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METAL-FREE OXIDATIVE CROSS-COUPLING OF PYRROLES WITH ELECTRON-RICH ARENES USING RECYCLABLE HYPERVALENT IODINE(III) REAGENT

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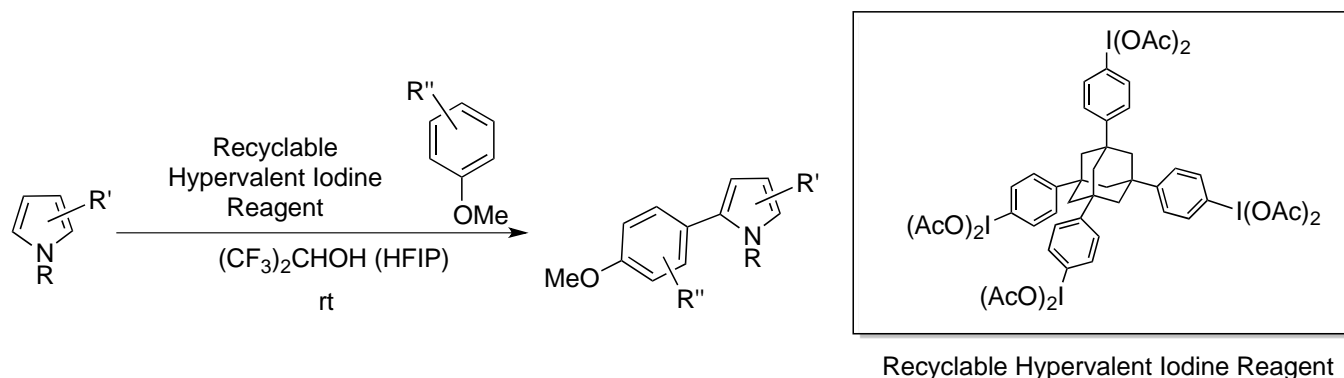
Abstract – The facile and clean oxidative cross-coupling reaction of pyrroles has been developed using the recyclable hypervalent iodine(III) reagents having an adamantane core. The recyclable iodine(III) reagent could be recovered from the reaction mixtures as the corresponding reduced forms, *i.e.*, the tetraiodide **2**, by a simple solid-liquid separation. By re-oxidizing the recovered **2** to the initial reagent **1a** using *m*-chloroperbenzoic acid (*m*CPBA), the reagent **1a** can be reused.

In Celebration of Professor Kiyoshi Tomioka on His 70th Birthday

Pyrrole-aryl derivatives are an important class of compounds exhibiting significant biological and photoelectronic properties.^{1,2} Therefore, many efforts have been devoted to developing efficient synthetic methods for the synthesis of these biaryls. Traditionally, these carbon-carbon biaryl bonds are formed in the presence of a transition metal catalyst by a cross-coupling reaction between an organometallic reagent and an aryl halide.³ Needless to say, these reactions required a pre-functionalization for obtaining the coupling partners. In addition, the unstable nature of some pyrrole organometallic and halide compounds makes it more difficult to synthesize by coupling reactions.⁴ As a new approach, the direct oxidative carbon-hydrogen (C-H) bond functionalization strategies of pyrroles^{5,6} might be expected to be an attractive methodology for enabling rapid

access to these molecules. Significant progress has been made toward improving various selectivities of the reactions, but many of these methods still have substrate limitations.

Hypervalent iodine reagents have received much attention as alternatives to toxic heavy metal reagents to their mild oxidizing ability, low toxicity, and ease of handling.⁷ In our laboratory, a novel oxidative coupling method of heteroaromatic compounds using a hypervalent iodine(III) reagent is under development and research, in the past years, we reported a useful biaryl coupling reaction of heteroaromatics compounds *via* the σ -heteroaromatic iodonium(III) species as an intermediate.⁸ In this regard, our research group has achieved a metal-free protocol for the synthesis of pyrrole-aryl. This new oxidative coupling is versatile in allowing the reactions under metal-free and mild conditions, tolerates a diverse series of functionalities of the pyrroles. In continuation of our interest in the oxidative coupling reaction of pyrroles, we now report that a recycling version of this oxidative coupling should become feasible and provide an eco-friendly synthetic method (Scheme 1) because many recent studies have demonstrated the utility of the recyclable hypervalent iodine reagents.



Scheme 1. Cross-Coupling Reaction of Pyrroles Using Recyclable Hypervalent Iodine(III) Reagent

The use of recyclable hypervalent iodine reagents during the reaction makes it possible to easily remove the reagents from the reaction mixture and it must be a more promising and ecological approach to reduce the co-production of stoichiometric amounts of the iodoarene. Therefore, various types of recyclable hypervalent iodine reagents have been reported.¹⁰ First, the polymer-supported hypervalent iodine reagents, such as poly(diacetoxyiodo)styrene (PDAIS) and poly[bis(trifluoroacetoxyiodo)]styrene (PBTIS), incorporating phenyliodine(III) diacetate (PIDA) and phenyliodine(III) bis(trifluoroacetate) (PIFA) in their polymer backbones were developed.^{10a-c} Inspired by this research, other chemists have also reported new recyclable hypervalent iodine(III) compounds with fluororous tags and ionic supports.^{10h-f} From an atom economy perspective, these are less than ideal, and from an environmental point of view, we have previously developed a structurally new recyclable hypervalent iodine(III) reagent **1a**, namely,

1,3,5,7-tetrakis[4-(diacetoxyiodo)phenyl]adamantane (Figure 1), which was easily recovered by precipitation utilizing the insolubility of the tetraiodide **2**, stoichiometrically produced from **1a** after the reactions, in common polar solvents.¹¹ The hypervalent iodine(III) reagent **1** with our reusable adamantane cores has several advantages over conventional polymer-supported reagents in reactivity and recyclability. Typically, it shows a higher reactivity compared to polymer-supported reagents and no decomposition of the backbone after repetitive use due to fact that the definite tetrahedral structure is observed. Considering the background of the recyclable iodine reagent, we improved the coupling reaction using recyclable iodine(III) reagent and avoided a stoichiometric amount of iodobenzene waste from the initial conditions.

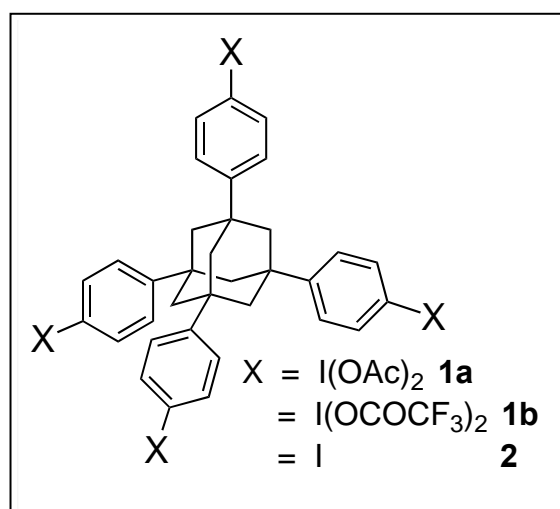
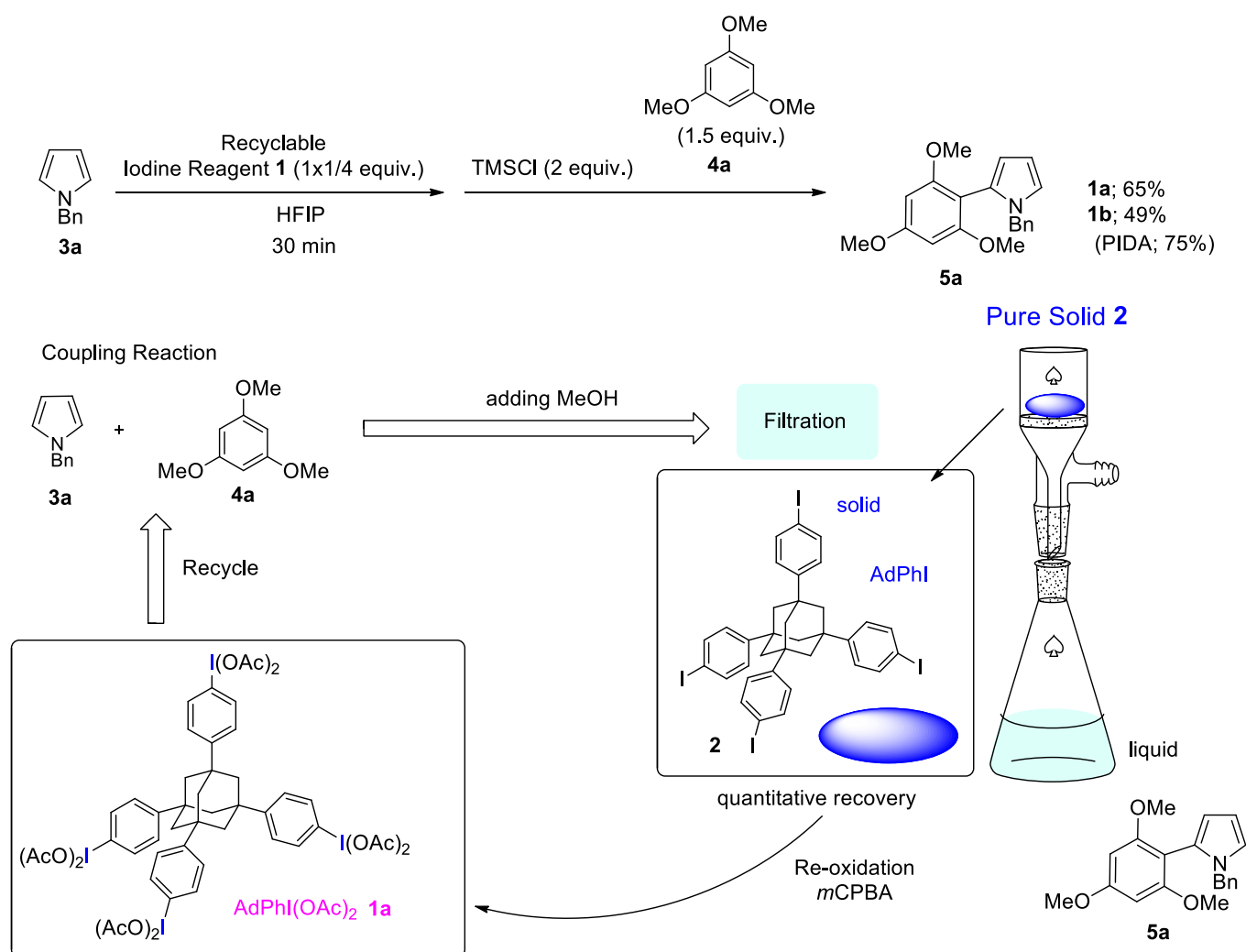


Figure 1. Recyclable Hypervalent Iodine(III) Reagents Having Adamantane Cores

Based on our initial studies, we conducted the oxidative cross-coupling reaction of *N*-benzylpyrrole **3a** with 1,3,5-trimethoxybenzene **4a** using the recyclable reagent **1a** based on the standard reaction conditions in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP, $(\text{CF}_3)_2\text{CHOH}$) in combination with TMSCl to give the cross-product **5a** in 65% yield (Scheme 2, Eq. 1). Screening of other adamantane-based recyclable iodine(III) reagent **1b** showed that the recyclable reagent **1a** is the most efficient oxidizing agent in this coupling reaction. The use of the polymer-supported reagent, the commercially available PDAIS, did not yield any product **5a** under the given conditions. As a result, the recyclable iodine(III) reagent **1a** and TMSCl in HFIP at room temperature gave the best result.

The oxidant **1a** could be easily separated from the reaction mixtures as the corresponding reduced forms, *i.e.*, the tetraiodide **2**, by a simple solid–liquid separation. The procedure for recovering the tetraiodide **2**

after the reaction is shown in Scheme 2. Methanol was then added to the reaction mixture to precipitate **2** without removing the solvent. Since **2** was hardly soluble in HFIP and methanol, it was precipitated as a white powder by adding methanol and recovered by filtration. By re-oxidizing the recovered **2** to the initial reagent **1a** using *m*-chloroperbenzoic acid (*m*CPBA), the reagent **1a** can be reused. In this way, the reagents were reproduced without reducing the purity and repeatedly used without losing any activities. The reuse of the reagent **1a** in the same reaction gave a comparable result (3 h, 65% yield of coupling product **5a**), and the tetraiodide **2** was also recovered in over 97% yield.

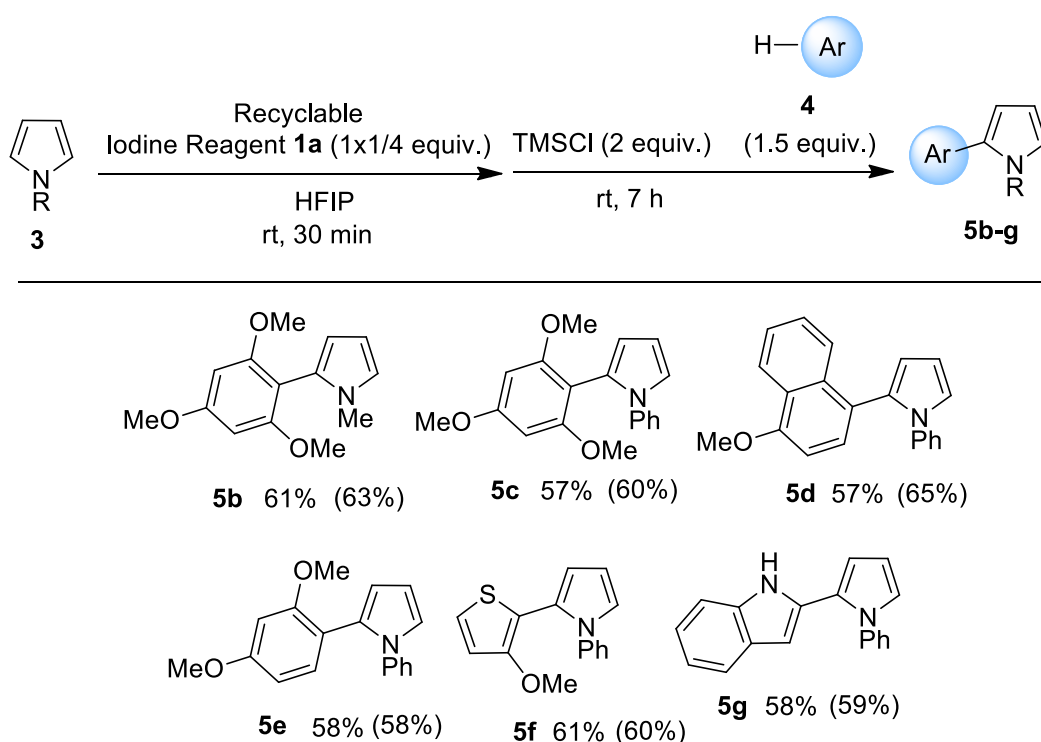


Scheme 2. Oxidative Cross-Coupling Reaction of Pyrrole **3a** with 1,3,5-Trimethoxybenzene **4a** Using Recyclable Hypervalent Iodine(III) Reagent **1**

With **1a** (1 x 1/4 equiv, 100 mol% of iodine(III) atom relative to the substrates), the developed conditions worked well for all the pyrroles **3** with arenes **4**, affording the corresponding biaryl products **5** (Table 1)

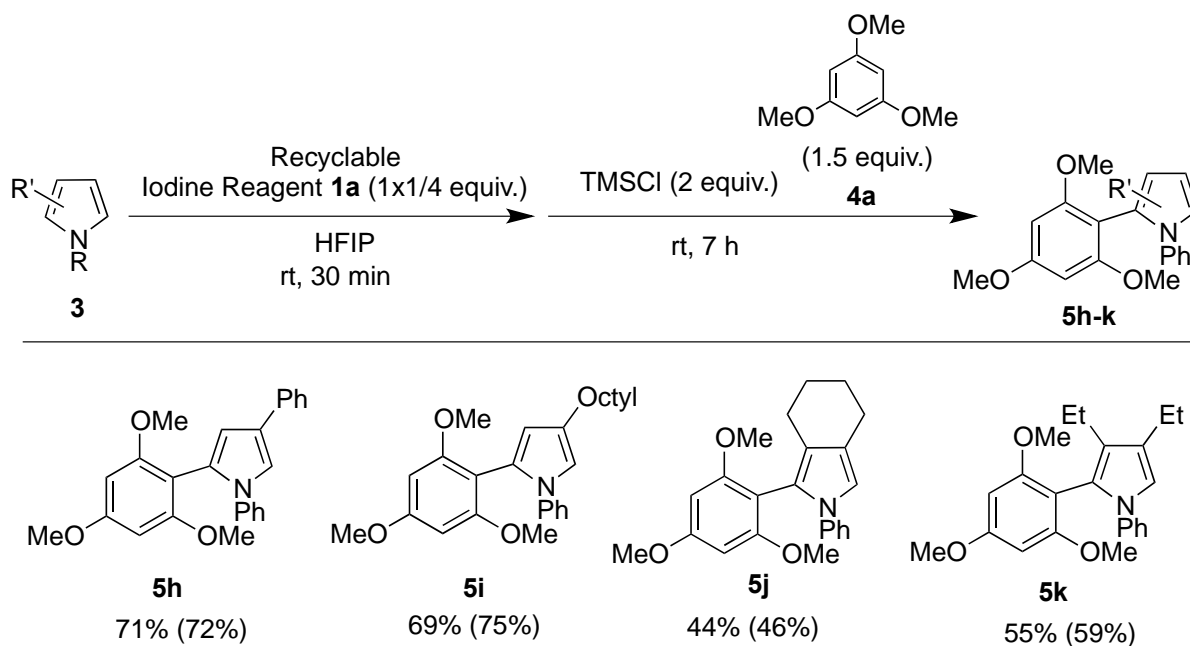
in good to moderate yields. As mentioned in the optimization studies, the *N*-benzylpyrrole **3a** provided the expected coupling product **5a** in 65% yield. In addition, the developed protocol worked well on pyrroles **3b** and **3c** having methyl and phenyl on the pyrrole ring and gave the corresponding products **5b** and **5c** in good yields. The different arenes **4b** and **4c** participated well in the reaction to give the desired coupling products **5d** and **5e**, respectively. In the case of heteroaromatic compounds, such as the electron-rich thiophene **4d** and indole **4e**, the coupling reactions smoothly proceeded.

Table 1. Coupling Reaction of *N*-Substituted Pyrroles **3** with Arenes **4** ^{[a],[b],[c]}



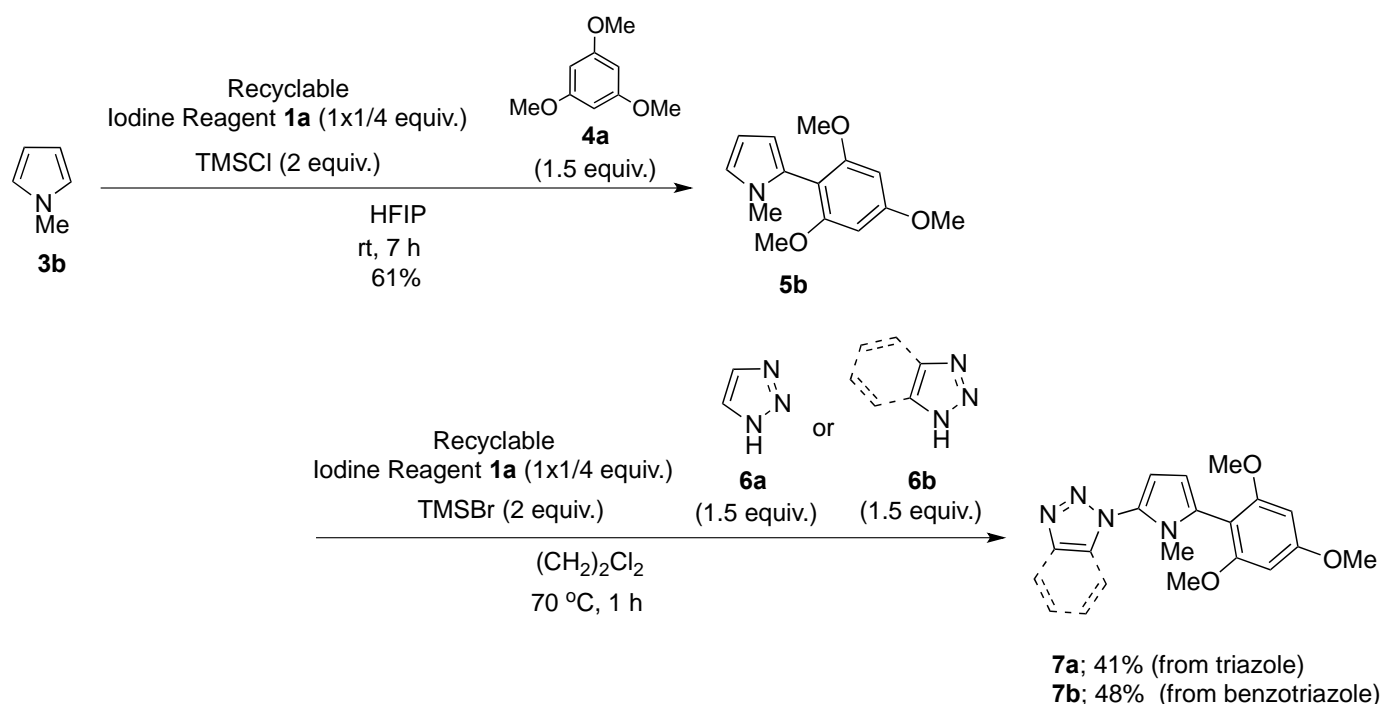
[a] Reaction conditions: pyrrole (0.40 mmol), arene (0.60 mmol), recyclable hypervalent iodine(III) reagent (0.40 x 1/4 mmol) and TMSCl (0.8 mmol) in HFIP (2 mL) at room temperature for 7 h. [b] Isolated yield. [c] The parenthesis showed the yield when PIDA was used.

Subsequently, the substrate was further extended to various substituted pyrroles **3** for the biaryl synthesis (Table 2). In the case of the 3-substituted pyrroles **3d** and **3e**, the coupling reaction selectively proceeded only by the C-5 arylation of the pyrroles without the formation of other isomers. The reactions of the electron-rich 3,4-dialkyl-substituted pyrroles, **3f** and **3g**, also occurred in an efficient manner and the coupling products, **5j** and **5k**, were obtained in good yields.

Table 2. Reaction of Various Pyrroles **3** with 1,3,5-Trimethoxybenzene **4a** ^{[a],[b],[c]}

[a] Reaction conditions: pyrrole (0.40 mmol), 1,3,5-trimethoxybenzene (0.60 mmol), recyclable hypervalent iodine(III) reagent (0.40 x 1/4 mmol) and TMSCl (0.80 mmol), in HFIP (2 mL) at room temperature for 7 h. [b] Isolated yield. [c] The parenthesis showed the yield when PIDA was used.

In order to further explore the applicability of the pyrrole cross-coupling, we examined the controllable arylation reaction of pyrrole for the iterative process. Utilizing the reaction of *N*-methylpyrrole **3b**, the C2-arylation developed in this study first gave coupling product **5b** in 61% yield. Subsequently, under the conditions we have previously developed,¹² the second *N*-arylation introduced the 1,2,3-triazole **6a** and 1,2,3-benzotriazole **6b** moieties took place and the diarylated products **7a** and **7b** were obtained (Scheme 3). Nitrogen heterocycles are known as core of various natural products and functional materials, among which azoles and pyrroles have the most frequent occurrence.¹³



Scheme 3. Iterative Arylation of Pyrrole **3b** Using Recyclable Hypervalent Iodine(III) Reagent **1a**

In conclusion, inspired by the fascinating environmentally benign chemistry, we have developed a clean oxidative cross-coupling reaction for pyrroles using the recyclable hypervalent iodine(III) reagent with TMSCl in HFIP at room temperature. Moreover, we have also established the synthesis of a pyrrole trimer by utilizing the iterative use of our developed direct coupling reactions. Considering the attractive features of the hypervalent iodine(III) reagent in synthetic chemistry, this methodology is a practical and convenient approach to synthesize biaryls under metal-free conditions.

EXPERIMENTAL

Melting point (mp) is uncorrected. All ^1H - and ^{13}C -NMR spectra of the products were measured in CDCl_3 by spectrometers operating at 400 MHz (100 MHz for ^{13}C NMR) at 25 °C. Chemical shifts of ^1H -NMR were recorded in parts per million (ppm, δ) relative to tetramethylsilane ($\delta = 0.00$ ppm) as an internal standard. Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, brs = broad singlet, m = multiplet), coupling constant (J) in Hz, and integration. Chemical shifts of ^{13}C -NMR were reported in ppm with the solvent as reference peak (CDCl_3 : $\delta = 77.0$ ppm). Absorptions of infrared spectra (IR) are reported in reciprocal centimeters (cm^{-1}) for representative peaks. Flash column chromatography was performed with Merck Silica Gel 60 (230-400 mesh) eluting with hexane and ethyl acetate for isolation of the products. Analytical thin-layer chromatography (TLC)

was carried out on Merck Silica Gel F₂₅₄ plates (0.25 mm). The spots and bands were detected by UV light of irradiation (254, 365 nm) and/or by staining with 5% phosphomolybdic acid followed by heating.

Preparation of a Recyclable Hypervalent Iodine Reagent 1a. To a stirred solution of 1,3,5,7-tetrakis(4-iodophenyl)adamantane **2** (1.42 g, 1.5 mmol) in CH₂Cl₂ (150 mL)-acetic acid (150 mL) was added *m*CPBA (ca. 69% purity, 3.12 g, 18 mmol) at room temperature. The mixture was stirred for 12 h under the same reaction conditions during which the cloudy solution became clear. The resultant mixture was filtered, and CH₂Cl₂ was removed using a rotary evaporator. Hexane was added to the residue to precipitate the 1,3,5,7-tetrakis[4-(diacetoxyiodo)phenyl]adamantane **1a**. After filtration, the almost pure product was obtained in nearly quantitative yield.

General Procedure for the Oxidative Cross-Coupling Reaction of Pyrroles

To a stirred solution of pyrrole **3a** (0.40 mmol 1 equiv.) in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP, 0.1 M), recyclable hypervalent iodine(III) reagent **1a** (0.40 x 1/4 mmol 1 equiv.) was added at room temperature. After 30 min, to the mixture, arene **4a** (0.60 mmol 1.5 equiv.) and TMSCl (0.80 mmol 2 equiv.) were added and then stirred for 7 h under the same conditions, while the reaction progress was checked by TLC. MeOH was added to the reaction mixture, and it was filtered to give the tetraiodide **2** (confirmed by ¹H-NMR analysis and TLC), which was washed several times with small portion of MeOH for purification. The filtrate was evaporated and subjected to column chromatography (SiO₂, hexane) to give the pure biaryl **5a**.

Characterization of the coupling products 5

1-Benzyl-2-[(2,4,6-trimethoxy)phenyl]-1*H*-pyrrole (**5a**)

White solid; mp 87-89 °C; ¹H-NMR (400 MHz, CDCl₃): δ 3.54 (s, 6H), 3.75 (s, 3H), 4.72 (s, 2H), 6.01-6.05 (m, 3H), 6.22 (t, 1H, *J* = 3.0 Hz), 6.65 (t, 1H, *J* = 2.0 Hz), 6.93 (d, 2H, *J* = 6.8 Hz), 7.08-7.16 (m, 3H) ppm; ¹³C-NMR (100 MHz, CDCl₃): δ 50.6, 55.3, 55.6, 90.4, 103.3, 107.9, 109.3, 120.7, 125.5, 126.8, 127.1, 128.1, 138.9, 160.1, 161.4 ppm; IR (KBr): 3942 w, 3053 w, 2987 w, 2945 w, 2685 w, 2305 w, 1610 w, 1421 w, 1263 s, 1155 w, 1126 w, 895 w, 814 w, 748 s, 706 m cm⁻¹; HRFABMS calcd for C₂₀H₂₁NO₃ [M]⁺ 323.1521, found 323.1537.

1-Methyl-2-[(2,4,6-trimethoxy)phenyl]-1*H*-pyrrole (**5b**)

White solid; mp 87-89 °C; ¹H-NMR (400 MHz, CDCl₃): δ 3.31 (s, 3H), 3.66 (s, 6H), 3.78 (s, 3H), 5.99 (dd, 1H, *J* = 3.7, 1.8 Hz), 6.12 (s, 2H), 6.15 (t, 1H, *J* = 3.0 Hz), 6.64 (t, 1H, *J* = 2.0 Hz) ppm; ¹³C-NMR (100 MHz, CDCl₃): δ 34.0, 55.3, 55.8, 90.5, 103.5, 107.1, 109.4, 121.4, 125.2, 159.9, 161.2 ppm; IR

(KBr): 2930 m, 1611 s, 1583 s, 1552 m, 1496 w, 1454 m, 1413 m, 1334 m, 1307 w, 1224 m, 1203 s, 1155 s, 1124 s, 1030 w, 812 w, 711 m cm^{-1} ; HRFABMS calcd for $\text{C}_{14}\text{H}_{17}\text{NO}_3$ $[\text{M}]^+$ 247.1208, found 247.1204.

1-Phenyl-2-[(2,4,6-trimethoxy)phenyl]-1H-pyrrole (5c)

White solid; mp 87-89 °C; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 3.51 (s, 6H), 3.78 (s, 3H), 6.03 (s, 2H), 6.27-6.30 (m, 1H), 6.40 (1H, t, $J = 2.8$ Hz), 6.98 (t, 1H, $J = 2.8$ Hz), 7.09-7.14 (m, 3H), 7.21 (t, 2H, $J = 7.6$ Hz) ppm; $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ 55.1, 55.4, 90.3, 103.9, 108.8, 111.6, 121.4, 124.1, 124.9, 125.6, 128.2, 141.3, 159.3, 161.1 ppm; IR (KBr): 3944 w, 3053 w, 2986 w, 2941 w, 2305 w, 1502 w, 1417 w, 1261 s, 1226 w, 1157 w, 1128 m, 895 w, 814 w, 763 s, 748 s, 704 m cm^{-1} ; HRFABMS calcd for $\text{C}_{19}\text{H}_{19}\text{NO}_3$ $[\text{M}]^+$ 309.1365, found 309.1357.

2-[(4-Methoxy)naphthalen-1-yl]-1-phenyl-1H-pyrrole (5d)

$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 3.95 (s, 3H), 6.42 (q, 1H, $J = 1.7$ Hz), 6.46 (t, 1H, $J = 3.2$ Hz), 7.03-7.16 (m, 8H), 7.35-7.42 (m, 2H), 7.87-7.90 (m, 1H), 8.22-8.26 (m, 1H) ppm; $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ 55.4, 103.2, 108.8, 112.4, 121.8, 122.5, 124.7, 125.0, 125.9, 126.0, 126.5, 128.7, 129.1 ppm; IR (KBr): 2925, 2853, 2362, 2252, 1723, 1586, 1498, 1459, 1384, 1237, 1096, 913, 744 cm^{-1} ; MALDI-TOFMS calcd for $\text{C}_{21}\text{H}_{17}\text{NO}$ $[\text{M}]^+$ 299.1310, found 299.1305.

2-[(2,4-Dimethoxy)phenyl]-1-phenyl-1H-pyrrole (5e)

Colorless oil; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 3.28 (s, 3H), 3.80 (s, 3H), 6.30 (s, 1H), 6.33 (s, 1H), 6.38 (t, 1H, $J = 3.2$ Hz), 6.50 (d, 1H, $J = 8.8$ Hz), 6.99 (s, 1H), 7.11-7.28 (m, 6H) ppm; $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ 54.7, 55.3, 98.6, 104.2, 108.8, 110.7, 115.5, 122.3, 124.1, 125.7, 128.5, 130.3, 132.0, 141.5, 157.6, 160.5 ppm; IR (KBr): 2932, 1614, 1502, 1465, 1305, 1209, 1161, 1034, 765 cm^{-1} ; HRFABMS calcd for $\text{C}_{18}\text{H}_{17}\text{NO}_2$ $[\text{M}]^+$ 279.1259, found 279.1254.

2-[(3-Methoxy)thiophen-2-yl]-1-phenyl-1H-pyrrole (5f)

Colorless oil; $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ 3.45 (s, 3H), 6.34 (t, 1H, $J = 3.3$ Hz), 6.46-6.48 (m, 1H), 6.71 (d, 1H, $J = 5.7$ Hz), 6.92-6.94 (m, 1H), 7.06 (d, 1H, $J = 5.4$ Hz), 7.20-7.32 (m, 5H) ppm; $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ 58.2, 109.1, 111.5, 112.2, 116.3, 123.2, 123.3, 124.0, 125.3, 126.6, 128.6, 140.6, 154.0 ppm; IR (KBr): 3105, 3051, 2958, 2931, 2850, 1597, 1523, 1500, 1427, 1379, 1321, 1259, 1236, 1103, 1070, 790, 763, 750, 717, 696 cm^{-1} . MALDI-TOFMS calcd for $\text{C}_{15}\text{H}_{13}\text{NOS}$ $[\text{M}]^+$ 255.0718, found 255.0713.

2-(1-Phenyl-1H-pyrrol-2-yl)-1H-indole (5g)

White solid; mp 144-145 °C; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 6.41 (t, 1H, $J = 2.8$ Hz), 6.52 (d, 1H, $J = 3.6$ Hz), 6.60 (d, 1H, $J = 2.4$ Hz), 6.94 (s, 1H), 7.07 (td, 1H, $J = 8.0, 1.2$ Hz), 7.16 (td, 1H, $J = 6.8, 1.2$ Hz), 7.20-7.27 (m, 5H), 7.31 (d, 1H, $J = 8.0$ Hz), 7.63 (d, 1H, $J = 8.0$ Hz), 7.99 (s, 1H) ppm; $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ 109.1, 109.3, 110.0, 110.9, 120.0, 120.2, 122.2, 122.7, 122.8, 125.8, 126.5, 126.6, 127.3,

128.8, 135.6, 140.8 ppm; IR (KBr): 3404, 3058, 2926, 1597, 1498, 1456, 1434, 1331, 1242, 1199, 1097, 81, 791, 741, 697 cm^{-1} ; MALDI-TOFMS calcd for $\text{C}_{18}\text{H}_{14}\text{N}_2$ $[\text{M}+\text{H}]^+$ 258.1157, found 258.1152.

1,4-Diphenyl-2-[(2,4,6-trimethoxy)phenyl]-1H-pyrrole (5h)

White solid; mp 59-61 $^{\circ}\text{C}$; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 3.51 (s, 6H), 3.79 (s, 3H), 6.03 (s, 2H), 6.61 (s, 1H), 7.12-7.32 (m, 9H), 7.58 (dd, 2H, $J = 8.4, 1.2$ Hz) ppm; $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ 55.2, 55.5, 90.5, 103.7, 110.1, 118.2, 124.0, 125.0, 125.1, 125.2, 125.8, 125.9, 128.3, 128.4, 135.8, 141.2, 159.3, 161.3 ppm; IR (KBr): 2936, 2837, 1583, 1500, 1454, 1415, 1336, 1227, 1204, 1155, 1126, 911, 812, 748, 695 cm^{-1} ; MALDI-TOFMS calcd for $\text{C}_{25}\text{H}_{24}\text{NO}_3$ $[\text{M}+\text{H}]^+$ 386.1756, found 386.1751.

4-Octyl-1-phenyl-2-[(2,4,6-trimethoxy)phenyl]-1H-pyrrole (5i)

Brown oil; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 0.88 (m, 3H), 1.22-1.45 (m, 10H), 1.69-1.65 (m, 2H), 2.55 (t, 2H, $J = 7.8$ Hz), 3.48 (s, 6H), 3.78 (s, 3H), 6.02 (s, 2H), 6.16 (s, 1H), 6.76 (s, 1H), 7.11-7.05 (m, 3H), 7.19 (t, 2H, $J = 7.3$ Hz) ppm; $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ 14.1, 22.7, 27.3, 29.3, 29.6, 29.9, 30.4, 31.9, 55.2, 55.4, 90.2, 90.4, 104.3, 112.5, 118.6, 123.7, 124.0, 125.1, 128.2, 141.6, 159.1, 160.9 ppm; IR (KBr): 2999, 2925, 2853, 2359, 1610, 1584, 1500, 1415, 1127, 812, 765, 695 cm^{-1} ; MALDI-TOFMS calcd for $\text{C}_{27}\text{H}_{36}\text{NO}_3$ $[\text{M}+\text{H}]^+$ 422.1365, found 422.2690.

2-Phenyl-1-[(2,4,6-trimethoxy)phenyl]-4,5,6,7-tetrahydro-2H-isoindole (5j)

White solid; mp 117-119 $^{\circ}\text{C}$; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 1.72-1.79 (m, 4H), 2.39 (t, 2H, $J = 5.8$ Hz), 2.48 (t, 2H, $J = 5.9$ Hz), 3.48 (s, 6H), 3.78 (s, 3H), 6.02 (s, 2H), 6.71 (s, 1H), 7.02-7.07 (m, 3H), 7.17 (t, 2H, $J = 7.6$ Hz) ppm; $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ 22.1, 22.2, 23.9, 24.1, 55.2, 55.4, 90.4, 103.4, 116.9, 119.7, 120.1, 121.7, 123.6, 124.9, 128.2, 141.7, 159.2, 161.0 ppm; IR (KBr): 2998, 2926, 2837, 1585, 1502, 1335, 1204, 1127, 813, 764, 696 cm^{-1} ; MALDI-TOFMS calcd for $\text{C}_{23}\text{H}_{25}\text{NO}_3$ $[\text{M}+\text{H}]^+$ 363.1834, found 363.1830.

3,4-Diethyl-1-phenyl-2-[(2,4,6-trimethoxy)phenyl]-1H-pyrrole (5k)

White solid; mp 97-99 $^{\circ}\text{C}$; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 1.02 (t, 3H, $J = 7.5$ Hz), 1.28 (t, 3H, $J = 7.5$ Hz), 2.30 (q, 2H, $J = 7.5$ Hz), 2.59 (q, 2H, $J = 7.5$ Hz), 3.50 (s, 6H), 3.78 (s, 3H), 6.02 (s, 2H), 6.74 (s, 1H), 7.01-7.06 (m, 3H), 7.14 (t, 2H, $J = 7.8$ Hz) ppm; $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ 12.4, 14.7, 18.6, 18.8, 55.2, 55.4, 90.3, 103.7, 117.8, 121.3, 123.8, 124.8, 125.0, 125.1, 128.1, 141.4, 159.7, 161.2 ppm; IR (KBr): 2960, 2927, 2852, 1583, 1501, 1462, 1412, 1204, 1128, 764, 697 cm^{-1} ; MALDI-TOFMS calcd for $\text{C}_{23}\text{H}_{28}\text{NO}_3$ $[\text{M}+\text{H}]^+$ 366.2069, found 366.2064.

General Procedure for Synthesis Pyrrole Trimer 7

To a stirred solution of pyrrole **3b** (0.40 mmol 1 equiv.) in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP, 0.1 M), recyclable hypervalent iodine(III) reagent **1a** (0.40 x 1/4 mmol 1 equiv.) was added at room temperature. After 15 min, to the mixture, arene **4a** (0.60 mmol 1.5 equiv.) and TMSCl (0.80 mmol 2

equiv.) was added and then stirred for 3 h under the same conditions, while the reaction progress was checked by TLC. MeOH was added to the reaction mixture, and it was filtered to give the tetraiodide **2** (confirmed by $^1\text{H-NMR}$ analysis and TLC), which was washed several times with small portion of MeOH for purification. The filtrate was evaporated and subjected to column chromatography (SiO_2 , hexane) to give the pure **5b**.

Next, azole **6a**, recyclable hypervalent iodine(III) reagent **1a** (0.40 x 1/4 mmol 1 equiv.) and TMSBr (0.8 mmol 2 equiv.) were added to a solution of pyrrole dimer **5b** (0.4 mmol 1 equiv.) in $(\text{CH}_2)_2\text{Cl}_2$ (0.1 M) at ambient temperature and the mixture was stirred under an inert atmosphere at 70 °C. After 1 h, saturated aqueous sodium hydrogen carbonate was added to the mixture at room temperature when the reaction completed. The aqueous phase was extracted with CH_2Cl_2 . The extract was dried over anhydrous Na_2SO_4 and then evaporated to dryness. MeOH was added to the reaction mixture, and it was filtered to give the tetraiodide **2** (confirmed by $^1\text{H-NMR}$ analysis and TLC), which was washed several times with small portion of MeOH for purification. The filtrate was evaporated and subjected to column chromatography (SiO_2 , hexane) to give 1-(1-methyl-5-(2,4,6-trimethoxyphenyl)-1*H*-pyrrol-2-yl)-1*H*-1,2,3-triazole **7a**.

1-(1-Methyl-5-(2,4,6-trimethoxyphenyl)-1*H*-pyrrol-2-yl)-1*H*-1,2,3-triazole (**7a**)

Brown oil; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 3.18 (s, 3H), 3.75 (s, 6H), 3.85 (s, 3H), 6.12 (d, 1H, $J = 3.4$ Hz), 6.19 (s, 2H), 6.34 (d, 1H, $J = 3.9$ Hz), 7.79-7.81 (m, 2H) ppm; $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ 31.0, 55.4, 55.8, 90.5, 102.3, 104.1, 108.4, 124.7, 126.2, 126.6, 133.0, 160.0, 161.8 ppm; IR (KBr): 3122, 2922, 2850, 1710, 1610, 1584, 1537, 1464, 1415, 1337, 1276, 1228, 1205, 1155, 1125, 1035, 1011, 947, 816, 750, 647 cm^{-1} ; MALDI-TOFMS calcd for $\text{C}_{16}\text{H}_{19}\text{N}_4\text{O}_3$ $[\text{M}+\text{H}]^+$ 315.1457, found 315.1452.

1-(1-Methyl-5-(2,4,6-trimethoxyphenyl)-1*H*-pyrrol-2-yl)-1*H*-benzo[*d*][1,2,3]triazole (**7b**)

$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 3.14 (s, 3H), 3.77 (s, 6H), 3.86 (s, 3H), 6.21-6.23 (m, 3H), 6.47 (d, 1H, $J = 4.0$ Hz), 7.40 (t, 1H, $J = 8.0$ Hz), 7.50-7.58 (m, 2H), 8.10 (d, 1H, $J = 8.4$ Hz) ppm; $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ 30.9, 55.4, 55.9, 90.7, 102.6, 105.1, 108.8, 110.6, 119.9, 123.1, 124.2, 126.4, 128.2, 134.9, 145.2, 160.1, 161.8 ppm; MALDI-TOFMS calcd for $\text{C}_{20}\text{H}_{21}\text{N}_4\text{O}_3$ $[\text{M}+\text{H}]^+$ 365.1614, found 365.1608.

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