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Palladium(II)-catalyzed synthesis of indenones through the cyclization of benzenecarbaldehydes with internal alkynes†

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The palladium(II)-catalyzed carbocyclization of benzenecarbaldehydes with internal alkynes to afford 2,3-disubstituted indenones was reported. The annulation reaction proceeded through the transmetalation of Pd(II) with an aromatic aldehyde and the insertion of internal alkynes, followed by cyclization *via* the intramolecular nucleophilic addition of intermediate organopalladium(II) species to the aldehyde group. This reaction proceeded in moderate to good yields with high regioselectivity.

Introduction

The transition metal-catalyzed oxidative C–H activation/carbocyclization of inactivated arene C–H bonds has evolved as a highly efficient route for a wide variety of building blocks.[1,2] In this respect, the direct embodiment of inactivated arene groups in the C–H functionalization reaction is the most excellent synthetic strategy that induces additional features. Mostly, carbocyclization is catalyzed by rhodium[3] or palladium[4] complexes. Palladium[4a–e]-catalyzed carbocyclization of C–H bonds has received enormous attention owing to high efficiency, broad scope and good functional group tolerance. Pd-catalyzed oxidative coupling of arenes with alkynes can result in a broad spectrum of homo and heterocycles such as napthalenes,[4a] carbolines,[4b] phenanthrenes,[4c] isoquinolones,[4d] and benzazepines.[4e] Some of these methodologies have been successfully applied to the synthesis of natural products.[4f–h] Inspite of their success, it is essential to explore the C–H activation of inactivated arenes expedited by directing groups, which not only coordinate to metals but also participate in the subsequent reactions to provide novel tandem transformations. This approach serves not only to broaden the scope of palladium-catalyzed C–H functionalization but also to achieve molecular complexity.

Indenones, which are an important class of carbocyclic compounds, form core moieties of many natural products.[5] They are used as estrogen binding receptors,[5a] pharmaceuticals[5a–e] and fungicides.[5f] Furthermore, they find applications in materials science and photochromic chemistry.[5g] They also serve as useful precursors in the synthesis of a variety of biomolecules such as the C-nor-D-homosteroid ring system,[5h] gibberellins[5i] and indenes.[5j] Liebeskind and South first reported the preparation of indenones from *o*-diiodo benzene and different alkynes employing nickel carbonyl as the catalyst.[6] Later, other transition metals such as iron,[7] palladium[8] and rhodium[9] (Scheme 1, eqn (1)) were utilized as catalysts for the syntheses of indenones using preactivated aldehydes, nitriles, amides, esters or halides as the starting materials;[6–9] among these synthesis methods, Pd-catalyzed annulation of alkynes with *ortho*-functionalized aryl-carbonyl and aryl-nitrile compounds forms a powerful synthetic strategy.[8] In recent times, the direct assembly of indenones *via* rhodium,[10] rhenium,[11] cobalt[12] and ruthenium[13]-catalyzed carbocyclization of benzoyl chlorides, benzimides, benzamides, azomethines, arylnitrones, benzaldehydes, nitrostyrenes[14a] and carboximides[14b] with alkynes and benzaldehydes with haloiodoketones[14c,d] (Scheme 1, eqn (2) and (4)) has been reported. However, these methods have certain drawbacks, which include harsh reaction conditions and the requirement of activated or preactivated arenes normally obtained from limited natural resources. Therefore, to overcome these problems, it is necessary to develop novel, convenient and efficient approaches and readily available starting materials for the synthesis of indenones. With this stated objective in the pursuance of our consistent efforts on the development of new synthetic methodologies,[15] the direct alkynylation of the aromatic rings of benzenecarbaldehydes with the corresponding diaryl alkynes in the presence of a catalytic

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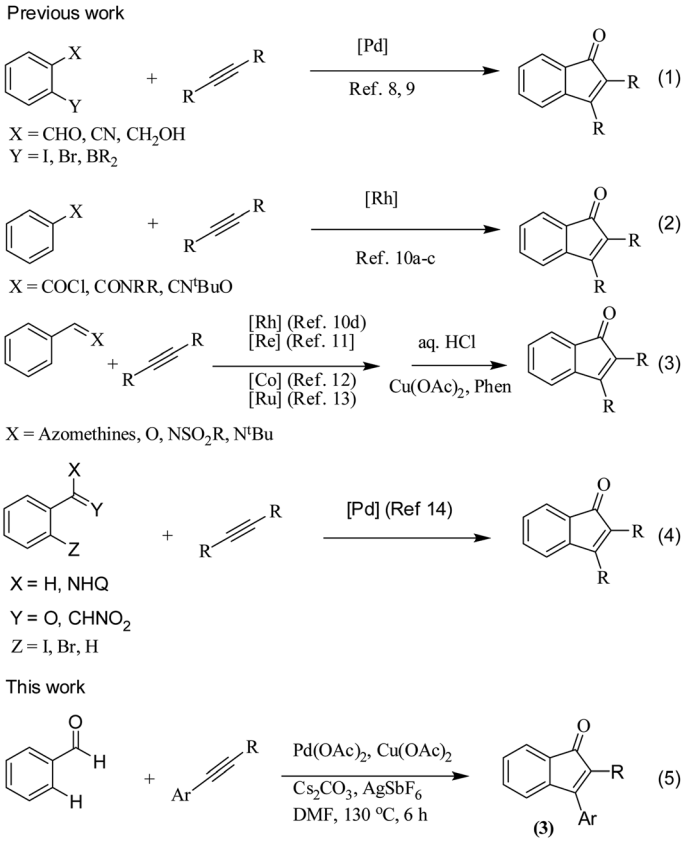


Scheme 1 Representative metal-catalyzed synthesis of indenones *via* C–H activation/carbocyclization.

amount of palladium acetate (Scheme 1, eqn (5)) was explored and reported.

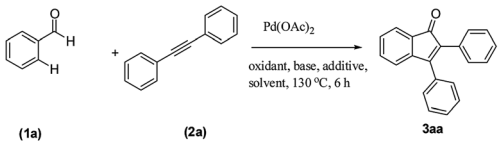
Results and discussion

We focused our studies on the metal-catalyzed direct C–H activation/carbocyclization of inactivated arenes and found that the palladium complexes possessed catalytic activity for the direct C–H activation/carbocyclization of benzenecarbaldehydes with diaryl alkynes. The reaction of the aldehyde (**1a**) with diphenylacetylene (**2a**) in the presence of palladium acetate (10.0 mol%), copper acetate (2.0 equiv.) and cesium carbonate (2.0 equiv.) in DMF (2 mL) at 130 °C for 6 h under a nitrogen atmosphere proceeded to give indenone **3aa**. Magnificently, we obtained 41% yield of the desired product (Table 1, entry 1). The yield of **3aa** improved to 69% when $AgSbF_6$ was used as the additive. The structure of **3aa** was established on the basis of its ^1H, ^{13}C NMR and ESI-HRMS results; this structure has been reported in the literature and was obtained by a different route.[16]

Intrigued by the above optimistic result, the effect of bases, oxidants, additives, solvents and temperatures on the reaction yield was further evaluated and some representative results are shown in Table 1. Various salts including $Cu(OAc)_2$, Cu_2O and CuO were examined; $Cu(OAc)_2$ was found to be the optimal choice for the carboannulation reaction (Table 1, entries 1 and 4). In the case of Cu_2O and CuO, the yield was <10% (Table 1, entries 8 and 9). The $Cu(OAc)_2$ loading was also evaluated, and the use of 0.5 equiv. of $Cu(OAc)_2$ led to a significant decrease in the yield (21%, entry 2). The use of $Cu(OAc)_2$ without Cs_2CO_3 produced only traces of the product (entry 3). However, the replacement of $Cu(OAc)_2$ with silver salts such as Ag_2CO_3, Ag_2O, AgOAc and AgF almost resulted in the same yields (entries 11–14). Other bases such as Li_2CO_3, Na_2CO_3, NaOAc, NaO^tBu, Na_3PO_4, K_2CO_3, KOAc and KO^tBu were not suitable for this conversion. A survey of the role of solvents revealed that DMF was the optimal candidate (entries 4–10) as the solvent. To probe the process further, the screening of additives disclosed $AgSbF_6$ as the most favored one to push the reaction forward, affording the desired product **3aa** in 69% yield (entries 4 and 12). Decreasing the reaction temperature to 100 °C resulted in a lower yield of 49% (entry 15), and no distinct change was detected by raising the reaction temperature (entry 16). When the reaction time was decreased to 3 h, a lower yield of 29% was obtained (entry 17). It may be noted that carboannulation did not proceed in the absence of $Pd(OAc)_2$ and the use of $AgSbF_6$ was critical for achieving a high yield.

With the optimized conditions in hand, we further checked for the substrate scope and generality by varying the structures of the alkynes. As shown in Table 2, various valuable indenones can be conveniently and efficiently obtained in moderate to good yields with high regioselectivity by this novel palladium-catalyzed carboannulation reaction, indicating that this method is general and practically useful.

Table 1 Optimization of the reaction conditions



Entry[a]	Oxidant	Additive	Base	Solvent	Yield[b] (%)
1	$Cu(OAc)_2$	—	Cs_2CO_3	DMF	41
2	$Cu(OAc)_2$	—	Cs_2CO_3	DMF	21
3	$Cu(OAc)_2$	—	—	DMF	Trace
4	$Cu(OAc)_2$	$AgSbF_6$	Cs_2CO_3	DMF	69
5	$Cu(OAc)_2$	$AgSbF_6$	Cs_2CO_3	DCE	32
6	$Cu(OAc)_2$	$AgSbF_6$	Cs_2CO_3	Dioxane	39
7	Cu_2O	$AgSbF_6$	Cs_2CO_3	DMF	Trace
8	CuO	$AgSbF_6$	Cs_2CO_3	DMF	Trace
9	CuI	$AgSbF_6$	Cs_2CO_3	DMF	Trace
10	$Cu(OAc)_2$	$AgSbF_6$	Cs_2CO_3	Toluene	13
11	Ag_2CO_3	—	—	DMF	31
12	Ag_2CO_3	$AgSbF_6$	Cs_2CO_3	DMF	63
13	AgOAc	$AgSbF_6$	Cs_2CO_3	DMF	56
14	AgF	$AgSbF_6$	Cs_2CO_3	DMF	48
15	$Cu(OAc)_2$	$AgSbF_6$	Cs_2CO_3	DMF	49
16	$Cu(OAc)_2$	$AgSbF_6$	Cs_2CO_3	DMF	66
17	$Cu(OAc)_2$	$AgSbF_6$	Cs_2CO_3	DMF	29

[a] Reaction conditions: benzaldehyde (**1a**) (0.5 mmol), alkyne (**2a**) (0.6 mmol), $Pd(OAc)_2$ (0.011 g, 0.05 mmol), oxidant (1 equiv.), additive (20 mol%), base(1 equiv.), solvent (2 mL). [b] Isolated yield after column chromatography.

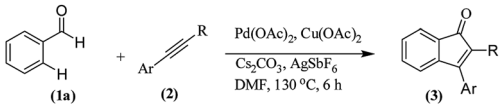
In general, both electron-rich and electron-deficient aromatic diaryl alkynes were suitable for this method, and a wide range of groups such as methyl, fluoro, chloro, methoxy, trifluoromethyl, and hydrogen were tolerated under the reaction conditions (**3aa–3am**). We further checked the generality of both electron-rich and electron-deficient aromatic disubstituted diaryl alkynes. In general, electron-rich disubstituted diaryl alkynes underwent carboannulation smoothly and gave moderate yields, whereas electron-deficient aromatic disubstituted diaryl alkynes were not suitable for this conversion. Unsymmetrical alkynes also underwent carbocyclization smoothly and gave moderate yields with high regioselectivity. Besides the fact that no traces of regioisomers were detected by *in situ* ^{1}H NMR analysis in all the annulations, the results demonstrated that this novel Pd-catalyzed carboannulation reaction exhibited high regioselectivity.

We further checked for the substrate scope and generality by varying the structures of benzaldehyde, as shown in Table 3. In general, both electron-rich and electron-deficient compounds were used to prepare different indenones following the above method. The electron-withdrawing groups containing benzenecarbaldehydes underwent C–H annulations smoothly and gave good yields, whereas the electron-rich benzenecarbaldehydes gave low yields of indenones and required a comparatively longer time.

Plausible pathway

On the basis of the current information,[8,17] a plausible mechanism for conversion is shown in Scheme 2. The formation of indenone **3aa** apparently started with the palladation of an

Table 2 Substrate scope of alkynes



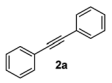
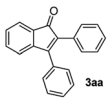
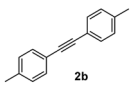
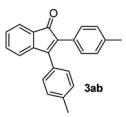
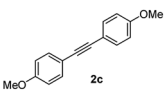
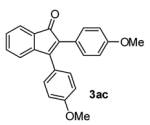
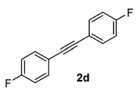
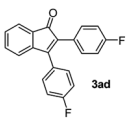
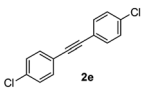
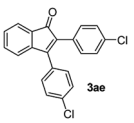
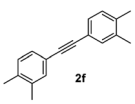
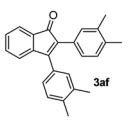
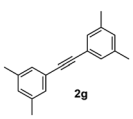
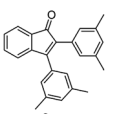
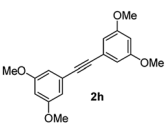
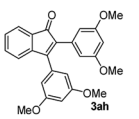
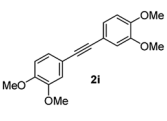
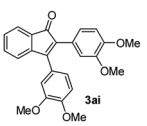
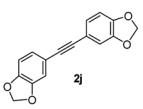
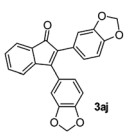
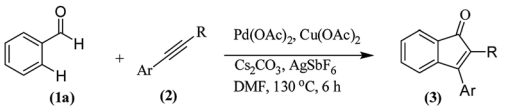
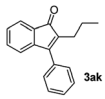
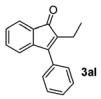
Entry[a]	Alkyne (2)	Product (3)	Yield[b] (%)
1			69
2			71
3			73
4			59
5			55
6			77
7			75
8			78
9			75
10			59

Table 2 (*Contd.*)



Entry[a]	Alkyne (2)	Product (3)	Yield[b] (%)
11			45
12			40

[a] Reaction conditions: benzaldehyde (**1**) (0.074 g, 0.5 mmol), alkyne (**2**) (0.6 mmol), $Pd(OAc)_2$ (0.011 g, 0.05 mmol), $Cu(OAc)_2$ (0.090 g, 0.5 mmol), Cs_2CO_3 (0.162 g, 0.5 mmol), $AgSbF_6$ (0.034 g, 0.1 mmol), DMF (2 mL). [b] Isolated yield after column chromatography.

aromatic aldehyde by $Pd(OAc)_2$ to yield the palladium complex **4**. *Syn*-addition of **4** to the triple bond of diphenylacetylene **2** yielded the palladium species **5**. This was followed by intramolecular cyclization, which would lead to **6**; it further underwent reductive elimination to yield the indenone **3aa**. $AgSbF_6$ may be speculated to facilitate the removal of an acetate anion by exchange with $[SbF_6]^-$, which could propel the forward reaction. In case of unsymmetrical alkynes, the *syn* addition of complex **4** to alkyne **2** occurred in such a way that the alkyne carbon bearing the bulky group coupled with the complex **4** to give **5** by possibly avoiding steric hindrance when annulating with the carbaldehyde carbon.

Finally, to express the practical applicability of this protocol on a preparative scale, some reactions were carried out on the gram scale (20 mmol) using the following combinations of substrates: **1a** with **2a** and **1a** with **2g**. As per our expectations, the reactions proceeded smoothly to afford the target compounds in high yields as obtained in similar reactions on the milligram scale (entries 1 and 7, Table 2), which demonstrated the practical utility of this method.

Conclusions

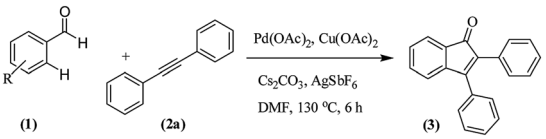
In conclusion, we developed one-pot palladium-catalyzed carboannulation between benzaldehyde and internal alkynes for the synthesis of indenones. The reaction involved challenging nucleophilic addition of an organopalladium species to benzaldehyde. With this protocol, generally, high regioselective addition across unsymmetrically substituted alkynes was achievable.

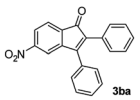
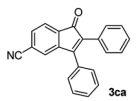
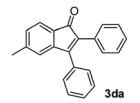
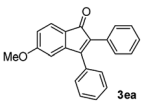
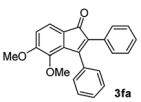
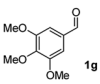
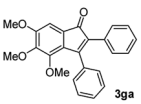
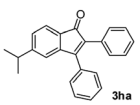
Experimental procedure

Materials and method

Solvents were dried according to known methods as appropriate. ^1H, ^{13}C spectra (^1H, 400 MHz; ^{13}C, 100 MHz) were recorded using a 400 MHz spectrometer in $CDCl_3$ with shifts referenced to $SiMe_4$ ($\delta = 0$). IR spectra were recorded on an FTIR spectrophotometer. Elemental analyses were carried out on a CHN analyzer. Mass spectra were recorded using LC-MS and HRMS (ESI-TOF analyzer) equipment. Column chromatography was performed on silica gel (250–400 mesh) using ethyl acetate (EtOAc)/hexane mixture.

Table 3 Substrate scope of benzaldehydes

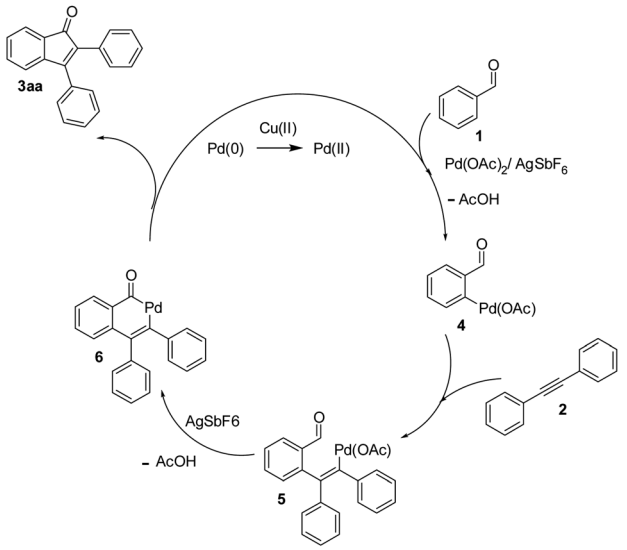


Entry[a]	Benzaldehyde (1)	Product (3)	Yield[b] (%)
1			43
2			49
3			55
4			51
5			55
6			57
7			53

[a] Reaction conditions: benzaldehyde (**1**) (0.5 mmol), alkyne (**2**) (0.6 mmol), $Pd(OAc)_2$ (0.011 g, 0.05 mmol), $Cu(OAc)_2$ (0.090 g, 0.5 mmol), Cs_2CO_3 (0.162 g, 0.5 mmol), $AgSbF_6$ (0.034 g, 0.1 mmol), DMF (2 mL). [b] Isolated yield after column chromatography.

General procedure for the synthesis of indenones

Benzaldehyde (0.053 g, 0.5 mmol), $Pd(OAc)_2$ (0.011 g, 0.05 mmol), $Cu(OAc)_2$ (0.090 g, 0.5 mmol), $AgSbF_6$ (0.034 g, 0.1 mmol), Cs_2CO_3 (0.162 g, 0.5 mmol), DMF (2 mL) and diaryl acetylene (0.6 mmol) were charged into an oven-dried 25 mL round bottomed flask under nitrogen. The mixture was stirred at 130 °C for 6 h. After cooling to room temperature and extracting with EtOAc (3 × 25 mL). The combined ethyl acetate



Scheme 2 A plausible pathway for the formation of **3aa**.

extract was washed with brine (75 mL), dried over anh. Na_2SO_4 and filtered. The solvent was removed under vacuum and the resulting crude product was purified by silica gel chromatography using hexane/ethyl acetate mixture to afford compounds **3aa–3al**. The details on the yields for all the compounds are presented in Tables 2 and 3

2,3-Diphenyl-1-indenone (3aa). A mixture of benzaldehyde **1a** (0.053 g, 0.5 mmol) and 1,2-diphenylethyne (0.6 mmol) was stirred at 130 °C for 6 h. The residue was purified by flash chromatography over silica gel (hexane/ethyl acetate, 99 : 1) to afford the desired product **3aa** as a red solid. IR (KBr, cm^{-1}) 2911, 1704, 1605, 1447; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 5.4 Hz, 1H), 7.42–7.35 (m, 6H), 7.30–7.21 (m, 6H), 7.17 (d, J = 5.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.4, 153.3, 145.2, 133.2, 132.7, 132.4, 130.7, 129.9, 129.2, 128.9, 128.7, 128.5, 128.0, 127.7, 122.9, 121.2; (HRMS (ESI) Calcd for $C_{21}H_{15}O$ [M + H]: m/z 283.1124. Found: 283.1123).

2,3-Bis(4-methyphenyl)-1-indenone (3ab). A mixture of benzaldehyde **1a** (0.053 g, 0.5 mmol) and 1,2-bis(4-methylphenyl)ethyne (0.6 mmol) was stirred at 130 °C for 6 h. The residue was purified by flash chromatography over silica gel (hexane/ethyl acetate, 99 : 1) to afford the desired product **3ab** as a red solid. IR (KBr, cm^{-1}) 2914, 1703, 1601, 1450; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.3 Hz, 1H), 7.39 (td, J = 7.3 and 1.2 Hz, 3H), 7.27–7.15 (m, 5H), 7.09 (d, J = 8.4 Hz, 2H), 2.42 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.7, 154.7, 145.5, 139.3, 137.5, 133.2, 132.0, 130.9, 129.9, 129.8, 129.4, 128.8, 128.7, 128.4, 127.9, 122.7, 121.1, 21.5, 21.3; (HRMS (ESI) Calcd for $C_{23}H_{19}O$ [M + H]: m/z 311.1436. Found: 311.136)

2,3-Bis(4-methoxyphenyl)-1-indenone (3ac). A mixture of benzaldehyde **1a** (0.053 g, 0.5 mmol) and 1,2-bis(4-methoxyphenyl)ethyne (0.6 mmol) was stirred at 130 °C for 6 h. The residue was purified by flash chromatography over silica gel (hexane/ethyl acetate, 99 : 1) to afford the desired product **3ac** as a red solid. IR (KBr, cm^{-1}) 2911, 1701, 1605, 1439; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.0 Hz, 1H), 7.39 (d, J = 8.1 Hz, 3H), 7.36–7.29 (m, 3H), 7.22 (d, J = 8.1 Hz, 1H), 6.97 (d, J = 8.1 Hz, 2H), 6.85 (d, J = 8.1 Hz, 2H), 3.88 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 159.1, 133.2, 131.2, 131.0, 130.2, 128.6, 125.1, 122.7, 120.9, 114.2, 113.6, 55.3, 55.2; (HRMS (ESI) Calcd for $C_{23}H_{19}O_3$ [M + H]: m/z 343.1335. Found: 343.1335).

2,3-Bis(4-fluorophenyl)-1-indenone (3ad). A mixture of benzaldehyde **1a** (0.053 g, 0.5 mmol) and 1,2-bis(4-fluorophenyl)ethyne (0.6 mmol) was stirred at 130 °C for 6 h. The residue was purified by flash chromatography over silica gel (hexane/ethyl acetate, 99 : 1) to afford the desired product **3ad** as a red solid. IR (KBr, cm^{-1}) 2989, 1714, 1608, 1440; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.0 Hz, 1H), 7.44 (t, J = 8.1 and 1.0 Hz, 3H), 7.41–7.30 (m, 3H), 7.19 (t, J = 8.1 and 1.0 Hz, 3H), 7.15–6.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2, 164.1, 162.1 (d, J_{C-F} = 244. 0 Hz), 154.1 (d, J_{C-F} = 244. 0 Hz),, 144.8 (d, J_{C-F} = 8. 0 Hz),, 133.6, 131.7 (d, J_{C-F} = 8. 0 Hz), 131.5, 130.5 (d, J_{C-F} = 8. 0 Hz), 129.2, 128.4, 126.5 (d, J_{C-F} = 8. 0 Hz),, 123.4, 121.1, 116.3, 116.1, 115.4, 115.2; (HRMS (ESI) Calcd for $C_{21}H_{12}F_2O_2$ [M + H]: m/z 319.0935. Found: 319.0959).

2,3-Bis(4-chlorophenyl)-1-indenone (3ae). A mixture of benzaldehyde **1a** (0.053 g, 0.5 mmol) and 1,2-bis(4-chlorophenyl)ethyne (0.6 mmol) was stirred at 130 °C for 6 h. The residue was purified by flash chromatography over silica gel (hexane/ethyl acetate, 99 : 1) to afford the desired product **3ae** as a red solid. IR (KBr, cm^{-1}) 2915, 1700, 1605, 1446; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.0 Hz, 1H), 7.43–7.36 (m, 3H), 7.34–7.29 (m, 3H), 7.26–7.23 (m, 2H), 7.20–7.18 (m, 2H), 7.11 (d, J = 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.1, 154.3, 144.6, 135.3, 134.1, 133.6, 131.4, 131.3, 130.9, 130.4, 129.9, 129.4, 128.7, 128.4, 123.3, 121.1; (HRMS (ESI) Calcd for $C_{21}H_{12}Cl_2O_2$ [M + H]: m/z 351.0235. Found: 351.0247).

2,3-Bis(3,4-dimethylphenyl)-1-indenone (3af). A mixture of benzaldehyde **1a** (0.053 g, 0.5 mmol) and 1,2-bis(3,4-dimethylphenyl)ethyne (0.6 mmol) was stirred at 130 °C for 6 h. The residue was purified by flash chromatography over silica gel (hexane/ethyl acetate, 99 : 1) to afford the desired product **3af** as a red solid. IR (KBr, cm^{-1}) 2915, 1704, 1600, 1446; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 5.0 Hz, 1H), 7.34 (dt, J = 5.6 and 0.8 Hz, 1H), 7.27 (dt, J = 5.7, 0.6 Hz, 1H), 7.22 (brs, 1H), 7.16 (brs, 2H), 7.15 (brs, 1H), 7.09 (d, J = 5.8 Hz, 1H), 7.00 (d, J = 5.8 Hz, 1H), 6.95 (d, J = 5.8 Hz, 1H), 2.32 (s, 3H), 2.28 (s, 3H), 2.24 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 154.8, 145.6, 137.9, 136.8, 136.1$_9$, 136.1$_1$, 133.2, 132.0, 131.0, 130.9, 130.3, 129.9, 129.3, 129.2, 128.6, 128.4, 127.3, 122.6, 121.1, 19.8, 19.6; HRMS (ESI) Calcd For $C_{25}H_{22}ONa$ [M + Na]: m/z 361.1568. Found: 361.1570.

2,3-Bis(3,5-dimethylphenyl)-1-indenone (3ag). A mixture of benzaldehyde (0.053 g, 0.5 mmol) and 1,2-bis(3,5-dimethylphenyl)ethyne (0.140 g, 0.6 mmol) was stirred at 130 °C for 6 h. The residue was purified by flash chromatography over silica gel (hexane/ethyl acetate, 99 : 1) to afford the desired product **3ag** as a red solid. IR (KBr, cm^{-1}) 2915, 1709, 1600, 1457; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 2.6 Hz, 1H), 7.37 (dt, J = 5.9, 0.9 Hz, 1H), 7.28 (dt, J = 5.8, 0.6 Hz, 1H), 7.14 (d, J = 5.8 Hz, 1H), 7.05 (brs, 1H), 7.00 (brs, 2H), 6.91 (brs, 2H), 6.89 (brs, 1H), 2.31 (s, 6H), 2.23 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 196.9, 156.4, 145.6, 138.8, 138.1, 137.2, 136.6, 133.3, 132.7, 132.3, 130.8, 130.6, 129.4, 128.7, 127.6, 126.0, 122.7, 121.2, 21.34, 21.32; HRMS (ESI) Calcd for $C_{25}H_{22}ONa$ [M + Na]: *m*/*z* 361.1568. Found: 361.1567.

2,3-Bis(3,5-dimethoxyphenyl)-1-indenone (3ah). A mixture of benzaldehyde **1a** (0.053 g, 0.5 mmol) and 1,2-bis(3,5-dimethoxyphenyl)ethyne (0.178 g, 0.6 mmol) was stirred at 130 °C for 6 h. The residue was purified by flash chromatography over silica gel (hexane/ethyl acetate, 95 : 5) to afford the desired product **3ah** as a red solid. IR (KBr, cm^{-1}) 2913, 1709, 1594, 1452; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 5.6 Hz, 1H), 7.37 (dt, J = 0.9, 5.9 Hz, 1H), 7.28 (dt, J = 0.6, 5.8 Hz, 1H), 7.17 (d, J = 5.8 Hz, 1H), 6.52 (d, J = 1.8 Hz, 2H), 6.49 (t, J = 1.8 Hz, 1H), 6.47 (d, J = 1.8 Hz, 2H), 6.36 (t, J = 1.8 Hz, 1H), 3.71 (s, 6H), 3.65 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2, 161.0, 160.2, 155.6, 145.0, 134.5, 133.5, 132.4, 132.2, 130.6, 129.0, 122.9, 121.4, 107.8, 106.3, 101.4, 100.8, 55.4, 55.2; HRMS (ESI) Calcd for $C_{25}H_{22}O_5Na$ [M + Na]: *m*/*z* 425.1365. Found: 425.1362.

2,3-Bis(3,4-dimethoxyphenyl)-1-indenone (3ai). A mixture of benzaldehyde **1a** (0.053 g, 0.5 mmol) and 1,2-bis(3,4-dimethoxyphenyl)ethyne (0.178 g, 0.6 mmol) was stirred at 130 °C for 6 h. The residue was purified by flash chromatography over silica gel (hexane/ethyl acetate, 95 : 5) to afford the desired product **3ai** as a red solid. IR (KBr, cm^{-1}) 2915, 1693, 1632, 1452; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 5.4 Hz, 1H), 7.39 (dt, J = 6.0, 0.8 Hz, 1H), 7.29 (dt, J = 5.9, 0.6 Hz, 1H), 7.21 (d, J = 5.8 Hz, 1H), 7.08 (dd, J = 6.6, and 1.5 Hz, 1H), 6.95 (d, J = 6.7 Hz, 2H), 6.88 (dd, J = 9.9 Hz and J = 1.5 Hz, 2H), 6.81 (d, J = 6.7 Hz, 1H), 3.95 (s, 3H), 3.88 (s, 3H), 3.73 (s, 3H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.8, 153.9, 149.9, 149.1, 148.7, 148.4, 145.3, 133.3, 131.3, 131.0, 128.7, 125.4, 123.6, 123.0, 122.7, 121.6, 120.9, 113.1, 111.9, 111.3, 110.9, 55.9, 55.8, 55.6; HRMS (ESI) Calcd for $C_{25}H_{22}O_5Na$ [M + Na]: *m*/*z* 425.1365. Found: 425.1363.

2,3-Bis(3,4-dimethoxymethylenephenyl)-1-indenone (3aj). A mixture of benzaldehyde **1a** (0.053 g, 0.5 mmol) and 1,2-bis(3,4-dimethoxymethylenephenyl)ethyne (0.159 g, 0.6 mmol) was stirred at 130 °C for 6 h. The residue was purified by flash chromatography over silica gel (hexane/ethyl acetate, 99 : 1) to afford the desired product as a red solid. IR (KBr, cm^{-1}) 2914, 1699, 1630, 1499; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 7.0 Hz, 1H), 7.38 (dt, J = 7.5, 1.1 Hz, 1H), 7.28 (dt, J = 7.7, 0.9 Hz, 1H), 7.17 (d, J = 7.2 Hz, 1H), 6.95 (dd, J ~8.1, J = 1.7 Hz, 1H), 6.86 (d, J = 8.0 Hz, 1H), 6.84 (dd, J ~8.4 Hz and J = 1.6 Hz, 2H), 6.79–6.77 (m, 2H), 6.05 (s, 2H), 5.96 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.5, 154.1, 148.5, 148.0, 147.4, 147.3, 145.2, 133.4, 131.6, 130.8, 128.8, 126.4, 124.6, 124.2, 122.9, 121.1, 110.2, 108.9, 108.8, 108.4, 101.4, 101.0; HRMS (ESI) Calcd for $C_{23}H_{15}O_5$ [M + H]: *m*/*z* 371.0919. Found: 371.0917.

2-Propyl,3-phenyl-1-indenone (3ak). A mixture of benzaldehyde **1a** (0.053 g, 0.5 mmol) and 1-phenylbutyne (0.6 mmol) was stirred at 130 °C for 6 h. The residue was purified by flash chromatography over silica gel (hexane/ethyl acetate, 99 : 1) to afford the desired product **3ak** as a red solid. IR (KBr, cm^{-1}) 2914, 1703, 1615, 1447; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.41 v(m, 6H), 7.39–7.18 (m, 2H), 7.12 (d, J = 7.0 Hz, 1H), 2.72–2.31 (m, 2H), 1.56–1.48 (m, 2H), 0.90 (t, J = 7.0 and 2.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3, 155.2, 145.9, 135.3, 133.1, 132.9, 130.9, 129.0, 128.1, 122.4, 120.5, 120.5, 25.3, 22.6, 14.2; HRMS (ESI) Calcd for $C_{17}H_{15}O$ [M + H]: *m*/*z* 235.1124. Found: 235.1100.

Conflicts of interest

There are no conflicts to declare.

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