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Novel hexadentate imidazolium salts in the rhodium-catalyzed addition of arylboronic acids to aldehydes

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Abstract

Four novel hexadentate imidazolium salts were synthesized from hexakis(bromomethyl)benzene and 1-substituted imidazole. The arylation of aldehydes with arylboronic acids was effected conveniently and in high yields by a catalyst system generated in situ from these hexadentate imidazolium salts, $[Rh(COD)Cl]_2$ and a base.

Keywords: Imidazolium salts; N-heterocyclic carbene; Aldehyde; Arylation; Rhodium

1. Introduction

In the last decade much attention has been paid to N-heterocyclic carbenes (NHCs) and their transition metal complexes because NHCs are easily generated from the corresponding imidazolium salts and have been employed with considerable success in various catalytic transformations [1]. Multi-coordinate transition metal complexes with multidentate ligands are known to provide powerful platforms for small molecule activation and functionalization [2,3]. However, only a few examples of multidentate NHC ligands and/or their transition metal complexes have been reported in the literature [4–11]. Among those multidentate NHC–transition metal complexes, so far just one type of tetradentate NHC–palladium complex has been used as catalyst for organic transformation [9].

Diarylmethanols are important intermediates for the synthesis of biologically and pharmaceutically active substances [12–14]. The addition of organometallic reagents to aldehydes has been one of the general methods for the synthesis of diarylmethanols. Of those organometallic reagents, organolithium and organomagnesium compounds are most frequently used for this purpose, but tolerate only a few electrophilic groups on themselves [15–18]. Examples of using other functionalized organometallic species [19–23] such as organocopper, organochromium, organotin, especially organozinc, have been described. However, these organometallic reagents are usually toxic and sensitive to air and moisture. The progress that has been achieved by recent publications describing the addition of arylboronic acid derivatives to aldehydes in the presence of catalytic amounts of Rh(I) and phosphine, nitrogen [24–27], especially NHC ligands [28–32] deserve particular mention. These methods present high efficiency with a reasonable tolerance towards polar substituents in the substrates and benefit from the stability and ready accessibility of the nontoxic boron derivatives. It is believed that the reaction involves a transmetallation of the boronic acid with formation of an organorhodium(I) species which is nucleophilic enough to transfer its aryl substituent to an aldehyde.

The above findings and our interests in NHCs and C–C formation reactions triggered our efforts to develop novel multidentate imidazolium salt as NHC ligand precursor for application in homogeneous catalysis. We now would like to report the straightforward synthesis of unprecedented hexadentate imidazolium salts and the efficiency

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of catalysts prepared in situ from them and $[Rh(COD)Cl]_2$ for the addition of arylboronic acids to aldehydes.

2. Results and discussion

2.1. Synthesis of hexadentate imidazolium salts

The four novel hexadentate imidazolium salts presented in Scheme 1 were prepared readily by refluxing hexakis(bromomethyl)benzene with 1-substituted imidazoles in THF in 90–96% yields. 1-Phenylimidazole, 1-(*p*-methylphenyl)imidazole, 1-mesitylimidazole were prepared according to the literature procedure [33].

2.2. Catalysis of NHC–rhodium complexes

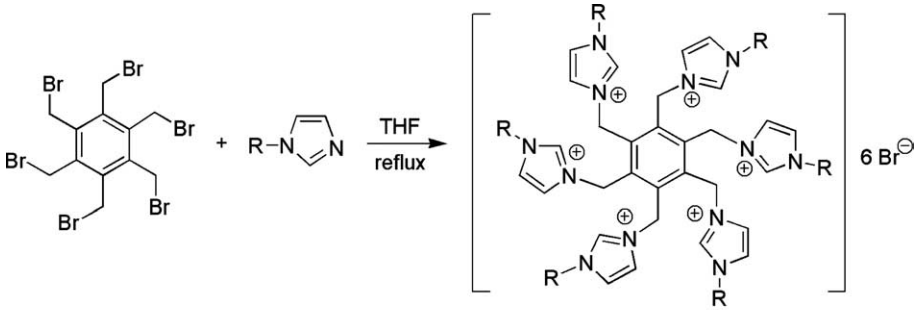
A combination of the ligand precursor **4** (1 mol%) with $[Rh(COD)Cl]_2$ (0.5 mol%) was first tested as a catalyst for the addition of phenylboronic acid to *p*-chlorobenzaldehyde in dimethoxyethane (DME)–H_2O (4:1) solution using KOBu-*t* as a base (Scheme 2). After refluxing for 16 h, the corresponding secondary alcohol was obtained in 21% yield (Table 1, entry 3). We then examined the influence of the molar ratio of imidazolium salt to $[Rh(COD)Cl]_2$. As can be seen, $[Rh(COD)Cl]_2$ (1.5 mol%) bearing ligand **4** gave excellent result, whereas the other molar ratio of $[Rh(COD)Cl]_2$ to **4** turned out to be less efficient (Table 1, entries 3–6). $[Rh(COD)Cl]_2$ alone did not exhibit any catalytic activity (Table 1, entry 2). Therefore, 3 mol of rhodium ligated 1 mol of NHC might be the possible pathway. However, we failed to isolate the active species. $RhCl_3 \cdot 3H_2O$ did not show any catalytic activity in this reaction under similar conditions (Table 1, entry 1).

We surveyed various other solvents such as H_2O, THF–H_2O, 1,4-dioxane–H_2O and *n*-BuOH–H_2O in 4:1 volume ratio for the reaction. As can be seen from Table 1, use of 1,4-dioxane–H_2O resulted in the highest yield (entry 9 versus entries 5, 7, 8, 10). This screening has also revealed that ether is better solvent in catalyzing the addition reaction and *n*-butyl alcohol showed inappreciable activity (entry 10). When water was used solely, the yield was depressed (Table 1, entry 7). This may be attributed to the poor solubility of the reactants in water.

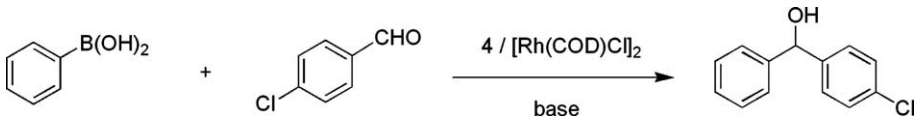
In order to indicate the base effect on the reaction, we changed the base to cesium carbonate and potassium hydroxide. Cesium carbonate resulted in low yield. Potassium hydroxide gave excellent yield but lower than potassium *t*-butoxide. When we doubled the amount of potassium *t*-butoxide, the addition yield increased to 95% (Table 1, entry 11). It is likely that the strong base can generate the NHC in situ by deprotonation of imidazolium salt **4** and enhance the catalyst activity.

The activity evaluation of ligand precursors **1**–**4** was carried out in 1,4-dioxane–H_2O with 2 equiv. of potassium *t*-butoxide. As can be seen from Table 1, all of the four hexadentate imidazolium salts in combination with $[Rh(COD)Cl]_2$ showed efficient catalytic activity in the addition reaction of phenylboronic acid to *p*-chlorobenzaldehyde. The imidazolium salt **4** bearing bulky substituent on its N-atom gave the best yield. However, the catalytic activity is not so sensitive to the steric hindrance of the substituent attached on the N-atom. Even the N-methyl-substituted **1** demonstrated excellent catalytic efficiency, which is not in accord with the case of monodentate NHC–rhodium complex [28].

Table 2 summarizes the **4**/$[Rh(COD)Cl]_2$-catalyzed addition of arylboronic acids to various aldehydes. The results reveal the wide scope of this method that is compatible with nitro, cyano, methoxy, chloro in aldehydes. *p*-Chlorobenzaldehyde, *p*-nitrobenzaldehyde and heliotropin



Scheme 1. Syntheses of hexadentate imidazolium salts.



Scheme 2. Addition of phenylboronic acid to *p*-chlorobenzaldehyde.

Table 1
Addition of phenylboronic acid to 4-chlorobenzaldehyde catalyzed by the NHC–Rh complex[a]

Entry	Imidazolium salt	Metal salt	Solvent	Base	Yield (%)
1	**4**	$RhCl_3 \cdot 3H_2O$[b]	DME–H_2O	KOBu-*t*	0
2	–	$[Rh(COD)Cl]_2$	DME–H_2O	KOBu-*t*	0
3	**4**	$[Rh(COD)Cl]_2$[c]	DME–H_2O	KOBu-*t*	21
4	**4**	$[Rh(COD)Cl]_2$[d]	DME–H_2O	KOBu-*t*	31
5	**4**	$[Rh(COD)Cl]_2$	DME–H_2O	KOBu-*t*	70
6	**4**	$[Rh(COD)Cl]_2$[e]	DME–H_2O	KOBu-*t*	41
7	**4**	$[Rh(COD)Cl]_2$	H_2O	KOBu-*t*	58
8	**4**	$[Rh(COD)Cl]_2$	THF–H_2O	KOBu-*t*	36
9	**4**	$[Rh(COD)Cl]_2$	1,4-dioxane–H_2O	KOBu-*t*	76
10	**4**	$[Rh(COD)Cl]_2$	*n*-BuOH–H_2O	KOBu-*t*	<5
11	**4**	$[Rh(COD)Cl]_2$	1,4-dioxane–H_2O	KOBu-*t*[f]	95
12	**4**	$[Rh(COD)Cl]_2$	1,4-dioxane–H_2O	Cs_2CO_3[f]	26
13	**4**	$[Rh(COD)Cl]_2$	1,4-dioxane–H_2O	KOH[f]	89
14	**1**	$[Rh(COD)Cl]_2$	1,4-dioxane–H_2O	KOBu-*t*[f]	81
15	**2**	$[Rh(COD)Cl]_2$	1,4-dioxane–H_2O	KOBu-*t*[f]	90
16	**3**	$[Rh(COD)Cl]_2$	1,4-dioxane–H_2O	KOBu-*t*[f]	86

[a] All reactions were carried out using metal salt (1.5 mol%), imidazolium salt (1 mol%), and a base (1 equiv. to the aldehyde) in mixture solvent (V:V = 4:1) at 80 °C for 16 h in argon unless stated otherwise. Yields represent isolated yield based on *p*-chlorobenzaldehyde.
[b] 3 mol% $RhCl_3 \cdot H_2O$.
[c] 0.5 mol% $[Rh(COD)Cl]_2$.
[d] 1 mol% $[Rh(COD)Cl]_2$.
[e] 3 mol% $[Rh(COD)Cl]_2$.
[f] 2 equiv. of base to aldehyde were used.

reacted very cleanly with various arylboronic acids in excellent yields (Table 2, entries 2, 3, 6–10).

3. Experimental

3.1. General

Reactions were carried out under argon to exclude oxygen from the reaction systems. The complex $[Rh(COD)Cl]_2$ [34] and hexakis(bromomethyl)benzene [35] were prepared according to the literature methods. All other reagents were used as they were received without any purification unless noted otherwise. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded on a Varian INOVA 400 MHz NMR spectrometer. Mass spectra were obtained by using Bruker Daltonics Data Analysis 3.2.

3.2. Procedure for the preparation of hexadentate imidazolium salts

1-Substituted imidazole (13.2 mmol) and hexakis(bromomethyl)benzene (2 mmol) were stirred in THF (15 ml) at reflux for 24–48 h. The precipitate was filtered and washed with dry THF (3 × 15 ml) to afford the product as a white powder. Pure sample was obtained after recrystallization from an appropriate solvent.

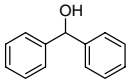
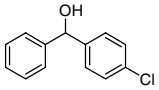
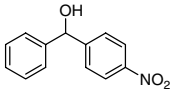
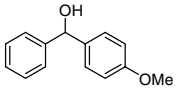
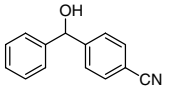
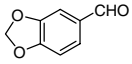
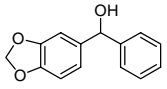
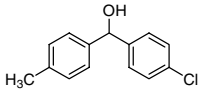
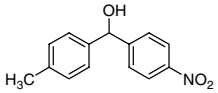
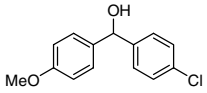
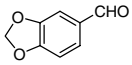
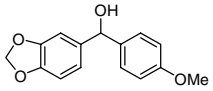
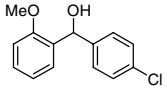
Hexakis[(3-methylimidazolio)methyl]benzene hexabromide (**1**): yield: 96%. m.p. 160–163 °C (ethanol). ^1H NMR (400 MHz, DMSO-d_6): $\delta = 9.32$ (s, 6H, NCHN), 7.78 and 7.66 (s, 2 × 6H, NCHCHN), 5.78 (s, 12H, NCH_2), 3.84 (s, 18H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 138.6$, 136.9, 123.1, 122.8, 47.5, 35.9. HRMS (ESI): *m*/*z* calcd for $C_{36}H_{48}Br_5N_{12}$ $[M - Br]^+$: 1043.0042. Found 1043.0036.

Hexakis[(3-phenylimidazolio)methyl]benzene hexabromide (**2**): yield: 93%. m.p. 248–250 °C (methanol). ^1H NMR (400 MHz, DMSO-d_6): $\delta = 9.89$ (s, 6H, NCHN), 8.31 and 8.27 (s, 2 × 6H, phenyl-CH), 7.87 (s, 12H, NCHCHN), 7.54–7.50 (m, 18H, phenyl-CH), 6.10 (s, 12H, NCH_2). ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 138.8$, 135.6, 134.4, 130.0, 124.2, 122.3, 120.6, 48.8. HRMS (ESI): *m*/*z* calcd for $C_{66}H_{60}Br_4N_{12}$ $[M - 2Br]^{2+}$: 668.0899. Found 668.0893.

Hexakis{[3-(*p*-methylphenyl)imidazolio]methyl} benzene hexabromide (**3**): yield: 95%. m.p. 255–257 °C (methanol). ^1H NMR (400 MHz, DMSO-d_6): $\delta = 9.80$ (s, 6H, NCHN), 8.26 and 8.21 (s, 2 × 6H, phenyl-CH), 7.71 and 7.70 (s, 2 × 6H, NCHCHN), 7.30 and 7.28 (s, 2 × 6H, phenyl-CH), 6.06 (s, 12H, NCH_2), 2.38 (s, 18H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 139.7$, 138.8, 135.2, 132.0, 130.3, 124.1, 122.0, 120.7, 48.7, 20.7. HRMS (ESI): *m*/*z* calcd for $C_{72}H_{72}Br_4N_{12}$ $[M - 2Br]^{2+}$: 710.1368. Found 710.1363.

Hexakis{[3-(2,4,6-trimethylphenyl)imidazolio]methyl} benzene hexabromide (**4**): yield: 90%. m.p. 262–263 °C (methanol). ^1H NMR (400 MHz, DMSO-d_6): $\delta = 9.77$ (s, 6H, NCHN), 8.09 and 7.99 (s, 2 × 6H, NCHCHN), 7.10 (s, 12H, phenyl-CH), 6.14 (s, 12H, NCH_2), 2.32 (s, 18H, CH_3), 2.07 (s, 36H, CH_3). ^{13}C NMR (100 MHz, DMSO) $\delta = 140.4$, 139.1, 138.1, 134.9, 131.2, 129.4, 123.8, 123.0, 48.4, 20.8, 18.2. HRMS (ESI): *m*/*z* calcd for $C_{84}H_{96}Br_4N_{12}$ $[M - 2Br]^{2+}$: 794.2307. Found 794.2302.

Table 2
The **4**/[Rh(COD)Cl]$_2$-catalyzed addition of arylboronic acids to various aldehydes[a]

Entry	Boronic acid	Aldehyde	Product	Time (h)	Yield (%)
1	$C_6H_5B(OH)_2$	C_6H_5CHO		19	89
2		*p*-Cl-C_6H_5CHO		16	95
3		*p*-NO_2-C_6H_5CHO		16	95
4		*p*-MeO-C_6H_5CHO		24	81
5		*p*-CN-C_6H_5CHO		17	88
6				16	99
7	*p*-Me-$C_6H_4B(OH)_2$	*p*-Cl-C_6H_5CHO		16	94
8		*p*-NO_2-C_6H_5CHO		16	95
9	*p*-MeO-$C_6H_4B(OH)_2$	*p*-Cl-C_6H_5CHO		16	95
10				16	96
11	*o*-MeO-$C_6H_4B(OH)_2$	*p*-Cl-C_6H_5CHO		16	86

[a] All reactions were carried out using [Rh(COD)Cl]$_2$ (1.5 mol%), imidazolium salt **4** (1 mol%), and KOBu-*t* (2 equiv.) in 1,4-dioxane–H_2O (V:V = 4:1) at 80 °C in argon unless stated otherwise. The reaction was monitored by TLC. Yields represent isolated yield based on aldehyde.

3.3. Representative procedure for NHC–rhodium complex catalyzed addition of arylboronic acids to aldehydes (Table 1, entry 11)

To 1,4-dioxane (40 ml) were introduced phenylboronic acid (2.39 g, 19.6 mmol), KOBu-*t* (1.10 g , 9.8 mmol), *p*-chloroaldehydes (0.69 g, 4.9 mmol), [Rh(COD)Cl]$_2$ (0.036 g, 0.075 mmol), imidazolium bromide **4** (0.086 g, 0.049 mmol), and then water (10 ml) was added. The resulting mixture was heated for 16 h at 80 °C in argon. The solvent was evaporated under reduced pressure. The residue was dissolved in ethyl acetate (50 ml) and washed with water. After dried over $MgSO_4$, the organic phase was evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate, 10/1) to afford the corresponding alcohol as a colorless syrup that slowly crystallized upon standing at room temperature (1.03 g, 95%).

4. Conclusion

In conclusion, a new type of NHC precursor, hexadentate imidazolium bromide was readily synthesized in high yields. The catalyst system generated in situ from the hexadentate imidazolium salts and [Rh(COD)Cl]$_2$ disclosed herein represents an easy to handle and high yielding procedure for the addition of arylboronic acids to aldehydes. The result of this research was the first observation that the addition of arylboronic acids to aldehydes was effected by multidentate NHC–rhodium complexes.

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References

[1] W.A. Herrmann, Angew. Chem. Int. Ed. 41 (2002) 1290, and references cited therein.
[2] D.M. Jenkins, T.A. Betley, J.C. Peters, J. Am. Chem. Soc. 124 (2002) 11238.
[3] L.H. Gade, Acc. Chem. Res. 35 (2002) 575.
[4] H.V.R. Dias, W. Jin, Tetrahedron Lett. 35 (1994) 1365.
[5] U. Kernbach, M. Ramm, P. Luger, W.P. Fehlhammer, Angew. Chem. Int. Ed. 35 (1996) 310.
[6] R. Frankel, C. Birg, U. Kernbach, T. Habereder, H. Noth, W.P. Fehlhammer, Angew. Chem. Int. Ed. 40 (2001) 1907.
[7] H. Nakai, Y. Tang, P. Gantzel, K. Meyer, Chem. Commun. (2003) 24.
[8] X. Hu, I. Castro-Rodriguez, K. Meyer, J. Am. Chem. Soc. 125 (2003) 12237.
[9] Y. Zhao, Y. Zhou, D. Ma, J. Liu, L. Li, T.Y. Zhang, H. Zhang, Org. Biomol. Chem. 1 (2003) 1643.
[10] X. Hu, Y. Tang, P. Gantzel, K. Meyer, Organometallics 22 (2003) 612.
[11] X. Hu, I. Castro-Rodriguez, K. Meyer, Organometallics 22 (2003) 3016.
[12] K. Meguro, M. Aizawa, T. Sohda, Y. Kawamatsu, A. Nagaoka, Chem. Pharm. Bull. 33 (1985) 3787.
[13] F. Tada, K. Tanaka, K. Koshiro, Tetrahedron: Asymmetry 2 (1991) 873.
[14] M. Botta, V. Summa, F. Corelli, G. DiPietro, P. Lombardi, Tetrahedron: Asymmetry 7 (1996) 1263.
[15] A. Fürstner, H. Brunner, Tetrahedron Lett. 37 (1996) 7009.
[16] A. Fürstner, Chem. Rev. 99 (1999) 991.
[17] A. Boudier, L.O. Bromm, M. Lotz, P. Knochel, Angew. Chem. Int. Ed. 39 (2000) 4414.
[18] C. Bolm, J. Rudolph, J. Am. Chem. Soc. 124 (2002) 14850.
[19] B. Weber, D. Seebach, Tetrahedron 50 (1994) 7473.
[20] R. Noyori, M. Kitamura, Angew. Chem. Int. Ed. 30 (1991) 49.
[21] K. Soai, S. Niwa, Chem. Rev. 92 (1992) 833.
[22] P.I. Dosa, J.C. Ruble, G.C. Fu, J. Org. Chem. 62 (1997) 444.
[23] C. Bolm, N. Hermanns, J.P. Hildebrand, K. Muñiz, Angew. Chem. Int. Ed. 39 (2000) 3465.
[24] M. Sakai, M. Ueda, N. Miyaura, Angew. Chem. Int. Ed. 37 (1998) 3279.
[25] M. Ueda, N. Miyaura, J. Organoment. Chem. 595 (2000) 31.
[26] C. Moreau, C. Hague, A.S. Weller, C.G. Frost, Tetrahedron Lett. 42 (2001) 6957.
[27] R.A. Batey, A.N. Thadani, D.V. Smil, Org. Lett. 1 (1999) 1683.
[28] A. Fürstner, H. Krause, Adv. Synth. Catal. 343 (2001) 343.
[29] I. Özdemir, S. Demir, J. Mol. Catal. 215 (2004) 45.
[30] N. Imlinger, M. Mayr, D. Wang, K. Wurst, M.R. Buchmeiser, Adv. Synth. Catal. 346 (2004) 1836.
[31] T. Focken, J. Rudolph, C. Bolm, Synthesis (2005) 429.
[32] W. Zhang, Y. Qin, S. Zhang, M. Luo, ARKIVOC 14 (2005) 39.
[33] M.C. Perry, X. Cui, M.T. Powell, D.-R. Hou, J.H. Reibenspies, K. Burgess, J. Am. Chem. Soc. 125 (2003) 113.
[34] J. Chatt, L.M. Venanzi, J. Chem. Soc. (1975) 4735.
[35] J. Závada, M. Pánková, P. Holý, M. Tichý, Synthesis (1994) 1132.