

A Palladium-Catalyzed Intramolecular Arene-Triflate Coupling for the Synthesis of Fluoranthenes and Benzofluoranthenes

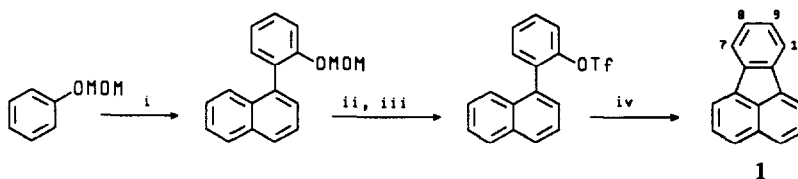
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Abstract: A method for the preparation of fluoranthenes and benzofluoranthenes from aryl bromides and aryl methoxymethyl ethers is described. The key step in this synthesis is an intramolecular triflate-arene coupling mediated by bis(triphenylphosphine)palladium(II)chloride. Fluoranthene, benzo[a]fluoranthene, benzo[b]fluoranthene, and indeno[1,2,3-cd]pyrene were prepared in yields of 84-91%. The regiospecific synthesis of substituted benzofluoranthenes was demonstrated by the preparation of 6-fluorobenzo[b]fluoranthene (72% yield) and 5- and 6-methoxybenzo[b]fluoranthene in yields of 73% and 62% respectively when the reaction was conducted in the presence of excess triphenylphosphine.

Several nonalternant polycyclic aromatic hydrocarbons including fluoranthene **1**, the isomeric benzofluoranthenes, and indeno[1,2,3-cd]pyrene are common environmental pollutants which can pose a significant human health risk.¹ While a number of methods for the synthesis of these compounds are known,² those involving formation of the five-membered ring suffer from low yields, inability to prepare substituted derivatives, and incompatibility with many functional groups.^{2c,d,4,i} As a result the efficient preparation of analogs substituted in the biologically important benzo ring (eg. positions 7-10 in **1**) is problematic. We report here a new high-yielding synthesis for these compounds in which a five-membered ring is formed by cyclization of a 1-(2-trifluoromethanesulfonyloxyphenyl)naphthalene (or benzannulated naphthalene) in the presence of a palladium catalyst (**Scheme 1**). While palladium-catalyzed coupling reactions of aromatic triflates with arylboronic acids,³ aryltin,⁴ and arylzinc derivatives⁵ have received much attention recently, there have been no reports detailing the intramolecular coupling of aryltriflates to unsubstituted aromatic carbons.⁶



Scheme 1. Reagents and conditions: (i) n-BuLi, ether, R.T., 3h; MgBr₂; 1-bromonaphthalene, Ni(dppe)Cl₂, 2:1 ether/THF, -78 °C then reflux, 94%. (ii) 4N HCl, THF, reflux, 2 h; 90%. (iii) Tf₂O, 2,6-lutidine, CH₂Cl₂, -30 °C, 1 h; 85%. (iv) Pd(PPh₃)₂Cl₂, LiCl, DBU, DMF, 140 °C, 6 h; 89%.

Table 1. Preparation of Fluoranthenes and Benzofluoranthenes by Intramolecular Triflate-Arene Coupling.

MOM-Ether	Aryl Bromide	Product of Ni(dppe)Cl ₂ Coupling ^a (% Yield)	Product of Pd(PPh ₃) ₂ Cl ₂ Coupling (% Yield)
"			
"			
"			
	"		
	"		
	"		

^a Product resulting from *ortho*-lithiation of the MOM-ether, transmetalation with MgBr₂, and coupling with the aryl bromide.

^b Without added PPh₃.

^c With the addition of 4 equivalents PPh₃.

The triflate substrates for these reactions were prepared in three steps starting from methoxymethyl (MOM) phenyl ethers and aryl bromides. *Ortho*-lithiation of the MOM ether^{7,8} followed by transmetalation with MgBr_2 afforded a Grignard reagent which was coupled in generally high yield with an aryl bromide in the presence of 1,2-diphenylphosphinoethanenickel(II)chloride $[\text{Ni}(\text{dppe})\text{Cl}_2]$.^{9,10} Hydrolysis of the MOM ether and treatment with triflic anhydride gave the triflates in good yields.¹¹

Treatment of the triflate of 1-(2-hydroxyphenyl)naphthalene with bis(triphenylphosphine)-palladium(II)chloride $[\text{Pd}(\text{PPh}_3)_2\text{Cl}_2]$ (0.1 equiv) in the presence of LiCl (3 equiv) and DBU (1.2 equiv) in DMF at 135-140 °C for 6 h afforded fluoranthene **1** in 89% yield.¹² Tetrakis(triphenylphosphine)palladium(0) was less effective at catalyzing the reaction. No identifiable products were isolated when the reaction was conducted in the absence of a base. The yields for benzo[a]fluoranthene **2**, benzo[b]fluoranthene **4**, and indeno[1,2,3-cd]pyrene **3** were comparable (84-91%) (Table 1).

Application of these reaction conditions for the preparation of compounds bearing substituents in the benzo-ring was also investigated. 4-Fluorophenyl MOM ether was lithiated at the 2-position and coupled with 9-bromophenanthrene followed by conversion to the triflate using the general procedures described above. Cyclization employing the standard conditions described above afforded 6-fluorobenzo[b]fluoranthene **5** in 72% yield. Coupling of 4-methoxyphenyl MOM ether with 9-bromophenanthrene and subsequent conversion to the triflate occurred in good overall yield. However, the palladium-catalyzed intramolecular coupling of this triflate gave 6-methoxybenzo[b]fluoranthene **6** in very low yield (<5%) along with recovered starting material. Apparently the electron-donating properties of the *p*-methoxy group was responsible for this dramatic decrease in yield since oxidative-addition of aryl halides to organopalladium species is known to be accelerated by electron-withdrawing groups on the aromatic ring.¹³ Placement of the methoxy group *meta* with respect to the triflate group¹⁴ had little effect on the yield of the intramolecular coupling reaction and gave 5-methoxybenzo[b]fluoranthene **7** in less than 5% yield along with recovered starting material. It was thought that addition of an excess of a donor ligand such as triphenylphosphine, might provide a sufficient increase in the electron-density at the metal to allow the oxidative-addition to proceed. This was found to be the case. When these cyclizations were repeated with the incorporation in the reaction mixture of 4 equiv (relative to palladium) of triphenylphosphine, the yields of **6** and **7** increased to 62% and 73% respectively. Triphenylphosphine had little effect on the formation of **1** (90%) and **5** (68%).

In summary, a new versatile and high-yielding reaction sequence for the synthesis of fluoranthenes and benzofluoranthenes from aryl halides and methoxymethyl phenyl ethers has been developed. The key step is an intramolecular $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ catalyzed coupling of an aryl triflate with an unsubstituted aromatic carbon. In difficult cases the yields are enhanced by the addition of excess triphenylphosphine.

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 11. All new compounds gave satisfactory ¹H and ¹³C-NMR spectra and C,H-analyses (±0.4%).
 12. General procedure for the palladium-catalyzed intramolecular coupling reaction: A solution of the triflate (0.15 mmol), Pd(PPh₃)₂Cl₂ (0.015 mmol), LiCl (0.45 mmol), and DBU (0.18 mmol) in DMF (2 mL) was heated under N₂ at 135-140 °C for 6 h. After cooling to RT, H₂O was added and the mixture extracted with EtOAc. The organic layer was dried over Na₂SO₄, concentrated, and purified by flash chromatography on SiO₂ eluting with hexanes to give the hydrocarbon.
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