 159.2. − ^{31}P NMR: δ = 32.3. − $C_{29}H_{30}NO_3P$ (471.5): calcd. C 73.87, H 6.41, N 2.97; found C 74.02, H 6.18, N 3.09.

General Procedure for the Synthesis of the Diarylenamines 16b−f: A solution of *n*BuLi (1.25 mL, 1.6 M in hexanes, 2 mmol) was added dropwise, at −78 °C under argon, over a period of 15 min, to a stirred solution of compounds **17**−**20** (2 mmol) in THF (20 mL). The solution was stirred for 15 min at this temperature and a solution of the appropriate aldehyde **21**−**23** (2 mmol) in THF (5 mL) was then added by syringe. The reaction mixture was allowed to warm to room temperature over a period of 1 h and stirred at this temperature for 8 h. Aqueous NH_4Cl was added and the mixture was extracted with Et_2O (75 mL). The organic layer was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo to a brown solid that was used directly in the next step without further purification.

General Procedure for the Synthesis of the Protected Phenanthrylamine Derivatives 29b−f: The crude solid residue obtained above was dissolved in toluene, freshly distilled from sodium (250 mL). The mixture was degassed by bubbling argon through it and then refluxed under argon. A solution of nBu$_3$SnH (875 mg, 3 mmol) and AIBN (330 mg, 2 mmol) in dry degassed toluene (20 mL) was then added dropwise over 10 min. Once addition was complete, refluxing was continued for a further 0.5 h. The toluene was evaporated under reduced pressure and the residue was dissolved in CH_3CN (100 mL). This solution was washed with hexane (5 × 50 mL) and concentrated in vacuo to a solid residue, which was purified by flash column chromatography on silica gel, using an AcOEt/hexanes mixture (1:1) as eluent, and finally recrystallized from hexane/toluene.

***N*-(4-Methoxyphenylmethyl)-*N*-(methylphenanthro[2,3-*d*][1,3]dioxol-6-yl)amine (29b):** 52%, m.p. 158−159 °C. − ^{1}H NMR: δ = 2.75 (s, 3 H, NCH_3), 3.81 (s, 3 H, OCH_3), 4.21 (s, 2 H, CH_2Ar), 6.11 (s, 2 H, OCH_2O), 6.88 (d, *J* = 8.3 Hz, 2 H, aromatic H), 7.27 (s, 1 H, aromatic H), 7.34 (d, *J* = 8.3 Hz, 2 H, aromatic H), 7.45−7.56 (m, 2 H, aromatic H), 7.75 (dd, *J* = 9.3, 4.1 Hz, 1 H, aromatic H), 7.88 (s, 1 H, aromatic H), 8.05 (s, 1 H, aromatic H), 8.41 (dd, *J* = 9.0, 2.4 Hz, 1 H, aromatic H). − ^{13}C NMR: δ = 41.7, 55.2, 60.3, 100.3, 102.4, 113.7, 114.5, 122.1, 124.9, 125.9, 126.0, 127.8, 127.9, 129.6, 130.6, 131.9, 147.7, 147.9, 158.7. − $C_{24}H_{21}NO_3$ (371.4): calcd. C 77.61, H 5.70, N 3.77; found C 77.72, H 5.86, N 3.53.

***N*-(4-Methoxyphenylmethyl)-*N*-methyl-*N*-(5,6,7-trimethoxyphenanthren-9-yl)amine (29c):** 57%, m.p. 141−142 °C. − ^{1}H NMR: δ = 2.82 (s, 3 H, NCH_3), 3.81 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 4.01 (s, 3 H, OCH_3), 4.04 (s, 3 H, OCH_3), 4.19 (s, 2 H, CH_2Ar), 6.90 (d, *J* = 8.2 Hz, 2 H, aromatic H), 7.29 (s, 1 H, aromatic H), 7.37 (d, *J* = 8.2 Hz, 2 H, aromatic H), 7.45−7.57 (m, 2 H, aromatic H), 7.75 (d, *J* = 6.8 Hz, 1 H, aromatic H), 7.80 (s, 1 H, aromatic H), 9.44 (d, *J* = 6.8 Hz, 1 H, aromatic H). − ^{13}C NMR: δ = 41.1, 55.3, 55.8, 60.3, 60.5, 61.2, 101.4, 113.8, 115.8, 120.4, 125.3, 125.6, 126.5, 127.3, 127.4, 127.6, 129.5, 130.8, 132.3, 142.7, 147.4, 152.2, 152.8, 158.7. − $C_{26}H_{27}NO_4$ (417.5): calcd. C 74.80, H 6.52, N 3.35; found C 74.75, H 6.47, N 3.41.

***N*-(4-Methoxyphenylmethyl)-*N*-methyl-*N*-(3,5,6,7-tetramethoxyphenanthren-9-yl)amine (29d):** 56%, m.p. 107−108 °C. − ^{1}H NMR: δ = 2.81 (s, 3 H, NCH_3), 3.82 (s, 3 H, OCH_3), 3.95 (s, 3 H, OCH_3), 4.01 (s, 3 H, OCH_3), 4.05 (s, 3 H, OCH_3), 4.07 (s, 3 H, OCH_3), 4.17 (s, 2 H, CH_2Ar), 6.91 (d, *J* = 8.3 Hz, 2 H, aromatic H), 7.19 (dd, *J* = 7.7, 1.4 Hz, 1 H, aromatic H), 7.28 (s, 1 H, aromatic H), 7.39 (d, *J* = 8.3 Hz, 2 H, aromatic H), 7.69 (d, *J* = 7.7 Hz, 1 H, aromatic H), 7.85 (s, 1 H, aromatic H), 9.07 (d, *J* = 1.4 Hz, 1 H, aromatic H). − ^{13}C NMR: δ = 41.2, 55.3, 55.4, 55.8, 60.5, 60.7, 61.3, 101.3, 107.9, 113.8, 115.8, 116.0, 119.9, 127.8, 128.2, 128.7, 129.05, 129.1, 130.9, 142.5, 145.5, 152.4, 152.7, 157.5, 158.7. − $C_{27}H_{29}NO_5$ (447.5): calcd. C 72.46, H 6.53, N 3.13; found C 72.36, H 6.48, N 3.21.

***N*-(2,3-Dimethoxyphenanthren-9-yl)-*N*-(4-methoxyphenylmethyl)-*N*-methylamine (29e):** 48%, m.p. 135−136 °C. − ^{1}H NMR: δ = 2.79 (s, 3 H, NCH_3), 3.81 (s, 3 H, OCH_3), 4.03 (s, 3 H, OCH_3), 4.10 (s, 3 H, OCH_3), 4.24 (s, 2 H, CH_2Ar), 6.90 (d, *J* = 7.8 Hz, 2 H, aromatic H), 7.16 (s, 1 H, aromatic H), 7.24 (s, 1 H, aromatic H), 7.35 (d, *J* = 7.8 Hz, 2 H, aromatic H), 7.56−7.63 (m, 2 H, aromatic H), 7.96 (s, 1 H, aromatic H), 8.47 (d, *J* = 7.9 Hz, 1 H, aromatic H), 8.55 (d, *J* = 7.9 Hz, 1 H, aromatic H). − ^{13}C NMR: δ = 41.5, 55.3, 55.9, 56.0, 60.6, 103.4, 107.8, 113.7, 114.7, 122.1, 122.6, 124.5, 125.3, 126.2, 127.5, 128.5, 130.0, 130.7, 131.1, 146.9, 148.3, 149.5, 158.7. − $C_{25}H_{25}NO_3$ (387.5): calcd. C 77.49, H 6.50, N 3.61; found C 77.65, H 6.52, N 3.49.

***N*-(4-Methoxyphenylmethyl)-*N*-methyl-*N*-(2,3,6-trimethoxyphenanthren-9-yl)amine (29f):** 59%, m.p. 134−135 °C. − ^{1}H NMR: δ = 2.76 (s, 3 H, NCH_3), 3.81 (s, 3 H, OCH_3), 4.02 (s, 6 H, 2 × OCH_3), 4.09 (s, 3 H, OCH_3), 4.22 (s, 2 H, CH_2Ar), 6.89 (d, *J* = 8.6 Hz, 2 H, aromatic H), 7.11 (s, 1 H, aromatic H), 7.14 (s, 1 H,

aromatic H), 7.22 (d, J = 9.0 Hz, 1 H, aromatic H), 7.33 (d, J = 8.6 Hz, 2 H, aromatic H), 7.83 (s, 1 H, aromatic H), 7.88 (s, 1 H, aromatic H), 8.38 (d, J = 9.0 Hz, 1 H, aromatic H). − ^{13}C NMR: δ = 41.5, 55.3, 55.5, 55.9, 56.1, 60.7, 103.6, 104.9, 107.8, 112.6, 113.7, 114.7, 121.6, 126.2, 128.1, 129.5, 132.5, 148.0, 149.6, 158.2, 158.7. − $C_{26}H_{27}NO_4$ (447.5): calcd. C 74.80, H 6.52, N 3.35; found C 74.71, H 6.65, N 3.26.

General Procedure for the Synthesis of the Phenanthrylamines 15b−f: A suspension of Pd on C (10%, 5 mg) and ammonium formate (189 mg, 3 mmol) in a solution of the benzylated phenanthrylamines **29b−f** (0.3 mmol) in MeOH (25 mL) was refluxed under argon over a period of 0.5 h. The reaction mixture was then filtered through Celite® and washed with MeOH, and the solvent was removed under reduced pressure. The crude product was dissolved in CH_2Cl_2 (10 mL) and the organic phase was washed with water and dried with Na_2SO_4. The crude solid obtained after solvent removal was purified by chromatography on aluminium oxide (Merck aluminium oxide 90 active basic, 70−230 mesh ASTM), using AcOEt/hexanes (3:7) as eluent, and finally recrystallized from hexane/toluene.

***N*-Methyl-*N*-(phenanthro[2,3-*d*][1,3]dioxol-6-yl)amine (15b):** 92%, m.p. 155−156 °C. − IR (KBr): $\tilde{\nu}$ = 3423 cm^{-1} (NH). − ^{1}H NMR: δ = 3.07 (s, 3 H, NCH_3), 4.10 (br. s, 1 H, NH), 6.10 (s, 2 H, OCH_2O), 6.74 (s, 1 H, aromatic H), 7.24 (s, 1 H, aromatic H), 7.34 (t, J = 7.9 Hz, 1 H, aromatic H), 7.43 (d, J = 7.8 Hz, 1 H, aromatic H), 7.70 (d, J = 7.8 Hz, 1 H, aromatic H), 8.03 (s, 1 H, aromatic H), 8.31 (d, J = 7.9 Hz, 1 H, aromatic H). − ^{13}C NMR: δ = 31.2, 98.6, 101.3, 101.4, 101.7, 121.4, 122.1, 122.7, 125.2, 126.1, 126.7, 127.3, 133.1, 142.2, 147.8. − $C_{16}H_{13}NO_2$ (251.3): calcd. C 76.48, H 5.21, N 5.57; found C 76.61, H 4.99, N 5.59.

***N*-Methyl-*N*-(5,6,7-trimethoxyphenanthren-9-yl)amine (15c):** 88%, m.p. 95−96 °C. − IR (KBr): $\tilde{\nu}$ = 3410 cm^{-1} (NH). − ^{1}H NMR: δ = 3.08 (s, 3 H, NCH_3), 3.99 (s, 3 H, OCH_3), 4.02 (s, 3 H, OCH_3), 4.04 (s, 4 H, OCH_3 + NH), 6.80 (s, 1 H, aromatic H), 7.09 (s, 1 H, aromatic H), 7.38−7.46 (m, 2 H, aromatic H), 7.71 (d, J = 7.9 Hz, 1 H, aromatic H), 9.38 (d, J = 7.9 Hz, 1 H, aromatic H). − ^{13}C NMR: δ = 31.4, 55.9, 60.3, 61.3, 97.6, 103.5, 123.4, 123.7, 125.0, 125.9, 126.5, 126.6, 133.3, 141.5, 152.3. − $C_{18}H_{19}NO_3$ (297.4): calcd. C 72.71, H 6.44, N 4.71; found C 72.89, H 6.47, N 4.63.

***N*-Methyl-*N*-(3,5,6,7-tetramethoxyphenanthren-9-yl)amine (15d):** 94%, m.p. 114−115 °C. − IR (KBr): $\tilde{\nu}$ = 3395 cm^{-1} (NH). − ^{1}H NMR: δ = 3.05 (s, 3 H, NCH_3), 3.97 (br. s, 4 H, OCH_3 + NH), 4.01 (s, 3 H, OCH_3), 4.03 (s, 3 H, OCH_3), 4.04 (s, 3 H, OCH_3), 6.79 (s, 1 H, aromatic H), 7.10 (s, 1 H, aromatic H), 7.14 (d, J = 8.5 Hz, 1 H, aromatic H), 7.63 (d, J = 8.5 Hz, 1 H, aromatic H), 9.00 (s, 1 H, aromatic H). − ^{13}C NMR: δ = 31.5, 55.4, 55.9, 60.5, 61.3, 97.7, 103.8, 108.1, 116.1, 119.5, 124.2, 125.9, 127.7, 127.8, 139.9, 142.5, 152.4, 153.0, 156.0. − $C_{19}H_{21}NO_4$ (327.4): calcd. C 69.71, H 6.47, N 4.28; found C 69.55, H 6.52, N 4.21.

***N*-(2,3-Dimethoxyphenanthren-9-yl)-*N*-methylamine (15e):** 91%, m.p. 138−139 °C. − IR (KBr): $\tilde{\nu}$ = 3441 cm^{-1} (NH). − ^{1}H NMR: δ = 3.07 (s, 3 H, NCH_3), 4.02 (br. s, 4 H, OCH_3 + NH), 4.07 (s, 3 H, OCH_3), 6.73 (s, 1 H, aromatic H), 7.12 (s, 1 H, aromatic H), 7.53 (dt, J = 8.1, 1.2 Hz, 1 H, aromatic H), 7.62 (dt, J = 8.2, 1.2 Hz, 1 H, aromatic H), 7.86 (dd, J = 8.1, 1.2 Hz, 1 H, aromatic H), 8.00 (s, 1 H, aromatic H), 8.53 (dd, J = 7.9, 1.2 Hz, 1 H, aromatic H). − ^{13}C NMR: δ = 31.8, 55.8, 56.1, 101.7, 103.8, 107.0, 119.2, 120.4, 123.0, 124.5, 125.2, 126.2, 128.8, 130.5, 141.3, 146.7, 149.7. − $C_{17}H_{17}NO_2$ (267.3): calcd. C 76.38, H 6.41, N 5.24; found C 76.53, H 6.19, N 5.36.

***N*-Methyl-*N*-(2,3,6-trimethoxyphenanthren-9-yl)amine (15f):** 96%, m.p. 198−199 °C. − IR (KBr): $\tilde{\nu}$ = 3408 cm^{-1} (NH). − ^{1}H NMR: δ = 3.05 (s, 3 H, NCH_3), 4.00 (br. s, 4 H, OCH_3 + NH), 4.01 (s, 3 H, OCH_3), 4.06 (s, 3 H, OCH_3), 6.60 (s, 1 H, aromatic H), 7.09 (s, 1 H, aromatic H), 7.16 (dd, J = 9.0, 2.4 Hz, 1 H, aromatic H), 7.76 (s, 1 H, aromatic H), 7.78 (dd, J = 9.0, 2.4 Hz, 1 H, aromatic H), 7.86 (d, J = 2.4 Hz, 1 H, aromatic H). − ^{13}C NMR: δ = 31.1, 55.5, 55.8, 56.2, 100.0, 104.0, 105.0, 107.0, 114.3, 118.5, 119.1, 122.0, 129.5, 132.0, 141.5, 146.4, 150.0, 158.1. − $C_{18}H_{19}NO_3$ (297.4): calcd. C 72.71, H 6.44, N 4.71; found C 72.62, H 6.32, N 4.94.

General Procedure for the Synthesis of the Dioxoaporphines 1b−d: A solution of the phenanthrylamines **15b−d** (0.5 mmol), oxalyl chloride (96 mg, 0.75 mmol), and DMF (2 drops) in anhydrous CH_2Cl_2 (10 mL) was stirred at room temperature for 30 min. The solvent and excess reagent were removed under vacuum and the solid residue was then dissolved in freshly distilled CH_2Cl_2 (10 mL). A solution of $SnCl_4$ (2.5 mL, 1 M in CH_2Cl_2, 2.5 mmol) was slowly added by syringe and the mixture was then stirred at room temperature for 48 h. Aqueous HCl (10%, 5 mL) and CH_2Cl_2 (20 mL) were then added and the organic phase was subsequently treated with water and brine, and dried with $MgSO_4$. After removal of the solvent, the crude residue was treated by flash column chromatography on silica gel, using an acetone/hexanes mixture (3:2) as eluent, to afford the targeted dioxoaporphines **1b−d**, which were finally recrystallized from ethanol/hexane (**1c** and **1d**) or acetone (**1b**).

5,6-Dihydro-6-methyl-4*H*-benzo[*g*][1,3]dioxolo[4′,5′,5,6]benzo-[*de*]quinoline-4,5-dione (1b): 78%, m.p. 351−352 °C. − IR (KBr): $\tilde{\nu}$ = 1660 cm^{-1} (C=O), 1594 cm^{-1} (C=O). − ^{1}H NMR [D$_6$]DMSO: δ = 3.70 (s, 3 H, NCH_3), 6.49 (s, 2 H, OCH_2O), 7.57−7.70 (m, 2 H, aromatic H), 7.90 (s, 1 H, aromatic H), 8.04 (d, J = 7.8 Hz, 1 H, aromatic H), 8.70 (d, J = 7.2 Hz, 1 H, aromatic H), 8.75 (s, 1 H, aromatic H). − ^{13}C NMR [D6]DMSO: δ = 31.2, 101.0, 106.1, 115.1 115.6, 120.3, 121.9, 122.9, 125.6, 125.7, 130.0, 130.8, 133.4, 136.3, 137.0, 146.9, 156.1, 175.5 (s, C=O). − $C_{18}H_{11}NO_2$ (305.3): calcd. C 70.82, H 3.63, N 4.59; found C 70.72, H 3.89, N 4.43.

***N*-Methylouregidione (1c):** 81%, m.p. 202−203 °C (ref.[30] 202−203 °C). The analytical and spectroscopic data of synthetic **1c** match those reported for the natural product.[31]

5,6-Dihydro-1,2,3,10-tetramethoxy-6-methyl-4*H*-dibenzo[*de*,*g*]-quinoline-4,5-dione (1d): 75%, m.p. 186−187 °C. − IR (KBr): $\tilde{\nu}$ = 1660 cm^{-1} (C=O), 1605 cm^{-1} (C=O). − ^{1}H NMR: δ = 3.75 (s, 3 H, NCH_3), 3.99 (s, 3 H, OCH_3), 4.06 (s, 3 H, OCH_3), 4.09 (s, 3 H, OCH_3), 4.16 (s, 3 H, OCH_3), 7.26 (dd, J = 8.7, 2.5 Hz, 1 H, aromatic H), 7.47 (s, 1 H, aromatic H), 7.75 (d, J = 8.7 Hz, 1 H, aromatic H), 8.96 (d, J = 2.5 Hz, 1 H, aromatic H). − ^{13}C NMR: δ = 30.7, 55.4, 61.2, 61.7, 62.1, 108.6, 114.9, 117.7, 120.5, 121.5, 126.1, 128.1, 129.9, 146.8, 156.8, 158.4, 158.9, 159.9, 174.3 (s, C=O). − $C_{21}H_{19}NO_6$ (381.4): calcd. C 66.14, H 5.02, N 3.67; found C 66.23, H 4.91, N 3.72.

General Procedure for the Synthesis of the Chloroacetamides 30e,f: A solution of the phenanthrylamines **15e** or **15f** (0.5 mmol) and triethylamine (76 mg, 0.75 mmol) in dry CH_2Cl_2 (10 mL) was cooled to 0 °C under argon, with stirring. A solution of chloroacetyl chloride (85 mg, 0.75 mmol) was added by syringe and the mixture was stirred at 0 °C for 2 h. After warming to room temperature, the solvent and excess reagent were removed under vacuum. The crude product was then dissolved in CH_2Cl_2 (20 mL) and the organic phase was washed successively with water and brine, and

dried with $MgSO_4$. Flash column chromatography on silica gel, with AcOEt/hexanes (7:3) as eluent, afforded the chloroacetamides **30e**,**f**, which were finally purified by recrystallization from hexane/toluene.

2-Chloro-*N*-(2,3-dimethoxyphenanthren-9-yl)-*N*-methylacetamide (30e): (96%), m.p. 155−156 °C. − IR (KBr): $\tilde{\nu}$ = 1663 cm^{-1} (C=O). − ^1H NMR: δ = 3.44 (s, 3 H, NCH_3), 3.74 (d, *J* = 13.3 Hz, 1 H, CH_2Cl), 3.90 (d, *J* = 13.3 Hz, 1 H, CH_2Cl), 4.05 (s, 3 H, OCH_3), 4.14 (s, 3 H, OCH_3), 7.23 (s, 1 H, aromatic H), 7.60−7.65 (m, 2 H, aromatic H), 7.70 (dt, *J* = 8.2, 1.3 Hz, 1 H, aromatic H), 7.80 (d, *J* = 7.1 Hz, 1 H, aromatic H), 8.00 (s, 1 H, aromatic H), 8.60 (d, *J* = 8.0 Hz, 1 H, aromatic H). − ^{13}C NMR: δ = 37.7, 41.8, 56.0, 56.1, 103.2, 108.4, 122.7, 123.1, 125.1, 125.7, 126.2, 127.0, 127.4, 127.5, 131.1, 135.4, 150.0, 150.4, 167.3 (s, C=O). − $C_{19}H_{18}ClNO_3$ (343.8): calcd. C 66.38, H 5.28, N 4.07; found C 66.27, H 5.41, N 4.11.

2-Chloro-*N*-methyl-*N*-(2,3,6-trimethoxyphenanthren-9-yl)acetamide (30f): (91%), m.p. 203−204 °C. − IR (KBr): $\tilde{\nu}$ = 1665 cm^{-1} (C=O). − ^1H NMR: δ = 3.42 (s, 3 H, NCH_3), 3.74 (d, *J* = 13.3 Hz, 1 H, CH_2Cl), 3.91 (d, *J* = 13.3 Hz, 1 H, CH_2Cl), 4.02 (s, 3 H, OCH_3), 4.03 (s, 3 H, OCH_3), 4.12 (s, 3 H, OCH_3), 7.26 (s, 1 H, aromatic H), 7.26 (dd, *J* = 8.8, 2.1 Hz, 1 H, aromatic H), 7.47 (s, 1 H, aromatic H), 7.71 (d, *J* = 8.8 Hz, 1 H, aromatic H), 7.86 (d, *J* = 8.8 Hz, 1 H, aromatic H), 7.91 (d, *J* = 2.1 Hz, 1 H, aromatic H). − ^{13}C NMR: δ = 37.8, 41.8, 55.7, 56.0, 56.2, 103.3, 105.1, 108.4, 116.3, 122.1, 123.1, 124.4, 124.5, 126.8, 132.7, 135.5, 150.1, 159.0, 167.3 (s, C=O). − $C_{20}H_{20}ClNO_4$ (373.8): calcd. C 64.26, H 5.39, N 3.75; found C 64.10, H 5.23, N 3.59.

General Procedure for the Synthesis of the Dioxoaporphines 1e,f: A solution of the chloroacetamide **30e** or **30f** (0.2 mmol) in aqueous MeOH (3:7, 40 mL) was placed in a Pyrex tube equipped with a magnetic stirrer. Irradiations were carried out in a Rayonet RPR 100 photoreactor, fitted with RPR 300- and 350-nm lamps. The mixture was irradiated with stirring for 4 h and oxygen was subsequently bubbled through the solution for 0.5 h. After removal of the solvent, the crude solid residue was triturated with a mixture of petroleum ether/ethanol (9:1), filtered, purified by flash column chromatography on silica gel using an acetone/hexanes mixture (1:1) as eluent, and finally recrystallized from ethanol/hexane (**1e**) or acetone (**1f**).

5,6-Dihydro-9,10-dimethoxy-6-methyl-4*H*-dibenzo[*de,g*]quinoline-4,5-dione (1e): 34%, m.p. 172−173 °C. − IR (KBr): $\tilde{\nu}$ = 1650 cm^{-1} (C=O), 1616 cm^{-1} (C=O). − ^1H NMR: δ = 3.97 (s, 3 H, NCH_3), 4.08 (s, 3 H, OCH_3), 4.13 (s, 3 H, OCH_3), 7.53 (s, 1 H, aromatic H), 7.58 (s, 1 H, aromatic H), 7.60 (t, *J* = 7.4 Hz, 1 H, aromatic H), 8.00 (dd, *J* = 9.2, 4.5 Hz, 1 H, aromatic H), 8.01 (s, 1 H, aromatic H), 8.53 (dd, *J* = 9.3, 4.5 Hz, 1 H, aromatic H). − ^{13}C NMR: δ = 30.6, 55.5, 55.7, 106.3, 107.4, 113.6, 120.4, 120.9, 123.5, 125.1, 129.7, 131.1, 132.6, 140.3, 149.1, 149.7, 151.0, 176.9 (s, C=O). − $C_{19}H_{15}NO_4$ (321.3): calcd. C 71.02, H 4.71, N 4.36; found C 71.00, H 4.98, N 4.54.

5,6-Dihydro-2,9,10-trimethoxy-6-methyl-4*H*-dibenzo[*de,g*]quinoline-4,5-dione (1f): 29%, m.p. 269−270 °C. − IR (KBr): $\tilde{\nu}$ = 1652 cm^{-1} (C=O), 1611 cm^{-1} (C=O). − ^1H NMR: δ = 3.83 (s, 3 H, NCH_3), 4.06 (s, 3 H, OCH_3), 4.07 (s, 3 H, OCH_3), 4.11 (s, 3 H, OCH_3), 7.24 (s, 1 H, aromatic H), 7.39 (s, 1 H, aromatic H), 7.81 (s, 1 H, aromatic H), 8.14 (d, *J* = 2.6 Hz, 1 H, aromatic H), 8.34 (d, *J* = 2.6 Hz, 1 H, aromatic H). − ^{13}C NMR: δ = 30.3, 55.5, 56.2, 56.5, 108.7, 112.1, 112.7, 116.5, 117.9, 119.0, 127.3, 127.8, 132.4, 135.5, 149.4, 150.9, 151.2, 161.5, 175.6 (s, C=O). − $C_{20}H_{17}NO_5$ (351.4): calcd. C 68.37, H 4.88, N 3.99; found C 68.05, H 5.02, N 4.10.

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