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# Direct Assembly of Polyarenes via C−C Coupling Using PIFA/$BF_3 \cdot Et_2O$

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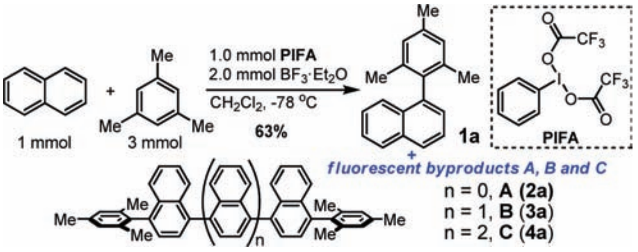
***Abstract:*** Direct oxidative Kita-type coupling between naphthalene and substituted benzenes was found to proceed via four-component coupling, leading to a linear tetraarene with a binaphthalene core. The methodology was extendable to the coupling of unfunctionalized 1,1′-binaphthalene with mesitylene to give a linear hexaarene product in a remarkably chemoselective manner in 87% yield. The method represents an attractive alternative to the traditional syntheses of related oligonaphthalene products via a sequence of metal-catalyzed cross-coupling steps.

Direct oxidative coupling of arenes dates back to 1912, when Scholl and Seer reported the formation of biaryls from arenes in the presence of stoichiometric $FeCl_3$.[1] Although several promising metal-catalyzed direct arene−arene (Ar−Ar) coupling reactions have been reported in recent years,[2] variants of the classical Scholl coupling continue enjoying widespread use, especially in intramolecular processes.[3] Despite the prevalent use of metal halides in such processes, Kita and co-workers have developed a combination of $BF_3 \cdot Et_2O$ with phenyliodine bis(trifluoroacetate) (PIFA) that is highly effective in promoting direct C−C coupling.[4,5] The method was initially used in intramolecular coupling reactions[4a] and later applied to direct intermolecular cross-coupling.[4b] Thus, Ar−Ar coupling between naphthalenes and polyalkylbenzenes was found to take place at the 1 position of the naphthalene.[4c] The process was later used by the Kita group for the arylation of thiophenes and pyrroles[4d] and by others in the construction of C−C[5a,b] and C−N bonds.[5d] The presence of $BF_3 \cdot Et_2O$ was found to be crucial in the activation of the hypervalent iodine reagent, although more recently Tse and co-workers[5b] showed that a catalytic amount of $HAuCl_4$ could be used in combination with $PhI(OAc)_2$ in a related arene−arene coupling.

***Scheme 1.*** Kita Coupling between Naphthalene and Mesitylene



As part of our group's work on new hypervalent iodine reagents, we applied the Kita conditions to the synthesis of 1-mesitylnaphthalene (**1a**).[4c] As reported in Scheme 1, the reaction between naphthalene and mesitylene in the presence of PIFA/$BF_3 \cdot Et_2O$ led to a 63% yield of **1a** after 3 h at −78 °C.

Surprisingly, the thin-layer chromatography analysis of the mixture revealed not only **1a** but also a ladder of spots that were fluorescent under 365 nm light, suggesting the presence of more extended aromatic systems. Mass spectrometric analysis of the principal component **A** ($m/z$ 490, largest $R_f$) suggested a formal dehydrodimerization of **1a**. Further assignment was guided by the observation by $^1H$ NMR spectroscopy of three Me resonances in a 6:6:6 integral ratio, indicating the inequivalence of the two *o*-Me groups within each mesityl moiety.[6] On the basis of these data, **A** was identified as 4,4′-dimesityl-1,1′-binaphthyl (**2a**), and this assignment was confirmed by X-ray diffraction analysis (Figure 1).[7,8] Similarly, the minor components **B** and **C** were identified as the tri- and tetranaphthalenes **3a** and **4a**, respectively (Scheme 1).

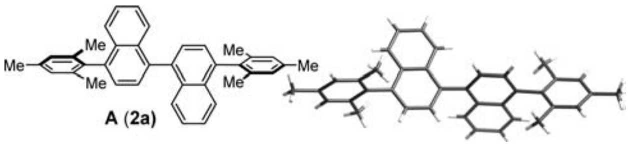


***Figure 1.*** (left) Connectivity of **2a**. (right) Molecular structure of **2a**, showing one of the two independent molecules. Dihedral angle ranges (deg): Mes−Naph, 81.6−86.9; Naph−Naph, 70.4−73.8.

Since in principle the formation of **2a**, **3a**, and **4a** corresponds to an overoxidation process, the **1a**/oligomer ratio should depend on the amount of the PIFA oxidant employed. Indeed, as shown in Figure 2, the process proved to be highly sensitive to the amount of the hypervalent iodine reagent, reaching optimal yields of **1a** at 1.0 equiv of PIFA and predominantly giving **2a** (45%) when this amount was raised to 1.8 equiv.

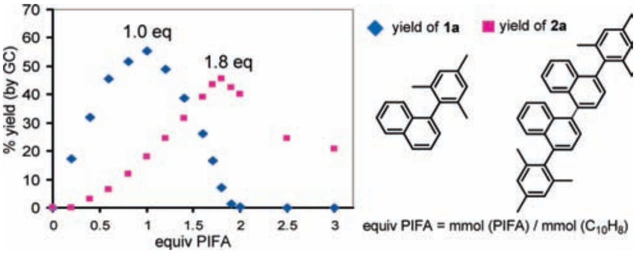


***Figure 2.*** Yields of **1a** and **2a** as a function of the amount of PIFA used. Reaction conditions: 0.5 mmol of $C_{10}H_8$, 1.5 mmol of mesitylene (3 equiv), 1.0 mmol of $BF_3 \cdot Et_2O$, and PIFA (as indicated) in $CH_2Cl_2$ at −78 °C. $n\text{-}C_{11}H_{24}$ was used as an internal standard.

The rest of the products were identified as a mixture of higher oligomers and bismesitylnaphthalene, the latter resulting from a second arylation of **1a**. We thought that the product ratios should be sensitive to the amount of mesitylene used and wondered whether

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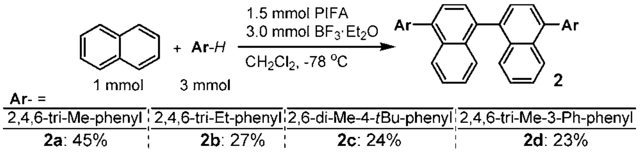
using less mesitylene would inhibit the formation of bismesitylnaphthalene in favor of an increased yield of **2a**. Unfortunately, while lowering the amount of mesitylene did suppress the second arylation of **1a**, no improvement in the yield of **2a** occurred; instead, a higher percentage of oligomeric products was obtained (see the Supporting Information).

Thus, with the use of an excess of PIFA, the protocol was extended to a series of electron-rich arenes and afforded the corresponding tetraaryl products **2a**−**d** in yields of 45−23% (Scheme 2), with the remaining products consisting of higher oligomers.[9] In these examples, 3 equiv of $BF_3 \cdot Et_2O$ was used to ensure complete activation of PIFA.

***Scheme 2.*** Direct Four-Component Coupling between Naphthalene and Substituted Arenes

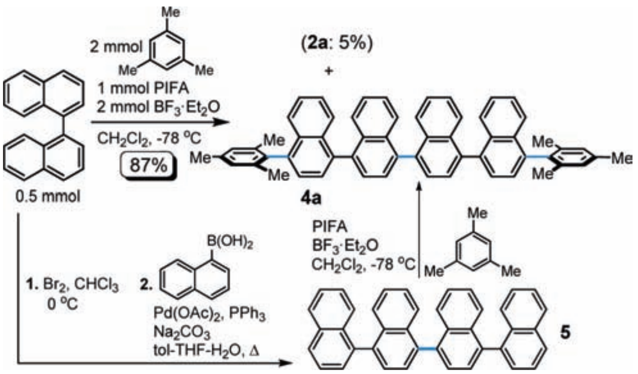


In order to extend the method to larger polyaromatic compounds, we considered two possible mechanistic sequences: (*a*) formation of **1a** followed by its dehydrodimerization and (*b*) initial oligomerization of naphthalene followed by C−C coupling at the 4 and 4′ positions. The viability of manifold *a* was confirmed by the efficient dehydrodimerization of **1a** (eq 1; see the Supporting Information).

$$\mathbf{1a} \xrightarrow{\text{Kita conditions}} \mathbf{2a} \quad \text{Yield: 45\%} \tag{1}$$

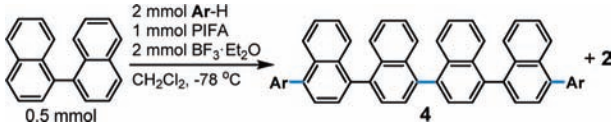
Next, route *b* was tested. Since this sequence might start with the formation of a bisnaphthalene through a known oxidative coupling reaction,[10] we submitted 1,1′-binaphthalene to the reaction conditions. To our surprise, this coupling only produced 5% **2a**, affording instead an 87% yield of hexaarene **4a** (Scheme 3 top). The connectivity of this product was confirmed by its independent synthesis via a bromination/Suzuki coupling sequence to give tetranaphthalene **5** (Scheme 3 bottom), which then underwent Kita coupling with mesitylene.

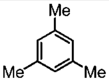
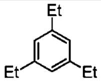
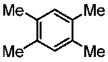
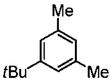
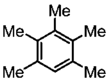
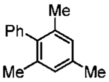
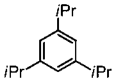
***Scheme 3.*** Coupling between 1,1′-Binaphthalene and Mesitylene



Intrigued by such a convergent transformation, we proceeded to test other polyalkylbenzenes. The effect of the substitution pattern of the Ar−H component was assessed by comparing tris-, tetra-, and pentamethylbenzenes (Table 1, entries **a**, **e**, and **f**). The **4**/**2** selectivity ratio was found to be 17.2 for mesitylene (entry **a**), decreased to 4.2 for the tetramethylbenzene (entry **e**), and was inverted for the pentamethylbenzene (0.03), which gave instead 95% **2f**. The trend is in line with the increased reactivity of tetra- and pentamethylbenzenes, which makes the capping reaction faster than the homocoupling of 1,1′-binaphthalene. High yields were also obtained in the case of **4b** and **4c** derived from 1,3,5-triethyl- and 1-*tert*-butyl-3,5-dimethylbenzene, respectively. Additionally, 2,4,6-trimethyl-1,1′-biphenyl and 1,3,5-triisopropylbenzene gave products **4d** and **4g** in 42 and 40% yield.

***Table 1.*** Oxidative Four-Component Kita Coupling Involving Binaphthalene and Electron-Rich Benzenes[a]

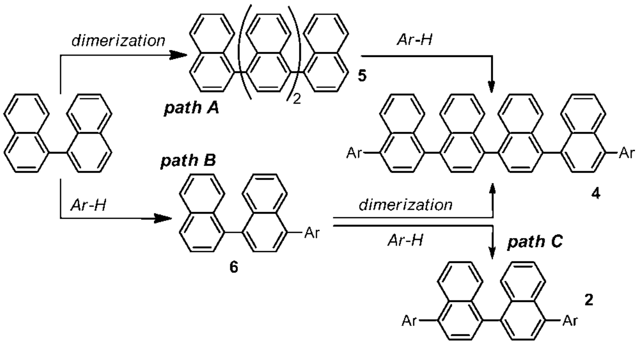


| Ar-H | | %4 | %2 | 4/2 | Ar-H | | %4 | %2 | 4/2 |
|---|---|---|---|---|---|---|---|---|---|
|  | **a** | 87 | 5 | 17.4 |  | **b** | 90 | <5 | >18 |
|  | **e** | 46 | 11 | 4.2 |  | **c** | 82 | <5 | >16 |
|  | **f** | 3 | 95 | 0.03 |  | **d** | 42 | <5 | >8 |
| | | | | |  | **g** | 40 | 7 | 5.7 |

[a] Isolated products.

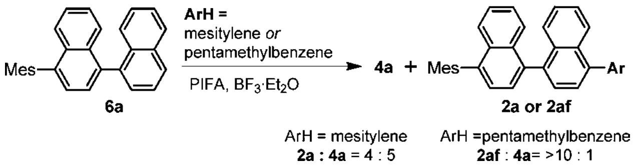
To further rationalize the ratios observed, we note that the formation of **4** from binaphthalene must follow either a dimerization/arylation sequence[11] (Scheme 4, path A) or a arylation/dimerization sequence (path B). Furthermore, the monarylation product **6**, an intermediate in path B, may undergo a second arylation to give **2** (path C).

***Scheme 4.*** Plausible Reaction Paths from Binaphthalene to **2** and **4**



Preliminary results indicated that all three paths may be operational under the reaction conditions and may compete to give different products. We found particularly interesting the possible competition between paths B and C, as these would lead to two different products. Our initial hypothesis was that mesitylene would favor path B to give **4** while the more reactive pentamethylbenzene would favor path C via a rapid second arylation. To probe this hypothesis, monomesitylated **6a** was prepared and was tested in two reactions, one with mesitylene and the other with pentamethylbenzene (Scheme 5). As expected, mesitylene gave **4a** as the main product (path B favored) while pentamethylbenzene produced almost exclusively the mixed diarylated product **2af** (72% yield, selectivity >10:1; path C favored) (see the Supporting Information). The somewhat reduced selectivity in the case of mesitylene to give **4a** may be explained by the exclusion of path A in this case.

***Scheme 5.*** Competition between Paths B and C Using Monomesitylbinaphthalene **6a** and Two Different Arenes



Following a suggestion by a referee, we also determined that, as Scheme 4 indicates, the rates associated with paths B and C (and therefore the **4**/**2** ratio) are sensitive to the amount of ArH employed. Thus, while the use of 4 equiv of mesitylene in the arylation of binaphthalene led to selective formation of **4a** (Table 1), the use of 12 equiv of mesitylene led to an erosion in the selectivity down to a **2a**/**4a** ratio of ~1:1. It is interesting to note, however, that even under such biased conditions, the reaction still affords significant amounts of the tetranaphthalene product **4a**.

There remains a question as to what governs the different reactivity of naphthalene, binaphthalene, and higher oligonaphthalenes under the Kita conditions. Thus, while monoarylated **1a** or dimeric **2a** was the principal product with naphthalene and selective dimerization was observed for binaphthalene, we found that both ternaphthyl and tetranaphthyl (**5**) underwent selective diarylation to give **3** and **4**, respectively. Although we were able to observe the presence of the formal dimerization product Ar−$(Nap)_6$−Ar from ternaphthyl by MALDI−TOF mass spectrometry, the yield of this oligomer did not exceed 3−4%. The difficulty in explaining this trend is due to the relatively scarce mechanistic studies of the Kita coupling. If the proposal of a radical-based mechanism is accepted,[4c] the differential reactivity must be governed by the relative redox potentials of the species involved. Our measurements in both $CH_2Cl_2$ and *N*,*N*-dimethylformamide confirmed that binaphthalene ($E_{ox} = 1.69$ V) and monarylated **6a** ($E_{ox} = 1.72$ V) are more easily oxidized than naphthalene ($E_{ox} = 1.80$ V), consistent with a greater tendency of the binaphthyl derivatives to undergo dimerization. However, further mechanistic studies are required to explain the reactivities of ter- and tetranaphthyl and to rule out a potential Scholl-type acid−base mechanism.

It is expected that the three stereogenic Ar−Ar junctions (a*R* or a*S*) present in **4a** would lead to the existence of atropisomeric forms. With a 23.5 kcal/mol interconversion barrier, these forms should be observable by NMR spectroscopy.[12,13] Indeed, the $^{13}$C NMR spectrum of **4a** contains a complex set of signals suggestive of the presence of several diastereomers (see the Supporting Information).[14]

Traditionally, oligonaphthalenes have been the subject of considerable interest in the field of dyes and organic optical devices, where they serve either as precursors to the long aromatic systems[15] or in their own right.[16] Since their synthesis has typically involved a sequence of metal-catalyzed cross-coupling reactions, the protocol reported herein represents a remarkably direct one-step access to **4a** by a regioselective *intermolecular* four-component assembly via the functionalization of six C−H bonds to give three new C−C bonds. Current work is focused on further establishing the scope and limitations of this approach.

**Acknowledgment.** This work is dedicated to Professor Carmen Nájera on the occasion of her 60th birthday. Financial support from the Ministerio de Ciencia e Innovación (MICINN) of Spain [Projects CTQ2008-05409-C02-01, CTQ2009-07881, and Consolider Ingenio 2010 (CSD2007-00006)] and DURSI-Generalitat de Catalunya (SGR 2009-1441) is gratefully acknowledged. We thank Dr. J. Orduna for the MALDI−TOF spectra and B. Noverges and Dr. G. Guirado for CV measurements; we also thank Prof. J. Marquet for insightful discussions.

**Supporting Information Available:** Experimental procedures, spectral and analytical data for all products, and crystallographic data for **2a** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(6) The diastereotopicity of the *o*-Me groups is due to their position above the mutually opposed termini of the remote naphthalene group (see the Supporting Information).

(7) X-ray data for **2a**: $C_{38}H_{34}$; $M_r = 490.65$,; monoclinic; *P*2/*c*; $a = 24.806(2)$ Å, $b = 9.6651(8)$ Å, $c = 24.423(2)$ Å, $\beta = 106.87(2)°$; $V = 5603.5(10)$ Å$^3$; $Z = 8$; Mo K$\alpha$, $\lambda = 0.71073$ Å; $T = 110(2)$ K; $2\theta_{max} = 52.74$; 118667/11450 reflns collected/independent ($R_{int} = 0.1170$); $R_1[I > 2\sigma(I)] = 0.0426$, $wR_2$(all data) $= 0.0900$; $\Delta\rho_{max} = 0.15$ e Å$^{-3}$; 697 parameters; two independent molecules in the asymmetric unit. The crystallographic data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(8) The connectivity of **2a** was also confirmed by its independent synthesis from 4,4′-dibromobinaphthalene via Negishi coupling with mesitylzinc chloride (see the Supporting Information).

(9) Lower yields of **2a** were obtained with other common oxidants, such as $PhI(OAc)_2$, PhI(OH)(OTs), and $MoCl_5$; and only traces of **2a** were obtained with $FeCl_3$, $CuCl_2/AlCl_3$, or $Pb(OAc)_4$ (see the Supporting Information).

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(13) The measured racemization barrier for 1,1′-binaphthalene is 23.5 kcal/mol. See: (a) Cooke, A. S.; Harris, M. M. *J. Chem. Soc.* **1963**, 2365. Also see: (b) Pu, L. *Chem. Rev.* **1998**, *98*, 2405–2494.

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