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Iodine-Catalyzed Functionalization of Primary Aliphatic Amines to Oxazoles, 1,4-Oxazines, and Oxazinones

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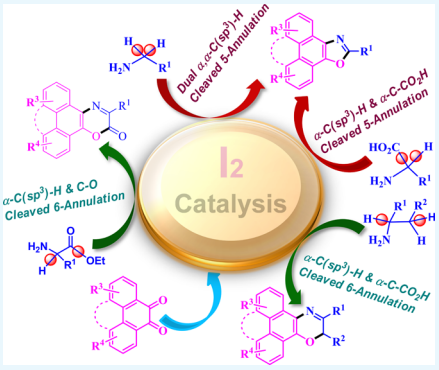
Supporting Information

ABSTRACT: Unprecedented I_2-catalyzed α,α-C(sp^3)-H, decarboxylative α-C(sp^3)-H, lactonized α-C(sp^3)-H, and α,β-C(sp^3)-H functionalized 5- and 6-annulation as well as α-C(sp^3)-H activated 6-lactonization of primary aliphatic amines are devised under aerobic conditions. The metal-free sustainable strategy was employed for the diverse construction of valuable five-and six-membered polycyclic *N,O*-heteroaromatics such as oxazoles, 1,4-oxazines, and oxazin-2-one with a rapid reaction rate and high yield. The viability of this mild nonmetallic catalysis is successfully verified through syntheses of labile chiral heterocyclic analogues. In contrast to the common practice, this method is not limited to use of prefunctionalized amines, directing groups (DGs) and/or transient DGs, metal catalysts, and traditional oxidants. The possible mechanistic pathway of the annulation reaction is investigated by control experiments and ESI-MS data collected for a reaction mixture of the ongoing reaction. The synthesized new compounds are potent organic nanobuilding blocks to achieve valuable organic nanomaterials of different sizes, shapes, and dimensions, which are under investigation for the discovery of high-tech devices of innovative organic nanoelectronics and photophysical properties.



INTRODUCTION

Aliphatic primary amines are represented in a wide range of chemical feedstock and display great biological, pharmaceutical, agricultural, materials, and synthetic applications.[1−6] Of late, functionalization of C(sp^3)-H has emerged as a promising synthetic tool.[7−10] The C(sp^3)-H activated functionalization of secondary and tertiary aliphatic amines is well investigated employing transition-metal catalysts.[11−14] However, site-selective functionalization of inactivated C(sp^3)-H bonds of primary aliphatic amines is more challenging because of their strong nucleophilic, reducing, chelation, and deactivating properties, which may hamper or deactivate catalytic power of the possible metal catalysts. Thus, use of prefunctionalized amines, directing group (DGs), and/or transient DG, their removal after the desired transformation, and intramolecular annulation are frequently exercised in the metal catalysis processes.[15−18] A limited number of approaches were devoted for the site-selective C(sp^3)-H functionalization of primary aliphatic amines, such as Zr^{IV}/Ni^{II}-catalyzed α-selective cyclization,[19,20] Pd^{II}-tuned β-arylation,[21] Pd^{II}-Ag^{I} guided γ-substitution,[18,22−25] and Pd^{II}-activated δ-arylation.[26,27] However, a metal-free C(sp^3)-H functionalization is always a more appealing strategy to be developed for minimizing the harmful impact on nature.[28−30]

So far, few nonmetallic C(sp^3)-H activation processes were developed utilizing pyridine-*N*-oxide, TBAI/TBHP, DTBP, hypervalent iodines, and iodine.[31−37] Molecular iodine has emerged as an excellent catalyst[38−43] because of its high solubility in the reaction media, easy handling, low cost, and environmentally friendly nature in comparison to heavy metals. The cyclization through C(sp^3)-H functionalization has become an indispensable synthetic strategy to deliver invaluable heterocyclic molecules.[44−50] Earlier, Schafer et al. introduced an α-C(sp^3)-H activated intramolecular 6-annulation with the $Zr(NM_2)_4$ catalyst ((i), Scheme 1).[19] We established $NiX_2 \cdot nH_2O$-catalyzed bimolecular 5-annulation ((ii), Scheme 1).[20] Chen et al. reported $Pd(OAc)_2$-$PhI(OAc)_2$-mediated intramolecular 4-annulation of protected primary aliphatic amines ((iii), Scheme 1).[26] The major limitations of these methods are the utilization of toxic heavy metal catalysts, intramolecular cyclization ((i) and (iii), Scheme 1), severe water susceptibility to catalysis ((ii), Scheme 1), high reaction temperature (145 °C), requirements of a stoichiometric oxidant [$PhI(OAc)_2$] and base in excess (2.5 equiv.), and slow reaction rates. In a continuous effort to synthesize novel polycyclic heteroaromatics for design, synthesis, and fabrication of new organic nanomaterials to discover their innovative organic electronic properties[51−54] for developing new generation devices,[55,56] herein, we disclose a direct C−O bond forming 5-annulation ((iv), Scheme 1) and 6-annulation ((v), Scheme 1) through C(sp^3)-H functionalization through nonmetallic catalysis to furnish polycyclic *N,O*-heteroaromatics.

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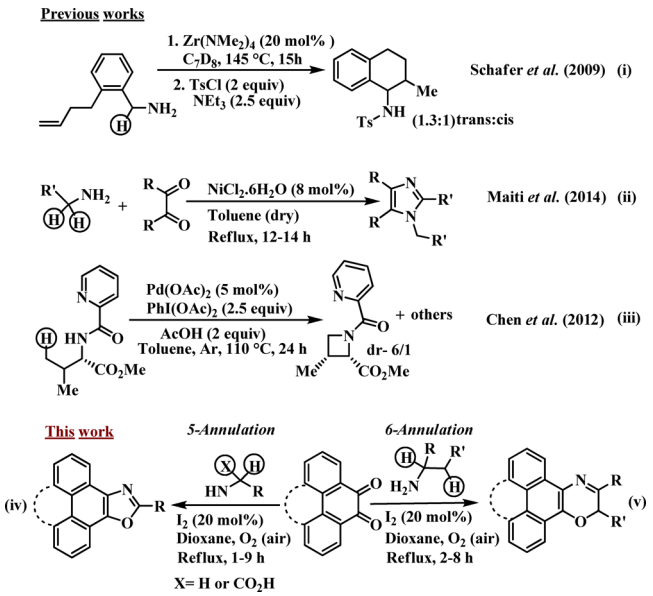
Scheme 1. Annulation with Primary Aliphatic Amine-C(sp^3)-H



1,3-Oxazoles are a fundamental class of five-membered privileged heterocyclic motifs that have profound importance in natural products, pharmaceuticals, agrochemicals, and materials.[57−62] For instance, the benzoxazole-based natural product nataxazoles (**A**, Figure 1) displayed anticancer,

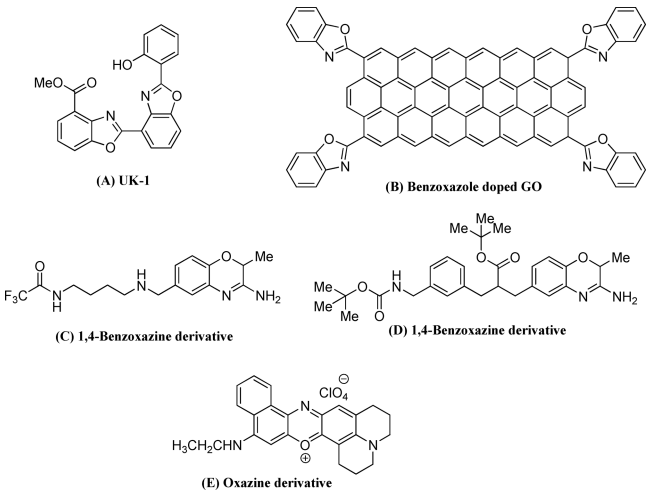


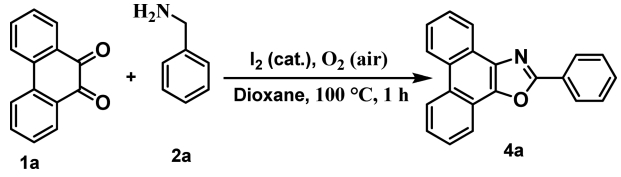
Figure 1. Important benzoxazole and oxazine analogues.

antibacterial, and cytotoxic bioactivities,[61] and the heterocycle-grafted graphene oxide organic material was used as a valuable high-performance supercapacitor electrode (**B**, Figure 1).[62] The widespread application of the heterocycles led to the development of several synthetic strategies such as Cu^{II}-catalyzed oxidative cyclization,[63] [2 + 2 + 1] annulation of alkyne and nitrile,[64] dehydrogenative annulation,[65] Pd^{II}-catalyzed annulation of amides,[66] and photocatalytic Ru catalysis.[67] The importance of metal-free synthesis was also realized using organocatalysis,[68] cyclization of aminoacids,[69] PhIO-TfOH,[70] and dehydrogenative I_2-TBHP cyclization.[71] 1,4-Oxazines have shown immense importance in biological and material sciences.[72−80] For example, oxazine derivatives (**C**, **D**, Figure 1) were employed in the treatment of neurodegenerative, inflammatory,[78] autoimmune, and cardiovascular[79] disorders, and the thin films of naphthoxazine-based materials (**E**, Figure 1) showed unique surface plasmon polarization with emission enhancement properties. Syntheses of oxazines were mainly achieved through Pd^{II} catalysis of bisvinylphosphate[81] and intramolecular cyclization with the CuI-catalyst[82] and triphenylphosphine.[83]

RESULTS AND DISCUSSION

Intending to synthesize the heterocyclic moiety through nonmetallic amine-C(sp^3)-H functionalization, at first, we focused on α-C(sp^3)-H functionalization, and for that, we have selected phenanthrenequinone (**1a**) and benzylamine (**2a**) as two reacting partners, which might yield the corresponding oxazole derivative (**4a**, Table 1). The feasibility of the 5-annulation catalysis was examined with 20 mol % triflic acid and camphor sulfonic acid (CSA) as possible catalysts (entries 1, 2, Table 1) under aerobic conditions in toluene at 100 °C (bath temperature) for 15 h. In these cases, the α,α-C(sp^3)-H-amine derived oxazole was obtained successfully in moderate yields (48, and 57%, respectively). To our delight, on the use of I_2, the reaction was rapidly completed (2 h), and the yield significantly improved (79%, entry 3). Keeping I_2 as a promising catalyst (20 mol %), different solvents such as protic EtOH (entry 4), relatively low boiling point EDC (entry 5), and highly polar DMF and DME (entries 6, 7, respectively) were screened to achieve moderate to high yields (58−78%). Gratifyingly, dioxane proved to be the best reaction medium providing the desired product (**4a**) rapidly (1 h), and **4a** was furnished almost in quantitative yield (98%, entry 8). The increase in reaction time (6 h) resulted in a decrease in yield of the desired product (95%, entry 9). In the absence of oxygen (argon atmosphere),

Table 1. Development of C(sp^3)-H-Functionalized 5-Annulation[a]



1a 2a 4a

entry	catalyst	solvent[b]	time (h)	yield (%)[c]
1	triflic acid	toluene	15	48
2	CSA	toluene	15	57
3	I_2	toluene	2	79
4[d]	I_2	EtOH	1.5	58
5	I_2	EDC	1.5	70
6	I_2	DMF	1.5	75
7	I_2	DME	1.5	78
8	I_2	dioxane	1	98
9[d]	I_2	dioxane	6	95
10[e]	I_2	dioxane	24	22
11[f]	I_2	dioxane	12	79
12[g]	I_2	dioxane	1	94
13		dioxane	24	ND[h]

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.5 mmol), catalyst (20 mol %). [b]Volume of solvent: 2 mL. [c]Yield of pure **4a** after silica gel column chromatography using ethyl acetate in petroleum ether as an eluent. [d]Under reflux (~80 °C for EtOH and ~100 °C for dioxane). [e]Under argon. [f]Catalyst (15 mol %). [g]Catalyst (25 mol %). [h]Not detected.

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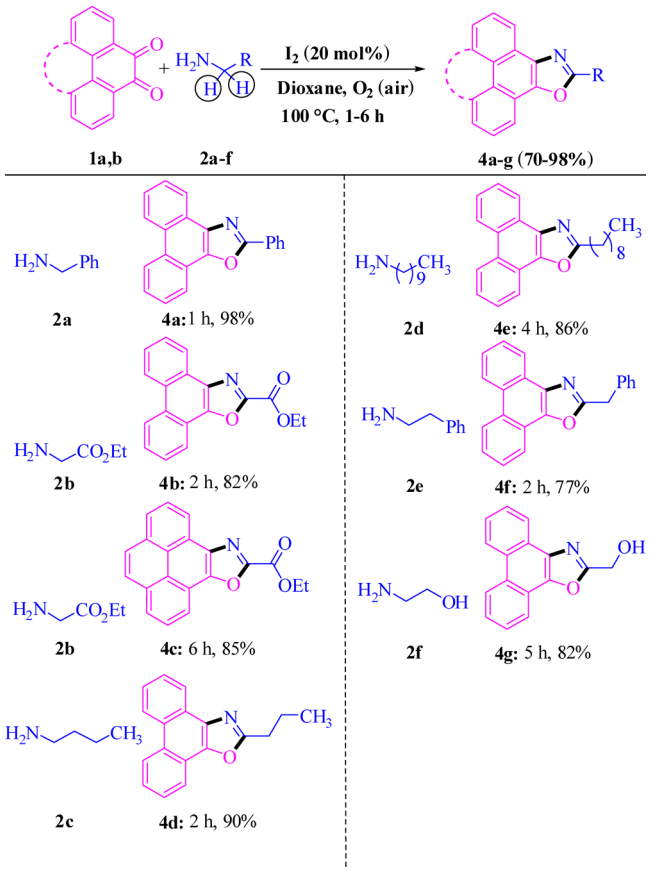
the yield drastically dropped to 22% even after continuation of the reaction for 24 h (entry 10). Surprisingly, the change of catalyst loading (entries 11, 12) led to a considerable decrease in the yield of the desired product (**4a**). The 5-annulation was unsuccessful in the absence of the catalyst under the same reaction conditions (entry 13).

The substrate scope of the dual α-C(sp^3)-H-functionalized 5-annulation was investigated using a wide range of primary aliphatic amines (**2a**–**f**, Scheme 2) and aromatic 1,2-diketones

Scheme 2. Dual α-C(sp^3)-H-Functionalized 5-Annulation to Oxazoles



(**1**) under the developed optimized reaction conditions (entry 8, Table 1). The ester-substituted primary amine (**2b**, Scheme 2) and phenanthrenequinone (**1a**) as well as pyrene-based 1,2-diketones (**1b**) smoothly transformed into the corresponding desired products (**4b**, **4c**, Scheme 2), which did not require any change in the developed reaction conditions (entry 8, Table 1).

The presence of weak hydrophobic interactions through the installation of the hydrocarbon residue is frequently needed for the generation of organic nanomaterials.[51−56] Herein, use of *n*-butyl-, decyl-, and phenethylamine (**2c**–**e**) was successful in achieving corresponding potent nanobuilding blocks (**4d**–**f**) with high yields (77−90%) in 2−4 h. Hydrogen bonding is one of the most common gluing interactions operating between the organic nanounits, and the synthesis of an oxazole derivative (**4g**) bearing the −OH group worked well with the coupling partner aminoethanol (**2f**).

After dual α-C(sp^3)-H functionalization of various primary aliphatic amines, we turned our attention for making the strategy more diverse and general through replacement of one of the α-C(sp^3)-H by $-CO_2H$ so that inexpensive and easily available amino acids may be employed as the key substrate for decarboxylative 5-annulation. To our delight, the attempted reaction between phenyl glycine (**3a**) and phenanthrenequinone (**1a**) rapidly (3 h) furnished the desired product (**4a**, Scheme 3) under similar reaction conditions (entry 8, Table 1) with high yield (80%). Many aliphatic and aromatic residues, phenolic −OH, alcoholic −OH, −SMe, and chirality were well tolerated to produce a variety of polycyclic oxazoles in high yield, and reaction rates were faster on use of a wide range of amino acids (**3a**–**k**). In a competitive experiment of cleaving C(sp^3)-H versus $-CO_2H$ in glycine (**3k**) possessing two α-C(sp^3)-H groups as well as one α-CO_2H group furnished oxazole derivative **4p** through a decarboxylation process exclusively, rather than formation of the $-CO_2H$ group tethered oxazole derivative (**4q**) by functionalization of consecutive two C(sp^3)-H. Thus, C-CO_2H breaking is more favorable under the catalytic conditions with respect to C(sp^3)-H cleavage. The structure of compound **4j** is established by single-crystal X-ray diffraction analysis.[84] Further, 2,7-dibromo-phenanthrene-9,10-dione under optimized reaction conditions (entry 8, Table 1) led to exclusive construction of corresponding oxazole derivatives **4r** and **4s** through the decarboxylation process.

Next, we envisioned functionalization of both α-C(sp^3)-H and β-C(sp^3)-H under the reaction conditions leading to the construction of valuable six-annulated polycyclic oxazine derivatives (Scheme 4). To verify that we have employed primary amines (**5**) possessing a β-C(sp^3)-H, which was obtained by just replacing the α-H with an alkyl group of **2** (Scheme 4). To our surprise, six-annulated desired oxazine derivative **6a** (Scheme 4) was rapidly (2 h) formed upon treatment of 1-phenylethylamine (**5a**) with 9,10-phenanthrenequinone (**1a**) under the catalytic conditions in high yield (80%). Herein, phenyl (**6a**, **6b**, **6e**, **6g**, **6i**) and activated aromatic residues such as naphthyl (**6c**), 4-tolyl (**6d**), 4-hydroxyphenyl (**6h**), and methyl [γ-C(sp^3)-H, **6e**) as well as the ester functionality (**6g**, **6h**) are well tolerated to furnish selectively polyaromatic oxazine systems (**6a**–**i**) in 2−8 h with high yields (68−81%). In the presence of the cyclohexyl group, the desired product tautomerized to **6f** through migration of a double bond. Probably, high steric and electronic repulsion appeared due to the presence of axial and equatorial C−H bonds (cyclohexyl residue) in the close vicinity of the C=N bond and lone pair in **6f'**, which led to release of unwanted repulsive forces to obtain thermodynamically stable and fully aromatic 3-cyclohexyl-4*H*-phenanthro[9,10-*b*][1,4]oxazines (**6f**).

To understand the reactivity and versatility of the C(sp^3)-H-functionalized annulation strategy, we have replaced the R group (**5**, Scheme 4) by a $-CO_2Et$ group in the aliphatic amines (**7a**–**c**, Scheme 5). To our surprise, a 6-annulation reaction occurred under the reaction conditions through α-C(sp^3)-H functionalization of the primary aliphatic amines as well as an O−C coupling with the ester group involving the release of −OEt to afford valuable polynuclearoxazine-2-ones (**8a**–**c**). The molecular-iodine-catalyzed synthesis of 3-alkyl-2*H*-phenanthro[9,10-*b*][1,4]oxazin-2-one (**8**) was rapid (2−4.5 h) and high yielding (72−77%). Formation of all new oxazoles, oxazines, oxazine-2-ones, and analogues was confirmed by spectroscopic analyses, recorded melting points (Supporting Information), and also single-crystal X-ray diffraction analyses of **4j**[84] and **6a**.[85] It is worthy to note that, although most of the reported metal catalysts for C−H-activated functionalization reactions are moisture-sensitive, herein, the catalyst I_2 efficiently performed

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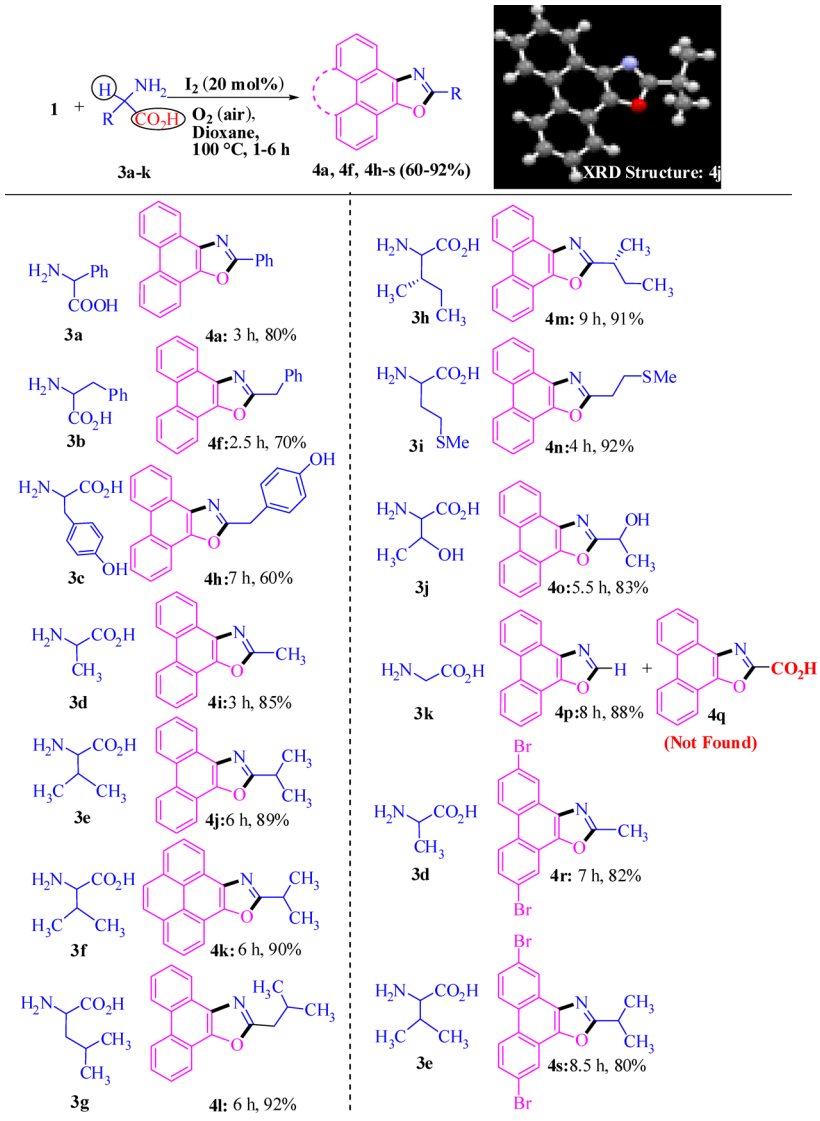
Scheme 3. Decarboxylative α-C(sp^3)-H-Functionalized 5-Annulation



the diverse C−H-functionalized annulation catalysis even in the presence of water.

Out of several possibilities,[86−91] the current catalysis is expected to pass through the initial formation of a monoimine **IA** and **IB**, which may proceed through activation of an α-C(sp^3)-H subsequent formation of a five-membered transition state (**II**) with the catalyst (I_2) to intermediates **IIIA** and **IIIB** (Scheme 6). The formation of intermediates **IA** and **IB**, as well as **IIIA** and **IIIB**, was detected in the mass spectral analyses of the ongoing reaction (Supporting Information). A second α-C(sp^3)-H activation of **IIIA** with the close vicinity of the iodine substituent possessing lone pairs and larger size (**IV**) may release HI to furnish the dual α-C(sp^3)-H-functionalized 5-annulated product (**4a**, path a). On the other hand, decarboxylative α-C(sp^3)-H 5-annulation of **IIIB** is possibly passing through a six-membered transition state (**V**) to **4i** (path b). In both cases, the generated HI is expected to oxidize immediately by aerial O_2 to regenerate I_2 for the next catalytic cycle. The role of inexpensive O_2 as an oxidant was verified (entry 10, Table 1) by performing the reaction in the absence of O_2 (argon atmosphere) where the yield of **4a** drastically reduced (22%) in the presence of the catalyst. Herein, decarboxylation through a six-membered transition state (**V**, path b, Scheme 6) is energetically more favorable than the second α-C(sp^3)-H activation by a four-membered one (**IV**, path a), which was reflected in the 5-annulation of glycine to produce exclusively **4p** instead of **4q**.

The 6-annulation is expected to proceed in a similar fashion through the initial formation of a monoimine **VI** (Scheme 7), which may proceed via an iodine-mediated activation of an α-C(sp^3)-H through an eight-membered transition state (**VII**). Removal of HI leads to the generation of the putative intermediate **VIII**, which further tautomerizes to transition state **IX**. It undergoes O−C coupled cyclization, oxidative C=N formation (**X**) to desired product **6**, and the regeneration of molecular iodine for the next catalytic cycle.

Next, we moved to investigate morphological characteristics of some final compounds through fabrication by the spin coating method. Thus, we choose three representative compounds, namely, **4n**, **6b**, and **6h**, carrying strong aromatic electron clouds, polar functional groups, phenolic −OH, van der Waals interaction, and $\pi-\pi$ stacking attractive forces, which might operate in between the small organic molecules (nanobuilding block) to fabricate the desired organic nanomaterials through the spin coating, deep coating, and Langmuir−Blodget

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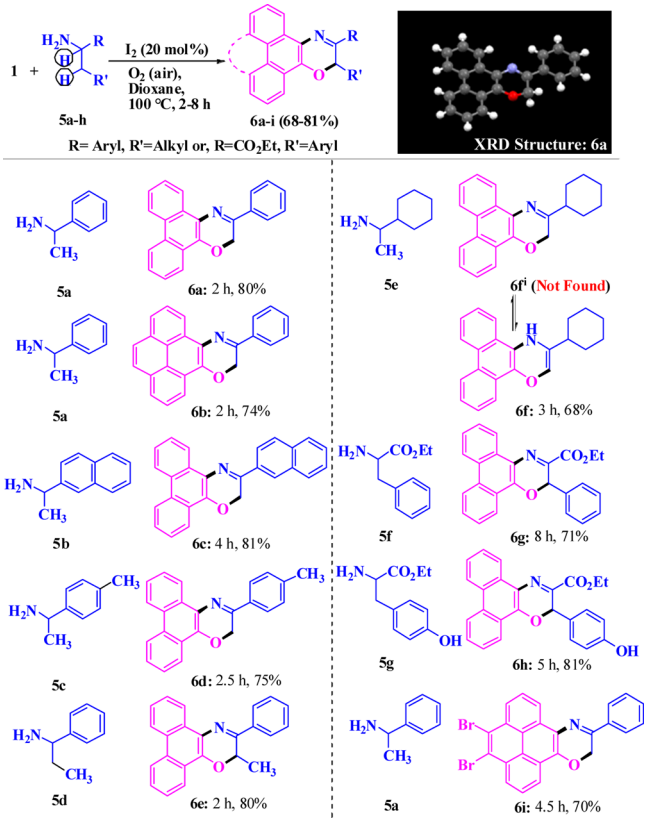
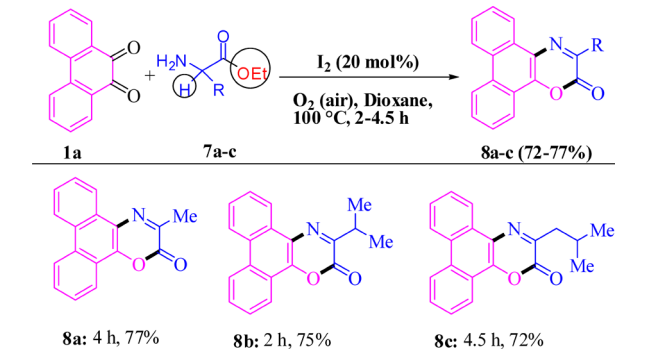
Scheme 4. α,β-C(sp^3)-H-Functionalized 6-Annulation to Oxazines



Scheme 5. α-C(sp^3)-H-Functionalized Lactonization to Oxazine-2-ones

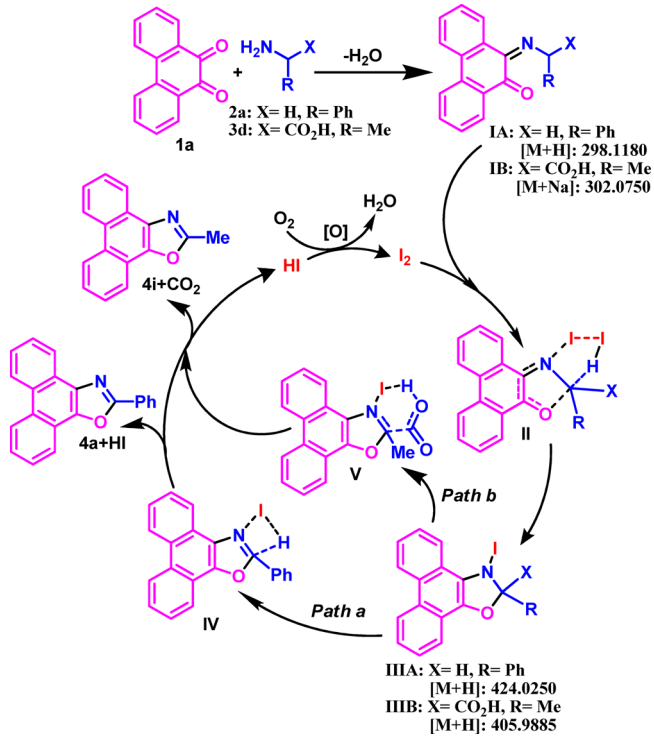


techniques. The SEM images of the spin-coated materials displayed nanomorphologies such as the existence of the rod-like structure of compound **4n** (Figure 2), the sheet-like architecture of compound **6b** (Figure 3), and the flower-like nanostructure of compound **6h** (Figure 4). We are now investigating the development of their innovative optical, nanoelectronics, and $I-V$ characteristics for potential application in the valuable solar cell, supercapacitor, and nonvolatile memory devices.

CONCLUSIONS

In conclusion, we have demonstrated a general nonmetallic synthetic strategy for diverse C(sp^3)-H functionalization of unprotected primary aliphatic amines with an I_2 catalyst to intermolecular 5- and 6-annulation. A variety of unsubstituted, substituted, acid, ester, alcohol, and thiol derivatives of primary

Scheme 6. Mechanistic Hypothesis for I_2-Catalyzed 5-Annulation



amines and their chiral analogues were successfully coupled to 1,2-diketone analogues to obtain a series of new polyaromaticoxazoles, 1,4-oxazines, oxazin-2-one, and chiral heterocycles with rapid reaction rates and high yields. This newly established I_2-catalyzed α,α-C(sp^3)-H, decarboxylative α-C(sp^3)-H, lactonized α-C(sp^3)-H, and α,β-C(sp^3)-H-functionalized 5- and 6-annulation as well as α-C(sp^3)-H-activated 6-lactonization of primary aliphatic amines will open up another avenue for developing a metal-free sustainable strategy for simple, rapid, and diverse construction of functional-group-decorated heteroaromatics, which will find considerable application in organic synthesis, medicinal chemistry, materials science, and organic nanoelectronics for smart devices.

EXPERIMENTAL SECTION

General Methods. All reagents were purchased from commercial suppliers and used without further purification. Petroleum ether used in our experiments was in the boiling range of 60−80 °C. Column chromatography was performed on silica gel (100−200 and 230−400 mesh). Reported melting points are uncorrected. Prior to melting point determination, recrystallization was carried out; for compounds whose NMR spectra were taken in $CDCl_3$, recrystallization was carried out in $CDCl_3$, and for those whose NMR spectra were taken in DMSO-d_6, recrystallization was carried out in an ethyl acetate/hexane mixture. ^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature in $CDCl_3$/DMSO-d_6 solution. Chemical shifts are reported in ppm (δ) relative to internal reference tetramethylsilane. Coupling constants are quoted in Hz (J). Proton multiplicities are represented as s (singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet), and m (multiplet). Splitting patterns that could not be interpreted are designated as multiplet (m). Infrared spectra were recorded on an FT-IR spectrometer in thin films. HR-MS data were

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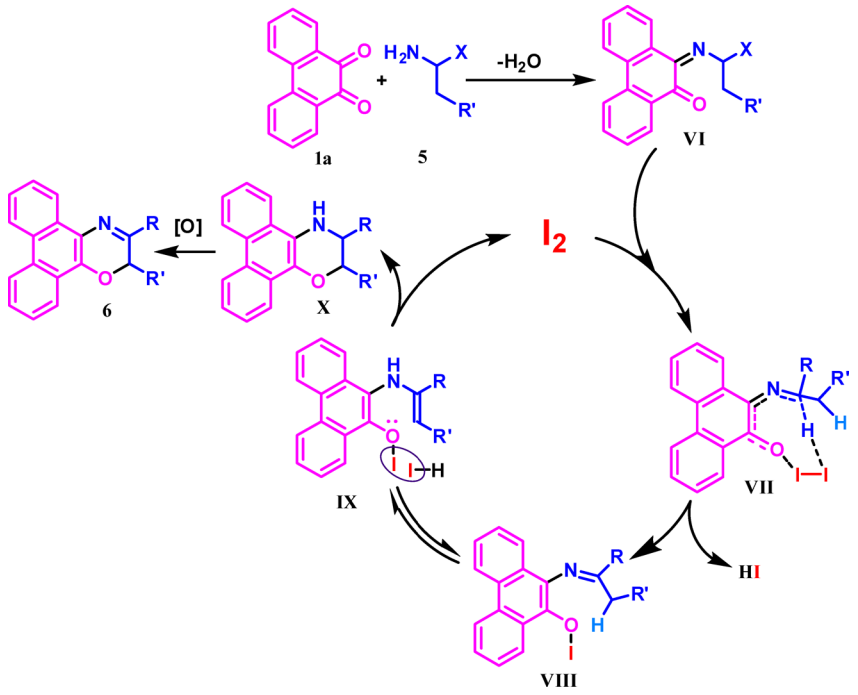
Scheme 7. Mechanistic Hypothesis for I_2-Catalyzed 6-Annulation



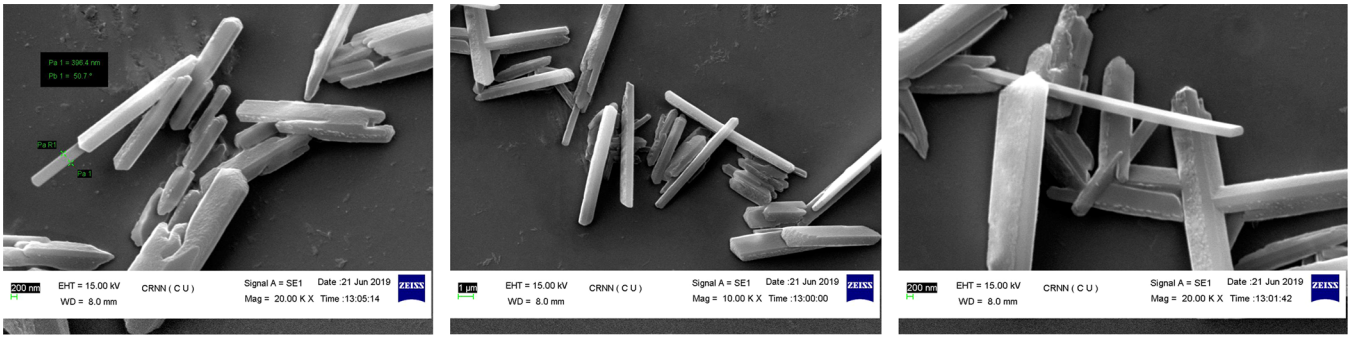


Figure 2. Rod-like nanostructures of **4n** observed in SEM imaging.

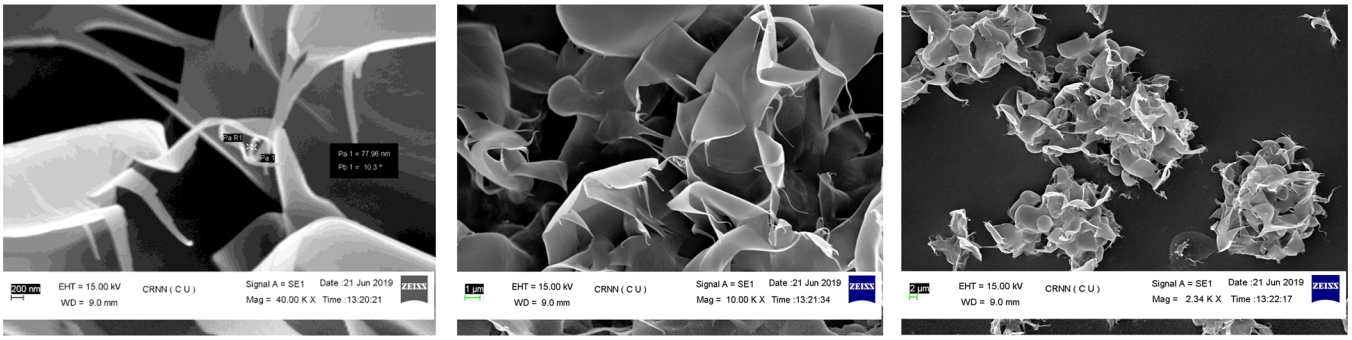


Figure 3. Sheet-like nanostructures of **6b** observed in SEM imaging.

acquired by electron spray ionization on a Q-tof-micro quadruple mass spectrophotometer. X-ray crystallographic data were taken using an X-ray diffractometry instrument.

General Procedure for the Synthesis of Oxazoles 4a−s (GP-I). To a mixture of phenanthrenequinone (**1**, 1.0 mmol) and amine (**2a−f**)/amino acid (**3a−k**, 1.1 mmol, 1.1 equiv.) in dioxane (2 mL), I_2 (20 mol %, 50 mg) was added, and the solution was refluxed under air to complete the reaction, which was monitored by TLC. Dioxane was removed from the reaction mixture, and the residue was purified by silica gel column chromatography using a suitable eluent to afford the desired product.

*2-Phenylphenanthro[9,10-d]oxazole (**4a**).*[92−94] The compound was prepared following **GP-I** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and benzylamine (1.1 mmol, 0.12 mL). Purification by column chromatography (8%

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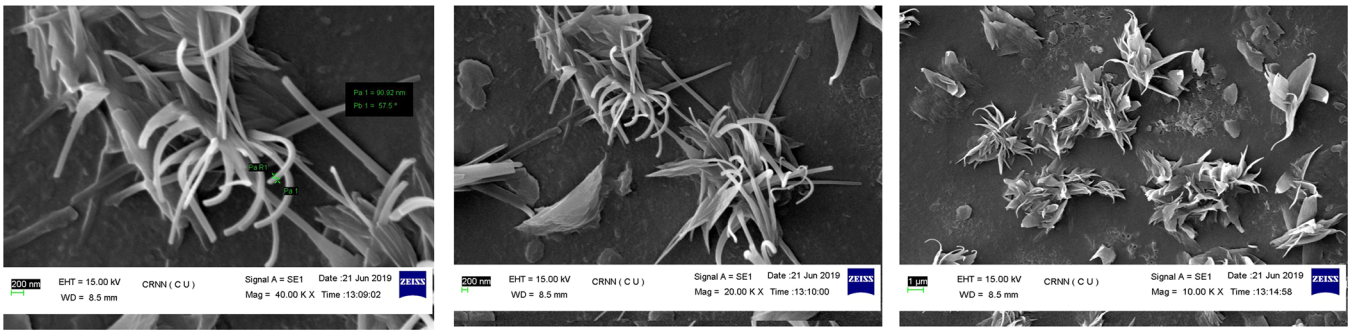

Figure 4. Flower-like nanostructures of **6h** observed in SEM imaging.

EtOAc-pet ether) afforded the title compound as a white solid (289 mg, 0.98 mmol, 98% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54−7.59 (m, 3H), 7.61−7.75 (m, 4H), 8.27−8.37 (m, 3H), 8.59−8.66 (m, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 120.7, 120.9, 122.8, 123.3, 123.6, 126.0, 126.1, 126.2, 127.0, 127.1, 127.3, 127.5, 128.8, 129.1, 130.8, 135.4, 144.7, 162.0; FT-IR (KBr, cm^{-1}): 708.3, 755.3, 1058.9, 1235.1, 1450.9, 1480.0, 1548.4, 2853.2, 2923.7.

*Ethyl Phenanthro[9,10-d]oxazole-2-carboxylate (**4b**).* The compound was prepared following **GP-I** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and ethyl glycinate (1.1 mmol, 112 mg). Purification by column chromatography (8% EtOAc-pet ether) afforded the title compound as a yellow solid (239 mg, 0.82 mmol, 82% yield). mp 168−170 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.50 (t, J = 7.2 Hz, 3H), 4.58 (q, J_1 = 6.9 Hz, J_2 = 15 Hz, 2H), 7.49−7.68 (m, 4H), 8.23−8.26 (m, 1H), 8.53−8.59 (m, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 14.3, 29.7, 63.0, 120.3, 121.7, 123.1, 123.4, 123.7, 125.6, 126.9, 127.5, 127.8, 127.9, 129.2, 130.6, 134.7, 146.3, 151.8, 156.3; FT-IR (KBr, cm^{-1}): 722.9, 755.4, 1148.0, 1278.8, 1451.1, 1534.4, 1733.4, 2857.4, 2925.2; HRMS (ESI-TOF) m/z calcd for $C_{18}H_{14}NO_3$ $[M + H]^+$: 292.0974, found 292.0971.

*Ethyl Pyreno[4,5-d]oxazole-10-carboxylate (**4c**).* The compound was prepared following **GP-I** employing pyrene-4,5-dione (1.0 mmol, 232 mg) and ethyl glycinate (1.1 mmol, 112 mg). Purification by column chromatography (3% EtOAc-pet ether) afforded the title compound as a reddish orange solid (268 mg, 0.85 mmol, 85% yield). mp 146−148 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.54 (t, J = 7.2 Hz, 3H), 4.63 (q, J_1 = 12 Hz, J_2 = 7.2 Hz, 2H), 7.97−8.13 (m, 4H), 8.18 (d, J = 6.9 Hz, 2H), 8.53 (d, J = 7.5 Hz, 1H), 8.81 (d, J = 7.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 14.3, 63.1, 119.0, 119.5, 120.6, 123.5, 124.4, 124.7, 126.1, 126.4, 126.7, 126.8, 127.3, 128.2, 131.7, 131.8, 135.5, 147.1, 152.1, 156.3; FT-IR (KBr, cm^{-1}): 668.9, 1215.8, 1732.5, 2927.6, 3019.7; HRMS (ESI-TOF) m/z calcd for $C_{20}H_{14}NO_3$ $[M + H]^+$: 316.0974, found 316.0977.

*2-Propylphenanthro[9,10-d]oxazole (**4d**).*[92−94] The compound was prepared following **GP-I** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and butyl amine (1.1 mmol, 0.11 mL). Purification by column chromatography (2% EtOAc-pet ether) afforded the title compound as a yellow solid (235 mg, 0.90 mmol, 90% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.02 (t, J = 6.9 Hz, 3H), 1.86−1.99 (m, 2H), 2.97 (t, J = 7.5 Hz, 2H), 7.50−7.64 (m, 4H) 8.08−8.11 (m, 1H), 8.42 (d, J = 7.8 Hz, 1H), 8.58 (q, J_1 = 4.5 Hz, J_2 = 7.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 13.9, 21.0, 30.8, 120.6, 121.1, 122.7, 123.4, 123.7, 128.8, 126.06, 126.13, 127.1, 127.3, 128.7, 128.9, 134.2, 144.7, 166.1.

*2-Nonylphenanthro[9,10-d]oxazole (**4e**).* The compound was prepared following **GP-I** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and decyl amine (1.1 mmol, 0.22 mL). Purification by column chromatography (2% EtOAc-pet ether) afforded the title compound as a brown solid (297 mg, 0.86 mmol, 86% yield). mp 52−54 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.84−0.89 (m, 3H), 1.34−1.47 (m, 12H), 1.88−1.96 (m, 2H), 3.02 (t, J = 7.2 Hz, 2H), 7.53−7.70 (m, 4H), 7.13 (d, J = 7.8 Hz, 1H), 8.48 (d. J = 7.8 Hz, 1H), 8.58−8.61 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 14.0, 22.6, 27.3, 28.8, 29.2, 29.3, 31.8, 120.4, 120.9, 122.5, 123.2, 123.5, 125.6, 125.8, 126.0, 127.0, 127.1, 128.5, 128.7, 134.1, 144.5, 166.0; FT-IR (KBr, cm^{-1}): 754.9, 1215.6, 1346.8, 1560.2, 1579.6, 2855.1, 2927.0; HRMS (ESI-TOF) m/z calcd for $C_{24}H_{28}NO$ $[M + H]^+$: 346.2171, found 346.2166.

*2-Benzylphenanthro[9,10-d]oxazole (**4f**).* The compound was prepared following **GP-I** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and phenethylamine (1.1 mmol, 0.14 mL). Purification by column chromatography (3% EtOAc-pet ether) afforded the title compound as a yellow solid (238 mg, 0.77 mmol, 77% yield). mp 98−100 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.41 (s, 2H), 7.25−7.35 (m, 3H), 7.43 (d, J = 7.2 Hz, 2H), 7.61−7.71 (m, 4H), 8.14−8.17 (m, 1H), 8.49 (d, J = 7.8 Hz, 1H), 8.66−8.70 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 35.2, 120.6, 120.9, 122.6, 123.3, 123.5, 125.8, 126.0, 126.1, 127.1, 127.2, 128.6, 128.7, 128.8, 134.2, 135.3, 145.1, 163.7; FT-IR (KBr, cm^{-1}): 711.3, 760.3, 1111.9, 1235.1, 1450.9, 1480.0, 1556.4, 2859.3, 2925.9; HRMS (ESI-TOF) m/z calcd for $C_{22}H_{16}NO$ $[M + H]^+$: 310.1232, found 310.1236.

*2-(Phenanthro[9,10-d]oxazol-2-yl)ethanol (**4g**).* The compound was prepared following **GP-I** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and ethanolamine (1.1 mmol, 0.07 mL). Purification by column chromatography (20% EtOAc-pet ether) afforded the title compound as a yellow solid (204 mg, 0.82 mmol, 82% yield). mp 174−176 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.99 (s, 2H), 6.14 (brs, 1H), 7.76−7.98 (m, 4H), 8.22−8.28 (m, 1H), 8.63 (d, 1H, J = 10.8 Hz), 9.25 (t, 2H, J = 9 Hz); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 56.1, 119.8, 119.9, 121.6, 123.6, 123.8, 125.0, 126.0, 126.4, 127.4, 127.5, 127.8, 128.1, 133.0, 143.7, 164.5; FT-IR (KBr, cm^{-1}): 669.1, 756.6, 1215.9, 1408.8, 1456.3, 1634.2, 1727.9, 2927.1, 3019.8; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{12}NO_2$ $[M + H]^+$: 250.0868, found 250.0871.

*4-(Phenanthro[9,10-d]oxazol-2-yl-methyl)phenol (**4h**).* The compound was prepared following **GP-I** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and tyrosine (1.1 mmol, 200 mg). Purification by column chromatography (20% EtOAc-pet ether) afforded the title compound as a yellow solid (195 mg, 0.60 mmol, 60% yield). mp 200−202 °C; ^{1}H NMR

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(300 MHz, DMSO-d_6): δ 4.29 (s, 2H), 6.72 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 7.60−7.75 (m, 4H), 8.03−8.06 (m, 1H), 8.28−8.31 (m, 1H), 8.79 (t, J = 6.6 Hz, 2H), 9.37 (s, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 33.0, 115.0, 119.7, 119.8, 121.7, 123.5, 123.7, 124.9, 125.1, 125.8, 126.1, 127.2, 127.3, 127.7, 127.8, 129.5, 133.2, 143.6, 156.0, 164.4; FT-IR (KBr, cm^{-1}): 723.7, 756.2, 809.8, 1256.7, 1450.9, 1518.7, 1594.6, 2924.0, 3399.9; HRMS (ESI-TOF) m/z calcd for $C_{22}H_{16}NO_2$ $[M + H]^+$: 326.1181, found 326.1178.

*2-Methylphenanthro[9,10-d]oxazole (**4i**).*[92−94] The compound was prepared following **GP-I** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and alanine (1.1 mmol, 98 mg). Purification by column chromatography (3% EtOAc-pet ether) afforded the title compound as a light green solid (198 mg, 0.85 mmol, 85% yield). mp 128−130 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 2.72 (s, 3H), 7.48−7.68 (m, 4H), 8.07−8.09 (m, 1H), 8.41 (d, J = 7.8 Hz, 1H), 8.60 (d, J = 7.5 Hz, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 14.5, 120.4, 120.9, 122.4, 123.2, 123.5, 125.7, 125.85, 125.92, 127.0, 127.2, 128.5, 128.7, 134.2, 144.7, 162.3; FT-IR (KBr, cm^{-1}): 723.1, 753.9, 1032.8, 1231.8, 1451.8, 1587.7, 1737.7, 2853.7, 2924.4.

*2-Isopropylphenanthro[9,10-d]oxazole (**4j**).* The compound was prepared following **GP-I** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and valine (1.1 mmol, 129 mg). Purification by column chromatography (2% EtOAc-pet ether) afforded the title compound as a yellow solid (232 mg, 0.89 mmol, 89% yield). mp 76−78 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 0.74 (s, J = 6.9 Hz, 6H), 2.54−2.63 (m, 1H), 6.73−6.89 (m, 4H), 7.36 (d, J = 7.5 Hz, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.80−7.83 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 20.7, 29.1, 120.5, 121.0, 122.6, 123.3, 123.5, 125.7, 125.9, 126.1, 127.0, 127.2, 128.5, 128.7, 134.0, 144.4; FT-IR (KBr, cm^{-1}): 722.7, 730.7, 755.7, 1033.7, 1078.8, 1350.7, 1450.3, 1558.0, 1578.4, 2928.9, 2962.1; HRMS (ESI-TOF) m/z calcd for $C_{18}H_{16}NO$ $[M + H]^+$: 262.1232, found 262.1229.

*10-Isopropylpyreno[4,5-d]oxazole (**4k**).* The compound was prepared following **GP-I** employing pyrene-4,5-dione (1.0 mmol, 232 mg) and valine (1.1 mmol, 129 mg). Purification by column chromatography (2% EtOAc-pet ether) afforded the title compound as a yellow solid (256 mg, 0.90 mmol, 90% yield). mp 96−98 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 1.61 (d, J = 6.9 Hz, 6H), 3.43−3.52 (m, 1H), 7.95−8.13 (m, 6H), 8.38 (d, J = 7.5 Hz, 1H); 8.72 (d, J = 7.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 20.8, 29.3, 117.4, 120.0, 120.3, 122.9, 124.8, 125.2, 126.0, 126.3, 127.3, 128.0, 131.7, 131.8, 145.2, 170.4; FT-IR (KBr, cm^{-1}): 716.1, 826.2, 1178.6, 1303.8, 1564.2, 1603.8, 1726.9, 2925.6, 2969.4; HRMS (ESI-TOF) m/z calcd For $C_{21}H_{16}NO$ $[M + H]^+$: 286.1232, found 286.1227.

*2-Isobutylphenanthro[9,10-d]oxazole (**4l**).* The compound was prepared following **GP-I** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and leucine (1.1 mmol, 144 mg). Purification by column chromatography (2% EtOAc-pet ether) afforded the title compound as a light brown solid (253 mg, 0.92 mmol, 92% yield). mp 68−70 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 1.03 (d, J = 6.6 Hz, 6H), 2.29−2.38 (m, 1H), 2.90 (d, J = 7.2 Hz, 2H), 7.54−7.67 (m, 4H), 8.13−8.16 (m, 1H), 8.46 (d, J = 7.8 Hz, 1H), 8.60−8.65 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 22.5, 27.9, 37.8, 120.6, 121.1, 122.7, 123.4, 123.6, 125.8, 126.05, 126.14, 127.1, 127.3, 128.6, 128.9, 134.3, 144.7, 165.5; FT-IR (KBr, cm^{-1}): 724.3, 751.8, 1051.7, 1323.7, 1450.5, 1556.5, 1578.9, 2870.9, 2926.6, 2959.9; HRMS (ESI-TOF) m/z calcd for $C_{19}H_{18}NO$ $[M + H]^+$: 276.1388, found 276.1393.

*(R)-2-sec-Butylphenanthro[9,10-d]oxazole (**4m**).* The compound was prepared following **GP-I** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and isoleucine (1.1 mmol, 144 mg). Purification by column chromatography (2% EtOAc-pet ether) afforded the title compound as yellow oil (250 mg, 0.91 mmol, 91% yield). $[\alpha]_D^{20}$: +1.46° (c 2.667, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 0.95 (t, J = 7.5 Hz, 3H), 1.47 (d, J = 6.9 Hz, 3H), 1.74−1.83(m, 1H), 1.94−2.10 (m, 1H), 3.13−3.20 (m, 1H), 7.56−7.67 (m, 4H), 8.16−8.19 (m, 1H), 8.45−8.48 (m, 1H), 8.64−8.69 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 11.8, 18.3, 28.4, 36.1, 120.6, 121.1, 122.7, 123.3, 123.6, 125.7, 125.9, 126.2, 126.5, 127.0, 127.2, 128.5, 128.8, 134.1, 144.5, 169.4; FT-IR (KBr, cm^{-1}): 724.1, 754.9, 1053.2, 1324.3, 1452.1, 1521.4, 1578.5, 1618.7, 2932.3, 2967.9; HRMS (ESI-TOF) m/z calcd for $C_{19}H_{18}NO$ $[M + H]^+$: 276.1388, found 276.1383.

*2-(2-(Methylthio)ethyl)phenanthro[9,10-d]oxazole (**4n**).* The compound was prepared following **GP-I** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and methionine (1.1 mmol, 164 mg). Purification by column chromatography (3% EtOAc-pet ether) afforded the title compound as a deep yellow solid (270 mg, 0.92 mmol, 92% yield). mp 82−84 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 2.17 (s, 3H), 3.07 (t, J = 7.5 Hz, 2H), 3.33 (s, J = 7.5 Hz, 2H), 7.57−7.69 (m, 4H), 8.11 (d, J = 7.5 Hz, 1H), 8.44 (d, J = 7.8 Hz, 1H), 8.60 (t, J = 4.1 Hz, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 15.6, 29.3, 31.3, 120.6, 120.9, 122.6, 123.4, 123.6, 125.9, 126.0, 126.2, 127.2, 127.3, 128.7, 128.9, 134.2, 144.8, 163.9; FT-IR (KBr, cm^{-1}): 726.6, 763.0, 1054.3, 1321.7, 1432.1, 1558.7, 1576.7, 2853.3, 2922.5; HRMS (ESI-TOF) m/z calcd for $C_{18}H_{16}NOS$ $[M + H]^+$: 294.0953, found 294.0957.

*1-(Phenanthro[9,10-d]oxazol-2-yl)ethanol (**4o**).* The compound was prepared following **GP-I** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and threonine (1.1 mmol, 131 mg). Purification by column chromatography (10% EtOAc-pet ether) afforded the title compound as a yellow solid (218 mg, 0.83 mmol, 83% yield). mp 178−180 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 1.61 (dd, J_1 = 1.8 Hz, J_2 = 1.8 Hz, 3H), 5.04−5.10 (m, 1H), 6.00 (brs, 1H), 7.66−7.78 (m, 4H), 8.19 (d, J = 7.5 Hz, 1H), 8.36 (d, J = 7.8 Hz, 1H), 8.89 (t, J = 8.1 Hz, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 21.0, 62.1, 119.8, 121.6, 123.6, 123.8, 125.0, 125.8, 126.3, 127.3, 127.4, 127.8, 128.0, 132.8, 143.4, 167.1; FT-IR (KBr, cm^{-1}): 715.8, 1245.9, 1426.8, 1501.3, 1654.2, 1729.5, 2928.7, 3087.5, 3325.6; HRMS (ESI-TOF) m/z calcd for $C_{17}H_{14}NO_2$ $[M + H]^+$: 264.1025, found 264.1030.

*Phenanthro[9,10-d]oxazole (**4p**).*[92−94] The compound was prepared following **GP-I** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and glycine (1.1 mmol, 83 mg). Purification by column chromatography (1% EtOAc-pet ether) afforded the title compound as a yellow solid (193 mg, 0.88 mmol, 88% yield). ^1H NMR (300 MHz, $CDCl_3$): δ 7.59−7.70 (m, 4H), 8.12−8.18 (m, 2H), 8.47 (d, J = 7.5 Hz, 1H), 8.59 (d, J = 6.3 Hz, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 120.85, 120.93, 122.7, 123.4, 123.6, 126.0, 126.2, 127.2, 128.9, 129.4, 133.4, 144.5, 151.2.

*5,10-Dibromo-2-methylphenanthro[9,10-d]oxazole (**4r**).* The compound was prepared following **GP-I** employing 1,6-dibromo-9,10-phenanthrenequinone (1.0 mmol, 366 mg) and alanine (1.1 mmol, 98 mg). Purification by column chromatography (2% EtOAc-pet ether) afforded the title compound as a light yellow solid (320 mg, 0.82 mmol, 82% yield). mp 150−152 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 2.62 (s, 3H), 6.89 (d, 1H, J = 2.4 Hz), 6.95−6.98 (m, 1H), 7.17−7.28 (m, 1H), 7.27 (d, 1H, J = 8.7 Hz), 7.46−7.53 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz,

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$CDCl_3$): δ 15.1, 119.8, 119.9, 121.4, 121.8, 122.8, 128.9, 130.8, 131.4, 131.8, 135.0, 136.5, 137.6, 139.6, 140.2, 141.1, 164.0; FT-IR (KBr, cm^{-1}): 744.7, 756.8, 1046.7, 1228.8, 1399.8, 1601.7, 1775.6, 2826.8, 2970.5; HRMS (ESI-TOF) *m/z* calcd for $C_{16}H_{10}Br_2NO$ $[M + H]^+$: 389.9129, found 389.9133 (one of the major peaks).

*5,10-Dibromo-2-isopropylphenanthro[9,10-d]oxazole (**4s**).* The compound was prepared following **GP-I** employing 1,6-dibromo-9,10-phenanthrenequinone (1.0 mmol, 366 mg) and valine (1.1 mmol, 129 mg). Purification by column chromatography (1% EtOAc-pet ether) afforded the title compound as a light yellow solid (335 mg, 0.80 mmol, 80% yield). mp 118−120 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 1.25 (d, *J* = 6 Hz, 6H), 2.85−2.94 (m, 1H), 6.98−7.04 (m, 1H), 7.07−7.11 (m, 1H), 7.32−7.41 (m, 1H), 7.53−7.66 (m, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 21.1, 30.2, 119.1, 119.8, 120.6, 122.3, 123.0, 125.5, 128.5, 130.3, 133.7, 138.7, 140.1, 140.6; FT-IR (KBr, cm^{-1}): 701.7, 748.7, 801.7, 1051.7, 1101.9, 1299.7, 1508.7, 1602.0, 1659.4, 2889.7, 2971.2; HRMS (ESI-TOF) *m/z* calcd for $C_{18}H_{14}Br_2NO$ $[M + H]^+$: 417.9442, found 417.9437 (one of the major peaks).

General Procedure for the Synthesis of Oxazines 6a-i (GP-II). To a mixture of phenanthrenequinone (**1**, 1.0 mmol) and α-substituted amine (**5a-e**)/amino acid ester (**5f, g**, 1.1 mmol, 1.1 equiv.) in dioxane (2 mL), I_2 (20 mol %, 50 mg) was added, and the solution was refluxed under air to complete the reaction, which was monitored by TLC. Dioxane was removed from the reaction mixture, and the residue was purified by silica gel column chromatography using a suitable eluent to afford the desired product.

*3-Phenyl-2H-Phenanthro[9,10-b][1,4]oxazine (**6a**).* The compound was prepared following **GP-II** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and α-methylbenzylamine (1.1 mmol, 0.14 mL). Purification by column chromatography (2% EtOAc-pet ether) afforded the title compound as a yellow solid (247 mg, 0.80 mmol, 80% yield). mp 136−138 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 5.22 (s, 2H), 7.49−7.68 (m, 7H), 8.10 (t, *J* = 3.6 Hz, 2H), 8.25−8.28 (m, 1H), 8.61 (t, *J* = 9.3 Hz, 2H), 8.74 (d, *J* = 8.1 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 62.8, 122.5, 122.7, 122.77, 122.82, 124.7, 124.8, 125.1, 126.7, 126.8, 127.0, 127.1, 127.2, 128.8, 130.2, 130.7, 130.9, 135.8, 139.0, 154.7; FT-IR (KBr, cm^{-1}): 722.6, 752.0, 1127.5, 1324.6, 1449.1, 2853.6, 2924.5; HRMS (ESI-TOF) *m/z* calcd for $C_{22}H_{16}NO$ $[M + H]^+$: 310.1232, found 310.1237.

*11-Phenyl-10H-pyreno[4,5-b][1,4]oxazine (**6b**).* The compound was prepared following **GP-II** employing pyrene-4,5-dione (1.0 mmol, 232 mg) and α-methylbenzylamine (1.1 mmol, 0.14 mL). Purification by column chromatography (20% DCM-pet ether) afforded the title compound as a yellow solid (246 mg, 0.74 mmol, 74% yield). mp 146−148 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 5.26 (s, 2H), 7.457.49 (m, 3H), 7.90−8.11 (m, 8H), 8.43 (d, *J* = 7.8 Hz, 1H), 8.90 (dd, J_1 = 1.5 Hz, J_2 = 6 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 62.8, 119.8, 120.0, 121.5, 123.8, 124.3, 125.3, 125.6, 126.0, 126.3, 126.7, 127.7, 128.7, 129.2, 130.9, 131.0, 135.7, 140.0, 155.0; FT-IR (KBr, cm^{-1}): 717.3, 825.1, 1051.7, 1384.6, 1455.5, 1567.5, 1646.3, 2857.4, 2932.2; HRMS (ESI-TOF) *m/z* calcd for $C_{24}H_{16}NO$ $[M + H]^+$: 334.1232, found 334.1227.

*3-(Naphthalen-2-yl)-2H-phenanthro[9,10-b][1,4]oxazine (**6c**).* The compound was prepared following **GP-II** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and 1-(naphthalen-2-yl)-ethylamine (1.1 mmol, 0.13 mL). Purification by column chromatography (2% EtOAc-pet ether) afforded the title compound as a yellow crystalline solid (291 mg, 0.81 mmol, 81% yield). mp 104−106 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 5.13 (s, 2H), 7.19−7.74 (m, 8H), 7.80−7.99 (m, 3H), 8.28−8.34 (m, 1H), 8.58−8.78 (m, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 65.6, 122.4, 122.67, 122.74, 122.9, 124.2, 124.6, 125.0, 125.2, 125.3, 125.9, 126.3, 126.6, 126.8, 127.0, 127.2, 127.3, 128.3, 128.6, 130.1, 130.7, 133.0, 134.1, 134.5, 139.0, 157.1; FT-IR (KBr, cm^{-1}): 718.6, 749.3, 756.5, 1026.2, 1235.2, 1508.1, 1674.4, 2852.0, 2923.0; HRMS (ESI-TOF) *m/z* calcd for $C_{26}H_{18}NO$ $[M + H]^+$: 360.1388, found 360.1393.

*3-p-Tolyl-2H-phenanthro[9,10-b][1,4]oxazine (**6d**).* The compound was prepared following **GP-II** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and 1-(4-methylphenyl)-ethylamine (1.1 mmol, 0.16 mL). Purification by column chromatography (2% EtOAc-pet ether) afforded the title compound as a yellow solid (242 mg, 0.75 mmol, 75% yield). mp 118−120 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 2.41 (s, 3H), 5.19 (s, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.54−7.68 (m, 4H), 7.99 (d, *J* = 8.1 Hz, 2H), 8.24−8.27 (m, 1H), 8.58−8.64 (m, 2H), 8.73−8.76 (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 21.5, 62.6, 122.3, 122.5, 122.6, 124.6, 124.7, 124.9, 126.5, 126.6, 127.0, 129.4, 130.1, 130.4, 133.0, 138.8, 141.3, 154.7; FT-IR (KBr, cm^{-1}): 721.9, 755.9, 1032.4, 1126.2, 1179.5, 1384.2, 1494.5, 1608.1, 2853.1, 2923.9; HRMS (ESI-TOF) *m/z* calcd for $C_{23}H_{18}NO$ $[M + H]^+$: 324.1388, found 324.1386.

*2-Methyl-3-phenyl-2H-phenanthro[9,10-b][1,4]oxazine (**6e**).* The compound was prepared following **GP-II** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and α-ethylbenzylamine (1.1 mmol, 0.16 mL). Purification by column chromatography (2% EtOAc-pet ether) afforded the title compound as a yellow solid (258 mg, 0.80 mmol, 80% yield). mp 172−174 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 1.43 (d, *J* = 6.6 Hz, 3H), 5.80 (q, *J* = 6.9 Hz, 1H), 7.42−7.72 (m, 7H), 8.12−8.15 (m, 2H), 8.30−8.33 (m, 1H), 8.60−8.66 (m, 2H), 8.82 (dd, J_1 = 0.6 Hz, J_2 = 9 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 16.1, 67.6, 122.4, 122.5, 122.7, 123.4, 124.9, 125.5, 126.6, 126.7, 126.8, 127.0, 127.9, 128.4, 128.7, 130.0, 130.7, 132.8, 135.4, 136.3, 157.8; FT-IR (KBr, cm^{-1}): 682.5, 760.5, 1057.9, 1427.8, 1564.1, 2853.9, 2925.5; HRMS (ESI-TOF) *m/z* calcd for $C_{23}H_{18}NO$ $[M + H]^+$: 324.1388, found 324.1383.

*3-Cyclohexyl-4H-phenanthro[9,10-b][1,4]oxazine (**6f**).* The compound was prepared following **GP-II** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and 1-cyclohexylethylamine (1.1 mmol, 0.16 mL). Purification by column chromatography (3% EtOAc-pet ether) afforded the title compound as a pale yellow low melting solid (215 mg, 0.68 mmol, 68% yield). ^1H NMR (300 MHz, $CDCl_3$): δ 1.51−1.63 (m, 4H), 1.73−1.77 (m, 2H), 1.84−1.88 (m, 2H), 2.13−2.23 (m, 2H), 2.84−2.92 (m, 1H),6.81 (s, 1H), 7.52−7.64 (m, 5H), 8.05−8.08 (m, 1H), 8.26−8.28 (m, 1H), 8.66 (d, *J* = 8.1 Hz, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 26.0, 29.7, 31.7, 37.8, 99.6, 120.3, 121.1, 122.6, 123.4, 123.6, 123.9, 124.8. 125.2, 126.75, 126.83, 127.6, 128.0, 128.4, 147.8, 163.1; FT-IR (KBr, cm^{-1}): 754.3, 1215.7, 1450.9, 1632.5, 1728.5, 2854.6, 2927.0, 3019.2; HRMS (ESI-TOF) *m/z* calcd for $C_{22}H_{22}NO$ $[M + H]^+$: 316.1701, found 316.1697.

*Ethyl 2-Phenyl-2H-phenanthro[9,10-b][1,4]oxazine-3-carboxylate (**6g**).*[95] The compound was prepared following **GP-II** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and phenylalanine ethyl ester (1.1 mmol, 193 mg). Purification by column chromatography (8% EtOAc-pet ether) afforded the title compound as a yellow solid (271 mg, 0.71 mmol, 71%

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yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.41 (t, J = 7.2 Hz, 3H), 4.41−4.46 (m, 2H), 6.60 (s, 1H), 7.17−7.22 (m, 3H), 7.33−7.37 (m, 2H), 7.54−7.68 (m, 4H), 8.32−8.35 (m, 1H), 8.54 (dd, J_1 = 8.1 Hz, J_2 = 15 Hz, 2H), 8.64 (dd, J_1 = 1.2 Hz, J_2 = 15 Hz, 1H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 14.1, 29.6, 62.2, 122.3, 122.7, 122.8, 123.4, 123.5, 124.4, 125.4, 126.7, 126.9, 127.4, 128.5, 128.6, 129.0, 129.5, 132.1, 135.6, 139.5, 147.4, 163.3.

*Ethyl 2-Phenyl-2H-phenanthro[9,10-b][1,4]oxazine-3-carboxylate (**6h**).* The compound was prepared following **GP-II** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and tyrosine ethyl ester (1.1 mmol, 209 mg). Purification by column chromatography (15% EtOAc-pet ether) afforded the title compound as a deep yellow solid (322 mg, 0.81 mmol, 81% yield). mp 192−194 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.39 (t, J = 7.2 Hz, 3H), 4.40 (q, J = 6.9 Hz, 2H), 6.49 (s, 1H), 6.60 (d, J = 8.7 Hz, 2H), 7.20 (d, J = 10.5 Hz, 2H), 7.51−7.66 (m, 5H), 8.28 (d, J = 7.8 Hz, 1H), 8.46−8.57 (m, 2H), 8.65 (d, J = 8.1 Hz, 1H); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 13.5, 61.2, 70.8, 115.1, 121.5, 122.2, 122.47, 122.54, 122.8, 123.5, 124.7, 125.2, 125.8, 126.9, 127.3, 128.2, 128.3, 128.5, 130.8, 138.2, 148.1, 158.0, 161.9; FT-IR (KBr, cm^{-1}): 724.4, 755.0, 1170.0, 1229.5, 1514.2, 1613.1, 1715.7, 2853.4, 2924.7, 3370.8; HRMS (ESI-TOF) m/z calcd For $C_{25}H_{20}NO_4$ [M + H]$^+$: 398.1392, found 398.1388.

*4,5-Dibromo-11-phenyl-10H-pyreno[4,5-b][1,4]oxazine (**6i**).* The compound was prepared following **GP-II** employing 4,5-dibromopyrene-4,5-dione (1.0 mmol, 390 mg) and α-methylbenzylamine (1.1 mmol, 0.14 mL). Purification by column chromatography (15% DCM-pet ether) afforded the title compound as a bright yellow solid (344 mg, 0.70 mmol, 70% yield). mp 156−158 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.93 (s, 2H), 7.64−7.68 (m, 3H), 8.10−8.30 (m, 8H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 60.7, 118.8, 119.0, 120.5, 122.8, 123.3, 124.3, 124.6, 124.7, 125.3, 125.7, 126.7, 127.7, 128.2, 129.9, 130.0, 135.1, 139.1, 155.0; FT-IR (KBr, cm^{-1}): 720.2, 900.1, 1021.5, 1121.5, 1314.9, 1422.7, 1601.7, 1678.6, 2823.2, 2954.7; HRMS (ESI-TOF) m/z calcd for $C_{24}H_{14}Br_2NO$ [M + H]$^+$: 489.9442, found 489.9447 (one of the major peaks).

General Procedure for the Synthesis of Oxazine-2-ones 8a−c (GP-III). To a mixture of phenanthrenequinone (**1**, 1.0 mmol) and amino acid ester (**5i−k**, 1.1 mmol, 1.1 equiv.) in dioxane (2 mL), I_2 (20 mol %, 50 mg) was added, and the solution was refluxed under air to complete the reaction, which was monitored by TLC. Dioxane was removed from the reaction mixture, and the residue was purified by silica gel column chromatography using a suitable eluent to afford the desired product.

*Ethyl 2-Phenyl-2H-phenanthro[9,10-b][1,4]oxazine-3-carboxylate (**8a**).* The compound was prepared following **GP-III** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and alanine ethyl ester (1.1 mmol, 117 mg). Purification by column chromatography (8% EtOAc-pet ether) afforded the title compound as a yellow solid (201 mg, 0.77 mmol, 77% yield). mp 198−200 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.66 (s, 3H), 7.63−7.75 (m, 4H), 8.42 (d, J = 8.1 Hz, 1H), 8.56−8.62 (m, 2H), 8.77−8.79 (m, 1H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 21.3, 122.4, 122.5, 122.7, 123.4, 126.9, 127.4, 127.7, 128.0, 128.3, 129.0, 130.8, 131.3, 141.1, 153.6; FT-IR (KBr, cm^{-1}): 723.7, 763.3, 1086.3, 1396.5, 1731.5, 1741.8, 2853.0, 2923.3. HRMS (ESI-TOF) m/z calcd For $C_{17}H_{12}NO_2$ [M + H]$^+$: 262.0868, found 262.0864.

*3-Isopropyl-2H-phenanthro[9,10-b][1,4]oxazin-2-one (**8b**).* The compound was prepared following **GP-III** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and valine ethyl ester (1.1 mmol, 145 mg). Purification by column chromatography (3% EtOAc-pet ether) afforded the title compound as a yellow solid (201 mg, 0.77 mmol, 77% yield). mp 148−150 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.40−1.43 (m, 6H), 3.48−3.56 (m, 1H), 7.61−7.70 (m, 4H), 8.39 (d, J = 7.8 Hz, 1H), 8.50−8.56 (m, 2H), 8.80 (d, J = 7.8 Hz, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 20.0, 32.1, 122.4, 122.6, 122.7, 123.4, 123.5, 126.9, 127.4, 127.6, 128.0, 128.6, 128.9, 131.2, 153.0, 160.5; FT-IR (KBr, cm^{-1}): 723.1, 751.1, 1036.3, 1451.7, 1623.9, 1731.3, 2853.6, 2925.8. HRMS (ESI-TOF) m/z calcd for $C_{19}H_{16}NO_2$ [M + H]$^+$: 290.1181, found 290.1176.

*3-Isopropyl-2H-phenanthro[9,10-b][1,4]oxazin-2-one (**8c**).* The compound was prepared following **GP-III** employing 9,10-phenanthrenequinone (1.0 mmol, 208 mg) and leucine ethyl ester (1.1 mmol, 159 mg). Purification by column chromatography (2% EtOAc-pet ether) afforded the title compound as a pale yellow solid (218 mg, 0.72 mmol, 72% yield). mp 106−108 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.01 (d, J = 6.6 Hz, 6H), 2.39−2.43 (m, 1H), 2.83 (d, J = 6.9 Hz, 2H), 7.54−7.66 (m, 4H), 8.25 (d, J = 7.8 Hz, 1H), 8.40−8.44 (m, 2H), 8.65−8.68 (m, 1H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 22.6, 26.3, 42.5, 122.3, 122.4, 122.6, 123.2, 123.3, 126.8, 127.2, 127.5, 127.8, 128.3, 128.8, 131.0, 140.6, 153.4, 155.7. FT-IR (KBr, cm^{-1}): 725.2, 764.7, 1193.4, 1293.8, 1397.2, 1451.1, 1495.8, 1554.6, 1734.2, 2870.4, 2926.6, 2955.6. HRMS (ESI-TOF) m/z calcd for $C_{20}H_{18}NO_2$ [M + H]$^+$: 304.1338, found 304.1333.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.9b03501.

Copies of ^{1}H and ^{13}C spectra of all synthesized compounds (**4a−p**, **4r**, **4s**, **6a−i**, **8a−c**), single-crystal XRD data (**4j** and **6a**), and copies of mass kinetics spectral data (PDF)

X-ray crystallographic data for **4j** (CIF)

X-ray crystallographic data for **6a** (CIF)

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Notes

The authors declare no competing financial interest.

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