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Sequential Sonogashira/Carbopalladative Cyclization/Suzuki Reactions Catalyzed by a Single Palladium Source by Using Protected Homopropargyl Alcohol

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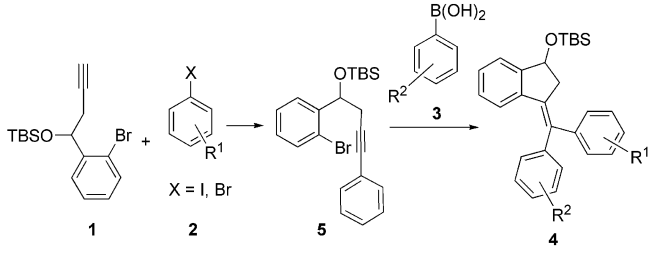
A novel cascade combination reaction catalyzed by a single palladium source for the synthesis of various indene derivatives is reported. The approach involved sequential Sonogashira/carbopalladative cyclization/Suzuki coupling reactions by using three readily available components, such as homopropargyl alcohol, aryl iodides or aryl bromides, and arylboronic acids. The overall domino reaction yields were up to 70 %.

Introduction

Arylalkynes play an important role as building blocks in many synthetic transformations and are common units of natural products, new materials, and pharmaceuticals.[1] In the field of alkyne chemistry, palladium-catalyzed domino reactions have attracted great interest and enabled the rapid establishment of molecular complexity in the total synthesis of complex natural products with minimized separation/purification efforts. Among such approaches, heteroarylalkyne are widely used with (hetero)aryl bromides or iodides for the synthesis of arylheterocyclic compounds by intramolecular Heck reaction involving terminations of insertion cascades as Sonogashira, Suzuki–Miyaura, or Heck cross-coupling reactions.[2] Zhu and co-workers reported a novel approach based on the multicomponent reaction concept by using a palladium-catalyzed domino Sonogashira/carbopalladation/C–H activation/C–C bond forming sequence for the synthesis of 3-arylidene oxindoles.[3] In comparison, few reports are concerned about the domino reactions of simple (alkyl)arylalkynes which are readily available for the synthesis of (benzo)carbocycles. Carbocycles are extremely important as basic skeletons of many biologically active natural products with specific structures. The synthesis of these carbocycles remains a challenge. Typical examples reported in the literature described the preparation of alkylidene indenols containing five-membered carbocycles by an intramolecular domino cyclocarbopalladation of alkynes following a Suzuki–Miyaura cross-coupling termination.[4] Recently, we developed an efficient method for the construction of various 2,5-disubstituted-3-bromofurans starting from protected homopropargyl alcohol.[5] As a continuation of our ongoing work on the further application of homopropargyl alcohols, which can be easily obtained by Barbier-type propargylation of aldehydes,[6] we designed a novel cascade combination involving a Sonogashira/carbopalladative cyclization/Suzuki sequential reaction by using *ortho*-bromo-substituted homopropargyl alcohol, which is relatively easily available and stable compared to the *ortho*-iodophenylhomopropargyl alcohol. The underlying principle of our approach is shown in Scheme 1. The Sonogashira coupling of protected homopropargyl alcohol **1** with aryl halide **2** in the presence of a palladium catalyst should give the disubstituted arylalkyne **5**, which would further react with arylboronic acid **3** to yield target compound **4** through a sequence of intramolecular carbopalladation/cyclization/Suzuki coupling (Scheme 1). By following this protocol and with simple variations in the structure of some of the starting materials, it would be very easy to access small libraries of differently substituted indene derivatives. Moreover, to the best of our knowledge, there are no reports on the synthesis of indene derivatives from homopropargyl alcohol derivatives through Sonogashira/carbopalladative cyclization/Suzuki multistep sequential transformations.



Scheme 1. Proposed three-component cascade reaction.

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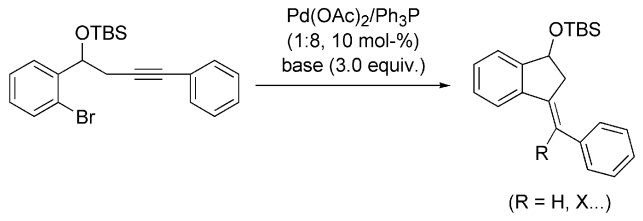
Results and Discussion

To probe the viability of the envisioned entire cascade reaction, we examined the reaction conditions step by step. The key step in these reactions is the *syn* addition of arylpalladium halide to the triple bond, which affords an intermediate that can participate in a wide variety of useful synthetic processes. Furthermore, the combination of mechanistically distinct reactions by a single catalyst is by far less developed owing to the specificity of each catalytic system to each individual reaction. Thus, in our initial studies, different bases were screened in the presence of the palladium catalyst to determine the optimal conditions for the first Sonogashira coupling reaction step (Table 1). Intriguingly, when HCOONa was used as a base, cyclization product **7** was observed. Thus, we considered the process shown in Scheme 2 as a potentially useful approach for the synthesis of indene derivative (Table 1, Entry 7). It should be noted that the termination of insertion cascades by using HCOONa to provide reductive protons has remained unexplored to date. The displacement of the Pd–Br bond in intermediate **6** by HCOO- afforded new intermediate **A**, which could further undergo decarboxylation to afford [H-Pd-C] species **B**. Intermediate **B** made the entire catalysis cycle complete through reductive elimination to finally yield target **7** (Scheme 1). Thus, the formation of intermediate **B** was the key step of the projected cyclization. For example, in the presence of other bases, no cyclization product was obtained due to the lack of a β-hydride elimination pathway for the Pd^{II} intermediate to recycle Pd^0 complexes (Table 1, Entries 3–6, 8, and 9) even when the reaction temperature was increased (Table 1, Entries 1and 2). In addition, when using the mixed solvents DMF/H_2O, we obtained trace amounts of the cyclic product (Table 1, Entry 10). This demonstrated that water had a great influence on this reaction.

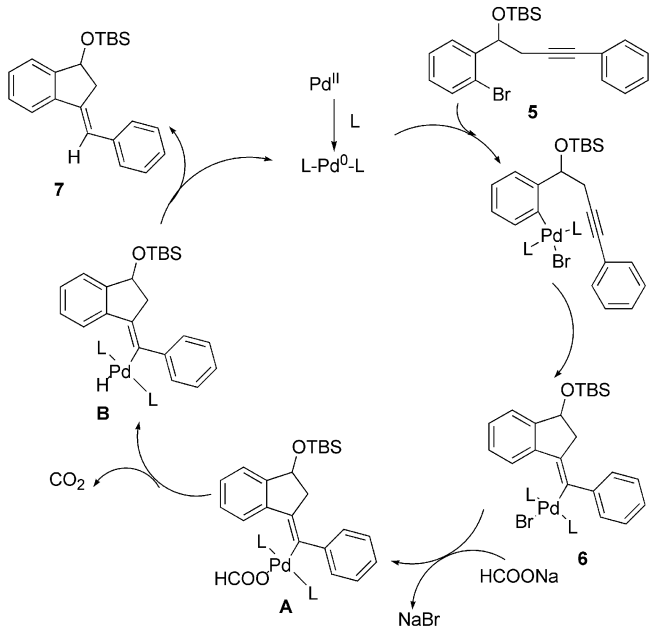
Preliminary investigations confirmed the viability of cyclocarbopalladation in the presence of the same palladium catalyst system that is optimal for the first Sonogashira coupling step. Notably, the indene skeleton of product **7** is present in a large number of drug candidates possessing interesting biological activities.[7] Such molecules are also used as ligands in metallocene complexes, especially group IV metallocene complexes used in the area of catalytic olefin polymerization.[8] With this promising result in hand, we defined an efficient catalytic system for the entire sequence, starting from readily available protected *ortho*-bromophenylhomopropargyl alcohol (**1**), phenyl iodide (**2**), and *para*-methoxyphenylboronic acid (**3a**). By this reaction in the presence of a suitable palladium catalyst, highly substituted indene derivative **4a** could be afforded. To improve the total yield of this sequential reaction, we attempted to vary the palladium source at different stages, one for the Sonogashira coupling and the other for the successive carbopalladative cyclization/Suzuki sequence. Regardless, the tandem reaction proceeded smoothly whether catalyzed by the same palladium source or by different palladium sources (Table 2, Entries 1–4). Even more interestingly, the reaction

Table 1. Screening the intramolecular cyclization.[a]



Entry	Base	*T* [°C]	Yield [%][b]
1	$NaHCO_3$	130	–
2	NaOAc	130	–
3	$NaHCO_3$	80	–
4	NaOAc	80	–
5	K_2CO_3	80	–
6	CH_3ONa	80	–
7	HCOONa	80	74
8	$N(C_2H_5)_3$	80	–
9	piperidine	80	–
10[c]	HCOONa	80	trace

[a] Reaction was carried out with the alcohol (0.2 mmol), **2** (0.21 mmol), the palladium catalyst (5 mol-%), and PPh_3 (8 equiv.) in piperidine (2 mL) at 80 °C under an atmosphere of N_2 for 12 h. [b] Isolated yield. [c] Using the mixed solvents DMF/H_2O, 9:1.

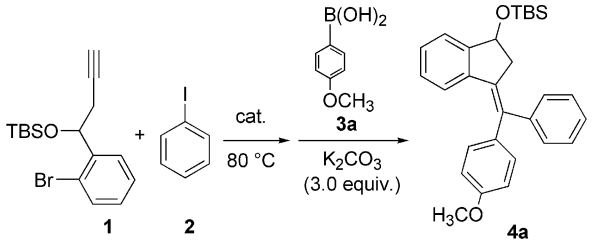


Scheme 2. Carbopalladative cyclization of protected homopropargyl alcohol.

also resulted in the corresponding product with a similar yield when only PPh_3 and K_2CO_3 were added without any additional palladium catalyst in the second step after the Sonogashira coupling (Table 2, Entry 5). We were intrigued enough by this result to explore the use of a single palladium catalyst in mechanistically distinct reactions. By using piperidine and K_2CO_3 as bases at different stages, only 10 mol-% $Pd(OAc)_2/PPh_3$ (1:8) with 5 mol-% CuI, necessary for the Sonogashira step, could catalyze the whole reaction sequence successfully with 59% yield (Table 2, En-

try 6). The reaction has unaffected by reducing the loading of $Pd(OAc)_2$ to 5 mol-%, yielding 60% of the product (Table 2, Entry 7). Adjusting the $Pd(OAc)_2/PPh_3$ ratio from 1:8 to 1:4 resulted in a decrease in the yield to 46% (Table 1, Entry 8). By further reducing the loading of $Pd(OAc)_2$ to 3 mol-%, only 42% product was obtained (Table 2, Entry 9). After optimization, we found that 5 mol-% of $Pd(OAc)_2/PPh_3$ (1:8) gave the best results with 60% yield for the entire cascade reaction sequence, although other different palladium catalysts [e.g., $Pd(CH_3CN)_2Cl_2$, $Pd(PPh_3)_4$, and $PdCl_2$] were also successful in this procedure. As such consecutive processes avoid the use of higher amounts of expensive palladium catalysts and avoids time consuming and costly purification processes, they are inherently environmentally benign and atom economic compared to the step-by-step reactions, although herein the overall yield by this cascade reaction (yield 60%) has no advantageous over that of the traditional step-by-step reactions [Sonogashira coupling, 10 mol-% $Pd(OAc)_2/PPh_3$ (1:2), yield 84%; cyclocarbopalladation/Suzuki coupling, 10 mol-% $Pd(OAc)_2/PPh_3$ (1:2), yield 83%].

Table 2. A survey of reaction conditions.[a]

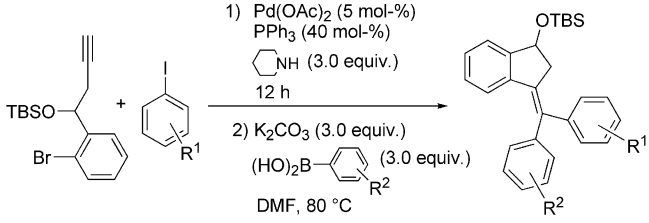


Entry	Sonogashira (mol-%)	Successive sequence (mol-%)	Yield[b] [%]
1	$Pd(PPh_3)_4$ (10)	$Pd(OAc)_2/PPh_3$ (10:20)	59
2	$Pd(CH_3CN)_2Cl_2/PPh_3$ (10:80)	$Pd(OAc)_2/PPh_3$ (10:20)	55
3	$Pd(OAc)_2/PPh_3$ (10:80)	$Pd(OAc)_2/PPh_3$ (10:20)	59
4	$Pd(OAc)_2/PPh_3$ (10:80)	$Pd(OAc)_2$ (10)	58
5	$Pd(OAc)_2/PPh_3$ (10:80)	PPh_3 (20)	55
6	$Pd(OAc)_2/PPh_3$ (10:80)	–	59
7	$Pd(OAc)_2/PPh_3$ (5:40)	–	60
8	$Pd(OAc)_2/PPh_3$ (5:20)	–	46
9	$Pd(OAc)_2/PPh_3$ (3:24)	–	42

[a] All reactions were carried out under an atmosphere of argon by using **1** (1.2 equiv.), **2** (1.0 equiv.), Pd catalyst, CuI (5 mol-%), and piperidine (3.0 equiv.) in DMF (2 mL) for 12 h at 80 °C. Then catalyst, base, and **3a** were added, followed by heating at 80 °C for 20 h. [b] Isolated yield.

Encouraged by the efficiency of the reaction protocol described above, different substituted aryl iodides and arylboronic acids were examined to probe the scope and limitation of this new three-component reaction (Table 3). As summarized in Table 3, a variety of arylboronic acids substituted by an electron-donating or an electron-withdrawing group were tolerated in moderate yields. In the cases of the same R^1 group, phenylboronic acids bearing an electron-donating group produced a higher yield than those with an electron-withdrawing group. Furthermore, when R^1 and R^2 were *p*-$COCH_3$ and *p*-OCH_3 groups, respectively, the reaction produced the highest yield of 70% (Table 3, Entry 9). These corresponding new indene derivatives products have single *Z* or *E* structures with different substitutions on the aromatic rings. Nevertheless, as for the *o*-substitution of R^1 or R^2 in the aromatic halide or arylboronic acid, this tandem reaction was either sluggish or complicated. This may be attributed to steric hindrance. When *p*-substitution R^1 was an electron-donating group, such as *p*-CH_3, a trace amount of the product was obtained.

Table 3. Scope of the tandem reaction of aryl iodides and arylboronic acids.[a]



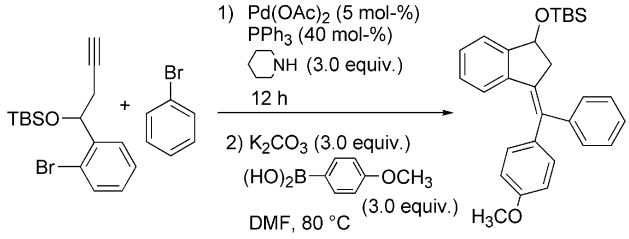
Entry	R^1	R^2	Yield [%][b]
1	H	H	44
2	H	*p*-CO_2CH_3	34
3	H	*p*-OCH_3 (**3a**)	60
4	*p*-F	H	50
5	*p*-F	*p*-CO_2CH_3	46
6	*p*-F	*p*-OCH_3	67
7	*p*-$COCH_3$	H	58
8	*p*-$COCH_3$	*p*-CO_2CH_3	48
9	*p*-$COCH_3$	*p*-OCH_3	70

[a] General conditions: All reactions were carried out under an atmosphere of argon by using **1** (1.2 equiv.), ArI (1.0 equiv.), CuI (5 mol-%), $Pd(OAc)_2$ (5 mol-%), PPh_3 (40 mol-%), and piperidine (3.0 equiv.) in DMF (2 mL) at 80 °C for 12 h; then K_2CO_3 (3.0 equiv.) and $ArB(OH)_2$ (3.0 equiv.) were added, followed by heating at 80 °C. [b] Isolated yield.

Compared to aryl iodides, aryl bromides have many advantages, including that they are widely commercially available at a low price. Thus we attempted to use aryl bromides instead of aryl iodides in the reaction. We found that the same product was made in 40% yield (Table 4, Entry 1). KI was added to the reaction in an attempt to enhance the reaction yield. However, the yield remained unchanged (36%) when adding KI (20 mol-%) at the beginning of the reaction (Table 4, Entries 2 and 3). However, after the Sonogashira coupling reaction, KI (20 mol-%) was added in addition to K_2CO_3 (3.0 equiv.), and the reaction yield increased to 57% (Table 4, Entry 3). The reason for this remains unexplained to date. In addition, we also tested the loading of KI, but no improvement was observed by increasing or decreasing the amount of KI (Table 4, Entries 5–7).

The scope of the reaction was also surveyed by probing changes in the aryl bromides and the substituted phenyl boronic acid substrates; the results are listed in Table 5. The outcome of this three-component reaction was influenced by the electronic properties of the phenylboronic acids, and a variety of products were synthesized in moderate levels or

Table 4. Screening reaction conditions of aryl bromides.[a]

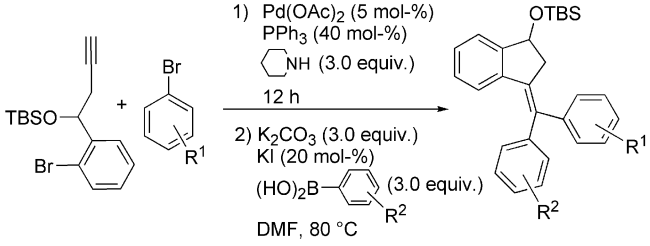


Entry	Sonogashira (mol-%)	Successive sequence (mol-%)	Yield[b] [%]
1	$Pd(OAc)_2/PPh_3$ (5:40)	–	40
2	$Pd(OAc)_2/PPh_3$ (5:40), KI (20)	–	36
3	$Pd(OAc)_2/PPh_3$ (5:40)	KI (20)	57
4	$Pd(OAc)_2/PPh_3$ (5:40)	$Pd(OAc)_2$ (5)	39
5	$Pd(OAc)_2/PPh_3$ (5:40)	KI (40)	47
6	$Pd(OAc)_2/PPh_3$ (5:40)	KI (50)	32
7	$Pd(OAc)_2/PPh_3$ (5:40)	KI (10)	50

[a] All reactions were carried out under an atmosphere of argon by using **1** (1.2 equiv.), **2a** (1.0 equiv.), $Pd(OAc)_2$ (5 mol-%), CuI (5 mol-%), and piperidine (3 equiv.) in DMF (2 mL) for 12 h at 80 °C. Then the base, additive, and **3a** were added into the above reaction mixture, followed by heating at 80 °C for 20 h. [b] Isolated yield.

somewhat higher yields. When R^1 = *p*-$COCH_3$ and R^2 = H, the reaction resulted in the best yield of 69% (Table 5, Entry 7). Among these results, some of the yields of the products were slightly higher than those obtained for iodobenzene (Table 5, Entries 1 and 7). This may be due to favorable Br/I exchange on the *ortho*-bromide of the substrate, which makes it easier to form the [ArPdX] intermediate (for Suzuki reaction) when KI (20 mol-%) was added.

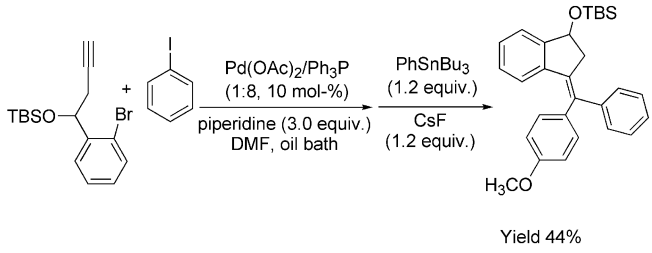
Table 5. Scope of the tandem reaction of aryl bromides and arylboronic acids.[a]



Entry	R^1	R^2	Yield [%][b]
1	H	H	57
2	H	*p*-CO_2CH_3	38
3	H	*p*-OCH_3 (**3a**)	57
4	*p*-F	H	57
5	*p*-F	*p*-CO_2CH_3	45
6	*p*-F	*p*-OCH_3	65
7	*p*-$COCH_3$	H	69
8	*p*-$COCH_3$	*p*-CO_2CH_3	45
9	*p*-$COCH_3$	*p*-OCH_3	68

[a] General conditions: All reactions were carried out under an atmosphere of argon by using **1** (1.2 equiv.), ArI (1.0 equiv.), CuI (5 mol-%), $Pd(OAc)_2$ (5 mol-%), PPh_3 (40 mol-%), and piperidine (3.0 equiv.) in DMF (2 mL) at 80 °C for 12 h; then K_2CO_3 (3.0 equiv.), KI (20 mol-%), and $ArB(OH)_2$ (3.0 equiv.) were added, followed by heating at 80 °C. [b] Isolated yield.

To challenge the methodology further, we also investigated the Sonogashira/carbopalladative cyclization/Stille coupling cascade sequence. By employing phenyltributyltin and CsF (1.2 equiv.), we obtained the desired product in 44% yield under the previously optimized conditions (Scheme 3). According to this result, we believe that the primary factor affecting the reaction yield is the efficiency of the Stille coupling.



Scheme 3. Sonogashira-carbopalladative cyclization-Stille reaction.

Conclusions

In conclusion, we developed a sequential reaction involving multi carbon–carbon bond formation by using protected homopropargyl alcohol in the presence of a single $Pd(OAc)_2$/triphenylphosphane catalytic system with good yields under mild conditions. The methodology that we described consists of Sonogashira/carbopalladative cyclization/Suzuki or Stille coupling reactions, leading to an efficient method to construct various indene derivatives, and this is the first report of such a cascade combination. Moreover, the wide tolerance of various substituents in the substrates and easy procedure to access the products efficiently from readily available starting materials may imply a potential synthetic application. Further experiments designed to explore the reaction scope are currently underway.

Experimental Section

General: All reagents were obtained from commercial suppliers and were used without further purification. DMF was distilled from CaH_2, ethyl acetate (anhydrous, 99.9%) was used as received. ^1H NMR and ^{13}C NMR spectra were obtained with a Bruker 400-AM spectrometer in $CDCl_3$. High-resolution mass spectra were determined with a Bruker Daltonics APEXII 47e FT-ICR spectrometer.

General Procedure: To the solution of [1-(2-bromophenyl)but-3-ynyloxy](*tert*-butyl)dimethylsilane in anhydrous DMF in a Schlenk flask under an atmosphere of nitrogen was added $Pd(OAc)_2$ (2.2 mg, 5 mol-%), PPh_3 (21 mg, 40 mol-%), and piperidine (51 mg, 0.6 mmol). The mixture was stirred vigorously at room temperature for 2 h. After addition of iodobenzene (40.8 mg, 0.2 mmol), the mixture was heated to 80 °C for 12 h until iodobenzene was totally consumed, as indicated by TLC. The mixture was cooled to room temperature. K_2CO_3 (82.8 mg, 0.6 mmol) and 4-methoxyphenylboronic acid (91.2 mg, 0.6 mmol) were added to the reaction system. Then the mixture was warmed to 80 °C for another 20 h. After

the reaction was complete, the mixture was quenched with brine (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layer was washed with brine and dried with anhydrous Na_2SO_4. The solvent was removed in vacuo, and the residue was purified by column chromatography to afford the white solid (266 mg, yield 60%).

***tert*-Butyl[3-(diphenylmethylene)-2,3-dihydro-1*H*-inden-1-yloxy]dimethylsilane:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.14 (s, 3 H), 0.19 (s, 3 H), 0.98 (s, 9 H), 2.94–3.21 (m, 2 H), 5.30 (t, J = 6.57 Hz, 1 H), 6.41 (d, J = 7.91 Hz, 1 H), 6.92 (t, J = 7.58 Hz, 1 H), 7.18 (t, J = 7.38 Hz, 1 H), 7.24–7.37 (m, 11 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.63, –5.35, 17.19, 24.89, 45.34, 72.90, 125.73, 126.09, 126.14, 126.76, 126.97, 127.68, 128.22, 128.91, 134.78, 135.18, 138.75, 141.53, 142.18, 147.91 ppm. HRMS: calcd. for $C_{28}H_{32}OSi$ 412.22224; found 412.22267.

(*Z*)-Methyl-4-{[3-(*tert*-Butyldimethylsilyloxy)-2,3-dihydro-1*H*-inden-1-ylidene](phenyl)methyl}benzoate: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.00 (s, 3 H), 0.05 (s, 3 H), 0.83 (s, 9 H), 2.80–3.06 (m, 2 H), 3.81 (s, 3 H), 5.15 (t, J = 6.43 Hz, 1 H), 6.29 (d, J = 7.84 Hz, 1 H), 6.78 (t, J = 7.58 Hz, 1 H), 7.03–7.24 (m, 9 H), 7.88 (s, 1 H), 7.90 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.56, –4.29, 18.24, 25.95, 46.65, 52.14, 73.84, 124.22, 124.81, 127.11, 127.30, 128.20, 128.92, 129.33, 130.09, 130.20, 134.71, 137.28, 139.25, 142.61, 147.54, 149.25, 167.08 ppm. HRMS: calcd. for $C_{30}H_{34}O_3Si$ 470.22772; found 470.22732.

(*Z*)-*tert*-Butyl{3-[(4-methoxyphenyl)(phenyl)methylene]-2,3-dihydro-1*H*-inden-1-yloxy}dimethylsilane: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.00 (s, 3 H), 0.05 (s, 3 H), 0.84 (s, 9 H), 2.82 (dd, J = 6.9, 15.1 Hz, 1 H), 3.02 (dd, J = 6.9, 15.2 Hz, 1 H), 3.71 (s, 3 H), 5.15 (t, J = 6.5 Hz, 1 H), 6.38 (d, J = 7.9 Hz, 1 H), 6.74–7.44 (m, 13 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.64, –5.36, 17.18, 24.89, 45.46, 54.16, 72.96, 113.00, 122.94, 123.74, 125.68, 126.08, 126.62, 126.91, 128.26, 130.07, 133.91, 134.40, 134.87, 138.95, 142.49, 147.85, 157.74 ppm. HRMS: calcd. for $C_{29}H_{34}O_2Si$ 442.23281; found 442.23288.

(*E*)-*tert*-Butyl{3-[(4-fluorophenyl)(phenyl)methylene]-2,3-dihydro-1*H*-inden-1-yloxy}dimethylsilane: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.10 (s, 3 H), 0.15 (s, 3 H), 0.93 (s, 9 H), 2.87–3.14 (m, 2 H), 5.26 (t, J = 6.45 Hz, 1 H), 6.38 (d, J = 6.38 Hz, 1 H), 6.84 (t, J = 7.60 Hz, 1 H), 6.93 (t, J = 8.67 Hz, 2 H), 7.08–7.33 (m, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.66, –5.38, 17.12, 24.86, 45.36, 72.81, 113.95 (d, J = 21.26 Hz), 122.99, 123.73, 126.10, 126.24, 126.82, 127.71, 128.81, 129.81 (d, J = 7.93 Hz), 135.27, 133.66, 138.14 (d, J = 3.23 Hz), 138.54, 141.26, 147.85, 160.48 (d, J = 246.64 Hz) ppm. HRMS: calcd. for $C_{28}H_{31}FOSi$ 430.21282; found 430.21222.

(*E*)-Methyl-4-{[3-(*tert*-Butyldimethylsilyloxy)-2,3-dihydro-1*H*-inden-1-ylidene](4-fluorophenyl)methyl}benzoate: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.00 (s, 3 H), 0.05 (s, 3 H), 0.82 (s, 9 H), 2.77–3.03 (m, 2 H), 3.77 (s, 3 H), 5.16 (t, J = 6.42 Hz, 1 H), 6.29 (d, J = 7.94 Hz, 1 H), 6.76 (t, J = 7.57 Hz, 1 H), 6.86 (t, J = 8.70 Hz, 2 H), 7.02–7.24 (m, 6 H), 7.87 (s, 1 H), 7.89 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.59, –4.32, 18.23, 25.91, 46.66, 52.15, 73.76, 115.14 (d, J = 21.38 Hz), 124.23, 124.74, 127.32, 128.31, 129.04, 130.12, 130.96 (d, J = 7.98 Hz), 133.61, 137.42, 138.60 (d, J = 3.28 Hz), 139.05, 147.24, 149.21, 161.73 (d, J = 247.07 Hz), 167.00 ppm. HRMS: calcd. for $C_{30}H_{33}FO_3Si$ 488.21830; found 488.21800.

(*E*)-*tert*-Butyl{3-[(4-Fluorophenyl)(4-methoxyphenyl)methylene]-2,3-dihydro-1*H*-inden-1-yloxy}dimethylsilane: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.00 (s, 3 H), 0.05 (s, 3 H), 0.83 (s, 9 H), 2.74–2.99 (m, 2 H), 3.69 (s, 3 H), 5.15 (t, J = 6.53 Hz, 1 H), 6.38 (d, J = 7.90 Hz, 1 H), 6.72–7.09 (m, 9 H), 7.21 (d, J = 7.51 Hz, 1 H), 7.34 (d, J = 8.82 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.64, –5.37, 17.18, 24.88, 45.49, 54.15, 72.90, 113.07, 113.82 (d, J = 21.25 Hz), 122.98, 123.70, 126.13, 126.67, 129.86 (d, J = 7.92 Hz), 130.02, 133.35, 133.66, 134.94, 138.79, 147.82, 157.85, 149.21, 160.51 (d, J = 254.89 Hz) ppm. HRMS: calcd. for $C_{29}H_{33}FO_2Si$ 460.22339; found 460.22399.

(*E*)-1-(4-{[3-(*tert*-Butyldimethylsilyloxy)-2,3-dihydro-1*H*-inden-1-yli-dene](phenyl)methyl}phenyl)ethanone: ^{1}H NMR (400 MHz, $CDCl_3$): δ = –0.05 (s, 3 H), 0.00 (s, 3 H), 0.78 (s, 9 H), 2.42 (s, 3 H), 2.75–3.00 (m, 2 H), 5.11 (t, J = 6.41 Hz, 1 H), 6.22 (d, J = 7.92 Hz, 1 H), 6.74 (t, J = 7.62 Hz, 1 H), 6.99–7.19 (m, 9 H), 7.74 (d, J = 8.28 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.57, –4.29, 18.24, 25.93, 29.73, 46.47, 73.86, 124.13, 125.04, 127.28, 127.55, 128.21, 128.33, 128.94, 129.46, 129.99, 134.76, 135.37, 138.06, 139.39, 141.88, 148.19, 149.22, 197.69 ppm. HRMS: calcd. for $C_{30}H_{34}O_2Si$ 454.23281; found 454.23224.

(*Z*)-Methyl-4-{(4-Acetylphenyl)[3-(*tert*-butyldimethylsilyloxy)-2,3-dihydro-1*H*-inden-1-ylidene]methyl}benzoate: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.05 (s, 3 H), 0.00 (s, 3 H), 0.77 (s, 9 H), 2.41 (s, 3 H), 2.76–3.00 (m, 2 H), 3.74 (s, 3 H), 5.11 (t, J = 6.41 Hz, 1 H), 6.24 (d, J = 7.78 Hz, 1 H), 6.74 (t, J = 7.55 Hz, 1 H), 7.00–7.20 (m, 6 H), 7.74 (d, J = 7.82 Hz, 2 H), 7.85 (d, J = 7.75 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.56, –4.29, 18.22, 25.93, 29.73, 46.71, 52.16, 73.75, 124.31, 124.97, 127.42, 128.33, 128.73, 129.27, 129.51, 130.23, 130.35, 133.64, 135.62, 138.85, 139.04, 146.77, 147.47, 149.49, 197.52, 166.87 ppm. HRMS: calcd. for $C_{32}H_{36}O_4Si$ 512.23829; found 512.23855.

(*Z*)-1-(4-{[3-(*tert*-Butyldimethylsilyloxy)-2,3-dihydro-1*H*-inden-1-ylidene](4-methoxyphenyl)methyl}phenyl)ethanone: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.00 (s, 3 H), 0.05 (s, 3 H), 0.83 (s, 9 H), 2.36 (s, 3 H), 2.82–3.06 (m, 2 H), 3.59 (s, 3 H), 5.16 (t, J = 6.21 Hz, 1 H), 6.42 (d, J = 7.90 Hz, 1 H), 6.68–7.25 (m, 9 H), 7.31 (d, J = 8.31 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.56, –4.26, 18.20, 25.97, 29.59, 46.63, 55.03, 73.99, 114.30, 124.18, 125.07, 126.52, 127.32, 128.17, 129.52, 131.18, 134.19, 134.56, 135.38, 137.80, 139.69, 148.47, 149.22, 159.16, 196.99 ppm. HRMS: calcd. for $C_{31}H_{36}O_3Si$ 484.24337; found 484.24373.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H and ^{13}C NMR spectra of selected compounds.

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[1] a) M. G. Organ, H. Ghasemi, *J. Org. Chem.* **2004**, *69*, 695–700; b) N. Ohyabu, T. Nishikawa, M. Isobe, *J. Am. Chem. Soc.* **2003**, *125*, 8798–8805; c) J. M. Altenburger, G. Y. Lassalle, M. Matrougui, D. Galtier, J. C. Jetha, Z. Bocskei, C. N. Berry, C. Lunven, J. Lorrain, J. P. Herault, P. Schaeffer, S. E. O'Connor, J. M. Herbert, *Bioorg. Med. Chem.* **2004**, *12*, 1713–1730; d) W.-M. Dai, K.-W. Lai, A. Wu, W. Hamaguchi, M. Y. H. Lee, L. Zhou, A. Ishii, S. Nishimoto, *J. Med. Chem.* **2002**, *45*, 758–761; e) S. H. Lee, T. Nakamura, T. Tsutsui, *Org. Lett.* **2001**, *3*, 2005–2007.

[2] a) D. M. D′Souza, F. Rominger, T. J. J. Müller, *Angew. Chem. Int. Ed.* **2005**, *44*, 153–158; b) W. S. Cheung, R. J. Patch, M. R. Player, *J. Org. Chem.* **2005**, *70*, 3741–3744; c) R. Yanada, S. Obika, T. Inokuma, K. Yanada, M. Yamashita, S. Ohta, Y.

Takemoto, *J. Org. Chem.* **2005**, *70*, 6972–6975; d) M. Arthuis, R. Pontikis, J.-C. Florent, *Tetrahedron Lett.* **2007**, *48*, 6397–6400.

[3] a) A. Pinto, L. Neuville, P. Retailleau, J. Zhu, *Org. Lett.* **2006**, *8*, 4927–4930; b) A. Pinto, L. Neuville, J. Zhu, *Angew. Chem. Int. Ed.* **2007**, *46*, 3291–3295.

[4] a) L. F. Tietze, K. Kahle, T. Raschke, *Chem. Eur. J.* **2002**, *8*, 401–407; b) S.-H. Min, S. J. Pang, C. G. Cho, *Tetrahedron Lett.* **2003**, *44*, 4439–4442; c) C. H. Oh, Y. M. Lim, *Tetrahedron Lett.* **2003**, *44*, 267–270; d) B. Salem, E. Delort, P. Klotz, J. Suffert, *J. Org. Lett.* **2003**, *5*, 2307–2310; e) E. Marchal, J. F. Cupif, P. Uriac, P. Weghe, *Tetrahedron Lett.* **2008**, *49*, 3713–3715; f) L.-N. Guo, X.-H. Duan, J. Hu, H.-P. Bi, X.-Y. Liu, Y.-M. Liang, *Eur. J. Org. Chem.* **2008**, 1418–1425.

[5] X. Wang, L.-Y. Liu, J. Li, *Sci. China Ser. B: Chem.* **2009**, *52*, 1314–1320.

[6] a) A. S. Y. Lee, S. F. Chu, Y. T. Chang, S. H. Wang, *Tetrahedron Lett.* **2004**, *45*, 1551–1553; b) Y. Masuyama, A. Ito, M. Fukuzawa, K. Terada, Y. Kurusu, *Chem. Commun.* **1998**, 2025–2026; c) Q. R. Li, C. Z. Gu, H. Yin, *Chin. J. Chem.* **2006**, *1*, 72–78; d) A. Kundu, S. Prabhakar, M. Vairamani, S. Roy, *Organometallics* **1999**, *18*, 2782–2785.

[7] a) S. Hagishita, M. Yamada, K. Shirahase, T. Okada, Y. Murakami, Y. Ito, T. Matsuura, M. Wada, T. Kato, *J. Med. Chem.* **1996**, *39*, 3636–3658; b) J. Palm, K. P. Boegesoe, T. Liljefors, *J. Med. Chem.* **1993**, *36*, 2878–2885; c) N. J. Clegg, S. Paruthiyil, D. C. Leitman, T. S. Scanlan, *J. Med. Chem.* **2005**, *48*, 5989–6003; d) D. T. Witiak, S. V. Kakodkar, G. E. Brunst, J. R. Baldwin, R. G. Rahwan, *J. Med. Chem.* **1978**, *21*, 1313–1315; e) H. Gao, J. A. Katzenellenbogen, R. Garg, C. Hansch, *Chem. Rev.* **1999**, *99*, 723–744.

[8] H. G. Alt, A. Koeppl, *Chem. Rev.* **2000**, *100*, 1205–1222.

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