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Synthesis of Pyrenes by Twofold Hydroarylation of 2,6-Dialkynylbiphenyls

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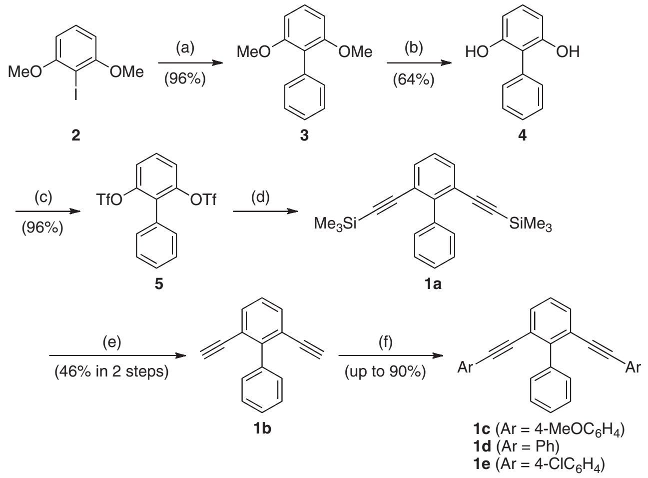
Cationic gold(I) complexes having Buchwald-type biarylphosphines effectively catalyzed twofold hydroarylation of 2,6-dialkynylbiphenyls to construct pyrene skeletons.

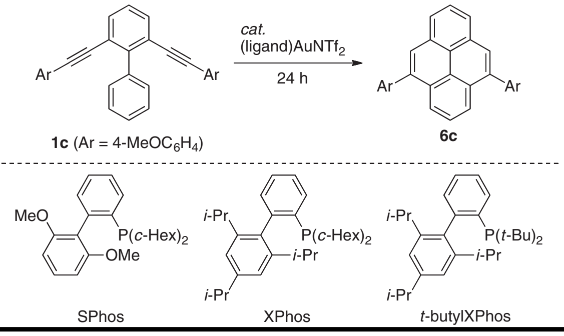
Synthesis of polycyclic aromatic hydrocarbons (PAHs)[1] has been the subject of intensive research because PAHs possess characteristic light-emitting and semiconducting properties.[2] Among them, pyrene derivatives are an important class of compounds that have been used as materials for organic light-emitting diodes[3] and fluorescent probes and sensors.[4] Several established methods are available for the synthesis of 1,3,6,8-substituted[5] and 2,7-substituted pyrenes[6] from pyrene. In contrast, substitution reactions of pyrene at the 4, 5, 9, and 10 positions have been scarcely developed.[7] Pyrene derivatives possessing substituents at these positions are often prepared via indirect routes involving partial reduction[8] and the Diels–Alder reaction[9] of pyrene. Fürstner reported that hydroarylation reaction[10] of 2-alkynylbiphenyls gives phenanthrenes and/or 9-alkylidenefluorenes depending on the catalyst employed.[11] We anticipated that pyrene skeletons could be directly constructed by twofold hydroarylation of dialkynylbiphenyls.[12,13] In this paper, we report that 4,10-disubstituted pyrenes are synthesized by gold(I)-catalyzed twofold hydroarylation of 2,6-dialkynylbiphenyls.

2,6-Dialkynylbiphenyls **1** requisite for twofold hydroarylation were prepared as shown in Scheme 1. Palladium-catalyzed cross-coupling of 2-iodo-1,3-dimethoxybenzene (**2**) with phenylboronic acid gave 2,6-dimethoxybiphenyl (**3**). Demethylation of **3** with BBr_3 afforded biphenyl-2,6-diol (**4**).[14] The two hydroxy groups of **4** were converted to the corresponding triflates, and subsequent palladium-catalyzed cross-coupling with trimethylsilylacetylene provided 2,6-bis[(trimethylsilyl)-ethynyl]biphenyl (**1a**). The trimethylsilyl groups were removed under basic conditions, and the resulting 2,6-diethynylbiphenyl (**1b**) underwent palladium-catalyzed cross-coupling with aryl halides to furnish 2,6-bis(arylethynyl)biphenyls **1c**–**1e** in up to 90% yields.[15]



Scheme 1. Conditions: (a) 1.1 equiv $PhB(OH)_2$, 1 mol % $[Pd_2(dba)_3]\cdot CHCl_3$, 2.4 mol % $[HP(t\text{-}Bu)_3]BF_4$, 3.3 equiv KF, THF, reflux. (b) 2 equiv BBr_3, CH_2Cl_2, −78 °C to rt. (c) 4 equiv Tf_2O, 3 equiv pyridine, CH_2Cl_2, 0 °C to rt. (d) 3 equiv $Me_3SiC{\equiv}CH$, 20 mol % $[PdCl_2(PPh_3)_2]$, 40 mol % CuI, 2 equiv Bu_4NI, 13 equiv Et_3N, DMF, 85 °C. (e) 2.3 equiv K_2CO_3, MeOH, rt. (f) 2 equiv ArI, 6 mol % $[PdCl_2(PPh_3)_2]$, 10 mol % CuI, Et_3N, rt.

Table 1. Hydroarylation of diyne **1c**

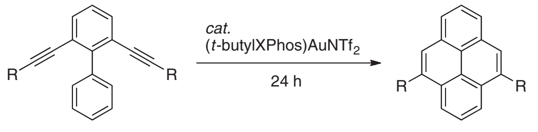


Entry	Gold(I) catalyst		Conditions	Yield[a]/%
	/mol %	Ligand		
1	20	SPhos	*p*-xylene, 150 °C	83
2	20	XPhos	*p*-xylene, 150 °C	83
3	20	*t*-butylXPhos	*p*-xylene, 150 °C	88
4	5	*t*-butylXPhos	DCE, 70 °C	73
5	5	*t*-butylXPhos	DCE, 60 °C	48

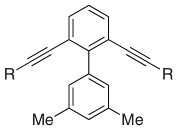
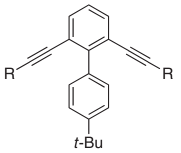
[a] Isolated yield.

2,6-Bis[(4-methoxyphenyl)ethynyl]biphenyl (**1c**) thus obtained was treated with $PtCl_2$ in *p*-xylene at 140 °C.[11] However, no formation of a pyrene derivative was observed, which led us to examine a hydroarylation reaction using gold(I) complexes having Buchwald-type biarylphosphine ligands (Table 1). When diyne **1c** was heated in *p*-xylene in the presence of $(SPhos)AuNTf_2$ (20 mol %) at 150 °C for 24 h, hydroarylation successfully occurred on both sides to afford 4,10-bis(4-methoxyphenyl)pyrene (**6c**) in 83% yield (Entry 1). $(XPhos)AuNTf_2$ worked equally well (Entry 2), and $(t\text{-butylXPhos})AuNTf_2$ gave the best result giving **6c** in 88% yield (Entry 3).[16,17] On the other hand, neutral chlorogold(I) complexes bearing the same biarylphosphine ligands failed to promote the hydroarylation. Both the catalyst loading and the reaction temperature could be reduced by the use of 1,2-dichloroethane (DCE) as the solvent; when the reaction was carried out in DCE at 70 °C with the use of 5 mol %

Table 2. Hydroarylation of **1** catalyzed by (t-butylXPhos)-$AuNTf_2$[a]



1 **6**

<table>
<tr><th>Entry</th><th>1</th><th>R</th><th>6</th><th colspan="2">Yield[b]/%</th></tr>
<tr><th></th><th></th><th></th><th></th><th>A</th><th>B</th></tr>
<tr><td>1</td><td>1f</td><td>
(R = 4-$MeOC_6H_4$)</td><td>6f</td><td>89</td><td>95</td></tr>
<tr><td>2</td><td>1g</td><td>
(R = 4-$MeOC_6H_4$)</td><td>6g</td><td>92</td><td>96</td></tr>
<tr><td>3</td><td>1d</td><td>Ph</td><td>6d</td><td>47[c]</td><td></td></tr>
<tr><td>4</td><td>1e</td><td>4-ClC_6H_4</td><td>6e</td><td>1[d]</td><td>52</td></tr>
<tr><td>5</td><td>1h</td><td>Me</td><td>6h</td><td>70</td><td>86</td></tr>
<tr><td>6</td><td>1b</td><td>H</td><td>6b</td><td>30</td><td>18</td></tr>
<tr><td>7</td><td>1a</td><td>$SiMe_3$</td><td>6b</td><td>16</td><td>42</td></tr>
</table>

[a]Method A: 5 mol % catalyst in DCE at 80 °C. Method B: 20 mol % catalyst in p-xylene at 150 °C. [b]Isolated yield. [c]20 mol % of catalyst was used. [d]A mixture with monohydroarylated phenanthrene (22%).

of (t-butylXPhos)$AuNTf_2$, pyrene **6c** was produced in 73% yield (Entry 4). However, incomplete conversion was observed when the reaction was carried out at 60 °C for 24 h (Entry 5), and no reaction occurred at room temperature.

The twofold hydroarylation was examined with various 2,6-dialkynylbiphenyls **1** in DCE (80 °C) and/or in p-xylene (150 °C) (Table 2). A distinct electronic effect was observed with the hydroarylation of 2,6-bis(arylethynyl)biphenyls. Electron-rich aryl substituents appended to a 2,6-bis[(4-methoxyphenyl)ethynyl]phenyl group accelerated the hydroarylation reaction; the reaction of diynes **1f** and **1g** having additional alkyl substituents on the biphenyl backbone gave high yields of the corresponding pyrenes **6f** and **6g**, respectively (Entries 1 and 2). The reaction of phenyl-substituted derivative **1d** was slower than that of the 4-methoxyphenyl-substituted derivative **1c**, and pyrene **6d** was isolated in 47% yield with the use of 20 mol % of the catalyst in DCE (Entry 3).[18] In the case of diyne **1e** equipped with 4-chlorophenyl groups, the reaction was even more sluggish, and when carried out in p-xylene at 150 °C, produced pyrene **6e** in moderate yield (Entry 4). No reaction occurred with a diyne having nitro groups on the *para*-positions of the phenyl rings. Thus, the reactivity of 2,6-bis(arylethynyl)biphenyls was highly dependent on the electronic character of the aryl groups. The hydroarylation reaction proceeded more facilely with more electron-donating aryl groups. In addition to those with arylethynyl substituents, 2,6-di(prop-1-ynyl)biphenyl (**1h**) also participated in the hydroarylation reaction to give 4,10-dimethylpyrene (**6h**) in good yield (Entry 5). On the other hand, the reaction of **1b** having terminal ethynyl groups suffered the formation of a by-product derived from the competing 5-*exo* cyclization to afford pyrene (**6b**) in low yield (Entry 6). Trimethylsilyl-substituted substrate **1a** also afforded **6b** through desilylation that occurred during the course of the reaction (Entry 7).[19]

In summary, we have established a new entry to 4,10-substituted pyrenes via gold(I)-catalyzed twofold hydroarylation of 2,6-dialkynylbiphenyls. Further studies to explore the reactivities peculiar to dialkynylbiphenyls are underway and the results will be reported in due course.

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16 Gold complex $[(4\text{-}CF_3C_6H_4)_3P]AuNTf_2$ exhibited a similar catalytic activity (20 mol %, p-xylene, 150 °C, 84%).

17 The reaction in p-xylene required a higher temperature to proceed than in DCE.

18 The reaction in the presence of 5 mol % gold(I) catalyst in DCE at 80 °C resulted in the formation of a mixture of pyrene **6d** (20%) and monohydroarylated phenanthrene (13%).

19 The reaction of **1a** was also accompanied by the formation of some unidentified by-products.