Palladium-catalysed reaction of aryl bromides with metallocenes to produce pentaarylated cyclopentadienes

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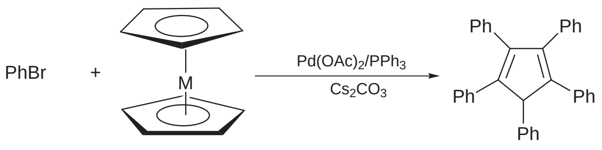
Aryl bromides can efficiently react with some metallocenes, typically zirconocene dichloride, in the presence of a palladium/phosphine catalyst system and an appropriate base to produce the corresponding pentaarylated cyclopentadienes.

Palladium-catalysed coupling reactions of aryl halides with alkenes, alkynes and organometallic species are now recognized to be highly useful and are widely employed for the preparation of substituted aromatic compounds.[1] It has been recently shown that intermolecular arylation of certain aromatic substrates, such as acenaphthylene,[2a–c] azulene[2a] and 2-phenylphenols,[3a] and a number of five-membered heteroaromatic substrates, including indoles,[4a] furans,[2b,4b] thiophenes[3b,4b] and azoles,[3b,4c] *i.e.* imidazole, oxazole and thiazole derivatives, with aryl halides can also proceed under palladium catalysis without the stoichiometric metalation of the aromatic compounds. In our investigation into the arylation of metallocenes as five-membered aromatic substrates, we observed an unprecedented reaction in which aryl bromides can efficiently react with some of them to produce the corresponding pentaarylated cyclopentadienes in good yields (Schemes 1 and 2), which is reported herein. Note that pentaphenylcyclopentadiene as well as cyclopentadienes having other bulky substituents are known to form stable complexes with various metals, and the synthesis and properties of the complexes have been the subjects of intense study.[5] Recently, the pentaphenyl compound was applied as a ligand of an iron-containing asymmetric catalyst[6] and also as a component of electroluminescent devices.[7] Thus, new, effective methods for the synthesis of its derivatives appear to be of widespread interest. However, only a limited number of the methods have been so far reported.[8–11]

The catalytic reaction was first examined using bromobenzene **1a** (6 mmol) and a number of metallocenes **2** (0.5 mmol) in the presence of $Pd(OAc)_2$ (0.125 mmol), PPh_3 (0.5 mmol), and Cs_2CO_3 (6 mmol) in DMF at 130 °C for 6 h (Scheme 1). From the reaction was obtained pentaphenylcyclopentadiene **3** as the major product; the reaction efficiency was found to be a marked function of the identity of metallocenes: The yields of **3** using **2a–e** (M = Fe, Co, Ni, $TiCl_2$, $ZrCl_2$) were <1, 23, 62, 64 and 70% (based on the cyclopentadiene moiety, *i.e.* 1 mmol = 100%), respectively. Thallium cyclopentadienide was only as effective as **2b**. It should be noted that the use of iodobenzene and K_2CO_3 in place of **1a** and Cs_2CO_3, respectively, in the reaction with **2c** significantly reduced the product yield, giving biphenyl as the major product. Analysis of the reaction mixture with **2c** or **2e** after a reaction time of 3 h by GLC–MS confirmed the formation of tri- and tetra-phenylcyclopentadienes together with **3** in comparable amounts, while the peaks of the tri- and tetra-substituted compounds disappeared after 6 h. From the reaction with **2e** using reduced amounts of **1a** (3 mmol) and of palladium acetate (0.0125 mmol) for 20 h, the intermediary products could also be isolated and identified to be 1,2,4-triphenyl- (21%) and 1,2,3,4-tetraphenylcyclopenta-1,3-diene (9%). These results suggest that phenylpalladium species generated in the medium can react with **2c** or **2e** effectively in the initial stages of the reaction, and the cyclopentadienyl moiety is further phenylated in a stepwise manner to the end product **3**.



1a **2a–e** **3**

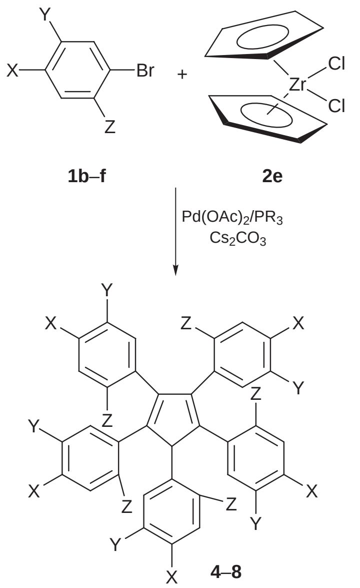
2a: M = Fe, **2b**: M = Co, **2c**: M = Ni, **2d**: M = $TiCl_2$, **2e**: M = $ZrCl_2$

Scheme 1

When the reaction using 4-fluorobromobenzene **1b** in place of **1a** was carried out, contamination by phenyl groups from PPh_3 in the product was observed.[12] Therefore, the applicability of $Pd(OAc)_2/P(o\text{-Tol})_3$ and $Pd_2(\mu\text{-OAc})_2/(P\text{-C})_2$ [P-C = $o\text{-}CH_2C_6H_4P(o\text{-Tol})_2$], which would avoid the scrambling of aryl moieties,[12] was examined for the reaction of **1a** with **2e**. The latter complex has recently been proven to be an efficient catalyst for the Heck reaction.[12] However, the use of these catalyst systems considerably retarded the reaction and it could not be completed. Consequently, the reaction of **1b** with **2e** was carried out using $P(4\text{-}FC_6H_4)_3$ as ligand. As expected, the corresponding product **4** could be cleanly isolated, although the yield was only moderate (Scheme 2 and Table 1).

One of the possible ways to promote the reaction could be the use of relatively more basic and sterically hindered phosphines.[13,14] It was found that PBu^t_3 can considerably enhance the reaction of **1a** and **2e**: the reaction was completed within 3 h to give **3** in an isolated yield of 77%. Furthermore, in the reactions of **1b** and 4-methyl-, 4-methoxy-, and 3-methylbromobenzenes **1c–e** using PBu^t_3, no incorporation of *tert*-butyl groups in the products was detected, giving the expected compounds **4–7**§ in fair to good isolated yields. The use of this phosphine was essential for the reaction of **1d** to take place. Remarkably, under the optimized conditions the amount of palladium catalyst can be reduced to 0.0125 mmol (0.25 mol% per transferred aryl group) while still achieving an acceptable isolated yield of **5** (60%).

In the reaction of a relatively bulky bromide, 2,5-dimethylbromobenzene **1f**, with **2e**, however, PPh_3 afforded a considerably better yield of product **8**§ (70%) compared with PBu^t_3 (31%). While the analysis of **8** obtained using PPh_3 by MS indicated contamination with $C_5H(Ph)(2,5\text{-}Me_2C_6H_3)_4$ (8%), fortunately the purity could be increased to 98% *via* a single recrystallization from $MeOH–C_6H_6$. The formation of **8** is of special interest, since it should be sterically very crowded. Compound **8** was found to consist of at least six rotamers at room temperature: its ^1H NMR showed six obvious methine proton peaks (three minor ones at δ 4.85, 5.07 and 5.25 and



Scheme 2

Table 1 Reaction of **1a–f** with **2e**[a]

Bromide				R in PR$_3$	t/h	Product	Yield (%)[b]
1	X	Y	Z				
a	H	H	H	Ph	6	**3**	70
a	H	H	H	Bu^t	3	**3**	77
b	F	H	H	4-FC$_6$H$_4$	24	**4**	38
b	F	H	H	Bu^t	1	**4**	60
c	Me	H	H	Bu^t	1	**5**	78
c[c]	Me	H	H	Bu^t	20	**5**	60
d	MeO	H	H	Bu^t	1.5	**6**	45
e	H	Me	H	Bu^t	1	**7**	80
f	H	Me	Me	Bu^t	22	**8**	31
f	H	Me	Me	Ph	24	**8**	70[d]

[a] See also Scheme 2. Reaction conditions: **1** (6 mmol), **2e** (0.5 mmol), Pd(OAc)$_2$ (0.125 mmol), PR$_3$ (0.5 mmol), Cs$_2$CO$_3$ (6 mmol), DMF (10 cm^3), 130 °C. Workup was carried out by adding TsOH (12 mmol) and filtering through a silica gel column, followed by chromatographic purification. [b] Isolated yield based on the amount of cyclopentadiene moiety (1 mmol = 100%). Satisfactory elemental and spectral (^{1}H and ^{13}C NMR and mass) analyses data were obtained for each compound. [c] Reaction with 0.0125 mmol of Pd(OAc)$_2$ and 0.05 mmol of PBu$^t_3$. [d] Contaminated with C$_5$H(Ph)(2,5-Me$_2$C$_6$H$_3$)$_4$ (8%).

three major ones at δ 5.10, 5.29 and 5.46 in CDCl$_3$) together with more than 20 methyl peaks. This resembles the previously reported spectrum for tetra(2-methylphenyl)cyclopentadienone at a lower temperature of −43 °C.[15] The peaks in the ^{1}H NMR spectrum of **8** in DMSO-d$_6$ were still notably sharp even at 100 °C, reflecting its crowded nature, while they were completely broadened at 150 °C.

In summary, we have shown that various homosubstituted pentaarylcyclopentadienes can be prepared *via* the treatment of aryl bromides with metallocenes, typically zirconocene dichloride, under palladium catalysis. This novel synthetic method represents an efficient and straightforward alternative to the rather tedious ‘tetracyclone route’,[5,8] opening up opportunities for the construction of even extremely sterically crowded pentaarylcyclopentadienes. Its synthetic application as well as the detailed reaction mechanism are currently under investigation.

Notes and References

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§ *Selected data* for **4**: mp 186–187 °C (Found: C, 78.13; H, 3.95. Calc. for C$_{35}$H$_{21}$F$_5$: C, 78.35; H, 3.94%); δ_H(400 MHz, CDCl$_3$) 4.90 (s, 1H), 6.73–6.77 (m, 4H), 6.84–6.95 (m, 14H), 7.07–7.10 (m, 2H), For **5**: mp 250 °C (Found: C, 92.56; H, 7.04. Calc. for C$_{40}$H$_{36}$: C, 92.98; H, 7.02%); δ_H(500 MHz, CDCl$_3$) 2.17 (s, 6H), 2.20 (s, 3H), 2.26 (s, 6H), 4.97 (s, 1H), 6.81–6.95 (m, 18H), 7.07 (d, *J* 7.8, 2H). For **6**: mp 193–194 °C (Found: C, 80.28; H, 6.07. Calc. for C$_{40}$H$_{36}$O$_5$: C, 80.51; H, 6.08%); δ_H(500 MHz, CDCl$_3$) 3.68 (s, 6H), 3.71 (s, 3H), 3.75 (s, 6H), 4.89 (s, 1H), 6.56–6.58 (m, 4H), 6.67–6.71 (m, 6H), 6.88–6.92 (m, 8H), 7.08–7.10 (m, 2H). For **7**: mp 163–164 °C (Found: C, 92.94; H, 7.10. Calc. for C$_{40}$H$_{36}$: C, 92.98; H, 7.02%); δ_H(400 MHz, CDCl$_3$) 2.08 (s, 6H), 2.15 (s, 6H), 2.23 (s, 3H), 5.02 (s, 1H), 6.77–6.93 (m, 15H), 6.99–7.04 (m, 5H). For **8**: mp 194–196 °C (Found: C, 91.92: H, 7.97. Calc. for C$_{45}$H$_{46}$: C, 92.10; H, 7.90%); δ_H(400 MHz, CDCl$_3$) 1.72–2.46 (m, 30H), 4.86–5.45 (m, 1H), 6.46–7.10 (m, 15H).

1 R. F. Heck, *Palladium Reagents in Organic Syntheses*, Academic Press, New York, 1985; A. de Meijere and F. E. Meyer, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 2379; J. Tsuji, *Palladium Reagents and Catalysts*, Wiley, Chichester, 1995.
2 (*a*) Review: G. Dyker, *Chem. Ber./Recueil*, 1997, **130**, 1567; (*b*) G. Dyker, *J. Org. Chem.*, 1993, **58**, 234; (*c*) G. Dyker, J. Körning, P. G. Jones and P. G. Bubenitschek, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 1733.
3 (*a*) T. Satoh, Y. Kawamura, M. Miura and M. Nomura, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 1740; (*b*) S. Pivsa-Art, T. Satoh, Y. Kawamura, M. Miura and M. Nomura, *Bull. Chem. Soc. Jpn.*, 1998, **71**, 467.
4 (*a*) Y. Akita, Y. Itagaki, S. Takizawa and A. Ohta, *Chem. Pharm. Bull.*, 1989, **37**, 1477; (*b*) A. Ohta, Y. Akita, T. Ohkuwa, M. Chiba, R. Fukunaga, A. Miyafuji, T. Nakata, N. Tani and Y. Aoyagi, *Heterocycles*, 1990, **31**, 1951; (*c*) Y. Aoyagi, A. Inoue, I. Koizumi, R. Hashimoto, K. Tokunaga, K. Gohma, J. Komatsu, K. Sekine, A. Miyafuji, J. Kanoh, R. Honma, Y. Akita and A. Ohta, *Heterocycles*, 1992, **33**, 257.
5 For recent work on complexes using C$_5$Ph$_5$: D. Matt, M. Huhn, M. Bonnet, I. Tkatchenko, U. Englert and W. Kläui, *Inorg. Chem.*, 1995, **34**, 1288; S. Barry, A. Kucht, H. Kucht and M. D. Rausch, *J. Organomet. Chem.*, 1995, **489**, 195; I. Kuksis and M. C. Baird, *Organometallics*, 1996, **15**, 4755; D. J. Hammack, M. M. Dillard, M. P. Castellani, A. L. Rheingold, A. L. Rieger and P. H. Rieger, *Organometallics*, 1996, **15**, 4791; I. Kuksis, I. Kovács, M. C. Baird and K. F. Preston, *Organometallics*, 1997, **15**, 4991; A. M. Bond, R. Colton, D. A. Fiedler, L. D. Field, D. Leslie, T. He, P. A. Humphery, C. M. Lindall, F. Marken, A. F. Masters, H. Schumann, K. Suehring and V. Tedesco, *Organometallics*, 1997, **16**, 2787; C. Janiak, R. Weimann and F. Görlitz, *Organometallics*, 1997, **16**, 4933.
6 J. C. Ruble, H. A. Latham and G. C. Fu, *J. Am. Chem. Soc.*, 1997, **119**, 1492.
7 For example: C. Adachi, T. Tsuji and S. Saito, *Appl. Phys. Lett.*, 1990, **56**, 799; Y. Ohmori, Y. Hironaka, M. Yoshida, N. Tada, A. Fujii and K. Yoshino, *Synth. Met.*, 1997, **85**, 1241.
8 W. Broser, P. Siegle and H. Kurreck, *Chem. Ber.*, 1968, **101**, 69; L. D. Field, K. M. Ho, C. M. Lindall, A. F. Masters and A. G. Webb, *Aust. J. Chem.*, 1990, **43**, 281.
9 T. R. Jack, C. J. May and J. Powell, *J. Am. Chem. Soc.*, 1977, **99**, 4707.
10 H. Schumann, H. Kucht and A. Kucht, *Z. Naturforsch.*, **1992**, 47b, 1281; R. H. Lowack and K. P. C. Vollhardt, *J. Organomet. Chem.*, 1994, **476**, 25.
11 Related reaction of iodocyclopentadienyl complexes with tributyl(cyclopentadienyl)stannane to give a mixture of 1,2,4,5- and 1,1,2,4-substituted cyclopentadienes: R. Boese, G. Bräunlich, J.-P. Gottenland, J.-T. Hwang, C. Troll and K. P. C. Vollhardt, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 995.
12 W. A. Herrmann, C. Brossmer, C.-P. Reisinger, T. H. Riermeier, K. Öffele and M. Beller, *Chem. Eur. J.*, 1997, **3**, 1357 and references cited therein.
13 V. V. Grushin and H. Alper, *Chem. Rev.*, 1994, **94**, 1047 and references cited therein.
14 M. Nishiyama, T. Yamamoto and Y. Koie, *Tetrahedron Lett.*, 1998, **39**, 617; T. Yamamoto, M. Nishiyama and Y. Koie, *Tetrahedron Lett.*, 1998, **39**, 2367.
15 R. Willem, A. Jans, C. Hoogzand, M. Gielen, G. V. Binst and H. Pepermans, *J. Am. Chem. Soc.* 1985, **107**, 28.

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