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Stereoselective Palladium-Catalyzed α-Arylation of 3-Aryl-1-Indanones: An Asymmetric Synthesis of (+)-Pauciflorol F

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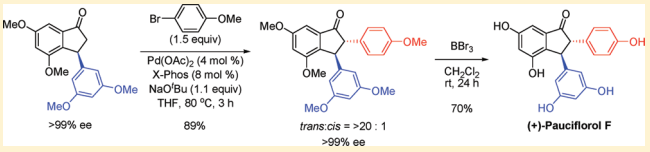
Supporting Information

ABSTRACT: Highly stereoselective, palladium-catalyzed α-arylation reactions of 3-aryl-1-indanones with aryl bromides are described. The use of sodium *tert*-butoxide as a base in this process is required to elevate the efficiencies and stereoselectivities of these reactions. The new methodology was successfully applied to a highly efficient route for the asymmetric synthesis of (+)-pauciflorol F.



INTRODUCTION

Transition-metal-catalyzed transformations and, in particular, those promoted by Pd catalysts serve as powerful methods for C−C bond formation.[1] Recently, catalytic α-arylation reactions of carbonyl compounds have begun to attract great attention in the areas of organic and medicinal chemistry owing to their use in the installation of aryl/heteroaryl groups α to carbonyl moieties.[2] In continuing efforts aimed at the development of catalytic processes that can be employed in concise routes for the synthesis of biologically active natural products and pharmaceuticals,[3] we have explored palladium-catalyzed α-arylation reactions of 3-aryl-1-indanones.[4]

Indanones, including a polyphenol family derived from resveratrol (**1**),[5] are frequently found in nature (Figure 1). Among members of this group, pauciflorol F (**2**),[6] quadrangularin A (**3a**),[7] and parthenocissin A (**3b**)[8] hold great interest as a consequence of their potential biological utility. Additionally, donepezil (Aricept, **4**)[9] and indacrinone (**5**),[10] both of which contain the 1-indanone core structure, have been developed as anti-Alzheimer and antihypertensive drugs, respectively. Compound **6**, bearing a 1-indenone scaffold, also was discovered to be a peroxisome proliferator-activated receptor γ (PPARγ) agonist for the treatment of type 2 diabetes.[11]

Total syntheses of pauciflorol F have been described by the Bo,[12] Snyder,[13] and Sarpong[14] groups. However, a selective asymmetric synthesis of (+)-pauciflorol F has not been reported to date. While this manuscript was being prepared, Yang and coworkers reported a concise synthesis of racemic pauciflorol F using an α-arylation approach.[15] In the key arylation process employed in their route, 2.2 equiv of a strong base, such as KHMDS, was required, and it resulted in the formation of significant amounts of an unwanted indenone product. Here, we describe the results of studies that have led to a new, mild, and efficient Pd-catalyzed α-arylation reaction of 1-indanones that takes place with high levels of stereoselectivity and have resulted in the first asymmetric synthesis of (+)-pauciflorol F.

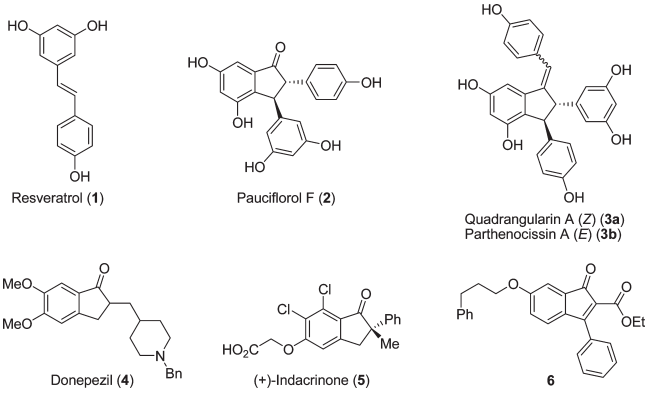


Figure 1. Indanones in nature and in pharmaceuticals.

RESULTS AND DISCUSSION

Stereoselective Pd-Catalyzed α-Arylation of 3-Aryl-1-indanone. For preparation of the requisite 3-aryl-1-indanones **10a** and **10b**, routes involving aldol condensations of the acetophenone derivative **7** with benzaldehydes **8a** and **8b** followed by acid-mediated cyclization were utilized (Scheme 1).[16]

With 3-aryl-1-indanone **10a** in hand, its α-arylation reaction with 4-bromoanisole was explored (Table 1). Initially, the Pd-catalyzed α-arylation reaction was attempted following the procedure and conditions developed by Buchwald.[17] When a combination of $Pd(OAc)_2$ (4 mol %), X-Phos (8 mol %), and

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Scheme 1. Synthesis of 3-Aryl-1-indanones 10a,b

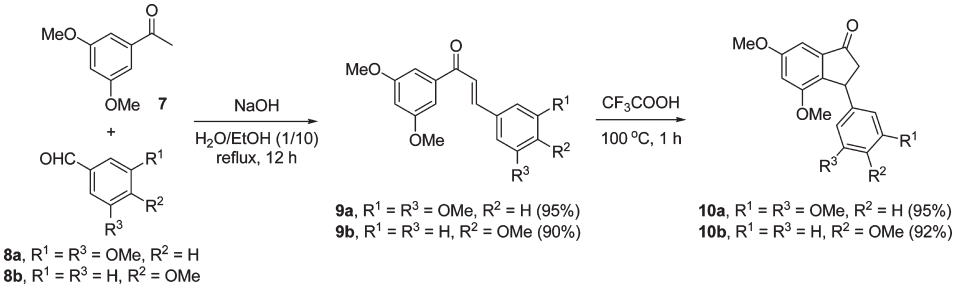
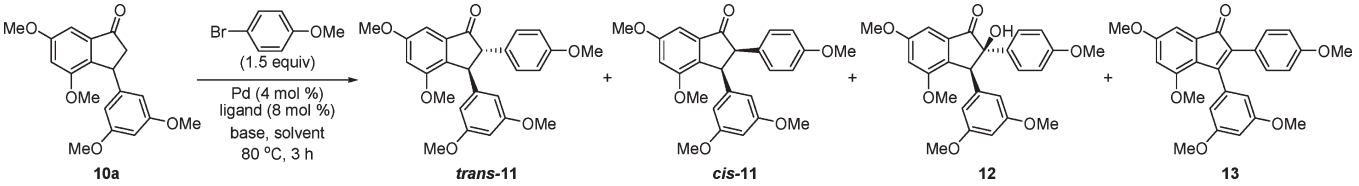


Table 1. Optimization of Pd-Catalyzed α-Arylation Reactions of 3-Aryl-1-indanone 10a with 4-Bromoanisole[a]



					Yield (%)[b]			
Entry	Pd	Ligand	Base (equiv)	Solvent	*trans*-**11**	*cis*-**11**	**12**	**13**
1	$Pd(OAc)_2$	X-Phos	NaO^{t}Bu (1.5)	toluene	56	20	18	6
2	$Pd(OAc)_2$	X-Phos	NaO^{t}Bu (1.2)	toluene	79 (78)[d]	12	5	4
3	$Pd(OAc)_2$	X-Phos	NaO^{t}Bu (1.1)	toluene	87	6	2	5
4	$Pd(OAc)_2$	X-Phos	NaO^{t}Bu (1.05)	toluene	85 (81)[d]	4	0	3
5	$Pd(OAc)_2$	X-Phos	NaO^{t}Bu (1.1)	THF	91 (89)[d]	4	2	3
6	$Pd_2(dba)_3$[c]	X-Phos	NaO^{t}Bu (1.1)	THF	90 (87)[d]	5	3	2
7	$Pd(OAc)_2$	X-Phos	Cs_2CO_3 (2.0)	THF	88	4	3	4
8	$Pd(OAc)_2$	X-Phos	Cs_2CO_3 (2.0)	CH_3CN	77	10	6	3
9	$Pd(OAc)_2$	S-Phos	NaO^{t}Bu (1.1)	THF	87	10	0	3
10	$Pd(OAc)_2$	DavePhos	NaO^{t}Bu (1.1)	THF	75	4	0	2
11	$Pd(OAc)_2$	t-Bu_3PHBF_4	NaO^{t}Bu (1.1)	THF	64	6	0	4
12	$Pd(OAc)_2$	BINAP	NaO^{t}Bu (1.1)	THF	36	7	4	0
13	$Pd(OAc)_2$	DPEphos	NaO^{t}Bu (1.1)	THF	31	6	5	0

[a] Conditions: **10a** (0.5 mmol), $Pd(OAc)_2$ (4 mol %), ligand (8 mol %), base, solvent (1.5 mL), 80 °C, 3 h. [b] ^{1}H NMR yields. [c] 2 mol % of $Pd_2(dba)_3$ was used. [d] Yields in parentheses.

NaO^{t}Bu (1.5 equiv) in toluene was used in this process, carried out at 80 °C for 3 h, a mixture of coupling products was produced (Table 1, entry 1). Careful column chromatographic separation led to the isolation of all characterizable products. These included the *trans* and *cis* coupling products **11**, which were present in a *ca.* 3:1 ratio as determined by ^{1}H NMR analysis. Surprisingly, the α-hydroxy compound **12**, whose structure had been unambiguously elucidated by Sarpong,[14] along with traces of 1-indenone **13** were also produced in this reaction. We believed that the use of excess base was responsible for the formation of α-hydroxy **12**, a proposal that was supported by the observation that *trans*-**11** could be readily converted to α-hydroxy **12** in 80% yield under basic conditions (Scheme 2).[18] When the amount of NaO^{t}Bu employed in this process was decreased to 1.2 equiv, the yield of α-hydroxy **12** was lowered to 5% and concurrently an improved (*ca.* 6.6:1 ratio) level of *trans*/*cis* diastereoselectivity was observed (Table 1, entry 2). With the use of 1.1 equiv of NaO^{t}Bu, the coupling reaction proceeded in 87% yield with a dr of *ca.* 14:1 (entry 3). However, a further decrease in the amount of this base to 1.05 equiv led to incomplete conversion of the starting materials (entry 4). Changing the reaction solvent to THF while maintaining the other conditions led to the generation of *trans*-**11** in an excellent 89% isolated yield and >20:1 dr (entry 5). $Pd_2(dba)_3$ also proved to be an effective catalyst for this α-arylation reaction, which yielded *trans*-**11** in a 87% and >20:1 dr (entry 6). The use of mild bases such as Cs_2CO_3 in either THF or CH_3CN solvent is less effective for this process (entries 7 and 8). Interestingly, when KO^{t}Bu was employed as the base, reaction of **14**[19] with 4-bromoanisole provided α-hydroxy **15** and indenone **16** in respective yields of 63% and 20% instead of the desired α-arylated product (Scheme 2).

The results of a study in which a broad range of ligands (S-Phos, DavePhos, BINAP, DPEphos, and t-Bu_3PHBF_4) were employed (entries 9−13) demonstrated that all were inferior to X-Phos and, except for S-Phos, did not promote reactions that proceeded to completion.

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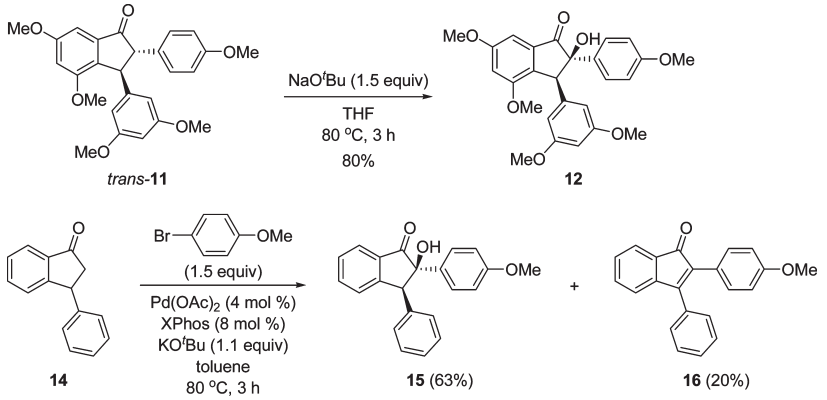
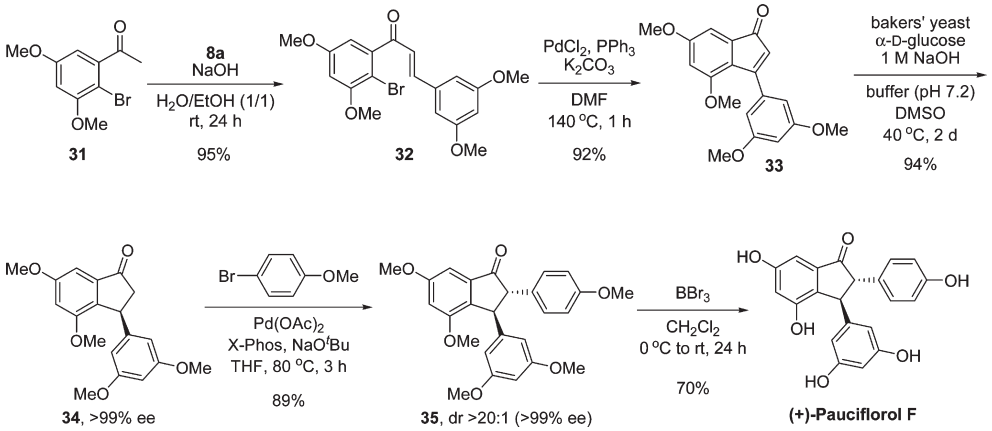
Scheme 2. Formation of α-Hydroxy 1-Indanones



Scheme 3. Asymmetric Synthesis of (+)-Pauciflorol F



Scope of Pd-Catalyzed α-Arylation. As illustrated in Table 2, the optimized conditions ($Pd(OAc)_2$ (4 mol %), X-Phos (8 mol %), and NaO^{t}Bu (1.1 equiv) in THF at 80 °C for 3 h) were applied in promoting coupling reactions of a wide range of aryl and heteroaryl bromides that yielded various *trans*-2,3-diaryl-1-indanones.

In the case of the tetramethoxy substituted 1-indanone **10a**, α-arylation with bromobenzene and *p*-bromotoluene provided the corresponding α-arylated products **17** and **18** in 91% and 76% yield with high degrees of diastereoselectivity (entries 1 and 2). However, aryl bromides bearing electron-withdrawing groups, such as chloro, cyano, and trifluoromethyl, participated in less efficient reactions that afforded coupling products **19**−**21** in 60−74% yields with 4−10:1 diastereoselectivities (entries 3−5). At this point, we thought that the low diastereoselectivity was caused by the increased acidity of α-proton on coupling products due to inductive effects of electron-withdrawing substituents. In the reaction of trimethoxy substituted 1-indanone **10b** with 1-bromo-3,5-dimethoxybenzene, the coupling product **22**, a potential precursor of quadranglularin A, was generated in 74% yield with an excellent (>20:1) diastereomeric ratio (entry 6).

α-Arylation reactions of indanone **14** also took place with aryl bromides that contain a range of substituents with different electronic and steric properties (entries 7−12). For example, reaction of **14** with *o*-bromotoluene afforded **28** in 66% yield and 17:1 dr (entry 12). The results of this investigation showed that reactions of indenone **14** take place with higher diastereoselectivities than those of the electron-rich tetramethoxy substituted analog **10a**. In addition, 2-naphthyl bromide as well as 3-pyridinyl bromide reacts with **14** to afford the corresponding products **29** and **30** in 86% and 30% yields, respectively (entries 13−14). Finally, observations made in this effort showed that reactions of electron-donating group appended aryl bromides take place more rapidly than those of aryl bromides with electron-withdrawing groups, probably due to the faster reductive elimination from electron-rich arylpalladium complexes.[20]

Asymmetric Total Synthesis of (+)-Pauciflorol F. With a highly efficient method for carrying out α-arylation reactions in hand, our attention turned to the asymmetric synthesis of (+)-pauciflorol F by using a strategy that employs an enantioselective, baker's-yeast-promoted conjugate reduction of 3-aryl-1-indenone **33** (Scheme 3). The key chalcone intermediate **32** was readily prepared by using aldol condensation of the acetophenone **31**[21] with the benzaldehyde **8a** under basic conditions. Intramolecular Heck reaction of chalcone **32** in highly dilute DMF afforded 1-indenone **33** in 92% yield. An attempt at enantioselective conjugate reduction of 3-aryl-1-indenone **33** following the procedure described by Clark and co-workers[22] was unsuccessful owing to the poor solubility of **33** in aqueous EtOH. However, when the

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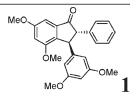
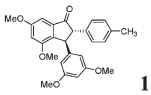
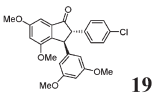
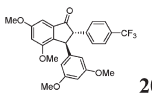
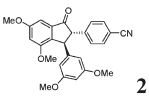
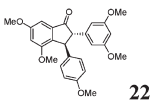
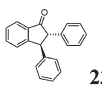
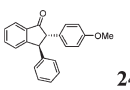
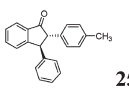
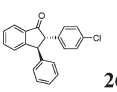
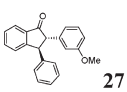
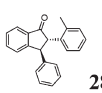
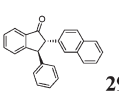
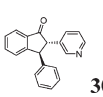
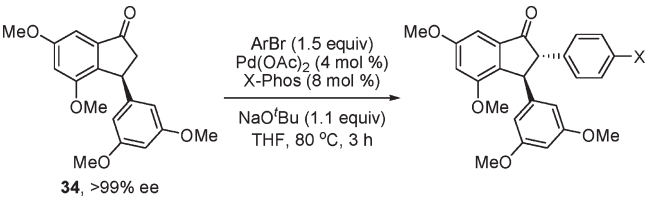
Table 2. Scope of Pd-Catalyzed α-Arylation Reaction[a]

Entry	3-Aryl-1-indanone	ArBr	Product	Yield (%)	*trans/cis* ratio[b]
1	**10a**		 **17**	91	18:1
2	**10a**		 **18**	76	>20:1
3	**10a**		 **19**	74	10:1
4	**10a**		 **20**	63	6.1:1
5[c]	**10a**		 **21**	60	4.8:1
6	**10b**		 **22**	74	>20:1
7	**14**		 **23**	76	17:1
8	**14**		 **24**	83	>20:1
9	**14**		 **25**	76	17:1
10	**14**		 **26**	61	17:1
11	**14**		 **27**	74	17:1
12	**14**		 **28**	66	17:1
13	**14**		 **29**	86	>20:1
14[d]	**14**		 **30**	30	6.7:1

[a] Reaction conditions: indanone (0.5 mmol), ArBr (1.5 equiv), $Pd(OAc)_2$ (4 mol %), X-Phos (8 mol %), NaO^tBu (1.1 equiv), THF (1.5 mL), 80 °C, 3 h. [b] The ratio was determined by ^1H NMR analysis. [c] $Pd_2(bda)_3$ (2 mol %) was the catalyst. Reaction time was 8 h. [d] 3-Bromopyridine (2.0 equiv) and NaO^tBu (1.2 equiv) were used. Reaction time was 24 h.

cosolvent was changed to DMSO the reduction process generating indanone **34**[23] proceeded smoothly (94% yield and >99% ee),

Table 3. Asymmetric Synthesis of Pauciflorol F Derivatives



Entry	ArBr	Product	Yield (%)	ee (%)[a]
1		X= H, **36**	92	>99
2		X = CH_3, **37**	85	99
3		X = Cl, **38**	78	>99[b]
4		X = CF_3, **39**	66	97[b,c]
5[d]		X = CN, **40**	60	>99

[a] Enantiomeric excess values were measured by HPLC analysis using a Chiralcel OD-H column (8:2 hexane/IPA, flow rate = 1 mL/min, λ = 230 nm). [b] 9:1 hexane/IPA was used. [c] HPLC flow rate was 0.25 mL/min. [d] Reaction was performed by using $Pd_2(bda)_3$ (2 mol %) for 8 h.

although a prolonged time (2 d) was required for complete consumption of **33**. Indanone **34** was then subjected to palladium-catalyzed α-arylation under the optimized reaction conditions described above to provide *trans*-indanone **35** with an excellent level of stereoselectivity (*trans*:*cis* = >20:1) and a 89% yield. Finally, global demethylation of **35** using BBr_3 provided (+)-pauciflorol F that has an $[\alpha]^{20}_D$ of +86 (*c* 0.5, MeOH),[24] which is in good agreement with the reported $[\alpha]^{25}_D$ of the enantiomer data of −80 (*c* 0.1, MeOH).[6]

Next, an investigation into the scope of the α-arylation established the asymmetric transformation of indanone **34** to be general for a range of aryl bromides (Table 3). Similar to the previous racemic results in Table 2, aryl bromides with electron-rich substituents proved to be excellent coupling partners in the reaction, affording good yields of permethylated pauciflorol F derivatives **36** and **37** with >99% enantiopurities (entries 1 and 2). In cases of electron-deficient substituents, the α-arylations were also effective to provide coupling products **38**−**40** with excellent enantiopurities, albeit in moderate to good yields (entries 3−5).

CONCLUSION

In summary, we have developed conditions for promoting highly efficient Pd-catalyzed α-arylation reactions of 3-aryl-1-indanones. Reactions employing the optimal catalytic system, involving $Pd(OAc)_2$, X-Phos, and NaO^tBu (1.1 equiv), are attended by decreased levels of formation of undesired products and take place with high degrees of stereoselectivity. Additionally, this study has led to the first asymmetric synthesis of (+)-pauciflorol F in 5 steps, starting from the known acetophenone **31**, in an overall 51% yield. The results of further studies aimed at elucidating the biological activities of the compounds prepared in this work will be discussed in following reports.

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EXPERIMENTAL SECTION

Typical Procedure for the Synthesis of (*E*)-1,3-Bis(3,5-dimethoxyphenyl)prop-2-en-1-one (9a). To a solution of acetophenone 7 (7.21 g, 40.0 mmol) in ethanol (10 mL) at 0 °C were added benzaldehyde **8a** (6.65 g, 40.0 mmol) and an aqueous solution of sodium hydroxide (1.92 g, 48.0 mmol) in H_2O (10 mL). After being stirred at room temperature for 12 h, the reaction mixture was quenched with H_2O (10 mL), and the aqueous phase was extracted with EtOAc (3 × 20 mL). The combined organic fractions were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. The resulting residue was purified by recrystallization from EtOAc/hexanes to give **9a** (12.5 g, 95% yield) as a yellow solid, mp 113−115 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, 1H, J = 15.7 Hz), 7.41 (d, 1H, J = 15.7 Hz), 7.14 (d, 2H, J = 2.2 Hz), 6.77 (d, 2H, J = 2.2 Hz), 6.67 (t, 1H, J = 2.2 Hz), 6.53 (t, 1H, J = 2.1 Hz), 3.86 (s, 6H), 3.84 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.0, 161.1, 160.9, 144.9, 140.1, 136.7, 122.5, 106.4, 160.4, 105.0, 102.8, 55.6, 55.5; HRMS (EI) calcd for $C_{19}H_{20}O_5$ [M^+] 328.1311, found 328.1310.

(*E*)-1-(3,5-Dimethoxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (9b). Yield 90%, white solid, mp 79−80 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, 1H, J = 15.6 Hz), 7.60 (d, 2H, J = 8.8 Hz), 7.35 (d, 1H, J = 15.6 Hz), 7.14 (d, 2H, J = 2.3 Hz), 6.94 (d, 2H, J = 8.8 Hz), 6.67 (t, 1H, J = 2.3 Hz), 3.87 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.2, 161.8, 161.0, 144.9, 140.6, 130.4, 127.7, 119.8, 114.6, 106.4, 104.9, 55.7, 55.5; HRMS (EI) calcd for $C_{18}H_{18}O_4$ [M^+] 298.1205, found 298.1202.

Typical Procedure for the Synthesis of 3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-2,3-dihydro-1*H*-inden-1-one (10a). Chalcone **9a** (6.57 g, 20.0 mmol) was dissolved in TFA (400 mmol, 30 mL). The reaction mixture was heated at 100 °C for 1 h. The solution was cooled to room temperature and diluted with toluene (30 mL). TFA was removed by fractional distillation. The solution was poured into $NaHCO_3$ (10 mL) and extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (1:9 EtOAc/hexanes) to afford **10a** (6.23 g, 95% yield) as a white solid, mp 105−107 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.84 (d, 1H, J = 2.0 Hz), 6.64 (d, 1H, J = 2.0 Hz), 6.29 (t, 1H, J = 2.2 Hz), 6.19 (d, 2H, J = 2.2 Hz), 4.50 (dd, 1H, J = 7.9, 2.1 Hz), 3.86 (s, 3H), 3.73 (s, 6H), 3.68 (s, 3H), 3.17 (dd, 1H, J = 19.2, 7.9 Hz), 2.59 (dd, 1H, J = 19.2, 2.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.2, 161.9, 160.9, 158.0, 146.7, 139.3, 139.1, 106.2, 105.4, 98.2, 96.4, 55.9, 55.7, 55.4, 47.6, 41.6; HRMS (EI) calcd for $C_{19}H_{20}O_5$ [M^+] 328.1311, found 328.1309.

4,6-Dimethoxy-3-(4-methoxyphenyl)-2,3-dihydro-1*H*-inden-1-one (10b). Yield 92%, white solid, mp 125−126 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.97 (d, 2H, J = 8.7 Hz), 6.84 (d, 1H, J = 2.1 Hz), 6.78 (d, 2H, J = 8.7 Hz), 6.63 (d, 1H, J = 2.1 Hz), 4.53 (dd, 1H, J = 7.9, 2.1 Hz), 3.86 (s, 3H), 3.77 (s, 3H), 3.66 (s, 3H), 3.19 (dd, 1H, J = 19.2, 7.9 Hz), 2.58 (dd, 1H, J = 19.2, 2.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.6, 161.8, 158.2, 158.0, 139.9, 139.1, 136.2, 128.3, 128.1, 113.9, 106.3, 95.9, 55.9, 55.7, 55.3, 47.9, 40.6; HRMS (EI) calcd for $C_{18}H_{18}O_4$ [M^+] 298.1205, found 298.1202.

Representative Procedure for α-Arylation. To a vial (3 mL) was added 1-indanone **10a** (150 mg, 0.457 mmol), 4-bromoanisole (128 mg, 0.6685 mmol), $Pd(OAc)_2$ (4.0 mg, 0.018 mmol), X-Phos (17.6 mg, 0.037 mmol), and NaO^{t}Bu (48.3 mg, 0.502 mmol) in a glovebox. THF (1.5 mL) was added, and then the vial was sealed with a screw cap. The reaction was heated at 80 °C for 3 h. The mixture was cooled to room temperature and filtered through a short pad of silica gel while rinsing with EtOAc (10 mL). The solution was concentrated *in vacuo*, and the residue was purified by silica gel column chromatography (ZEOprep 15−25 μm, 1:4:16 EtOAc/CH_2Cl_2/hexanes) to afford *trans*-**11** (178 mg, 89% yield) and *cis*-**11**, along with **12** and **13**.

***trans*-3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-2-(4-methoxyphenyl)-2,3-dihydro-1*H*-inden-1-one (*trans*-11)[14].** Yield 89%, white solid, mp 137−138 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.02 (d, 2H, J = 8.7 Hz), 6.89 (d, 1H, J = 2.0 Hz), 6.84 (d, 2H, J = 8.7 Hz), 6.70 (d, 1H, J = 2.1 Hz), 6.32 (t, 1H, J = 2.2 Hz), 6.15 (d, 2H, J = 2.2 Hz), 4.44 (d, 1H, J = 2.8 Hz), 3.88 (s, 3H), 3.78 (s, 3H), 3.71 (s, 6H), 3.69 (s, 3H), 3.65 (d, 1H, J = 2.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.8, 162.1, 160.9, 158.8, 157.9, 146.0, 138.8, 137.7, 131.6, 128.9, 114.4, 106.5, 105.3, 98.3, 96.6, 64.2, 55.8 55.7, 55.3, 52.0 ; HRMS (EI) calcd for $C_{26}H_{26}O_6$ [M^+] 434.1729, found 434.1733.

***cis*-3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-2-(4-methoxyphenyl)-2,3-dihydro-1*H*-inden-1-one (*cis*-11)[14].** White solid, mp 134−136 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.96 (d, 1H, J = 1.7 Hz), 6.73 (d, 3H, J = 8.5 Hz), 6.63 (d, 2H, J = 8.4 Hz), 6.08 (t, 1H, J = 2.1 Hz), 5.67 (d, 2H, J = 2.0 Hz), 4.85 (d, 1H, J = 7.9 Hz), 4.32 (d, 1H, J = 7.9 Hz), 3.90 (s, 3H), 3.73 (s, 3H), 3.71 (s, 3H), 3.53 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.7, 161.9, 160.2, 158.4, 157.9, 143.1, 139.4, 136.2, 131.3, 128.5, 113.5, 107.3, 106.3, 98.4, 96.4, 61.2, 56.0, 55.9, 55.3, 55.3, 48.4; HRMS (EI) calcd for $C_{26}H_{26}O_6$ [M^+] 434.1729, found 434.1741.

3-(3,5-Dimethoxyphenyl)-2-hydroxy-4,6-dimethoxy-2-(4-methoxyphenyl)-2,3-dihydro-1*H*-inden-1-one (12)[14]. White solid, mp 78−79 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.00 (d, 1H, J = 2.1 Hz), 6.93 (d, 2H, J = 8.6 Hz), 6.74 (d, 1H, J = 2.0 Hz), 6.58 (d, 2H, J = 8.6 Hz), 6.07 (t, 1H, J = 2.1 Hz), 5.82 (s, 2H), 4.62 (s, 1H), 3.92 (s, 3H), 3.68 (s, 3H), 3.65 (s, 3H), 3.55 (s, 6H), 2.91 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.6, 162.1, 160.0, 158.8, 158.4, 141.8, 137.4, 135.6, 132.5, 128.2, 112.9, 107.5, 107.4, 98.7, 97.0, 85.6, 56.7, 56.0, 55.8, 55.3; HRMS (EI) calcd for $C_{26}H_{26}O_7$ [M^+] 450.1679, found 450.1671.

3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-2-(4-methoxyphenyl)-1*H*-inden-1-one (13)[14]. Dark purple solid, mp 163−164 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12 (d, 2H, J = 8.9 Hz), 6.86 (d, 1H, J = 2.0 Hz), 6.75 (d, 2H, J = 8.8 Hz), 6.49 (d, 2H, J = 2.2 Hz), 6.43 (d, J = 1.5 Hz, 2H), 3.86 (s, 3H), 3.76 (s, 3H), 3.70 (s, 6H), 3.61 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6, 162.5, 160.2, 158.7, 156.6, 154.7, 137.0, 134.1, 131.0, 130.6, 123.6, 122.7, 113.4, 106.6, 104.1, 102.8, 101.0, 77.4, 77.0, 76.6, 55.9, 55.8, 55.3, 55.2; HRMS (EI) calcd for $C_{26}H_{24}O_6$ [M^+] 432.1573, found 432.1561.

2-Hydroxy-2-(4-methoxyphenyl)-3-phenyl-2,3-dihydro-1*H*-inden-1-one (15). To a vial (3 mL) were added 1-indanone **14**[19] (100 mg, 0.5 mmol), 4-bromoanisole (140 mg, 0.75 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), X-Phos (19 mg, 0.04 mmol), and KO^{t}Bu (62 mg, 0.55 mmol) in a glovebox. THF (1.7 mL) was added, and then the vial was sealed with a screw cap. The reaction was heated at 80 °C for 3 h. The mixture was cooled to room temperature and filtered through a short pad of silica gel while rinsing with EtOAc (10 mL). The solution was concentrated *in vacuo*, and the residue was purified by silica gel column chromatography (2% EtOAc/hexanes) to afford **15** (104 mg, 63% yield) as a light yellow solid, along with **16** (32 mg, 20% yield) as a red solid. Data for **15**: mp 145−146 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, 1H, J = 7.9 Hz), 7.68 (t, 1H, J = 7.3 Hz), 7.54 (t, 1H, J = 7.3 Hz), 7.33 (d, 1H, J = 7.6 Hz), 7.09 (d, 3H, J = 5.1 Hz), 6.82 (d, 2H, J = 4.6 Hz), 6.75 (d, 2H, J = 8.7 Hz), 6.50 (d, 2H, J = 8.6 Hz), 4.85 (s, 1H), 3.65 (s, 3H), 3.13 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.5, 158.9, 153.9, 137.9, 136.2, 135.8, 133.0, 129.8, 128.0, 127.9, 127.3, 127.0, 124.1, 113.0, 86.6, 59.3, 55.2; HRMS (EI) calcd for $C_{22}H_{18}O_3$ [M^+] 330.1256, found 330.1236.

2-(4-Methoxyphenyl)-3-phenyl-1*H*-inden-1-one (16)[25]. Red solid, mp 114−116 °C (lit.[2] mp 118−119.5 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, 1H, J = 7.0 Hz), 7.41 (d, 4H, J = 2.1 Hz), 7.38 (d, 1H, J = 3.9 Hz), 7.34 (d, 1H, J = 7.1 Hz), 7.28 (s, 1H), 7.23 (d, 2H, J = 8.5 Hz), 7.11 (d, 1H, J = 7.2 Hz), 6.80 (d, 2H, J = 8.6 Hz), 3.79 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.0, 159.2, 153.8, 145.6, 133.4, 133.1, 131.9, 131.3, 130.7, 129.1, 128.8, 128.6, 128.5, 123.1, 122.9, 120.9, 113.7, 55.2; HRMS (EI) calcd for $C_{22}H_{16}O_2$ [M^+] 312.1150, found 312.1144.

3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-2-phenyl-2,3-dihydro-1*H*-inden-1-one (17). Yield 91%, white solid, mp 107−109 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32−7.24 (m, 3H), 7.10 (d, 2H, J = 6.4 Hz), 6.90 (d, 1H, J = 2.1 Hz), 6.70 (d, 1H, J = 2.1 Hz), 6.32 (t, 1H, J = 2.2 Hz), 6.16 (d, 2H, J = 2.2 Hz), 4.49 (d, 1H, J = 2.7 Hz), 3.88 (s, 3H), 3.71 (s, 6H), 3.71−3.69 (m, 1H), 3.69 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.6, 162.2, 160.9, 157.9, 146.0, 139.5, 138.9, 137.8, 128.9, 127.9, 127.2, 106.6, 105.3, 98.3, 96.6, 65.0, 55.9, 55.7, 55.3, 51.9; HRMS (EI) calcd for $C_{25}H_{24}O_5$ [M^+] 404.1624, found 404.1618.

3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-2-(*p*-tolyl)-2,3-dihydro-1*H*-inden-1-one (18). Yield 76%, white solid, mp 70−75 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (d, 2H, J = 8.1 Hz), 6.98 (d, 2H, J = 8.0 Hz), 6.89 (d, 1H, J = 2.1 Hz), 6.70 (d, 1H, J = 2.1 Hz), 6.31 (t, 1H, J = 2.2 Hz), 6.15 (d, 2H, J = 2.2 Hz), 4.46 (d, 1H, J = 2.7 Hz), 3.88 (s, 3H), 3.71 (s, 6H), 3.69 (s, 3H), 3.67 (d, 1H, J = 2.7 Hz), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.7, 162.0, 160.8, 157.8, 146.0, 138.8, 137.7, 136.7, 136.4, 129.6, 127.7, 106.5, 105.2, 98.2, 96.5, 64.6, 55.8, 55.7, 55.2, 51.8, 21.1; HRMS (EI) calcd for $C_{26}H_{26}O_5$ [M^+] 418.1780, found 418.1783.

2-(4-Chlorophenyl)-3-(3,5-dimethoxyphenyl)-4,6-dimethoxy-2,3-dihydro-1*H*-inden-1-one (19). Yield 74%, white solid, mp 66−69 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (s, 1H), 7.03 (d, 2H, J = 8.5 Hz), 6.89 (d, 1H, J = 2.0 Hz), 6.70 (d, 1H, J = 2.0 Hz), 6.32 (t, 1H, J = 2.2 Hz), 6.14 (d, 2H, J = 2.2 Hz), 4.42 (d, 1H, J = 2.9 Hz), 3.88 (s, 3H), 3.71 (s, 6H), 3.69 (s, 3H), 3.67 (d, 1H, J = 2.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.0, 162.3 (s), 161.0, 157.9, 145.7, 138.6, 137.9, 137.5, 133.1, 129.4, 129.1, 106.8, 105.3, 98.6, 96.3, 64.3, 55.7, 55.8, 55.3, 51.8; HRMS (EI) calcd for $C_{25}H_{23}ClO_5$ [M^+] 438.1234, found 438.1230.

3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-2-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-inden-1-one (20). Yield 63%, white solid, mp 46−48 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, 2H, J = 8.2 Hz), 7.22 (d, 2H, J = 8.0 Hz), 6.90 (d, 1H, J = 1.9 Hz), 6.72 (d, 1H, J = 2.0 Hz), 6.33 (t, 1H, J = 1.9 Hz), 6.14 (d, 2H, J = 2.1 Hz), 4.46 (d, 1H, J = 2.9 Hz), 3.89 (s, 3H), 3.76 (d, 1H, J = 2.9 Hz), 3.72 (s, 6H), 3.69 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.5, 162.3, 160.9, 157.8, 145.4, 143.2, 138.5, 137.4, 128.3, 125.9, 125.8, 125.8, 125.7, 106.8, 105.2, 98.3, 96.5, 64.5, 55.8, 55.7, 55.3, 51.6; HRMS (EI) calcd for $C_{26}H_{23}F_3O_5$ [M^+] 472.1498, found 472.1495.

4-(3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-1-oxo-2,3-dihydro-1*H*-inden-2-yl)benzonitrile (21). Yield 60%, light yellow solid, mp 65−68 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, 2H, J = 8.1 Hz), 7.22 (d, 2H, J = 8.3 Hz), 6.89 (d, 1H, J = 2.0 Hz), 6.72 (d, 1H, J = 2.0 Hz), 6.33 (t, 1H, J = 2.2 Hz), 6.13 (d, 2H, J = 2.2 Hz), 4.44 (d, 1H, J = 2.9 Hz), 3.88 (s, 3H), 3.76 (d, 1H, J = 2.9 Hz), 3.72 (s, 6H), 3.69 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.1, 162.5, 161.1, 158.0, 145.3, 144.7, 138.4, 137.5, 132.8, 128.9, 118.8, 111.2, 107.0, 105.3, 98.4, 96.7, 64.8, 55.9, 55.8, 55.4, 51.6; HRMS (EI) calcd for $C_{26}H_{23}NO_5$ [M^+] 429.1576, found 429.1582.

***trans*-2-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-3-(4-methoxyphenyl)-2,3-dihydro-1*H*-inden-1-one (22).** Yield 74%, white solid, mp 163−164 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.94 (d, 2H, J = 8.6 Hz), 6.89 (d, 1H, J = 1.9 Hz), 6.79 (d, 2H, J = 8.7 Hz), 6.69 (d, 1H, J = 1.9 Hz), 6.36 (t, 1H, J = 2.1 Hz), 6.24 (d, 2H, J = 2.1 Hz), 4.51 (d, 1H, J = 2.5 Hz), 3.88 (s, 3H), 3.78 (s, 3H) 3.74 (s, 6H), 3.66 (s, 3H), 3.60 (d, 1H, J = 2.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.6, 162.1, 161.1, 158.3, 157.9, 141.7, 138.7, 138.6, 135.6, 128.1, 114.0, 106.7, 106.2, 99.1, 96.6, 65.5, 56.0, 55.8, 55.4, 55.3, 51.0; HRMS (EI) calcd for $C_{26}H_{26}O_6$ [M^+] 434.1729, found 434.1734.

2,3-Diphenyl-2,3-dihydro-1*H*-inden-1-one (23)[26]. Yield 76%, light red-orange oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, 1H, J = 7.6 Hz), 7.63 (t, 1H, J = 7.4 Hz), 7.49 (dd, 1H, J = 11.0, 3.9 Hz), 7.35−7.27 (m, 6H), 7.25 (dd, 1H, J = 4.6, 0.6 Hz), 7.11−7.07 (m, 4H), 4.57 (d, 1H, J = 4.7 Hz), 3.81 (d, 1H, J = 4.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.3, 156.2, 142.6, 138.6, 136.3, 135.5, 129.0, 128.9, 128.5, 128.4, 128.0, 127.3, 126.8, 124.1, 64.7, 55.0; HRMS (EI) calcd for $C_{21}H_{16}O$ [M^+] 284.1201, found 284.1201.

2-(4-Methoxyphenyl)-3-phenyl-1*H*-inden-1-one (24). Yield 83%, light red-orange oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, 1H, J = 7.4 Hz), 7.64 (t, 1H, J = 7.4 Hz), 7.48 (t, 1H, J = 7.4 Hz), 7.30 (d, 4H, J = 6.7 Hz), 7.09 (d, 2H, J = 6.3 Hz), 7.03 (d, 2H, J = 8.5 Hz), 6.86 (d, 2H, J = 8.6 Hz), 4.52 (d, 1H, J = 4.9 Hz), 3.79 (s, 3H), 3.76 (d, 1H, J = 4.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.7, 158.9, 156.1, 142.7, 136.3, 135.5, 130.6, 129.5, 129.0, 128.4, 128.0, 127.3, 126.8, 124.1, 114.4, 64.1, 55.4, 55.1; HRMS (EI) calcd for $C_{22}H_{18}O_2$ [M^+] 314.1307, found 314.1310.

3-Phenyl-2-(*p*-tolyl)-2,3-dihydro-1*H*-inden-1-one (25). Yield 76%, light red-orange oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, 1H, J = 7.6 Hz), 7.64 (td, 1H, J = 7.6, 1.1 Hz), 7.48 (t, 1H, J = 7.4 Hz), 7.35−7.27 (m, 4H), 7.13 (d, 2H, J = 8.0 Hz), 7.09 (dd, 2H, J = 7.7, 1.7 Hz), 7.00 (d, 2H, J = 8.0 Hz), 4.56 (d, 1H, J = 4.9 Hz), 3.78 (d, 1H, J = 4.9 Hz), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.6, 156.3, 142.7, 137.0, 136.4, 135.6, 135.5, 129.7, 129.0, 128.4, 128.0, 127.3 126.8, 124.1, 64.5, 55.0, 21.2; HRMS (EI) calcd for $C_{22}H_{18}O$ [M^+] 298.1358, found 298.1360.

2-(4-Chlorophenyl)-3-phenyl-2,3-dihydro-1*H*-inden-1-one (26). Yield 61%, yellow solid, mp 79−81 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, 1H, J = 7.5 Hz), 7.65 (td, 1H, J = 7.6, 0.9 Hz), 7.50 (t, 1H, J = 7.4 Hz), 7.37−7.27 (m, 6H), 7.08 (dd, 2H, J = 7.7, 1.7 Hz), 7.04 (d, 2H, J = 8.4 Hz), 4.51 (d, 1H, J = 5.0 Hz), 3.78 (d, 1H, J = 5.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 155.8, 142.1, 136.8, 136.0, 135.6, 133.1, 129.8, 129.0, 128.4, 127.9, 127.4, 126.7, 124.1, 64.0, 54.8; HRMS (EI) calcd for $C_{21}H_{15}ClO$ [M^+] 318.0811, found 318.0801.

2-(3-Methoxyphenyl)-3-phenyl-2,3-dihydro-1*H*-inden-1-one (27). Yield 74%, yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, 1H, J = 7.6 Hz), 7.64 (td, 1H, J = 7.5, 1.1 Hz), 7.48 (t, 1H, J = 7.5 Hz), 7.34−7.26 (m, 4H), 7.23 (dd, 1H, J = 8.2, 5.5 Hz), 7.09 (dd, 2H, J = 7.7, 1.6 Hz), 6.82 (dd, 1H, J = 8.0, 2.2 Hz), 6.69 (d, 1H, J = 7.6 Hz), 6.65 (t, 1H, J = 2.1 Hz), 4.58 (d, 1H, J = 4.7 Hz), 3.78 (d, 1H, J = 4.8 Hz), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.0, 159.9, 156.2, 142.6, 140.0, 136.2, 135.5, 129.9, 128.9, 128.3, 127.9, 127.2, 126.7, 124.1, 120.6, 114.3, 112.6, 64.6, 55.2, 54.8; HRMS (EI) calcd for $C_{22}H_{18}O_2$ [M^+] 314.1307, found 314.1306.

3-Phenyl-2-(*o*-tolyl)-2,3-dihydro-1*H*-inden-1-one (28). Yield 66%, light red-orange solid, mp 121−123 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, 1H, J = 7.7 Hz), 7.64 (td, 1H, J = 7.6, 1.1 Hz), 7.50 (t, 1H, J = 7.4 Hz), 7.29 (t, 4H, J = 7.0 Hz), 7.16−7.12 (m, 3H), 7.09 (dd, 2H, J = 7.4, 1.8 Hz), 6.93 (d, 1H, J = 6.2 Hz), 4.50 (d, 1H, J = 5.0 Hz), 4.03 (d, 1H, J = 5.1 Hz), 2.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.8, 156.1, 142.6, 142.6, 137.4, 136.9, 136.4, 135.3, 130.7, 128.9, 128.3, 127.9, 127.2, 126.6, 126.4, 123.9, 55.0, 20.0; HRMS (EI) calcd for $C_{22}H_{18}O$ [M^+] 298.1358, found 298.1355.

2-(Naphthalen-2-yl)-3-phenyl-2,3-dihydro-1*H*-inden-1-one (29). Yield 86%, light red-orange solid, mp 55−57 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, 1H, J = 7.8 Hz), 7.85−7.79 (m, 2H), 7.75 (dd, 1H, J = 6.0, 3.5 Hz), 7.67 (t, 1H, J = 7.4 Hz), 7.59 (s, 1H), 7.52 (t, 1H, J = 7.4 Hz), 7.45 (dq, 2H, J = 6.7, 3.5 Hz), 7.35−7.32 (m, 2H), 7.30−7.28 (m, 2H), 7.20 (dd, 1H, J = 8.4, 1.4 Hz), 7.11 (d, 1H, J = 2.0 Hz), 7.09 (s, 1H), 4.68 (d, 1H, J = 4.8 Hz), 3.97 (d, 1H, J = 4.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.3, 156.2, 142.5, 136.3, 135.9, 135.5, 133.6, 132.6, 129.0, 128.8, 128.4, 128.0, 127.8, 127.7, 127.2, 126.8, 126.2, 126.0, 125.8, 124.1, 64.9, 54.9; HRMS (EI) calcd for $C_{25}H_{18}O$ [M^+] 334.1358, found 334.1358.

3-Phenyl-2-(pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-one (30). The reaction was performed by following the typical procedure except for 3-bromopyridine (2.0 equiv) and NaO^{t}Bu (1.2 equiv) for 24 h to provide **30** in 30% yield as a yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (d, 1H, J = 4.2 Hz), 8.38 (s, 1H), 7.90 (d, 1H, J = 7.7 Hz), 7.67 (t, 1H, J = 7.5 Hz), 7.56−7.44 (m, 2H), 7.38−7.26 (m, 5H), 7.10 (dd, 2H, J = 7.4, 1.6 Hz), 4.55 (d, 1H, J = 5.3 Hz), 3.84 (d, 1H, J = 5.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.1, 155.8, 150.0, 148.8, 141.8, 135.97, 135.91, 135.85, 129.3, 128.7, 128.0, 127.7, 126.8, 124.2, 123.9, 62.3, 54.6; HRMS (EI) calcd for $C_{20}H_{15}NO$ [M^+] 285.1154, found 285.1144.

(*E*)-1-(2-Bromo-3,5-dimethoxyphenyl)-3-(3,5-dimethoxyphenyl)prop-2-en-1-one (32). To a solution of acetophenone **31**[21] (3.2 g, 12 mmol) and benzaldehyde **8a** (2.3 g 14 mmol) in ethanol (40 mL) was added 20% aq NaOH solution (10 mL, 15 mmol) dropwise. The mixture was stirred at room temperature for 24 h. The mixture was extracted with H_2O (10 mL) and EtOAc (3 × 10 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (10% EtOAc/hexanes) to afford chalcone **32** (4.8 g, 95% yield) as a white solid, mp 101−103 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (d, 1H, J = 16.1 Hz), 6.99 (d, 1H, J = 16.1 Hz), 6.68 (d, 2H, J = 2.2 Hz), 6.57 (d, 1H, J = 2.7 Hz), 6.51 (t, 2H, J = 2.7 Hz), 3.92 (s, 3H), 3.82 (s, 3H), 3.81 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.2, 161.2, 160.2, 157.0, 146.9, 143.2, 136.4, 126.8, 106.5, 104.6, 103.5, 101.2, 100.0, 56.6, 55.9, 55.6; HRMS (EI) calcd for $C_{19}H_{19}BrO_5$ [M^+] 406.0416, found 406.0402.

3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-1*H*-inden-1-one (33). To a vial (3 mL) was added chalcone **32** (204 mg, 0.5 mmol), $PdCl_2$ (4.4 mg, 5 mol %), K_2CO_3 (173 mg, 2.5 mmol), and triphenylphosphine (6.7 mg, 15 mol %) sequentially. The mixture was suspended in DMF (5.0 mL). Then, the reaction mixture was heated at 140 °C for 1 h. The mixture was purified by silica gel column chromatography (10% EtOAc/hexanes) to provide 1-indenone **33** (150 mg, 92% yield) as a red solid, mp 149−154 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.81 (d, 1H, J = 2.1 Hz), 6.78 (d, 2H, J = 2.3 Hz), 6.54 (t, 1H, J = 2.3 Hz), 6.45 (d, 1H, J = 2.1 Hz), 5.71 (s, 1H), 3.86 (s, 3H), 3.82 (s, 6H), 3.72 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.7, 166.4, 163.3, 160.2, 154.7, 136.9, 136.2, 122.5, 121.1, 106.1, 103.3, 102.8, 102.3, 56.0, 55.7, 55.6; HRMS (EI) calcd for $C_{19}H_{18}O_5$ [M^+] 326.1154, found 326.1149.

(*S*)-3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-2,3-dihydro-1*H*-inden-1-one (34). A 500 mL, two neck, round-bottomed flask is fitted with a mechanistic stirrer and a digital pH meter. The flask was charged with baker's yeast (1.9 g) and α-D-glucose (1.5 g) in an aqueous phosphate pH 7.2 buffer solution (300 mL). To the reaction mixture at 40 °C was added a solution of 1-indenone **33** (50 mg) in hot DMSO (3.0 mL). The reaction was stirred for 4 h, and a range of neutral pH (6.7−7.0) was maintained through the addition of 1 mL aliquots of 1 M NaOH (total *ca.* 10−15 mL). After 1 day, additional baker's yeast (1.9 g) and α-D-glucose (1.5 g) were added to the mixture, and a neutral pH was also kept by addition of 1 mL aliquots of 1 M NaOH (total *ca.* 10−15 mL). After an additional 1 day, the reaction mixture cooled to room temperature and quenched with EtOH (100 mL). The resulting mixture was filtered through a Celite pad to remove the yeast, and then the filtrate was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic fractions were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (10% EtOAc/hexanes) to afford 1-indenone **34** (47 mg, 94% yield, > 99% ee) as a white solid, mp 95−97 °C; $[\alpha]^{20}_D$ = +8.9 (*c* 0.5, MeOH). The enantiomeric excess was determined by HPLC using Chiralcel OD-H column (9:1 hexane/IPA, flow rate = 1 mL/min, λ = 230 nm), t_R = 12.4 min (*S*), 19.8 min (*R*); ^{1}H and ^{13}C NMR spectra are identical with those of the racemic compound **10a**.

(2*S*,3*S*)-3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-2-(4-methoxyphenyl)-2,3-dihydro-1*H*-inden-1-one (35). The reaction followed the typical procedure for α-arylation to provide **35** (89% yield, >99% ee) as a white solid. $[\alpha]^{20}_D$ = +137 (*c* 0.4, MeOH); Chiralcel OD-H column (8:2 hexane/IPA, flow rate = 1 mL/min, λ = 230 nm), t_R = 23.3 min (2*R*,3*R*), 39.1 min (2*S*,3*S*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.02 (d, 2H, J = 8.7 Hz), 6.89 (d, 1H, J = 2.0 Hz), 6.84 (d, 2H, J = 8.7 Hz), 6.70 (d, 1H, J = 2.1 Hz), 6.32 (t, 1H, J = 2.2 Hz), 6.15 (d, 2H, J = 2.2 Hz), 4.44 (d, 1H, J = 2.8 Hz), 3.88 (s, 3H), 3.78 (s, 3H), 3.71 (s, 6H), 3.69 (s, 3H), 3.65 (d, 1H, J = 2.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.8, 162.1, 160.9, 158.8, 157.9, 146.0, 138.8, 137.7, 131.6, 128.9, 114.4, 106.5, 105.3, 98.3, 96.6, 64.2, 55.8, 55.7, 55.3, 52.0; HRMS (EI) calcd for $C_{26}H_{26}O_6$ [M^+] 434.1729, found 434.1733.

(+)-Pauciflorol F (2). To a solution of **35** (0.39 mmol, 170 mg) in CH_2Cl_2 (4.0 mL) at 0 °C was added BBr_3 (3.9 mL, 3.9 mmol, 1 M in CH_2Cl_2) over 10 min. The reaction was allowed to warm to room temperature and then stirred for 24 h. The reaction was quenched with methanol (5 mL) and poured into water (5 mL). The aqueous layer washed with CH_2Cl_2 and extracted with the EtOAc (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried over $MgSO_4$. After concentration, the crude product was purified by silica gel column chromatography (10% MeOH/CH_2Cl_2) to provide (+)-pauciflorol F (99 mg, 70% yield) as a yellow amorphous powder. $[\alpha]^{20}_D$ = +86 (*c* 0.5, MeOH) (lit.[6] enantiomer $[\alpha]^{25}_D$ = −80 (*c* 0.1, MeOH)); ^{1}H NMR (500 MHz, acetone-d_6) δ 8.76 (s, 1H), 8.49 (s, 1H), 8.26 (s, 1H), 8.06 (s, 2H), 6.96 (d, 2H, J = 8.5 Hz), 6.78 (d, 2H, J = 8.5 Hz), 6.72 (s, 2H), 6.19 (d, 1H, J = 2.0 Hz), 6.02 (d, 2H, J = 2.1 Hz), 4.38 (d, 1H, J = 2.6 Hz), 3.50 (d, 1H, J = 2.6 Hz); ^{13}C NMR (125 MHz, acetone-d_6) δ 205.6, 160.3, 159.5, 157.2, 156.7, 147.4, 140.1, 134.8, 131.9, 129.6, 116.3, 110.3, 106.4, 101.7, 100.6, 65.4, 52.1; HRMS (EI) calcd for $C_{21}H_{16}O_6$ [M^+] 364.0946, found 364.0935.

(2*S*,3*S*)-3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-2-phenyl-2,3-dihydro-1*H*-inden-1-one (36). The reaction was followed the typical procedure for α-arylation to provide **36** (92% yield, 99% ee) as a white solid. $[\alpha]^{20}_D$ = +135 (*c* 0.5, MeOH); Chiralpak OD-H column (8:2 hexane/IPA, flow rate = 1 mL/min, λ = 230 nm), t_R = 7.0 min (2*R*,3*R*), 13.5 min (2*S*,3*S*).

(2*S*,3*S*)-3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-2-(*p*-tolyl)-2,3-dihydro-1*H*-inden-1-one (37). The reaction was followed the typical procedure for α-arylation to provide **37** (85% yield, 99% ee) as a white solid. $[\alpha]^{20}_D$ = +150 (*c* 0.5, MeOH); Chiralpak OD-H column (8:2 hexane/IPA, flow rate = 1 mL/min, λ = 230 nm), t_R = 6.7 min (2*R*,3*R*), 11.0 min (2*S*,3*S*).

(2*S*,3*S*)-2-(4-Chlorophenyl)-3-(3,5-dimethoxyphenyl)-4,6-dimethoxy-2,3-dihydro-1*H*-inden-1-one (38). The reaction was followed the typical procedure for α-arylation to provide **38** (78% yield, >99% ee) as a white solid. $[\alpha]^{20}_D$ = +154 (*c* 0.5, MeOH); Chiralpak OD-H column (9:1 hexane/IPA, flow rate = 1 mL/min, λ = 230 nm), t_R = 10.3 min (2*R*,3*R*), 11.7 min (2*S*,3*S*).

(2*S*,3*S*)-3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-2-(4-(trifluoromethyl)-phenyl)-2,3-dihydro-1*H*-inden-1-one (39). The reaction was followed the typical procedure for α-arylation to provide **41** (66% yield, 98% ee) as a white solid. $[\alpha]^{20}_D$ = +118 (*c* 0.5, MeOH); Chiralpak OD-H column (9:1 hexane/IPA, flow rate = 0.25 mL/min, λ = 230 nm), t_R = 38.5 min (2*R*,3*R*), 41.4 min (2*S*,3*S*).

(2*S*,3*S*)-4-(3-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-1-oxo-2,3-dihydro-1*H*-inden-2-yl)benzonitrile (40). The reaction was followed the typical procedure for α-arylation to provide **42** (67% yield, >99% ee) as a white solid. $[\alpha]^{20}_D$ = +177 (*c* 0.5, MeOH); Chiralpak OD-H column (8:2 hexane/IPA, flow rate = 1 mL/min, λ = 230 nm), t_R = 14.5 min (2*R*,3*R*), 20.8 min (2*S*,3*S*).

■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures and spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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