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Direct arylation of heteroaromatic compounds by $Pd(OAc)_2$/tetrakis(*N*-benzimidazoliummethyl)benzene salt system

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Dedicated to C. Bruneau for his outstanding contribution to organometallic chemistry and catalysis

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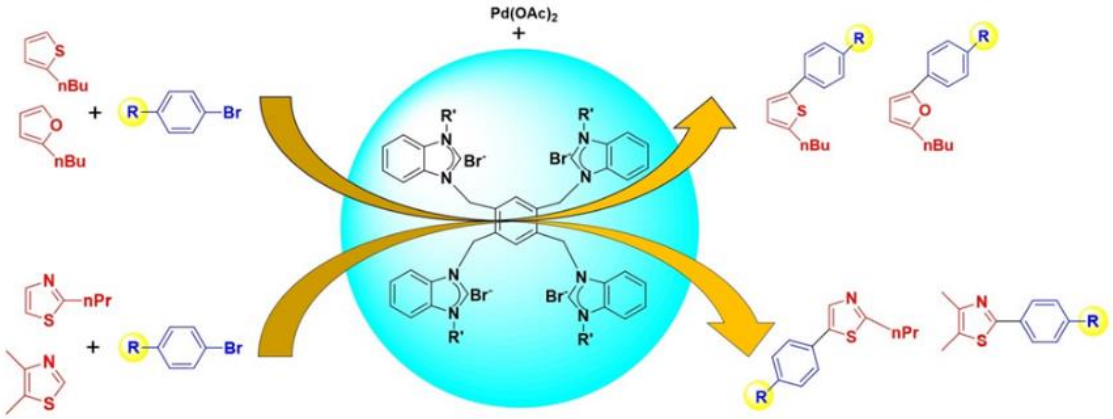
Abstract

Six novel tetrakis(*N*-benzimidazoliummethyl)benzene salts were synthesized using 1,2,4,5-tetrakis-(bromomethyl)benzene with 1-alkylbenzimidazole. The structures of all isolated compounds were elucidated based on spectroscopic methods (^{1}H and ^{13}C NMR, and FT-IR spectroscopy) and were investigated for their catalytic activities in the direct arylation of 2-n-propylthiazole, 2-n-buthyltiophene, 2-n-butylfuran, and 4,5-dimethylthiazole. All synthesized salts showed high catalytic activity for direct arylation of heteroaromatic compounds.



Keywords: Palladium, catalytic activity, direct arylation, *N*-heterocyclic carbene

Introduction

The discovery of N-heterocyclic carbenes (NHCs) as a unique ligand for transition metals is one of the most important advances for both organometallic chemistry and catalysis.[1,2,3] The strong σ-donor and weak π-acceptor binding properties of these ligands allow them to form more stable compounds with metals compared to their phosphine analogs. In addition, NHC ligands have less tendency to leave the metal center than phosphines, which interrupts the cocatalyst deactivation/decomposition pathways. In the 1960s, earlier studies by Wanzlick[4] and Ofele,[5] and then, synthesis of the first stable carbene by Arduengo[6] in 1991 led to an increase of experimental studies of novel NHCs. The intensive interest in NHCs has led to the parallel development of poly-NHCs[7-13] bearing bis-, tris-, tetra, and hexa ligands as well as mono-NHCs.[14,15] The use of poly-NHCs as chelating or bridging ligands provides more stability to the resulting metal complex and allows the synthesis of polynuclear complexes due to the robustness of metal-carbene interaction.[16-19]

The investigation of poly-NHCs leads not only to the preparation of their metal complexes but also applications in catalysis (cross coupling reactions,[20,21] C-H activation and functionalization,[22] hydrogenation,[23] allylation[24] e.g.), medicinal chemistry,[25,26] and photophysics.[27,28] The first example regarding poly-NHC catalyzed reaction had been published by Hermann's group in 1995.[29] From then on, many studies were reported about poly-NHCs and their catalytic activities in cross-coupling reactions,[20,21] C-H activation,[22] or direct arylation reactions.[30]

The cross coupling reactions such as Suzuki-Miyaura, Mizoroki-Heck, Sonogashira, Hiyama, and Kumada-Tamao-Corriu have been generally used for the formation of carbon-carbon bonds. The use of organometallic partners and the formation of by-products in these reactions has resulted in palladium-catalyzed direct C-H bond arylation during the past decades. Particularly, direct arylation of heteroaromatics attracted the researcher's attention due to their biological and physical properties.[31,32] In 1990 it was reported that Otha's group achieved good yields by direct arylation (C2- or C5-) of heteroaromatics with aryl bromides to yield the corresponding aromatic heterocycles using Pd catalyst. After these amazing results, palladium catalyzed direct arylation of assorted heteroaromatics with aryl halides has become an efficient method for the synthesis of various heteroaryls.[34-38] Additionally, our group has reported various studies about direct arylation of heteroaromatics catalyzed by Pd-NHC complexes.[39-44]

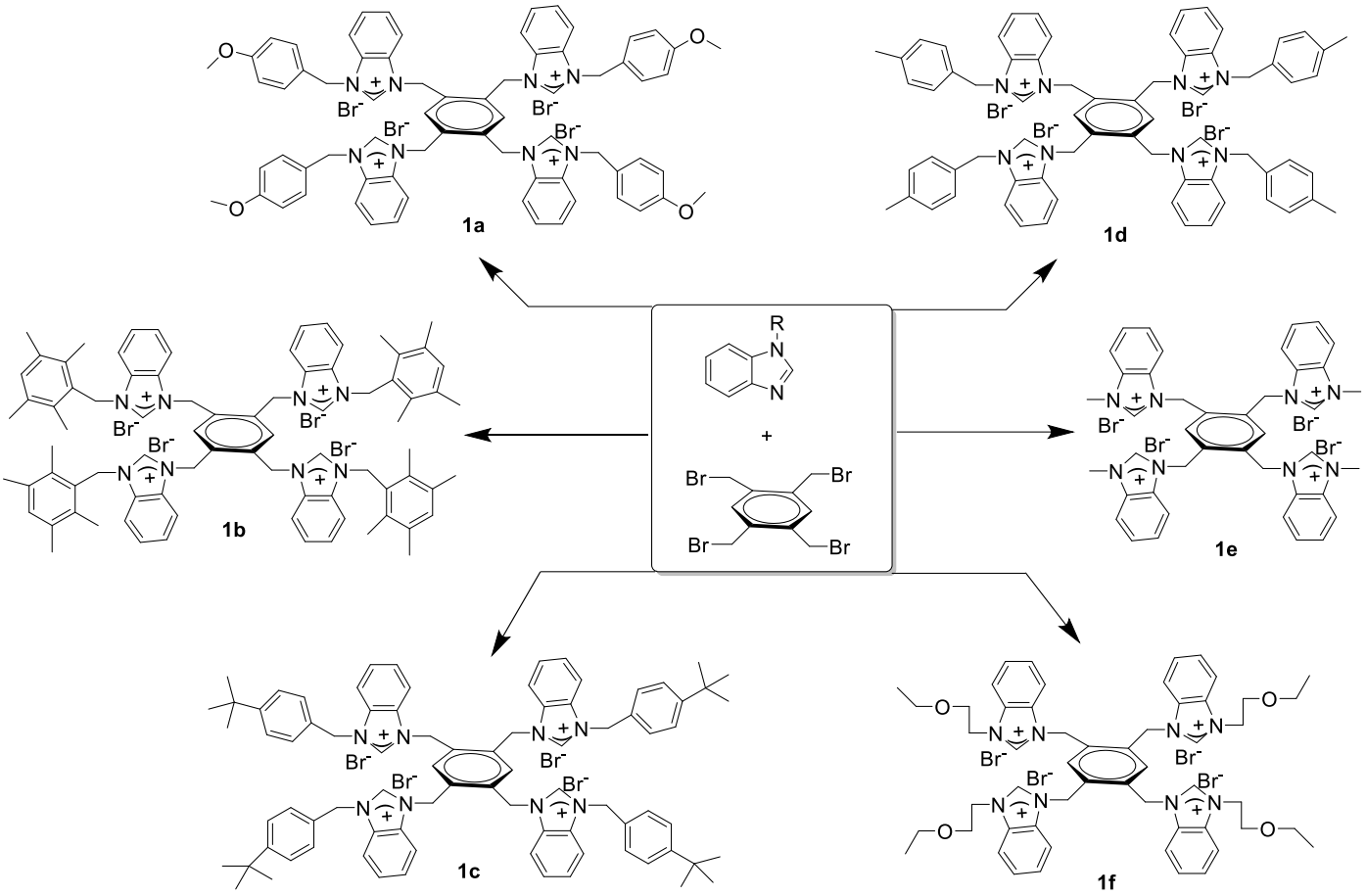
In the current work, we prepared six novel tetrakis(N-benzimidazoliummethyl)benzene salts (**1a-1f**) using 1,2,4,5-tetrakis(bromomethyl)benzene with 1-alkylbenzimidazole. After that, we investigated the *in situ* generated catalytic system using $Pd(OAc)_2$ as the palladium source and the tetrakis(N-benzimidazoliummethyl)benzene salts **(1a-1f)** as a carbene precursor for direct C2- and C5-arylation of heteroaromatics. The catalytic activities of these salts in the direct arylation of 2-n-propylthiazole, 2-n-butylthiophene, 2-n-butylfuran, and 4,5-dimethylthiazole were tested and the synthesized salts showed high catalytic activity.

Results and Discussion

Synthesis of 2,3,5,6-tetrakis(*N*-benzimidazoliummethyl) salts

2,3,5,6-tetrakis(*N*-benzimidazoliummethyl) salts were synthesized according to the literature.[24] The reaction of 2,3,5,6-tetrakis(bromomethyl)benzene with 1-alkylbenzimidazole in DMF at 80 °C for 12 h gave the corresponding salts (**1a-1f**) as shown in Scheme 1. The new tetraazolium salts (**1a-f**) were obtained with higher yields (79-93%). The *N*-heterocyclic carbene precursors stable to air and moisture are soluble in polar solvents

such as ethanol, dichloromethane, and dimethylformamide. The structure of these salts was elucidated with ^{1}H and ^{13}C NMR, and FT-IR spectroscopies. The ^{1}H NMR spectroscopy shows that the NCHN proton of the benzimidazolium salts appeared between 9.43-10.28 ppm. Additionally, the ^{13}C NMR reveals that the values for C(2) carbon are between 159.9-163.0 ppm. All data for these salts are compatible with the literature.[24]



Scheme 1. The procedure for the synthesis of tetraazolium salts.

Direct arylation of heteroaromatics

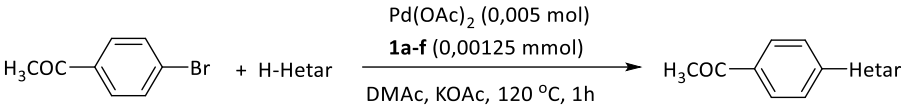
In the current work, we researched the activity of *in-situ* generated $Pd(OAc)_2$/1(a-f) catalyst systems for direct C2- and C5- arylation of heteroaromatics. For this purpose, we investigated the binding of aryl bromides (4-bromoasetofenone and 4-bromobenzene) to the C5-position of 2-*n*-buthyltiophene, 2-*n*-propylthiazole, 2-*n*-butylfuran, and C2- position of 4,5-dimethylthiazole. Based on previous studies on Pd-catalyzed direct arylation, for this study, DMAc (N,N-dimethylacetamide) and KOAc (potassium acetate) were selected as the solvent and base, respectively. The experiments were performed at 120 ^{o}C for 1 h. As shown in Table 1 and Table 2, the high GC yields were obtained using low $Pd(OAc)_2$/NHC precursor loadings at the end of the reaction.

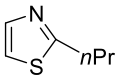
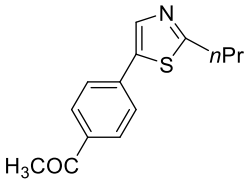
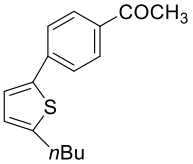
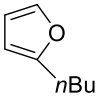
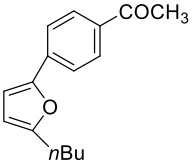
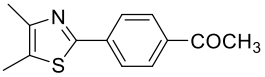
Firstly, we used bromoacetophenone as the aryl bromide for the direct arylation of heteroaromatics. Referring the Table 1, the yields at between 92-99% for 2-n-propylthiazole; 91-95% for 2-n-buthyltiophene; 91-98% for 2-n-butylfuran and 92-98% for 4,5-dimethylthiazole were obtained, respectively.

At the end of the reaction of 4-bromoacetophenone and 2-n-propylthiazole, the yield was obtained 99% using **1a** precatalyst. When the 2-n-buthyltiophene, 2-n-butylfuran, and 4,5-dimethylthiazole were used as a heteroaromatic compound, 95% yield was obtained for precatalyst **1a**, 98% yield was obtained for precatalyst

1a and **1c**, and 98% yield was obtained for precatalyst **1a** and **1c**, respectively. When the tetrazolium salts 1**e** and **1f** were used as the precatalyst in the arylation of heteroaromatics, partly lower yields were obtained (Table 1, entries 5-6,11-12,17-18, and 23-24).

Table 1. Arylation of heteroaryl derivatives with 4-bromoacetophenone



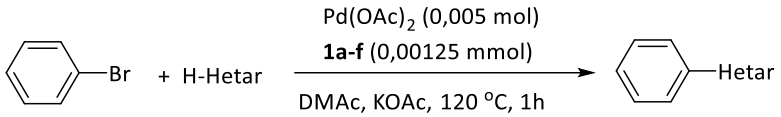
Entry	Catalyst	Heteroaryl derivative	Product	Yield (Isolated yield) (%)
1	**1a**			99 (81)
2	**1b**			96 (79)
3	**1c**			95 (78)
4	**1d**			96 (80)
5	**1e**			92 (76)
6	**1f**			93 (78)
7	**1a**			95 (89)
8	**1b**			92 (81)
9	**1c**			91 (79)
10	**1d**			93 (80)
11	**1e**			85 (74)
12	**1f**			83 (70)
13	**1a**			98 (89)
14	**1b**			97 (84)
15	**1c**			98 (83)
16	**1d**			96 (79)
17	**1e**			90 (73)
18	**1f**			91 (70)
19	**1a**			98 (90)
20	**1b**			94 (82)
21	**1c**			98 (87)
22	**1d**			96 (83)
23	**1e**			92 (79)
24	**1f**			93 (82)

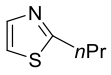
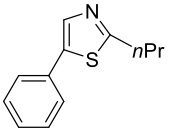
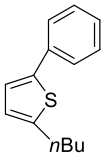
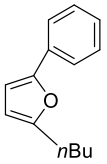
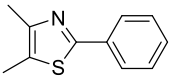
Reaction conditions: Heteroaryl derivative (2 mmol), 4-bromoacetophenone (1 mmol), Catalyst (**1a-1f**) (0.00125 mmol), $Pd(OAc)_2$ (0.005 mmol), KOAc (1mmol), DMAc (3 mL), 120°C, 1 h. Yields were calculated relative to aryl bromide by GC.

In addition, direct arylation of heteroaromatics with bromobenzene was researched and C2- and C5-arylated products were obtained with good yields (Table 2, entries 1-24). Arylation of 2-n-butylfuran gave the

highest yields in the range of 95-99% (Table 2, entries 13-18). The reaction of 4-bromobenzene with 2-n-propylthiazole gave the desired product with 91% yield using precatalyst **1a**. The yields of 80-90% were obtained for other precatalysts (Table 2, entries 2-6).

Table 2. Arylation of heteroaryl derivatives with bromobenzene



Entry	Catalyst	Heteroaryl derivative	Product	Yield (Isolated yield) (%)
1	**1a**			91 (80)
2	**1b**			88 (74)
3	**1c**			89 (76)
4	**1d**			90 (79)
5	**1e**			80 (69)
6	**1f**			82 (71)
7	**1a**			97 (85)
8	**1b**			97 (83)
9	**1c**			94 (80)
10	**1d**			95 (81)
11	**1e**			90 (77)
12	**1f**			92 (80)
13	**1a**			98 (84)
14	**1b**			99 (86)
15	**1c**			97 (81)
16	**1d**			98 (80)
17	**1e**			95 (79)
18	**1f**			96 (77)
19	**1a**			93 (80)
20	**1b**			89 (71)
21	**1c**			91 (77)
22	**1d**			88 (70)
23	**1e**			80 (67)
24	**1f**			82 (69)

Reaction conditions: Heteroaryl derivative (2 mmol), bromobenzene (1 mmol), Catalyst (1a-1f) (0.00125 mmol), $Pd(OAc)_2$ (0.005 mmol), KOAc (1mmol), DMAc (3 mL), 120°C, 1 h. Yields were calculated relative to aryl bromide by GC.

Similarly, when 2-n-buthyltiophene and 2-n-butylfuran were used as heteroaromatic compounds, C-5 arylated product was obtained with 97% and 99% high yields for catalyst **1b**, respectively. Moreover, close similar yields were obtained (90–97% for 2-n-buthyltiophene and 95–98% for 2-n-butylfuran) using the catalysts **1a** and **1c-f**. The coupling of 4,5-dimethylthiazole with neutral bromobenzene proceeds fairly. In the arylation

reactions of 4,5-dimethyl thiazole and 2-n-propylthiazole with bromobenzene were obtained C2- and C5-arylated products with the lowest yields in the range of 82-93% and 82-91% (Table 2, entries 19-24, 1-6). **1a** precatalyst showed the highest activity for these heteroaromatics as shown in Table 2, entries 1 and 19. When **1e** and **1f** were used in the $Pd(OAc)_2$/NHC catalyst system for arylation of heteroaromatics with bromobenzene, C2- and C5- arylated products were obtained with the lowest yields.

In this study, under optimal conditions, C2- and C5- arylated products were obtained with the reaction of heteroaromatics with 4-bromoacetofenone and 4-bromobenzene at high yields. Particularly, 4-bromoacetophenone was found to be more active than 4-bromobenzene due to its electron-attracting group (Table 1). When 2-n-butylfuran was used as heteroaromatic derivative in direct arylation reactions, the C5-arylated product was obtained with higher yields (Table 1 and 2). This is due to the ability of the oxygen atom in the ring to activate the C5- carbon in heteroaromatics.[45] In addition, arylated products were obtained with good yields in the direct arylation reactions where the other heteroaromatic compounds were used.

Eventually, we researched tetrazolium salts which we used as NHC precursor for the $Pd(OAc)_2$/NHC catalyst system in the direct arylation reactions of heteroaromatics with aryl bromides. All of the tetrazolium salts are active compounds for this reaction. There are no significant differences between the catalytic activities of tetraazolium salts used in the catalytic system with $Pd(OAc)_2$. However, It was found that the most effective catalyst is **1a** containing 4-methoxybenzyl group in the direct C2- and C5-arylation of heteroaromatics. On the contrary, the tetraazoluim salt **1e** showed lower activity in all direct arylation reactions. The steric and electronic properties of the alkyl group bearing to the compound may be the reason for this difference.

Conclusions

In summary, the novel six tetraazolium salts (**1a-f**) which are stable to air and moisture were synthesized from 2,3,5,6-tetrakis(bromomethyl)benzene according to the literature[12]. The characterization of the synthesized compounds was determined using ^{1}H NMR, ^{13}C NMR, and FT-IR spectroscopies. Also, the catalytic activities of tetraazolium salts/$Pd(AOc)_2$ systems were investigated in the direct C5-arylation of 2-n-butylthiophene, 2-n-propylthiazole and 2-n-butylfuran and C2-arylation of 4,5-dimethylthiazole with 4-bromobenzene /4-bromoacetophenone. It was found that prepared tetrazolium salts/$Pd(AOc)_2$ systems were efficient catalysts for the arylation of heteroaromatic compounds. Particularly, these *in situ* generated system showed very high activity especially in the direct arylation of 2-n-butylfuran. According to the obtained results, salt **1a** showed the highest activity for all reactions when compared to other salts. Finally, the desired products were obtained in high yields for direct arylation of heteroaromatics with different aryl bromides in the presence of low catalyst loading. This study is more environmentally benign and economical than other classic coupling reactions due to low catalyst loading and short reaction time.

Experimental Section

General. Tetrakis(benzimidazoliummethyl)benzene salts were synthesized under argon using standard Schlenk-type flasks and standard high vacuum line techniques. Some of the chemicals were synthesized in our laboratory. The other chemicals and solvents were purchased commercially. 4-methoxybenzyl chloride, 4-tert-butylbenzyl chloride, 2,3,5,6-tetramethylbenzyl chloride, methyl iodide, 2-ethoxyethyl chloride, 2,3,5,6-tetrakis(bromomethyl)benzene, 4,5-dimethylthiazole, 2-n-butyl thiophene, 2-*n*-butylfuran,

dimethylformamide, dimethylacetamide, pentane and diethyl ether were purchased from Sigma-Aldrich and Merck. ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d_6 on Bruker AC300P FT spectrometer. IR spectra were recorded on an FT-IR PerkinElmer Spectrum 100 spectrometer with absorption in cm^{-1}. Melting points were determined with an Electrothermal-9200 melting point device.

General procedure for the synthesis of tetrakis(benzimidazoliummethyl)benzene salts. To a solution of 1-alkylbenzimidazole (10 mmol) in DMF, 2,3,5,6-tetrakis(bromomethyl)benzene (2.5 mmol) was added slowly at 25 °C and the mixture was stirred at 80 °C for 12 h. The obtained white solid was filtered off and was washed with diethyl ether (4x10 ml), was dried under vacuum. The experiments carried out cover a part of the thesis work.[46]

2,3,5,6-Tetrakis(N-4-methoxybenzylbenzimidazoliummethyl)benzene tetrabromide (1a). Yield : 3.18 g (91%). Mp 265-266 °C, $\nu_{(CN)}$= 1551.9 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ= 10.28 (s, 4H, NC*H*N), 6.88-7.96 (m, 32 H, NC_6H_4N, $CH_2C_6H_4(OCH_3)$-4), 7.88 (s, 2H, $(CH_2)_4C_6H_2$), 6.09 (s, 8H, $(CH_2)_4C_6H_2$), 5.70 (s, 8H, $CH_2C_6H_4(OCH_3)$-4), 3.70 (s, 12H, $CH_2C_6H_4(OCH_3)$-4). ^{13}C NMR (75 MHz, DMSO-d_6) δ= 159.9 (N*C*HN), 114.3, 114.6, 126.1, 127.1, 127.4, 130.6, 134.3, 142.7 (NC_6H_4N, $CH_2C_6H_4(OCH_3)$-4), 130.9, 131.5 ($(CH_2)_4C_6H_2$), 55.6 ($CH_2C_6H_2(OCH_3)$-4), 49.9 ($(CH_2)_4C_6H_2$), 47.7 ($CH_2C_6H_2(OCH_3)$-4). Anal.calcd. for $C_{70}H_{66}N_8O_4Br_4$: C: 59.93, H: 4.74, N: 7.99. Found C: 59.52, H: 4.65, N: 7.80.

2,3,5,6-Tetrakis(*N*-4-tert-butylbenzylbenzimidazoliummethyl)benzene tetrabromide (1b). Yield : 3.43 g (93%). Mp 250-251 °C, $\nu_{(CN)}$= 1562.3 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ= 10.12 (s, 4H, NC*H*N), 7.30-8.26 (m, 32 H, NC_6H_4N, $CH_2C_6H_4(C(CH_3)_3)$-4), 7.98 (s, 2H, $(CH_2)_4C_6H_2$), 6.08 (s, 8H, $(CH_2)_4C_6H_2$), 5.72 (s, 8H, $CH_2C_6H_4(C(CH_3)_3)$-4), 1.16 (s, 36H, $CH_2C_6H_4(C(CH_3)_3)$-4). ^{13}C NMR (75 MHz, DMSO-d_6) δ= 162.9 (N*C*HN), 114.1, 126.0, 127.1, 128.8, 130.7, 131.2, 142.7 151.8, (NC_6H_4N, $CH_2C_6H_4(C(CH_3)_3)$-4), 131.4, 134.5 ($(CH_2)_4C_6H_2$) 40.7 ($(CH_2)_4C_6H_2$), 40.4 ($CH_2C_6H_4(C(CH_3)_3)$-4), 34.7 ($CH_2C_6H_4(C(CH_3)_3)$-4), 31.3 ($CH_2C_6H_4(C(CH_3)_3)$-4).). Anal.calcd. for $C_{82}H_{90}N_8Br_4$: C: 65.34, H: 6.02, N: 7.43. Found C: 65.31, H: 6.00, N: 7.40

2,3,5,6-Tetrakis(*N*-2,3,5,6-tetramethylbenzylbenzimidazoliummethyl)benzene tetrabromide (1c). Yield : 3.10 g (83%). Mp 228-229 °C, $\nu_{(CN)}$= 1556.3 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ= 9.39 (s, 4H, NC*H*N), 7.34-8.20 (m, 16 H, NC_6H_4N), 7.96 (s, 2H, $(CH_2)_4C_6H_2$), 7.11 (s, 4H, $CH_2C_6H(CH_3)_4$-2,3,5,6), 5.97 (s, 8H, $(CH_2)_4C_6H_2$), 5.77 (s, 8H, $CH_2C_6H(CH_3)_4$-2,3,5,6), 2.20 (s, 24H, $CH_2C_6H(CH_3)_4$-2,3), 2.15 (s, 24H, $CH_2C_6H(CH_3)_4$-5,6). ^{13}C NMR (75 MHz, DMSO-d_6) δ= 162.7 (N*C*HN), 142.2 ($CH_2C_6H(CH_3)_4$-2,3,5,6), 114.4, 114.7, 129.0, 131.3, 132.2, 134.1 (NC_6H_4N), 131.7, 134.3 ($(CH_2)_4C_6H_2$), 47.9 ($(CH_2)_4C_6H_2$), 46.7 ($CH_2C_6H_4(CH_3)_4$-2,3,5,6), 20.6 ($CH_2C_6H(CH_3)_4$-2,3), 15.6 ($CH_2C_6H(CH_3)_4$-5,6). Anal.calcd. for $C_{82}H_{90}N_8Br_4$: C: 65.34, H: 6.02, N: 7.43. Found C: 65.3, H: 6.0, N: 7.39.

2,3,5,6-Tetrakis(*N*-4-methylbenzylbenzimidazoliummethyl)benzene tetrabromide (1d). Yield : 2.95 g (89%). Mp 210-211 °C, $\nu_{(CN)}$= 1558.2 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ= 10.27 (s, 4H, NC*H*N), 7.12-7.98 (m, 32 H, NC_6H_4N, $CH_2C_6H_4(OCH_3)$-4), 7.85 (s, 2H, $(CH_2)_4C_6H_2$), 6.10 (s, 8H, $(CH_2)_4C_6H_2$), 5.71 (s, 8H, $CH_2C_6H_4(OCH_3)$-4), 2.26 (s, 12H, $CH_2C_6H_4(CH_3)$-4). ^{13}C NMR (75 MHz, DMSO-d_6) δ= 162.9 (N*C*HN), 114.3, 127.1, 127.4, 128.8, 129.8, 130.9, 131.2, 138.6 (NC_6H_4N, $CH_2C_6H_4(OCH_3)$-4), 131.5, 134.3 ($(CH_2)_4C_6H_2$), 50.1 ($(CH_2)_4C_6H_2$), 47.7 ($CH_2C_6H_2(OCH_3)$-4), 21.1 ($CH_2C_6H_2(CH_3)$-4).). Anal.calcd. for $C_{70}H_{66}N_8Br_4$: C: 62.79, H: 4.97, N: 8.37. Found C: 62.77, H: 4.96, N: 8.34

2,3,5,6-Tetrakis(*N*-methylbenzimidazoliummethyl)benzene tetrabromide (1e). Yield : 1.91 g (79%). Mp 276-278 °C, $\nu_{(CN)}$= 1570.1 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ= 9.66 (s, 4H, NC*H*N), 7.46-8.28 (m, 16 H, NC_6H_4N), 7.87 (s, 2H, $(CH_2)_4C_6H_2$), 6.01 (s, 8H, $(CH_2)_4C_6H_2$), 3.99 (s, 12H, NCH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ= 163.0 (N*C*HN), 113.8, 113.9, 127.3, 130.9, 139.1 (NC_6H_4N), 131.9, 133.9 ($(CH_2)_4C_6H_2$), 47.4 ($(CH_2)_4C_6H_2$), 36.4 (NCH_3) . Anal.calcd. for $C_{42}H_{42}N_8Br_4$: C: 51.56, H: 4.33, N: 11.45. Found C: 51.52, H: 4.29, N: 11.44

2,3,5,6-Tetrakis(*N*-2-ethoxyethylbenzimidazoliummethyl)benzene tetrabromide (1f). Yield : 2.43 g (80%). Mp 247-248 °C, $\nu_{(CN)}$= 1558.5 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ= 9.96 (s, 4H, NC*H*N), 7.23-8.04 (m, 16 H, NC_6H_4N), 8.01 (s, 2H, $(CH_2)_4C_6H_2$)), 6.11 (s, 8H, $(CH_2)_4C_6H_2$), 4.67 (m, 8H, $CH_2CH_2OCH_2CH_3$), 3.80 (m, 8H, $CH_2CH_2OCH_2CH_3$), 3.43 (q, *J*=6.9 Hz, 8H, $CH_2CH_2OCH_2CH_3$), 1.00 (t, *J*=7.2 Hz, 12H, $CH_2CH_2OCH_2CH_3$). ^{13}C NMR (75 MHz, DMSO-d_6) δ= 162.4 (N*C*HN), 113.4, 114.0, 125.8, 126.1, 126.7, 130.2, 139.0 (NC_6H_4N), 131.2, 133.3 ($(CH_2)_4C_6H_2$), 67.0 ($CH_2CH_2OCH_2CH_3$), 65.6 ($CH_2CH_2OCH_2CH_3$), 56.0 ($CH_2CH_2OCH_2CH_3$), 47.1 ($(CH_2)_4C_6H_2$), 18.2 ($CH_2CH_2OCH_2CH_3$) . Anal.calcd. for $C_{54}H_{66}N_8O_4Br_4$: C: 53.57, H: 5.49, N: 9.25. Found C: 53.32, H: 5.26, N: 8.91.

General procedure for direct arylation of heteroaromatics

Under argon atmosphere, heteroaryl derivative (2-*n*-propylthiazole, 2-*n*-butylthiophene, 2-*n*-butylfuran and 4,5-dimethylthiazole) (2 mmol), 4-bromobenzene or 4-bromoacetophenone (1 mmol), KOAc (2 mmol), $Pd(OAc)_2$ (0.005 mmol), **1a-1f** (0.00125 mmol), DMAc (3 mL) were added into Schlenk tube. The mixture was stirred strongly at 130 °C for 1h. The solvent was removed under a vacuum. The product was eluted using a pentane–diethyl ether mixture (3:1). The reaction mixture was purified by flash chromatography on silica gel. GC yields were calculated relative to aryl bromide.

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