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The amine exchange/biaryl coupling sequence: a direct entry to the phenanthro[9,10-*d*]heterocyclic framework

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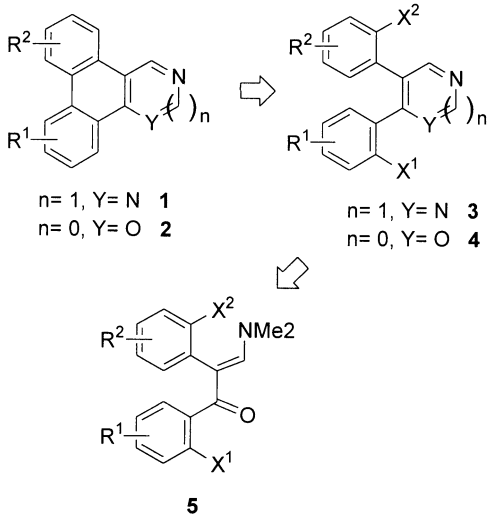
Abstract—Novel phenanthro[9,10-*d*]pyrimidines and phenanthro[9,10-*d*][1,2]oxazoles are regioselectively prepared by the application of a straightforward synthetic pathway, starting from new *o*,*o*′-dihalogenated and non-halogenated 4,5-diarylpyrimidines and 4,5-diarylisoxazoles, respectively, prepared via a tandem amine exchange/heterocyclization of diarylenaminones. A comparative study of biaryl coupling methodologies provides two highly efficient, complementary procedures to accomplish the final coupling step: an intramolecular Stille–Kelly stannylation/coupling of halogenated diarylpyrimidines and diarylisoxazoles, and a PIFA-mediated non-phenolic oxidative coupling of the corresponding non-halogenated substrates. In addition, other alternative approaches to the same target tetracyclic systems are also examined.

1. Introduction

The last few years have witnessed significant advances in the chemistry of phenanthro[9,10-*d*]heterocycles.[1] Apart from the already known naturally occurring products (anthofine, tylophorine, clyptopleurine or curcupital, inter alia),[2] a number of DNA intercalating agents,[3] novel nucleosides,[4] and antitumour agents[5] include the phenanthro[9,10]heterocyclic core. In addition, this heterocyclic system has gained much attention as an useful precursor of more complex, interesting molecules[6] such as porphyrins used in photodynamic therapy,[7] and the D_3-symmetric molecular propeller hexabenzotriphenylene.[8]

But the most promising applications of phenanthro[9,10]-heterocycles are based in their pronounced photoconducting, optoelectrical switching, electroluminiscence and photovoltaic properties,[7,9] which make them suitable for dyes, discotic liquid crystals, non-linear optics, xerography, solar cells, optical memory and data storage, sensors, etc.[10]

Following our investigations on the amine-exchange and biaryl coupling reactions as useful tools for the construction of heterocyclic systems,[11] we planned the preparation of novel phenanthro[9,10-*d*]pyrimidines **1** and phenanthro[9,10-*d*]isoxazoles **2** by an intramolecular *o*,*o*′-biaryl coupling of 4,5-diaryl substituted pyrimidines **3** and isoxazoles **4**, respectively as the final step. Although the application of biaryl coupling to the synthesis of phenanthrenes has already been reported,[12] our approach implied a challenging ring closure in conformationally highly constrained molecules[13] employing mild conditions in order to avoid the opening of the labile heterocycle framework.[14] The most outstanding results and full experimental details of this synthetic work are described here.



2. Results and discussion

2.1. Synthesis of 4,5-diarylpyrimidines

A series of dihalogenated enaminoketones **5**, readily obtained from the corresponding 1,2-diarylethanones,[11a,14c] were submitted to Leuckart reductive amination conditions, giving rise to 4,5-diarylpyrimidines in a regioselective way (Table 1). According to these results, the above used

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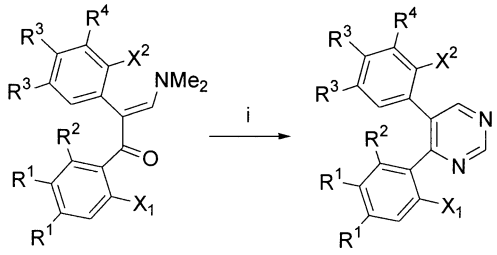
Table 1. Synthesis of diarylpyrimidines **3**



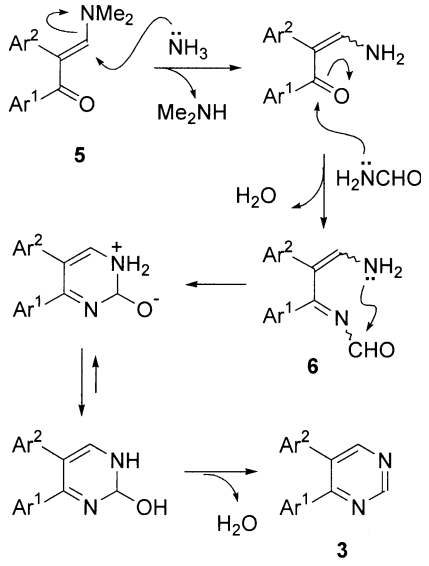
5 **3**

i: $NH_4^+HCOO^-$, $HCONH_2$, HCOOH, 150–165°C

R^1	R^2	R^3	R^4	X^1	X^2	**3** (%)[a]
H	H	H	H	Br	Br	**3a** (71)
H	H	H	H	I	I	**3b** (81)
OMe	H	OMe	H	Br	Br	**3c** (76)
OMe	H	OMe	H	I	I	**3d** (68)
OMe	H	H	H	Br	Br	**3e** (73)
OMe	H	H	H	I	I	**3f** (66)
H	H	OMe	H	Br	Br	**3g** (79)
H	H	OMe	H	I	I	**3h** (61)
H	H	OMe	H	Br	I	**3i** (66)
H	H	OMe	H	I	Br	**3j** (76)
H	H	OCH_2O[b]	H	Br	Br	**3k** (66)
H	H	H	H	H	H	**3l** (67)
OMe	H	OMe	H	H	H	**3m** (78)
OMe	H	H	H	H	H	**3n** (79)
OMe	OMe	OMe	H	H	H	**3o** (75)
OMe	H	OMe	OMe	H	H	**3p** (77)

[a] Yield of pure crystallized compound (MeOH).
[b] $R^3+R^3=OCH_2O$.

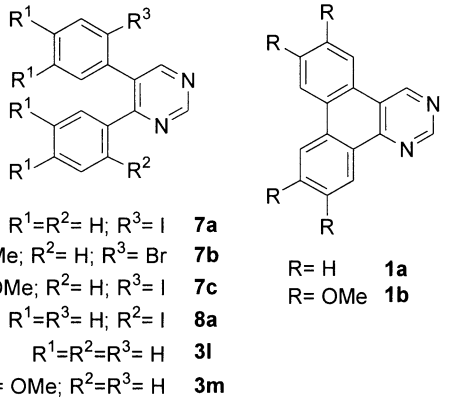
procedure[15] allows the presence of different halo functionalities without affecting the reaction yield, thus expanding significantly its scope. A mechanism for this selective, high yielding heteroring construction has been already proposed (Scheme 1).[15] The key step consists in an amine-exchange reaction of enaminoketones in which an unexpectedly easy removal of the dimethylamino group by other nitrogen nucleophiles allows the introduction of a vast array of moieties, providing a versatile, efficient tool for the synthesis of heterocycles.[16] In our mechanistic proposal, after the introduction of the nucleophile ammonia via amine-exchange, a condensation of formamide with the carbonyl group provides formyliminoenamines **6**, which undertake intramolecular heterocyclization, affording diarylpyrimidines **3**. A definitive proof for such a mechanism was obtained by detection of intermediates **6** when employing *o*,*o*′-dihaloenaminones **5**, probably due to a slightly longer reaction time needed in this case for the next step.[17]



Scheme 1.

2.2. Biaryl coupling of dihalogenated pyrimidines

In order to accomplish the key step of the programmed synthetic path leading to tetracycles **1**, a comparative study of methodologies for the cross coupling of selected *o*,*o*′-dihaloarylpyrimidines **3b–d** was carried out, revealing several marked differences if compared to the previously reported coupling of dihaloarylpyrazoles (Table 2).[11] No alkylstannanes or boronates were obtained in any case, neither by initial metal–halogen exchange followed by reaction with R_3SnCl or $B(OR)_3$ nor by treatment with Miyaura's reagent or pinacolborane.[18] Apart from starting material, only dehalogenation products **7**, **8** and **3l**,**m** could be isolated in low to moderate yield. Therefore it can be proposed that an unusually stable aggregation state of the so-formed organometallic species could avoid the attack of bulky electrophiles.[11b,19]



R^1=R^2= H; R^3= I **7a**
R^1= OMe; R^2= H; R^3= Br **7b**
R^1= OMe; R^2= H; R^3= I **7c**
R^1=R^3= H; R^2= I **8a**
R^1=R^2=R^3= H **3l**
R^1= OMe; R^2=R^3= H **3m**

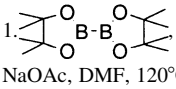
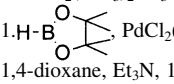
R= H **1a**
R= OMe **1b**

Otherwise, although Ullmann reaction was attempted by means of a wide range of experimental conditions, no target phenanthro derivative **1** was obtained, probably due to the instability of the pyrimidine ring under such reaction conditions, as only complex mixtures of products were detected in all cases, even when mild variants of this classic reaction were employed.[20]

However, a palladium catalyzed intramolecular tandem stannylation/biaryl coupling (Table 2, entries 25–27) provided directly the desired phenanthro[9,10-*d*]pyrimidines **1a**,**b** in high yields.[17] This method was then applied to the rest of *o*,*o*′-dihalogenated 4,5-diarylpyrimidines **3**, affording the corresponding phenanthroderivatives **1** with the results summarized in Table 3. In a similar fashion to pyrazole derivatives,[11b] both *o*,*o*′-diiodo and *o*,*o*′-dibromo derivatives, and even bromo-iodo mixed compounds were suitable substrates for the latter procedure, according to the comparable, good to excellent yields obtained. An additional feature of the versatility of our method is the fact

Table 2. Selected cross-coupling assays performed on pyrimidines **3b–d**

3b-d ---------→ **1a-b**

Entry	3	Reaction conditions	References	1 (%)[a]	Dehalogenation product (%)[a]	Conversion (%)
1	**3b**	1. Buli, THF; 2. R_3SnCl; 3. [Pd][b]	18b, 21	–	**7a–3l** (92)[c]	96
2	**3c**			–	**7b–3m** (85)[c]	93
3	**3d**			–	**7c–3m** (96)[c]	95
4	**3b**	1. BuLi, THF; 2. $B(OR)_3$; 3. [Pd][b]	18a, 21	–	**7a–3l** (95)[c]	98
5	**3c**			–	**7b–3m** (88)[c]	72
6	**3d**			–	**7c–3m** (91)[c]	91
7	**3b**	1.  , $PdCl_2(PPh_3)_2$,	18c,d, 21a	–	**7a–3l** (65)	51
8	**3c**	NaOAc, DMF, 120°C, sealed tube		–	**7b–3m** (80)	47
9	**3d**	2. $PdCl_2(PPh_3)_2$, K_3PO_4, DMF, 120°C, sealed tube		–	**7c–3m** (51)	63
10	**3b**	1.  , $PdCl_2(PPh_3)_2$, NaOAc,	18e,f, 21a	–	**7a–3l** (34)	60
11	**3c**	1,4-dioxane, Et_3N, 120°C, sealed tube		–	**7b–3m** (55)	52
12	**3d**	2. $PdCl_2(PPh_3)_2$, K_3PO_4, DMF, 120°C, sealed tube		–	**7c–3m** (31)	68
13	**3b**	[Cu], solvent[d]	20	–	**7a–3l** (18)[c]	100
14	**3c**			–	**7b–3m** (20)[c]	82
15	**3d**			–	**7c–3m** (13)[c]	96
16	**3b**	$(CuOTf)_2$·PhH, DMF, 100°C	20f	–	**7a–3l** (<5)	45
17	**3c**			–	**7b–3m** (16)	53
18	**3d**			–	**7c–3m** (9)	51
19	**3b**	CuTC,[e] NMP, 170°C		–	**7a–3l** (30)	88
20	**3c**		20c	–	**7b–3m** (18)	39
21	**3d**			–	**7c–3m** (26)	71
22	**3b**	Cu_2O, DMF, 190°C		–	**7a–3l** (74)	100
23	**3c**		20g	–	**7b–3m** (<5)	87
24	**3d**			–	**7c–3m** (59)	100
25	**3b**	Me_6Sn_2, $Pd(PPh_3)_4$ (5 mol%), 1,4-dioxane,		**1a** (96) *91*	**7a–3l** (<5)	100
26	**3c**	140°C, sealed tube[f]	12b	**1b** (94) *85*	**7b–3m** (<5)	95
27	**3d**			**1b** (91) *80*	**7c–3m** (8)	100
28	**3b**	Me_6Sn_2, $PdCl_2(PPh_3)_2$ (5 mol%), 1,4-dioxane,		**1a** (99) *93*	–	100
29	**3c**	140°C, sealed tube[f]	12b	**1b** (95) *91*	–	100
30	**3d**			**1b** (92) *88*	–	100

[a] GCMS yields. Isolated yields are indicated in italics.

[b] $Pd(Ph_3)_4$ and $PdCl_2(PPh_3)_2$ were used as catalysts under different conditions. The intermediate arylstannane, arylboronate or arylboronic acids were not observed in any case. When ^{t}BuLi or activated magnesium were employed instead of ^{n}BuLi similar results were obtained, although with slightly lower conversion. No significative changes were observed by the addition of metal-complexing agents such as TMEDA and crown ethers (18-crown-6).

[c] Averaged value.

[d] Different reaction conditions were assayed, employing either commercially available copper bronze or activated copper, which was prepared by treatment of copper bronze with EDTA·Na_2 and dried over P_2O_5 at 0.1 mmHg. The experiments were carried out in dimethylformamide, pyridine, quinoline and nitrobenzene as solvents.

[e] CuTC: Copper(I) 2-thiophenecarboxylate.

[f] The use of $^n Bu_6Sn_2$ as the stannylating agent led to mixtures of dehalogenation products. The use of heavy-wall pressure tubes was crucial for the success of the target transformation, as only dehalogenation products **7**, **8** and **3l**,**m** were observed when the reaction was performed under atmospheric pressure. Several palladium catalyst–ligand systems were assayed in order to optimize the procedure. See Ref. 12b for a more detailed discussion on the choice of the catalytic system.

that similar results were obtained from methoxylated substrates, which are generally accepted to undergo a slower transmetallation step.[22]

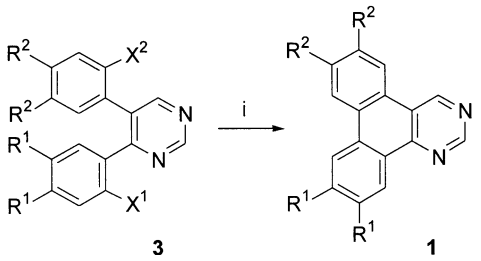
Otherwise, the coupling rate of diarylpyrimidines **3a–k** was observed to be much higher than the previously reported[11b] for *o*,*o*′-dihalogenated *N*-phenyl-4,5-diarylpyrazole analogs (21–27 h vs 40–76 h). In order to explain these rate-differences, we propose that the presence of the bulky phenyl group at the *N*-1 position in pyrazoles can sterically hinder the oxidative addition step, key process in our mechanistic proposal (Scheme 2).

2.3. Biaryl coupling of dihalogenated isoxazoles

A similar array of cross-coupling methodologies were assayed on *o*,*o*′-dihalogenated 4,5-diarylisoxazoles **4a–c**, readily obtained from enaminoketones **5a–c** and hydroxylamine by a regiocontrolled tandem amine-exchange/heterocyclization effected in heavy-wall pressure tubes.[11a] According to the results shown in Table 4, it was evident the high lability of the isoxazole ring under most of the conditions assayed. Although ring opening of isoxazoles bearing no substitution at C-3 under strongly basic conditions is already known, the behaviour showed by derivatives **4a–c** was unexpected and worthy to be examined.

A mixture of dehalogenation products **9**,**10** and **4l–m** and ketonitriles **11** were obtained when treating substrates **4a–c** with BuLi and different electrophiles such as $B(OMe)_3$, Me_3SnCl, Me_3SiCl, etc (entries 1–6 in Table 4). Taking into account our previous reports on the ring opening reactions of non-halogenated diarylisoxazoles, which usually need both the action of a strong base and high temperatures to undertake such reactions,[14c] we can conclude that the

Table 3. Phenanthropyrimidines **1** prepared



i: Me_6Sn_2, $PdCl_2(PPh_3)_2$ (5 mol%), 1,4-dioxane, 140°C, sealed tube

Substrate	R^1	R^2	X^1	X^2	Product (%)[a]
3a	H	H	Br	Br	**1a** (90)
3b	H	H	I	I	**1a** (93)
3c	OMe	OMe	Br	Br	**1b** (91)
3d	OMe	OMe	I	I	**1b** (88)
3e	OMe	H	Br	Br	**1c** (81)
3f	OMe	H	I	I	**1c** (86)
3g	H	OMe	Br	Br	**1d** (80)
3h	H	OMe	I	I	**1d** (84)
3i	H	OMe	Br	I	**1d** (67)
3j	H	OMe	I	Br	**1d** (62)
3k	H	OCH_2O[b]	Br	Br	**1e** (89)

[a] Yield of pure crystallized compound.
[b] $R^2+R^2=OCH_2O$.

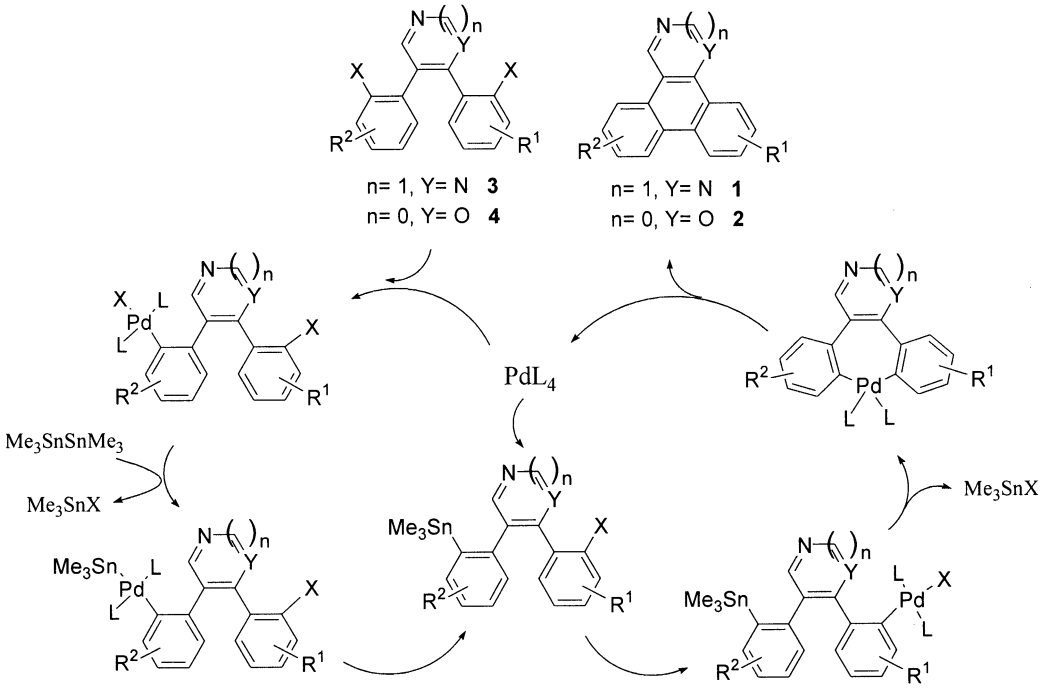
presence of the halo substituents induces significantly the cleavage of the heterocycle, even at low temperatures.

In order to generate the organolithium intermediates, reductive lithiation was assayed by reacting with lithium metal (entries 7–9). Surprisingly, instead of the expected lithium–halogen exchange reaction intermediates, the main products obtained from these assays were again α-ketonitriles **11** generated by a lithium metal promoted cleavage of isoxazole ring with no precedents so far.

Although the aimed biaryl coupling reaction was again effected under Stille–Kelly conditions[23] (Me_6Sn_2, $PdCl_2(PPh_3)_2$ (5 mol%), 1,4-dioxane, 115°C, sealed tube), phenanthro[1,2]oxazole **2a** was only obtained from *o*,*o*′-diiodo derivative **4b**, as *o*,*o*′-dibromo 4,5-diarylisoxazoles **4a** and **4c** provided phenanthroles **13a** and **12b**, respectively. The latter procedure was consequently applied to the rest of diiodinated substrates **4**, affording the corresponding tetracycles **2** with the yields summarized in Table 5.[24]

Diiodo isoxazoles **4b**, **4d**, **4f** and **4h** reacted even faster than the analog pyrimidine derivatives **3** (1.5–2.5 h), probably due to the lack of a bulky group at the *O*-1 position in comparison to previously reported *o*,*o*′-dihalogenated *N*-phenyl-4,5-diarylpyrazoles,[11b] although the electronic nature of isoxazole ring should also be considered to some extent.

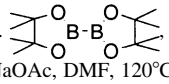
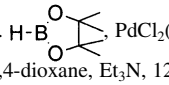
As a result of a ring cleavage of the heterocycle after the biaryl coupling reaction all the *o*,*o*′-dibromo and mixed *o*,*o*′-bromoiodo diarylisoxazoles afforded mixtures of phenanthroles **12** and **13** under the same reaction conditions. The latter side products were also isolated when the coupling reaction of diiodo derivatives was carried out for longer times than required. Ab initio, three possible factors were examined as responsible of such anomalous behaviour: (i) a possible thermal instability of the isoxazole ring in the phenanthro[1,2]oxazole system, (ii) a deprotonation at the C-3 position effected by the weakly basic phosphine ligands which would provoke a cleavage of the N–O bond analogous to that observed when using BuLi, or (iii) an



Scheme 2.

Table 4. Selected cross-coupling assays performed on isoxazoles **4a–c**

4a-c ---------► **2a-b**

Entry	4	Reaction conditions	2 (%)[a]	Dehalogenation product (%)[a]	Nitriles 11 (%)[a]	Phenanthroles (%)[a]
1	**4a**	1. BuLi, THF; 2. R_3SnCl; 3. [Pd][b]	–	**9a–4l** (62)[c]	**11a** (8), **11d** (15)[c]	–
2	**4b**		–	**9b–4l** (79)[c]	**11f** (13)[c]	–
3	**4c**		–	**9c–4m** (76)[c]	**11c** (6), **11e** (11)[c]	–
4	**4a**	1. BuLi, THF; 2. $B(OR)_3$; 3. [Pd][b]	–	**9a–4l** (65)[c]	**11a** (10), **11d** (11)[c]	–
5	**4b**		–	**9b–4l** (77)[c]	**11f** (19)[c]	–
6	**4c**		–	**9c–4m** (61)[c]	**11c** (12), **11e** (18)[c]	–
7	**4a**	1. Li, THF, −78°C; 2. −78°C→rt	–	**9a–4l** (<5)	**11a** (82) *77*[d]	–
8	**4b**	3. Reflux	–	**9b–4l** (<5)	**11b** (79) *74*[d]	–
9	**4c**		–	–	**11c** (97) *94*[d]	–
10	**4a**	1.  , $PdCl_2(PPh_3)_2$,	**2a** (*22*)[d]	**9a–4l** (6)	**11a** (7)	**12a** (25) *23*
11	**4b**	NaOAc, DMF, 120°C, sealed tube	**2a** (*36*)[d]	**9b–4l** (8)	–	**12a** (29) *26*
12	**4c**	2. $PdCl_2(PPh_3)_2$, K_3PO_4, DMF, 120°C, sealed tube	**2b** (*19*)[d]	–	**11c** (11)	**12b** (21) *19*
13	**4a**	1.  , $PdCl_2(PPh_3)_2$, NaOAc,	**2a** (*23*)[d]	–	**11a** (10)	**12a** (22)
14	**4b**	1,4-dioxane, Et_3N, 120°C, sealed tube	**2a** (*39*)[d]	–	–	**12a** (30)
15	**4c**	2. $PdCl_2(PPh_3)_2$, K_3PO_4, DMF, 120°C, sealed tube	**2b** (*17*)[d]	–	**11c** (6)	**12b** (15)
16	**4a**	[Cu], solvent[e]	–	**9a–4l** (15)[c]	**11d** (27), **11f** (10)[c]	–
17	**4b**		–	**9b–4l** (23)[c]	**11f** (17)[c]	–
18	**4c**		–	**9c–4m** (8)[c]	**11e** (16)[c]	–
19	**4a**	$(CuOTf)_2$·PhH, DMF, 100°C	–	**9a–4l** (22)	**11d** (18), **11f** (9)	–
20	**4b**		–	**9b–4l** (10)	**11f** (19)	–
21	**4c**		–	**9c–4m** (13)	**11e** (7)	–
22	**4a**	CuTC, NMP, 170°C[f]	–	**9a–4l** (27)	**11d** (18), **11f** (9)	–
23	**4b**		–	**9b–4l** (29)	**11f** (8)	–
24	**4c**		–	**9c–4m** (16)	**11e** (17)	–
25	**4a**	Cu_2O, DMF, 190°C	–	**9a–4l** (12)	**11f** (15)	–
26	**4b**		–	**9b–4l** (15)	**11f** (13)	–
27	**4c**		–	**9c–4m** (26)	**11e** (20)	–
28	**4a**	Me_6Sn_2, $Pd(PPh_3)_4$ (5 mol%)	–	**9a–4l** (8)	**11a** (6)	**13a** (*23*)
29	**4b**	1,4-Dioxane, 140°C, sealed tube[g]	**2a** (*81*)	**9b–4l** (5)	–	**12a** (*7*)
30	**4c**		–	**9c–4m** (6)	**11c** (9)	**12b** (*51*)
31	**4a**	Me_6Sn_2, $PdCl_2(PPh_3)_2$ (5 mol%)	–	–	–	**13a** (*12*)
32	**4b**	1,4-Dioxane, 140°C, sealed tube[g]	**2a** (*89*)	–	–	–
33	**4c**		–	–	–	**12b** (*49*)

[a] GCMS yields. Isolated yields are indicated in italics. Conversion was complete unless indicated.

[b] $Pd(Ph_3)_4$ and $PdCl_2(PPh_3)_2$ were used as catalysts under different conditions. The intermediate arylstannane, arylboronate or arylboronic acids were not observed in any case. When ^{t}BuLi or activated magnesium were employed instead of ^{n}BuLi similar results were obtained, although with slightly lower conversion. No significative changes were observed by the addition of metal-complexing agents such as TMEDA and crown ethers (18-crown-6).

[c] Averaged value.

[d] The conversion-rates for entries 7, 8, 9, 10, 11, 12, 13, 14 and 15 were 79, 96, 78, 27, 30, 25, 29, 33 and 25%, respectively.

[e] Different reaction conditions were assayed, employing either commercially available copper bronze or activated copper, which was prepared by treatment of copper bronze with EDTA·Na_2 and dried over P_2O_5 at 0.1 mmHg. The experiments were carried out in dimethylformamide, pyridine, quinoline and nitrobenzene as solvents.

[f] CuTC: Copper(I) 2-thiophenecarboxylate.

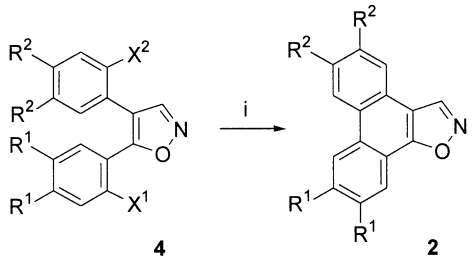
[g] The use of $^n Bu_6Sn_2$ as the stannylating agent led to mixtures of dehalogenation products. The use of heavy-wall pressure tubes was crucial for the success of the target transformation, as only dehalogenation products **9**, **10** and **4l**,**m** were observed when the reaction was performed under atmospheric pressure. Several palladium catalyst–ligand systems were assayed in order to optimize the procedure. See Ref. 12b for a more detailed discussion on the choice of the catalytic system.

insertion of the palladium catalyst in the C_3–H_3 bond by oxidative addition followed by N–O bond fragmentation.

The former two explanations based on the thermal instability of isoxazole and the ability of phosphine ligand to deprotonate the C-3 position were discarded when, after heating at 160°C in a thick-walled reaction vessel for 10 h equimolecular mixtures of Ph_3P and product **2a** or Ph_3P and substrate **4a** in 1,4-dioxane, no phenanthrol derivatives were isolated. On the other hand, the use of palladium catalysts highly stabilized by bidentate ligands ($PdCl_2$(dppe), Pd_2dba_3/BINAP or Pd_2dba_3/dppf) afforded starting material.[25] However, phenanthroles **12** and **13** were obtained after heating a solution of phenanthro[1,2]oxazole **2a** and catalytic amounts of $Pd(PPh_3)_4$ or $PdCl_2(PPh_3)$ (4 mol%) at 120°C for 3 h in a thick-walled reaction vessel.

All these experimental facts led us to propose the following considerations: (i) the ring-opening was caused by an unusual oxidative insertion of the palladium catalyst to the C_3–H_3 bond,[26] and (ii) the reason for the dissimilar behaviour observed for diiodo and dibromo or bromoiodo mixed substrates is based on the different biaryl coupling rates of diiodinated derivatives and the other halogenated substrates. Thus, as coupling of brominated isoxazoles is much slower, the rate of palladium insertion/ring opening becomes

Table 5. Phenanthro[9,10-*d*][1,2]oxazoles **2** prepared



4 **2**

i: Me_6Sn_2, $PdCl_2(PPh_3)_2$ (5 mol%), 1,4-dioxane, 140°C, sealed tube

Substrate[a]	R^1	R^2	X^1	X^2	Product (%)[b]
4b	H	H	I	I	**2a** (89)
4d	OMe	Ome	I	I	**2b** (73)
4f	OMe	H	I	I	**2c** (81)
4h	H	OMe	I	I	**2d** (78)

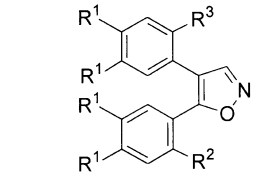
[a] See Ref. 12a.
[b] Yield of pure crystallized compound.

comparable and all the initially formed phenanthro[1,2]oxazoles **2** undergo cleavage to provide phenanthroles **12** and **13**. Diiodo derivatives couple much faster, so by the time that most of them have turned into **2**, no appreciable amount of phenanthroles **12** or **13** can be detected yet.

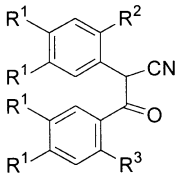
Unlike halogenated diarylpyrimidines **3**, isoxazoles **4** provided the corresponding tetracycles **2** by a sequential generation of arylboronates/biaryl coupling. As shown in Table 4 (entries 10–15), the coupling was carried out by using either bis(pinacolate)diboron or pinacolborane as the source of intermediate arylboronates, but low to moderate yields were obtained in all cases due to the formation of ring-cleavage products **12**. In addition, the conversion was rather low (25–33%) although it is worth mentioning that the target phenanthro[1,2]oxazole system **2** could be obtained from dibromo derivatives **4a** and **4c**.

2.4. Non-phenolic oxidative coupling mediated by PIFA

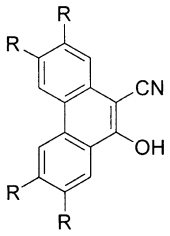
Oxidative coupling reactions constitute an useful, versatile tool to effect the biaryl linkage from phenols and phenol ethers.[27] Considering that no halogenated substrates are required, oxidative coupling can be used as an alternative methodology to cross coupling procedures such as Ullmann,



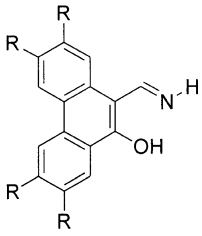
R^1=R^2=H; R^3=Br **9a**
R^1=R^2=H; R^3=I **9b**
R^1=OMe; R^2=H; R^3=Br **9c**
R^1=R^3=H; R^2=I **10a**
R^1=R^2=R^3=H **4l**
R^1=OMe; R^2=R^3=H **4m**



R^1=H; R^2=R^3=Br **11a**
R^1= H; R^2=R^3=I **11b**
R^1=OMe; R^2=R^3=Br **11c**
R^1=R^3=H; R^2=Br **11d**
R^1= OMe; R^3=H; R^2=Br **11e**
R^1=R^2=R^3=H **11f**



R^1=R^2= H **12a**
R^1=R^2=OMe **12b**
R^1= OMe;R^2= H **12c**
R + R^2= OCH_2O **12d**



R^1=R^2= H **13a**
R^1=R^2=OMe **13b**
R^1= OMe;R^2= H **13c**
R + R^2= OCH_2O **13d**

Suzuki or Stille reactions. In addition, it allows a wider range of substitution patters than photochemical approaches.[28] In fact, the synthesis of a number of natural products (e.g. kreysigine,[29] sanguinine,[30] tylophorine,[31] and bipowine,[32]) have been efficiently accomplished in the last few years by means of synthetic pathways based on phenol ether coupling procedures.

Taking into account these precedents and the availability of non-halogenated 4,5-diarylisoxazoles and 4,5-diarylpyrimidines,[14c,15] a range of different oxidative coupling procedures were assayed in order to achieve a simple, complementary entry to the phenanthropyrimidine and phenanthro[1,2]oxazole systems. As shown in Table 6, 4,5-bis-(3,4-dimethoxyphenyl)isoxazole **4m** was treated with Fe(III), I(III), Tl(III), Ru(IV) and V(V) oxidants to effect the target non-phenolic oxidative coupling. Good yields of the corresponding phenanthro[1,2]oxazole **2b**

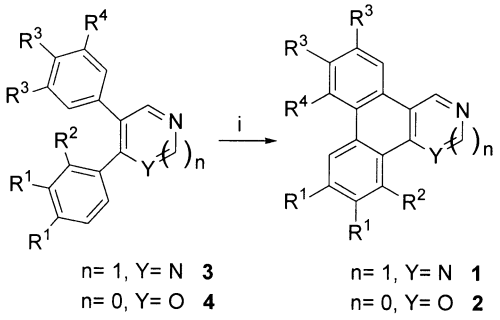
Table 6. Selected oxidative coupling assays performed on isoxazole **4m**

4m ----------→ **2b**

Entry	Reaction conditions	References	**2b** (%)[a]
1	TTFA[b] (1.1 equiv.), CH_2Cl_2, rt, 6.5 h	35a	42
2	TTFA[b] (1.1 equiv.), TFAA,[c] TFA,[d] $BF_3{\cdot}OEt_2$, 0°C, 4 h	35b	67
3	TTFA[b] (1.1 equiv.), CH_3CN, CH_2Cl_2, $BF_3{\cdot}OEt_2$, 40→0°C, 7 h	35c	72
4	$RuO_2{\cdot}2H_2O$ (4 equiv.), TFAA,[c] TFA,[d] $BF_3{\cdot}OEt_2$, CH_2Cl_2, −10°C→rt, 7 h	35d	71
5	VOF_3 (3.3 equiv.), $BF_3{\cdot}OEt_2$, CH_2Cl_2, rt, 0.15 h	35e	49
6	VOF_3 (3 equiv.), TFA,[d] CH_2Cl_2, −45°C→rt, 6 h	35f	69
7	$FeCl_3$ (6 equiv.), CH_2Cl_2, rt, 7 h	35g	80
8	PIFA (1.1 equiv.),[e] $BF_3{\cdot}OEt_2$, CH_2Cl_2, −40°C, 0.25 h	35h	85

[a] Yield of pure crystallized compound.
[b] TTFA: $Tl(OCOCF_3)_3$.
[c] TFAA: $(CF_3CO)_2O$.
[d] TFA: CF_3COOH.
[e] PIFA: $PhI(OCOCF_3)_2$.

Table 7.



i: PIFA, $BF_3{\cdot}OEt_2$, CH_2Cl_2, −40°C

Substrate	R^1	R^2	R^3	R^4	Product (%)[a]
3l	H	H	H	H	**1a** (23)
3m	OMe	H	OMe	H	**1b** (74)
3n	OMe	H	H	H	**1c** (81)
3o	OMe	OMe	OMe	H	**1f** (51)
3p	OMe	H	OMe	OMe	**1g** (88)
4l	H	H	H	H	**2a** (<5)[b]
4m	OMe	H	OMe	H	**2b** (85)
4n	OMe	H	H	H	**2c** (80)
4o	OMe	OMe	OMe	H	**2e** (61)

[a] Yield of pure crystallized compound.
[b] Only traces of phenantro[1,2]oxazole **2a** were detected from the crude ^1H NMR and GCMS spectra.

were obtained by using either $FeCl_3$ or PIFA (phenyliodine(III) bis(trifluoroacetate)), but the use of $FeCl_3$ involved a difficult removal of the metal oxidant in the work-up and further purification,[33] so PIFA, an hypervalent iodine reagent which combines easy handling, low toxicity,[34] and that avoids the formation of electrophilic metallation side-products,[35a] was chosen as the most convenient reagent to be assayed on the rest of non-halogenated isoxazoles **4l–o** and pyrimidines **3l–p**.[36] Thus, the application of the later methodology provided regioselectively[37] target phenanthropyrimidines **1** and phenanthro[1,2]oxazoles **2** with the results summarized in Table 7.

It should be pointed out that in contrast to the good yield obtained for most tetracycles **1** and **2**, poor results or no reaction were observed when both aryl substituents were phenyl groups (substrates **3l** and **4l**, respectively). Previous reports on the mechanism involved in oxidative coupling reactions have proposed that electron-rich aryl groups can efficiently stabilize the aromatic radical cation intermediate derived from a SET process[27,30,34] so that it can undergo either nucleophilic attack of another aromatic ring or radical coupling with another radical cation moiety.[35,38]

Comparing the results obtained from **3l** and **4l** it can be proposed that pyrimidine heterocycle, unlike isoxazole, can promote a slight stabilization of the above mentioned aromatic radical cation, otherwise very unstable due to the lack of electron-donating groups, thus leading to a low yield but meaningful coupling. As far as we know, there are very few examples of coupling reactions between two phenyl moieties effected by oxidants.[39]

Finally, the good yields obtained in the coupling of derivatives **3n** and **4n** are also remarkable if the lack of activation at one of the aryl rings (phenyl) is considered.

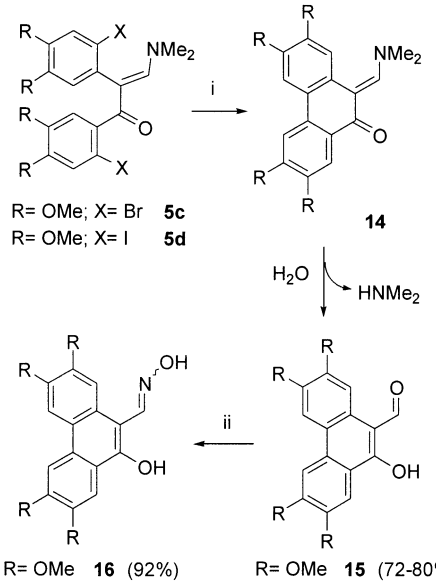
2.5. Alternative synthetic approaches to the phenanthroheterocyclic framework

On the basis of the excellent results obtained from the above developed diarylenaminoketone→diarylheterocycle→phenanthroheterocycle synthetic strategy, we planned an alternative approach to the target tetracyclic systems **1** and **2** by an initial biaryl coupling of enaminoketones followed by heterocyclization. This pathway had an additional interest as a test of the versatility of our already-optimized cross coupling procedure (Me_6Sn_2, $PdCl_2(PPh_3)_2$ (5 mol%), 1,4-dioxane,140°C, sealed tube) in such a labile system as that of enaminoketones **5**.

Methoxylated enaminoketones **5c** and **5d** were chosen as suitable substrates to apply this alternative approach, and the initial coupling reaction was successfully accomplished in both cases (80 and 72% yields, respectively). However, probably due to the hydrolysis of the coupled enaminone **14**, the reaction product was 10-formylphenanthrole **15**. Unfortunately, as all the attempts to prepare target tetracycle **2b** by a tandem oximation/heterocyclization[40] afforded intermediate 10-hydroxyminophenanthrole **16** (Scheme 3), this synthetic strategy was discarded.

Nevertheless, there still remained an alternative approach to tetracycles **1** and **2** closely related to the latter strategy, involving the cross-coupling of the synthetic precursors of halogenated diarylenaminoketones **5**, deoxybenzoins **17**, followed by aminomethylenation with dimethylformamide dimethyl acetal (DMFDMA)[11a,14c] and amine-exchange/heterocyclization of the corresponding enaminones **5**.

Again the same Stille–Kelly conditions proved to be an efficient procedure for the coupling of deoxybenzoins **17c–d** (61 and 66% yield, respectively) although longer



Scheme 3. i: Me_6Sn_2, $PdCl_2(PPh_3)_2$ (5 mol%), 1,4-dioxane, 140°C, sealed tube. ii: $NH_2OH{\cdot}HCl$, Na_2CO_3, AcOH, ^iPrOH, 140°C, sealed tube.

reaction times (6–7 days) were required and stannane intermediates **18** could be detected. In a similar fashion to derivatives **15**, the gain in stabilization in a more extended aromatic system provoked complete enolization of the coupled product, providing 9-phenanthrole **19** (Scheme 4), which turned out to be unreactive towards amino-methylenation with the Vilsmeier–Haack type reagent DMFDMA.

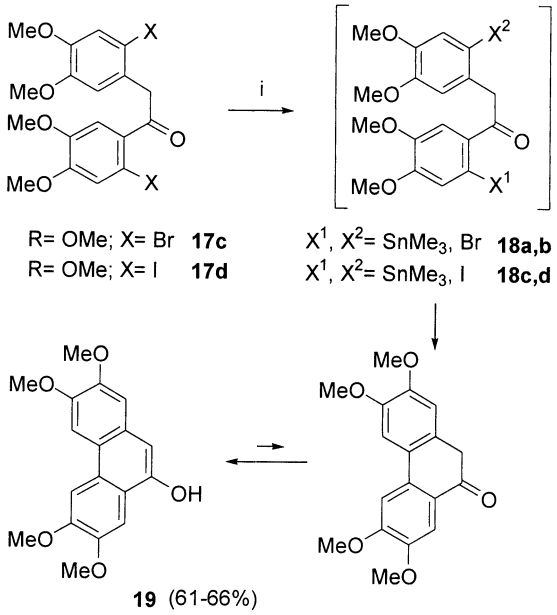
To sum up, a series of new phenanthro[9,10-*d*]pyrimidines and phenanthro[1,2]oxazoles have been regioselectively prepared by an straightforward, efficient synthetic pathway based on an initial tandem amine-exchange/heterocyclization of readily available diaryl enaminoketones followed by a biaryl coupling step. Towards this end, an exhaustive, comparative study of the main cross-coupling methodologies of halogenated substrates was performed, leading to an intramolecular Stille type tandem stannylation/coupling as the best procedure to effect the target coupling reaction of *o*,*o*′-dihalogenated 4,5-diarylheterocycles. In addition, non-phenolic oxidative coupling of non-halogenated substrates was also explored, featuring PIFA oxidation conditions as a valid complementary methodology for the access to the target tetracyclic systems with the additional bonus of its easy handling and non-toxicity. Finally, an evaluation of other alternative synthetic pathways revealed the importance of scheduling the biaryl coupling as the final step.

3. Experimental

3.1. General

For general experimental details, see Ref. 14c.

3.1.1. Synthesis of diarylpyrimidines. 4,5-Bis(2-bromophenyl)pyrimidine (3a). Typical procedure. A mixture of enaminoketone **5a** (2.491 g, 6.09 mmol), ammonium formate (3.864 g, 0.061 mol), $HCONH_2$ (0.62 mL, 0.0167 mol) and HCO_2H (0.62 mL, 0.0153 mol) was heated to 165°C until evaporation of water vapour stopped (50 min). Then the temperature was increased up to 180°C until complete consumption of the starting material was observed (1.5 h, monitored by TLC, silicagel, 25% EtOAc/CH_2Cl_2). After cooling the reaction mixture to room temperature, ice (25 g) was added and the resulting brown solution was extracted with dichloromethane (5×10 mL). Organic extracts were dried over anhydrous were dried over anhydrous sodium sulfate, evaporated under reduced pressure and the resulting residue was purified by flash chromatography using 40×50% EtOAc/CH_2Cl_2 as eluent. The obtained solid was crystallized from MeOH to afford pyrimidine **3a** (1.686 g, 71%) as a colorless powder: mp 144–146°C (MeOH); R_f 0.54 (45% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 7.11–7.24 (6H, m), 7.53–7.61 (2H, m), 8.82 (1H, s), 9.35 (1H, s); ^{13}C NMR ($CDCl_3$) δ 121.8, 123.4, 127.0, 127.2, 130.0, 130.2, 131.4, 133.6, 133.7, 135.6, 138.2, 157.5, 158.9, 164.2; FTIR (neat film, cm^{-1}): 1596; EIMS (*m*/*z*, %) 391 (M+2, 17), 390 (M^+, 32), 388 (M−2, 18), 311 (M−Br^{79}, 47), 309 (M−Br^{81}, 47), 230 (M−2Br, 100). Anal. Calcd for $C_{16}H_{10}Br_2N_2$: C, 49.27; H, 2.58; N, 7.18. Found: C, 49.39; H, 2.46; N, 7.25.



Scheme 4. Me_6Sn_2, $PdCl_2(PPh_3)_2$ (5 mol%), 1,4-dioxane, 140°C, sealed tube.

By use of the same procedure the following compounds were prepared.

3.1.2. 4,5-Bis(2-iodophenyl)pyrimidine (3b). 81%; colorless powder; mp 160–162°C (MeOH); R_f 0.42 (20% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 6.91 (1H, dd, *J*=7.6, 1.8 Hz), 6.97 (1H, dd, *J*=7.1, 1.9 Hz), 7.08–7.22 (4H, m), 7.79–7.88 (2H, m), 8.78 (1H, s), 9.32 (1H, s); ^{13}C NMR ($CDCl_3$) δ 96.6, 99.5, 127.7, 128.1, 129.2, 130.0, 130.1, 130.6, 139.3, 139.5, 136.0, 141.6, 157.6, 159.4, 165.7; FTIR (neat film, cm^{-1}): 1609; EIMS (*m*/*z*, %) 484 (M^+, 45), 357 (M−I, 13), 230 (M−2I, 100). Anal. Calcd for $C_{16}H_{10}I_2N_2$: C, 39.70; H, 2.08; N, 5.79. Found: C, 39.87; H, 2.19; N, 5.77.

3.1.3. 4,5-Bis(2-bromo-4,5-dimethoxyphenyl)pyrimidine (3c). 76%; colorless powder; mp 134–135°C (MeOH); R_f 0.37 (20% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.66 (3H, s), 3.70 (3H, s), 3.85 (3H, s), 3.86 (3H, s), 6.60 (1H, s), 6.67 (1H, s), 6.98 (1H, s), 7.01 (1H, s), 8.81 (1H, s), 9.31 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.9, 56.0, 112.0, 112.5, 113.3, 113.5, 114.8, 115.0, 127.7, 130.4, 147.9, 149.4, 149.7, 157.3, 159.0, 164.5; FTIR (neat film, cm^{-1}): 1596; EIMS (*m*/*z*, %) 512 (M+2, 1), 510 (M^+, 1), 508 (M^+−2, 1), 350 (M−2Br, 100). Anal. Calcd for $C_{20}H_{18}Br_2N_2O_4$: C, 47.08; H, 3.56; N, 5.49. Found: C, 46.97; H, 3.69; N, 5.23.

3.1.4. 4,5-Bis(4,5-dimethoxy-2-iodophenyl)pyrimidine (3d). 68%; colorless powder; mp 149–151°C (MeOH); R_f 0.31 (20% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.67 (6H, s), 3.83 (6H, s), 6.67 (2H, s), 7.21 (2H, s), 8.76 (1H, s), 9.32 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.9, 56.0, 56.1, 84.6, 87.2, 112.2, 113.3, 120.9, 121.2, 132.2, 134.5, 136.2, 148.8, 149.1, 149.3, 149.4, 157.4, 159.3, 166.0; FTIR (neat film, cm^{-1}): 1600; EIMS (*m*/*z*, %) 604 (M^+, 3), 350 (M−2I, 100). Anal. Calcd for $C_{20}H_{18}I_2N_2O_4$: C, 39.76; H, 3.00; N, 4.64. Found: C, 40.02; H, 3.08; N, 4.38.

3.1.5. 4-(2-Bromo-4,5-dimethoxyphenyl)-5-(2-bromophenyl)pyrimidine (3e). 73%; colorless powder; mp 104–105°C (MeOH); R_f 0.42 (20% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.60 (3H, s), 3.85 (3H, s), 6.58 (1H, s), 7.02 (1H, s), 7.14–7.24 (3H, m), 7.55 (1H, dd, J=7.8, 1.5 Hz), 8.86 (1H, s), 9.32 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.4, 55.6, 113.0, 114.9, 121.4, 126.8, 129.8, 129.9, 132.3, 138.5, 147.5, 149.0, 156.9, 158.9, 164.1; FTIR (neat film, cm^{-1}): 1601; EIMS (*m/z*, %) 452 (M+2, 9), 450 (M^+, 19), 448 (M−2, 9), 290 (M−2Br, 100). Anal. Calcd for $C_{18}H_{14}Br_2N_2O_2$: C, 48.03; H, 3.13; N, 6.22. Found: C, 48.08; H, 3.19; N, 6.16.

3.1.6. 4-(4,5-Dimethoxy-2-iodophenyl)-5-(2-iodophenyl)-pyrimidine (3f). 66%; colorless powder; mp 80–82°C (MeOH); R_f 0.41 (40% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.62 (3H, s), 3.83 (3H, s, OMe), 6.63 (1H, s), 6.97 (1H, ddd, J=7.9, 7.5, 1.6 Hz), 7.13 (1H, dd, J=7.5, 1.6 Hz), 7.23 (1H, s), 7.24 (1H, ddd, J=7.5, 7.5, 1.2 Hz), 7.88 (1H, d, J=7.9, 1.2 Hz), 8.74 (1H, s), 9.35 (1H, s); ^{1}H NMR ($CDCl_3$) δ 55.8, 56.0, 84.8, 99.5, 112.3, 121.6, 128.3, 130.0 130.7, 133.8, 136.3, 139.2, 140.0, 148.5, 149.3, 157.6, 159.1, 165.4; FTIR (neat film, cm^{-1}): 1595; EIMS (*m/z*, %) 544 (M^+, 16), 290 (M−2I, 100). Anal. Calcd for $C_{18}H_{14}I_2N_2O_2$: C, 39.73; H, 2.59; N, 5.15. Found: C, 39.79; H, 2.48; N, 5.15.

3.1.7. 5-(2-Bromo-4,5-dimethoxyphenyl)-4-(2-bromophenyl)pyrimidine (3g). 79%; colorless powder; mp 65–67°C (MeOH); R_f 0.28 (30% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.65 (3H, s), 3.84 (3H, s), 6.66 (1H, s), 6.99 (1H, s), 7.10–7.23 (3H, m), 7.60 (1H, dd, J=7.1, 2.0 Hz), 8.78 (1H, s), 9.34 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.8, 56.0, 112.2, 112.8, 115.4, 123.4, 127.3, 129.9, 130.0, 131.4, 132.7, 133.8, 136.0, 147.7, 149.6, 157.5, 158.7, 163.4; FTIR (neat film, cm^{-1}): 1600; EIMS (*m/z*, %) 452 (M+2, 11), 450 (M^+, 21), 448 (M−2, 11), 290 (M−2Br, 100). Anal. Calcd for $C_{18}H_{14}Br_2N_2O_2$: C, 48.03; H, 3.13; N, 6.22. Found: C, 48.19; H, 3.16; N, 6.08.

3.1.8. 5-(4,5-Dimethoxy-2-iodophenyl)-4-(2-iodophenyl)-pyrimidine (3h). 61%; colorless powder; mp 148–149°C (MeOH); R_f 0.36 (40% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.64 (3H, s), 3.84 (3H, s), 6.66 (1H, s), 7.00 (1H, ddd, J=7.5, 7.5, 1.6 Hz), 7.12 (1H, dd, J=7.5, 1.6 Hz), 7.21–7.26 (2H, m), 7.87 (1H, d, J=7.5 Hz), 8.83 (1H, s), 9.34 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.9, 56.0, 87.2, 96.5, 113.2, 121.1, 128.0, 129.2, 130.2, 131.6, 135.7, 139.2, 142.2, 148.8, 149.2, 157.4, 159.7, 166.2; FTIR (neat film, cm^{-1}): 1591; EIMS (*m/z*, %) 544 (M^+, 16), 290 (M−2I, 100). Anal. Calcd for $C_{18}H_{14}I_2N_2O_2$: C, 39.73; H, 2.59; N, 5.15. Found: C, 39.44; H, 2.32; N, 5.07.

3.1.9. 4-(2-Bromophenyl)-5-(4,5-dimethoxy-2-iodophenyl)-pyrimidine (3i). 66%; yellow powder; mp 134–135°C (MeOH); R_f 0.29 (50% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.61 (3H, s), 3.84 (3H, s), 6.62 (1H, s), 7.15–7.23 (4H, m), 7.56 (1H, dd, J=7.5, 2.4 Hz), 8.84 (1H, s), 9.33 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.6, 55.9, 87.2, 113.0, 121.0, 121.7, 127.1, 129.8, 130.2, 131.4, 132.6, 136.0, 138.5, 148.7, 149.1, 157.2, 159.4, 164.1; FTIR (neat film, cm^{-1}): 1594; EIMS (*m/z*, %) 498 (M+1, 8), 496 (M−1, 10), 290 (M−Br−I, 100). Anal. Calcd for $C_{18}H_{14}BrIN_2O_2$: C, 43.49; H, 2.84; N, 5.64. Found: C, 43.53; H, 2.88; N, 5.51.

3.1.10. 5-(2-Bromo-4,5-dimethoxyphenyl)-4-(2-iodophenyl)pyrimidine (3j). 76%; yellow powder; mp 114–115°C (MeOH); R_f 0.33 (50% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.64 (3H, s), 3.85 (3H, s), 6.62 (1H, s), 7.00 (1H, ddd, J=7.7, 7.6, 2.0 Hz), 7.02 (1H, s), 7.09 (1H, dd, J=7.7, 1.7 Hz), 7.24 (1H, ddd, J=7.6, 7.6, 1.7 Hz), 7.86 (1H, dd, J=7.9, 1.0 Hz), 8.86 (1H, s), 9.33 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.5, 55.6, 96.1, 113.0, 113.3, 114.7, 126.7, 127.5, 129.0, 129.6, 132.5, 138.7, 141.7, 147.5, 148.9, 156.8, 159.0, 165.9; FTIR (neat film, cm^{-1}): 1598; EIMS (*m/z*, %) 498 (M+1, 6), 496 (M−1, 6), (M−Br–I, 100). Anal. Calcd for $C_{18}H_{14}BrIN_2O_2$: C, 43.49; H, 2.84; N, 5.64. Found: C, 43.19; H, 2.96; N, 5.69.

3.1.11. 4-(2-Bromophenyl)-5-(5-bromo-1,3-benzodioxol-6-yl)pyrimidine (3k). 66%; colorless powder; mp 159–160°C (MeOH); R_f 0.41 (50% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 5.94 (2H, s), 6.59 (1H, s), 7.01 (1H, s), 7.14–7.25 (3H, m), 7.57 (1H, dd, J=8.0, 1.6 Hz), 8.76 (1H, s), 9.31 (1H, s); ^{13}C NMR ($CDCl_3$) δ 102.0, 110.6, 112.8, 114.4, 121.7, 127.1, 128.5, 130.1, 130.3, 133.0, 133.6, 138.2, 147.2, 148.6, 157.5, 159.4, 164.4; FTIR (neat film, cm^{-1}): 1594; EIMS (*m/z*, %) 436 (M+2, 3), 434 (M^+, 6), 432 (M−2, 3), 274 (M−2Br, 100). Anal. Calcd for $C_{17}H_{10}Br_2N_2O_2$: C, 47.04; H, 2.32; N, 6.45. Found: C, 47.17; H, 2.09; N, 6.49.

3.1.12. 4,5-Diphenylpyrimidine (3l). 67%; colorless powder; mp 130–131°C (MeOH) (lit.[41] 130–131°C (MeOH)).

3.1.13. 4,5-Bis(3,4-dimethoxyphenyl)pyrimidine (3m). 78%; colorless powder; mp 143–145°C (MeOH)(lit.[42] 125–127°C (EtOH)); R_f 0.30 (30% EtOAc/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.67 (6H, s), 3.87 (3H, s), 3.89 (3H, s), 7.11 (6H, m), 8.63 (1H, s), 9.20 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.5, 55.7, 110.3, 111.3, 112.3, 112.4, 121.5, 122.9, 128.9, 129.5, 132.4, 148.3, 148.8, 148.9, 150.0, 156.9, 157.9, 162.5; FTIR (neat film, cm^{-1}): 1620; EIMS (*m/z*, %) 353 (M+1, 21), 352 (M^+, 97), 351 (M−1, 100). Anal. Calcd for $C_{20}H_{20}O_4N_2$: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.34; H, 5.50; N, 7.66.

3.1.14. 4-(3,4-Dimethoxyphenyl)-5-phenylpyrimidine (3n). 78%; colorless powder; mp 115–116°C (MeOH); R_f 0.40 (30% EtOAc/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.57 (3H, s), 3.85 (3H, s), 6.76 (1H, d, J=8.4 Hz), 6.93 (1H, d, J=1.8 Hz), 7.14 (1H, dd, J=8.5, 1.8 Hz), 7.21–7.42 (5H, m), 8.65 (1H, s), 9.19 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.4, 55.7, 110.5, 112.8, 123.1, 127.9, 128.8, 129.2, 129.4, 132.7, 136.7, 148.2, 150.2, 157.2, 158.0, 162.5; FTIR (neat film, cm^{-1}): 1684; EIMS (*m/z*, %) 293 (M+1, 18), 292 (M^+, 93), 291 (M−1, 100). Anal. Calcd for $C_{18}H_{16}O_2N_2$: C, 73.95; H, 5.52; N, 9.58. Found: C, 73.68; H, 5.50; N, 9.35.

3.1.15. 5-(3,4-Dimethoxyphenyl)-4-(2,3,4-trimethoxyphenyl)pyrimidine (3o). 75%; colorless oil; R_f 0.20 (30% EtOAc/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.44 (3H, s), 3.58 (3H, s), 3.66 (3H, s), 3.80 (3H, s), 3.82 (3H, s), 6.58 (1H, s), 6.64

(1H, d, J=8.6 Hz), 6.71–6.84 (2H, bs), 6.95 (1H, d, J=8.6 Hz), 8.72 (1H, s), 9.14 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.4, 55.7, 55.9, 60.6, 60.7, 107.0, 110.9, 111.8, 120.9, 124.9, 125.1, 128.5, 134.1, 141.7, 148.5, 148.7, 150.9, 154.7, 155.6, 156.5, 162.2; FTIR (neat film, cm^{-1}): 1602; EIMS (*m/z*, %) 383 (M+1, 16), 382 (M^+, 91), 383 (M−1, 100). Anal. Calcd for $C_{21}H_{22}O_5N_2$: C, 65.96; H, 5.80; N, 7.33. Found: C, 65.82; H, 5.65; N, 7.18.

3.1.16. 4-(3,4-Dimethoxyphenyl)-5-(3,4,5-trimethoxyphenyl)pyrimidine (3p). 77%; colorless powder; mp 95–96°C (MeOH); R_f 0.20 (30% EtOAc/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.70 (9H, s), 3.85 (6H, s), 6.42 (2H, s), 6.76 (1H, d, J=8.4 Hz), 7.06 (1H, d, J=1.9 Hz), 7.11 (1H, dd, J=8.3, 1.9 Hz), 8.67 (1H, s), 9.17 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.4, 55.8, 56.1, 60.8, 106.4, 110.5, 112.6, 123.1, 129.4, 132.0, 132.7, 137.9, 148.4, 150.2, 153.5, 157.3, 157.7, 162.5; FTIR (neat film, cm^{-1}): 1602; EIMS (*m/z*, %) 383 (M+1, 24), 382 (M^+, 100), 381 (M−1, 29). Anal. Calcd for $C_{21}H_{22}O_5N_2$: C, 65.96; H, 5.80; N, 7.33. Found: C, 65.74; H, 5.50; N, 7.61.

When the same procedure was performed on enaminones **5f** and **5k**, the corresponding intermediate formyliminoenamines **6a** and **6b**, respectively were detected by means of the following selected spectroscopic data: ^{1}H NMR ($CDCl_3$) δ 6.70–7.45 (H_{arom}, =CH), 7.78–8.19 (1H, s, HCO); ^{13}C NMR ($CDCl_3$) δ 140.5–141.6 (=CH–N), 158.4–162.0 (CO); FTIR (neat film, cm^{-1}): 3270–3460 (N–H), 1710 (C=O), 1620–1615 (C=O), 1570 (C=C); EIMS (*m/z*, %) **6a** 534 (M−CHO, 4), 408 (M−I–CHO, 17), 280 (M−2I–CHO, 100); **6b** 429 (M+2-CHO, 3), 427 (M−CHO, 6), 425 (M−2-CHO, 4), 374 (M−Br^{79}, 14), 372 (M−Br^{81}, 14), 346 (M−Br^{79}–CHO, 77), 344 (M−Br^{81}–CHO, 77), 264 (M−2Br–CHO, 100).

3.2. Attempts at synthesis of arylboronic acids or aryltrimethylstannanes by the corresponding organolithium derivatives. Typical procedure

A solution of isoxazole **4c** (241 mg, 0.49 mmol) in dry THF (45 mL) at −78°C was treated with *n*-BuLi (0.74 mL, 1.19 M solution in hexane, 0.88 mmol) under Ar. This mixture was stirred at the same temperature for 35 min. A solution of $B(OMe)_3$ (tridistilled from Na) (0.74 mL, 2.45 mmol) in dry THF (1 mL) was added slowly during which time the solution changed color from pale yellow to dark orange. The resulting mixture was stirred for 2 h at −78°C, allowed to reach room temperature and poured onto a HCl 5% solution (80 mL) and stirred for 15 min. Brine (5 mL) was added and the aqueous layer was separated and extracted with Et_2O (5×25 mL). The combined organic layers were washed with H_2O (1×50 mL) and brine (1×50 mL), dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography using 40–80% de EtOAc/hexane as eluent, affording the following products.

3.2.1. 2-(2-Bromo-4,5-dimethoxyphenyl)-3-(3,4-dimethoxyphenyl)-3-oxopropanonitrile (13e). (87 mg, 18%) as a colorless powder: mp 120–121°C (Et_2O); R_f 0.77 (50% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 3.84 (3H, s), 3.86 (3H, s), 3.91 (3H, s), 3.94 (3H, s), 6.03 (1H, s), 6.89 (1H, d, J=8.6 Hz), 6.95 (1H, s), 7.05 (1H, s), 7.47 (1H, d, J=2.0 Hz), 7.67 (1H, dd, J=8.6, 2.0 Hz); ^{13}C NMR ($CDCl_3$) δ 45.4, 56.0, 56.2, 109.4, 110.3, 110.9, 114.1, 115.5, 116.1, 122.6, 124.0, 126.5, 149.3, 150.2, 154.5, 187.2; FTIR (neat film, cm^{-1}): 1684; EIMS (*m/z*, %) 421 (M+1, 5), 419 (M−1, 6). Anal. Calcd for $C_{19}H_{18}BrNO_5$: C, 54.30; H, 4.31; N, 3.33. Found: C, 54.21; H, 4.09; N, 3.30.

3.2.2. 2,3-Bis(2-bromo-4,5-dimethoxyphenyl)-3-oxopropanonitrile (11c). (12%) as a colorless powder: mp 119–120°C (30% EtOAc/hexane); R_f 0.72 (50% EtOAc/hexano); ^{1}H NMR ($CDCl_3$) δ 3.84 (3H, s), 3.86 (3H, s), 3.89 (3H, s), 3.91 (3H, s), 6.14 (1H, s), 6.85 (1H, d, J=8.4 Hz), 6.89 (1H, s), 6.98 (2H, s), 7.04 (1H, s); ^{13}C NMR ($CDCl_3$) δ 48.4, 56.2, 56.3, 111.9, 112.2, 112.6, 114.4, 115.4, 115.8, 116.7, 121.9, 128.7, 148.1, 149.3, 150.3, 152.4, 189.8; FTIR (neat film, cm^{-1}): 2207, 1707; EIMS (*m/z*, %) 501 (M+2, 1), 499 (M^+, 1), 497 (M−2, 1), 339 (M−2Br, 16). Anal. Calcd for $C_{19}H_{17}Br_2NO_5$: C, 45.72; H, 3.43; N, 2.81. Found: C, 45.67; H, 3.59; N, 2.83.

3.2.3. 4-(2-Bromo-4,5-dimethoxyphenyl)-5-(3,4-dimethoxyphenyl)isoxazole (9c). (49%) as a colorless oil: R_f 0.68 (6% EtOAc/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.76 (6H, s), 3.88 (3H, s), 3.93 (3H, s), 6.78 (1H, s), 6.80 (1H, d, J=8.2 Hz), 7.07 (1H, dd, J=8.3, 1.9 Hz), 7.13 (1H, d, J=1.8 Hz), 7.15 (1H, s), 8.29 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.7, 55.8, 56.1, 56.2, 109.3, 110.9, 113.6, 114.0, 115.6, 120.1, 120.3, 123.2, 148.6, 148.8, 149.6, 150.4, 152.3, 164.2; FTIR (neat film, cm^{-1}): 1604; EIMS (*m/z*, %) 421 (M+1, 6), 419 (M−1, 7), 340 (M−Br^{79}, 11), 339 (M−Br^{81}, 11). Anal. Calcd for $C_{19}H_{18}BrNO_5$: C, 54.30; H, 4.32; N, 3.33. Found: C, 54.32; H, 4.41; N, 3.39.

3.2.4. 4,5-Bis(3,4-dimethoxyphenyl)isoxazole (4m). (12%) as a colorless powder: mp 122–123°C (MeOH) (lit.[15c] 126–128°C (MeOH)).

The variation of the reaction conditions (temperature (−100→−40°C), stoichiometry of the organolithium reagent (1.1–2.3 equiv.), nature of the organolithium (^{n}BuLi, ^{t}BuLi) and of the electrophile reagents (($B(OMe)_3$, $B(O^iPr)_3$, TMSCl, Me_3SnCl)) led to the obtention of the former products in different yields ranged in Tables 2 and 4.

3.2.5. Ring opening of isoxazoles by treatment with lithium metal. 2,3-Bis(2-bromo-4,5-dimethoxyphenyl)-3-oxopropanonitrile (11c). Typical procedure. A solution of isoxazole **4c** (250 mg, 0.51 mmol) in dry THF (2 mL) was added to a stirred suspension of lithium shots (15 mg, 2.16 mmol, washed three times with hexane) in dry THF (10 mL) at −78°C under argon. After stirring for 15 min, the reaction was allowed to warm to room temperature and then heated to 85°C for 3.5 h until complete comsuption of the starting material was observed (monitored by TLC, silicagel, (30% EtOAc/hexane)). After cooling, the lithium excess was quenched by dropwise addition of methanol (3 mL). The reaction mixture was concentrated in vacuo and the resulting orange residue was purified by flash column chromatography using 35% de EtOAc/CH_2Cl_2 as

eluent, providing ketonitrile **11c** (156 mg, 73%) as a colorless powder.

The same procedure on isoxazole **4a** provided *2,3-bis(2-bromophenyl)-3-oxopropanonitrile (11a)* (61%) as a colorless oil: R_f 0.64 (5% EtOAc/CH_2Cl_2). Due to its instability, the structure of derivative **11a** was determined according to the following spectroscopic data: ^{1}H NMR (DMSO-d_6) δ 6.28–6.50 (3H, m), 6.61–6.74 (4H, m), 6.87 (1H, d, J=7.9), 6.94 (1H, d, J=7.9 Hz); EIMS (*m/z*, %) 379 (M^+, 3), 219 (M−2Br, 16).

The same procedure on isoxazole **4b** provided *2,3-bis(2-iodophenyl)-3-oxopropanonitrile (11b)* (71%) as a colorless powder: mp 199–201°C (40% EtOAc/hexane), R_f 0.60 (5% EtOAc/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 6.01 (1H, s), 7.07 (1H, ddd, J=7.8, 7.8, 1.5 Hz), 7.17–7.26 (2H, m), 7.35–7.49 (1H, m, H_{arom}), 7.54 (1H, dd, J=7.5, 1.8, H_{arom}), 7.63 (1H, dd, J=7.8, 1.6, H_{arom}), 7.92 (1H, d, J=7.0, H_{arom}) y 8.01 (1H, d, J=8.0, H_{arom}); ^{13}C NMR (CD_3COCD_3) δ 31.9, 95.3, 96.4, 101.0, 102.1, 118.2, 129.1, 130.6, 132.3, 137.2, 140.2, 141.1, 168.9; FTIR (neat film, cm^{-1}): 2212, 1613; EIMS (*m/z*, %) 473 (M^+, 3), 231 (M−2I+2H, 100), 219 (M−2I, 20).

3.2.6. Synthesis of phenanthro[9,10-*d*]pyrimidines via stannylation/biaryl coupling. Phenanthro[9,10-*d*]pyrimidine (1a). Typical procedure. A heavy wall-pressure tube was charged with diarylpyrimidine **3a** (53 mg, 0.14 mmol), $Pd(PPh_3)_2Cl_2$ (7.9 mg, 6.8 μmol), and degassed dioxane (4.2 mL) under nitrogen. A solution of Me_6Sn_2 (49 mg, 0.15 mmol) in degassed 1,4-dioxane (1.5 mL) was added dropwise to the resulting suspension, and after flushing with nitrogen at room temperature for 15 min, the mixture was heated at 140°C in an autoclave for 40 h. After cooling, the resulting black suspension was centrifuged and the deposited black palladium was washed with CH_2Cl_2 (1×3 mL). The combined organic solvents were washed with a saturated KF solution, dried over anhydrous Na_2SO_4 and the solvent was evaporated in vacuo. The residue was purified by flash chromatography using 20% hexane/EtOAc as eluent. Crystallization of the resulting yellow powder from MeOH afforded phenanthro[9,10-*d*]pyrimidine **1a** (25 mg, 90%) as a colorless powder: mp 172–173°C (MeOH); R_f 0.40 (45% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 7.69–7.84 (4H, m), 8.51–8.58 (3H, m), 9.21 (1H, dd, J=7.9, 1.5 Hz), 9.42 (1H, s), 10.0 (1H, s); ^{13}C NMR ($CDCl_3$) δ 121.6, 122.3, 122.6, 123.4, 125.5, 126.5, 127.7, 127.9, 128.6, 129.3, 130.8, 133.0, 151.0, 153.3, 156.0; FTIR (neat film, cm^{-1}): 1609; EIMS (*m/z*, %) 230 (M^+, 100). Anal. Calcd for $C_{16}H_{10}N_2$: C, 83.46; H, 4.38; N, 12.16. Found: C, 83.59; H, 4.48; N, 11.93.

The same procedure on diarylpyrimidine **3b** provided phenanthro[9,10-*d*]pyrimidine (1a) (93%).

The same procedure on diarylpyrimidine **3c** provided *6,7,10,11-tetramethoxyphenanthro[9,10-d]pyrimidine (1b)* (91%) as a colorless powder: mp 236–237°C (Et_2O); R_f 0.55 (8% MeOH/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 4.12 (3H, s), 4.14 (3H, s), 4.16 (6H, s), 7.65 (1H, s), 7.70 (1H, s), 7.89 (1H, s), 8.61 (1H, s), 9.36 (1H, s), 9.77 (1H, s; ^{13}C NMR ($CDCl_3$) δ 55.8, 56.0, 102.4, 102.5, 103.2, 105.3, 119.6, 122.0, 123.4, 127.1, 132.1, 151.7, 148.7, 148.9, 149.0, 149.8, 152.1, 154.4; FTIR (neat film, cm^{-1}): 1616; EIMS (*m/z*, %) 350 (M^+, 100), 335 (M−CH_3, 17), 307 (23), 292 (15), 263 (10), 221 (10), 175 (11). Anal. Calcd for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.61; H, 5.24; N, 8.09.

The same procedure on diarylpyrimidine **3d** provided *6,7,10,11-tetramethoxyphenanthro[9,10-d]pyrimidine (1b)* (88%).

The same procedure on diarylpyrimidine **3e** provided *10,11-dimethoxyphenanthro[9,10-d]pyrimidine (1c)* (81%) as a colorless powder: mp 234–235°C (Et_2O); R_f 0.26 (30% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 4.17 (3H, s), 4.18 (3H, s), 7.67–7.78 (1H, m), 7.94 (1H, s), 8.52 (1H, dd, J=8.3, 1.6 Hz), 8.49 (1H, dd, J=8.0, 1.2 Hz), 8.66 (1H, dd, J=6.9, 1.5 Hz), 8.68 (1H, s), 9.42 (1H, s), 9.96 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.8, 56.0, 103.1, 105.3, 120.0, 122.2, 122.8, 122.6, 125.8, 126.8, 127.6, 128.2, 129.0, 149.4, 150.0, 151.9, 152.9, 155.5; FTIR (neat film, cm^{-1}): 1617; EIMS (*m/z*, %) 290 (M^+, 100), 275 (M−CH_3, 24). Anal. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.29; H, 4.81; N, 9.55.

The same procedure on diarylpyrimidine **3f** provided *10,11-dimethoxyphenanthro[9,10-d]pyrimidine (1c)* (86%).

The same procedure on diarylpyrimidine **3g** provided *6,7-dimethoxyphenanthro[9,10-d]pyrimidine (1d)* (80%) as a colorless powder: mp 215–216°C (50% hexane/EtOAc); R_f 0.27 (30% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 7.73 (1H, ddd, J=8.1, 8.1, 1.1 Hz), 7.85 (1H, ddd, J=8.1, 8.1, 1.5 Hz), 7.98 (1H, s), 8.00 (1H, s), 8.49 (1H, dd, J=8.1, 1.1 Hz), 9.29 (1H, dd, J=8.1, 1.5 Hz), 9.43 (1H, s), 9.87 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.9, 102.8, 104.2, 120.6, 122.0, 124.2, 125.6, 126.7, 130.7, 132.5, 149.8, 150.2, 152.6, 155.0; FTIR (neat film, cm^{-1}): 1603; EIMS (*m/z*, %) 290 (M^+, 100), 275 (M−CH_3, 10). Anal. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.41; H, 4.89; N, 9.35.

The same procedure on diarylpyrimidine **3h** provided *6,7-dimethoxyphenanthro[9,10-d]pyrimidine (1d)* (84%).

The same procedure on diarylpyrimidine **3i** provided *6,7-dimethoxyphenanthro[9,10-d]pyrimidine (1d)* (67%).

The same procedure on diarylpyrimidine **3j** provided *6,7-dimethoxyphenanthro[9,10-d]pyrimidine (1d)* (62%).

The same procedure on diarylpyrimidine **3k** provided [1,3]dioxolo[2,3-*d*]phenanthro[9,10-*d*]pyrimidine (1e) (89%) as a colorless powder: mp 240–241°C (MeOH); R_f 0.38 (30% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 6.17 (2H, s), 7.71 (1H, dd, J=8.3, 7.1 Hz), 7.80 (1H, dd, J=7.9, 7.1 Hz), 7.90 (1H, s), 7.93 (1H, s), 8.37 (1H, d, J=8.3 Hz), 9.26 (1H, d, J=7.9 Hz), 9.40 (1H, s), 9.74 (1H, s); ^{13}C NMR ($CDCl_3$) δ 100.7, 101.9, 102.1, 122.2, 122.4, 125.6, 127.0, 128.0, 130.8, 132.8, 148.7, 149.3, 150.1, 153.1, 155.2; FTIR (neat film, cm^{-1}): 1621; EIMS (*m/z*, %) 274 (M^+, 100). Found: C, 74.21; H, 3.59; N, 10.28.

Anal. Calcd for $C_{17}H_{10}N_2O_2$: C, 74.44; H, 3.67; N, 10.21. Found: C, 74.21; H, 3.59; N, 10.28.

3.2.7. Synthesis of phenanthro[9,10-*d*][1,2]oxazoles via stannylation/biaryl coupling. Phenanthro[9,10-*d*]-[1,2]oxazole (2a). Typical procedure. A heavy wall-pressure tube was charged with diarylisoxazole **4b** (418 mg, 0.89 mmol), $Pd(PPh_3)_2Cl_2$ (19.3 mg, 27 μmol), and degassed dioxane (19 mL) under nitrogen. A solution of Me_6Sn_2 (440 mg, 1.33 mmol) in degassed 1,4-dioxane (7.4 mL) was added dropwise to the resulting suspension, and after flushing with nitrogen at room temperature for 15 min, the mixture was heated at 115°C in an autoclave for 50 min. After cooling, the resulting black suspension was centrifuged and the deposited black palladium was washed with CH_2Cl_2 (1×3 mL). The combined organic solvents were washed with a saturated KF solution (1×7 mL), dried over anhydrous Na_2SO_4 and the solvent was evaporated in vacuo. The resulting yellow residue was purified by flash chromatography using 30% hexane/EtOAc as eluent, providing a colorless oil which was crystallized from MeOH. Phenanthro[1,2]oxazole **2a** (0.173 g, 89%) was obtained as a colorless powder: mp 235–236°C (MeOH) (lit.[43] 241°C (C_6H_6)); R_f 0.34 (30% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 7.63–7.71 (2H, m), 7.73–7.84 (2H, m), 8.14 (1H, dd, *J*=6.7, 2.2 Hz), 8.46 (1H, dd, *J*=8.0, 1.6 Hz), 8.66–8.73 (2H, m), 9.11 (1H, s); ^{13}C NMR ($CDCl_3$) δ 119.8, 122.7, 123.7, 123.8, 123.9, 125.4, 126.3, 127.4, 127.7, 127.9, 129.0, 129.6, 131.5, 145.6; FTIR (neat film, cm^{-1}): 1615; EIMS (*m/z*, %) 219 (M^+, 100). Anal. Calcd for $C_{15}H_9NO$: C, 82.18; H, 4.14; N, 6.39. Found: C, 82.02; H, 4.29; N, 6.38.

The same procedure on diarylisoxazole **4d** provided *5,6,9,10-tetramethoxyphenanthro[9,10-d][1,2]oxazole (2b)* (73%) as a colorless powder: mp 216–217°C (20% EtOAc/hexane); R_f 0.30 (30% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 4.06 (6H, s), 4.11 (3H, s), 4.14 (3H, s), 7.37 (1H, s), 7.67 (1H, s), 7.72 (2H, s), 8.99 (1H, s); ^{13}C NMR ($CDCl_3$) δ 56.0, 56.9, 102.5, 103.7, 104.3, 112.5, 113.1, 119.1, 122.1, 125.7, 128.3, 132.0, 145.2, 148.3, 149.1, 149.5, 150.5; FTIR (neat film, cm^{-1}): 1606; EIMS (*m/z*, %) 339 (M^+, 100), 324 ($M-CH_3$, 25). Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 67.39; H, 5.27; N, 4.09.

The same procedure on diarylisoxazole **4f** provided *9,10-dimethoxyphenanthro[9,10-d][1,2]oxazole (2c)* (81%) as a colorless powder: mp 249–250°C (MeOH); R_f 0.56 (20% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 4.10 (3H, s), 4.14 (3H, s), 7.62–7.65 (2H, m), 7.71 (1H, s), 7.96 (1H, s), 8.13 (1H, dd, *J*=8.1, 1.4 Hz), 8.50 (1H, dd, *J*=7.6, 1.4 Hz), 9.06 (1H, s); ^{13}C NMR ($CDCl_3$) δ 56.0, 56.2, 102.7, 104.4, 112.8, 114.2, 123.2, 124.0, 124.7, 125.8, 126.3, 127.0, 128.2, 145.6, 149.9, 150.8, 160.3; FTIR (neat film, cm^{-1}): 1601; EIMS (*m/z*, %) 279 (M^+, 100), 264 ($M-CH_3$, 10). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.10; H, 4.69; N, 5.01. Found: C, 73.21; H, 4.84; N, 5.17.

The same procedure on diarylisoxazole **4h** provided *5,6-dimethoxyphenanthro[9,10-d][1,2]oxazole (2d)* (78%) as a yellow powder: mp 219–220°C (MeOH); R_f 0.57 (30% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 4.11 (3H, s), 4.20 (3H, s), 7.43 (1H, s), 7.68 (1H, ddd, *J*=7.9, 7.1, 1.3 Hz), 7.76 (1H, ddd, *J*=7.1, 7.1, 1.6 Hz), 7.99 (1H, s), 8.43 (1H, dd, *J*=7.1, 1.2 Hz), 8.54 (1H, dd, *J*=7.9, 1.6 Hz), 9.05 (1H, s); ^{13}C NMR ($CDCl_3$) δ 56.0, 56.1, 104.5, 104.9, 113.8, 118.8, 119.9, 122.7, 122.8, 123.1, 126.6, 128.6, 131.0, 145.3, 148.5, 150.2, 160.0; FTIR (neat film, cm^{-1}): 1620; EIMS (*m/z*, %) 279 (M^+, 100). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.10; H, 4.69; N, 5.01. Found: C, 73.14; H, 4.55; N, 5.09.

When the same procedure was applied to dibromoarylisoxazole **4a** at 140°C for 16–18 h, *10-iminomethylen-9-phenanthrol (13a)* was obtained (12%) as a colorless oil: R_f 0.17 (30% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 6.41 (1H, bs), 7.32 (1H, dd, *J*=8.0 Hz), 7.39 (1H, dd, *J*=7.0, 6.5 Hz), 7.51 (1H, dd, *J*=7.6, 7.4 Hz), 7.56–7.68 (2H, m), 8.32 (1H, dd, *J*=8.7, 8.3 Hz), 8.39–8.50 (2H, m), 11.96 (1H, bs); ^{13}C NMR ($CDCl_3$) δ 104.6, 118.5, 122.5, 123.5, 123.7, 124.6, 126.6, 126.8, 127.8, 131.0, 131.6, 132.9, 135.6, 152.4, 182.6; FTIR (neat film, cm^{-1}): 3254, 1619; EIMS (*m/z*, %) 221 (M^+, 88), 220 ($M-1$, 100). Anal. Calcd for $C_{15}H_{11}NO$: C, 81.49; H, 5.01; N, 6.33. Found: C, 81.49; H, 5.17; N, 6.46.

When the same procedure was applied to dibromoarylisoxazole **4c** at 140°C for 16–18 h, *10-hydroxy-2,3,6,7-tetramethoxy-9-phenanthrenecarbonitrile (12b)* was obtained (49%) as a colorless powder: mp 229–230°C (50% hexane/EtOAc); R_f 0.27 (40% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 4.05 (6H, s), 4.09 (3H, s), 4.14 (3H, s), 7.31 (1H, s), 7.66 (3H, s); ^{13}C NMR ($CDCl_3$) δ 56.1, 56.2, 102.5, 103.4, 104.9, 117.3, 119.5, 123.8, 128.4, 131.0, 132.2, 135.8, 148.3, 149.0, 150.2, 152.0, 155.6; FTIR (neat film, cm^{-1}): 3224, 2204; EIMS (*m/z*, %) 339 (M^+, 100). Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 67.31; H, 5.19; N, 4.08.

When the same procedure was applied to dibromoarylisoxazole **4e** at 140°C for 16–18 h, the following products were isolated.

3.2.8. 2,3-Dimethoxy-10-hydroxy-9-phenanthrenecarbonitrile (12c). (56%); as a colorless oil: R_f 0.37 (20% hexane/EtOAc); ^{1}H NMR (DMSO-d_6) δ 2.97 (3H, s), 3.08 (3H, s), 6.58 (1H, dd, *J*=8.0, 7.6 Hz), 6.64 (1H, dd, *J*=8.0, 7.6 Hz), 6.84 (1H, s), 6.92 (1H, d, *J*=8.0 Hz), 7.18 (1H, s), 7.77 (1H, d, *J*=8.0 Hz); ^{13}C NMR (DMSO-d_6) δ 55.9, 56.2, 88.4, 104.0, 104.5, 117.2, 119.2, 123.7, 125.0, 127.8, 128.2, 129.2, 132.1, 149.6, 150.0, 158.3; FTIR (neat film, cm^{-1}): 3251, 2222; EIMS (*m/z*, %) 279 (M^+, 100). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.01. Found: C, 72.99; H, 4.85; N, 5.05.

3.2.9. 2,3-Dimethoxy-9-iminomethylen-10-hydroxyphenanthrene (13c). (19%) as a mixture of *cis*/*trans* isomers; colorless oil: R_f 0.19 (30% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 4.05 (3H, s), 4.09 (3H, s), 6.59 (1H, bs), 7.28 (1H, ddd, *J*=8.0, 8.0, 1.3 Hz), 7.43–7.68 (3H, m), 7.96 (1H, s), 8.14 (1H, dd, *J*=8.1, 1.3 Hz), 8.44 (1H, bs), 11.93 (1H, bs); ^{13}C NMR ($CDCl_3$) δ 56.0, 103.7, 104.2, 107.1, 118.6, 122.9, 123.6, 124.5, 127.1, 128.5, 128.6, 130.6, 131.5, 132.0, 132.1, 132.6, 133.1, 149.0, 152.6, 181.6;

FTIR (neat film, cm^{-1}): 3228, 1626; EIMS (*m/z*, %) 281 (M^+, 100), 139 (11).

When the same procedure was applied to dibromoarylisoxazole **4k** at 140°C for 16–18 h, the following products were isolated.

3.2.10. 5-Cyano-6-hydroxyphenanthro[2,3-*d*][1,3]dioxole (12d). (44%); colorless oil: R_f 0.54 (30% hexane/EtOAc); ^1H NMR (DMSO-d_6) δ 5.27 (2H, s), 6.35 (1H, s), 6.74 (1H, dd, J=7.8, 7.6 Hz), 6.85 (1H, dd, J=8.0, 7.6 Hz), 7.37 (1H, s), 7.42 (1H, d, J=8.0 Hz), 7.79 (1H, d, J=8.4 Hz); ^{13}C NMR (DMSO-d_6) δ 91.0, 101.5, 102.2, 117.0, 121.1, 123.9, 125.9, 126.6, 128.5, 130.2, 132.5, 147.3, 149.2, 157.7; FTIR (neat film, cm^{-1}): 3263, 2223; EIMS (*m/z*, %) 263 (M^+, 100). Anal. Calcd for $C_{16}H_9NO_3$: C, 73.00; H, 3.44; N, 5.32. Found: C, 73.,09; H, 3.61; N, 5.37.

3.2.11. 6-Hydroxy-5-iminomethylenphenanthro[2,3-*d*]-[1,3]dioxole (13d). (16%); colorless oil: R_f 0.24 (30% hexane/EtOAc); ^1H NMR ($CDCl_3$) δ 6.02 (2H, s), 6.12 (1H, bs), 7.13 (1H, s), 7.46 (1H, dd, J=7.9, 7.3 Hz), 7.65 (1H, dd, J=7.9, 7.3 Hz), 7.71 (1H, s), 8.11 (1H, d, J=7.9 Hz), 8.26–8.34 (1H, m), 8.50 (1H, d, J=8.5 Hz), 12.09 (1H, bs); FTIR (neat film, cm^{-1}): 3261, 1618; EIMS (*m/z*, %) 265 (M^+, 100), 264 (M−1, 38). Anal. Calcd for $C_{16}H_{11}NO_3$: C, 72.44; H, 4.18; N, 5.28. Found: C, 72.41; H, 4.29; N, 5.37.

3.2.12. Sequential generation of arylboronates/biaryl coupling using bis(pinacolato)diboron. Phenanthro-[9,10-*d*][1,2]oxazole (2a). Typical procedure. A heavy wall-pressure tube was charged with diarylisoxazole **4b** (840 mg, 1.80 mmol), $PdCl_2(PPh_3)_2$ (241 mg, 0.342 mmol), bis(pinacolato)diboron (501 mg, 2.0 mmol), NaOAc (990 mg, 5.4 mmol) and degassed DMF (7.5 mL) and purged with Ar at room temperature for 15 min. After closing the tube, the mixture was heated at 120°C in an autoclave for 17 h until TLC showed the completion of the reaction. After cooling, the resulting black suspension was centrifugated and the deposited black palladium was removed. The reaction mixture was degassed again and anhydrous K_3PO_4 (1.47 g, 9 mmol) and $PdCl_2(PPh_3)_2$ (64.6 mg, 91.9 μmol) were added. After closing the tube, the resulting mixture was heated at 120°C in an autoclave for 55 h. After cooling, the resulting black suspension was centrifugated and the deposited black palladium was abundantly washed with dichlromethane. The combined organic solvents were washed with saturated NH_4Cl solution (2×10 mL), dried over anhydrous sodium sulfate and filtered off. The solvent was evaporated under pressure (1 mmHg, 90°C). The resulting residue was purified by flash column chromatography using 20% EtOAc/hexane as eluent providing phenanthro[1,2]oxazole **2a** (43.1 mg, 11%) as a colorless powder.

The same procedure on isoxazole **4a** provided phenanthro[9,10-*d*][1,2]oxazole (2a) (6%).

The same procedure on isoxazole **4c** provided *5,6,9,10-tetramethoxyphenanthro[9,10-d][1,2]oxazole (2b)* (5%).

3.2.13. Sequential generation of arylboronates/biaryl coupling using pinacolborane. Phenanthro[9,10-*d*]-[1,2]oxazole (2a). Typical procedure. A heavy wall-pressure tube was charged with diarylisoxazole **4b** (800 mg, 1.71 mmol), $PdCl_2(PPh_3)_2$ (143.9 mg, 0.205 mmol), anhydrous Et_3N (0.7 mL, 5.1 mmol) and degassed 1,4-dioxane (25 mL). Pinacolborane (0.29 mL of a stock solution prepared as previously reported,[18f] 2.93 mmol) was added dropwise and the mixture was purged with Ar at room temperature for 15 min. After closing the tube, the mixture was heated at 120°C in an autoclave for 6 h. After cooling, the resulting black suspension was centrifugated and the deposited black palladium was removed. The reaction mixture was diluted with H_2O (80 mL) and extracted with Et_2O (5×10 mL). The organic layer was dried over anhydrous sodium sulfate, filtered off and the solvent was evaporated in vacuo. The residue was dried under pressure (1 mmHg) at room temperature over P_2O_5 for 6 h. It was transferred into a heavy-wall presure tube and disolved in degassed DMF (3 mL). A mixture of K_3PO_4 (1.38 g, 8.38 mmol) and $PdCl_2(PPh_3)_2$ (59.8 mg, 85 μmol) were added, and after closing the tube, the resulting mixture was heated at 120°C in an autoclave for 55 h until TLC showed the completion of the reaction. After cooling, the resulting black suspension was centrifugated and the deposited black palladium was abundantly washed with CH_2Cl_2. The combined organic solvents were washed with saturated NH_4Cl solution (2×15 mL), dried over anhydrous sodium sulfate and filtered off. The solvent was evaporated under pressure (1 mmHg, 90°C) and the resulting residue was purified by flash column chromatography using 20% EtOAc/hexane as eluent, providing phenanthro[1,2]oxazole **2a** (48 mg, 13%) as a colorless powder.

The same procedure on isoxazole **4a** provided phenanthro[9,10-*d*][1,2]oxazole (2a) (7%).

The same procedure on isoxazole **4c** provided *5,6,9,10-tetramethoxyphenanthro[9,10-d][1,2]oxazole (2b)* (4%).

3.2.14. Synthesis of phenanthro[9,10-*d*]pyrimidines and phenanthro[9,10-*d*][1,2]oxazoles via oxidative coupling reaction. 5,6,9,10-Tetramethoxyphenanthro[9,10-*d*]-[1,2]oxazole (2b). Typical procedure. A solution of PIFA (84 mg, 0.19 mmol) in dry dichloromethane (0.6 mL) was added to a stirred solution of isoxazole **4m** (61 mg, 0.17 mmol) in dry dichloromethane (2.5 mL) at −40°C under argon. After adding $BF_3{\cdot}Et_2O$ (0.02 mL, 0.18 mmol), the resulting brown solution was stirred for 15 min. at −40°C, allowed to warm at room temperature and absorbed on silica gel (0.5 g). Purification by flash cromatography using 50–80% EtOAc/hexane as eluent provided phenanthro[1,2]oxazole **2b** (0.049 g, 85%) as a colorless powder.

The same procedure on diarylisoxazole **4n** provided *9,10-dimethoxyphenanthro[9,10-d][1,2]oxazole 2c* (80%) as a colorless powder.

The same procedure on diarylisoxazole **4o** provided *5,6,9,10,11-pentamethoxyphenanthro[9,10-d][1,2]oxazole 2e* (61%) as a yellow powder: mp 221–222°C (MeOH); R_f 0.31 (20% hexane/EtOAc); ^1H NMR ($CDCl_3$) δ 4.06 (3H, s), 4.11 (3H, s), 4.12 (3H, s), 4.14 (3H, s), 4.19 (3H, s), 7.43

(1H, s), 7.67 (1H, s), 7.81 (1H, s), 9.03 (1H, s); ^{13}C NMR ($CDCl_3$) δ 56.1, 56.2, 61.4, 62.0 (OMe), 100.5, 104.4, 105.0, 110.0, 113.8, 120.1, 122.0, 128.4, 144.5, 142.0, 148.5, 149.2, 150.2, 154.5, 159.0; FTIR (neat film, cm^{-1}): 1629; EIMS (*m/z*, %) 369 (M^+, 100), 354 ($M-CH_3$, 37). Anal. Calcd for $C_{20}H_{19}NO_6$: C, 65.03; H, 5.18; N, 3.79. Found: C, 65.29; H, 5.22; N, 3.86.

When the same procedure was applied to diarylisoxazole **4l** only traces of **phenanthro[9,10-*d*][1,2]oxazole 2a** (<5%) could be detected according to the following significant signals in crude ^{1}H NMR and GC-MS spectra: ^{1}H NMR ($CDCl_3$) δ 8.46 (1H, dd, J=8.0, 1.6 Hz, H_{arom}), 8.66–8.73 (2H, m, H_{arom}), 9.11 (1H, s, H-3); EIMS (*m/z*, %) 219 (M^+, 100).

The same procedure on diarylpyrimidine **3l** provided phenanthro[9,10-*d*]pyrimidine (1a) (23%).

The same procedure on diarylpyrimidine **3m** provided *6,7,10,11-tetramethoxyphenanthro[9,10-d]pyrimidine (1b)* (74%).

The same procedure on diarylpyrimidine **3n** provided *10,11-dimethoxyphenanthro[9,10-d]pyrimidine (1c)* (81%).

The same procedure on diarylpyrimidine **3o** provided *6,7,10,11,12-pentamethoxyphenanthro[9,10-d]pyrimidine (1f)* (51%) as a colorless powder: mp 238–239°C (MeOH); R_f 0.34 (2% MeOH/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.13 (3H, s), 3.21 (3H, s), 3.22 (3H, s), 3.24 (3H, s), 3.33 (3H, s), 7.02 (1H, s), 7.12 (1H, s), 7.32 (1H, s), 8.55 (1H, s), 9.28 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.9, 56.0, 56.2, 60.5, 60.9, 101.5, 104.6, 105.9, 114.0, 120.1, 123.5, 130.7, 142.6, 147.7, 150.2, 150.7, 153.0, 156.0; FTIR (neat film, cm^{-1}): 1600; EIMS (*m/z*, %) 380 (M^+, 39), 365 ($M-CH_3$, 100). Anal. Calcd for $C_{21}H_{20}N_2O_5$: C, 66.31; H, 5.30; N, 7.36. Found: C, 66.46; H, 5.25; N, 7.21.

The same procedure on diarylpyrimidine **3p** provided *6,7,8,10,11-pentamethoxyphenanthro[9,10-d]pyrimidine (1g)* (88%) as a colorless powder: mp 228–229°C (MeOH); R_f 0.31 (2% MeOH/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.84 (3H, s), 3.91 (3H, s), 3.94 (3H, s), 3.96 (3H, s), 4.17 (3H, s), 8.13 (1H, s), 8.47 (1H, s), 8.88 (1H, s), 9.36 (1H, s.), 10.26 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.0, 55.4, 56.4, 101.8, 105.2, 107.9, 117.3, 122.0, 123.3, 127.5, 143.9, 148.3, 149.5, 151.6, 151.6, 151.9, 152.8; FTIR (neat film, cm^{-1}): 1601; EIMS (*m/z*, %) 380 (M^+, 100), 365 ($M-CH_3$, 34). Anal. Calcd for $C_{21}H_{20}N_2O_5$: C, 66.31; H, 5.30; N, 7.36. Found: C, 66.38; H, 5.21; N, 7.49.

3.2.15. Stannylation/biaryl coupling of *o*,*o*′-dihalogenated deoxybenzoins. 2,3,6,7-Tetramethoxy-9-phenanthrol (19). Typical procedure. A heavy wall-pressure tube was charged with deoxybenzoin **17c** (90 mg, 0.19 mmol), $Pd(PPh_3)_2Cl_2$ (6.8 mg, 9.5 μmol), and degassed 1,4-dioxane (5.7 mL) under nitrogen. A solution of Me_6Sn_2 (93 mg, 0.28 mmol) in degassed 1,4-dioxane (2.7 mL) was added dropwise to the resulting suspension, and after flushing with nitrogen at room temperature for 15 min, the mixture was heated at 140°C in an autoclave for 7 days, adding additional amounts of the catalyst (3×1 mg, 7.9 μmol) every 36–48 h. After cooling, the resulting black suspension was centrifuged and the deposited black palladium was washed with CH_2Cl_2 (1×3 mL). The combined organic solvents were washed with a saturated aqueous KF solution (1×7 mL), dried over anhydrous Na_2SO_4 and the solvent was evaporated in vacuo. The residue was purified by flash chromatography using 40–50% hexane/EtOAc as eluent. Crystallization of the resulting yellow oil from Et_2O afforded phenanthrol **19** (0.036 g, 61%) as a colorless powder: mp 188–189°C (Et_2O); R_f 0.54 (10% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.94 (3H, s), 3.95 (3H, s), 3.96 (3H, s), 4.29 (3H, s), 5.72 (1H, bs), 6.86 (1H, s), 7.01 (1H, s), 7.60 (1H, s), 7.72 (1H, s), 7.75 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.7, 55.8, 55.9, 102.5, 102.7, 103.1, 103.4, 104.2, 106.7, 119.2, 120.0, 127.0, 147.3, 148.0, 148.4, 149.0; FTIR (neat film, cm^{-1}): 3401; EIMS (*m/z*, %) 315 (M+1, 6), 165 (100). Anal. Calcd for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77%). Found: C, 68.66; H, 5.69.

The same procedure on deoxybenzoin **17d** provided *2,3,6,7-tetramethoxy-9-phenanthrol (19)* (66%) as a colorless powder.

When the same procedure on deoxybenzoin **17c** was employed using shorter reaction times, mixtures of *2-(2-bromo-4,5-dimethoxyphenyl)-1-(2-trimethylstannyl-4,5-dimethoxyphenyl)ethanone* and *1-(2-bromo-4,5-dimethoxyphenyl)-2-(2-trimethylstannyl-4,5-dimethoxyphenyl)ethanone (18a)* and **(18b)** were detected by means of the following selected spectroscopic data: R_f 0.59 (40% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 0.11 (satel. Sn, $^2J(^{119}Sn-^1H)$=29 Hz), 0.22 (9H, s, Me_3Sn), 0.33 (satel. $^2J(^{117}Sn-^1H)$=27 Hz), 3.65 (3H, s, OMe), 3.69 (3H, s, OMe), 3.89 (3H, s, OMe), 3.96 (3H, s), 4.22 (2H, s, CH_2CO); ^{13}C NMR ($CDCl_3$) δ −7.42 (Me_3Sn), 55.2, 55.6, 56.0, 56.6 (OMe), 113.4, 114.7, 185 (CO); EIMS (*m/z*, %) 559 (M+1, 16), 557 (M−1, 15), 316 (M−Br−Me_3Sn, 80).

3.2.16. Stannylation/biaryl coupling of *o*,*o*′-dihalogenated enaminoketones. 9-Hydroxy-2,3,6,7-tetramethoxy-10-phenanthrenecarbaldehyde (15). Typical procedure. A heavy wall-pressure tube was charged with enaminone **5c** (150 mg, 0.24 mmol), $Pd(PPh_3)_2Cl_2$ (8.6 mg, 12 μmol), and degassed 1,4-dioxane (5.7 mL) under nitrogen. A solution of Me_6Sn_2 (119 mg, 0.36 mmol) in degassed 1,4-dioxane (3.4 mL) was added dropwise to the resulting suspension, and after flushing with nitrogen at room temperature for 15 min, the mixture was heated at 140°C in an autoclave for 6.5 h. After cooling, the resulting black suspension was centrifuged and the deposited black palladium was washed with CH_2Cl_2 (1×3 mL). The combined organic solvents were washed with a saturated aqueous KF solution (1×7 mL), dried over anhydrous Na_2SO_4 and the solvent was evaporated in vacuo. The residue was purified by flash chromatography using 1–2% MeOH/EtOAc as eluent. Crystallization of the resulting yellow oil from MeOH afforded phenanthrol **15** (59 mg, 72%) as a colorless powder: mp 209–211°C (MeOH); R_f 0.51 (10% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 4.05 (3H, s), 4.07 (3H, s), 4.09 (3H, s), 4.15 (3H, s), 7.62 (1H, s), 7.65 (1H, s), 7.67 (1H, s), 7.80 (1H, s), 10.65 (1H, s), 14.39 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.7, 56.0, 56.2, 100.0, 102.4, 103.9, 104.4, 107.2, 117.9, 118.7, 124.3, 130.4, 147.4,

148.7, 149.6, 153.0, 162.5, 192.2; FTIR (neat film, cm^{-1}): 3200, 1607; EIMS (*m/z*, %) 342 (M^+, 100), 327 ($M-CH_3$, 24). Anal. Calcd for $C_{19}H_{18}O_6$: C, 66.66; H, 5.30. Found: C, 66.34; H, 5.46.

The same procedure on enaminone **5d** provided *9-hydroxy-2,3,6,7-tetramethoxy-10-phenanthrenecarbaldehyde (15)* (72%).

3.2.17. Heterocyclization assays using hydroxylamine. 10-Hydroxy-9-hydroxyiminomethylen-2,3,6,7-tetramethoxyphenanthrene (16). Ground Na_2CO_3 (91 mg, 0.85 mmol) and $NH_2OH{\cdot}HCl$ (13.3 mg, 0.19 mmol) were added to a solution of aldehyde **15** (59 mg, 0.17 mmol) in dry ^{i}PrOH (2 mL) in a heavy-wall screw capped tube at room temperature. After closing the tube, it was heated in an oven at 140°C for 17 h. After cooling, the mixture was poured onto a saturated aqueous NH_4Cl solution (10 mL). The aqueous layer was extracted with dichloromethane (3×5 mL) and the combined organic layers were dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was crystallized from $CHCl_3$, providing hydroxyiminophenanthrol **16** (37 mg, 71%) as a colorless powder: mp 205–207°C ($CHCl_3$); R_f 0.58 (20% hexane/EtOAc); ^{1}H NMR (CD_3COCD_3) δ 3.89 (3H, s), 3.90 (3H, s), 3.91 (3H, s), 4.12 (3H, s), 7.59 (1H, s), 7.71 (1H, s), 7.96 (1H, s), 7.98 (1H, s), 9.21 (1H, s), 11.96 (1H, bs); ^{13}C NMR (CD_3COCD_3) δ 55.8, 56.0, 56.2, 56.3, 103.1, 104.2, 105.6, 119.7, 120.4, 125.5, 127.6, 148.4, 150.0, 150.7, 152.1; FTIR (neat film, cm^{-1}): 3431, 1612; EIMS (*m/z*, %) 357 (M^+, 21), 339 ($M-H_2O$, 100). Anal. Calcd for $C_{19}H_{19}NO_6$: C, 63.86; H, 5.36; N, 3.92. Found: C, 63.74; H, 5.49; N, 4.08.

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