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Synthesis of 9-Fluorenylidenes and 9,10-Phenanthrenes through Palladium-Catalyzed Aryne Annulation by *o*-Halostyrenes and *o*-Halo Allylic Benzenes

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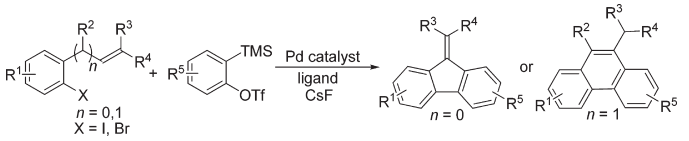

A number of functionally substituted 9-fluorenylidenes and 9,10-phenanthrenes have been synthesized from substituted *o*-halostyrenes and *o*-halo allylic benzenes respectively in good yields by the palladium-catalyzed annulation of arynes. The methodology tolerates a variety of functional groups, including cyano, ester, aldehyde, and ketone groups, occurs under relatively mild reaction conditions, and involves the generation of two new carbon−carbon bonds, thus providing these important carbocyclic ring systems in a single synthetic step.

Introduction

Derivatives of 9-fluorenylidenes and phenanthrenes are known to possess significant biological activity. Many dermatological and photostable cosmetic compositions[1] use the 9-fluorenylidene derivative Lumefantrine. Paranylene, a 9-fluorenylidene derivative, is used in dispersible formulations of anti-inflammatory agents.[2] Thus, derivatives of 9-fluorenylidenes are significant in the cosmetic and pharmaceutical fields. The thermochromic properties of 3-fluoren-9-ylidene-2′-hydroxy-3-phenylpropiophenone are known,[3] and 2,4,7-trinitro-9-fluorenylmethacrylate (TNFMN) has been used to study the donor−acceptor interactions of poly(FIMA)s with different tacticities.[4] The phenanthrene derivative 3,7-dihydroxy-2,4,8-trimethoxyphenanthrene is known for its anti-inflammatory properties,[5] while the derivative aristolochic acid exhibits tumor-inhibitory properties.[6] The phenanthrene derivatives 3-hydroxy-2,4-dimethoxy-7,8-methylenedioxyphenanthrene and 2,7-dihydroxy-1-methyl-5-vinylphenanthrene exhibit cytotoxicity.[7]

Since 9-fluorenylidene and phenanthrene derivatives are biologically and pharmaceutical important, the synthesis of these vital classes of compounds is of paramount importance. 9-Fluorenylidenes are mainly synthesized from 9*H*-fluoren-9-one derivatives using a Wittig reaction[8] or from 9*H*-fluorene derivatives.[9] Several methods have been reported for the synthesis of phenanthrene derivatives, and some of these approaches have significant disadvantages, including the use of toxic chemicals, harsh reaction conditions, or multistep reaction sequences.[10] The synthesis of phenanthrenes by the cocyclization of arynes and alkynes is also known,[11] but in most cases these reactions are not regioselective.

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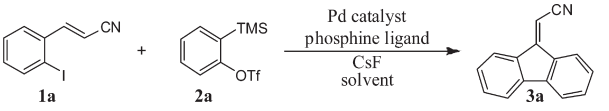
In synthetic organic chemistry, transition-metal-catalyzed annulation reactions have played a particularly valuable role of late.[12] For instance, a variety of carbocycles and heterocycles have been synthesized by the Pd-catalyzed annulation of alkynes by substituted aryl and vinylic halides.[13] However, the major difficulty in applying these reactions to arynes is the high reactivity of arynes[14] compared to alkynes, and the harsh reaction conditions often needed to generate arynes *in situ*, which also severely limits the functional group compatibility of the chemistry. Arynes often undergo Pd-catalyzed cyclotrimerization[15] to form polycyclic aromatic hydrocarbons as a result of their high reactivity. A very mild method of aryne generation from silylaryl triflate **2a** in the presence of CsF[16] has been used in our research laboratories and reported in the literature for a variety of Pd-catalyzed annulation reactions,[17] cycloaddition reactions,[18] electrophilic and nucleophilic reactions,[19] and insertion reactions.[20]

We have previously reported palladium-catalyzed alkyne annulations using ethyl (*E*)-4-(2-iodophenyl)-2-butenoate to obtain naphthalenes,[21] and the palladium-catalyzed alkyne annulation of methyl 3-(2-iodophenyl)acrylate has also been reported in the literature.[22] We recently reported the palladium-catalyzed aryne insertion and subsequent cyclization of *o*-halostyrenes to give 9-fluorenylidenes.[23] We report herein full details of our work on the synthesis of 9-fluorenylidenes and extensions of our methodology to obtain phenanthrenes from *o*-halo allylic benzenes by palladium-catalyzed aryne insertion and subsequent cyclization.

Results and Discussion

The focus of our early studies on this project was the palladium-catalyzed aryne annulation of substituted *o*-halostyrenes to give substituted 9-fluorenylidenes in good yields. (*E*)-3-(2-Iodophenyl)acrylonitrile (**1a**) was used as a model system for optimization of the reaction conditions, and 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2a**) was used as the aryne precursor. Early in this work, the reaction was run with 0.3 mmol of **1a**, 2.0 equiv of **2a**, 5 mol % $Pd(dba)_2$, 5 mol % P(*o*-tolyl)$_3$, and 3 equiv of CsF as the base in 5 mL of 1:9 acetonitrile/toluene at 110 °C in a sealed vial to obtain a 28% isolated yield of the desired 2-(9*H*-fluoren-9-ylidene)acetonitrile (**3a**) (eq 1; Table 1, entry 1).



(1)

Previously in our laboratories, we have found that the polarity of the acetonitrile/toluene solvent system greatly affects the yields of the aryne products under our experimental conditions, as it controls the rate of aryne formation. An increase in the polarity of the solvent system only slightly increased the yield of the desired product **3a** (entries 2−5). When the reaction was run in pure acetonitrile, the yield dropped to 25% (entry 6) with a simultaneous increase in the amount of the triphenylene side product resulting from palladium-catalyzed cyclotrimerization of the benzyne. None of the desired product was obtained when pure toluene was used as the solvent for the reaction, and both the starting *o*-halostyrene **1a** and the benzyne precursor **2a** remained unreacted under those conditions (entry 7). We believe that this is due to the low solubility of the fluoride source in toluene, which hinders formation of the benzyne. With 1:1 acetonitrile/toluene as the optimized solvent system for the reaction, we tried to improve the yield of the desired product **3a** by increasing the amount of the $Pd(dba)_2$ catalyst to 10 mol % and the P(*o*-tolyl)$_3$ ligand to 10 mol %. There was only a slight increase in the yield of the desired product **3a** to 39% (entry 8). An increase in the P(*o*-tolyl)$_3$ ligand to 20 mol % further increased the yield to 49% (entry 9). While maintaining a 1:2 ratio of the $Pd(dba)_2$ to the P(*o*-tolyl)$_3$ but further increasing the amount of the catalyst and the ligand, no significant increase in the yield was observed (entry 10). The reaction in the absence of P(*o*-tolyl)$_3$ did not yield the desired product **3a** (entry 11).

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TABLE 1. Optimization of Palladium-Catalyzed Benzyne Insertion into (*E*)-3-(2-Iodophenyl)acrylonitrile Using Various Solvents and Ligands (eq 1)[a]

entry	mol % $Pd(dba)_2$	phosphine ligand (mol %)	solvent (CH_3CN/$PhCH_3$)	% yield[b]
1	5	P(*o*-tolyl)$_3$ (5)	1:9	28[c]
2	5	P(*o*-tolyl)$_3$ (5)	1:7	36[c]
3	5	P(*o*-tolyl)$_3$ (5)	1:5	35[c]
4	5	P(*o*-tolyl)$_3$ (5)	1:3	35[c]
5	5	P(*o*-tolyl)$_3$ (5)	1:1	37[c]
6	5	P(*o*-tolyl)$_3$ (5)	1:0	25[c]
7	5	P(*o*-tolyl)$_3$ (5)	0:1	0[c]
8	10	P(*o*-tolyl)$_3$ (10)	1:1	39[c]
9	10	P(*o*-tolyl)$_3$ (20)	1:1	49[c]
10	15	P(*o*-tolyl)$_3$ (30)	1:1	48[c]
11	20		1:1	0[c]
12	10	tris(2,4,6-trimethoxyphenyl)-phosphine (20)	1:1	40[c]
13	10	tris(2,6-dimethoxyphenyl)-phosphine (20)	1:1	75
14	10	tri(2-methoxyphenyl)phosphine (20)	1:1	84
15	10	tri(2-furyl)phosphine (20)	1:1	30
16	10	$[(CH_3)_3P\cdot AgI]_4$ (20)	1:1	25[c]
17	10	tri(*tert*-butyl)phosphine (20)	1:1	< 5[c,d]
18	10	2-(di-*tert*-butylphosphino)biphenyl (20)	1:1	32
19	10	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos) (20)	1:1	35
20	10	1,3-bis(diphenylphosphino)-propane (dppp) (20)	1:1	< 5[c,d]
21	10	1,1′-bis(diphenylphosphino)-ferrocene (dppf) (20)	1:1	< 5[d]
22	10	1,1-bis(diphenylphosphino)-methane (dppm) (20)	1:1	91

[a]Representative procedure: (*E*)-3-(2-iodophenyl)acrylonitrile (0.3 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (2.0 equiv), $Pd(dba)_2$, ligand, CsF (3 equiv), and solvent (5 mL) were placed in a 4-dram vial. The vial was sealed with a screw cap. The reaction was then stirred at 110 °C for 24 h. [b]Isolated yields. [c]Some starting material **1a** was left. [d]GC yields.

Noting the importance of the ligand in the reaction, various ligands have been screened with the aim of increasing the yield of the 9-fluorenylidene **3a**. Electron-rich tris(2,4,6-trimethoxyphenyl)phosphine gave a reduced yield of 40% (entry 12), while tris(2,6-dimethoxyphenyl)-phosphine increased the yield to 75% (entry 13). Relatively unhindered tri(2-methoxyphenyl)phosphine improved the yield still further to 84% (entry 14). Along with steric factors, the electronic nature of the phosphine ligand seems to have an effect on the overall yield of the desired product **3a** (compare entries 12−14). To further study the effect on the yield of the desired product, in the presence of an oxygen moiety in the phosphine ligand (compare entries 9 and 14), the reaction was carried out with tri(2-furyl)phosphine as the ligand, which gave a poor 30% yield of **3a** (entry 15). The ligand trimethylphosphine obtained from $[(CH_3)_3P\cdot AgI]_4$ gave a poor 25% yield of the desired product **3a** (entry 16). The bulkier phosphine ligand tri(*tert*-butyl)phosphine gave an extremely poor yield (< 5%), while 2-(di-*tert*-butylphosphino)-biphenyl gave only a 32% yield of the fluorenylidene (entries 17 and 18). We have also screened bidentate ligands with a view toward improving the yield of the desired 9-fluorenylidene **3a**. The bidentate Xantphos ligand did not improve the yield of the reaction (entry 19), affording only a 35% yield of **3a**. The phosphine ligands dppp and dppf gave extremely poor yields (entries 20 and 21), but to our surprise dppm improved the yield to 91% (entry 22).

TABLE 2. Optimization of the Palladium-Catalyzed Benzyne Insertion into (*E*)-3-(2-Iodophenyl)acrylonitrile with dppm as the Ligand (eq 1)[a]

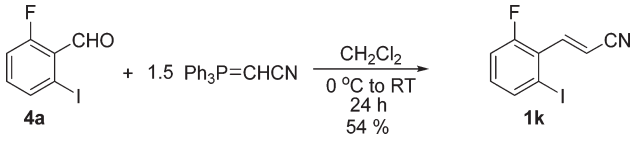
entry	$Pd(dba)_2$ (mol %)	dppm (mol %)	precursor (equiv)	CsF (equiv)	time (h)	temp (°C)	% yield[b] **3a**
1	10	20	2.0	3	24	85	52[c]
2	10	20	2.0	3	24	100	68[c]
3	10	20	2.0	3	24	120	92
4	10	20	1.5	3	24	110	91
5	10	20	1.2	3	24	110	69[c]
6	10	20	1.5	2	24	110	78
7	10	20	1.5	5	24	110	86
8	5	5	1.5	3	24	110	49[c]
9	5	10	1.5	3	24	110	62[c]
10	10	10	1.5	3	24	110	69[c]
11	20	10	1.5	3	24	110	42
12	10	40	1.5	3	24	110	76
13	10	20	1.5	3	12	110	71[c,d]

[a]Representative procedure: (*E*)-3-(2-iodophenyl)acrylonitrile (0.3 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate, $Pd(dba)_2$, dppm, CsF, and solvent (5 mL) were placed in a 4 dram vial. The vial was sealed with a screw cap. The reaction was then stirred at the desired temperature for the indicated time. [b]Isolated yields. [c]Some starting material **1a** was left. [d]GC yields.

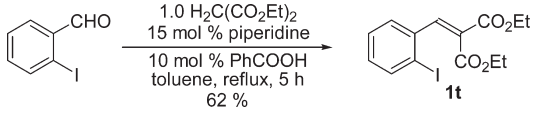
With dppm as the apparent ligand of choice, the reaction has been carried out at a lower temperature. At 85 °C, the desired product **3a** was obtained in a lower 52% yield (Table 2, entry 1), and the reaction did not go to completion. When the reaction was run at 100 °C, the yield increased to 68% (entry 2), while a further increase in the temperature to 120 °C did not have much effect on the yield of the product (compare Table 1, entry 22 and Table 2, entry 3). Reducing the amount of the benzyne precursor to 1.5 equiv did not affect the yield of the desired product **3a** (entry 4), but a further reduction of **2a** to 1.2 equiv decreased the yield of **3a** to 69% (entry 5). Either a decrease or an increase in the amount of the base CsF gave reduced yields of 78% and 86%, respectively (compare entries 4, 6, and 7). This variation in yields probably reflects a variation in the rate of benzyne formation from the 2-(trimethylsilyl)phenyl trifluoromethanesulfonate.

After optimization of the reaction conditions with respect to the solvent system, the phosphine ligand, the temperature, the amount of the aryne precursor and the base, we also studied if the reaction can be carried out at a lower catalyst loading with different palladium catalyst to phosphine ligand ratios. When the reaction was run with only 5 mol % of the $Pd(dba)_2$ catalyst and 5 mol % of the dppm ligand, the yield decreased to 49% (entry 8). An increase in the amount of the dppm ligand to 10 mol % increased the yield to 62% (entry 9), indicating that a ratio of $Pd(dba)_2$ to the dppm ligand of 1:2 works better than the ratio of 1:1, even at a lower catalyst loading. To double check this finding, the reaction was carried out with 10 mol % of $Pd(dba)_2$ and 10 mol % of the dppm ligand, which afforded only a 69% yield of the desired product **3a** (compare entries 4 and 10). A higher $Pd(dba)_2$ to dppm ligand ratio or a further excess of the dppm ligand decreased the yields of **3a** to 42% and 76% respectively (entries 11 and 12). A reduced reaction time gave a lower yield of 71% (entry 13). Thus, our optimized

SCHEME 1



SCHEME 2



conditions for the palladium-catalyzed aryne annulation are 0.3 mmol of **1a**, 1.5 equiv of **2a**, 10 mol % of $Pd(dba)_2$, 20 mol % of dppm, 3 equiv of CsF in 5 mL of 1:1 acetonitrile/toluene at 110 °C in a sealed vial for 24 h.

Using our best reaction conditions for the aryne annulation, we further examined the scope of this reaction on various substrates. Aryl halide **1k** was prepared by standard Wittig chemistry (Scheme 1), using commercially available aldehyde **4a**. The aryl halide **1t** was prepared by condensation of *o*-iodobenzaldehyde with diethyl malonate (Scheme 2). Aryl halides **1a**, **1h**, and **1r** were obtained from commercial sources, and **1b**,[24] **1c**,[24] **1d**,[25] **1e**,[26] **1f**,[23] **1g**,[27] **1i**,[23] **1j**,[23] **1l**,[28] **1m**,[28] **1n**,[21] **1o**,[28] **1p**,[28] **1q**,[29] and **1s**[30] were prepared according to literature procedures. The benzyne precursor **2a** is commercially available, and the aryne precursors **2b**,[18] 2c,[18] **2d**,[18] and **2e**[18] were prepared according to literature procedures.

The model system **1a** under our optimized conditions with 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2a**) as the benzyne precursor gave an 91% isolated yield of the desired product **3a** (Table 3, entry 1). To study the more facile oxidative addition of aryl iodides over aryl bromides, the reaction was carried out using the corresponding aryl bromide, (*E*)-3-(2-bromophenyl)acrylonitrile (**1b**). Compound **3a** was indeed obtained in a slightly lower 79% yield (entry 2). The *cis* isomer (*Z*)-3-(2-bromophenyl)acrylonitrile (**1c**) gave a slightly lower yield of 72% than the corresponding *trans* isomer, (*E*) 3-(2-bromophenyl)acrylonitrile (**1b**) (compare entries 2 and 3). With a methyl ester as the electron-withdrawing group (EWG) on the double bond of the *o*-halostyrene **1d**, the yield dropped to 76% under our optimized conditions (compare entries 1 and 4). Similar results were obtained using the corresponding bromide-containing ethyl ester (compare entries 2 and 5). With an aldehyde as the EWG on the *o*-halostyrene **1f**, a 76% yield of the desired product **3d** was obtained (entry 6), which is comparable to that obtained with an ester group present on the double bond of the *o*-halostyrene, but with a ketone present in the *o*-halostyrene **1g**, the yield dropped to 61% (entry 7). Previously aryl triflates have proved to work well in oxidative palladium insertion chemistry. Thus, we carried out a reaction with 2-(3-oxo-3-phenylpropenyl)phenyl trifluoromethanesulfonate, but none of the desired product was obtained. When a stronger electron-withdrawing nitro group was placed on the *o*-halostyrene, the reaction also failed to give the desired product **3f** (entry 8). Instead, we got a polymeric residue in the reaction flask. We believe 2-(2-nitrovinyl)iodobenzene (**1h**) undergoes polymerization under our reaction conditions. We therefore carried out the reaction at a lower temperature but again failed to get the desired product **3f**. Also, when an electron-donating methyl group was placed on the double bond of the *o*-halostyrene, as in 1-iodo-2-(1-propenyl)benzene, the reaction with 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2a**) failed to give the desired fluorenylidene under our reaction conditions. When electron-donating methoxy groups were placed on the *o*-halostyrene, we obtained an extremely poor yield (< 5%), presumably because oxidative addition of palladium is unfavorable in such electron-rich aryl halides (compare entries 5 and 9). On the other hand, the electron-rich substrate **1j** with a carbon−iodine bond, instead of a carbon−bromine bond, gave the desired product in a 73% yield (entry 10). The fluorine-containing *o*-halostyrene **1k** reacted with **2a** to give a 46% yield of the fluorenylidene (entry 11). However, the reaction was slow and did not go to completion even at the higher temperature of 140 °C. The structure of the major product has not been rigorously established but is assumed to be the less hindered *E*-isomer. Five percent of a minor isomer has also been observed.

We have also studied the scope of the reaction using various aryne precursors. The model system **1a** on reaction with the aryne precursor **2b** gave the desired compounds **3k** and **3l** as a 11:1 mixture of inseparable isomers in an 82% overall yield (entry 12). It is unclear as to which stereoisomer is the major product. The aryne precursor **2c** with two electron-rich methoxy groups gave a slightly lower yield of 78% when allowed to react with the model system **1a**; a 4:1 ratio of stereoisomers was obtained (entry 13). Again, the stereochemistry of the major isomer is unknown. The slightly lower yield may be due to the slower rate of aryne formation from precursor **2c**, as observed previously by us.

When we carried out the palladium-catalyzed aryne annulation using aryne precursor 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2a**) and *o*-halostyrene **1r**, bearing a trisubstituted double bond, under our optimized reaction conditions, the reaction was messy and the desired product **3w** was obtained in an extremely low (< 5%) yield as determined by GC analysis (Scheme 3). We have also tried an analogous reaction with *o*-halostyrene **1s**, where the electron-withdrawing groups on the double bond of the styrene were ester groups, instead of cyano groups. The desired product **3x** was again obtained in a very low (< 5%) yield as determined by GC analysis. A reaction with the corresponding aryl iodide **1t** only slightly improved the yield to ~5−10%, and the reaction was cleaner when compared to that of aryl bromide **1s**.

We have also been able to extend our methodology to the synthesis of phenanthrene derivatives from the corresponding *o*-halo allylic benzenes. Ethyl (*E*)-4-(2-iodophenyl)but-2-enoate (**1l**) on reaction with **2a** gave a 62% yield of the desired 9-phenanthrene **3o** (entry 14).

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TABLE 3. Synthesis of 9-Fluorenylidenes and Phenanthrenes by Palladium-Catalyzed Aryne Annulation of *o*-Halostyrenes and *o*-Halo Allylic Benzenes[a]

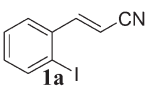
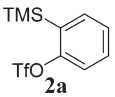
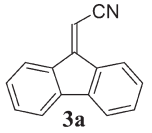
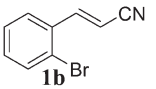
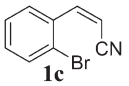
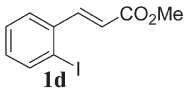
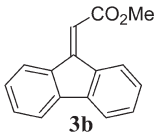
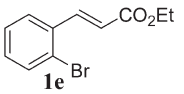
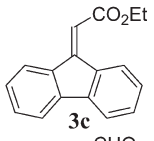
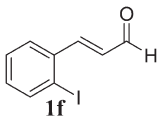
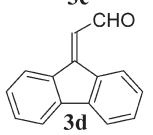
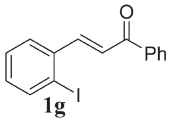
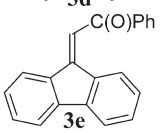
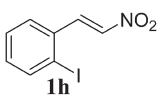
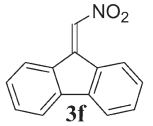
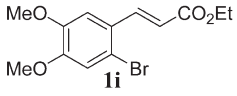
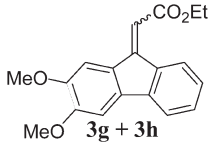
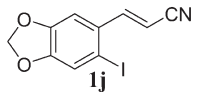
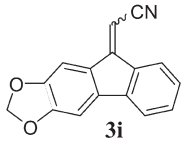
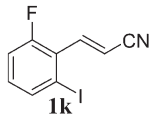
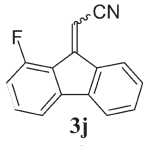
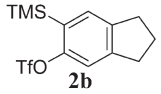
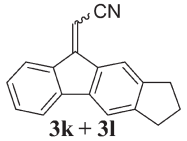
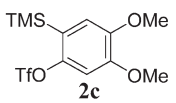
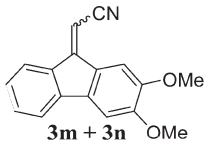
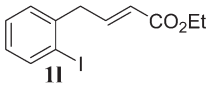
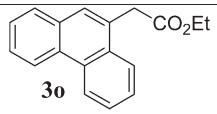
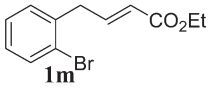
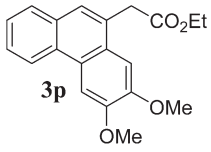
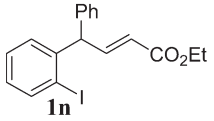
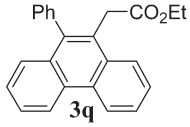
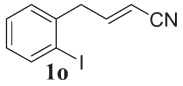
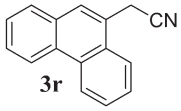
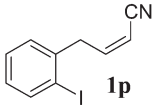
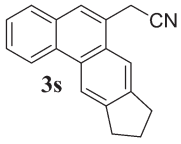
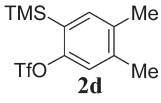
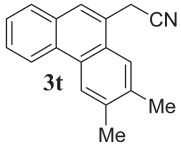
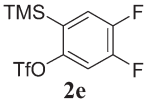
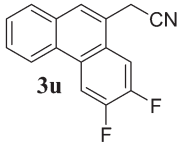
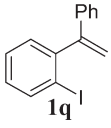
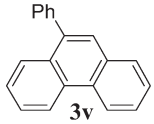
entry	unsaturated arene	benzyne precursor	product(s)	% isolated yield
1	 **1a**	 **2a**	 **3a**	91
2	 **1b**	**2a**	**3a**	79
3	 **1c**	**2a**	**3a**	72
4	 **1d**	**2a**	 **3b**	76
5	 **1e**	**2a**	 **3c**	75
6	 **1f**	**2a**	 **3d**	76
7	 **1g**	**2a**	 **3e**	61
8	 **1h**	**2a**	 **3f**	0
9	 **1i**	**2a**	 **3g + 3h**	<5%[b]
10	 **1j**	**2a**	 **3i**	73[c]
11	 **1k**	**2a**	 **3j**	46[d,e]
12	**1a**	 **2b**	 **3k + 3l**	82[f] [11:1]
13	**1a**	 **2c**	 **3m + 3n**	78[f] [4:1]

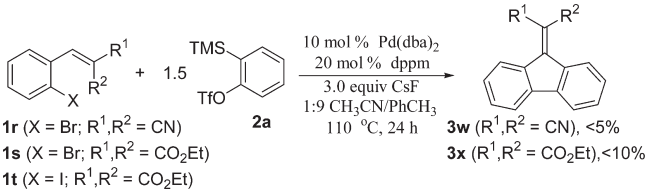
TABLE 3. Continued

entry	unsaturated arene	benzyne precursor	product(s)	% isolated yield
14	 **1l**	**2a**	 **3o**	62
15	 **1m**	**2a**	**3o**	49
16	**1l**	**2c**	 **3p**	45
17	 **1n**	**2a**	 **3q**	~20[b]
18	 **1o**	**2a**	 **3r**	58
19	 **1p**	**2a**	**3r**	47
20	**1o**	**2b**	 **3s**	52
21	**1o**	 **2d**	 **3t**	50
22	**1o**	 **2e**	 **3u**	0
23	 **1q**	**2a**	 **3v**	35[b]

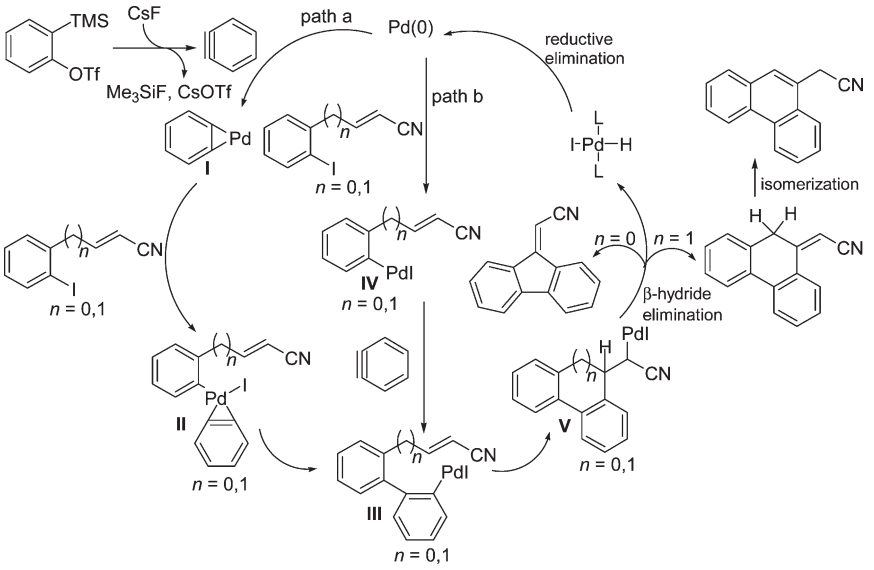
[a]Representative procedure: aryl halide **1(a−r)** (0.3 mmol), silylaryl triflate **2(a−e)** (2.0 equiv), 10 mol % of $Pd(dba)_2$, 20 mol % of dppm, CsF (3 equiv), and 1:1 $CH_3CN/PhCH_3$ (5 mL) were placed in a 4-dram vial. The vial was sealed with a screw cap. The reaction was then stirred at 110 °C for 24 h. [b]GC yields. [c]Eight percent of a minor isomer is observed by GC analysis. [d]Some starting material **1k** was left. The reaction did not go to completion even at 140 °C. [e]Five percent of a minor isomer is observed by GC analysis. [f]The ratio was determined by H^1 NMR spectroscopy.

Ethyl (*E*)-4-(2-bromophenyl)but-2-enoate (**1m**) gave a slightly lower yield of 49% of **3o**, presumably as a result of reasons mentioned previously. Ethyl (*E*)-4-(2-iodophenyl)-but-2-enoate, when allowed to react with the electron-rich aryne precursor **2c**, gave a somewhat lower yield of 45% of the desired phenanthrene **3p** (compare entries 14 and 16). The *o*-halo allylic benzene **1n** gave a poor ~20% yield of the desired phenanthrene **3q**, but the product could not be

SCHEME 3



SCHEME 4



purified (entry 17). An electron-withdrawing cyano group on the *o*-halo allylic benzene **1o**, instead of an ester group, gave a slightly lower 58% yield of the desired phenanthrene **3r**, contrary to our observations with the analogous fluorenylidenes (compare entries 14 and 18, and entries 1 and 4). (*Z*)-4-(2-Iodophenyl)-2-butenenitrile (**1p**) gave a 47% yield of the desired phenanthrene, which was slightly less than the (*E*)-isomer (compare entries 18 and 19). *o*-Halo allylic benzene **1o**, when treated with the aryne precursors **2b** and **2d**, gave 52% and 50% yields, respectively, of the corresponding phenanthrenes **3s** and **3t** (entries 20 and 21). Thus, the yield of the reaction decreases when more electron-rich aryne precursors are used. When inductively electron-withdrawing fluorine atoms were placed on the aryne precursor **2e**, none of the desired product was obtained for reasons not known to us. The *o*-halostyrene **1q** gave the phenanthrene **3v** in a 35% yield. This product, however, could not be separated from the corresponding triphenylene, which is the major side product in all of these reactions.

On the basis of the known reactions of organopalladium compounds with alkynes,[13] we propose two possible mechanistic pathways, path a or path b, for these reactions (Scheme 4). In path a, the aryne generated from the triflate in the presence of the fluoride source coordinates with Pd(0), affording palladacycle **I**.[31] Oxidative addition of the aryl halide to **I** might generate an arylpalladium(IV) complex **II**. Upon reductive elimination, complex **II** could afford a new arylpalladium intermediate **III**. Alternatively, according to path b, Pd(0) might add oxidatively to the aryl halide to afford the arylpalladium(II) intermediate **IV**, which in turn might add to the aryne[32] to afford arylpalladium intermediate **III**. Regardless of how intermediate **III** is generated, the palladium−carbon bond in this intermediate can then add across the neighboring carbon−carbon double bond to afford intermediate **V**, which directly affords the fluorenylidene product by β-hydride elimination when $n = 0$. When $n = 1$, the phenanthrene is obtained by further isomerization of the resulting olefin. This isomerization may be promoted by the base present in the reaction or by the palladium hydride generated during the process. Similar intramolecular palladium-catalyzed Heck reactions, followed by olefin isomerization, have been reported by us during the carbopalladation of alkynes to generate naphthalenes.[21]

Conclusions

A range of substituted fluorenylidenes and phenanthrenes have been obtained using a one-step palladium-catalyzed aryne insertion of *o*-halostyrenes and *o*-halo allylic benzenes, respectively, from starting materials that are readily available or easily synthesized. The arynes are obtained *in situ* under mild reaction conditions from the corresponding 2-(trimethylsilyl)aryl trifluoromethanesulfonates and CsF, thus rendering the methodology tolerant of a variety of functional groups, including cyano, ester, aldehyde, ketone, and methoxy groups. This provides a handle for further organic transformations. A fluorine moiety can also be introduced into the products. This methodology provides a very convenient and general approach to these two important classes of aromatic hydrocarbons.

Experimental Section

3-(2-Fluoro-6-iodophenyl)acrylonitrile (1k). This compound was prepared by the following procedure. To a solution of (triphenylphosphoranylidene)acetonitrile (4.5 mmol) in 30 mL of CH_2Cl_2 was added dropwise a solution of the 2-fluoro-6-iodobenzaldehyde (3.0 mmol) in 6 mL of CH_2Cl_2 at 0 °C under an inert argon atmosphere. The resulting mixture was stirred at 25 °C for 24 h and monitored by TLC. The solvent was then evaporated under reduced pressure. The solid residue was dissolved in 15 mL of hexanes, and the mixture was stirred at 25 °C for 30 min. The Ph_3PO was filtered off, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel using hexanes/EtOAc as the eluent to afford the desired product as a white solid: mp 82−83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (d, J = 16.8 Hz, 1H),

(31) (a) Yoshida, H.; Ikadai, J.; Shudo, M.; Ohshita, J.; Kunai, A. *Organometallics* **2005**, *24*, 156. (b) Yoshida, H.; Tanino, K.; Ohshita, J.; Kunai, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 5052.

(32) Henderson, J. L.; Edwards, A. S.; Greaney, M. F. *Org. Lett.* **2007**, *9*, 5589.

7.03−7.16 (m, 2H), 7.41 (d, J = 16.8 Hz, 1H), 7.75 (d, J = 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 101.64, 101.66, 104.0, 3104.2, 115.4, 116.8, 117.0, 117.8, 124.9, 125.0, 132.70, 132.79, 136.35, 136.39, 148.54, 148.57, 159.6, 162.1 (extra peaks due to splitting by fluorine); HRMS m/z 272.94554 (calcd C_9H_5FIN, 272.94508).

Diethyl [(2-Iodophenyl)methylene]propanedioate (1t). This compound was prepared by the following procedure. To a solution of 2-iodobenzaldehyde (10 mmol), diethyl malonate (10 mmol), and piperidine (1.5 mmol) in 60 mL of toluene was added benzoic acid (1.0 mmol). The reaction mixture was refluxed for 5 h using a Dean−Stark condenser for water removal. The mixture was cooled to room temperature and diluted with diethyl ether (100 mL) and EtOAc (100 mL). The organic layer was separated and washed two times each with 2 N HCl, satd aq $NaHCO_3$, and brine. The organic layer was then dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel using hexanes/EtOAc as the eluent and further subjected to distillation to remove traces of diethyl malonate (bp 195−196 °C) at ∼200 °C to afford the desired product as a brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14 (t, J = 7.0 Hz, 3H), 1.34 (t, J = 7.1 Hz, 3H), 4.19 (q, J = 7.2 Hz, 2H), 4.33 (q, J = 7.0 Hz, 2H), 7.03−7.07 (m, 1H), 7.29−7.39 (m, 2H), 7.83 (s, 1H), 7.89 (d, J = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 14.2, 61.6, 61.8, 99.6, 128.2, 128.6, 128.9, 131.1, 137.4, 139.4, 145.9, 163.5, 165.4; IR (neat, cm^{-1}) 3060, 2979, 1746, 1627, 1458, 1361; HRMS m/z 374.00220 (calcd $C_{14}H_{15}IO_4$, 374.00151).

(33) Dibbiase, S. A.; Lipisko, B. A.; Haag, A.; Wolak, R. A.; Gokel, G. W. *J. Org. Chem.* **1979**, *44*, 4640.

General Procedure for the Palladium-Catalyzed Annulation of Arynes by *o*-Halostyrenes and *o*-Halo Allylic Benzenes. To 0.3 mmol of the aryl halide were added the *o*-silylaryl triflate (1.5 equiv), $Pd(dba)_2$ (10 mol %), dppm (20 mol %), and 1:1 CH_3CN/$PhCH_3$ (5 mL). CsF (3.0 equiv) was then added, and the vial was sealed with a screw cap. The reaction mixture was then stirred at 110 °C for 24 h. After the reaction was complete, the resulting solution was washed with brine (25 mL) and extracted with EtOAc (25 mL). The combined EtOAc fractions were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using hexanes/EtOAc as the eluent to afford the desired product.

2-(9*H*-Fluoren-9-ylidene)acetonitrile (3a). This compound was obtained as a yellow solid: mp 109−111 °C (lit.[33] 109−110 °C); ^{13}C NMR (100 MHz, $CDCl_3$) δ 88.6, 120.3, 120.4, 121.7, 125.5, 128.0, 128.5, 131.9, 132; HRMS m/z 203.07381 (calcd $C_{15}H_9N$, 203.07350). The ^{1}H NMR spectrum matches the literature data.[33]

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Supporting Information Available: General experimental procedures and spectral data for all previously unreported starting materials and products. This material is available free of charge via the Internet at http://pubs.acs.org.