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First synthesis of bidentate NHC–Pd complexes with anthracene and xanthene skeletons

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Abstract—We synthesized a series of new bidentate NHC (N-heterocyclic carbene) precursors with anthracene and xanthene skeletons. The corresponding NHC–Pd complexes were prepared from these precursors. The catalytic activity of these Pd complexes was examined.

N-Heterocyclic carbenes (NHCs) derived from imidazolium salts and its derivatives have been widely employed as ligands for the synthesis of a number of NHC–Pd complexes.[1] Subsequently, the catalytic activity of the complexes was examined and some complexes turned out to be better alternative catalysts for the commonly employed phosphine–Pd catalysts. Various monodentate NHC–Pd complexes[1a–d] as well as Pd complexes with two tethered NHC moieties have been reported to date. As for the tethered NHC–Pd complexes, the two NHC components were connected with various functional groups such as methylene (ethylene) group (**A**),[2] binaphthyl group (**B**),[3] 2,6-dimethylenepyridyl group (**C**),[4–6] *m*-dimethylenephenyl group (**D**),[5,7] and so on (Fig. 1).[8] However, despite the observed unique properties of the xanthene-based diphosphine ligands in organometallic chemistry,[9,10] the corresponding bidentate NHC ligands with rigid anthracene or xanthene skeleton have not been reported. In this Letter we report the first synthesis of the bidentate NHC precursors with anthracene and xanthene skeletons. The corresponding NHC–Pd complexes were prepared, and the catalytic activity of the complexes was examined.

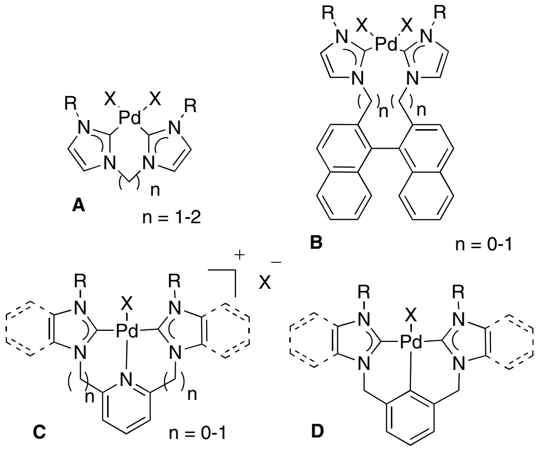

Figure 1. Examples of Pd catalysts with two tethered NHC moieties.

The results of the synthesis of a bidentate NHC–Pd complex (**6a**) with anthracene skeleton are summarized in Scheme 1. 1,8-Diiodoanthracene (**1**)[11] reacted with pinacolborane in the presence of Pd catalyst[12] to yield 1,8-bis(pinacolboryl)anthracene (**2**). Suzuki–Miyaura coupling[13] of **2** with 1-(4-iodophenyl)-1*H*-imidazole (**3**)[14] gave bisimidazole **4**, which was alkylated[15] to provide imidazolium salts **5a**–**b** in good yields. The bidentate NHC–Pd complex **6a**[16] was isolated in 66% yield by the palladation[17,18] of **5a** with Pd(OAc)$_2$. The methylated Pd NHC complex, however, was not isolated under similar reaction condition: the isolation (purification) of the product from the reaction mixture turned out to be extremely difficult due to the low solubility of the crude reaction mixture.

We also synthesized a series of bidentate NHC–Pd complexes (**12a**–**d**) with xanthene skeleton and the results are summarized in Scheme 2. By Ogino's method, disilylation of **7** was accomplished in high yield by the reaction of chlorotrimethylsilane with dilithiated xanthene.[19]

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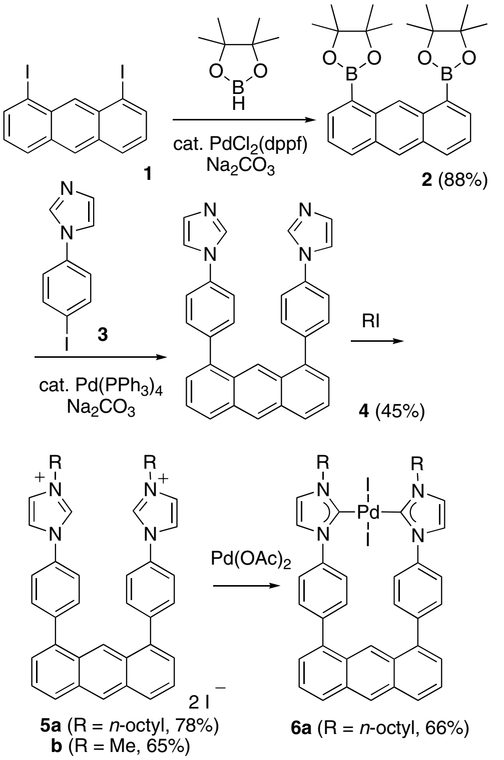
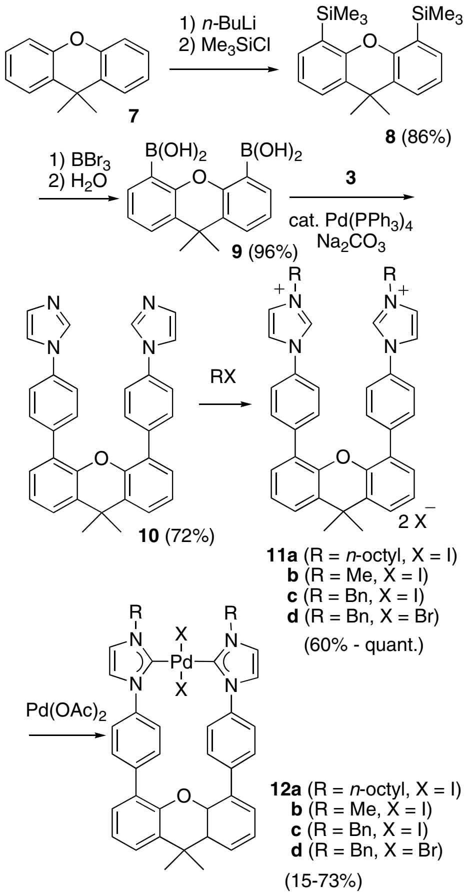


Scheme 1. Synthesis of a bidentate NHC–Pd complex (**6a**) with anthracene skeleton.

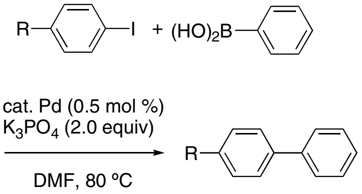
Subsequently, *ipso* substitution[20] of **8** with BBr_3 was carried out, and the hydrolysis of the bis(dibromoboryl) compound gave **9**. Suzuki–Miyaura coupling of bisboronic acid **9** with **3** gave **10**, which was alkylated and palladated to provide the corresponding Pd complexes **12a**–**d**.[21] Unlike the corresponding anthracene complex, methyl derivative **12b** was isolated without difficulty. The compounds were characterized by NMR and the monomeric structure of the complex was confirmed by an ESI-MS analysis of **12c**.[22]

The catalytic activity of these new Pd complexes for some reactions was examined. The results of Suzuki–Miyaura coupling reaction are summarized in Table 1. The reactions of various aryl iodides and phenylboronic acid were carried out in the presence of Pd catalyst (0.5 mol %) and K_3PO_4 (2.0 equiv) in DMF. The catalytic activity of the Pd complexes was compared by carrying out the reaction of 4-nitroiodobenzene with phenylboronic acid at 80 °C.[23] The catalytic activity of **6a** was much lower compared to other catalysts we examined, and the coupling product was isolated in low yield even after the reaction mixture was heated for 72 h (entry 1). On the other hand, the catalytic activity of the xanthene complexes with alkyl substituents (**12a**, **b**) was much higher: the reaction completed in 19 h, and the products were isolated in high yields (entries 2 and 3). The catalytic activity of **12c** was, however, much lower (entry 4). The results demonstrate that the catalytic activity of these complexes could be controlled by the bridging group (xanthene/anthracene skeleton) as well as the substituents bound to the NHC moiety.



Scheme 2. Synthesis of bidentate NHC–Pd complexes (**12a**–**d**) with xanthene skeleton.

Table 1. Palladium-catalyzed coupling reactions of aryl iodides with phenylboronic acid (Suzuki–Miyaura coupling)



Entry	R	Catalyst	Time (h)	Yield (%)
1	NO_2	**6a**	72	15
2	NO_2	**12a**	19	82
3	NO_2	**12b**	19	96
4	NO_2	**12c**	19	Trace
5	CH_3	**12b**	48	96
6	OCH_3	**12b**	19	86
7	CO_2CH_3	**12b**	32	96
8[a]	CO_2CH_3	**12b**	32	81

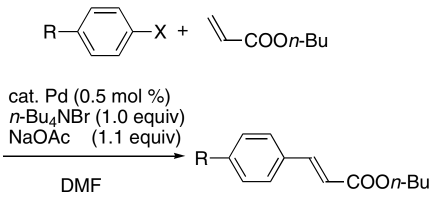
[a] A smaller amount (0.1 mol %) of **12b** was used.

Since **12b** was the most efficient catalyst, we examined the reactions of various iodoarenes with phenylboronic acid in the presence of **12b**. The reactions of electron-rich iodoarenes such as 4-iodotoluene and 4-iodoanisole, as well as ethyl 4-iodobenzoate proceeded smoothly and the corresponding biphenyls were isolated in high yields (entries 5–7). The reaction of ethyl 4-iodobenzoate proceeded even in the presence of 0.1 mol % of **12b**, and the product was isolated in 81% yield (entry 8).[24]

We next examined Mizoroki–Heck reaction of various aryl halides and *n*-butyl acrylate, and the results are summarized in Table 2. The reactions were carried out in the presence of Pd catalyst (0.5 mol %), Bu_4NBr (1.0 equiv), and NaOAc (1.1 equiv) in DMF.[25,26] Compared to Suzuki–Miyaura reaction, higher temperature (120 °C) was required for the Mizoroki–Heck reaction. The anthracene complex **6a** turned out to be a good catalyst for the reaction of 4-iodonitrobenzene with *n*-butyl acrylate, and the product was isolated in 92% yield (entry 1). Moreover, the catalytic activity of xanthene complexes was much higher, and the reactions completed in shorter periods (entries 2–5). It is noteworthy that the benzyl derivatives were also efficient catalysts for this reaction (entries 4 and 5, see also Table 1, entry 4). The reactions of various iodoarenes were examined in the presence of **12b** and the corresponding esters were isolated in good yields (entries 6–8). The observed substituent effects on the reactivity of the iodoarenes were in accordance with those reported in Table 1, and similar results were also reported in general: electron-deficient haloarenes were more reactive. The reactions of a bromoarene proceeded at 140 °C, while the reaction of 4-chloronitrobenzene was very slow (entries 9 and 10).[27]

In summary, we synthesized new bidentate NHC precursors with anthracene and xanthene skeletons and prepared a series of bidentate NHC–Pd complexes. The catalytic activity of the complexes for Mizoroki–Heck reactions and Suzuki–Miyaura coupling was examined. The bidentate NHC precursors prepared in this study could be utilized for the synthesis of various bidentate NHC–metal complexes. The study of the detailed structure of the complexes, as well as the examination of the catalytic activity of related complexes, is on going.

Table 2. Palladium-catalyzed coupling reactions of aryl halides with *n*-butyl acrylate (Mizoroki–Heck reaction)



Entry	R	X	Catalyst	Temperature (°C)	Time (h)	Yield (%)
1	NO_2	I	**6a**	120	26	92
2	NO_2	I	**12a**	120	16	80
3	NO_2	I	**12b**	120	16	92
4	NO_2	I	**12c**	120	16	91
5	NO_2	I	**12d**	120	16	92
6	CH_3	I	**12b**	120	22	83
7	OCH_3	I	**12b**	120	40	85
8	CO_2CH_3	I	**12b**	120	16	76
9	NO_2	Br	**12b**	140	17	70
10	NO_2	Cl	**12b**	140	48	7

Acknowledgment

We thank Professor Shinji Toyota (Okayama University of Science) for providing the detailed procedures for the synthesis of **1**.

Supplementary data

Experimental details for the synthesis of **2**, **4**–**6** and **8**–**12** and spectral data of the compounds. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.08.064.

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16. Compound **6a**: A gray solid; mp 271–274 °C; ^{1}H NMR (270 MHz, $CDCl_3$) 8.89 (s, 1H), 8.55 (s, 1H), 8.07–8.04 (d, $J = 8.4$ Hz, 2H), 7.96–7.93 (d, $J = 8.1$ Hz, 4H), 7.65–7.62 (d, $J = 8.1$ Hz, 4H), 7.57–7.51(t, $J = 8.1$ Hz, 2H), 7.42–7.40 (d, $J = 5.9$ Hz, 2H), 7.13–7.12 (d, $J = 1.9$ Hz, 2H), 7.10–7.09 (d, $J = 1.6$ Hz, 2H), 4.73–4.67 (t, $J = 7.7$ Hz, 4H), 2.20–2.09 (qui, $J = 7.7$ Hz, 4H), 1.53–1.23 (m, 20H), 0.92–0.87 (t, $J = 6.8$ Hz, 6H); ^{13}C NMR (150 MHz, DMSO-d_6) 162.4, 160.7, 137.8, 137.1, 129.9, 129.2, 127.1, 126.4, 124.7, 124.2, 123.1, 122.0, 121.4, 49.3, 34.2, 29.7, 27.9, 27.4, 27.1, 24.9, 20.6, 12.4; IR (KBr) 2923, 2852, 2360, 1669, 1513, 1455, 1421, 1266, 842, 747, 695, 419 cm^{-1}. Anal. Calcd for $C_{48}H_{56}I_2N_4OPd$: C, 54.95; H, 5.38; N, 5.34. Found: C, 54.93; H, 5.14; N, 5.55.
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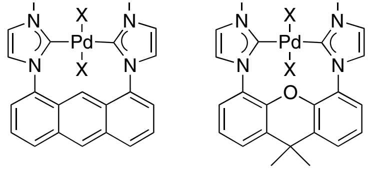
21. *Selected analytical data*: Compound **12b**: Mp >300 °C; ^{1}H NMR (270 MHz, $CDCl_3$) 7.72–7.69 (d, $J = 8.6$ Hz, 4H), 7.59–7.55 (d, $J = 8.6$ Hz, 4H), 7.44–7.40 (q, $J = 3.2$ Hz, 2H), 7.14–7.12 (m, 4H), 7.02–7.01 (d, $J = 2.2$ Hz, 2H), 6.98–6.97 (d, $J = 1.9$ Hz, 2H), 4.09 (s, 6H), 1.68 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) 167.7, 147.8, 138.9, 137.7, 131.3, 130.4, 130.1, 128.6, 125.2, 125.1, 123.4, 123.1, 122.9, 39.0, 34.6, 31.8; IR (KBr) 2923, 2852, 1519, 1469, 1433, 1395, 1216, 841, 790, 745, 696 cm^{-1}. Anal. Calcd for $C_{35}H_{34}I_2N_4OPd$: C, 47.40; H, 3.86; N, 6.32. Found: C, 47.20; H, 3.57; N, 6.25. Compound **12c**: Mp >300 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 7.80–7.78 (d, $J = 8.6$ Hz, 4H), 7.66–7.63 (d, $J = 8.6$ Hz, 4H), 7.57–7.54 (m, 4H), 7.49–7.46 (q, $J = 2.8$ Hz, 2H), 7.35–7.33 (d, $J = 6.4$ Hz, 6H), 7.21–7.19 (m, 4H), 7.04–7.03 (d, $J = 1.9$ Hz, 2H), 6.74–6.73 (d, $J = 1.9$ Hz, 2H), 5.77 (s, 4H), 1.73 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) 167.4, 147.8, 139.0, 137.6, 135.2, 131.3, 130.3, 130.0, 129.5, 128.8, 128.5, 128.4, 125.3, 125.2, 123.4, 121.1, 55.3, 34.6, 31.7; IR (KBr) 2924, 1731, 1520, 1470, 1432, 1393, 1280, 1215, 839, 792, 753, 725, 701 cm^{-1}; HR-MS (ESI) Calcd for $C_{47}H_{38}I_2N_4OPdNa$ ($[M+Na]^+$): 1057.0079. Found: 1057.0051.
22. The attempted synthesis of the following Pd complexes failed since the palladation of the corresponding imidazolium salts did not proceed. The details will be reported in due course.



23. Lower catalytic activity of **12b** was observed when aryl bromides or chlorides were used as the substrate.
24. *General procedure for Suzuki–Miyaura reaction*: A mixture of Pd complex (0.5 mol %), K_3PO_4 (424 mg, 2.0 mmol), aryl halide (1.0 mmol), and phenylboronic acid (183 mg, 1.5 mmol) in DMF (4 mL) was heated under Ar, and the course of the reaction was monitored by GC. After the reaction completed, the mixture was extracted with Et_2O, and the organic layer was dried over $MgSO_4$. The filtrate was concentrated and the residue was purified by column chromatography.
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26. *General procedure for Mizoroki–Heck reaction:* To a mixture of Pd complex (0.5 mol %), aryl halide (1.0 mmol), AcONa (90 mg, 1.1 mmol) and tetra-*n*-butylammounium bromide (322 mg, 1.0 mmol) in DMF (4 mL) was added *n*-butylacrylate (0.20 mL, 1.4 mmol), and the mixture was heated under Ar. The mixture was worked up as described for the Suzuki–Miyaura reaction.
27. It should be noted that the Pd black formed by the decomposition of the NHC–Pd complexes at high temperature (120–140 °C) could be the true catalytic species.