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Intramolecular Dehydrogenative Coupling of 2,3-Diaryl Acrylic Compounds: Access to Substituted Phenanthrenes

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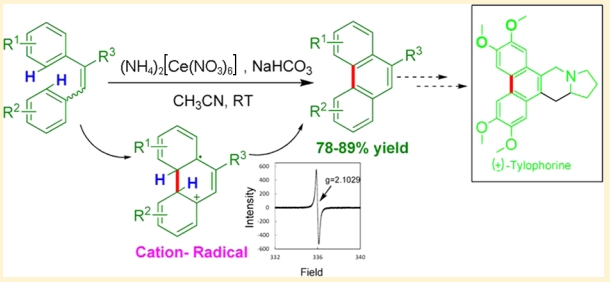
Supporting Information

ABSTRACT: A simple, facile, and environmentally benign intramolecular dehydrogenative coupling of various 1,2-diarylethylenes for the synthesis of phenanthrenes in excellent yield has been described. This new methodology uses ceric ammonium nitrate (CAN) as a promoter at room temperature and has been extended to intermolecular synthesis of biaryl compounds. The electron transfer from methoxyarene to cerium leads to cationic radical formation, which further proceeds to intramolecular coupling. Preliminary mechanistic investigation by EPR spectroscopy and density functional theory calculation suggested a similar view.



The π-conjugated substructure or a biaryl unit is common building scaffold for various natural products, biosimilars, dyes and functional materials.[1] For instance, polymethoxy phenanthroindolizidine and phenanthro- quinolizidine alkaloids are an important class of π-conjugated molecules displaying a very broad spectrum of biological activities ranging from antibacterial to antitumor properties.[2] A few representatives of this family are (−)-tylophorine, (−)-antofine, (−)-tylocrebrine, (−)-cryptopleurine, (−)-deoxytylophorinine, and (+)-tylophoridicine E (Figure 1). The common architectural motif among all these alkaloids is a phenanthrene ring and biaryl substructure, which plays a key role in their pharmacological activity.[2,3]

Conventionally, these can be synthesized by radical coupling,[4] Ullmann reaction,[5] or transition-metal-catalyzed cross-coupling reactions of the prefunctionalized synthons.[6] The cross-coupling reactions have emerged as an important tool for C−C bond formation in modern organic synthesis. Nevertheless, the cross-coupling protocols have the following common drawbacks for any transformation: (i) generation of a stoichiometric amount of metallic waste and (ii) less availability of the synthons such as aryl halides and aryl metal reagents. A more concise, environmentally benign, and atom economical approach would be dehydrogenative cross-coupling reactions of unsaturated compounds with aromatic compounds without utilizing a previously installed functional group.[7]

To date, most of the procedures using aryls for obtaining phenanthrene rings have explored the use of many heavy metal reagents such as $MoCl_5/TiCl_4$,[8] thallium(III) trifluoroacetate,[9] lead(IV) tetraacetate,[10] Ru (IV),[7b] early transition metal salts, e.g., vanadium oxytrifluoride (VOF_3) or vanadium oxy trichloride ($VOCl_3$),[11] MnO_2−BF_3·OEt_2,[12] iron(III) chloride,[13] and metal-free oxidants such as hypervalent iodine, phenyliodine(III) bis(trifluoroacetate) (PIFA), phenyliodine-(III) diacetate (PIDA),[14,15] DDQ/CH_3SO_3H,[16] and photocyclization in the presence of iodine.[17] Unfortunately, the poor substrate scope, average reaction yields, harsh reaction conditions, and high toxicity associated with the reagents limit the application of these methodologies. Thus, undoubt-

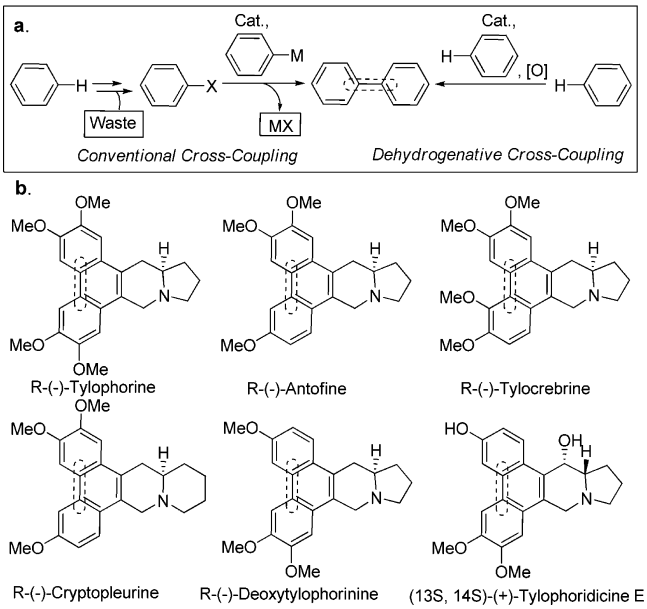


Figure 1. (a) Strategies to biaryl synthesis. (b) Selected important phenanthrene alkaloids.

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edly, there is a need for developing a highly efficient, cheap, and green alternative to these methodologies for a broad range of phenanthrenes.

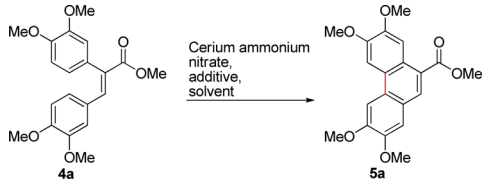
Since, the dehydrogenative cross-coupling reaction requires an electron-transfer oxidation of aryls via metal salts, a greener alternative must substitute the catalyst. Among all the one-electron oxidants, cheap commercially available and eco-friendly Ce(IV) salts are most attractive.

We have explored here the use of ceric ammonium nitrate (CAN) as an oxidative coupling promoter due to its high reduction potential, excellent Lewis acid property and high reactivity. Its easy solubility in water makes it an environment friendly catalyst, and it has already been effectively used as a catalyst in many synthetic transformations leading to important heterocyclic cores of biological importance.[18] We report an environmentally friendly, CAN mediated synthesis of phenanthrenes by dehydrogenative coupling of 1,2-diaryl ethylenes and biaryls by intermolecular coupling of aryls.

As a representative reaction, transformation of methyl-(*E*)-2,3-bis(3,4-dimethoxyphenyl)acrylate **4a** to the phenanthrene derivative **5a** is shown in Table 1. While the intramolecular oxidative coupling of **4a** was not observed in the presence of only ceric ammonium nitrate in CH_2Cl_2 (entry 1, Table 1), the presence of a suitable additive yielded the cyclized product **5a**. Lewis acids such as $BF_3{\cdot}OEt_2$, $Cu(OTf)_2$, and $SnCl_4$, as well as a Brønsted acid such as CH_3SO_3H, were examined as an additive in an oxidative biaryl coupling reaction. Unfortunately, none of the acid additives were helpful in providing the cyclized product (entries 2−5, Table 1). On the other hand, introduction of a weak base as an additive enabled the reaction to yield **5a** albeit in less than 5% yield. The reaction did not benefit by increasing the reaction time, as the unreacted starting material was recovered even after 18 h (entry 6, Table 1). To make the oxidative coupling reaction conditions more productive, various solvents were screened (entries 7−11, Table 1). It was observed that a highly polar solvent such as acetonitrile could give the best yields of the coupled product (entry 7, Table 1). It was observed that the concentrations of both base and the oxidating agent CAN were affecting the reaction efficiency (entries 12−16, Table 1). Performing the coupling using CAN (2 equiv) and $NaHCO_3$ (4 equiv) in CH_3CN at ambient temperature was identified as being ideal (entry 17, Table 1).

With the optimized reaction conditions in hand, we exploited the scope of the reaction with a variety of 2,3-diaryl acryl compounds. A number of 2,3-diaryl acrylates and its derivatives were synthesized by following the standard protocol of the Perkin reaction,[19] starting from arylacetic acid and the appropriate aryl aldehyde. To explore the scope of the reaction, we decided to investigate the effect of the substituents at the double bond (Table 2). Hence various 2,3-diaryl acrylic derivatives such as acrylic esters (*E*-**4a** and *E*-**4b**), acrylic acid (*E*-**4c**), acrylic aldehydes (*E*-**4d**), and acrylic amides (*E*-**4e**−**j**) were screened for the oxidative cyclization reaction under the optimized conditions. All of them showed excellent reactivity for the corresponding cyclized products **5a**−**j** in excellent yield. To check the impact of the configuration on the intramolecular oxidative coupling reaction, cyclization of acrylic nitrile *Z*-**4k** was opted. It gave a very high yield of the corresponding coupling product **5k**, which clearly indicates that the configuration of the double bond does not affect the oxidative coupling reaction.

Table 1. Optimization of Intramolecular Oxidative Coupling[a]



4a **5a**

entry	cerium(IV) ammonium nitrate (equiv)	additive (equiv)	solvent	yield[b] (%)
1	1.0	–	CH_2Cl_2	–
2	1.0	$BF_3{\cdot}OEt_2$ (1.0)	CH_2Cl_2	–
3	1.0	$Cu(OTf)_2$ (1.0)	CH_2Cl_2	–
4	1.0	$SnCl_4$ (1.0)	CH_2Cl_2	–
5	1.0	CH_3SO_3H (1.0)	CH_2Cl_2	–
6	1.0	$NaHCO_3$ (1.0)	CH_2Cl_2	<5
7	1.0	$NaHCO_3$ (1.0)	CH_3CN	29
8	1.0	$NaHCO_3$ (1.0)	THF	23
9	1.0	$NaHCO_3$ (1.0)	Et_2O	<5
10	1.0	$NaHCO_3$ (1.0)	1,4-Dioxane	24
11	1.0	$NaHCO_3$ (1.0)	Hexane	–
12	1.0	$NaHCO_3$ (2.0)	CH_3CN	32
13	1.0	$NaHCO_3$ (3.0)	CH_3CN	60
14	1.0	$NaHCO_3$ (4.0)	CH_3CN	64
15	2.0	$NaHCO_3$ (2.0)	CH_3CN	37
16	2.0	$NaHCO_3$ (3.0)	CH_3CN	53
17	2.0	$NaHCO_3$ (4.0)	CH_3CN	87

[a]Genral reaction conditions: **4a** (0.1 mmol), Cerium ammonium nitrate, additive in solvent (1.0 mL) at room temperature for 6 h, unless stated otherwise. [b]Isolated yield of **5a**

Further, we also investigated the effect of methoxy substitution with respect to its position on the aryl ring and the corresponding reaction yield. We observed that the 2-position veratryl group with a benzo[1,3]dioxole moiety in 2,3-diaryl acrylate did not affect the conversion to **5l**. Similarly substitution of the 3-position veratryl group with a benzo-[1,4]dioxole moiety did not impact the conversion significantly in **5m**. Also substitution of both veratryl groups with benzo[1,3]dioxole and benzo[1,4]dioxole did not impact the yield in **5n**. However, the number of electron-donating substituents on both aryl rings are extremely important for the feasibility of the oxidative coupling reaction. In the absence of the methoxyl group on one of the aryls of the acrylate, the reaction did not lead to the corresponding cyclized product **5o**. However, a substrate with more than two methoxyl groups on the phenyl of the acrylic compound gave both cyclized product **5p** and an intermolecular coupled product due to the enhanced reactivity. A slight deactivation of the substrate by substituting one methoxyl with fluorine on phenyl gave 62% of the cyclized product **5q**. Substrates with a reduced ester group of **4a** such as

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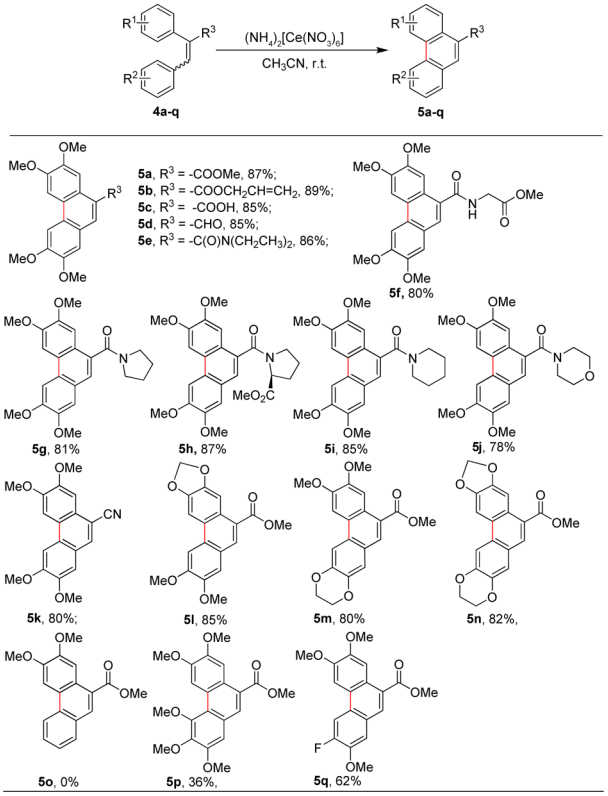
Table 2. Substrate Scope for Oxidative Coupling of 1,2-Diarylethylenes[a,b]

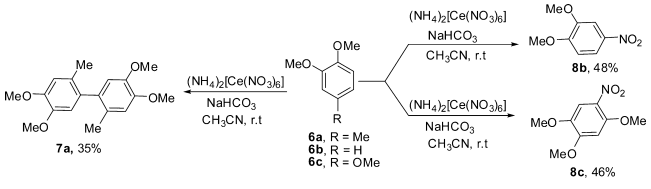


[a]Unless otherwise noted, the reactions were carried out with **4** (0.1 mmol), CAN (109.6 mg, 0.2 mmol), $NaHCO_3$ (33.6 mg, 0.4 mmol), and CH_3CN (1 mL) as solvent. [b]The yield refers to the isolated product.

corresponding allylic alcohol **4s** and methyl substituted alkene **4r** lead to the cyclized aldehyde (**5d**) instead of phenanthrenyl methyl alcohol and nitrated phenanthrene (**5r′**) respectively (see the Supporting Information).

As a result of the progression of the intramolecular biaryl coupling reaction, the CAN/$NaHCO_3$ system was also screened for the intermolecular biaryl coupling. It was found that substrates with two methoxy groups and a methyl group at the aryl ring (**6a**) give the corresponding coupled polymethoxy biaryl compound (**7a**). Substrates with poor-electron density such as anisole with one methoxy group at the aryl ring could not deliver the coupled product. Also other less reactive substrates such as toluene, halobenzene, and benzene did not afford the coupled product under the above-mentioned optimized conditions (Scheme 1). Substrates with two and three methoxy groups at the aryl ring gave the corresponding nitro products (**8b** and **8c**)[20] in place of a biaryl compound (Scheme 1).

Scheme 1. CAN-Mediated Oxidative Reactions



To learn about the mechanistic details of this reaction, full quantum chemical calculations were done with density functional theory (DFT) at the PBE/TZVP level of theory in order to understand the mechanism of the reaction. [For more details about the calculations, please see the SI.] As shown in Figure 2, the reaction can go through two possible mechanisms: **A** and **B**.

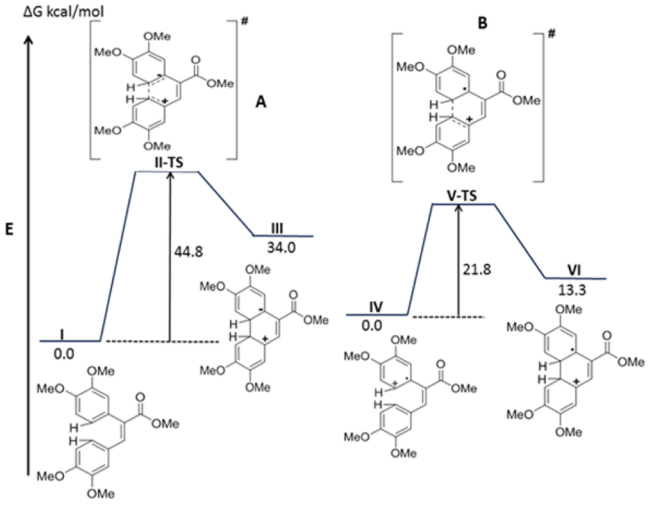


Figure 2. Calculations with density functional theory (DFT) comparing the free energy profiles: **A** (neutral pathway) and **B** (cation radical pathway) for the intramolecular cyclization process.

In **A**, the cyclization of the neutral starting reactant species **I** leads to the formation of the neutral complex **III**. This process is seen to be unfavorable: **III** is less stable in comparison to **I** by 34.0 kcal/mol. Furthermore, the transition state (**II**) for this reaction is seen to lie 44.8 kcal/mol higher than the reactant complex **I.** Given the unfavorability of this reaction, an alternate pathway (**B**) was considered. In this pathway, the cation radical species **IV** is considered as the reactant. Such a species will be formed if **I** loses an electron. Since cerium ammonium nitrate $(NH_4)_2[Ce(NO_3)_6]$ has been employed in the system, the loss of an electron from **I** to $(NH_4)_2[Ce(NO_3)_6]$ is a feasible possibility. The cation radical species **IV** is converted to the corresponding cyclized cation radical species **VI** by a pathway that is significantly more favorable than **A**. The barrier for this pathway is 21.8 kcal/mol, which is 23.0 kcal/mol lower in energy than the barrier in **A**. The large difference in the barrier heights between Pathway **A** and **B** makes it clear the Pathway **A** is not feasible and the reaction would only proceed through Pathway **B**. This indicates that **IV** is an important intermediate species that is formed during the reaction.

The reason for the preference for the cation radical pathway **B** can be explained by the fact that pathway **B** is a charge transfer process while pathway **A** is not. The natural bond orbital (NBO) charges have been calculated for the species **I** to **VI**, and they indicate that during the cyclization from **IV** to **VI**, charge is transferred from the **C1** carbon atom [see SI] in species **IV** to the **C2** carbon [see SI] in the transition state **V-TS**. However, a similar charge transfer process is not observed in pathway **A**. Since charge transfer processes are known to be facile, this explains why the cation radical pathway is seen to be more favorable than the neutral pathway.

As proposed, the CAN promoted intramolecular dehydrogenative cross-coupling might undergo a radical process. To

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investigate this possibility, we performed a radical trapping experiment. Although the oxidative coupling of methyl-(*E*)-2,3-bis(3,4-dimethoxyphenyl)acrylate **4a** with $(NH_4)_2[Ce(NO_3)_6]$ and $NaHCO_3$ in the presence of 1 equiv of TEMPO did not provide the corresponding TEMPO-coupled product, a lower yield of the phenanthrene **5a** was observed. The CAN-promoted dehydrogenative cross-coupling of **4a** was also monitored by electron paramagnetic resonance (EPR), and the results are shown in Figure 3. A sharp EPR signal at g = 2.1029 was detected (Figure 3B), which confirms the formation of a radical species in the reaction mixture. The formed radicals are assignable to aryl radicals obtained from **4a**.

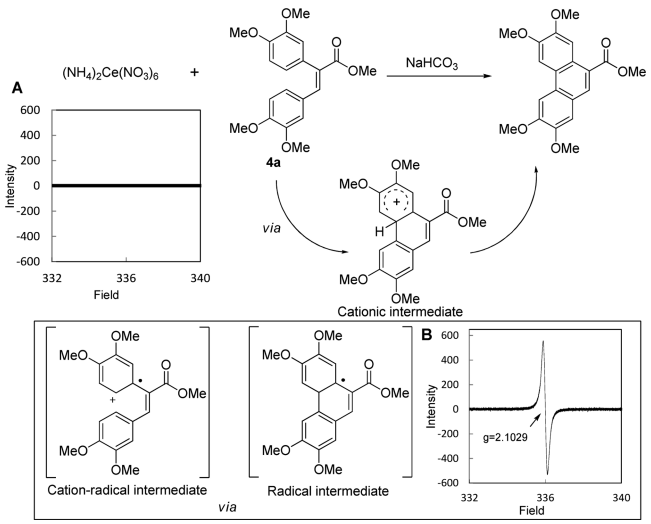
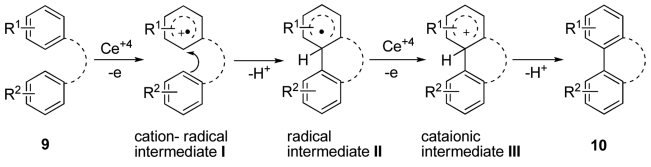


Figure 3. Capture experiment of aryl radical. (A and B) The EPR spectra of (A) $(NH_4)_2Ce(NO_3)_6$ in THF and (B) the reaction mixture of $(NH_4)_2Ce(NO_3)_6$ and **4a** in THF at room temperature.

Based on above-mentioned experimental findings (EPR spectoscopic study) and the DFT calculation, a plausible reaction mechanism for the CAN mediated oxidative coupling was proposed (Scheme 2). In the mechanism we propose that an electron-rich aromatic compound leads to an electron transfer from one of the aryl rings of the substrate to CAN to form a cationic radical intermediate and reduced form of CAN. Subsequently, a neutral second aryl ring of the substrate leads to the intramolecular substitution reaction on the cationic radical ring to deliver a radical intermediate. Further electron transfer from the radical intermediate to CAN gave a cationic intermediate, which after dehydroaromatization gave the biaryl product.

Scheme 2. Plausible Mechanism for CAN-Promoted Oxidative Coupling Reaction



In conclusion, an oxidative dehydrogenative coupling method for the synthesis of biaryl compounds in good to excellent yields by utilizing inexpensive, comparatively milder one-electron oxidant CAN and $NaHCO_3$ under room temperature was developed. The above-mentioned oxidation system which facilitates C−C bond formation can be employed for the intermolecular and intramolecular coupling reaction. The reaction showed tolerance for a broad range of functional groups. The present system is economical, greener, and easy to execute in comparison to a previously reported procedure for the coupling reaction.

EXPERIMENTAL SECTION

General Information. An NMR instrument (300 MHz) was used to record ^1H and ^{13}C NMR spectra in deuterated solvents with residual protonated solvent signals as internal reference. The ^1H NMR data are reported as follows: chemical shift (δ, ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), integration, coupling constant (Hz). The ^{13}C NMR data are recorded in terms of chemical shift (δ, ppm). An FT-IR spectrometer was used to record the infrared spectra which are reported in frequency of absorption. An MS-TOF mass spectrometer and ESI mass spectrometer were used to record low resolution and high resolution mass spectra. Column chromatographic separations were carried out on silica gel (100−200 mesh). Cerium(IV) ammonium nitrate was purchased from Sigma-aldrich and used without further purification. Anhydrous sodium hydrogen carbonate was used. In all reactions, dry solvents were used. All starting materials were prepared according to the known literature procedure. 2,3-Diaryl acrylic acid derivatives were prepared by perking condensation of aromatic aldehyde with phenylacetic acid derivatives according to the reported procedure.[13] Acrylic acid was converted into esters **4a**, **4b**,[13b] **4l**−**4o**,[14] **4p**,[7d] **4q**,[8c] and corresponding nitrile **4k**[14] by a well known literature procedure. 2,3-Diaryl acrylamide (**4e**−**4j**)[3b] derivatives were prepared according to the literature procedure.

General Procedure for Oxidative Degydrogenative Coupling. 2,3-Diaryl acrylic compound **4a**−**q** (0.1 mmol) was taken in 1 mL of CH_3CN. To this solution sodium hydrogen carbonate (0.4 mmol) and then cerium ammonium nitrate (0.2 mmol) were added under a nitrogen gas atmosphere. The suspension was stirred at room temperature until the reaction completed and then was filtered through Celite and washed with dichloromethane (3 × 2 mL). The resulting combined solution was concentrated on a rotavap to give the organic residue which was purified by column chromatography on silica gel (eluent: EtOAc/Pet ether) to give the corresponding 9-substituted phenanthrene derivatives.

*2,3,6,7-Tetramethoxy-phenanthrene-9-carboxylic Acid Methyl Ester (**5a**).*[13b] The reaction was run according to the general procedure for 6 h to give the compound **5a** as a yellow solid (31 mg, 87% yield); mp 202−206 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 4.02 (s, 3H), 4.04 (s, 3H), 4.09 (s, 3H), 4.13 (s, 3H), 4.14 (s, 3H), 7.26 (s, 1H), 7.75 (s, 1H), 7.79 (s, 1H), 8.41 (s, 1H), 8.65 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.9, 55.8, 55.9, 56.1, 102.5, 102.7, 106.9, 109.3, 122.2, 124.2, 124.6, 125.1, 127.1, 130.4, 149.1, 149.3, 151.3, 168.2. HRMS-ESI [M + Na], calcd for $C_{20}H_{20}O_6Na$ 379.1152, found 379.1170. IR (KBr): 1515, 1620, 1710, 2945, 3115 cm^{-1}.

*2,3,6,7-Tetramethoxy-phenanthrene-9-carboxylic Acid Allyl Ester (**5b**).* The reaction was run according to the general procedure for 4 h to give the compound **5b** as a yellow solid (34 mg, 89% yield); mp 170−174 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 4.05 (s, 3H), 4.08 (s, 3H), 4.13 (s, 3H), 4.14 (s, 3H), 4.94 (d, J = 6 Hz, 2H), 5.36 (d, J = 12 Hz, 1H), 5.51 (d, J = 18 Hz, 1H), 6.10−6.21 (m, 1H), 7.28 (s, 1H), 7.75 (s, 1H), 7.80 (s, 1H), 8.45 (s, 1H), 8.64 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.8, 55.9, 55.9, 56.0, 65.5, 102.5, 102.7, 106.9, 109.2, 118.4, 122.2, 124.2, 124.5, 125.1, 127.1, 130.4, 132.5, 149.0, 149.3, 151.3, 167.4. HRMS-ESI [M + Na], calcd for $C_{22}H_{22}NaO_6$ 405.1308, found 405.1290. IR (KBr): 1257, 1424, 1458, 1510, 1592, 1696, 2038, 2835, 2944, 3371 cm^{-1}.

*2,3,6,7-Teramethoxy-phenanthrene-9-carboxylic Acid (**5c**).*[13b] The reaction was run according to the general procedure for 5 h to give the compound **5c** as a yellow solid (29 mg, 85% yield); mp 282−286 °C. ^1H NMR (300 MHz, DMSO-d_6) δ 3.03 (s, 3H), 3.05 (s, 3H), 3.19 (s, 3H), 3.20 (s, 3H), 6.71 (s, 1H), 7.16 (s, 1H), 7.20 (s, 1H), 7.56 (s, 1H), 7.68 (s, 1H), 11.99 (b, 1H). ^{13}C NMR (75 MHz, DMSO-d6) δ 55.3, 55.6, 55.9, 56.0, 103.5, 104.0, 106.8, 109.6, 122.8,

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123.5, 124.2, 125.0, 126.5, 129.7, 148.8, 148.9, 151.2, 169.1. HRMS-ESI [M + Na], calcd for $C_{19}H_{18}O_6Na$ 365.0996, found 365.0993. IR (KBr): 1382, 2854, 3084, 3444 cm^{-1}.

2,3,6,7-Tetramethoxy-phenanthrene-9-carbaldehyde (5d).[3d] The reaction was run according to the general procedure for 4 h to give the compound **5d** as a yellow solid (28 mg, 85% yield); mp 212−214 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 4.07 (s, 3H), 4.11 (s, 3H), 4.14 (s, 3H), 4.16 (s, 3H), 7.33 (s, 1H), 7.76 (s, 2H), 8.05 (s, 1H), 8.96 (s, 1H), 10.26 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.9, 55.9, 56.1, 102.6, 106.2, 109.4, 122.9, 124.6, 125.0, 127.9, 139.1, 149.1, 149.4, 150.1, 152.1, 193.8. HRMS-ESI [M + Na], calcd for $C_{19}H_{18}O_5Na$ 349.1046, found 349.1058. IR (KBr): 1474, 1516, 1614, 1681, 2922, 3466 cm^{-1}.

2,3,6,7-Tetramethoxy-phenanthrene-9-carboxylic Acid Diethylamide (5e).[13c] The reaction was run according to the general procedure for 3.5 h to give the compound **5e** as a yellow solid (34 mg, 86% yield); mp 153−157 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 1.03 (t, J = 6 Hz, J = 9 Hz, 3H), 1.40 (t, J = 9 Hz, J = 6 Hz, 3H), 3.16 (m, 2H), 3.45 (m, 1H), 3.97 (s, 4H), 4.04 (s, 3H), 4.13 (s, 6H), 7.18 (s, 1H), 7.20 (s, 1H), 7.50 (s, 1H), 7.79 (s, 1H), 7.82 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.0, 14.4, 38.9, 43.1, 55.8, 55.9, 56.1, 56.1, 102.8, 103.1, 105.4, 108.5, 121.5, 122.8, 124.5, 124.8, 125.5, 131.3, 149.1, 149.5, 149.8, 170.7. HRMS-ESI [M + Na], calcd for $C_{23}H_{27}NNaO_5$ 420.1781, found 420.1782. IR (KBr): 1257, 1469, 1512, 1618, 2926, 3435.

[(2,3,6,7-Tetramethoxy-phenanthrene-9-carbonyl)-amino]-acetic Acid Methyl Ester (5f).[21] The reaction was run according to the general procedure for 5 h to give the compound **5f** as a yellow solid (33 mg, 80% yield); mp 250−254 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 3.85 (s, 3H), 4.05 (s, 6H), 4.14 (s, 6H), 4.38 (d, J = 6 Hz, 2H), 6.66 (bs, 1H), 7.23 (s, 1H), 7.76 (s, 1H), 7.79 (s, 1H), 7.82 (s, 1H), 7.93(s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 41.1, 52.1, 55.9, 56.0, 56.1, 102.5, 102.7, 106.4, 108.6, 123.1, 124.2, 124.8, 125.0, 125.6, 129.6, 149.2, 149.5, 150.5, 155.9, 169.9, 170.5. HRMS-ESI [M + Na], calcd for $C_{22}H_{23}NNaO_7$ 436.1366, found 436.1352. IR (KBr): 1472, 1514, 1658, 1754, 2363, 2936, 3375 cm^{-1}.

Pyrrolidin-1-yl-(2,3,6,7-teramethoxy-phenanthrene-9-yl)-methanone (5g). The reaction was run according to the general procedure for 5 h to give the compound **5g** as a light yellow solid (32 mg, 81% yield); mp 205−209 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 1.80−1.89 (m, 2H), 1.97−2.06 (m, 2H), 3.23 (t, 2H), 3.82 (t, 2H), 3.99 (s, 3H), 4.03 (s, 3H), 4.13 (s, 6H), 7.20(s, 1H), 7.28 (s, 1H), 7.56 (s, 1H), 7.78 (s, 1H), 7.82 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.6, 23.3, 29.7, 31.6, 55.9, 56.0, 56.1, 102.6, 103.0, 105.5, 108.5, 122.4, 124.7, 124.9, 125.4, 131.8, 149.1, 149.2, 149.4, 149.9, 169.7. HRMS-ESI, calcd [M + H] $C_{23}H_{26}NO_5$ 396.1805, found 396.1809. IR (KBr): 1467, 1511, 1616, 1717, 2930, 3480 cm^{-1}.

(S)-Methyl 1-(2,3,6,7-Tetramethoxyphenanthrene-9-carbonyl)-pyrrolidine-2-carboxylate (5h).[3b] The reaction was run according to the general procedure for 4.5 h to give the compound **5h** as a yellow solid (39 mg, 87% yield); mp 198−202 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 1.83−1.97 (m, 2H), 2.05−2.12 (m, 1H), 2.31−2.40 (m, 1H), 3.22−3.30 (m, 1H), 3.37−3.44 (m, 1H), 3.84 (s, 3H), 4.03 (s, 3H), 4.09 (s, 3H), 4.13 (s, 6H), 4.85 (dd, J = 3.0 Hz, J = 9.0 Hz, 1H), 7.21 (s, 1H), 7.58 (s, 1H), 7.70 (s, 1H), 7.79 (s, 1H), 7.81 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.1, 29.8, 48.9, 52.5, 56.1, 56.2, 56.2, 56.5, 58.6, 102.8, 102.9, 106.2, 108.7, 122.2, 122.7, 124.8, 125.0, 125.4, 131.4, 149.2, 149.6, 150.0, 170.1, 172.9. HRMS-ESI [M + Na], calcd for $C_{25}H_{27}NNaO_7$ 476.1679, found 476.1663. IR (KBr): 1467, 1514, 1625, 1742, 2954, 3462 cm^{-1}.

Piperidin-1-yl-(2,3,6,7-tetramethoxy-phenanthrene-9-yl)-methanone (5i).[3b] The reaction was run according to the general procedure for 5 h to give the compound **5i** as solid (35 mg, 85% yield); mp 200−204 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 1.71 (m, 6H), 3.22 (bs, 2H), 3.81 (s, 1H), 4.01−4.04 (m, 7H), 4.14 (s, 6H), 7.17 (s, 1H), 7.23 (s, 1H), 7.51 (s, 1H), 7.79 (s, 1H), 7.82 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.5, 26.0, 26.8, 42.8, 48.4, 55.9, 55.9, 56.0, 56.1, 102.6, 102.9, 105.5, 108.4, 121.9, 122.7, 124.5, 124.7, 125.4, 130.9, 149.0, 149.0, 149.4, 149.7, 169.7. HRMS-ESI [M + H], calcd for $C_{24}H_{28}NO_5$ 410.1961, found 410.1958. IR (KBr): 1465, 1510, 1622, 1736, 2356, 2855, 2926, 3444, 3575 cm^{-1}.

Morpholin-4-yl-(2,3,6,7-teramethoxy-phenanthrene-9-yl)-methanone (5j). The reaction was run according to the general procedure for 4.5 h to give the compound **5j** as a solid (32 mg, 78% yield); mp 202−206 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 3.29 (bs, 2H), 3.55−3.59 (m, 2H), 3.85−3.87 (m, 2H), 3.95−4.04 (m, 8H), 4.14 (s, 6H), 7.21 (s, 1H), 7.23 (s, 1H), 7.53 (s, 1H), 7.79 (s, 1H), 7.83 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 42.3, 47.7, 55.9, 56.1, 56.1, 67.1, 102.7, 103.2, 105.3, 108.5, 122.5, 122.6, 124.8, 124.8, 125.2, 129.9, 149.2, 149.3, 149.7, 150.1, 170.0. HRMS-ESI [M + Na], calcd for $C_{23}H_{25}NNaO_6$ 434.1574, found 434.1578. IR (KBr): 1469, 1512, 1626, 2927, 3430 cm^{-1}.

2,3,6,7-Tetramethoxy-phenanthrene-9-carbonitrile (5k).[13b] The reaction was run according to the general procedure for 4 h to give the compound **5k** as a yellow solid (26 mg, 80% yield); mp 264−268 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 3.98 (s, 3H), 4.02 (s, 3H), 4.07 (s, 3H), 4.08 (s, 3H), 7.14 (s, 1H), 7.47 (s, 1H), 7.67 (s, 1H), 7.69 (s, 1H), 7.95 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.2, 56.3, 56.3, 56.3, 102.7, 103.2, 105.9, 106.1, 108.8, 118.9, 124.3, 124.4, 124.7, 126.9, 132.2, 149.7, 150.3, 150.4, 151.9. HRMS-ESI [M + H], calcd for $C_{19}H_{18}NO_4$ 324.1230, found 324.1201. IR (KBr): 1474, 1512, 1619, 2210, 2358, 2927, 3451 cm^{-1}.

2,3-Dimethoxy-phenanthro[2,3-d][1,3]dioxol-6-carboxylic Acid Methyl Ester (5l).[14] The reaction was run according to the general procedure for 4.5 h to give the compound **5l** as a yellow solid (29 mg, 85% yield); mp 208−212 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 4.00 (s, 3H), 4.02 (s, 3H), 4.10 (s, 3H), 6.10 (s, 2H), 7.20 (s, 1H), 7.66 (s, 1H), 7.81 (s, 1H), 8.31 (s, 1H), 8.44 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.1, 55.9, 55.9, 100.1, 101.4, 102.5, 104.4, 108.9, 123.2, 124.5, 125.1, 126.6, 127.4, 130.0, 147.7, 147.8, 149.1, 151.1, 168.2. HRMS-ESI [M + Na], calcd for $C_{19}H_{16}NaO_6$ 363.0839, found 363.0853. IR (KBr): 1233, 1471, 1513, 1619, 1709, 2939, 3484 cm^{-1}.

2,3-Dimethoxy-9,10-dihydro-8,11-dioxa-benzo[a]anthracene-5-carboxylic Acid Methyl Ester (5m).[14] The reaction was run according to the general procedure for 5 h to give the compound **5m** as a yellow solid (28 mg, 80% yield); mp 205−209 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 4.02 (s, 3H), 4.08 (s, 3H), 4.10 (s, 3H), 4.42 (s, 4H), 7.38 (s, 1H), 7.80 (s, 1H), 7.93 (s, 1H), 8.34 (s, 1H), 8.59 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.0, 55.8, 64.4, 64.7, 102.9, 106.9, 108.9, 115.7, 122.6, 123.8, 125.1, 127.6, 130.4, 143.5, 145.9, 148.9, 149.2, 168.2. HRMS-ESI [M + Na], calcd for $C_{20}H_{18}NaO_6$ 377.1001, found 377.0988 IR (KBr): 1243, 1464, 1512, 1619, 1706, 2333, 2943, 3449, 3490 cm^{-1}.

9,10-Dihydro-1,3,8,11-tetraoxa-indeno[5,6-a]anthracene-5-carboxylic Acid Methyl Ester (5n). The reaction was run according to the general procedure for 4.5 h to give the compound **5n** as a solid (28 mg, 82% yield); mp 228−232 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 4.01 (s, 3H), 4.40 (s, 4H), 6.11 (s, 2H), 7.36 (s, 1H), 7.83 (s, 1H), 7.86 (s, 1H), 8.27 (s, 1H), 8.41 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.1, 64.4, 64.7, 100.6, 101.4, 104.6, 109.2, 115.4, 123.7, 124.8, 125.1, 126.6, 127.9, 130.1, 143.7, 145.9, 147.7, 147.9, 168.3. HRMS-ESI [M + Na], calcd for $C_{19}H_{14}NaO_6$ 361.0688, found 361.0678. IR (KBr): 1252, 1465, 1506, 1630, 1712 cm^{-1}.

2,3,4,6,7-Pentamethoxy-phenanthrene-9-carboxylic Acid Methyl Ester (5p).[7d] The reaction was run according to the general procedure for 3.5 h to give the compound **5p** as a yellow solid (14 mg, 36% yield); mp 112−116 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 4.01 (s, 3H), 4.02 (s, 3H), 4.03 (s, 3H), 4.08 (s, 3H), 4.09 (s, 3H), 4.11 (s, 3H), 7.16 (s, 1H), 8.35 (s, 1H), 8.58 (s, 1H), 9.20 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.1, 55.7, 55.9, 60.6, 61.4, 106.3, 106.4, 107.3, 120.8, 124.1, 124.4, 125.5, 127.4, 130.7, 144.8, 148.5, 148.6, 151.1, 152.1, 168.2. HRMS-ESI [M + Na], calcd for $C_{21}H_{22}NaO_7$ 409.1258, found 409.1256. IR (KBr): 1411, 1469, 1524, 1611, 1709, 2943 cm^{-1}.

Methyl 3-Fluoro-2,6,7-trimethoxyphenanthrene-9-carboxylate (5q).[8c] The reaction was run according to the general procedure for 7 h to give the compound **5q** as light green solid (22 mg, 62% yield); mp 203−207 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 4.03 (s, 3H), 4.03 (s, 3H), 4.07 (s, 3H), 4.11 (s, 3H), 7.33 (d, J = 9 Hz, 1H), 7.74 (s, 1H), 8.10 (d, J = 15 Hz, 1H), 8.39 (s, 1H), 8.57 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.3, 56.0, 56.3, 102.9, 107.0, 108.5 (d, J = 90 Hz), 111.4, 124.0, 124.2, 125.5, 126.8, 129.9, 147.4 (d, J = 51 Hz), 149.6,

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149.8, 152.4, 155.7, 168.2. HRMS-ESI [M + Na], calcd for $C_{19}H_{17}FNaO_5$ 367.0952, found 367.0954. IR (KBr): 1267, 1469, 1515, 1622, 1719, 2327, 2935, 3525 cm^{-1}.

4,4′,5,5′-Tetramethoxy-2,2′-dimethylbiphenyl (7a).[13b] The reaction was run according to the general procedure for 1 h to give the compound **7a** as a yellow solid (10 mg, 35% yield); mp 102−106 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 2.02 (s, 6H), 3.84 (s, 6H), 3.91 (s, 6H), 6.65 (s, 2H), 6.77 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.4, 56.1, 56.2, 113.1, 113.3, 128.4, 133.6, 146.8, 148.0. HRMS-ESI [M + Na], calcd for $C_{18}H_{22}NaO_4$ 325.1410, found 325.1409. IR (KBr): 1255, 1325, 1455, 1511, 2922, 3565 cm^{-1}.

1,2-Dimethoxy-4-nitrobenzene (8b).[20f] The reaction was run according to the general procedure for 35 min to give the compound **8b** as a yellow solid (9 mg, 48% yield); mp 128−132 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 3.97 (s, 3H), 3.98 (s, 3H), 6.91 (d, J = 9 Hz, 1H), 7.75 (s, 1H), 7.92 (d, J = 9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.5, 56.6, 106.7, 110.0, 117.9, 141.7, 149.1, 154.7. GC-MS (m/z): 183 [M^+]. IR (KBr): 1276, 1343, 1509, 1589, 2841, 2925.

1,2,4-Trimethoxy-5-nitrobenzene (8c).[20e] The reaction was run according to the general procedure for 10 min to give the compound **8c** as a yellow solid (10 mg, 46% yield); mp 172−176 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 3.90 (s, 3H), 3.98 (s, 6H), 6.56 (s, 1H), 7.59 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.6, 56.7, 57.4, 97.8, 109.2, 131.1, 142.6, 150.5, 154.9. GC-MS (m/z): 213 [M^+]. IR (KBr): 1270, 1349, 1515, 1586, 2840.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00507.

^1H and ^{13}C NMR spectra for all pure products; DFT calculation tables are also available (PDF)

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Notes

The authors declare no competing financial interest.

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