Synthesis of 9-Alkylidene-9*H*-fluorenes by a Novel, Palladium-Catalyzed Cascade Reaction of Aryl Halides and 1-Aryl-1-alkynes

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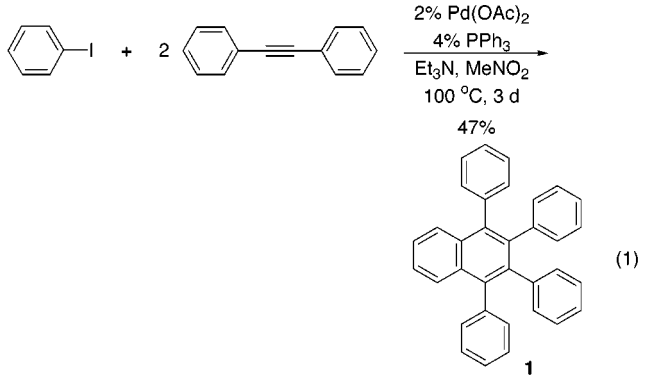
In the presence of a palladium catalyst and NaOAc, aryl iodides react with 1-aryl-1-alkynes to afford 9-alkylidene-9*H*-fluorenes in good yields. The products from this reaction are highly dependent on the base employed. This process appears to involve (1) oxidative addition of the aryl iodide to Pd(0), (2) alkyne insertion, (3) rearrangement of the resulting vinylic palladium intermediate to an arylpalladium species, and (4) aryl−aryl coupling with simultaneous regeneration of the Pd(0) catalyst. Consistent with this mechanism is the fact that 9-alkylidene-9*H*-fluorenes can also be prepared by the Pd-catalyzed rearrangement of 1,1-diaryl-2-iodo-1-alkenes.

Introduction

Annulation processes are extremely important in organic synthesis for the construction of heterocycles and carbocycles. Palladium-mediated annulations are particularly important.[1] Among these processes, the annulation of alkynes, which often involves cascade insertion processes, has proven a useful route for the synthesis of a wide variety of heterocycles and carbocycles from simple synthetic building blocks.[2] One unique feature of organopalladium chemistry is the extraordinary effect seemingly minor variations in the reaction conditions can have on the course of the reaction and the yield of the product. For example, Heck has reported the formation of a substituted naphthalene **1** from the palladium-catalyzed reaction of iodobenzene and 2 equiv of diphenylacetylene when PPh_3 and Et_3N are used (eq 1).[3] Dyker reversed the ratio of the reactants but added *n*-Bu_4NBr and K_2CO_3 as base instead and observed a totally new product, the substituted phenanthrene **2** (eq 2).[4] Cacchi has employed the same organic substrates in the presence of a formate salt and obtained triphenylethylene (**3**) (eq 3).[5]



With our own ongoing interests in palladium annulation chemistry,[1e−g] we had reason to reinvestigate the reaction of iodobenzene and diphenylacetylene. Employing our more-or-less standard palladium reaction conditions with NaOAc as the base, an unusual 1:1 adduct, 9-benzylidene-9*H*-fluorene (**4**), has been observed (eq 4).[6] This result encouraged us to further investigate this unusual reaction. Herein, we wish to report our "optimal"

(1) (a) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081. (b) Tsuji, J. *Palladium Reagents and Catalysts*; John Wiley & Sons: New York, 1996. (c) Pfeffer, M. *Recl. Trav. Chim. Pays-Bas* **1990**, *109*, 567. (d) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635. (e) Larock, R. C. Palladium-Catalyzed Annulation. *J. Organomet. Chem.* **1999**, *576*, 111. (f) Larock, R. C. Palladium-Catalyzed Annulation. In *Perspectives in Organopalladium Chemistry for the XXI Century*; Tsuji, J., Ed.; Elsevier Press: Lausanne, Switzerland, 1999. (g) Larock, R. C. Palladium-Catalyzed Annulation. *Pure Appl. Chem.* **1999**, *71*, 1435.

(2) (a) Trost, B. M.; Dumas, J. *Tetrahedron Lett.* **1993**, *34*, 19. (b) Zhang, Y.; Wu, G.; Angel, G.; Negishi, E. *J. Am. Chem. Soc.* **1990**, *112*, 8590. (c) Grigg, R.; Loganathan, V.; Sridharan, V. *Tetrahedron Lett.* **1996**, *37*, 3399. (d) Zhang, Y.; Negishi, E. *J. Am. Chem. Soc.* **1989**, *111*, 3454. (e) Lee, G. C. M.; Tobias, B.; Holmes, J. M.; Harcourt, D. A.; Garst, M. E. *J. Am. Chem. Soc.* **1990**, *112*, 9330. (f) Silverberg, L. J.; Wu, G.; Rheingold, A. L.; Heck, R. F. *J. Organomet. Chem.* **1991**, *409*, 411.

(3) Wu, G.; Rheingold, A. L.; Geib, S. J.; Heck, R. F. *Organometallics* **1987**, *6*, 1941.

(4) Dyker, G.; Kellner, A. *Tetrahedron Lett.* **1994**, *35*, 7633.

(5) Cacchi, S.; Felici, M.; Pietroni, B. *Tetrahedron Lett.* **1984**, *25*, 3137.

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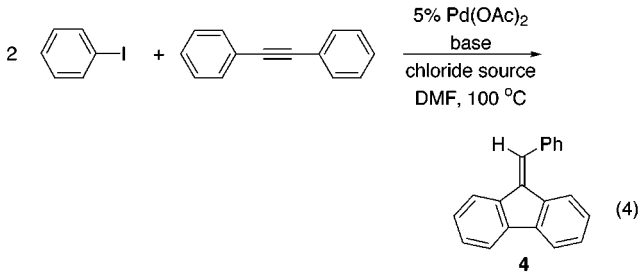


(4)

4

reaction conditions for this reaction and our efforts to extend this reaction to a variety of aryl iodides and 1-aryl-1-alkynes.

Results and Discussion

Our original reaction conditions employing NaOAc as the base for the reaction shown in eq 4 afforded a 23% yield of 9-benzylidene-9*H*-fluorene (**4**) (Table 1, entry 1). Obviously, the reaction conditions needed to be optimized before further testing the scope and limitations of the reaction. The effect of various bases, the chloride source, and the ligand (PPh_3) were therefore examined. The results are summarized in Table 1.

As indicated in eq 4, the formation of product **4** is the result of a 1:1 adduct of iodobenzene and diphenylacetylene; therefore, only 1 equiv of diphenylacetylene is actually required in the reaction. Indeed, we have found that the yield of the reaction was actually improved when only 1 equiv of diphenylacetylene was employed in the reaction (compare entries 1 and 2 of Table 1).

In an attempt to further improve the yield of the reaction, we examined the use of PPh_3 in the reaction. The addition of 10 mol % PPh_3, which presumably behaves as a ligand for palladium, showed a significant effect on the reaction. Good yields were obtained when the reactions employed only catalytic amounts of PPh_3 (Table 1, entries 4, 5, and 7).

An appropriate chloride source is also important for the reaction. Without chloride present, the reaction afforded only a 37% yield of **4** (Table 1, entry 5). The addition of LiCl improved the yield to 41% (Table 1, entry 4). The use of *n*-Bu_4NCl as the chloride source further improved the yield to 62% (Table 1, entry 7). Different amounts of *n*-Bu_4NCl were employed in the reaction, but no significant difference in the yield has been observed (Table 1, entries 7−9). One equivalent of *n*-Bu_4NCl appears to be enough.

Like much of our previous palladium annulation chemistry,[1e−g] the choice of base is critical to the reaction. Without any base, no reaction is observed (Table 1, entry 6). Thus, a number of bases have been examined in the reaction. When NaOAc was used as the base, compound **4** was the only product obtained from the reaction (Table 1, entries 1−9). However, a mixture of products **2** and **4** was obtained when other bases were employed (Table 1, entries 10−12). The base KOAc favored formation of the fluorene (Table 1, entry 10), while Na_2CO_3 gave a 3:2 mixture favoring the phenanthrene **2** (Table 1, entry 11). Using conditions similar to Dyker's[4] (only replacing *n*-Bu_4NBr with *n*-Bu_4NCl), the reaction afforded **2** as the major product in 71% yield (Table 1, entry 12). This result is dramatically different from that observed when NaOAc was employed as the base in the reaction (Table 1, entry 7).

Table 1. Palladium-Catalyzed Reaction of Iodobenzene and Diphenylacetylene (Eq 4)[a]

entry	alkyne (equiv)	base (equiv)	chloride source (equiv)	PPh_3 (%)	time (h)	% isolated yield **2**	% isolated yield **4**
1	2	NaOAc (2)	LiCl (1)		17		23
2	1	NaOAc (2)	LiCl (1)		30		37
3	1	NaOAc (2)	*n*-Bu_4NCl (1)		24		44
4	1	NaOAc (2)	LiCl (1)	10	8		41
5	1	NaOAc (2)		10	24		37
6	1		*n*-Bu_4NCl (1)	10	24	NR[b]	
7	1	NaOAc (2)	*n*-Bu_4NCl (1)	10	24		62
8	1	NaOAc (2)	*n*-Bu_4NCl (2)	10	24		61
9	1	NaOAc (2)	*n*-Bu_4NCl (3)	10	24		57
10	1	KOAc (2)	*n*-Bu_4NCl (1)	10	24	12	42
11	1	Na_2CO_3 (2)	*n*-Bu_4NCl (1)	10	48	30	20
12	1	K_2CO_3 (2)	*n*-Bu_4NCl (1)	10	48	71	8

[a] All reactions were run in the presence of 5 mol % $Pd(OAc)_2$ in DMF at 100 °C. [b] No reaction.

This investigation led to the following standard reaction procedure. One equivalent of aryl halide, 1 equiv of alkyne, 5 mol % of $Pd(OAc)_2$, 10 mol % of PPh_3, 2 equiv of NaOAc, and 1 equiv of *n*-Bu_4NCl were heated in DMF at 100 °C.

With this standard procedure in hand, we next explored the scope and limitations of the reaction by first examining other aryl alkynes. As shown in Table 2, entries 1−3, the alkynes that have been successful in this reaction all have an aryl group on one end of the carbon−carbon triple bond and another sterically hindered group, such as an aryl, *tert*-butyl, or similar group, on the other end (Table 2, entries 1−3). Thus, 1-phenyl-3,3-dimethyl-1-butyne (Table 2, entry 2) and 4-phenyl-2-methyl-3-butyn-1-ol (Table 2, entry 3) gave 9-alkylidene-9*H*-fluorenes in yields similar to the parent system (Table 2, entry 1). 1-Phenylpropyne gave a messy reaction with little or no fluorene evident. The structural features required of the alkyne can be rationalized by the mechanism proposed for the reaction, which will be discussed later.

The product of the reaction of iodobenzene and phenyl(trimethylsilyl)acetylene was quite unexpected (Table 2, entry 4). Fluorene **4** was obtained in 66% yield. There appear to be two different paths by which the product **4** may be formed. As shown in Scheme 1, the reaction may involve formation of the anticipated product **17**, followed by desilylation and a subsequent Heck reaction with iodobenzene to form the final product **4**. An alternative route to compound **4** starts with the desilylation of phenyl(trimethylsilyl)acetylene, followed by cross-coupling with iodobenzene (Scheme 2). The resultant diphenylacetylene can then react in the usual fashion with iodobenzene to give the final product **4**.

To further examine the scope of this reaction, a variety of aryl iodides have been employed in the reaction. The results are summarized in Table 2, entries 5−14. Various functionally substituted aryl iodides generally work as well as iodobenzene. The functional group can be either an electron-donating or an electron-withdrawing group. Aryl iodides bearing an electron-withdrawing substituent in the ortho position, such as 2-iodobenzotrifluoride (Table 2, entry 5) and 2-iodobenzonitrile (Table 2, entry 6), afforded the expected *E* isomers in better yields than iodobenzene, indicating that steric hindrance is not a major factor in this reaction. The substrate 1-*tert*-butyl-

(6) For a preliminary communication, see: Tian, Q.; Larock, R. C. *Org. Lett.* **2000**, *2*, 3329.

Table 2. Palladium-Catalyzed Reaction of Aryl Iodides and 1-Aryl-1-alkynes[a]

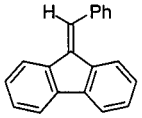
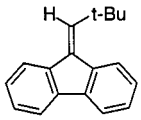
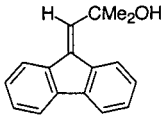
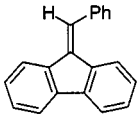
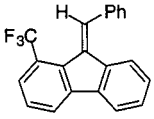
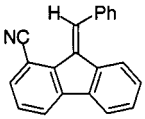
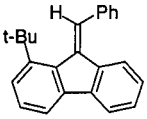
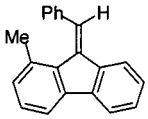
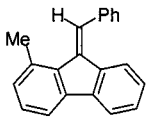
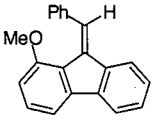
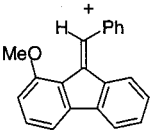
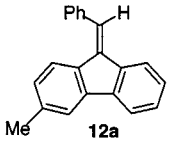
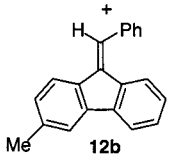
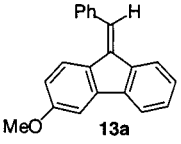
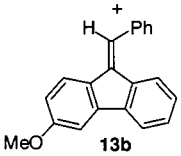
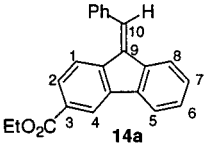
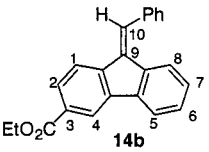
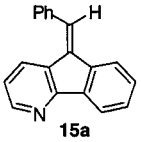
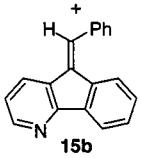
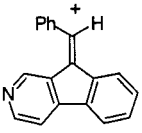
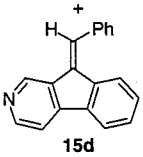
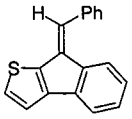
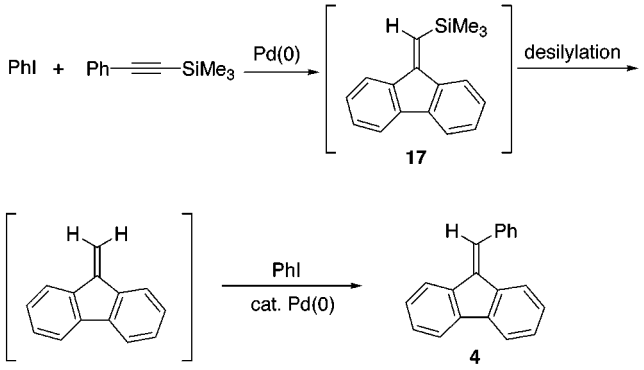
entry	aryl iodide	alkyne	time (h)	product(s)	% isolated yield (*Z*:*E*)
1	C_6H_5I	Ph—≡—Ph	12	 **4**	62
2	–	Ph—≡—t-Bu	20	 **5**	61
3	–	Ph—≡—CMe_2OH	20	 **6**	55
4	–	Ph—≡—$SiMe_3$	20	 **4**	66[b]
5	*o*-$F_3CC_6H_4I$	Ph—≡—Ph	48	 **7**	75
6	*o*-NCC_6H_4I	–	10	 **8**	63
7	*o*-*t*-BuC_6H_4I	–	96	 **9**	35
8	*o*-MeC_6H_4I	–	12	 **10a** +  **10b**	61 (40 : 60)
9	*o*-$MeOC_6H_4I$	–	158	 **11a** +  **11b**	25 (42 : 58)

Table 2 (Continued)

entry	aryl iodide	alkyne	time (h)	product(s)	% isolated yield (*Z*:*E*)
10	*p*-MeC_6H_4I	–	20	 **12a** +  **12b**	60 (40 : 60)
11	*p*-$MeOC_6H_4I$	–	18	 **13a** +  **13b**	45 (40 : 60)
12	*p*-$EtO_2CC_6H_4I$	–	15	 **14a** +  **14b**	45 (40 : 60)
13		–	48	 **15a** +  **15b** +  **15c** +  **15d**	76 (19 : 14 40 : 27)
14		–	19		24

[a] Reaction conditions: 5 mol % $Pd(OAc)_2$, 10 mol % PPh_3, 1 equiv of alkyne, 2 equiv of NaOAc, and 1 equiv of *n*-Bu_4NCl in DMF at 100 °C. [a] The yield is based upon the consumption of iodobenzene.

Scheme 1



Scheme 2

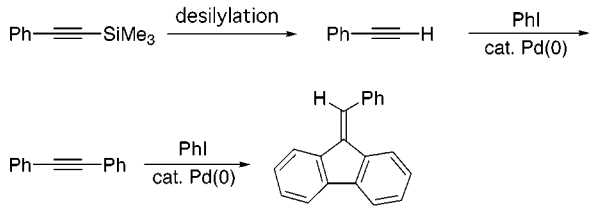


Table 3. Effects of Temperature and Reaction Time on the Reaction of Ethyl 4-Iodobenzoate and Diphenylacetylene[a]

entry	*T* (°C)	reaction time (h)	% isolated yield[b]	ratio **14a**/**14b**
1	80	4	5	21:79
2	80	8	10	30:70
3	80	16	20	37:63
4	80	48	33	42:58
5	100	4	10	32:68
6	100	8	30	40:60
7	100	16	44	42:58
8	100	32	44	39:61
9	100	72	44	40:60

[a] All reactions were run in the presence of 5 mol % of $Pd(OAc)_2$, 10 mol % of PPh_3, 2 equiv of NaOAc, and 1 equiv of *n*-Bu_4NCl in DMF at 100 °C. [b] The yield was determined by ^1H NMR spectroscopy using undecane as an internal standard.

2-iodobenzene with a highly hindered electron-donating group also afforded a single stereoisomer, but in a considerably lower yield presumably due to the substantial steric hindrance present in the alkyne and the product (Table 2, entry 7). However, other substrates with electron-donating groups, such as 2-iodotoluene (Table 2, entry 8) and 2-iodoanisole (Table 2, entry 9), produced mixtures of *Z* and *E* isomers. Furthermore, aryl iodides bearing either electron-donating or electron-withdrawing groups in the para position also afforded mixtures of *Z* and *E* isomers (Table 2, entries 10−12). In all systems where *Z* and *E* stereoisomers have been produced, the ratio has been approximately 40:60.

The structural assignment of the *Z* and *E* isomers is based on 1D and 2D NMR spectroscopy. 2D NOESY spectroscopy[7] is a powerful tool to identify the structure of these isomers. For example, the 2D NOESY spectrum of **9** (Table 2, entry 7) clearly shows a cross-peak between the protons of the *tert*-butyl group and the vinylic proton H-10. This confirms that **9** exists in the *E* configuration. In some cases, the 1D ^1H NMR spectra provide sufficient information to assign the stereochemistry. For example, the ^1H NMR spectra of compounds **14a** and **14b** (Table 2, entry 12) exhibit doublets for proton H-4 at 8.37 and 8.39 ppm. In the *Z* isomer **14a**, the phenyl ring present on the vinylic carbon C-10 can exhibit an anisotropic effect[8] on the ring that bears the ester group. This interaction may shield the protons on that ring, and as a result, the chemical shift of proton H-4 on that ring should appear at higher field. No such anisotropic interaction can exist in the *E* isomer **14b**, and the signal for H-4 should appear at lower field. Therefore, the configurations of **14a** and **14b** are tentatively assigned as *Z* and *E*, respectively.

The reactions of 1-*tert*-butyl-2-iodobenzene (Table 2, entry 7) and 2-iodoanisole (Table 2, entry 9) deserve special mention here. Dyker has reported that 1-*tert*-butyl-2-iodobenzene alone reacts with a palladium catalyst to give a strained 1,2-dihydrocyclobutabenzene derivative,[9] while 2-iodoanisole produces a substituted dibenzopyran under the same reaction conditions.[10] Under our reaction conditions, we only observe fluorene products (Table 2, entries 7 and 9). Clearly, addition of an alkyne completely changes the nature of the reaction. As shown in entry 9 (Table 2), the reaction of 2-iodoanisole did not afford a good yield even after a long reaction time (158 h). GC−MS analysis of the reaction indicated that a significant amount of the 2-iodoanisole still had not participated in the reaction. On the other hand, 4-iodoanisole reacted with diphenylacetylene much faster and also gave a much better yield (Table 2, entry 11).

Heteroaromatic iodides have also been examined in the reaction. The reaction of 3-iodopyridine afforded a good yield of a mixture of regioisomers and *Z*/*E* isomers (Table 2, entry 13). All of these isomers are known compounds, and the structural assignments are thus based on the literature.[11] On the other hand, only one isomer **16** was obtained from the reaction of 2-iodothiophene, although the yield was low (Table 2, entry 14).

As one can see from Table 2, in many cases, the *E* isomers are the sole or predominant products in the reaction. However, mixtures are often obtained. Previous literature has shown that these types of fluorenes undergo interconversions when heated to 140 °C in Decalin.[11a] We, therefore, suspected that the formation of isomers is due to thermal isomerization of the initially formed *E* isomer, which is expected by our mechanism to be produced in the reaction. This has been proven to be true by the following experiments.

The *Z* and *E* isomers **14a** and **14b** from the reaction of ethyl 4-iodobenzoate and diphenylacetylene have been separated by preparative TLC (Table 2, entry 12). When submitted to the standard palladium reaction conditions, each pure isomer **14a** and **14b** gave the same 40:60 mixture of isomers **14a** and **14b** as that obtained from the reaction of ethyl 4-iodobenzoate and diphenylacetylene. However, without $Pd(OAc)_2$ present, simple heating of the *E* isomer **14b** for the same period of time

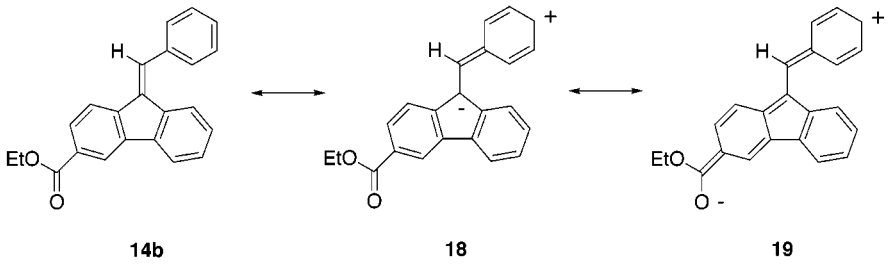
(7) Jeener, J.; Meier, B. H.; Bachmann, P.; Ernst, R. R. *J. Chem. Phys.* **1979**, *71*, 4546.

(8) Günther, H. *NMR Spectroscopy*, 2nd ed.; John Wiley & Sons: New York, 1995; pp 85−93.

(9) Dyker, G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 103.

(10) Dyker, G. *Chem. Ber.* **1994**, *127*, 739.

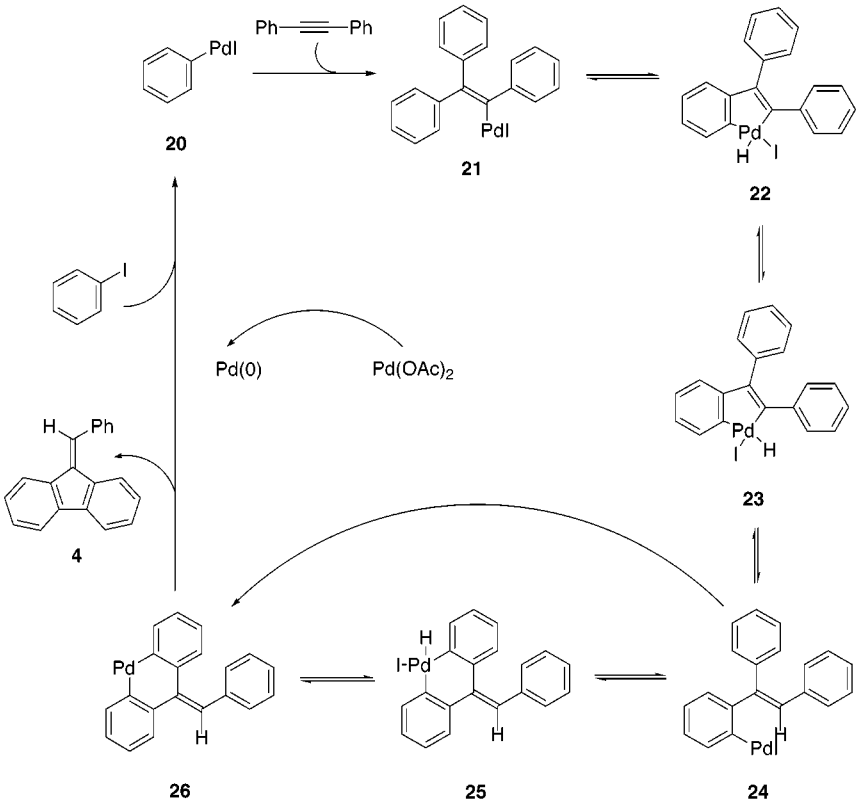
(11) (a) Prostakov, N. S.; Moiz, S. S.; Soldatenkov, A. T.; Zvolinskii, V. P.; Cherenkova, G. I. *Khim. Geterotsikl. Soedin.* **1971**, 1398. (b) Prostakov, N. S.; Varlamov, A. V.; Anismov, B. N.; Mikhailova, N. M.; Vasil'ev, G. A.; Zakharov, P. I.; Galiullin, M. A. *Khim. Geterotsikl. Soedin.* **1978**, 1234.



14b **18** **19**

Figure 1. Resonance structures for the *E* isomer **14b**.

Scheme 3



in DMF generated a 12:88 mixture of isomers **14a** and **14b**. This indicates that $Pd(OAc)_2$ or perhaps reduced Pd(0) may play an important role in the isomerization process and that it is not a simple thermal isomerization.

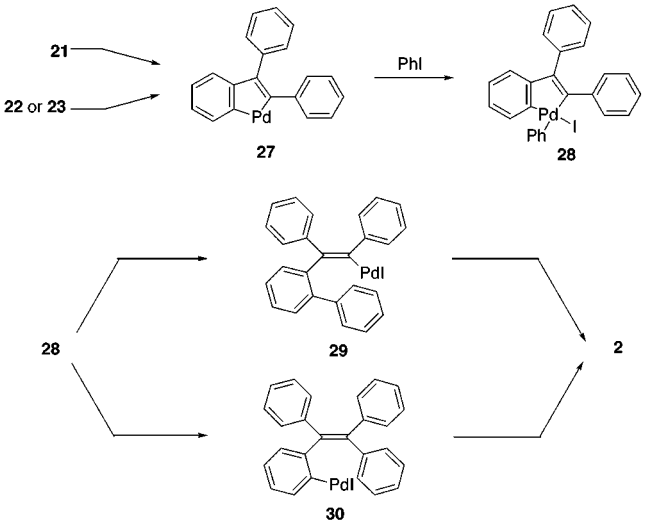
We have also examined the effects of temperature and reaction time on the isomerization process. From Table 3, one can see that different ratios were observed at different reaction times. At the beginning of the reaction, the percent of the *E* isomer **14b** in the mixture was relatively high, presumably because there has been insufficient time to effect significant isomerization. After a period of time (16 h for the reaction at 80 °C or 8 h for the reaction at 100 °C), the ratio of **14a** to **14b** levels off at approximately 40:60 and little further isomerization is observed (Table 3, entries 7−9). We have also found that the actual temperature is very important for the isomerization process. Higher temperatures (100 °C) accelerate the process. After the same period of time (4 h), the reaction at the higher temperature (100 °C) afforded a higher percentage of isomer **14a** in the mixture than that at the lower temperature (80 °C) (compare entries 1 and 5 of Table 3). It appears to take somewhat more than 16 h at 80 °C or approximately 8 h at 100 °C for this isomerization to reach equilibrium.

The mechanism of the isomerization process about the exocyclic double bond in the fluorene system has not been fully elucidated. However, examination of the resonance structures for the *E* isomer **14b** reveals particularly favorable resonance structures **18** and **19** (Figure 1). In resonance structure **18**, the two π-electrons of the exocyclic double bond are shifted to the five-membered ring of the fluorene ring system to give a stable 6π-electronic arrangement, which is similar to that of fulvene.[12] Resonance structure **19** is also particularly favorable due to the electron-withdrawing effect of the ester group. We suggest that, due to the resonance contributions of **18** and **19**, the exocyclic double bond may be of low enough energy to allow thermal isomerization to the *Z* isomer **14b**. We suspect that the Pd(0) catalyst may also form an olefin complex with this exocyclic double bond further weakening the double bond and thus accelerating the isomerization process.

Based on the structure of the products from this reaction (Table 2) and our present understanding of organopalladium chemistry, especially the active role of

(12) Lo, D. H.; Whitehead, M. A. *Tetrahedron* **1969**, *25*, 2615. (b) Griffiths, J.; Lockwood, M. *J. Chem. Soc., Perkin Trans. 1* **1976**, 48.

Scheme 4

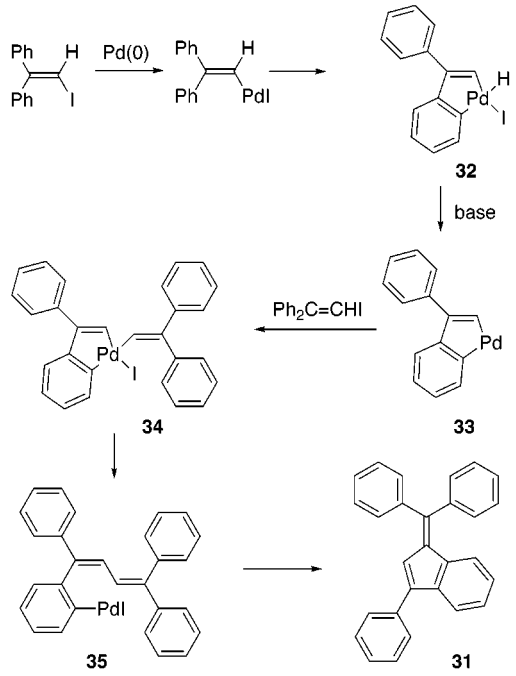


Pd(IV) as an intermediate in organopalladium chemistry,[13] we propose the following mechanism for this reaction (Scheme 3).

The mechanism appears to involve the formation, transformation, and reductive elimination of Pd(IV) intermediates. The oxidative addition of Pd(0) to iodobenzene produces an arylpalladium intermediate **20**, which rapidly inserts the alkyne to produce a vinylic palladium(II) species **21**. It is obvious why the alkyne must have an aryl group at one end of the carbon−carbon triple bond and an even more hindered group on the other end, since previous work on the carbopalladation of alkynes has indicated that this process is controlled by steric effects with the carbon moiety adding to the less hindered end of the triple bond.[1c,e−g] Intermediate **21** in turn apparently undergoes oxidative addition to the neighboring aryl C−H bond to generate a Pd(IV) intermediate **22**, which isomerizes to afford a new Pd(IV) intermediate **23**. Reductive elimination of **23** leads to arylpalladium(II) intermediate **24**. It is not clear if either the former or the latter process is reversible. Intermediate **24** can further cyclize to the fluorene product **4** by either of two possible mechanisms. It can undergo single bond rotation and oxidative addition to the neighboring phenyl ring to afford new organopalladium(IV) intermediate **25**. Two consecutive reductive eliminations finally afford the product **4** and HI and regenerate the Pd(0) catalyst. Alternatively, arylpalladium intermediate **24** may undergo electrophilic aromatic substitution on the neighboring arene to directly produce **26**, which affords the final product and Pd(0) by simple reductive elimination.

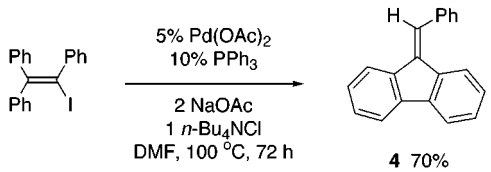
The profound effect that the choice of base has on the products formed in this process (Table 1, entries 9−12) raises the question as to how formation of the phenanthrene **2** and flourene **4** are related mechanistically. It appears that the phenanthrene **2** arises by either cyclization of **21** to palladacycle **27** or reductive elimination of HI from intermediates **22** or **23** to produce the five-membered ring palladacycle **27**, which in turn undergoes oxidation addition by another molecule of iodobenzene,

Scheme 5



producing a palladium(IV) intermediate **28** (Scheme 4). This intermediate can undergo reductive elimination to either vinylic palladium(II) species **29** or arylpalladium(II) intermediate **30**, either of which can further cyclize by oxidative addition or electrophilic aromatic substitution pathways similar to those shown for the formation of the fluorene in Scheme 3. Apparently, the presence of K_2CO_3 favors formation of palladacycle **27** and the use of NaOAc favors the complete migration of palladium from the vinylic position to the aromatic species **24**. Indeed, Dyker[14] has proposed the formation of an intermediate like **27** by oxidative addition of vinylic halides and removal of HI, but he has not previously observed the apparent migration of palladium from a vinylic position to an aryl position as required for formation of the fluorene.

As shown in the proposed mechanism in Scheme 3, vinylic palladium intermediate **21** is a proposed intermediate in the formation of the fluorene **4**. Since this intermediate should be easily generated by the oxidative addition of Pd(0) to the corresponding vinylic iodide, 1,2,2-triphenyl-1-iodoethylene, we might expect to observe the formation of product **4** from this vinylic iodide under our usual reaction conditions. Indeed, this turned out to be true. The fluorene **4** was obtained from the reaction in 70% yield (eq 5).

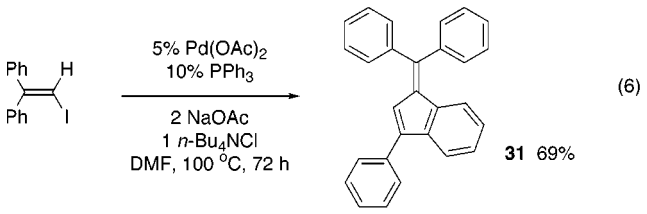


(5)

Encouraged by this result, we have also examined the analogous reaction of 1-iodo-2,2-diphenylethylene (eq 6).

(13) (a) Canty, A. J. *Acc. Chem. Res.* **1992**, *25*, 83 and references therein. (b) Catellani, M.; Frignani, F.; Rangoni, A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 119. (c) Catellani, M.; Chiusoli, G. P.; Costa, M. *Pure Appl. Chem.* **1990**, *62*, 623.

(14) (a) Dyker, G.; Nerenz, F.; Siemsen, P.; Bubenitschek, P.; Jones, P. G. *Chem. Ber.* **1996**, *129*, 1265. (b) Dyker, G.; Siemsen, P.; Sostman, S.; Wiegand, A.; Dix, I.; Jones, P. G. *Chem. Ber.* **1997**, *130*, 261.



(6)

To our surprise, this reaction provided the annulated pentafulvene **31** in 69% yield. This is the same product that Dyker obtained from the same starting material under similar reaction conditions.[14a] This reaction presumably proceeds as shown in Scheme 5 via key intermediates **32** and **33**, instead of forming the anticipated fluorene product. Intermediate **32** apparently undergoes reductive elimination of HI to form **33** faster than rearrangement to the arylpalladium species required to form the fluorene. Subsequent oxidative addition of the vinylic halide $Ph_2C{=}CHI$ to **33** eventually leads to the fulvene product **31**. The intervening steps may involve reductive elimination to an arylpalladium intermediate **35** as shown or reductive elimination to a vinylic palladium intermediate (not shown). Subsequent intramolecular Heck coupling of either species would provide the fulvene **31**.

Conclusion

The Pd-catalyzed coupling of aryl or heterocyclic iodides and 1-aryl-1-alkynes in the presence of NaOAc provides an efficient, general synthetic route to 9-alkylidene-9*H*-fluorenes. The process proceeds by an unusual cascade migration/coupling process involving the novel rearrangement of a vinylic palladium intermediate to an arylpalladium species. On the basis of the proposed mechanism, the synthesis of a 9-alkylidene-9*H*-fluorene has also been achieved starting with a vinylic iodide.

Experimental Section

General Methods. All ^1H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz, respectively. Thin-layer chromatography (TLC) was performed using commercially prepared 60 mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) or a basic $KMnO_4$ solution (3 g of $KMnO_4$ + 20 g of K_2CO_3 + 5 mL of NaOH (5%) + 300 mL of H_2O).

Reagents. All reagents were used directly as obtained commercially unless otherwise noted. Anhydrous forms of NaOAc, LiCl, DMF, CH_2Cl_2, hexanes, and ethyl acetate were purchased from Fisher Scientific. $Pd(OAc)_2$ was donated by Johnson Matthey, Inc., and Kawaken Fine Chemicals Co., Ltd. Iodobenzene, 2-iodobenzotrifluoride, 2-iodotoluene, 2-iodoanisole, 4-iodoanisole, 2-iodothiophene, triphenylphosphine, phenyl(trimethylsilyl)acetylene, and diphenylacetylene were obtained from Aldrich Chemical Co., Inc. Ethyl 4-iodobenzoate and *n*-Bu_4NCl were purchased from Lancaster Synthesis, Inc. 2-Iodobenzonitrile was purchased from Trans World Chemicals, Inc. 4-Phenyl-2-methyl-3-butyn-2-ol was obtained from Farchan Scientific Co. 3,3-Dimethyl-1-phenyl-1-butyne,[15] 3-iodopyridine,[16] 1-*tert*.-butyl-2-iodobenzene,[17] 1-iodo-1,2,2-triphenylethylene,[18] and 1-iodo-2,2-diphenylethylene[19] were prepared according to previous literature procedures.

General Procedure for the Palladium-Catalyzed Reaction of Aryl Iodides and Internal Alkynes. Palladium acetate (2.8 mg, 0.0125 mmol), PPh_3 (6.7 mg, 0.025 mmol), NaOAc (42 mg, 0.50 mmol), *n*-Bu_4NCl (70 mg, 0.25 mmol), the aryl iodide (0.25 mmol), the alkyne (0.25 mmol), and 5 mL of DMF (or appropriate modifications) were placed in a 4 dram vial, which was heated in an oil bath at 100 °C for the period of time indicated in Tables 1−3. The reaction mixture was cooled, diluted with ether, washed with saturated NH_4Cl, dried over anhydrous $MgSO_4$, and filtered. The solvent was evaporated under reduced pressure, and the product was isolated by chromatography or preparative TLC. The following compound is representative of those prepared by this procedure. All other fluorenes are reported in the Supporting Information.

9-Benzylidene-9*H*-fluorene (4) (Table 2, Entry 1). Obtained as a white solid in 62% yield after purification by column chromatography (hexanes): mp 73−74 °C (lit.[20] mp 73−74 °C); ^1H NMR ($CDCl_3$) δ 7.06 (dt, J = 1.2, 7.5 Hz, 1 H), 7.29−7.50 (m, 6 H), 7.54−7.61 (m, 3 H), 7.70−7.74 (m, 3 H), 7.78−7.82 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 119.6, 119.7, 120.2, 124.4, 126.7, 127.0, 127.3, 128.1, 128.2, 128.6, 129.3, 136.5, 136.6, 136.9, 139.2, 139.5, 141.3 (one sp^2 C missing due to overlap); IR ($CDCl_3$) 3053, 1490 cm^{-1}; HRMS *m*/*z* 254.1088 (calcd for $C_{20}H_{14}$ 254.1096).

The following compounds were prepared using the general procedure reported earlier, except that no alkynes were employed.

9-Benzylidene-9*H*-fluorene (4) (Eq 5). Obtained as a white solid in 70% yield from the reaction of 1-iodo-1,2,2-triphenylethylene[18] after purification by column chromatography (hexanes). The melting point and ^1H and ^{13}C NMR spectra were identical to those in the literature.[20]

Compound 31 (Eq 6). Obtained as an orange solid in 69% yield from the reaction of 1-iodo-2,2-diphenylethylene[19] after purification by column chromatography (hexanes). The melting point and ^1H and ^{13}C NMR spectra match those in the literature.[14a]

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Supporting Information Available: Full characterization of compounds **5**−**16** and ^1H and ^{13}C NMR spectra for compounds **8**, **11a**,**b**, **12a**,**b**, **16**, and **31** (the ^1H and ^{13}C NMR spectra for the other major products can be found in the Supporting Information for the communication[6]). This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) Larock, R. C.; Doty, M. J.; Cacchi, S. *J. Org. Chem*. **1993**, *58*, 4579.
(16) Wang, Y. Ph.D. Dissertation, Iowa State University, 1995.
(17) Lesslie, M. S.; Mayer, U. J. H. *J. Chem. Soc.* **1961**, 611.
(18) Miller, L. L.; Kaufman, D. A. *J. Am. Chem. Soc.* **1968**, *90*, 7282.
(19) Curtin, D. Y.; Flynn, E. W. *J. Am. Chem. Soc.* **1959**, *81*, 4714.
(20) Sprinzak, Y. *J. Am. Chem. Soc.* **1956**, *78*, 466.
(21) Miller, R. B.; McGarvey, G. *Synth. Commun.* **1978**, *8*, 291.