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Tetrahedron Letters 44 (2003) 3817–3820

TETRAHEDRON LETTERS

Microwave-assisted Suzuki coupling on a KF–alumina surface: synthesis of polyaryls

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Received 6 January 2003; revised 5 March 2003; accepted 14 March 2003

Abstract—A range of conjugated polyaryls has been synthesized through one-pot microwave assisted palladium-catalyzed consecutive Suzuki coupling reactions on a KF–alumina surface with notable features including rapid reaction times, solvent-free conditions, high yields, atom economic and air-insensitive reactions.

Biaryls and higher homologues are an important class of conjugated polyaromatic compounds, originating from benzene as unique building blocks. On the one hand, multinuclear aromatics develop the concept of aromaticity and supramolecular benzene chemistry,[1] and on the other hand, lead to wide applications in material and biological sciences.[2] Polyaryls find several applications as liquid crystals,[2a] laser-dyes[2b] and conducting polymers.[2c,d] For example, the terphenyls (*o*-, *m*-, *p*-isomers) are used industrially as heat storage and transfer agents and as textile dye carriers whilst the *p*-isomer has found application as a laser dye. 9,10-Diphenylanthracene is used as a fluorescer in a peroxyoxalate chemiluminescence system.[3] In addition, biaryls and higher homologues are often present as subunits in numerous biologically active natural products, pharmaceuticals and agrochemicals.[4] The synthesis of polyaromatic hydrocarbons (PAHs) and their derivatives has therefore been of considerable interest to organic and physical chemists for many years.

A variety of methods are available for the synthesis of biaryls via coupling of benzene rings promoted by different reagents.[5] The transition metal-catalyzed cross-coupling of Grignard reagents with dihalobenzenes[5b,c] and other methods[5d] produce the desired terphenyls in poor yields. However, most of the classical methods are often complicated by harsh reaction conditions, lack of selectivity and generality, or the requirement of expensive reagents. Moreover, many of the methods are not being recognized from the viewpoint of green chemistry. Recent literature reports confirm that palladium-catalyzed Suzuki coupling reactions of aryl halides with aryl boronic acids (or esters) have become convenient and widely used synthetic methods for regioselective aryl–aryl bond formation.[5,6] The reasons are manifold: ease of access of the organoboronic species, broad range of functional group tolerance, low toxicity of the inorganic residues, etc. However, although the Suzuki coupling reaction is one of the most useful methods yet developed for the syntheses of both symmetrical and unsymmetrical biaryls, there are still improvements and further applications that could be made to render it more effective. Surprisingly, little attempt has been made to investigate consecutive cross-couplings in a one-pot reaction. A few sporadic examples of bis-Suzuki couplings are known in the literature[5e,7] and therefore much new research should be extended towards the scope and the amelioration of the economical and ecological parameters of the Suzuki reaction. We envisaged that a multi-Suzuki coupling of di-, tri- or tetra-haloaromatics with aryl boronic acids could lead to terphenyls and higher homologues in a one-pot reaction. Kabalka et al.[8a] and Villemin et al.[8b] have reported that Suzuki cross-coupling reactions can be efficiently performed on the surface of KF–alumina with microwave irradiation. In conjunction with our interest in hetero cross-coupling reactions on KF–alumina surfaces,[8c] we investigated microwave-assisted palladium-catalyzed coupling of polyhaloaromatics with arylboronic acids on KF–alumina and other inorganic oxides. In this letter, we report our results, which expand the scope of the Suzuki reaction on a solvent-free inorganic surface leading to the synthesis of a large variety of polyaromatics.

Keywords: polyaromatic hydrocarbons; Suzuki coupling; palladium; KF–alumina; microwave assisted reactions.

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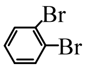
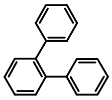
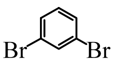
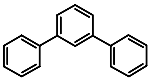
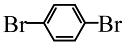
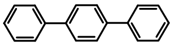
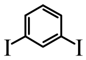
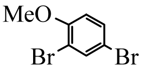
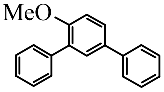
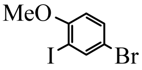
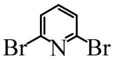
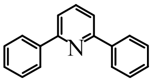
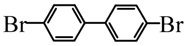
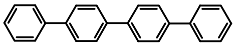
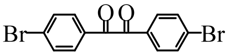
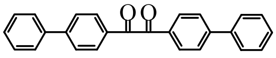
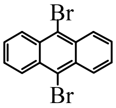
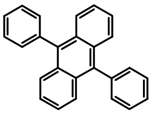
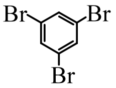
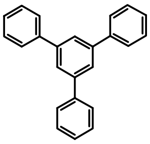
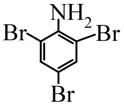
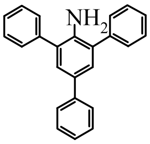
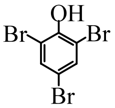
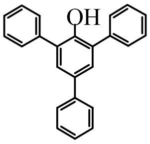
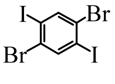
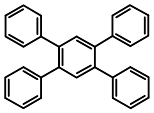
0040-4039/03/$ - see front matter
doi:10.1016/S0040-4039(03)00731-7

Table 1. Solid-supported [KF–Al_2O_3] polyarylations of polyhaloaromatics with phenyl boronic acid using catalytic $Pd(OAc)_2$ under microwave irradiation

Entry	Haloaromatics	Conditions Power (W)/ Time	Products [a]	% Isolated Yields [b]
1	 **1**	80 W / 10 min	 **2**	58
2	 **3**	80 W / 15 min	 **4**	83
3	 **5**	160 W / 15 min	 **6**	63
4	 **7**	320 W / 7 min	**4**	88
5	 **8**	80 W / 20 min	 **9**	63
6	 **10**	80 W / 20 min	**9**	65
7	 **11**	160 W / 10 min	 **12**	91
8	 **13**	400 W / 5 min	 **14**	53
9	 **15**	240 W / 10 min	 **16**	58
10	 **17**	320 W / 10 min	 **18**	88
11	 **19**	240 W / 7 min	 **20**	90
12	 **21**	240 W / 10 min	 **22**	75
13	 **23**	240 W / 10 min	 **24**	76
14	 **25**	320 W / 7 min	 **26**	55

[a] All the products gave satisfactory spectral data (^{1}H- and ^{13}C-NMR) and the known compounds were compared with reported mps; [b] Yields refer to the average from 2-3 runs.

We initially focused our attention on the cross-coupling of dibromoaromatics with phenylboronic acids on KF– alumina using microwave irradiation. As can be seen from the results presented in Table 1, the dibromobenzenes afforded the corresponding terphenyls as the major products (entries 1–3). Varying amounts of mono-substituted biaryls (15–20%) were detected on TLC, which could be easily separated from the terphenyls by column chromatography. While comparing the reaction rate between dibromo- and diiodoarenes (entries 2 and 4), the latter afforded the corresponding terphenyl **4** in a slightly better yield. However, different conditions were required to accomplish the desired bis-coupling. 2,4-Dibromoanisole (entry 5) and 4-bromo-2-iodoanisole (entry 6) afforded the terphenyl **9** in almost comparable yields. Thus, no significant reactivity difference between bromo- and iodo-substituents was observed. Among the other dibromoarenes, 2,6-dibromopyridine (entry 7) and 9,10-dibromoanthracene (entry 10) yielded the desired products **12** and **18**, respectively, in excellent yields. The biphenyl systems (entries 8 and 9) produced the corresponding products **14** and **16** in yields of 50–60%. In the case of tribromoaromatics (entries 11–13), the corresponding tris-coupled compounds **20**, **22** and **24** were isolated as the major products (Table 1). Small amounts of mono- or bis-coupled products were detected by TLC. The 1,4-dibromo-2,5-diiodobenzene **25** yielded the tetraphenylbenzene **26** in 55% yield (entry 14). Villemin and co-workers obtained their best results on Suzuki couplings with aryl iodides using mono-mode microwave irradiation.[8b] Our conditions using KF–alumina (1:4) and irradiation from a domestic microwave oven, however, enabled polyarylations in good to excellent yields. We also examined such poly-Suzuki couplings on other inorganic surfaces (Table 2). The results were best on the surface of KF–alumina (1:4). The reactions were carried out in air. All the reactants were intimately mixed with the inorganic surface before being placed in a domestic microwave oven (Kenstar; Model OM-9925E) and irradiated at the appropriate power (W) and time (Table 1). In many Suzuki cross-couplings, a crucial role is played by the ligands,[9] which complex with palladium salts. The above solvent-free conditions, however, required no such ancillary ligands, which is advantageous in view of atom economy in the reaction.

Table 2. Multi-Suzuki reactions on different inorganic surfaces under microwave irradiation without solvent [A/B/Pd(OAc)$_2$ = 1/2.5/0.04 mmol on 1.5 g of B]

Entry	Substrate (A)	Surface (B)	Conditions	Yield (%)
1	1,3-Dibromobenzene	KF–Al$_2$O$_3$ (1:4)	80 W/15 min	83
2	1,3-Dibromobenzene	Al$_2$O$_3$	80 W/15 min	20–25
3	1,3-Dibromobenzene	MgO	80 W/15 min	25
4	1,3-Dibromobenzene	MgO–K$_2$CO$_3$ (3:2)	80 W/15 min	30

In summary, we have demonstrated that it is possible to perform palladium-catalyzed Suzuki couplings of polyhaloaromatics with phenyl boronic acid on a surface of KF–alumina with the aid of microwave irradiation from a domestic microwave oven. The method is fast, operationally simple, and allows rapid access to a variety of polyaromatic hydrocarbons.

Representative procedure for a multi-Suzuki coupling: 1,3-Dibromobenzene **3** (236 mg, 1.0 mmol), phenyl boronic acid (305 mg, 2.5 mmol) and palladium acetate (10 mg, 0.04 mmol) were intimately mixed with 1.5 g of KF–alumina (prepared according to Ref. 8c) and the mixture was irradiated in a domestic microwave oven at 80 W for 15 min. The solid mixture was then placed on a silica gel column and eluted with petroleum ether:EtOAc (99:1) to furnish *m*-terphenyl **4** (190 mg, 83%); mp 87–88°C (lit.[10] 89°C); ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.30–7.84 (m, 14H); ^{13}C NMR (CDCl$_3$, 100 MHz): δ 126.1, 127.2, 127.4, 128.8, 129.2, 141.1, 141.7.

Acknowledgements

We gratefully acknowledge financial assistance from the Department of Science and Technology, New Delhi (Grant No. SP/S1/G13/97). P.D. is a Junior Research Fellow under this project.

References

1. Watson, M. D.; Fechtenkotter, A.; Mullen, K. *Chem. Rev.* **2001**, *101*, 1267 and references cited therein.
2. (a) Gary, G. W.; Winsor, P. A. *Liquid Crystals and Plastic Crystals*; John Wiley and Sons: New York, 1974; Vol. 1; (b) Schneider, D. J.; Landis, D. A.; Fleitz, P. A.; Seliskar, C. J.; Kaufman, J. M.; Steppel, R. N. *Laser Chem.* **1991**, *11*, 49; (c) Baker, K. N.; Fratini, A. V.; Resch, T.; Knachel, H. C.; Adams, W. W.; Socci, E. P.; Farmer, B. L. *Polymer* **1993**, *34*, 1571; (d) Heeger, A. J. *J. Phys. Chem. B* **2001**, *105*, 8475; (e) Yang, S.-M.; Shie, J.-J.; Fang, J.-M.; Nandy, S. K.; Chang, H.-Y.; Lu, S.-H.; Wang, G. *J. Org. Chem.* **2002**, *67*, 5208 and references cited therein.
3. Zhi, Z.; Yang, X.; Wang, X. *Chem. Educ.* **2000**, *5*, 187.
4. (a) Trujillo, J. M.; Jorge, R. E.; Navarro, E.; Boada, J. *Phytochemistry* **1990**, *29*, 2991; (b) Tsuji, K.; Nakamura, K.; Ogino, T.; Konishi, N.; Tojo, T.; Ochi, T.; Seki, N.; Matsuo, M. *Chem. Pharm. Bull.* **1998**, *46*, 279; (c) Becker, F. F.; Mukhopadhyay, C.; Hackfeld, L.; Banik, I.; Banik, B. K. *Bioorg. Med. Chem.* **2000**, *8*, 2693.
5. (a) Sainsbury, M. *Tetrahedron* **1980**, *36*, 3327; (b) Li, S.; Wei, B.; Low, P. M. N.; Lee, H. K.; Hor, T. S. A.; Xue, F.; Mak, T. C. W. *J. Chem. Soc., Dalton Trans.* **1997**, 1289; (c) Minato, A.; Tamao, K.; Hayashi, T.; Suzuki, K.; Kumada, M. *Tetrahedron Lett.* **1980**, *21*, 845; (d) Nakada, M.; Miura, C.; Nishiyama, H.; Higashi, F.; Mori, T. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 3122; (e) Hassan, J.; Sevignon, M.; Gozzi, C.; Chulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359.

6. (a) Miyaura, H.; Yanagi, T.; Suzuki, A. *Synth. Commun.* **1981**, *11*, 513; (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457; (c) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147; (d) Suzuki, A. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F.; Stang, P. J., Eds.; VCH: Weinheim, 1998; p. 49; (e) Yin, J.; Rainka, M. P.; Zhang, X.-X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1162.
7. (a) Goldfinger, M. B.; Crawford, K. B.; Swager, T. M. *J. Org. Chem.* **1998**, *63*, 1676; (b) Cox, P. J.; Wang, W.; Snieckus, D. *Tetrahedron Lett.* **1992**, *33*, 2253; (c) Toyata, S.; Woods, C. R.; Benaglia, M.; Siegel, J. S. *Tetrahedron Lett.* **1998**, *39*, 2697.
8. (a) Kabalka, W.; Pagni, L.; Hair, R. M. *Org. Lett.* **1999**, *1*, 1423; (b) Villemin, D.; Caillot, F. *Tetrahedron Lett.* **2001**, *42*, 639; (c) Basu, B.; Jha, S.; Mridha, N. K.; Bhuiyan, M. M. H. *Tetrahedron Lett.* **2002**, *43*, 7967.
9. Urgaonkar, S.; Nagarajan, M.; Verkade, J. G. *Tetrahedron Lett.* **2002**, *43*, 8921 and references cited therein.
10. France, H.; Heilbron, I. M.; Hey, D. H. *J. Chem. Soc.* **1939**, 1288.