JOC The Journal of Organic Chemistry
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pubs.acs.org/joc

Palladium-Catalyzed Annulation of Alkynes with *Ortho*-Halide-Containing Benzyl Alcohols in Aqueous Medium

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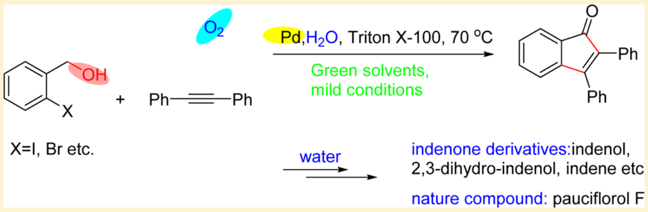
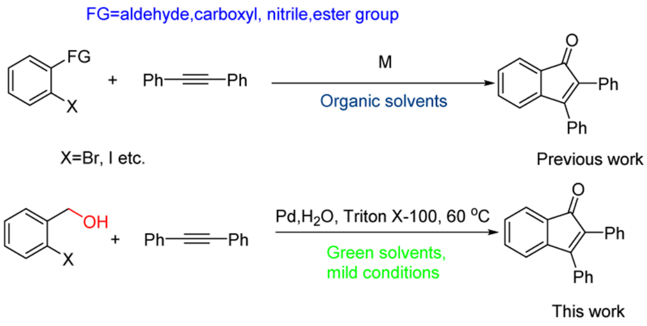
Ⓢ *Supporting Information*

ABSTRACT: The Pd-catalyzed annulations of *ortho*-halide-containing benzyl alcohols with alkynes for the synthesis of indenones were achieved in aqueous Triton X-100 micelles with good yields and wide substrate scopes. Moreover, the indenones obtained in this procedure can be further functionalized to form some more synthetic useful derivatives via an environmental-friendly way.



Indenones are a class of important compounds since they are ubiquitous in synthetic chemistry, biology, pharmacology, and material chemistry.[1] Consequently, preparation of indenones and their derivatives has aroused great interest among synthetic chemists over the past decades.[2] Typically, indenones have been synthesized by transition metal (Pd,[3] Co,[4] Ru[5] etc.)-catalyzed annulations of alkynes with ortho-bifunctionalized arenes (Scheme 1).[6] In recent years, guided by powerful C−H activation technologies, Rh-catalyzed direct annulations of aldehydes with alkynes have appeared.[7] In addition, other approaches such as trimerization, cross-couplings, and amino transfer reactions have also been developed for the formation of indenones.[8]

Scheme 1. Preparation of Indeones via Annulation of Alkynes



Despite all these advances, development of greener methods for the preparation of indenones is in high demand, as the existing methods usually require high reaction temperatures, expensive reagents, and the use of potential toxic organic solvents.

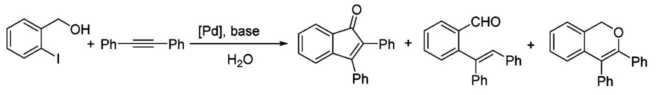
Water is an ideal green medium for organic synthesis.[9] Meanwhile, nonionic surfactants develop well that enable transition-metal catalyzed cross-couplings to be performed in water. The surfactants may spontaneously self-aggregate to form nanomicelles that serve as nanoreactors for many valued types of couplings.[10]

Alone this line, we herein wish to explore a novel approach to synthesize indenones via Pd-catalyzed annulation in water under relatively mild conditions. We originally planned to furnish the Pd-catalyzed annulations with *ortho*-halogenated benzaldehydes and alkynes in water. In the course of exploring this reaction, it was found that *ortho*-halide-containing benzyl achohols could also efficiently convert to indenones. To date, there is no report describing the synthesis of indenones from *ortho*-halide-containing benzyl achohols. In addition, the usage of benzyl achohols may broaden the scope of substrates to prepare indenones. In this regard, the Pd-catalyzed annulations using cheaper benzyl alcohols instead of corresponding aldehydes (for example, 2-iodobenzaldehyde \$20/g vs 2-iodobenzyl alcohol \$1/g from Aldrich) deserved further investigation.

As a representative example, the annulation of 2-iodobenzyl alcohol and diphenylethyne was selected to optimize the reaction (Table 1). The present reaction could not occur in the absence of a palladium catalyst (entry 1). The use of surfactant is crucial for the reaction, and the yield increased from 5% to 69% in the presence of a surfactant (entries 2, 3). Screening ionic and nonionic surfactants revealed that Triton X-100 was still the best choice (entries 3−6). Next, the reaction temperature was examined in a quest to improve the yield. There was a sharp decrease in the reactivity at lower temperature (entries 3, 7−9), but side reactions could be inhibited at the same time. Avoiding the nasty byproducts, the reaction was finally conducted at 70 °C. To our delight, a satisfactory yield could be obtained when the reaction was extended to 24 h (entry 10). Considering that the annulation of 2-iodobenzyl alcohol with diphenylethyne may need the consumption of molecular oxygen, an oxygen balloon was introduced. As expected, oxygen promoted the reaction with

Received: July 7, 2014
Published: October 13, 2014

Table 1. Optimizations for the Preparation of Indenone[a]

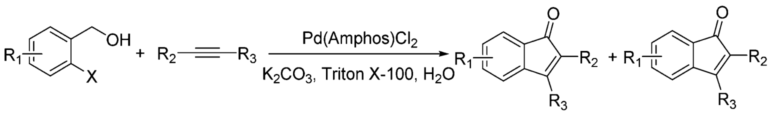


1a **2a** **3a** **4a** **5a**

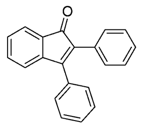
entry	catalysts	additives	bases	temp (°C)	time (h)	yield (%)[b]
1	–	TX-100[c]	K_2CO_3	110	2	0
2	Pd(Amphos[d])Cl_2	–	K_2CO_3	–	2	5
3	Pd(Amphos)Cl_2	TX-100	K_2CO_3	110	2	69 (15[e],10[f])
4	Pd(Amphos)Cl_2	TBAC	K_2CO_3	110	2	23
5	Pd(Amphos)Cl_2	SDS	K_2CO_3	110	2	50
6	Pd(Amphos)Cl_2	Brij L23	K_2CO_3	110	2	55
7	Pd(Amphos)Cl_2	TX-100	K_2CO_3	90	2	53 (13[e])
8	Pd(Amphos)Cl_2	TX-100	K_2CO_3	25	2	0
9	Pd(Amphos)Cl_2	TX-100	K_2CO_3	70	2	31 (2[e])
10	Pd(Amphos)Cl_2	TX-100	K_2CO_3	70	24	80 (9[e])
11[h]	Pd(Amphos)Cl_2	TX-100	K_2CO_3	70	24	86 (6[e])
12[h]	Pd(dppf)Cl_2	TX-100	K_2CO_3	70	24	70 (17[e])
13[h]	$Pd(PPh_3)_2Cl_2$	TX-100	K_2CO_3	70	24	17 (10,[e] 23[f])
14[h]	Pd(Xphos)Cl_2	TX-100	K_2CO_3	70	24	44 (15[e])
15[h]	Pd(Amphos)Cl_2	TX-100	NaOAc	70	24	16 (62[e])
16[h]	Pd(Amphos)Cl_2	TX-100	$KHCO_3$	70	24	7 (41[e])
17[h]	Pd(Amphos)Cl_2	TX-100	*t*-BuOK	70	24	40[f]

[a]Reaction conditions: 2-iodobenzyl alcohol 0.5 mmol, 1,2-diphenylethyne 0.55 mmol, palladium complex 0.01 mmol, base 0.5 mmol, 2 wt % surfactants/H_2O, 2 mL, in air, 24 h. [b]Determined by GC. [c]Tx-100 was Triton X-100. [d]Amphos = di-*tert*-butyl(4-dimethylaminophenyl)phosphine. [e]The yield of **5a**. [f]The yield of **4a**. [h]With O_2 balloon.

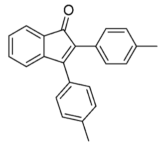
Table 2. Scope of Substrates[a,b]



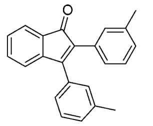
1 **2** **3** **3'**



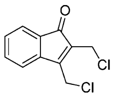
3a X=I, 86%; X=Br, 75%[c]
X=Cl, 7%[c]



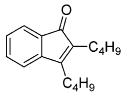
3b X=I, 87%; X=Br, 77%[c]



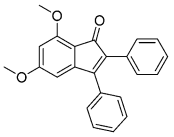
3c X=I, 81%



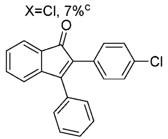
3d X=I, 0%



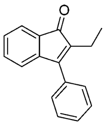
3e X=I, 77%



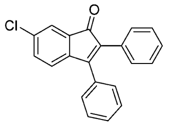
3f X=I, 68%[d](77%[e]); X=Br, 35%[c]



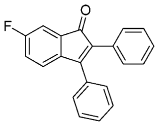
3g X=I, 84%[f](50:50)[g]



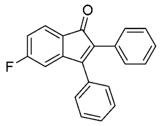
3h X=I, 80%



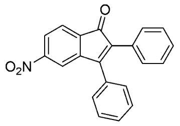
3i X=I, 87%, X=Br, 65%[c]



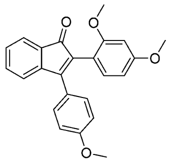
3j X=I, 90%, X=Br, 78%[c]



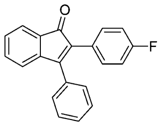
3k X=I, 85%



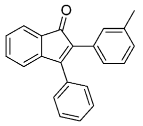
3l X=I, trace



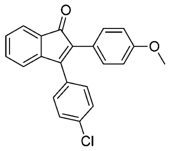
3m X=I, 68%[f](56:44)[g]



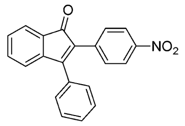
3n X=I, 93%[f](50:50)[h]



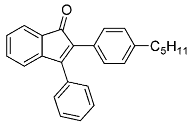
3o X=I, 82%[f](50:50)[h]



3p X=I, 81%[f](51:49)[g]



3q X=I, 83%[f](75:25)[h]

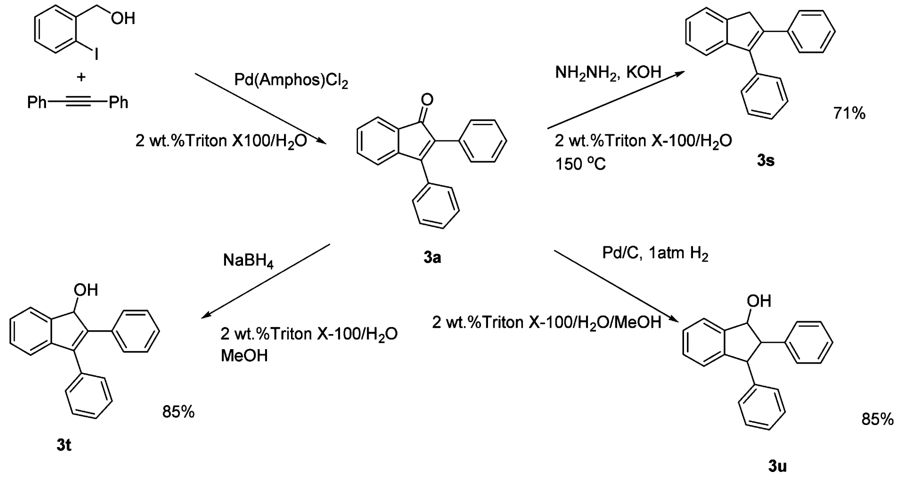


3r X=I, 73%[f](77:23)[h]

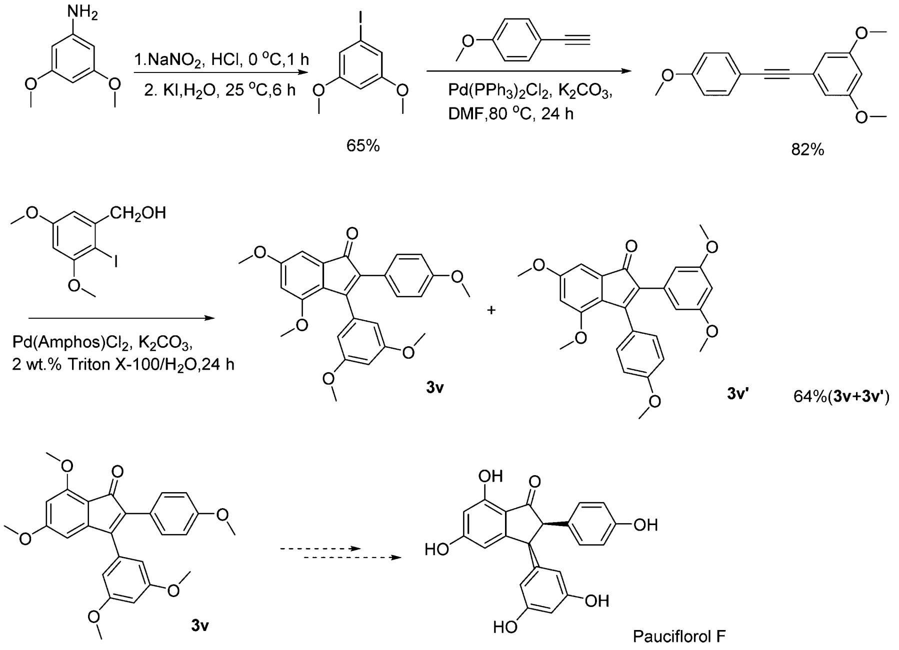
[a]Reaction conditions: 2-halobenzyl alcohol 0.5 mmol, alkyne 0.55 mmol, palladium complex 0.01 mmol, base, 0.5 mmol, 2 wt % Triton X-100/H_2O 2 mL, with O_2 balloon, 70 °C, 24 h. [b]Isolated yields. [c]The reaction was conducted at 110 °C. [d]The reaction was conducted at 80 °C. [e]2 wt % Triton X-100/H_2O 2 mL was replaced by 2 wt % Brij L23/H_2O. [f]Yield of all the isomers. [g]The two isomers were separated, and the ratio of two isomers(**3**/**3′**) was determined by isolated yield. [h]The two isomers were unseparated, the ratio of two isomers (**3**/**3′**) was determined by ^1H NMR, and the regioselectivty was not determined.

the yield increased to 86% (entry 11). Then some other commercially available palladium complexes were tested (entries 12–14). However, palladium complexes, such as Pd(dppf)Cl_2, $Pd(PPh_3)_2Cl_2$, and Pd(Xphos)Cl_2, did not give

Scheme 2. Sequence Reactions with Indenones in Aqueous Medium



Scheme 3. A Potential Application of the Protocol in Total Synthesis



any improvement. Finally, an examination of the bases demonstrated that K_2CO_3 was the most effective base for this transformation, and other bases were not suitable for this reaction (entries 11, 15−17).

With the optimized conditions in hand, a series of internal alkynes and 2-halobenzyl alcohols were chosen to establish the scope and generality of the method (Table 2). Symmetric diarylethynes bearing a methyl substituent at different positions coupled with 2-iodobenzyl alcohol to afford the indenones in good yields (**3b**, **3c**). Notably, an alkyl-substituted internal alkyne was also tolerated (**3e**), but propargyl chloride failed to provide the desired product (**3d**).

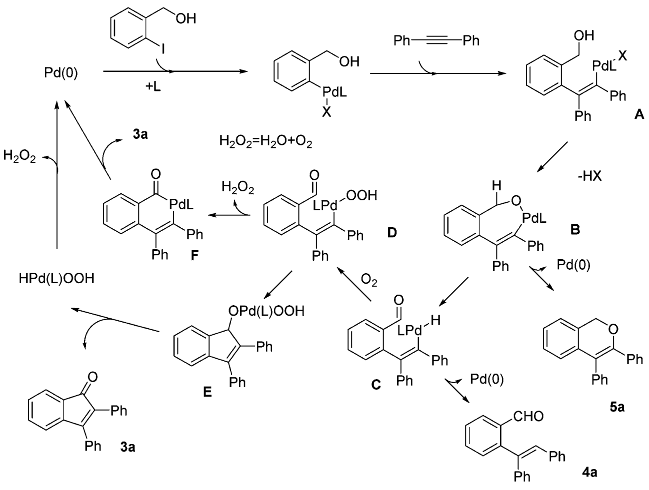
As for asymmetric diarylacetylenes, most of them underwent smooth coupling with two isomers obtained (**3g**, **3n**−**3p**). The electronic effect seems to have little influence on the regioselectivity except for **3q**, while the steric effect plays an important role in the regioselectivity. For example, the usage of but-1-yn-1-ylbenzene only afforded a sole product (**3h**). Similarly, a regioselective product was obtained when 1-pentyl-4-(phenylethynyl)benzene was used (**3r**). After that, substituted 2-iodobenzyl alcohols were examined. Variation of the substituents showed obvious effects on the reaction efficiency. Chloro or fluoro substituted 2-iodobenzyl alcohols survived the reaction with satisfactory yields (**3i**−**3k**). However, 2-iodobenzyl alcohol substituted with an electron-donating group afforded the corresponding product in only 68% yield even at a higher temperature (**3f**). Gratefully, a higher yield could be obtained when Triton X-100 was replaced by Brij L23. 2-Iodo-4-nitrobenzyl alcohol was also subjected to the reaction. But unfortunately, the deiodination product instead of the desired indenone was observed in this case (**3l**). We further used 2-bromobenzyl alcohol and 2-chlorobenzyl alcohol to replace 2-iodobenzyl alcohol. 2-Bromobenzyl alcohol survived this reaction with moderate to good yields at a higher temperature (110 °C) (**3a**, **3b**, **3f**, **3i**, **3j**). As for 2-chlorobenzyl alcohol, only a trace amount of product could be observed at 110 °C for 24 h (**3a**).

Next, we performed several experiments to explore the sequence reactions of the above-mentioned annulation (Scheme 2). 2,3-Diphenyl-1*H*-inden-1-one (**3a**) could easily convert to 2,3-diphenyl-1*H*-indene (**3s**) with hydrazine in the presence of KOH. When **3a** was treated with $NaBH_4$, the corresponding indenol (**3t**) was obtained, whereas in Pd/C hydrogenation conditions, 2,3-diphenyl-2,3-dihydro-1*H*-inden-1-ol (**3u**) was produced. All the reactions were conducted in the Triton X-100/water system (methanol needed to be added in some cases) which does not need separation of indenones from the original reaction system. Thus, these synthetic useful structures (indenol, 2,3-dihydro-indenol, indene, etc.) can be achieved in one pot via an environmental-friendly approach.

To further highlight the potential advantage of our methodology, the developed method was utilized for preparation of 2-(3,5-dimethoxyphenyl)-5,7-dimethoxy-3-(4-methoxyphenyl)-1*H*-inden-1-one (**3v**), a key intermediate which can eventually convert to *Pauciflorol F* (a kind of polyphenolic natural products[1e]) (Scheme 3). 1,3-Dimethoxy-5-((4-methoxyphenyl)ethynyl)benzene was first synthesized via iodidation and Sonogashira couplings using 3,5-dimethoxyaniline as the starting material.[11] Next, 1,3-dimethoxy-5-((4-methoxyphenyl)ethynyl)benzene reacted with (2-iodo-3,5-dimethoxyphenyl)methanol under the developed conditions to obtain two isomers in moderate yields (64% total yields). Indenone **3v** was separated by preparative HPLC. According to the literature,[1e] further hydrogenation and demethylation of **3v** can finally yield the *Pauciflorol F*.

Finally, we tried to go through the mechanism of the developed reaction. The reaction could not proceed under an argon atmosphere which means oxygen is necessary for this reaction. To clarify when benzyl alcohol was oxidized, 2-iodobenzyl alcohol was stirred under the optimal conditions. It failed to convert to 2-iodobenzaldehyde under the optimal conditions without adding alkyne. However, the oxidative addition of 2-iodobenzyl alcohol to the active Pd(0) complex occurred with a self-coupling product obtained. It indicates that the insertion of alkyne may occur before the oxidation. Although details about the mechanism remain to be ascertained, based on the above-mentioned results and the well documented annulation of *ortho*-halobenzaldehyde with an alkyne,[3a,6b] a proposed mechanism was outlined in Scheme 4.

Scheme 4. Proposed Mechanism of the Pd-Catalyzed Annulation



The palladium complex $Pd(Amphos)Cl_2$ was a precursor for the active Pd(0) complex. The oxidative addition of 2-iodobenzyl alcohol to the Pd(0) complex first took place. Then the alkyne was inserted to the C−Pd bond to form the intermediate **A**. After dehydrohalogenation, intermediate **B** was formed. The intermediate **B** can directly lead to byproduct **5a** via the reductive elimination of palladium. Also, intermediate **B** can convert to intermediate **C** through hydrogen transfer. The formation of intermediate **C** provided a good explanation for the formation of byproduct **4a**. According to the paper reported by Uemura,[14] a palladium hydroperoxide intermediate **D** may be further formed. Then there may exist two ways to close the ring. Intermediate **D** could transfer to the intermediate **E** via the insertion of the C═O double bond. Then β-H elimination of intermediate **E** would give the indenone and HPdOOH species. The HPdOOH species could further decompose to the Pd(0) complex and H_2O_2 which finished the catalytic cycle. On the other hand, intermediate F was produced via the intramolecular oxidative addition along with the detachment of H_2O_2. Intermediate F could also form the desired indenone **3a** and Pd(0) species. The H_2O_2 formed in the two paths may produce H_2O and O_2 *in situ*. In this procedure, ligand and Triton X-100 may help to stabilize and improve the reactivity of the Pd(0) species in water (it is possible to form nanomicelles), avoiding the formation of palladium black.

In summary, we have described a novel synthesis of indenones via Pd-catalyzed annulation of an *ortho*-halobenzyl alcohol with internal alkynes in an aqueous system. This new procedure is environmental-friendly because no toxic solvent is required in the coupling step. In addition, the indenones formed in the procedure can undergo some sequence reactions without any separation process which can decrease the consumption of energy and reagents. The protocol also exhibits good yields and broad substrate scopes, thereby offering considerable potential applications to complex targets (*Pauciflorol F* intermediate) in water.

■ EXPERIMENTAL SECTION

Melting points are uncorrected. All commercial materials were used without further purification. Asymmetric diarylacetylenes were synthesized according to the literature;[12] 2-iodo-4,6-dimethoxybenzyl alcohol was synthesized according to the literature.[13] The proton (^1H) and carbon (^{13}C) NMR spectra were obtained in $CDCl_3$ using a 500 MHz spectrometer referenced to TMS and are reported in δ units. Coupling constants (*J* values) are reported in Hz. Mass spectra were obtained using the EI technique. Elemental analysis was performed on a C/H mode. Preparative high performance liquid chromatography was performed on the column XDB-C18 (9.6 mm × 250 mm) with methanol/water (70:30) as eluent.

General Procedure for Synthesis of Indenones. A mixture of 2-iodobenzyl alcohol (0.5 mmol), alkyne (0.55 mmol), Pd(Amphos)-Cl_2 (0.01 mmol), and K_2CO_3 (0.50 mmol) was stirred in 2 wt % Triton X-100/H_2O (2 mL) in a 5 mL vial with an oxygen balloon at 70 °C for 24 h. The reaction mixture was then cooled and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo to give a crude mixture which was purified by silica gel column chromatography to afford the desired product.

*2,3-Diphenyl-1H-inden-1-one (**3a**).* Starting material: 2-iodobenzyl alcohol 117 mg (0.5 mmol), 1,2-diphenylethyne 97.9 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, 1:100) to give 121 mg of product as a red solid (86% yield); mp 152−153 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.0 Hz, 1H), 7.36−7.28 (m, 6H), 7.20 (dt, *J* = 6.5, 5.3 Hz, 6H), 7.08 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.6, 154.4, 144.3, 132.5, 131.8, 131.4, 129.8, 129.0, 128.4, 128.0, 127.8, 127.6, 127.1, 126.8, 122.0, 120.3. GC/MS, *m/z*: 282 [M$^+$]. Anal. Calcd for $C_{21}H_{14}O$: C, 89.34; H, 5.00. Found: C, 89.65; H, 5.15.

2,3-Di-p-tolyl-1H-inden-1-one (***3b***). Starting material: 2-iodobenzyl alcohol 117 mg (0.5 mmol), 1,2-di-*p*-tolylethyne 113 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, 1:100) to give 135 mg of product as a red solid (87% yield); mp 143−145 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.0 Hz, 1H), 7.36 (s, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.22 (m, 2H), 7.20−7.10 (m, 4H), 7.07 (d, *J* = 12.0 Hz, 2H), 2.36 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.7, 154.5, 144.5, 137.4, 136.5, 132.5, 131.8, 129.7, 129.1, 127.9, 127.7, 127.6, 126.9, 126.1, 124.8, 121.9, 120.3, 20.5. GC/MS, *m/z*: 310 [M$^+$]. Anal. Calcd for $C_{23}H_{18}O$: C, 89.00; H, 5.85. Found: C, 88.79; H, 5.69.

2,3-Di-m-tolyl-1H-inden-1-one (***3c***). Starting material: 2-iodobenzyl alcohol 117 mg (0.5 mmol), 1,2-di-*m*-tolylethyne 113 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, 1:100) to give 125 mg of product as a red solid (81% yield); mp 141−143 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.0 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.30−7.23 (m, 3H), 7.21 (d, *J* = 7.8 Hz, 2H), 7.15 (dd, *J* = 13.7, 7.6 Hz, 3H), 7.07 (d, *J* = 7.8 Hz, 2H), 2.39 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.8, 153.8, 144.5, 138.4, 136.6, 132.3, 131.1, 130.0, 128.9, 128.5, 127.9, 127.7, 127.5, 127.0, 121.8, 120.2, 20.5, 20.4. GC/MS, *m/z*: 310 [M$^+$]. Anal. Calcd for $C_{23}H_{18}O$: C, 89.00; H, 5.85. Found: C, 88.63; H, 5.71.

2,3-Dipropyl-1H-inden-1-one(***3e***). Starting material: 2-iodobenzyl alcohol 117 mg (0.5 mmol), dec-5-yne 76 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, 1:20) to give 82 mg of product as a red oil (77% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 7.0 Hz, 1H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.01 (d, *J* = 7.2 Hz, 1H), 2.57−2.48 (m, 2H), 2.27−2.20 (m, 2H), 1.61−1.54 (m, 2H), 1.48−1.38 (m, 4H), 1.33 (dd, *J* = 14.9, 7.2 Hz, 2H), 0.96 (dd, *J* = 13.8, 6.5 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.5, 156.7, 144.7, 133.9, 132.1, 130.2, 126.9, 120.7, 118.0, 30.5, 29.0, 25.0, 22.1, 21.8, 21.7, 12.9. GC/MS, *m/z*: 214 [M$^+$]. Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.39; H, 8.38.

5,7-Dimethoxy-2,3-diphenyl-1H-inden-1-one(***3f***). Starting material: 2-iodo-4,6-dimethoxybenzyl alcohol 147 mg (0.5 mmol), 1,2-diphenylethyne 97.9 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, 1:20) to give 116 mg of product as a red oil (68% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (m, 5H), 7.17 (d, *J* = 7.4 Hz, 3H), 7.11 (d, *J* = 6.9 Hz, 2H), 6.87 (s, 1H), 6.42 (s, 1H), 3.86 (s, 3H), 3.56 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.2, 161.8, 157.3, 154.0, 134.0, 133.3, 130.2, 130.1, 128.9, 127.7, 127.4, 126.8, 126.5, 126.0, 121.6, 106.2, 103.1, 101.9, 54.9, 54.7. GC-MS, *m/z*: 342 [M$^+$]. Anal. Calcd for $C_{23}H_{18}O_3$: C, 80.68; H, 5.30. Found: C, 80.29; H, 5.45.

2-(4-Chlorophenyl)-3-phenyl-1H-inden-1-one (***3g***) *and 3-(4-Chlorophenyl)-2-phenyl-1H-inden-1-one* (***3g′***). Starting material: 2-iodobenzyl alcohol 117 mg (0.5 mmol), 1-chloro-4-(phenylethynyl)-benzene 117 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, 1:20) to give 132 mg of product (mixture of **3g**, **3g′**, the ratio is 1:1 which is determined by ^{1}H NMR) as a red oil (84% yield). **3g** and **3g′** were separated by preparative HPLC (methonol/water, 70:30).

2-(4-Chlorophenyl)-3-phenyl-1H-inden-1-one (***3g***). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.0 Hz, 1H), 7.41 (d, *J* = 8.3 Hz, 3H), 7.35 (d, *J* = 8.5 Hz, 2H), 7.33−7.24 (m, 7H), 7.14 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.2, 154.8, 144.1, 132.8, 132.6, 131.5, 129.7, 128.6, 128.2, 128.0, 127.4, 122.1, 120.4; GC-MS, *m/z*: 316 [M$^+$]. Anal. Calcd for $C_{21}H_{13}ClO$: C, 79.62; H, 4.14. Found: C, 80.01; H, 4.28.

3-(4-Chlorophenyl)-2-phenyl-1H-inden-1-one (***3g′***). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.0 Hz, 1H), 7.49−7.43 (m, 3H), 7.42−7.36 (m, 3H), 7.32 (t, *J* = 7.3 Hz, 1H), 7.24 (q, *J* = 8.7 Hz, 4H), 7.16 (d, *J* = 7.2 Hz, 1H);^{13}C NMR (126 MHz, $CDCl_3$) δ 195.2, 152.9, 143.9, 134.3, 132.6, 131.9, 130.2, 129.6, 129.4, 129.0, 128.2, 127.2, 127.0, 122.2, 120.0. GC-MS, *m/z*: 316 [M$^+$]. Anal. Calcd for $C_{21}H_{13}ClO$: C, 79.62; H, 4.14. Found: C, 79.97; H, 4.31;

2-Ethyl-3-phenyl-1H-inden-1-one (***3h***). Starting material: 2-iodobenzyl alcohol 117 mg (0.5 mmol), but-1-yn-1-ylbenzene 71.5 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, 1:50) to give 94 mg of product as an orange oil (80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.0 Hz, 2H), 7.45 (t, *J* = 8.6 Hz, 4H), 7.28 (s, 1H), 7.19 (s, 1H), 7.00 (d, *J* = 7.2 Hz, 1H), 2.35 (q, *J* = 7.5 Hz, 2H), 1.10 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.2, 153.7, 144.9, 135.7, 132.2, 131.8, 130.1, 128.1, 127.8, 127.2, 126.8, 121.4, 119.6, 76.3, 76.0, 75.8, 15.7, 13.0; GC-MS, *m/z*: 234 [M$^+$]. Anal. Calcd for $C_{17}H_{14}O$: C, 87.15; H, 6.02. Found: C, 87.39; H, 5.84.

6-Chloro-2,3-diphenyl-1H-inden-1-one (***3i***). Starting material: 5-chloro-2-iodo benzyl alcohol 134 mg (0.5 mmol), 1,2-diphenylethyne 97.9 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, 1:100) to give 137 mg of product as an orange-red solid (87% yield); mp 183−184 °C; ^{1}H NMR (500 MHz, CDCl3) δ 7.54 (d, *J* = 1.6 Hz, 1H), 7.44−7.41 (m, 3H), 7.39−7.32 (m, 3H), 7.25 (d, *J* = 7.6 Hz, 5H), 7.09 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.1, 154.1, 142.3, 134.1, 131.7, 131.4, 131.3, 129.4, 129.0, 128.6, 127.9, 127.4, 127.2, 127.0, 122.6, 121.2. GC-MS, *m/z*: 316 [M$^+$]. Anal. Calcd for $C_{21}H_{13}ClO$: C, 79.62; H, 4.14. Found: C, 79.89; H, 3.97.

6-Fluoro-2,3-diphenyl-1H-inden-1-one (***3j***). Starting material: 5-fluoro-2-iodo benzyl alcohol 126 mg (0.5 mmol), 1,2-diphenylethyne 97.9 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, 1:100) to give 135 mg of product as an orange-red oil (90% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (ddd, *J* = 7.0, 5.8, 3.4 Hz, 4H), 7.33−7.15 (m, 7H), 7.11 (dd, *J* = 8.0, 4.5 Hz, 1H), 7.03 (td, *J* = 8.7, 2.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.9, 166.5, 152.2, 147.6, 132.7, 131.3, 129.4, 129.0, 128.5, 128.0, 127.4, 127.2, 127.1, 125.6, 123.8, 123.8, 113.5, 113.4, 109.3, 109.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ −111.53. GC-MS, *m/z*: 300[M$^+$]. Anal. Calcd for $C_{21}H_{13}FO$: C, 83.98; H, 4.36. Found: C, 83.79; H, 4.53.

5-Fluoro-2,3-diphenyl-1H-inden-1-one (***3k***). Starting material: 4-fluoro-2-iodo benzyl alcohol 126 mg (0.5 mmol), 1,2-diphenylethyne 97.9 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, 1:100) to give 128 mg of product as an orange oil (85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 7.9, 5.2 Hz, 1H), 7.47−7.41 (m, 3H), 7.37 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.27 (d, *J* = 3.9 Hz, 5H), 6.94 (td, *J* = 9.0, 2.1 Hz, 1H), 6.87 (dd, *J* = 8.5, 2.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.7, 166.5, 152.2, 147.6, 132.7, 131.3, 129.4, 129.0, 128.5, 128.0, 127.4, 127.2, 127.1, 125.6, 123.8,123.8, 113.5, 113.4, 109.3, 109.1. ^{19}F NMR (470 MHz, $CDCl_3$) δ −104.02; GC-MS, *m/z*: 300 [M$^+$]. Anal. Calcd for $C_{21}H_{13}FO$: C, 83.98; H, 4.36. Found: C, 83.76; H, 4.47.

2-(2,4-Dimethoxyphenyl)-3-(4-methoxyphenyl)-1H-inden-1-one (***3m***) *and 3-(2,4-Dimethoxyphenyl)-2-(4-methoxyphenyl)-1H-inden-1-one* (***3m′***). Starting material: 2-iodobenzyl alcohol 117 mg (0.5 mmol), 1,3-dimethoxy- 5-((4-methoxyphenyl)ethynyl)benzene 147 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, from 1:200 to 1:20) to give 126 mg of product (mixture of **3m**, **3m′**, the ratio is 56:44 which is determined by ^{1}H NMR) as a red oil (68% yield). **3m** and **3m′** were separated by preparative HPLC (methonol/water, 70:30).

2-(2,4-Dimethoxyphenyl)-3-(4-methoxyphenyl)-1H-inden-1-one (***3m***). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 6.8 Hz, 1H), 7.33 (dd, *J* = 14.5, 7.8 Hz, 3H), 7.23 (s, 2H), 7.05 (d, *J* = 8.3 Hz, 1H), 6.87 (d, *J* = 8.2 Hz, 2H), 6.47 (d, *J* = 8.3 Hz, 1H), 6.39 (s, 1H), 3.80 (m, 6H), 3.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.2, 160.9, 158.0, 157.4, 150.9, 145.1, 132.3, 131.4, 129.8, 129.6, 129.5, 127.2, 123.6, 121.3, 120.1, 114.0, 112.5, 104.0, 98.3, 54.4, 54.3, 54.2; MS, *m/z*: 372 [M$^+$]. Anal. Calcd for $C_{24}H_{20}O_4$: C, 77.40; H, 5.41. Found: C, 77.67; H, 5.49.

3-(2,4-Dimethoxyphenyl)-2-(4-methoxyphenyl)-1H-inden-1-one (***3m′***). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.1 Hz, 1H), 7.29 (d, *J* = 7.4 Hz, 1H), 7.24 (m, 2H), 7.20 (s, 1H), 7.15 (d, *J* = 9.0 Hz, 1H), 6.91 (d, *J* = 7.2 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 2H), 6.51 (s, 2H), 3.85 (s, 3H), 3.77 (s, 3H), 3.55 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.6, 160.0, 159.2, 157.7, 154.3, 144.4, 131.9, 131.3, 130.7, 129.1, 128.5, 127.4, 125.3, 121.6, 120.0, 112.8, 103.7, 98.1, 54.3, 54.3, 54.2; MS, m/z: 372 [M^+]. Anal. Calcd for $C_{24}H_{20}O_4$: C, 77.40; H, 5.41. Found: C, 77.73; H, 5.54.

*2-(4-Fluorophenyl)-3-phenyl-1H-inden-1-one (**3n**) and 3-(4-Fluorophenyl)-2-phenyl-1H-inden-1-one (**3n′**).* Starting material: 2-iodobenzyl alcohol 117 mg (0.5 mmol), 1-fluoro-4-(phenylethynyl)-benzene 108 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, 1:100) to give 139.5 mg of product (mixture of **3n**, **3n′**, the ratio is 1:1 which is determined by ^{1}H NMR) as a red oil (93% yield). **3n** and **3n′** could hardly be separated.

Mixture of **3n**, **3n′**, the ratio is 1:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60−7.54 (m, 1H), 7.45−7.32 (m, 4H), 7.32−7.20 (m, 4H), 7.16−7.05 (m, 2H), 6.94 (t, J = 8.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.4, 195.2, 170.1, 163.1, 162.3, 161.1, 160.4, 154.3, 153.2, 144.2, 144.0, 132.5, 132.5, 131.6, 130.8, 130.8, 130.4, 129.6, 129.0, 128.8, 128.4, 128.1, 127.9, 127.7, 127.5, 127.2, 126.9, 125.8, 122.1, 120.3, 120.1, 115.2, 115.0, 114.3, 114.1; GC-MS, m/z: 300 [M^+]. Anal. Calcd for $C_{21}H_{13}FO$: C, 83.98; H, 4.36. Found: C, 84.18; H, 4.53.

*2-(3-Methylphenyl)-3-phenyl-1H-inden-1-one (**3o**) and 3-(3-Methylphenyl)-2-phenyl-1H-inden-1-one (**3o′**).* Starting material: 2-iodobenzyl alcohol 117 mg (0.5 mmol), 1-methyl-4-(phenylethynyl)-benzene 106 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, 1:100) to give 121 mg of product (mixture of **3o**, **3o′**, the ratio is 1:1 which is determined by ^{1}H NMR) as a red oil (82% yield). **3o** and **3o′** could hardly be separated.

Mixture of **3o** and **3o′** (50:50); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, 1H), 7.41−7.35 (m, 3H), 7.24 (m, 6H), 7.12 (dd, J = 13.7, 6.9 Hz, 2H), 7.04 (d, J = 7.5 Hz, 0.5 × 1H), 6.99 (d, J = 7.6 Hz, 0.5 × 1H), 2.34 (s, 0.5 × 3H), 2.26 (s, 0.5 × 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.2, 195.6, 154.2, 144.4, 136.6, 132.4, 131.3, 129.8, 129.6, 129.1, 129.0, 128.2, 127.9, 127.7, 127.6, 127.5, 127.0, 126.9, 126.7, 126.1, 124.7, 121.9, 120.3, 20.5. GC-MS, m/z: 296 [M^+]. Anal. Calcd for $C_{22}H_{16}O$: C, 89.16; H, 5.44. Found: C, 88.98; H, 5.52.

*3-(4-Chlorophenyl)-2-(4-methoxyphenyl)-1H-inden-1-one (**3p**) and 2-(4-Chlorophenyl)-3-(4-methoxyphenyl)-1H-inden-1-one (**3p′**).* Starting material: 2-iodobenzyl alcohol 117 mg (0.5 mmol), 1-chloro-4-((4-methoxyphenyl)ethynyl)benzene 133 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, from 1:200 to 1:20) to give 140 mg of product (mixture of **3p**, **3p′**, the ratio is 51:49 which is determined by ^{1}H NMR) as a red oil (81% yield). **3p** and **3p′** were separated by preparative HPLC (methanol/water, 70:30).

*3-(4-Chlorophenyl)-2-(4-methoxyphenyl)-1H-inden-1-one (**3p**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 7.0 Hz, 1H), 7.39 (d, J = 8.3 Hz, 2H), 7.34 (t, J = 8.6 Hz, 2H), 7.27 (d, J = 7.3 Hz, 1H), 7.20 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 7.3 Hz, 1H), 6.81 (d, J = 8.7 Hz, 2H), 3.79 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.6, 158.5, 151.3, 144.2, 134.1, 132.5, 131.4, 130.5, 130.3, 129.6, 129.0, 128.2, 127.8, 122.1, 121.8, 119.7, 112.8, 54.2; GC-MS, m/z:346 [M^+]. Anal. Calcd for $C_{22}H_{15}ClO_2$: C, 76.19; H, 4.36. Found: C, 76.38; H, 4.47.

*2-(4-Chlorophenyl)-3-(4-methoxyphenyl)-1H-inden-1-one (**3p′**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 7.0 Hz, 1H), 7.37 (t, J = 7.4 Hz, 1H), 7.34−7.27 (m, 3H), 7.21 (dd, J = 15.8, 7.3 Hz, 4H), 6.93 (d, J = 8.6 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.2, 159.7, 154.7, 144.0, 132.6, 132.4, 130.3, 130.0, 129.2, 128.6, 128.1, 127.4, 123.6, 121.9, 120.4, 113.4, 54.4; GC-MS, m/z: 346 [M^+]. Anal. Calcd for $C_{22}H_{15}ClO_2$: C, 76.19; H, 4.36. Found: C, 76.39; H, 4.45.

*2-(4-Nitrophenyl)-3-phenyl-1H-inden-1-one (**3q**) and 3-(4-Nitrophenyl)-2-phenyl-1H-inden-1-one (**3q′**).* Starting material: 2-iodobenzyl alcohol 117 mg (0.5 mmol), 1-nitro-4-((4-methoxyphenyl)-ethynyl)benzene 123 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, from 1:20 to 1:10) to give 135 mg of product (mixture of **3q**, **3q′**, the ratio is 75:25 which is determined by ^{1}H NMR, but the regioselectivity is not determined) as a red oil (total yield 83%). **3q** and **3q′** could hardly be separated.

Mixture of **3q** and **3q′** (75:25). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.83 (s, 1H), 8.27 (d, J = 8.6 Hz, 1H), 8.10 (d, J = 8.7 Hz, 0.75 × 1H), 8.08 (d, J = 8.7 Hz, 0.25 × 1H), 8.06 (m, 1H), 7.62 (m, 1H), 7.56 (m, 1H), 7.50−7.38 (m, 3H), 7.34 (m, 2H), 7.28 (m, 1H), 7.19 (t, J = 6.5 Hz, 0.75 × 2H), 7.07 (d, J = 7.2 Hz, 0.25 × 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.3, 157.4, 145.8, 143.5, 136.8, 132.9, 130.9, 129.7, 129.6, 129.1, 128.9, 128.2, 127.3, 125.2, 122.4, 122.3, 121.1, 111.3; GC-MS, m/z: 327 [M^+]. Anal. Calcd for $C_{21}H_{13}NO_3$: C, 77.05; H, 4.00. Found: C, 76.77; H, 4.25.

*2-(4-Pentylphenyl)-3-phenyl-1H-inden-1-one (**3r**) and 3-(4-Pentylphenyl)-2-phenyl-1H-inden-1-one (**3r′**) (77:23).* Starting material: 2-iodobenzyl alcohol 117 mg (0.5 mmol), 1-pentyl-4-(phenylethynyl)benzene 136 mg (0.55 mmol). The crude material was purified by column chromatography (ethyl acetate/petroleum ether, from 1:200 to 1:10) to give 135 mg of product (mixture of **3r**, **3r′**, the ratio is 77:23 which is determined by ^{1}H NMR, but the regioselectivity is not determined) as a red oil (73% yield). **3r** and **3r′** could hardly be separated.

Mixture of **3r** and **3r′**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, J = 7.0 Hz, 1H), 7.43−7.34 (m, 2H), 7.27 (dd, J = 16.1, 6.7 Hz, 7H), 7.19 (dd, J = 10.8, 8.1 Hz, 3H), 7.09 (dd, J = 24.2, 7.6 Hz, 1H), 2.59 (dt, J = 42.1, 7.8 Hz, 2H), 1.69−1.59 (m, 2H), 1.39−1.28 (m, 4H), 0.90 (dd, J = 13.7, 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.6, 154.6, 144.3, 143.6, 132.3, 131.1, 130.0, 130.0, 129.0, 128.9, 128.8, 128.2, 127.9, 127.8, 127.5, 127.2, 127.1, 126.6, 121.9, 120.4, 120.1, 34.9, 34.8, 30.6, 29.9, 21.6, 13.1. MS, m/z: 352 [M^+]. Anal. Calcd for $C_{26}H_{24}O$: C, 88.60; H, 6.86. Found: C, 88.27; H, 6.51.

Synthesis of 2,3-Diphenyl-1*H*-indene 3s. A mixture of 2-iodobenzyl alcohol 117 mg (0.5 mmol), 1,2-diphenylethyne 97.9 mg (0.55 mmol), Pd(Amphos)Cl_2 8 mg (0.01 mmol), K_2CO_3 69 mg (0.50 mmol) was stirred in 2 wt % Triton X-100/H_2O (2 mL) in a 5 mL vial with an oxygen balloon at 60 °C for 24 h. Then the resulting indenone mixture was transferred to a sealed tube. Then KOH 31 mg (0.55 mmol), hydrazine 28 mg (0.55 mmol), and H_2O 1 mL were added. The resulting mixture was stirred at 150 °C for 24 h. Upon completion, the mixture was cooled, extracted with ethyl acetate (15 mL), and washed with diluted hydrochloric acid (3 × 15 mL), sat. aq. $NaHCO_3$ (3 × 15 mL), and dried over anhydrous Na_2SO_4. After filtration, the organic layer was concentrated in vacuo and the residue was purified by column chromatography on silica gel (pure petroleum ether) to give 95 mg of **3s** (71% total yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 7.1 Hz, 1H), 7.44 (d, J = 6.7 Hz, 2H), 7.41−7.36 (m, 3H), 7.32−7.19 (m, 8H), 3.95 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.0, 141.4, 140.1, 139.0, 135.6, 135.1, 128.4, 127.8, 127.3, 127.2, 126.4, 125.9, 125.5, 124.1, 122.6, 119.4, 40.2. GC-MS, m/z: 268 [M^+]. Anal. Calcd for $C_{21}H_{16}$: C, 93.99; H, 6.01. Found: C, 93.79; H, 5.89.

Synthesis of 2,3-Diphenyl-1*H*-indenol 3t. A mixture of 2-iodobenzyl alcohol 117 mg (0.5 mmol), 1,2-diphenylethyne 97.9 mg (0.55 mmol), Pd(Amphos)Cl_2 8 mg (0.01 mmol), and K_2CO_3 69 mg (0.50 mmol) were stirred in 2 wt % Triton X-100/H_2O (2 mL) in a 5 mL vial with an oxygen balloon at 60 °C for 24 h. Then the resulting indenone mixture was added to 3 mL of methanol and cooled to 0 °C, and $NaBH_4$ (3 mmol) was then added in portions over 30 min. The resulting mixture was stirred at 0 °C for another 3 h. Afterward, the mixture was treated with diluted hydrochloric acid, extracted with ethyl acetate (15 mL), washed with sat. aq. $NaHCO_3$ (3 × 15 mL), and dried over anhydrous Na_2SO_4. After filtration, the organic layer was concentrated in vacuo and the residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) to give 121 mg of **3t** (85% total yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, J = 6.7 Hz, 1H), 7.35 (d, J = 6.9 Hz, 2H), 7.30 (dd, J = 17.2, 9.0 Hz, 5H), 7.24 (t, J = 6.6 Hz, 2H), 7.21 (s, 1H), 7.18 (s, 1H), 7.16 (d, J = 7.0 Hz, 1H), 7.11 (d, J = 6.8 Hz, 1H), 5.65 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3, 142.9, 142.8, 138.8, 133.8, 133.1, 128.3, 128.1, 127.8, 127.7, 127.3, 127.1, 126.8, 126.4, 125.4, 122.7, 119.7, 76.3; GC-MS, m/z: 284 [M^+]. Anal. Calcd for $C_{21}H_{16}O$: C, 88.70; H, 5.67. Found: C, 88.57; H, 5.74.

Synthesis of 2,3-Diphenyl-2,3-dihydro-1*H*-inden-1-ol 3u. A mixture of 2-iodobenzyl alcohol 117 mg (0.5 mmol), 1,2-diphenylethyne 97.9 mg (0.55 mmol), Pd(Amphos)Cl_2 8 mg (0.01 mmol), and K_2CO_3 69 mg (0.50 mmol) was stirred in 2 wt % Triton X-100/H_2O (2 mL) in a 5 mL vial with an oxygen balloon at 60 °C for 24 h. Then the resulting indenone mixture was added to 10% Pd/C (50 mg), 3 mL of methanol and introduced to a pressure reactor. The suspension was stirred at room temperature for 6 h under 5 atm of hydrogen. After the reaction, the pressure was released. The reaction mixture was then extracted with ethyl acetate (15 mL) and filtered through a pad of Celite. After filtration, the organic layer was concentrated in vacuo and the residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) to give 109 mg of **3u** (78% total yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 7.4 Hz, 1H), 7.35 (t, J = 7.4 Hz, 1H), 7.28 (t, J = 7.4 Hz, 1H), 7.15 (d, J = 7.4 Hz, 1H), 7.08–7.00 (m, 4H), 6.97 (t, J = 7.4 Hz, 2H), 6.85 (dd, J = 6.2, 3.0 Hz, 2H), 6.65 (d, J = 7.3 Hz, 2H), 5.45 (t, J = 7.0 Hz, 1H), 4.68 (d, J = 7.4 Hz, 1H), 4.02 (t, J = 6.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.8, 142.6, 139.1, 135.5, 129.2, 128.6, 127.3, 127.0, 126.7, 126.5, 126.0, 125.4, 124.5, 122.9, 76.3, 76.0, 75.8, 58.5, 53.2. GC-MS, *m*/*z*: 286 [M^+]. Anal. Calcd for $C_{21}H_{18}O$: C, 88.08; H, 6.34. Found: C, 88.27; H, 6.19.

Synthesis of *Paucif lorol F* Intermediate 3v. A mixture of (2-iodo-3,5-dimethoxyphenyl)methanol 147 mg (0.5 mmol), 1,3-dimethoxy-5-((4-methoxyphenyl)phenylethyne 147 mg (0.55 mmol), Pd(Amphos)Cl_2 8 mg (0.01 mmol), and K_2CO_3 69 mg (0.50 mmol) were stirred in 2 wt % Triton X-100/H_2O (2 mL) in a 5 mL vial with an oxygen balloon at 100 °C for 24 h. The reaction mixture was then cooled to room temperature, extracted with EtOAc (15 mL), washed with sat. aq. $NaHCO_3$ (3 × 15 mL), and dried over anhydrous Na_2SO_4. After filtration, the organic layer was concentrated in vacuo affording a mixture of indenone isomers (138 mg, 64% yield). **3v** and **3v′** were separated by preparative HPLC (methanol/water, 70:30). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 1.9 Hz, 1H), 6.75 (d, J = 8.7 Hz, 2H), 6.49 (d, J = 2.1 Hz, 2H), 6.43 (d, J = 2.0 Hz, 2H), 3.86 (s, 3H), 3.76 (s, 3H), 3.70 (s, 6H), 3.60 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.6, 161.5, 159.2, 157.8, 155.6, 153.7, 136.0, 133.1, 130.0, 129.7, 122.6, 121.8, 112.5, 105.6, 103.2, 101.8, 100.0, 54.9, 54.8, 54.4, 54.2. Anal. Calcd for $C_{26}H_{24}O_6$: C, 72.21; H, 5.59. Found: C, 72.37; H, 5.44.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge the Natural Science Foundation of Jiangsu Province (BK 20131346) for financial support.

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