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Synthesis of [N,P] ligands based on pyrrole. Application to the total synthesis of arnottin I

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ABSTRACT

This paper describes the synthesis of a new class of [N,P] ligands based on pyrrole with a dimethylamino group as hard donor and a phosphine moiety as soft base. We have also modified the phosphine fragment to change the electronic and steric properties of these ligands. Palladium complex **3a** proved to be very efficient in Heck cross-coupling reactions and in intramolecular aryl–aryl couplings of esters and amides. We have demonstrated the applicability and efficiency of this novel catalyst in the total synthesis of the natural product arnottin I.

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1. Introduction

The structural diversity of natural products has been driven by imagination and creativity in organic synthesis, and has achieved extraordinary progress in the development of procedures for obtaining complex molecules.[1] In this context, the development of novel strategies to achieve coupling reactions promoted by a transition metal has made possible to obtain structurally complex molecules, forming extremely selective bonds despite the presence of a wide variety of reactive functional groups.[2] Therefore, the development of new bidentate ligands has acquired great significance and currently a large number of ligands with wide-ranging structural motifs are known.[3] Mixed donor ligands [N,P][4] have been successfully used in a large number of catalytic processes such as polymerization and oligomerization of olefins,[5] C–C coupling reactions,[6] hydrogenation, and hydroformylation reactions,[7] among others.

However, despite the variety of frameworks used to obtain bidentate ligands, only a few examples contain pyrrole as the main structural motif.[8,9] Some of them are based on 2-phosphanyl-1-arylpyrrole ligands (PAP ligands), which have demonstrated a broad range of catalytic applications, and are commercially available as CataCXium-P®.[8] In all cases, the substituents connected to the pyrrole nitrogen atom are based on aryl substituents forming an N–C bond. More recently, Enthaler and co-workers[9a] described a new class of PAP ligands, in which the carbon group was replaced by an amine functionality to generate an N–N bond. Thus, the amine-based group can be an additional donor, which can be coordinated to the metal center. However, their coordination behavior continues to be that of a monodentate ligand in the presence of iron (0) carbonyl precursors, a fact, which can be attributed to the steric hindrance of introduced diphenylamino groups. Inspired by this concept, we have envisaged introducing a dimethylamino group at 1-position of the pyrrole backbone with the idea of reducing the steric hindrance of this amino group and increasing the σ-donor character, to allow its coordination as a bidentate ligand. We report below an efficient synthesis of new [N,P] ligands based on pyrrole, with a combination of hard and soft donor atoms (Fig. 1).

We have applied variations of the phosphine fragment in order to modify the electronic and steric properties of these ligands. The Pd complexes derived from these ligands are very efficient in inter- and intramolecular coupling reactions, and the applicability of these couplings became evident with the total synthesis of arnottin I, a coumarin-based natural product.

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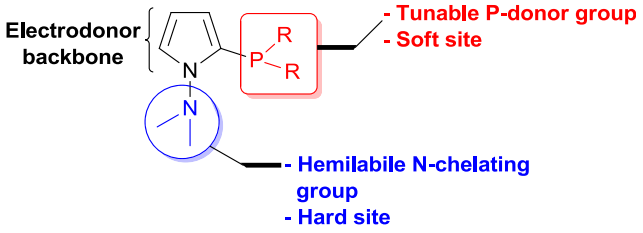
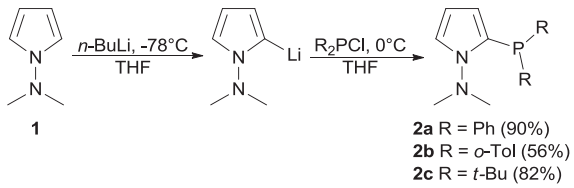


Fig. 1. Features of [N,P] ligands based on pyrrole.

2. Results and discussion

2.1. Synthesis of [N,P] ligands based on pyrrole and their palladium (II) complexes

The synthesis of bifunctional ligands **2** was made taking advantage of the regioselective lithiation of 1-(dimethylamino)pyrrole 1.[10] This metalation was easily accomplished using *n*-BuLi at −78 °C in anhydrous THF. Thus, the 2-lithiopyrrole obtained was quenched with the corresponding chlorophosphine at 0 °C, making possible to obtain good yields of bidentate ligands **2a**–**c** (Scheme 1).



Scheme 1. Preparative route to of [N,P] ligands based on pyrrole.

The [N,P] ligands based on pyrrole **2a**–**c** were characterized by spectroscopic techniques and obtained data were consistent with the literature for this kind of compounds; ^{31}P NMR spectra reveal interesting properties for these ligands, showing that the signals for the phosphanyl pyrrole **2a**–**c** are shifted to lower frequencies in comparison to phenyl phosphines (Table 1),[11] as a result of the electron-releasing effect of the pyrrole ring.

Table 1
^{31}P NMR chemical shift for [N,P] ligands based on pyrrole and their phosphine analogues

R	PyrrolePR$_2$ (**2**)	PhPR$_2$	Δδ
Ph	−29.2	−6	23.2
o-Tolyl	−45.7	−21.7	24
t-Bu	−1.2	40.5	41.7

The structural arrangement for **2a** was unequivocally established by X-ray diffraction analysis; one phenyl ring in this structure is in disorder generating two orientations in 78:22 ratio. Only the major contributor is shown in Fig. 2.

Once ligands **2a**–**c** were obtained, we studied their coordination ability to Pd (II). We prepared complexes **3a**–**c** by treating **2a**–**c** with Pd(CH$_3$CN)$_2$Cl$_2$ in CHCl$_3$, obtaining, in all cases, a yellow powder, after recrystallization from hexane–CH$_2$Cl$_2$ (Scheme 2).

As expected, the ^{31}P NMR spectra showed that the coordinated phosphine signals are shifted to higher frequencies regarding the free ligands, due to coordination with the Pd atom. Likewise, in ^{1}H NMR the signal assigned to the dimethylamine moiety coordinated to Pd (II) is shifted by approximately 1 ppm to a higher frequency in

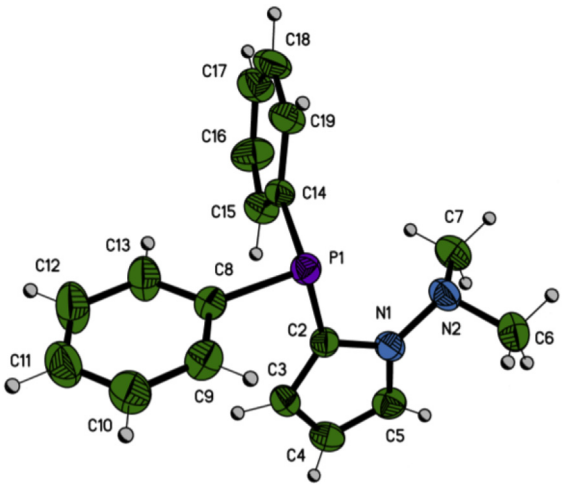
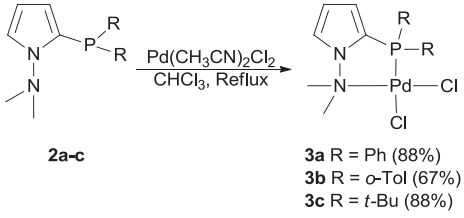


Fig. 2. ORTEP representation of ligand **2a**. Ellipsoids are shown at 30% probability level. Selected bond length (Å) and bond angles (°): P(1)–C(14B), 1.776(19); P(1)–C(2), 1.815(2); P(1)–C(8), 1.839(2); P(1)–C(14), 1.879(12); N(1)–C(5), 1.362(3); N(1)–C(2), 1.370(3); N(1)–N(2), 1.411(3); N(2)–C(7), 1.460(4); N(2)–C(6), 1.462(3); C(14B)–C(15B), 1.377 (12); C(14B)–C(19B), 1.393(12); C(15B)–C(16B), 1.401(12); C(16B)–C(17B), 1.376(11); C(17B)–C(18B), 1.374(11); C(18B)–C(19B), 1.372(11); C(14B)–P(1)–C(2), 104.5(8); C(14B)–P(1)–C(8), 103.0(12); C(2)–P(1)–C(8), 97.60(10); C(2)–P(1)–C(14), 99.7(5); C(8)–P(1)–C(14), 101.3(8); C(5)–N(1)–C(2), 109.6(2); C(5)–N(1)–N(2), 128.65(19); C(2)–N(1)–N(2), 121.76(18); N(1)–N(2)–C(7), 110.9(2); N(1)–N(2)–C(6), 109.90(19); C(7)–N(2)–C(6), 111.3(2); C(15B)–C(14B)–C(19B), 117.0 (13); C(15B)–C(14B)–P(1), 125.5(15); C(19B)–C(14B)–P(1), 117.4(14); C(19)–C(14)–P(1), 118.3(9); N(1)–C(2)–C(3), 106.7(2); N(1)–C(2)–P(1), 120.70(16); C(3)–C(2)–P(1), 132.45(19); C(13)–C(8)–C(9), 117.2(2); C(13)–C(8)–P(1), 124.62(19); C(9)–C(8)–P(1), 118.13(18); C(15)–C(14)–P(1), 123.0(9).



Scheme 2. Coordination of [N,P] ligands **2a**–**c** with Pd(MeCN)$_2$Cl$_2$.

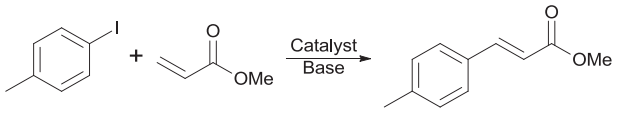
comparison to **2a**–**c**. This behavior has also been observed in ^{13}C NMR (Δδ ≈ 9 ppm). These spectroscopic data lead us to suggest that these ligands behave as bidentate donors.

2.2. Catalytic evaluation of complexes 3a–c in coupling reactions

To evaluate the potential of complexes **3a**–**c** as catalyst precursors in the Mizoroki–Heck reaction, we performed a series of experiments using cross-coupling between methyl acrylate and 4-iodotoluene as a model reaction. To determine optimal conditions, the reaction was performed under different conditions, screening parameters such as base, reaction time, and catalyst loading under conventional heating at 140 °C. The results are summarized in Table 2.

Our initial exploration of reaction conditions focused on catalyst loading using complex **3a** as a catalyst, DMF as a solvent, and Et$_3$N as a base. As shown in Table 2, it is evident that the highest TON value (entry 6) was achieved with low catalyst loading (0.01 mol %) after 2 h of reaction time. When we used higher catalyst loading under the same conditions (entries 2 and 3), the reaction produced high conversions of the coupled product but the isolated yield was slightly decreased. Naturally, no reaction took place in the absence of the catalyst (entry 1).

Table 2
Evaluation of catalytic conditions for Mizoroki–Heck cross-coupling of 4-iodotoluene with methyl acrylate[a]



Entry	Catalyst	Time (h)	[Pd] (mol %)	Base	Yield[b] (%)	TON	TOF
1	**3a**	2	0	Et_3N	0	0	0
2	**3a**	2	0.5	Et_3N	90	180	90
3	**3a**	2	0.1	Et_3N	97	970	485
4	**3a**	0.5	0.01	Et_3N	31	3100	6200
5	**3a**	1	0.01	Et_3N	95	9500	9500
6	**3a**	2	0.01	Et_3N	99	9900	4950
7	**3a**	3	0.01	Et_3N	90[c]	9000	3000
8	**3a**	1	0.01	K_3PO_4	91	9100	9100
9	**3a**	1	0.01	K_2CO_3	97	9700	9700
10	**3a**	1	0.01	Na_3PO_4	61	6100	6100
11	**3a**	1	0.01	Na_2CO_3	55	5500	5500
12	**3b**	1	0.01	Et_3N	97	9700	9700
13	**3c**	1	0.01	Et_3N	72	7200	7200
14	**3a**	1	0.005	Et_3N	99	19,800	19,800
15	**3b**	1	0.005	Et_3N	99	19,800	19,800
16	**3c**	1	0.005	Et_3N	77	15,400	15,400
17	**3a**	12[d]	0.005	Et_3N	90	18,000	1500
18	**3a**	36[e]	0.005	Et_3N	93	18,600	517
19	$(dppe)PdCl_2$	1	0.005	Et_3N	43	8600	8600
20	$(BINAP)PdCl_2$	1	0.005	Et_3N	79	15,800	15,800

[a] All reactions were performed with 5.0 mmol of the 4-iodotoulene, 6.0 mmol of the alkene, 5 mL of DMF, and 5.6 mmol of base at reflux conditions.
[b] Isolated yields.
[c] The formation of side-products is observed.
[d] Temperature: 120 °C.
[e] Temperature: 100 °C.

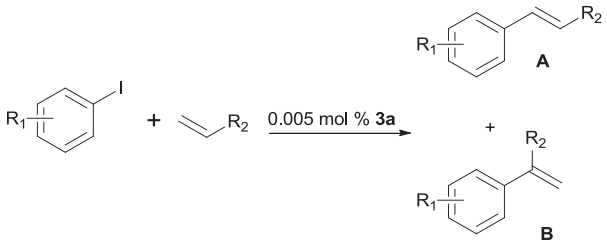
The results listed in Table 2 clearly show that optimal reaction time was 2 h of heating in DMF at 140 °C. After 3 h of reaction time (entry 7), the expected methyl cinnamate was obtained in only 90% yield. We then examined the effect of the base on the Mizoroki–Heck coupling reactions yield using 0.01 mol % catalyst loading of **3a**. After screening a variety of inorganic bases, K_2CO_3 was found to be the most effective base (entry 9), while K_3PO_4 also provided good results (entry 8). In contrast, low conversions were achieved when the counter-ion of the base was changed (entries 10 and 11), probably due to the poor solubility of Na_2CO_3 and Na_3PO_4. When we used an organic base, high yields were also obtained when the reaction was carried out with Et_3N (entry 5). Based on these results, Et_3N, an inexpensive and effective base, was selected as the best base for the Heck reaction using the mixed [N,P] bidentate ligand **3a**.

We carried out optimization studies testing the same model reaction (entries 12–16) using some precatalyst with different substituents on the phosphine moiety, in an effort to select the most effective precatalyst for the Heck reaction. Based on results in Table 2, it can be seen that the activity of the precatalyst bearing an *o*-tolyl phosphine group (**3b**) resulted in an identical yield of the desired product (entry 15) in comparison with complex **3a**, which contains a diphenyl phosphine group. However, when the coupling reaction was performed employing complex **3c**, there was a significantly lower yield (entry 16). This behavior could be explained considering that aliphatic phosphines have a strong σ-donor behavior, thereby increasing the electron density on the palladium atom, unfavorable to the reductive elimination in the Heck catalytic cycle. The steric effect of the phosphine moiety could also play an important role in the catalytic cycle, disfavoring the olefin coordination to palladium atom, and in consequence providing a poor yield of coupling product.

Additionally, two experiments at different temperatures were carried out (entries 17 and 18). As expected, the reaction proceeds more slowly at lower temperatures, but remains effective toward the formation of coupling product, in good yields. As a further step, we also compared these findings with known related catalysts in order to make evident the performance of these new complexes. Thus, two experiments were carried out using as commercial palladium complexes, $(dppe)PdCl_2$ and $(rac\text{-}BINAP)PdCl_2$ in the same reaction conditions (Table 2, entries 19 and 20). The results obtained indicate that complex **3a** is more active and efficient in this coupling reaction than commercial palladium catalyst at these reaction conditions.

Having established an effective catalytic system for this cross-coupling reaction, we next examined the scope of this procedure. As shown in Table 3, treatment of various aryl iodides with olefins, under optimized conditions as described above, was efficiently carried out in moderate to good yields of the corresponding cross-coupled products. The results indicated that catalyst **3a** is active and tolerant for a range of functionalities.

Table 3
Scope of Mizoroki–Heck cross-coupling using **3a**[a]



Entry	R^1	R^2	Time (h)	Yield[b]		TON	TOF
				A	**B**		
1	4-OMe	COOMe	1	98	—	19,600	19,600
2	4-NH_2	COOMe	2	90	—	18,000	9000
3	4-Me	COOMe	2	99	—	19,800	19,800
4	2-Me	COOMe	2	76	—	15,200	7600
5	3-Me	COOMe	1	90	—	18,000	18,000
6	4-H	COOMe	2	90	—	18,000	9000
7	4-Br	COOMe	4	66	—	13,200	3300
8	4-CF_3	COOMe	4	95	—	19,000	4750
9	4-OMe[c]	COOMe	48	26	—	26	0.54
10	4-Me	Ph	21	88	11	20,000	952
11	2-Me	Ph	24	87	7	18,800	783
12	3-Me	Ph	21	72	4	15,200	723
13	4-OMe	Ph	29	69	0	13,800	476
14	4-NH_2	Ph	7	21	1	4400	629
15	4-H	Ph	23	86	11	19,400	844
16	4-Me	Fc	2	32	16	9600	457
17	4-Me	4-Py	24	46	7	10,600	442

[a] All reactions were performed with 5.0 mmol of the aryl iodide, 6.0 mmol of the alkene, 5 mL of DMF, 0.005 mol % **3a**, and 5.6 mmol of Et_3N at reflux conditions.
[b] Isolated yields.
[c] 5.0 mmol 4-Bromoanisole as aryl halide, 6.0 mmol of the alkene, 5 mL of DMF, and 5.6 mmol of Et_3N, 20 mol % of TBAB, 1 mol % [Pd] at reflux conditions.

The effect of the substituent on the aromatic ring of the iodobenzene was examined. For this purpose, we performed a reaction between activated and deactivated aryl iodides with methyl acrylate (Table 3, entries 1–9). In every case, the substrate was converted to the desired methyl cinnamate with isolated yields ranging from 66 to 99%. From the results, it is evident that the more electron-rich aryl iodides induce faster reactions, obtaining excellent yields of the coupling products (entries 1–3). In the case of 4-bromo iodobenzene, we observed the formation of other by-products in trace amount (entry 7). To probe the effectiveness of this catalytic system in the case of other aryl halides, we also tested 4-bromoanisole as substrate (entry 9), obtaining the corresponding cinnamate in 26% yield after 48 h, although 20 mol % of TBAB as additive and 1 mol % of catalyst loading were required. This result

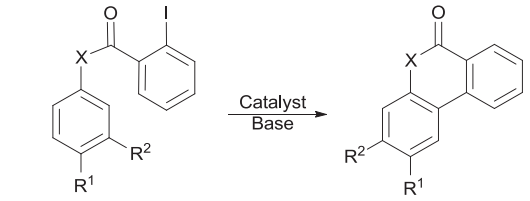
showed a poor activity of this catalytic system during the oxidative addition into the above mentioned aryl bromide.

Substrate scope of the reaction could be extended to non-activated olefins (entries 10–15). Thus, we decided to perform the Mizoroki–Heck reaction with some iodobenzenes and styrene. We observed a significant electronic effect of the *para*-substituents on the aryl iodide on the yield of the reaction. For example, when 0.005 mol % **3a** was used in presence of iodotoluene, iodoanisole, or iodoaniline (entries 10, 13, and 14), we obtained the corresponding stilbene in 88, 69, and 21% yields, respectively. These results show that strong releasing groups caused a decrease in reaction yield while a weak electron-donor group or iodobenzene (entries 10 and 15) makes possible to achieve good stilbene yields. The position of the substituent on aryl iodide causes a slightly positive effect on the regioselectivity of this reaction (entries 11 and 12), thus *ortho* or *meta* groups on the aryl iodide favor the formation of the corresponding stilbene product.

The Mizoroki–Heck reaction of 4-iodotoluene was also extended to 4-vinylpyridine and vinylferrocene in the presence of **3a** as catalysts (entries 16 and 17). In both cases, the corresponding coupling products were obtained in moderate yields. In every case, moderate regioselectivity toward internal olefins was observed with a small amount of terminal olefins.

Before testing our catalyst in the total synthesis of arnottin I, we investigated a biaryl cyclization reaction of ester **4a** and amide **4b**,[12] with an iodine atom as a leaving group in order to demonstrate the viability of our catalyst to generate the chromone **5a** or the phenanthridinone **5b**, respectively (Table 4).

Table 4
Evaluation of catalytic conditions for biaryl cyclization reaction[a]



4a $R^1 = OCH_3$; R^2 = H; X = O
4b $R^1 = CH_3$; R^2 = H; X = N

5a-b

Entry	Ar–I	Product	Catalyst	Base	[Pd] (mol %)	Time (h)	Yield[b] (%)
1	**4a**	**5a**	$Pd(PPh_3)_2Cl_2$	AcONa	20	21	79
2	**4a**	**5a**	**3a**	Et_3N	1	5	0
3	**4a**	**5a**	**3a**	AcONa	5	2	50[c]
4	**4a**	**5a**	**3a**	AcONa	1	1.5	80
5	**4a**	**5a**	**3a**	AcONa	0.5	2	92
6	**4b**	**5b**	**3a**	AcONa	0.5	10	60[c]

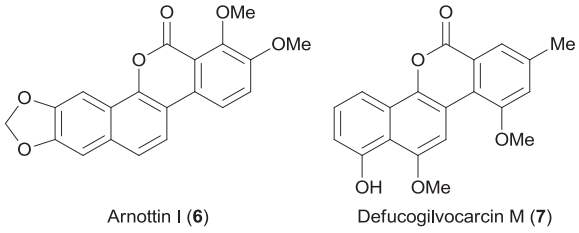
[a] All reactions were performed with 1.0 mmol of the aryl iodide, 6 mL of DMF and 1.2 mmol of base at 160 °C.
[b] Isolated yields.
[c] A complex mixture of side-products is observed by TLC, decreasing the yield of desired product.

Initially, we performed aryl–aryl coupling of ester **4a** using a commercially available palladium catalyst. When the reaction was carried out with $Pd(PPh_3)Cl_2$, AcONa as a base in DMF at 160 °C (entry 1), a catalyst loading of 20 mol % was needed to achieve, after 21 h of reaction, a good yield (79%) of the corresponding chromone. With the expectation that our catalyst could provide better results, we applied our findings in the Mizoroki–Heck reaction on this aryl–aryl coupling. Unfortunately, when Et_3N was used as a base (entry 2), the desired product was not obtained. In the presence of AcONa as a base, better results were accomplished and moderate to good yields of chromone **5a** were obtained (entries 3–5).

The effect of catalyst loading on aryl–aryl coupling reactions using catalyst **3a** was then examined. Thus, the reaction of **4a** using a catalyst loading of 5 mol % of **3a** (entry 3) affords 50% yield of the expected compound. The yield of **5a** was increased to 80% when the reaction was carried out with 1 mol % of **3a** (entry 4). We found that 0.5 mol % of complex **3a** provides the best results, with an optimum yield of the coupled product (entry 5). Optimized conditions for aryl–aryl coupling involved the use of AcONa as a base and 0.5 mol % of **3a** in DMF at 140 °C. As a further step, we evaluated the scope of this reaction toward the arylation of amide **4b** (entry 6), obtaining **5b** in moderate yield.

2.3. Total synthesis of arnottin I

Encouraged by our results, and in order to demonstrate the applicability of the catalysts reported in this paper, we decided to carry out the total synthesis of a pharmacologically significant natural product. Arnottin I (**6**) is a coumarin-based natural product isolated from *Xanthoxylum arnottuanum* as a non-alkaloid minor component.[13] Its close structural relationship to the aglycon of gilvocarcins (defucogilvocarcins) and its pharmacological properties make it a very interesting synthetic target (Fig. 3).[14] Recently, our group reported a formal total synthesis of defucogilvocarcin M **7**, which consisted in the first place in the preparation of a key α-tetralone by a free radical addition–cyclization sequence. In one of the final steps, an intramolecular Pd(0)-catalyzed aryl–aryl coupling was performed, providing compound **7** product after a final deprotection step.[15]

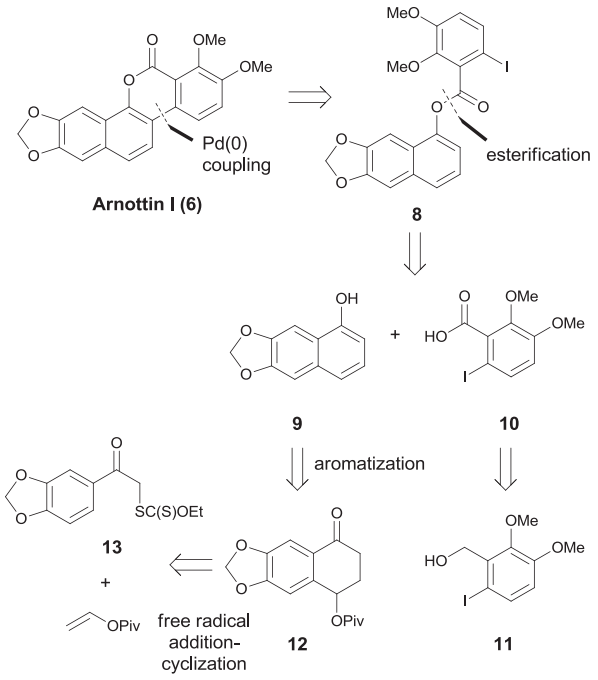


Arnottin I (**6**) Defucogilvocarcin M (**7**)

Fig. 3. Arnottin I (**6**) and defucogilvocarcin M (**7**).

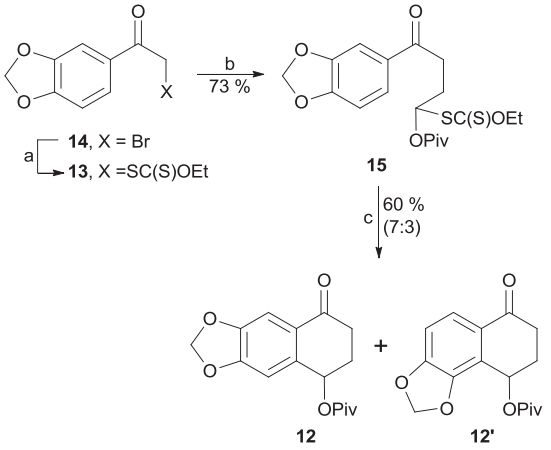
Thus, we decided to perform total synthesis of arnottin I using a similar strategy as that for defucogilvocarcin M (**7**). As shown in the retrosynthetic analysis (Scheme 3), arnottin I (**6**) would be obtained from ester **8** through an aryl–aryl coupling catalyzed by complex **3a**. Ester **8** would be assembled by esterification of naphthol **9** with acid **10**,[16] the latter being prepared from known alcohol **11**. Although naphthol **9** had been prepared by other means,[14d,17] we chose to prepare it by aromatization of compound **12** because, as demonstrated by Zard,[18] α-tetralones like **12** are easily accessible through a free radical addition–cyclization sequence between acetophenone xanthates and an appropriate radical acceptor. Moreover, **12** is a very valuable synthetic intermediate that could serve to prepare a variety of naphthalene derivatives,[19] such as naphthylamines, allowing the synthesis of other similar natural products like nitidine[16,20] or chelerythrine.[21] In this way, the required α-tetralone would be obtained from a free radical addition–cyclization sequence between xanthate **13** and vinyl pivalate.

Based on this plan, the first part of the synthesis consisted in the preparation of tetralone **12**. Thus, as shown in Scheme 4, reaction of compound **14**[22] with potassium *O*-ethylxantogenate yielded the desired radical precursor **13** (68% yield). When the latter reacted with vinyl pivalate in the presence of 0.4 equiv of dilauroyl peroxide (DLP, added portionwise), a 73% yield of adduct **15** was isolated. The next step consisted in the radical cyclization onto the aromatic ring, which was expected to furnish the two possible regioisomers. In



Scheme 3. Retrosynthetic analysis for arnottin I (**6**).

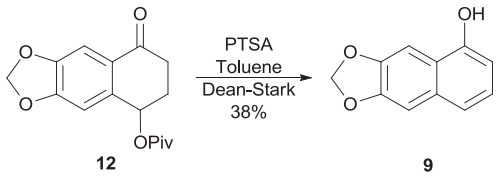
practice, when we performed the reaction with 1.4 equiv of DLP (added portionwise) in refluxing 1,2-dichloroethane, a separable mixture of desired tetralone **12** and undesired product **12′** was obtained in a 7:3 ratio in favor of **12** in 60% combined yield, probably due to a steric repulsion between the OPiv group and the 3,4-ethylendioxy moiety.



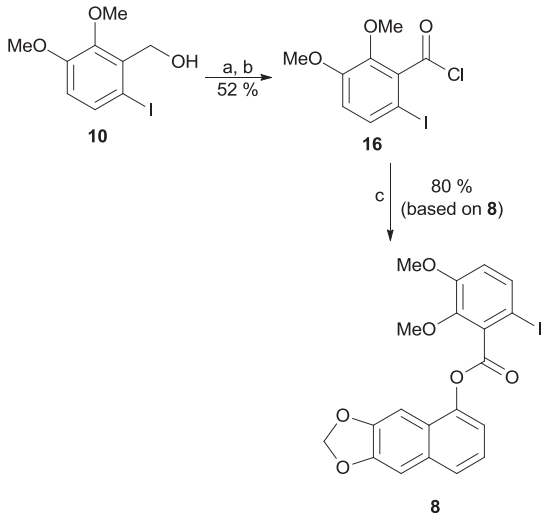
Scheme 4. Reagents and conditions: (a) KSC(S)OEt, acetone, rt; (b) vinyl pivalate, DLP (0.4 equiv), 1,2-dichloroethane, reflux; (c) DLP (1.4 equiv), 1,2-dichloromethane, reflux.

With the desired key tetralone in hand, we proceeded to transform it into the key naphthol **9**. We found that when a solution of **12** in toluene was treated with 3 equiv of PTSA, aromatization took place, albeit providing a low yield (38%, Scheme 5). Attempts to optimize the reaction by varying the acids, solvents, and reaction times were unsuccessful, leading to incomplete reactions and/or even lower yields.

On the other hand, the required acid chloride **16** was prepared in two steps from known alcohol **10**[16] by Jones oxidation and treatment with oxalyl chloride. Once formed, the acid chloride was immediately subjected to esterification with naphthol **9** under standard conditions yielding 80% compound **8** (Scheme 6).

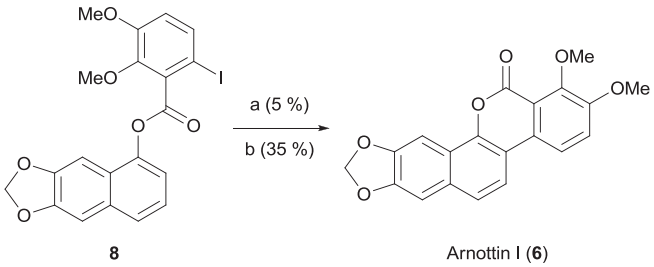


Scheme 5. Aromatization of tetralone **12**.



Scheme 6. Reagents and conditions: (a) Jones reagent, acetone, rt; (b) $(COCl)_2$, NEt_3, DMF cat., CH_2Cl_2, 0 °C to rt; (c) **8**, NEt_3, DMAP cat., CH_2Cl_2, 0 °C to rt.

At this stage, we proceeded to carry out final cyclization for the synthesis of arnottin I. In order to compare the efficiency of our catalyst with a commercially available one, we first repeated Harayama's work,[14a] treating ester **8** with different sources of Pd(0), obtaining arnottin I in moderate to good yields. Thus, we decided to repeat the reaction with substrate **8** and $Pd(PPh_3)_2Cl_2$, which was reported to produce a 52% yield of arnottin I. Disappointingly, in our hands, the expected compound **6** could only be observed as a minor product and isolated at a very low yield (5%) even with a large load (20%) of catalyst. Next, our catalyst (**3a**) was tested with the same substrate and under the same conditions (sodium acetate in refluxing DMF). Unlike $Pd(PPh_3)_2Cl_2$, only a 0.5 mol % charge of complex **3a** was needed for the complete conversion of **8** into arnottin I (**6**) in 35% yield, recovering a small amount of the starting material. Even if the yield remained low due to the presence of some traces amount of unidentified by-products, the reaction was cleaner and easier to purify than when a commercially available palladium complex was used (Scheme 7).



Scheme 7. Reagents and conditions: (a) $Pd(PPh_3)_2Cl_2$ (20 mol %), AcONa, DMF, 140 °C; (b) **3a** (0.5 mol %), AcONa, DMF, reflux.

3. Conclusions

We have developed efficient bidentate [N,P] ligands based on pyrrole, with a combination of hard and soft donor atoms.

Palladium complex **3a** proved to be a very efficient precursor catalyst in Heck cross-coupling reactions and in intramolecular aryl–aryl couplings of esters and amides. In order to demonstrate the applicability and efficiency of this catalyst, we completed a total synthesis of arnottin I. To obtain the key naphthalene derivative we applied a free radical strategy during the first stage of synthesis. In the crucial final step of synthesis, an aryl–aryl coupling promoted by catalyst **3a** was used, giving the desired product in better yields and in cleaner reaction conditions than commercial sources of Pd(II), and also remarkably reducing the load of palladium catalyst.

4. Experimental section

4.1. General considerations

All operations were carried out under an inert atmosphere of nitrogen or argon gas using standard Schlenk techniques. Anhydrous THF was obtained by distillation under an inert atmosphere over sodium and benzophenone. Column chromatography was performed using 70–230 mesh silica gel. All reagents and solvents were obtained from commercial suppliers and used without further purification. All compounds were characterized by IR spectra, recorded on a Perkin–Elmer 283B or 1420 spectrophotometer, by means of film and KBr techniques, and all data are expressed in wave numbers (cm^{-1}). Melting points were obtained on a Melt-Temp II apparatus and are uncorrected. NMR spectra were measured with a Bruker Avance+300 and a Varian Unity (300 MHz), using $CDCl_3$ and C_2D_6SO as solvents. Chemical shifts are in parts per million (ppm) (δ), relative to TMS. The MS-FAB$^+$ and MS-EI spectra were obtained on a JEOL SX 102A, the values of the signals are expressed in mass/charge units (m/z), followed by the relative intensity with reference to a 100% base peak.

4.2. Structure determination by X-ray crystallography

Suitable X-ray quality crystals of **2a** were grown through slow evaporation of a dichloromethane/*n*-hexane solvent mixture at −5 °C. Single white crystals of compounds **2a** were mounted on a glass fiber at room temperature. The crystals were then placed on a Bruker SMART APEX CCD diffractometer, equipped with Mo-Kα radiation; decay was negligible in both cases. Details of crystallographic data collected on compound **2a** are provided in Supplementary data of this article.[23] Systematic absences and intensity statistics were used in space group determinations. The structures were determined using direct methods.[24] Anisotropic structure refinements were achieved using full-matrix, least-squares techniques on all non-hydrogen atoms. All hydrogen atoms were placed in idealized positions, based on hybridization, with isotropic thermal parameters fixed at 1.2 times the value of the attached atom. Structure solutions and refinements were performed using SHELXTL v 6.10.[25]

*4.2.1. General synthesis of N,N-dimethyl-1H-pyrrol-1-amine-2-dialkylphosphine (**2a**–**c**).* A solution of *N*,*N*-dimethyl-1*H*-pyrrol-1-amine (8.3 mmol) in anhydrous THF (30 mL) under nitrogen atmosphere, was cooled at −78 °C and then *n*-butyl lithium (9.9 mmol, 1.2 equiv, Sol. 2.5 M in *n*-hexane) was added dropwise by syringe. The mixture was gradually warmed to room temperature. After reaching this temperature, the reaction mixture was cooled at 0 °C, followed by the addition of chlorodiphenylphosphine (8.3 mmol) and stirring at room temperature for 2 h. The solvent was evaporated at reduced pressure and the crude was purified by column chromatography. Elution with hexane/ethyl acetate.

Compound (**2a**): White powder, mp 106–108 °C (2.2 g, 90%). Elemental analysis: found C, 73.70; H, 6.69; N, 9.56; calcd C, 73.45; H, 6.50; N, 9.51. IR (KBr, cm^{-1}) ν_{max}: 3090, 3059, 2960, 2000–1600, 748–696. ^{31}P NMR (50 MHz, $CDCl_3$): δ=−29.2 ppm. ^{1}H NMR (300.53 MHz, $CDCl_3$, ppm): 7.32 (m, 10H), 7.07 (m, 1H), 6.18 (t, J=3.3 Hz, 1H), 5.51 (dd, J=1.8, 1.7 Hz, 1H), δ 2.57 (s, 6H). ^{13}C NMR (75.58 MHz, $CDCl_3$, ppm): 137.7 (d, J=8.6 Hz), 132.8 (d, J=18.9 Hz), 133.5 (d, J=20.0 Hz), 128.4 (dd, J=6.9 Hz); 128.6, 116.5, 113.3, 108.4, 47.9. MS (EI) m/z (%): 294 [M$^+$] (22), 251 [M$^+$−$C_{16}H_{14}$NP] (100), 250 [M$^+$−$C_{16}H_{13}$NP] (62), 174 [M$^+$−$C_{10}H_9$NP] (37), 143 [M$^+$−$C_{10}H_9$N] (31), 77 [M$^+$−C_6H_5] (5).

Compound (**2b**): White powder, mp 86–88 °C (0.76 g, 56%). Elemental analysis: found C, 76.85; H, 7.10; N, 8.80; calcd C, 74.51; H, 7.19; N, 8.69. IR (KBr, cm^{-1}) ν_{max}: 3048, 2957, 2000–1600, 752–709. ^{31}P NMR (50 MHz, $CDCl_3$): δ=−45.7 ppm. ^{1}H NMR (300.53 MHz, $CDCl_3$, ppm): 7.22 (d, J=1.5 Hz, 1H), 7.19 (m, 4H), 7.07 (m, 2H); 6.80 (dd, J=1.5 Hz, 2H), 6.18 (ddd, J=0.6 Hz, 1H), 5.48 (dd, J=1.8 Hz, 1H), 2.74 (s, 6H), 2.40 (d, J=1.56 Hz, 6H). ^{13}C NMR (75.58 MHz, $CDCl_3$, ppm): 142 (d, J=26.2 Hz), 135.8 (d, J=8.7 Hz), 132.9, 129.9 (d, J=4.7 Hz), 128.3, 125.8, 116.6, 114.3, 108.4, 48, 21.1 (d, J=21.5 Hz). MS (EI) m/z (%): 322 [M$^+$] (34), 279 [M$^+$−$C_{18}H_{18}$NP] (100), 264 [M$^+$−$C_{17}H_{15}$NP] (31), 197 [M$^+$−$C_{13}H_{10}$P] (42).

Compound (**2c**): White powder, mp 48–50 °C (1.7 g, 82%). Elemental analysis: found C, 67.25; H, 10.95; N, 10.75; calcd C, 66.11; H, 10.70; N, 11.01. IR (KBr, cm^{-1}) ν_{max}: 3104, 2957, 2000–1600, 1390–1359. ^{31}P NMR (50 MHz, $CDCl_3$, 25 °C): δ=1.9 ppm. ^{1}H NMR (300.53 MHz, $CDCl_3$, ppm): 7.16 (m, 1H), 6.37 (dd, J=1.6 Hz, 1H), 6.24 (dd, J=2.9, 3.1 Hz, 1H), 2.83 (s, 6H), 1.18 (d, J=12.1 Hz, 18H). ^{13}C NMR (75.58 MHz, $CDCl_3$, ppm): 127.1, 115.5, 113.3 (d, J=5.2 Hz), 107.4, 48.4, 32.4 (d, J=17.2 Hz), 30.4 (d, J=14.9 Hz). MS (EI) m/z (%): 255 [M$^+$] (47), 211 [M$^+$−$C_{12}H_{21}$NP] (100), 155 [M$^+$−C_8H_{13}NP] (17), 99 [M$^+$−C_4H_5NP] (50).

4.2.2. General synthesis of palladium complexes. A solution of the corresponding ligand (0.68 mmol) and $Pd(CH_3CN)_2Cl_2$ (0.68 mmol) in chloroform (30 mL) was heated at reflux for 2 h. The solution was allowed to cool to room temperature. The solvent was removed under vacuum, leaving a yellow residue, which was dissolved in the minimum amount of dichloromethane. The resulting solution was filtered through Celite, and then the slow addition of hexane induced the formation of a yellow solid, which was filtered, washed with hexane, and dried under vacuum to give the corresponding complexes **3a**–**c**.

Compound (**3a**): Yellow powder, mp 280 °C (0.29 g, 88%). Elemental analysis: found C, 43.39; H, 4.01; N, 5.63; calcd C, 45.83; H, 4.06; N, 5.93. IR (KBr, cm^{-1}) ν_{max}: 3105, 2928, 2000–1600, 748–693. ^{31}P NMR (50 MHz, $CDCl_3$): δ=16.7 ppm. ^{1}H NMR (300.53 MHz, $CDCl_3$, ppm): 7.85 (4H, J=2.2 Hz), 7.5 (ddd, J=4.5 Hz, 6H), 7.39 (d, J=1.2 Hz, 1H), 6.67 (d, J=1.2 Hz, 1H), 6.32 (t, J=1.6 Hz, 1H), 3.71 (s, 6H). ^{13}C NMR (75.58 MHz, $CDCl_3$, ppm): 133.6 (d, J=12.0 Hz), 132.5 (d, J=3.0 Hz), 129.2 (d, J=12.7 Hz), 127.9 (d, J=68.2 Hz), 121.9 (d, J=73.5 Hz), 117.5 (d, J=8.0 Hz), 117.1 (d, J=8.0 Hz), 113.2, 57.3. MS (FAB$^+$) m/z (%): 472 [M$^+$] (2), 437 [M$^+$−$C_{18}H_{19}ClN_2PPd$] (2), 294 [M$^+$−$C_{18}H_{19}N_2P$] (15), 251 [M$^+$−$C_{16}H_{14}$NP] (100), 174 [M$^+$−$C_{10}H_9$NP] (37), 143 [M$^+$−$C_{10}H_9$N] (32), 77 [M$^+$−C_6H_5] (5).

Compound (**3b**): Yellow powder, mp 280 °C (0.12 g, 67%). Elemental analysis: found C, 47.85; H, 4.84; N, 5.45; calcd C, 48.06; H, 4.60; N, 5.60. IR (KBr, cm^{-1}) ν_{max}: 3101, 2930, 2000–1600, 756–716. ^{31}P NMR (50 MHz, $CDCl_3$): δ=15.4 ppm. ^{1}H NMR (300.53 MHz, $CDCl_3$, ppm): 7.20–7.35 (m, 9H), 6.57 (dd, J=1.5 Hz, 1H), 6.26 (dd, J=1.5 Hz, 1H), 3.68 (d, J=6 Hz, 6H), 2.57 (d, J=21.9 Hz, 6H). ^{13}C NMR (75.58 MHz, $CDCl_3$, ppm): 141.9 (d, J=8.2 Hz), 136.9 (d, J=17.0 Hz), 134 (d, J=12.7 Hz), 132.6 (dd, J=22.6 Hz), 126.6 (d, J=12.1 Hz), 123, 116.4 (dd, J=7.7 Hz), 113.3 (d, J=2.2 Hz), 57.0 (d, J=76.3 Hz), 23.5 (d, J=24.2 Hz).

Compound (**3c**): Yellow powder, mp 300 °C (0.13 g, 88%). Elemental analysis: found C, 39.35; H, 6.54; N, 6.10; calcd C, 38.95; H,

6.30; N, 6.49. IR (KBr, cm^{-1}) ν_{max}: 3112, 2960, 1396–1366, 743. ^{31}P NMR (50 MHz, $CDCl_3$): δ=60.5 ppm. ^1H NMR (300.53 MHz, $CDCl_3$, ppm): 7.26 (m, 1H), 6.65 (dd, *J*=1.1 Hz, 1H), 6.42 (dd, *J*=1.4 Hz, 1H), 3.69 (s, 6H), 1.56 (s, 9H), 1.51 (s, 9H). ^{13}C NMR (75.58 MHz, $CDCl_3$, ppm): 127.1, 115.7, 113.6, 108.0, 57.3, 39.5 (d, *J*=21.8 Hz), 29.3.

4.2.3. General procedure for Mizoroki–Heck coupling reactions. In a 25-mL round-bottomed flask, a mixture of aryl iodide (5 mmol), alkene (6 mmol), and base (5.6 mmol) was placed in 4 mL of DMF, then a solution of the complex **3** (0.005 mol %) in 1 mL of DMF was added. The reaction mixture was refluxed for the time stated in Tables 3 and 4 at 140 °C. The reaction mixture was poured into water (20 mL) and extracted with ether or hexane (2×30 mL). The combined organic layers were dried over anhydrous sodium sulfate. After the removal of the solvent in vacuo, the resulting crude was purified by column chromatography on silica gel (hexane/ethyl acetate) to give the corresponding cross-coupling product (the purified product was identified by means of determination of mp and by ^1H and ^{13}C NMR, the data obtained are consistent with literature).[26] The entire flasks used in the each coupling reaction were meticulously cleaned with aqua regia to avoid the presence of unseen palladium catalyst.

4.2.4. General procedure for aryl–aryl coupling reaction. In a 25-mL round-bottomed flask, compound **4** (1.0 mmol) and base (1.2 mmol) were placed in 4 mL of DMF, then a solution of the complex **3a** (0.5 mol %) in 1 mL of DMF was added. The reaction mixture was refluxed for the time stated in Table 4 at 140 °C. The reaction mixture was poured into water (20 mL) and extracted with ether or hexane (2×30 mL). The combined organic layers were dried over anhydrous sodium sulfate. After the removal of the solvent in vacuo, the resulting crude was purified by column chromatography on silica gel (hexane/ethyl acetate) to give chromone **5a** or phenanthridinone **5b** (the purified product was identified by determination of mp and by ^1H and ^{13}C NMR, the data obtained are consistent with literature).[27] The entire flasks used in the each coupling reaction were meticulously cleaned with aqua regia to avoid the presence of unseen palladium catalyst.

4.3. Total synthesis of arnottin I (6)

*4.3.1. S-2-(Benzo[d][1,3]dioxol-5-yl)-2-oxoethyl O-ethyl carbonodithioate (**13**).* To a solution of 2-bromo-3′,4′-methylenedioxiacetophenone (5.930 g, 24.3 mmol) in 60 mL of acetone at 0 °C was added portionwise 3.91 g (24.3 mmol) of potassium *O*-ethyl xanthogenate. The resulting mixture was stirred at room temperature for 2 h, the solvent was evaporated, and the resulting mixture partitioned between water and CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2, the combined organic extracts were dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, hexane/AcOEt, 8:2) to give xanthate **13** (68% yield) as a white solid (mp 50 °C). ^1H NMR ($CDCl_3$, 300 MHz) δ=7.64 (dd, *J*=8.1, 1.8 Hz, 1H), 7.47 (d, *J*=1.8 Hz, 1H), 6.88 (d, *J*=8.1 Hz, 1H), 6.06 (s, 2H), 4.64 (q, *J*=7.2 Hz, 2H), 4.59 (s, 2H), 1.40 (t, *J*=7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ=213.3, 190.3, 152.3, 148.3, 130.5, 124.9, 108.1, 108.0, 102.0, 70.6, 43.4, 13.7. HRMS (FAB+) calcd for $C_{12}H_{13}O_4S_2$ 285.0255, found 285.0255.

*4.3.2. 4-(Benzo[d][1,3]dioxol-5-yl)-1-(ethoxycarbonothioylthio)-4-oxobutyl pivalate (**15**).* A solution of xanthate **13** (2.0 g, 7.03 mmol) and vinyl pivalate (1.802 g, 14.05 mmol) in 8 mL of 1,2-dichloroethane (DCE) was refluxed for 15 min under N_2. Lauroyl peroxide (DLP) (0.14 g, 0.087 mmol) was then added to the refluxing solution, followed by additional portions (0.056 g, 0.35 mmol every 90 min). When starting material was completely consumed, the mixture was cooled to room temperature, concentrated under reduced pressure, and purified by flash column chromatography (silica gel, hexane/dichloromethane, 1:1) to afford the title compound in 73% yield as a yellow oil. ^1H NMR ($CDCl_3$, 300 MHz) δ=7.53 (dd, *J*=8.2, 1.8 Hz, 1H), 7.41 (d, *J*=1.8 Hz, 1H), 6.84 (d, *J*=8.1 Hz, 1H), 6.70 (t, *J*=6.0 Hz, 1H), 6.04 (s, 2H), 4.63 (qd, *J*=1.2, 7.2 Hz, 2H), 3.04 (td, *J*=2.1, 7.2 Hz, 2H), 2.42–2.34 (m, 2H), 1.41 (t, *J*=7.2 Hz, 3H), 1.19 (s, 9H). ^{13}C NMR: δ=210.1, 195.8, 176.6, 151.8, 148.2, 131.4, 124.2, 107.8, 107.8, 101.8, 80.2, 70.1, 38.8, 33.9, 28.7, 26.9, 13.6.

*4.3.3. 8-Oxo-5,6,7,8-tetrahydronaphtho[2,3-d][1,3]dioxol-5-yl pivalate (**12**).* A solution of **15** (1.859 g, 4.669 mmol) in 1,2-dichloroethane (47 mL) was refluxed for 15 min under N_2. Lauroyl peroxide (DLP) was then added portionwise (0.372 g, 0.933 mmol, 20 mol % per hour) to the refluxing solution. When the starting material was completely consumed (after addition of 1.6 equiv of DLP), the crude mixture was cooled to room temperature, concentrated under reduced pressure, and purified by flash column chromatography (silica gel, hexane/dichloromethane, 3:7, a small pad of basic alumina was packed on the top of the column to eliminate the lauric acid generated during the reaction) and recrystallized with hexane/dichloromethane to give a mixture of tetralones **12** and **12′** (7:3, 60% combined yield). The mixture was separated by crystallization from hexane/dichloromethane (95:5), to isolate tetralone **12** as a brown solid (mp 105 °C). ^1H NMR ($CDCl_3$, 300 MHz) δ=7.47 (s, 1H), 6.83 (s, 1H), 6.04 (s, 2H), 5.98 (dd, *J*=6.3, 3.9 Hz, 1H), 2.84 (ddd, *J*=17.4, 9.4, 5.3 Hz, 1H), 2.61 (ddd, *J*=17.4, 7.2, 4.8 Hz, 1H), 2.41–2.18 (m, 2H), 1.21 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ=195.2, 177.8, 152.2, 148.4, 137.8, 127.4, 107.5, 106.3, 101.9, 68.9, 38.9, 34.0, 28.6, 27.0. HRMS (FAB+) calcd for $C_{16}H_{18}O_5$ 290.1154, found 290.1152. Spectral data for tetralone **12′** (white solid, mp 122–123 °C): ^1H NMR ($CDCl_3$, 300 MHz) δ=7.65 (d, *J*=8.4 Hz, 1H), 6.85 (d, *J*=8.4 Hz, 1H), 6.19 (t, *J*=4.2 Hz, 1H), 6.15 (d, *J*=7.5 Hz, 2H), 2.77 (ddd, *J*=16.9, 9.7, 6.9 Hz, 1H), 2.55 (dt, *J*=17.1, 4.9 Hz, 1H), 2.24–2.30 (m, 2H), 1.16 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ=195.3, 177.6, 152.2, 145.3, 126.9, 123.2, 121.5, 109.0, 102.5, 63.8, 39.0, 33.82, 28.0, 27.1.

*4.3.4. Naphtho[2,3-d][1,3]dioxol-5-ol (**9**).* A solution of tetralone **12** (0.050 g, 0.172 mmol) and 0.098 g (0.515 mmol) of PTSA in 5.8 mL of dry toluene was refluxed for 45 min with a Dean–Stark apparatus. The reaction mixture was allowed to cool at room temperature and neutralized with a saturated solution of Na_2CO_3. The aqueous phase was extracted with CH_2Cl_2, the combined organic extracts were dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, hexane/dichloromethane, 3:7) to give naphthol **9** (38% yield) as a brown solid (mp 120 °C). ^1H NMR ($CDCl_3$, 300 MHz) δ=7.48 (s, 1H), 7.27–7.24 (m, 1H), 7.14 (t, *J*=7.5 Hz, 1H), 7.08 (s, 1H), 6.67 (dd, *J*=9.0, 3.0 Hz, 1H), 6.02 (s, 2H), 5.15 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ=150.8, 148.0, 147.2, 132.0, 124.3, 120.7, 119.8, 107.7, 103.7, 100.9, 98.4. HRMS (FAB+) calcd for $C_{11}H_8O_3$ 188.0473, found 188.0472.

*4.3.5. 6-Iodo-2,3-dimethoxybenzoic acid (**10**).* To a cold (0 °C), stirred solution of 2-iodo-5,6-dimethoxybenzylalcohol (0.5 g, 1.70 mmol) in acetone (8.6) was added dropwise 3.3 mL (0.51 mmol) of Jones reagent. The reaction was stirred for a further hour at room temperature, the acetone was evaporated at reduced pressure, and then the residue partitioned between saturated aqueous K_2CO_3 solution and CH_2Cl_2. After separation of the organic layer, the aqueous phase was acidified with concentrated HCl (pH=2). The mixture was then extracted with dichloromethane; the combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by recrystallization from hexane/dichloromethane (95:5) to give **10** in

53% yield. All spectroscopic and physical data matched with those reported in the literature.[16]

*4.3.6. 6-Iodo-2,3-dimethoxybenzoyl chloride (**16**).* To a suspension of acid **10** (0.195 g, 0.632 mmol) and one drop of DMF in CH_2Cl_2 (21 mL) at 0 °C was slowly added oxalyl chloride (0.401 g, 3.159 mmol) under N_2. The ice bath was removed, and the reaction mixture was stirred at room temperature for 1 h. The resulting clear pale yellow solution was concentrated in vacuo to afford crude **16** as a pale yellow solid, which was used immediately for the next reaction without further purification.

*4.3.7. Naphtho[2,3-d][1,3]dioxol-5-yl 6-iodo-2,3-dimethoxybenzoate (**8**).* To a solution of naphthol **9** (0.092 g, 0.489 mmol), triethylamine (0.148 g, 1.462 mmol), and a catalytic amount of 4-DMAP in dry CH_2Cl_2 (21 mL) at 0 °C was slowly transferred a solution of freshly prepared acid chloride **16** (0.207 g, 0.634 mmol) in anhydrous CH_2Cl_2 (5 mL). The reaction mixture was allowed to warm to room temperature and stirred for 2.5 h. The mixture was extracted with CH_2Cl_2, the organic phase was washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, hexane/dichloromethane 3:7) to give ester **7** (79% yield) as a white solid (mp 162 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ=7.60–7.56 (m, 2H), 7.54 (s, 1H), 7.39–7.32 (m, 2H), 7.15 (s, 1H), 6.79 (d, J=8.7 Hz, 1H), 6.04 (s, 2H), 4.00 (s, 3H), 3.91 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ=165.7, 153.0, 148.4, 148.1, 147.1, 146.3, 134.9, 134.5, 132.1, 125.3, 124.0, 116.7, 115.6, 103.8, 101.1, 98.5, 79.3, 61.7, 56.1. HRMS (FAB+) calcd for $C_{20}H_{15}O_6$ 477.9913, found 477.9909.

*4.3.8. Arnottin I (**6**).* Following the general method for the aryl–aryl coupling, the title compound was obtained from ester **8** (0.230 g, 0.481 mmol), sodium acetate (0.094 g, 1.145 mmol), and complex **3a** (0.001 g, 0.002 mmol) in 5 mL of DMF. After 8 h of reaction, the compound was purified by flash chromatography (silica gel, dichloromethane/methanol 98:2) to give ester arnottin I **1** in 35% yield as a white solid (mp 260 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ=7.90 (d, J=8.7 Hz, 1H), 7.85 (d, J=8.4 Hz, 1H), 7.83 (s, 1H), 7.54 (d, J=9.0 Hz, 1H), 7.46 (d, J=9.0 Hz, 1H), 7.15 (s, 1H), 6.11 (s, 2H), 4.03 (s, 3H), 3.99 (s, 3H). MS (EI) m/z (rel intensity): 350 (65), 335 (25), 279 (25), 167 (65), 149 (100). Spectroscopic data fully matched with those reported in the literature.[13]

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2014.01.002.

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