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First intermolecular palladium catalyzed arylation of an unfunctionalized aromatic hydrocarbon

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Abstract

Azulene is arylated by iodobenzene and by 4-nitro-chlorobenzene under palladium catalysis at the electron-rich 1-position.

Keywords: Arylation; Azulene; Palladium catalysis

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1. Introduction

For the synthesis of biaryl compounds palladium catalyzed processes found widespread application [1,2]. Among these methods the Suzuki [3] and the Stille coupling reaction [4] are the most popular. For both reactions a transmetalation of an intermediary aryl palladium halide (or triflate) with an arylboronic acid or an aryl stannane, respectively, is the crucial reaction step. From a preparative point of view the direct palladium catalyzed coupling reaction of an aryl halide with an aromatic CH-group would be highly desirable. Unfortunately such a reaction was restricted to intramolecular cases until recently [2,5,6]. Miura and coworkers reported that 2-phenylphenol is arylated in the 2′-position, revealing a precoordination via an arylpalladium phenolate [7]. Certain heterocycles such as imidazole derivatives undergo an efficient palladium catalyzed arylation in the presence of caesium carbonate as the base [8]. Nevertheless, for unfunctionalized aromatic hydrocarbons this type of coupling reaction is still a challenging problem. Herein we report on the arylation of azulene (**1**), an aromatic hydrocarbon that exhibits an increased reactivity due to its dipolar nature.

2. Results and discussion

Recently we reported on the first palladium-catalyzed intermolecular arylation of a tetrasubstituted carbon–carbon double bond [9a,b]; an excess of aryl halide was crucial for a successful reaction. Moreover we succeeded in the multifold arylation of metallocenes resulting in a new synthesis of pentaarylcyclopentadienes [9c]. These findings prompted us to try the intermolecular arylation of several polycyclic aromatic hydrocarbons such as azulene (**1**), anthracene, phenanthrene and pyrene under similar reaction conditions. However, among these exclusively azulene (**1**) was arylated to some extent (Schemes 1 and 2): under Jeffery-conditions [10] (5 mol% Pd(OAc)$_2$, eight equivalents K$_2$CO$_3$, two equivalents n-Bu$_4$NBr, 10 ml DMF, N$_2$, 3 days, 100°C) with five equivalents of iodobenzene (**2a**) a small amount of 1-phenylazulene **3a** (5% yield) was isolated besides biphenyl [11] as the main product. With a thirtyfold excess of **2a** the yield of **3a** increased to 13%. Under the same reaction conditions 1-chloro-4-nitrobenzene (**2b**) turned out to be the superior arylating agent, since a fivefold excess of **2b** was sufficient to accomplish a similar result. So far the best result, a 16% yield of **3b** (54% based on recovered starting material), was achieved at 140°C; because of partial decomposition at this temperature n-Bu$_4$NBr was omitted in this case. Also for some other reaction conditions [12] and catalysts that we tested, such as cyclopalladated com-

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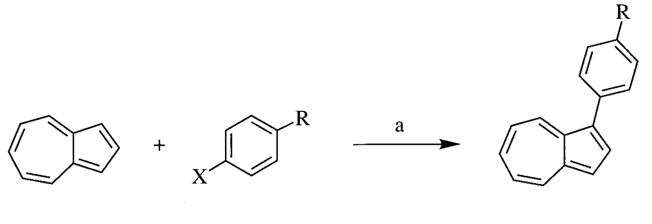
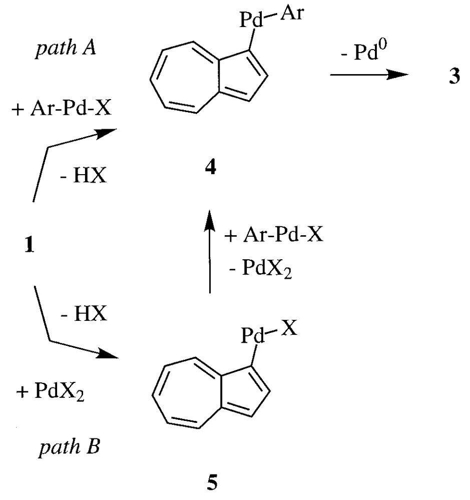
plexes [13], palladium clusters [14], palladium on activated carbon and in the presence of silver salts, the maximum turnover number was around 3. Under Jeffery-conditions 1-chloro-2,4-dinitrobenzene led to the formation of polymeric material, whereas with benzyl bromide a 19% yield of 1-benzylazulene was obtained [15].



1 2a: X = I, R = H 3a: R = H
2b: X = Cl, R = NO$_2$ 3b: R = NO$_2$

Scheme 1. Reaction conditions a; for the formation of **3a**: 1 mmol **1**, 5 mol% Pd(OAc)$_2$, eight equivalents K_2CO_3, two equivalents *n*-Bu$_4$NBr, 10 ml DMF, N_2, 3 days, 100°C, with five equivalents **2a** the yield of **3a** is 5%, with thirty equivalents **2a** the yield of **3a** is 13%; for the formation of **3b**: 1 mmol **1**, five equivalents **2b**, eight equivalents K_2CO_3, no *n*-Bu$_4$NBr, 10 ml DMF, N_2, 3 days, 140°C, with 5 mol% Pd(OAc)$_2$ the yield of **3b** is 16% (54% based on recovered starting material), with 15 mol% Pd(OAc)$_2$ added in 3 portions every 24 h the yield of **3b** is 28%.



Scheme 2. Mechanistic pathways for the Pd-catalyzed arylation of azulene (**1**).

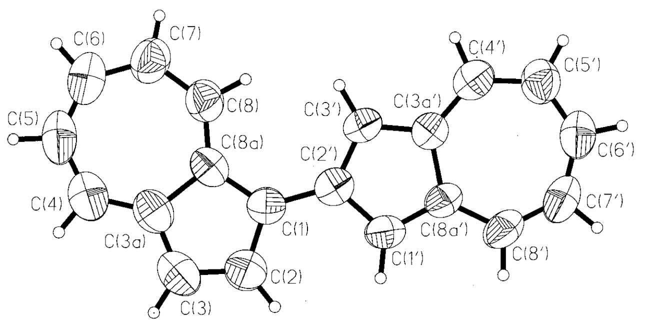


Fig. 1. Structure of 1,2′-biazulenyl in the crystal.

Obviously, the arylation as well as the benzylation takes place regioselectively at the electron-rich 1-position suggesting an electro-philic attack of a Pd(II)-species as a crucial reaction step [16]. According to the mechanistic pathway A the key intermediate **4** is formed via a palladation of azulene **1** with an arylpalladium halide. Presumably this step proceeds in the sense of an electrophilic aromatic substitution. The alternative pathway B explains the formation of **4** via a ligand exchange reaction between a palladated azulene **5** and the arylpalladium halide. This rather speculative pathway requires both Pd(0)- and Pd(II)-catalysts and could explain the deactivation of the catalytic system. However, appropriate reaction conditions (Pd-clusters in DMSO in the presence of oxygen [17]) were unsuccessful. The mechanistic pathways A and B were tested by performing stochiometric reactions. The result from the reaction of azulene (**1**) with a stochiometric amount of phenylpalladium chloride [18] in acetonitrile at room temperature is in accord with pathway A: the crude product was identified by ^{1}H-NMR spectroscopy as a mixture of azulene (**1**), 1-phenylazulene (**3a**) and biphenyl in the ratio 1:2:7. An attempt to prepare an azulene–Pd-complex of type **5** from **1** and a stochiometric amount of palladium acetate resulted in the isolation of a 10% yield of 1,2′-biazulenyl, which was identified by a X-ray structure analysis (Fig. 1) [19].

Due to its dipolar nature azulene (**1**) is one of the most reactive aromatic hydrocarbons. Therefore the relatively low yields we have achieved exemplify the difficulties that are connected with the Pd-catalyzed intermolecular arylation. Especially for less reactive substrates such as phenanthrene and pyrene further studies should concentrate on high pressure techniques and on palladium catalysts that are active at elevated temperatures.

3. Experimental

*3.1. 1-(4-Nitrophenyl)-azulene (**3b**)*

A mixture of 128 mg (1.00 mmol) of azulene (**1**), 788 mg (5.00 mmol) of 1-chloro-4-nitrobenzene (**2b**), 1.1 g (8.0 mmol) K_2CO_3 and 11 mg (50 μmol) of Pd(OAc)$_2$ in dry DMF (10 ml) was stirred under N_2 in a sealed tube for 3 days at 140°C. After dilution with water (50 ml), the reaction mixture was extracted thrice with 30 ml of dichloromethane. The combined organic extracts were washed with water (20 ml), filtered through a pad of silica and evaporated in vacuo (50°C/100 mbar). The residue was fractionated by flash chromatography (silica, 50:1

hexanes–ethyl acetate). First fraction ($R_f = 0.39$): 90 mg (70%) recovered starting material **1**. Second fraction ($R_f = 0.14$): 40 mg (16%) green crystals of **3b** with m.p. 94–96°C. Selected spectroscopic data of **3b**: UV (acetonitrile): λ_{max} (l g ε) = 232 nm (4.45), 284 (4.53), 335 (3.94, sh), 407 (4.20). ^{1}H-NMR (500 MHz, $CDCl_3$, TMS): $\delta = 7.28$ ppm (t, $J = 10$ Hz, 2H, 5-H, 7-H), 7.47 (d, $J = 4.0$ Hz, 1H, 3-H), 7.69 (t, $J = 10$ Hz, 1H, 6H), 7.76 (d, $J = 9$ Hz, 2H, 2′/6′-H), 8.06 (d, $J = 4.0$ Hz, 1H, 2-H), 8.34 (d, $J = 9$ Hz, 2H, 3′/5′-H), 8.42 (d, $J = 9.3$ Hz, 1H), 8.57 (d, $J = 10$ Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): $\delta = 118.33$ ppm (d), 124.12 (d), 124.53 (d), 124.78 (d), 128.47 (s), 129.75 (d), 135.32 (d), 135.87 (s), 137.32 (d), 138.01 (d), 138.95 (d), 142.82 (s), 144.38 (s), 145.86 (s). MS (70 eV); m/z (%): 250 (19), 249 [100, M^+], 219 (11), 204 (39), 202 (89), 201 (17), 200 (16), 101 (16), 88 (11). Calc. for $C_{16}H_{11}NO_2$ (259.27): C, 77.10; H, 4.45; N, 5.62. Found: C, 76.87; H, 4.53; N, 5.67%.

Selected spectroscopic data of 1-phenylazulene (**3a**) [20]: blue crystals with m.p. 53–54°C. ^{1}H-NMR (500 MHz, $CDCl_3$, TMS): $\delta = 7.14$ ppm (t, $J = 10$ Hz, 2H, 5-H, 7-H), 7.34 (t, $J = 7.4$ Hz, 1H, 4′-H), 7.43 (d, $J = 3.9$ Hz, 1H, 3-H), 7.49 (t, $J = 7.5$ Hz, 2H, 3′/5′-H), 7.58 (t, $J = 9.9$ Hz, 1H, 6-H), 7.62 (d, $J = 8.3$ Hz, 2H, 2′/6′-H), 8.02 (d, $J = 3.6$ Hz, 1H, 2-H), 8.34 (d, $J = 8.8$ Hz, 1H, 4-H), 8.55 (d, $J = 9.7$ Hz, 1H, 8-H). ^{13}C-NMR (125 MHz, $CDCl_3$): $\delta = 117.48$ ppm (d), 123.07 (d), 123.34 (d), 126.31 (d), 128.66 (d), 129.79 (d), 131.35 (s), 135.25 (s), 136.64 (d), 137.18 (d), 137.31 (d), 137.54 (s), 138.23 (d), 141.71 (s).

Selected spectroscopic data of 1-benzylazulene: blue crystals with m.p. 58–59°C. ^{1}H-NMR (500 MHz, $CDCl_3$, TMS): $\delta = 4.45$ ppm (s, 2H), 7.08 (t, $J = 9.8$ Hz, 2H, 5-H, 7-H), 7.14–7.20 (m, 3H), 7.24 (d, $J = 7.8$ Hz, 2H), 7.33 (d, $J = 3.6$ Hz, 1H, 3-H), 7.53 (t, $J = 9.9$ Hz, 1H, 6-H), 7.72 (d, $J = 3.6$ Hz, 1H, 2-H), 8.26 (d, $J = 9.4$ Hz, 1H), 8.29 (d, $J = 9.7$ Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): $\delta = 33.69$ ppm (t), 116.88 (s), 121.81 (d), 122.42 (d), 125.84 (d), 128.40 (d), 128.59 (d), 129.11 (d), 133.64 (d), 135.93 (s), 136.55 (d), 137.48 (d), 138.05 (d), 140.84 (s), 141.90 (s).

Selected spectroscopic data of 1,2′-biazulenyl: green crystals with m.p. 140–141°C from pentane (lit. [21] m.p. 144–145°C). ^{1}H-NMR (500 MHz, $CDCl_3$, TMS): $\delta = 7.21$–7.15 ppm (m, 3H), 7.27 (t, $J = 9.9$ Hz, 1H), 7.49–7.45 (m, 2H), 7.63 (t, $J = 9.9$ Hz, 1H), 7.75 (s, 2H), 8.29 (d, $J = 9.2$ Hz, 2H), 8.34–8.33 (m, 2H), 9.06 (d, $J = 9.8$ Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): $\delta = 116.50$ ppm (d), 118.97 (d), 123.81 (d), 124.20 (d), 124.46 (d), 127.19 (s), 134.57 (d), 135.14 (d), 136.26 (d), 136.27 (s), 137.29 (d), 138.51 (d), 138.60 (d), 141.28 (s), 143.55 (s), 146.67 (s).

4. Supplementary material

The crystallographic data (without structure factors) have been deposited as supplementary publication no. CCDC-139097 at the Cambridge Crystallographic Data Centre. Copies of the data may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk)

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References

[1] J. Tsuji, Palladium Reagents and Catalysts: Innovations in Organic Synthesis, Wiley, Chichester, 1995.
[2] G. Bringmann, R. Walter, R. Weirich, Angew. Chem. 102 (1990) 1006; Angew. Chem. Int. Ed. Engl. 29 (1990) 977.
[3] (a) N. Miyaura, T. Yanagi, A. Suzuki, Synth. Commun. 11 (1981) 513. (b) U. Schmidt, R. Meyer, U. Leitenberger, A. Lieberknecht, Angew. Chem. 101 (1989) 946; Angew. Chem. Int. Ed. Engl. 28 (1989) 929. (c) Y. Miura, H. Oka, M. Momoki, Synthesis (1995) 1419.
[4] A.M. Echavarren, J.K. Stille, J. Am. Chem. Soc. 109 (1987) 5478.
[5] G. Dyker, Chem. Ber./Recl. 130 (1997) 1567.
[6] Benzo[b]furan is arylated by 1,8-diiodonaphthalene under palladium catalysis: G. Dyker, J. Org. Chem. 58 (1993) 234.
[7] (a) T. Satoh, T. Itaya, M. Miura, M. Nomura, Chem. Lett. 1996, 823. (b) T. Satoh, Y. Kawamura, M. Miura, M. Nomura, Angew. Chem. 109 (1997) 1820; Angew. Chem. Int. Ed. Engl. 36 (1997) 1740.
[8] M. Miura, T. Satoh, T. Itaya, Y. Kawamura, S. Pivsa-Art, M. Nomura, 9th IUPAC Symposium on Organometallic Chemistry, OMCOS 9, 1997, final program p. 130, poster 42.
[9] (a) G. Dyker, J. Körning, P.G. Jones, P. Bubenitschek, Angew. Chem. 105 (1993) 1805; Angew. Chem. Int. Ed. Engl. 32 (1993) 1733. (b) G. Dyker, J. Körning, P.G. Jones, P. Bubenitschek, Liebigs. Ann./Recueil (1997) 203. (c) M. Miura, S. Pivsa-Art, G. Dyker, J. Heiermann, T. Satoh, M. Nomura, J. Chem. Soc. Chem. Commun. (1998) 1889.
[10] T. Jeffery, Tetrahedron Lett. 26 (1985) 2667.
[11] G. Dyker, J. Org. Chem. 58 (1993) 234.
[12] Caesium carbonate did not facilitate the arylation in this case.
[13] W.A. Herrmann, C. Brossmer, C.-P. Reisinger, T.H. Riermeier, K. Öfele, M. Beller, Chem. Eur. J. 3 (1997) 1357.
[14] M.T. Reetz, G. Lohmer, J. Chem. Soc. Chem. Commun. (1996) 1921.
[15] A related cross coupling reaction of a bromomethylindole with 1,2-dimethoxybenzene has recently been described: (a) W.G. Rajeswaran, P.C. Srinivasan, Synthesis (1994) 270. (b) W.G. Rajeswaran, P.C. Srinivasan, Synthesis (1992) 835.
[16] Our attempts to apply phenyl triflate in order to achieve arylation via cationic Pd-complexes were unsuccessful.

[17] (a) M. Rönn, P.G. Andersson, J.-E. Bäckvall, Tetrahedron Lett. 38 (1997) 3603. (b) R.A.T.M. van Bethem, H. Hiemstra, P.W.N.M. van Leeuwen, J.W. Geus, W.N.J. Speckamp, Angew. Chem. 107 (1995) 500503; Angew. Chem. Int. Ed. Engl. 34 (1995) 457. (c) R.C. Larock, T.R. Hightower, J. Org. Chem. 58 (1993) 5298. (d) R.C. Larock, T.R. Hightower, J. Org. Chem. 61 (1996) 3584.

[18] Phenylpalladium chloride was prepared in situ from lithium tetrachloropalladate (dried 2 h at 120°C in vacuo) and phenylmercuric acetate: H. Horino, M. Arai, N. Inoue, Tetrahedron Lett. (1974) 647.

[19] X-ray structure analysis: Siemens P4 four-circle diffractometer, Mo–K_α radiation ($\lambda = 0.71073$ Å), graphite monochromator, scintillation counter, 293 K, empirical absorption correction, SHELXTL and SHELXL93 programs, direct methods, full-matrix least-squares refinement on F^2 one scaling factor, one isotropic extinction parameter. $C_{20}H_{14}$; formula weight 254.31 g mol^{-1}, orthorhombic, space group $Pca2_1$, $a = 26.100(8)$, $b = 6.344(2)$, $c = 8.092(3)$ Å, $V = 1339.9(8)$ Å^3, $Z = 4$, ($\rho = 1.261$ g cm^{-3}, $\mu(\text{Mo–K}_\alpha) = 0.071$ mm^{-1}, transmission range 0.980–0.963, crystal dimensions ca. 0.45 × 0.30 × 0.25 nun, green blocks, ω–2θ-scans, $2\theta_{\max} = 50°$, 1300 unique reflections, $R_1(wR_2) = 0.0576(0.1568)$, 861 observed reflections for R_1 ($I > 2\sigma(I)$), 182 variables, GOF = 0.996, C-atoms anisotropic, H atoms at idealized positions.

[20] V.A. Nefedov, N.A. German, A.I. Lutsenko, G.I. Nikishin, J. Org. Chem. USSR 23 (1987) 154.

[21] T. Morita, K. Takase, Bull. Chem. Soc. Jpn. 55 (1982) 1144.