Efficient Assembly of 1-Methylene-1*H*-indenes via Palladium-Catalyzed Tandem Reaction of 1-(2,2-Dibromovinyl)-2-alkenylbenzene with Arylboronic Acid

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Highly efficient palladium-catalyzed reaction of 1-(2,2-dibromovinyl)-2-alkenylbenzene with arylboronic acid is disclosed, which generates the functionalized 1-methylene-1*H*-indenes in good yields. Tandem Suzuki−Miyaura coupling and Heck reactions are involved in this process.

Introduction

Expanding interest in combinatorial chemistry has been directed toward the development of tandem reactions[1,2] for the generation of small molecules. These reactions provide an efficient and powerful tool for natural product-like compound construction using simple starting materials. For instance, Grigg reported a general palladium catalyzed cycloaddition strategy using several different protocols for 5- and 6- membered ring formation.[2f] Ma and co-workers described efficient construction of *cis*-fused bicyclo[4.3.0]-nonenes via palladium-catalyzed three-component cascade cyclization reaction of bisallenes with propargylic carbonates and organoboronic acids.[2c] Moreover, the indene core exists in many natural products and drug candidates with remarkable biological activities.[3] In addition, several applications have been discovered for the use of indene-related compounds in the field of materials science.[4] The need for novel pathways to indene substructures has resulted in several new synthetic approaches to this carbacycle.[5−8] 1-Methyleneindene, a member of indene family, has recently attracted much attention[9−11] because of its unique structure in drug candidates. These functionalized indenes can be easily obtained starting from 1-methyleneindenes. Thus, it is of high interest to develop novel routes for efficient assembly of functionalized 1-methyleneindenes, especially in a combinatorial format.

Recently, we reported an efficient route for the 1-methyleneindenes generation via palladium-catalyzed tandem reactions[2] of 1-(2,2-dibromovinyl)-2-alkynylbenzenes with arylboronic acids.[12] In this transformation, *gem*-dibromoolefin,[13] which could be easily accessible from an aldehyde in the presence of CBr_4/PPh_3, was utilized as an electrophile in the process. It is well recognized that *gem*-dihaloolefin is a versatile building block in various organic reactions with good stereoselectivity.[14−20] For instance, Lautens and co-workers reported several efficient routes for the carbo- and heterocycles formation starting from *gem*-dihaloolefins.[17−19] Prompted by these results and with an expectation to generate diverse 1-methyleneindenes, we conceived that 1-(2,2-dibromovinyl)-2-alkenylbenzene **1** was a suitable substrate as well. As described in Scheme 1, a coupling partner such as arylboronic acid can react with 1-(2,2-dibromovinyl)-2-alkenylbenzene to form functionalized 1-methyleneindenes. We reasoned that in this reaction process, the Suzuki−Miyaura coupling would occur first to generate intermediate **B**, with the concurrent release of Pd(0). Subsequently, oxidative addition of vinyl bromide **B** with Pd(0) afforded the intermediate **C**, which then underwent intramolecular insertion and β-hydrogen elimination to produce the desired 1-methyleneindene **3**. In the reaction process, according to the Heck reaction mechanism (*syn*-carbopalladation followed by bond rotation and *syn*-β-hydride elimination),[20] (*Z*)-methyleneindene would be afforded. On the basis of these considerations, we started to investigate the palladium-

Scheme 1. Proposed Synthetic Route for Palladium-Catalyzed Reaction of 1-(2,2-Dibromovinyl)-2-alkenylbenzene **1** with Arylboronic Acid **2**

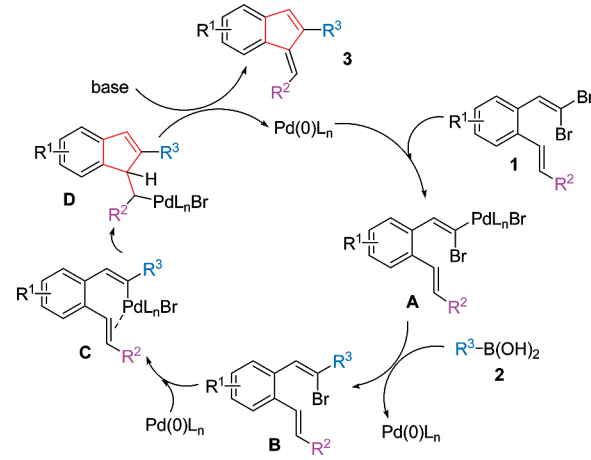

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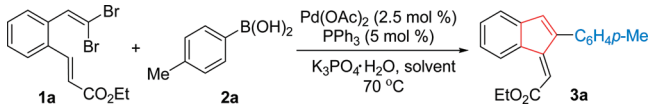
Table 1. Solvents Screening for Palladium-Catalyzed Reaction of 1-(2,2-Dibromovinyl)-2-alkenylbenzene **1a** with Arylboronic Acid **2a**



entry	solvent	time	yield (%)[a]
1	THF	3 h	42
2	toluene	3 h	60
3	DMAc	12 h	trace
4	1,4-dioxane	3 h	52
5	DCE	3 h	47
6	MeCN	3 h	26

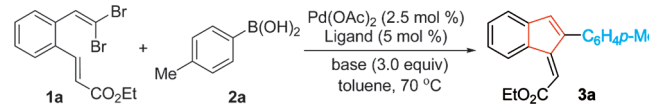
[a] Isolated yield based on 1-(2,2-dibromovinyl)-2-alkenylbenzene **1a**.

catalyzed reaction of 1-(2,2-dibromovinyl)-2-alkenylbenzene **1** with arylboronic acid **2**.[21]

Result and Discussion

The initial attempt was carried out with (*E*)-ethyl 3-(2-(2,2-dibromovinyl)phenyl)acrylate **1a** and 4-methylphenylboronic acid **2a** in the presence of palladium acetate (2.5 mol %), PPh_3 (5 mol %), and $K_3PO_4 \cdot H_2O$ (3.0 equiv) in different solvents at 70 °C (Table 1). The expected product **3a** was afforded in 42% yield when the reaction was performed in tetrahydrofuran (THF; Table 1, entry 1). The structure of compound **3a** was confirmed by ^1H and ^{13}C NMR. The yield was increased to 60% when the solvent was changed to toluene (Table, entry 2). In these two reactions the starting material, (*E*)-ethyl 3-(2-(2,2-dibromovinyl)phenyl)acrylate **1a**, was consumed in 3 h, accompanied with the generation of a small amount of unknown byproducts. Inferior results were observed when other solvents were examined. For instance, only a trace amount of product was observed when the reaction occurred in DMAc after 12 h (Table 1, entry 3). The expected product was isolated in 26% yield when MeCN was used as the solvent (Table 1, entry 6). In these two cases, the reactions of (*E*)-ethyl 3-(2-(2,2-dibromovinyl)phenyl)acrylate **1a** could not go to completion, even if the time was prolonged to 24 h. We reasoned that in this transformation, the presence of heteroatomic solvents might deactivate the reactivity of the palladium catalyst. Further screening of bases (3.0 equiv) revealed that the reaction worked efficiently in the presence of Cs_2CO_3 or KOH (Table 2, entries 3 and 5, 66% yield). These two reactions were finished in 3 h as observed by the disappearance of 1-(2,2-dibromovinyl)-2-alkenylbenzene **1a**. Lower yield was obtained when the amount of base was reduced to 1.0 or 2.0 equiv. No reaction took place when $NaHCO_3$ or NaOAc was employed as the base (Table 2, entries 2 and 6), and the starting material was recovered after 12 h. When the base was replaced by *t*-BuOK, 1-(2,2-dibromovinyl)-2-alkenylbenzene **1a** was retained after 12 h; however, a trace amount of product was also detected (Table 2, entry 4). Again, no improvement was observed when the reaction was prolonged to 24 h. Other phosphine ligands were tested but failed to improve the efficacy of the reaction (Table 2, entries 9−14). In these cases, 1-(2,2-dibromovinyl)-2-alkenylbenzene **1a** was not completely absent after 12 h, and the reactions were accompanied by the formation of various byproducts. When the reaction occurred at 100 °C in the presence of KOH as a base, compound **3a** was isolated in 81% yield and the reaction time was shortened to 1 h (Table 2, entry 15). Other palladium catalysts were also examined. However, only lower yields were obtained ($PdCl_2$, $PdCl_2(PPh_3)_2$, $PdCl_2(MeCN)_2$, $Pd(PPh_3)_4$). On the basis of the above results, we recognized that another pathway might be possible in which the Heck reaction proceeded first after the oxidative addition of the palladium catalyst to the (*Z*)-bromide. This result was indicated as well by Lautens.[21] The reaction worked well to generate the desired product **3** when small monodentate phosphines were used as ligands, while the Heck reaction might occur first when an electron-rich, sterically crowded ligand is used.

Table 2. Ligands and Bases Screening for Palladium-Catalyzed Reaction of 1-(2,2-Dibromovinyl)-2-alkenylbenzene **1a** with Arylboronic Acid **2a**

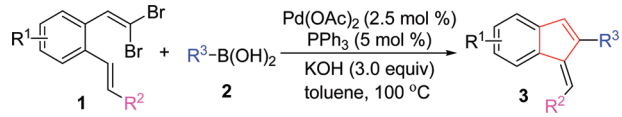


entry	ligand	base	temp (deg)	time	yield (%)[a]
1	PPh_3	K_2CO_3	70	3 h	56
2	PPh_3	$NaHCO_3$	70	12 h	*b*
3	PPh_3	Cs_2CO_3	70	3 h	66
4	PPh_3	*t*-BuOK	70	12 h	trace
5	PPh_3	KOH	70	3 h	66
6	PPh_3	NaOAc	70	12 h	*b*
7	PPh_3	NaOH	70	12 h	28
8	PPh_3	$K_2HPO_4 \cdot 3H_2O$	70	12 h	11
9	PCy_3	Cs_2CO_3	70	12 h	27
10	P(*o*-Tol)$_3$	Cs_2CO_3	70	12 h	26
11	DPPF	Cs_2CO_3	70	12 h	37
12	BINAP	Cs_2CO_3	70	12 h	38
13	John-Phos	Cs_2CO_3	70	12 h	9
14	XPhos	Cs_2CO_3	70	12 h	21
15	PPh_3	KOH	100	1 h	81
16	PPh_3	Cs_2CO_3	100	1 h	80

[a] Isolated yield based on 1-(2,2-dibromovinyl)-2-alkenylbenzene **1a**. [b] No reaction occurred.

Under the optimized conditions [$Pd(OAc)_2$ (2.5 mol %), PPh_3 (5 mol %), KOH (3.0 equiv), toluene, 100 °C], the scope of this tandem reaction was examined with a series of 1-(2,2-dibromovinyl)-2-alkenylbenzenes **1** and arylboronic acids **2**. Results are shown in Table 3. All reactions went to completion in 1−2 h, which afforded the expected (*Z*)-methyleneindenes in good yields with excellent selectivity (>95:5, determined by ^1H NMR). For instance, 1-(2,2-dibromovinyl)-2-alkenylbenzene **1a** reacted with 4-methoxyphenylboronic acid **2b** leading to the desired (*Z*)-ethyl 2-(2-(4-methoxyphenyl)-1*H*-inden-1-ylidene)acetate **3b** in 71% yield (Table 3, entry 2). A similar result was obtained when phenylboronic acid **2c** was used as a replacement (70% yield, Table 3, entry 3). Reaction of 1-(2,2-dibromovinyl)-2-alkenylbenzene **1a** with 4-fluorophenylboronic acid **2b** gave rise to the corresponding product **3d** in 80% yield (Table 3, entry 4). Other substrates were explored as well. Reaction of 1-(2,2-dibromovinyl)-2-alkenylbenzenes **1b**-**1e** with arylboronic acids proceeded efficiently to generate the desired products in good to excellent yields (Table 3, entries 5−11).

Table 3. Palladium-Catalyzed Reaction of 1-(2,2-Dibromovinyl)-2-alkenylbenzene **1** with Arylboronic Acid **2**



entry	R^1, R^2	R^3	time (h)	product	yield (%)[a]
1	R^1 = H, R^2 = COOEt (**1a**)	4-MeC_6H_4 (**2a**)	1	**3a**	81
2	R^1 = H, R^2 = COOEt (**1a**)	4-$MeOC_6H_4$ (**2b**)	1	**3b**	71
3	R^1 = H, R^2 = COOEt (**1a**)	C_6H_5 (**2c**)	1	**3c**	70
4	R^1 = H, R^2 = COOEt (**1a**)	4-FC_6H_4 (**2d**)	2	**3d**	80
5	R^1 = H, R^2 = COOMe (**1b**)	4-MeC_6H_4 (**2a**)	1	**3e**	78
6	R^1 = H, R^2 = COOMe (**1b**)	4-FC_6H_4 (**2d**)	1	**3f**	77
7	R^1 = H, R^2 = COO^{n}Bu (**1c**)	4-MeC_6H_4 (**2a**)	1	**3g**	90
8	R^1 = H, R^2 = COO^{n}Bu (**1c**)	4-FC_6H_4 (**2d**)	2	**3h**	83
9	R^1 = H, R^2 = COO^{t}Bu (**1d**)	4-MeC_6H_4 (**2a**)	1	**3i**	71
10	R^1 = H, R^2 = CN (**1e**)	4-MeC_6H_4 (**2a**)	2	**3j**	98
11	R^1 = H, R^2 = CN (**1e**)	4-FC_6H_4 (**2d**)	2	**3k**	93
12	R^1 = 4-F, R^2 = COOEt (**1f**)	4-MeC_6H_4 (**2a**)	2	**3l**	85
13	R^1 = 4-F, R^2 = COOEt (**1f**)	4-FC_6H_4 (**2d**)	2	**3m**	80
14	R^1 = 5-F, R^2 = COOEt (**1 g**)	4-MeC_6H_4 (**2a**)	2	**3n**	80
15	R^1 = 5-F, R^2 = COOEt (**1 g**)	4-FC_6H_4 (**2d**)	2	**3o**	87
16	R^1 = 5-Cl, R^2 = COOEt (**1 h**)	4-MeC_6H_4 (**2a**)	1	**3p**	81
17	R^1 = 5-Cl, R^2 = COOEt (**1 h**)	4-FC_6H_4 (**2d**)	2	**3q**	85
18	R^1 = 4,5-$(OMe)_2$, R^2 = COOEt (**1i**)	4-MeC_6H_4 (**2a**)	2	**3r**	70
19	R^1 = 5-Me, R^2 = COOEt (**1j**)	4-MeC_6H_4 (**2a**)	1	**3s**	76
20	R^1 = 5-Me, R^2 = COOEt (**1j**)	4-FC_6H_4 (**2d**)	2	**3t**	67

[a] Isolated yield based on 1-(2,2-dibromovinyl)-2-alkenylbenzene **1**.

For example, almost quantitative yield of compound **3j** was obtained when (*E*)-3-(2-(2,2-dibromovinyl)phenyl)acrylonitrile **1e** was employed in the reaction of 4-methylphenylboronic acid (98% yield, Table 3, entry 10). Under standard conditions, the cyano group was well tolerated. Further, the fluoro-, chloro-, methyl-, and methoxy-substituted 1-(2,2-dibromovinyl)-2-alkenylbenzenes **1f**−**1j** were examined in the reactions of arylboronic acids (Table 3, entries 12−20). As expected, all reactions gave rise to the desired products in good yields, and the electron effect on the aromatic backbone of the substrates was not observed.

Conclusion

In summary, we have described a highly efficient palladium-catalyzed reaction of 1-(2,2-dibromovinyl)-2-alkenylbenzene with arylboronic acid, which generates the functionalized 1-methylene-1*H*-indenes in good yields. Tandem Suzuki−Miyaura coupling and Heck reactions are involved in this transformation. We believe that this method provides an excellent complement to the 1-methylene-1*H*-indene synthesis. The good substrate generality combined with the easily availability of the starting materials makes this novel method attractive for further focused library construction.

Experimental Section

General procedure for palladium-catalyzed reaction of 1-(2,2-dibromovinyl)-2-alkenylbenzene **1** with arylboronic acid **2**: 1-(2,2-Dibromovinyl)-2-alkenylbenzene **1** (0.2 mmol) was added to a solution of $Pd(OAc)_2$ (2.5 mol %), PPh_3 (5 mol %), arylboronic acid **2** (0.3 mmol, 1.5 equiv), and KOH (0.6 mmol, 3 equiv) in toluene (3.0 mL). The solution was then stirred at 100 °C. After completion of the reaction as indicated by TLC, the solvent was evaporated and the residue was purified by flash chromatography column on silica gel to produce the desired product **3**.

(*E*)-Ethyl 2-(2-*p*-tolyl-1*H*-inden-1-ylidene)acetate (3a). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (t, J = 7.3 Hz, 3H), 2.40 (s, 3H), 4.28 (q, J = 7.3 Hz, 2H), 6.33 (s, 1H), 6.83 (s, 1H), 7.18−7.30 (m, 7H), 8.58 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 21.2, 60.8, 120.6, 120.8, 126.5, 127.3, 129.1, 129.2, 130.1, 131.8, 133.4, 133.6, 137.6, 143.7, 144.2, 150.9, 166.3; HRMS (ESI) calcd for $C_{20}H_{18}O_2$: 313.1204 (M + Na^{+}), found: 313.1209.

(*E*)-Ethyl 2-(2-(4-methoxyphenyl)-1*H*-inden-1-ylidene)-acetate (3b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, J = 7.3 Hz, 3H), 3.85 (s, 3H), 4.29 (q, J = 7.3 Hz, 2H), 6.31 (s, 1H), 6.80 (s, 1H), 6.96 (d, J = 8.7 Hz, 2H), 7.17−7.21 (m, 2H), 7.25−7.31 (m, 3H), 8.57 (d, J = 7.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 55.3, 60.8, 113.9, 120.6, 120.8, 126.5, 127.2, 127.3, 130.1, 130.5, 133.3, 133.4, 143.8, 143.9, 151.1, 159.4, 166.3; HRMS (ESI) calcd for $C_{20}H_{18}O_3$: 329.1154 (M + Na^{+}), found: 329.1155.

(*E*)-Ethyl 2-(2-phenyl-1*H*-inden-1-ylidene)acetate (3c). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (t, J = 7.3 Hz, 3H), 4.29 (q, J = 7.3 Hz, 2H), 6.33 (s, 1H), 6.86 (s, 1H), 7.19−7.21 (m, 2H), 7.28 (d, J = 6.8 Hz, 1H), 7.35−7.45 (m, 5H), 8.59 (d, J = 7.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 60.8, 120.7, 120.9, 126.7, 127.3, 127.8, 128.4, 129.3, 130.2, 133.4, 134.0, 134.8, 143.6, 144.2, 150.8, 166.2; HRMS (ESI) calcd for $C_{19}H_{16}O_2$: 299.1048 (M + Na^{+}), found: 299.1054.

(*E*)-Ethyl 2-(2-(4-fluorophenyl)-1*H*-inden-1-ylidene)acetate (3d). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, J = 7.3 Hz, 3H), 4.29 (q, J = 7.3 Hz, 2H), 6.25 (s, 1H), 6.83 (s, 1H), 7.11 (t, J = 8.7 Hz, 2H), 7.21 (t, J = 7.8 Hz, 2H), 7.27−7.34 (m, 3H), 8.58 (d, J = 7.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 60.8, 115.4 (d, $^2J_{CF}$ = 21.9 Hz), 120.6, 121.0, 126.8, 127.4, 130.2, 130.7, 130.9 (d, $^3J_{CF}$ =

8.0 Hz), 133.3, 134.2, 143.1, 143.4, 150.8, 162.5 (d, $^1J_{CF}$ = 247.1 Hz), 166.1; HRMS (ESI) calcd for $C_{19}H_{15}FO_2$: 317.0954 (M + $Na^{+)}$, found: 317.0955.

(*E*)-Methyl 2-(2-*p*-tolyl-1*H*-inden-1-ylidene)acetate (3e). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.39 (s, 3H), 3.81 (s, 3H), 6.33 (s, 1H), 6.82 (s, 1H), 7.18−7.29 (m, 7H), 8.58 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2, 51.7, 120.0, 120.9, 126.6, 127.3, 129.1, 129.2, 130.2, 131.8, 133.4, 133.7, 137.6, 143.7, 144.2, 151.3, 166.6; HRMS (ESI) calcd for $C_{19}H_{16}O_2$: 299.1048 (M + $Na^{+)}$, found: 299.1048.

(*E*)-Methyl 2-(2-(4-fluorophenyl)-1*H*-inden-1-ylidene)-acetate (3f). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (s, 3H), 6.25 (s, 1H), 6.83 (s, 1H), 7.11 (t, *J* = 8.3 Hz, 2H), 7.20−7.24 (m, 2H), 7.28−7.32 (m, 3H), 8.59 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 51.8, 115.4 (d, $^2J_{CF}$ = 20.7 Hz), 120.0, 121.0, 126.8, 127.4, 130.3, 130.7, 130.9 (d, $^3J_{CF}$ = 8.0 Hz), 133.2, 134.3, 143.0, 143.4, 151.2, 162.5 (d, $^1J_{CF}$ = 245.7 Hz), 166.5; HRMS (ESI) calcd for $C_{18}H_{13}FO_2$: 303.0797 (M + $Na^{+)}$, found: 303.0807.

(*E*)-Butyl 2-(2-*p*-tolyl-1*H*-inden-1-ylidene)acetate (3g). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.3 Hz, 3H), 1.36−1.43 (m, 2H), 1.63−1.69 (m, 2H), 2.39 (s, 3H), 4.23 (t, *J* = 7.3 Hz, 2H), 6.34 (s, 1H), 6.82 (s, 1H), 7.19 (t, *J* = 7.8 Hz, 2H), 7.22−7.29 (m, 5H), 8.58 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.6, 19.1, 21.2, 30.6, 64.7, 120.6, 120.8, 126.5, 127.3, 129.1, 129.2, 130.1, 131.8, 133.4, 133.6, 137.6, 143.7, 144.2, 150.8, 166.4; HRMS (ESI) calcd for $C_{22}H_{22}O_2$: 341.1517 (M + $Na^{+)}$, found: 341.1500.

(*E*)-Butyl 2-(2-(4-fluorophenyl)-1*H*-inden-1-ylidene)acetate (3h). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (t, *J* = 7.3 Hz, 3H), 1.37−1.44 (m, 2H), 1.65−1.70 (m, 2H), 4.24 (t, *J* = 7.3 Hz, 2H), 6.25 (s, 1H), 6.83 (s, 1H), 7.11 (t, *J* = 8.6 Hz, 2H), 7.19−7.22 (m, 2H), 7.27−7.33 (m, 3H), 8.58 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.6, 19.1, 30.6, 64.8, 115.4 (d, $^2J_{CF}$ = 20.7 Hz), 120.6, 121.0, 126.8, 127.4, 130.2, 130.9 (d, $^3J_{CF}$ = 7.8 Hz), 133.3, 134.2, 143.0, 143.4, 150.7, 162.5 (d, $^1J_{CF}$ = 245.8 Hz), 166.2; HRMS (ESI) calcd for $C_{21}H_{19}FO_2$: 345.1267 (M + $Na^{+)}$, found: 345.1245.

(*E*)-tert-Butyl 2-(2-*p*-tolyl-1*H*-inden-1-ylidene)acetate (3i). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.54 (s, 9H), 2.40 (s, 3H), 6.28 (s, 1H), 6.81 (s, 1H), 7.18−7.29 (m, 7H), 8.52 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2, 28.1, 81.3, 120.7, 122.7, 126.3, 126.9, 129.1, 129.2, 129.8, 132.0, 133.1, 133.5, 137.5, 143.6, 144.1, 149.2, 165.8; HRMS (ESI) calcd for $C_{22}H_{22}O_2$: 341.1517 (M + $Na^{+)}$, found: 341.1504.

(*E*)-2-(2-*p*-Tolyl-1*H*-inden-1-ylidene)acetonitrile (3j). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.39 (s, 3H), 5.80 (s, 1H), 6.84 (s, 1H), 7.20−7.25 (m, 6H), 7.32 (t, *J* = 7.3 Hz, 1H), 8.24 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2, 94.6, 117.0, 121.4, 124.2, 127.0, 128.6, 129.5, 130.4, 131.1, 133.4, 134.7, 138.3, 141.8, 142.9, 156.5; HRMS (ESI) calcd for $C_{18}H_{13}N$: 266.0946 (M + $Na^{+)}$, found: 266.0947.

(*E*)-2-(2-(4-Fluorophenyl)-1*H*-inden-1-ylidene)acetonitrile (3k). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.74 (s, 1H), 6.87 (s, 1H), 7.13 (t, *J* = 8.3 Hz, 2H), 7.23−7.36 (m, 5H), 8.25 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 94.7, 115.8 (d, $^2J_{CF}$ = 21.0 Hz), 116.8, 121.6, 124.2, 127.3, 129.4, 130.4 (d, $^3J_{CF}$ = 8.5 Hz), 131.3, 133.2, 135.3, 140.7, 142.6, 156.3, 162.7 (d, $^1J_{CF}$ = 246.8 Hz); HRMS (ESI) calcd for $C_{17}H_{10}FN$: 270.0695 (M + $Na^{+)}$, found: 270.0698.

(*E*)-Ethyl 2-(6-fluoro-2-*p*-tolyl-1*H*-inden-1-ylidene)acetate (3l). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (t, *J* = 7.3 Hz, 3H), 2.39 (s, 3H), 4.28 (q, *J* = 7.3 Hz, 2H), 6.35 (s, 1H), 6.78 (s, 1H), 6.96 (dt, *J* = 2.5, 8.6 Hz, 1H), 7.09 (dd, *J* = 5.5, 8.6 Hz, 1H), 7.23 (s, 4H), 8.43 (dd, *J* = 2.0, 10.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 21.2, 60.9, 115.8 (d, $^2J_{CF}$ = 27.6 Hz), 116.0 (d, $^2J_{CF}$ = 22.8 Hz), 121.1 (d, $^3J_{CF}$ = 7.8 Hz), 121.5, 129.1, 129.2, 131.5, 132.9, 135.2 (d, $^3J_{CF}$ = 10.0 Hz), 137.7, 139.6, 150.3 (d, $^4J_{CF}$ = 2.1 Hz), 162.3 (d, $^1J_{CF}$ = 241.7 Hz), 165.9; HRMS (ESI) calcd for $C_{20}H_{17}FO_2$: 331.1110 (M + $Na^{+)}$, found: 331.1114.

(*E*)-Ethyl 2-(6-fluoro-2-(4-fluorophenyl)-1*H*-inden-1-ylidene)acetate (3m). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.33 (t, *J* = 7.3 Hz, 3H), 4.30 (q, *J* = 7.3 Hz, 2H), 6.28 (s, 1H), 6.79 (s, 1H), 6.98 (dt, *J* = 2.0, 8.7 Hz, 1H), 7.10−7.13 (m, 3H), 7.19−7.32 (m, 2H), 8.43 (dd, *J* = 2.0, 10.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 61.0, 115.5 (d, $^2J_{CF}$ = 20.7 Hz), 115.9 (d, $^2J_{CF}$ = 25.5 Hz), 116.2 (d, $^2J_{CF}$ = 22.7 Hz), 121.3 (d, $^3J_{CF}$ = 9.0 Hz), 121.5, 130.5, 130.8 (d, $^3J_{CF}$ = 7.8 Hz), 133.5, 135.1 (d, $^3J_{CF}$ = 9.8 Hz), 139.3, 142.9, 150.2, 162.4 (d, $^1J_{CF}$ = 241.6 Hz), 162.5 (d, $^1J_{CF}$ = 246.5 Hz), 165.8; HRMS (ESI) calcd for $C_{19}H_{14}F_2O_2$: 335.0860 (M + $Na^{+)}$, found: 335.0837.

(*E*)-Ethyl 2-(5-fluoro-2-*p*-tolyl-1*H*-inden-1-ylidene)acetate (3n). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (t, *J* = 7.3 Hz, 3H), 2.40 (s, 3H), 4.27 (q, *J* = 7.3 Hz, 2H), 6.30 (s, 1H), 6.75 (s, 1H), 6.82−6.89 (m, 2H), 7.24 (s, 4H), 8.61 (dd, *J* = 5.5, 9.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 21.2, 60.8, 108.5 (d, $^2J_{CF}$ = 23.7 Hz), 112.2 (d, $^2J_{CF}$ = 21.7 Hz), 120.6, 129.0 (d, $^3J_{CF}$ = 9.0 Hz), 129.2, 131.4, 132.2, 137.9, 146.2, 149.9, 164.3 (d, $^1J_{CF}$ = 247.8 Hz), 166.1; HRMS (ESI) calcd for $C_{20}H_{17}FO_2$: 331.1110 (M + $Na^{+)}$, found: 331.1116.

(*E*)-Ethyl 2-(5-fluoro-2-(4-fluorophenyl)-1*H*-inden-1-ylidene)acetate (3o). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.33 (t, *J* = 7.3 Hz, 3H), 4.28 (q, *J* = 7.3 Hz, 2H), 6.22 (s, 1H), 6.76 (s, 1H), 6.84−6.90 (m, 2H), 7.12 (t, *J* = 8.6 Hz, 2H), 7.29−7.32 (m, 2H); 8.62 (dd, *J* = 5.0, 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 60.9, 108.7 (d, $^2J_{CF}$ = 23.7 Hz), 112.5 (d, $^2J_{CF}$ = 22.8 Hz), 115.5 (d, $^2J_{CF}$ = 20.8 Hz), 120.6, 129.1, 129.2 (d, $^3J_{CF}$ = 8.6 Hz), 130.4, 130.9 (d, $^3J_{CF}$ = 8.0 Hz), 132.8, 145.1, 145.9, 149.8, 162.5 (d, $^1J_{CF}$ = 203.2 Hz), 164.5 (d, $^1J_{CF}$ = 204.1 Hz), 166.0; HRMS (ESI) calcd for $C_{19}H_{14}F_2O_2$: 335.0860 (M + $Na^{+)}$, found: 335.0845.

(*E*)-Ethyl 2-(5-chloro-2-*p*-tolyl-1*H*-inden-1-ylidene)acetate (3p). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (t, *J* = 7.3 Hz, 3H), 2.40 (s, 3H), 4.27 (q, *J* = 7.3 Hz, 2H), 6.34 (s, 1H), 6.77 (s, 1H), 7.14−7.16 (m, 2H), 7.24 (m, 4H), 8.55 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 21.2, 60.9, 121.1, 121.4, 126.0, 128.4, 129.2, 129.3, 131.3, 131.6, 132.3, 136.0, 138.0, 145.4, 145.8, 149.9, 166.1; HRMS (ESI) calcd for $C_{20}H_{17}ClO_2$: 347.0815 (M + $Na^{+)}$, found: 347.0794.

(*E*)-Ethyl 2-(5-chloro-2-(4-fluorophenyl)-1*H*-inden-1-ylidene)acetate (3q). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.33 (t, *J* = 7.3 Hz, 3H), 4.29 (q. *J* = 7.3 Hz, 2H), 6.26 (s, 1H), 6.77 (s, 1H), 7.10−7.18 (m, 4H), 7.31 (dd, *J* = 5.5, 8.0 Hz,

2H), 8.55 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 61.0, 115.5 (d, $^2J_{CF} = 21.4$ Hz), 121.3 (d, $^3J_{CF} = 5.4$ Hz), 126.3, 128.5, 130.2 (d, $^4J_{CF} = 3.1$ Hz), 130.9, 131.0, 131.4, 132.9, 136.1, 144.6, 145.1, 149.8, 162.6 (d, $^1J_{CF} = 247.3$ Hz), 165.9; HRMS (ESI) calcd for $C_{19}H_{14}ClFO_2$: 351.0564 ($M + Na^{+}$), found: 351.0543.

(*E*)-ethyl 2-(5,6-dimethoxy-2-*p*-tolyl-1*H*-inden-1-ylidene)acetate (3r). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (t, $J = 7.3$ Hz, 3H), 2.40 (s, 3H), 3.93 (s, 3H), 3.96 (s, 3H), 4.27 (q, $J = 7.3$ Hz, 2H), 6.24 (s, 1H), 6.71 (s, 1H), 6.78 (s, 1H), 7.23 (s, 4H), 8.51 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 21.2, 56.0, 56.3, 60.6, 104.8, 112.8, 119.4, 125.9, 129.1, 129.2, 132.0, 133.1, 137.4, 137.9, 143.4, 147.4, 150.6, 151.8, 166.5; HRMS (ESI) calcd for $C_{22}H_{22}O_4$: 373.1416 ($M + Na^{+}$), found: 373.1395.

(*E*)-Ethyl 2-(5-methyl-2-*p*-tolyl-1*H*-inden-1-ylidene)acetate (3s). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (t, $J = 7.3$ Hz, 3H), 2.36 (s, 3H), 2.39 (s, 3H), 4.27 (q, $J = 7.3$ Hz, 2H), 6.27 (s, 1H), 6.77 (s, 1H), 6.99−7.01 (m, 2H), 7.21−7.25 (m, 4H), 8.48 (d, $J = 7.7$ Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 21.2, 21.6, 60.6, 119.6, 121.9, 126.9, 127.3, 129.1, 129.2, 130.7, 131.9, 133.6, 137.5, 140.5, 144.0, 144.5, 151.1, 166.4; HRMS (ESI) calcd for $C_{21}H_{20}O_2$: 327.1361 ($M + Na^{+}$), found: 327.1346.

(*E*)-Ethyl 2-(2-(4-fluorophenyl)-5-methyl-1*H*-inden-1-ylidene)acetate (3t). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (t, $J = 7.3$ Hz, 3H), 2.37 (s, 3H), 4.28 (q, $J = 7.3$ Hz, 2H), 6.19 (s, 1H), 6.78 (s, 1H), 7.00−7.02 (m, 2H), 7.11 (t, $J = 8.4$ Hz, 2H), 7.31 (dd, $J = 5.5$, 8.7 Hz, 2H), 8.48 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 21.6, 60.7, 115.4 (d, $^2J_{CF} = 21.4$ Hz), 119.6, 122.1, 127.2, 127.4, 130.6, 130.9 (d, $^3J_{CF} = 7.6$ Hz), 134.2, 140.6, 143.4, 143.8, 151.0, 162.5 ($^1J_{CF} = 245.7$ Hz), 166.2; HRMS (ESI) calcd for $C_{20}H_{17}FO_2$: 331.1110 ($M + Na^{+}$), found: 331.1091.

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Supporting Information Available. Experimental procedures, characterization data, ^{1}H and ^{13}C NMR spectra of compounds **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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