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Iron-Catalyzed Quick Homocoupling Reaction of Aryl or Alkynyl Grignard Reagents Using a Phosphonium Ionic Liquid Solvent System

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ABSTRACT: *The iron-catalyzed homocoupling reaction of aryl Grignard reagent was completed very quickly when the reaction was carried out in a phosphonium salt ionic liquid solvent system at 0°C for 5 min. Using a similar reaction system, the first example of the iron-catalyzed homocoupling reaction of alkynyl Grignard reagents has also been accomplished using the ionic liquid technology.* © 2011 Wiley Periodicals, Inc. Heteroatom Chem 22:397–404, 2011; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.20696

INTRODUCTION

Iron is recognized as an economical and pollution-free metal source, and various types of iron metal-catalyzed organic transformations have been reported during the past decades [1]. We were also fascinated by the possibility of iron-catalyzed reactions and developed several of them, that is the intramolecular cyclization of cyclopropanedithioacetals [2], the [2 + 2]-cycloaddition of *trans*-anethol [3], the [2 + 3]-type cycloaddition of styrene derivatives with 1,4-benzoquinone [4], the 1,4-addition of β-ketoesters to vinylketones [5], the alkylation of indoles and pyrrole [6,7], the Nazaov cyclization of thiophenes [8] or pyrroles [9], and the enantioselective Michael addition of thiols to α, β-unsaturated carbonyl compounds [10].

Excellent examples have also been reported recently by two groups on the iron-catalyzed biaryl-coupling reaction, including Hayashi [11] and Cahiez [12] independently. The iron-catalyzed homo- or heterocoupling reaction of aryl Grignard reagents has been recognized as an easy and efficient access to the production of symmetrical di- or polyaromatic compounds [13].

Ionic liquids (ILs) are now widely recognized as suitable for use in organic reactions and provide possibilities for improvement in the control of product distribution, enhanced reactivity, ease of product recovery, catalyst immobilization, and recycling. However, ILs have been considered inappropriate for strong base-mediated reactions. Recently, several examples have been reported, which show the possibility of using these liquids as reaction media for strong base-mediated reactions such as the Grignard reaction [14–16]. We also succeeded in designing an IL that is appropriate for this reaction; introduction of alkyl ether moiety on the side arm of phosphonium salt was quite effective in improving the capability of the phosphonium salt ILs as solvent for the Grignard reaction; methoxyethyl(tri-*n*-butyl)phosphonium bis(trifluoromethanesulfonyl)imide ($[P_{444ME}][NTf_2]$) was thus synthesized [17].

Clyburne and his colleagues reported that an alkyl Grignard reagent was reacted with

Dedicated to Professor Kin-ya Akiba on the occasion of his 75th birthday.

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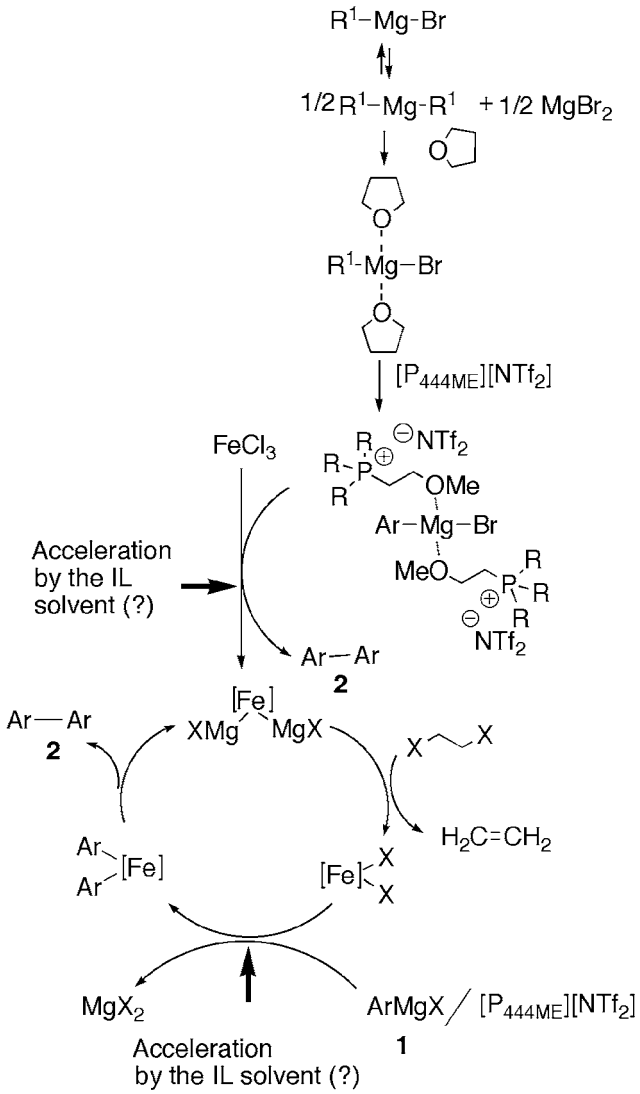


FIGURE 1 Working hypothesis of iron-catalyzed quick homocoupling of aryl Grignard reagent in the IL solvent system.

benzoquinone to provide not the simple addition product, but the corresponding coupling product with hydroquinone through a single electron transfer and transmetallation process [18].

Hayashi and Nagano proposed the reaction mechanism for the iron(III) chloride-mediated homocoupling reaction of the aryl Grignard reaction: The key step might be a reduction step of iron(III) cation by an aryl Grignard reagent or a transmetallation step on the iron as illustrated in Fig. 1 [11b]. We previously reported that iron(III)-catalyzed [2 + 3]-type cycloaddition of *trans*-anethol with benzoquinone was drastically accelerated when the reaction was changed by acetonitrile to an IL [4]. Fuchigami and co-workers reported that formation of a charge-separated transition state did accelerate in ILs solvent, but the form was unstable in ILs due to their noncoordinating property; and the reaction was thus significantly accelerated [19]. In fact, we found that a charge-separated transition pathway was involved in our the iron(III) salt-mediated [2 + 3]-type cycloaddition reaction by observing positive solvatochromism during the course of the reaction [4c]. Hence, we hypothesized that acceleration of iron(III) chloride-mediated homocoupling of the aryl Grignard reagent might be expected if the reactions were conducted in ILs because both electron transfer and transmetallation might take place easily in the solvent. On the basis of this working hypothesis, we tested the iron-catalyzed homocoupling reaction of the aryl Grignard reagent developed by Hayashi [11b] in our phosphonium IL ($[P_{444M}E][NTf_2]$) [17] as a solvent and found that a desired homocoupling reaction did, in fact, proceed very quickly.

Conventional organic synthesis generally appreciates high productivity and selectivity. However, recently, the development of quick reactions has also become very important in many stages of organic synthesis. For example, the criteria for synthetic efficiency in an in vivo PET (positron emission tomography) study using ^{11}C or ^{18}F as a positron nuclide are different. The investigation requires a rapid chemical reaction for the incorporation of these atoms into bioactive organic compounds, because of the time limitation of the short-lived positron emitter (half-life of ^{11}C is 20.3 min and that of ^{18}F is 110 min) [20].

In this article, we report the results of iron-catalyzed types of the quick homocoupling reaction of aryl Grignard reagents or alkylnyl Grignard reagents in the IL solvent system [21].

RESULTS AND DISCUSSION

Homocoupling Reaction of Aryl Grignard Reagents

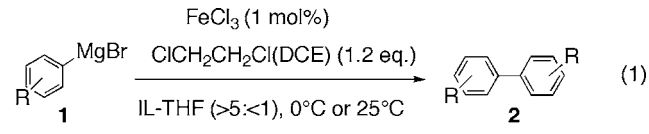
We tested the reaction of phenyl magnesium bromide (PhMgBr) in the presence of 1 mol% of iron(III) chloride using 1,2-dichloroethane as an oxidant (Eq. (1)): The desired coupling reaction of PhMgBr (**1a**) was completed in less than 5 min at 0°C, and biaryl **2a** was obtained in excellent yield in a pure $[P_{444ME}][NTf_2]$ solvent. Since PhMgBr was prepared in a tetrahydrofurane (THF) solvent, we initially prepared an IL solution of PhMgBr by removing this solvent under reduced pressure at 0°C and then mixing it with $FeCl_3$ and the oxidant. However, we soon found that we could bypass such a nuisance process because no significant reduction in the reaction rate

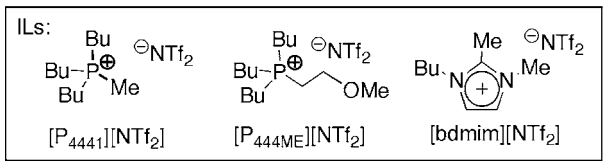
TABLE 1 Iron-Catalyzed Homocoupling of Aryl Grignard Reagents **1**

Entry	*Substrate* ***1***	*Solvent*[a]	*Temperature (°C)*	*Time (min)*	*Product* ***2***	*Yield (%)*[b]
1	**1a**	$[P_{444ME}][NTf_2]$	0	5	**2a**	100
2	**1a**	$[P_{4441}][NTf_2]$	0	5	**2a**	99
3	**1a**	[bdmim][NTf_2]	0	5	**2a**	90
4	**1a**	THF	40	60	**2a**	90
5	**1a**	HMPA	0	55	**2a**	2
6	**1a**	$[P_{444ME}][NTf_2]$[c]	0	5	**2a**	100
7	**1b**	$[P_{444ME}][NTf_2]$	0	5	**2b**	99
8	**1c**	$[P_{444ME}][NTf_2]$	25	5	**2c**	86
9	**1d**	$[P_{444ME}][NTf_2]$	25	30	**2d**	18[d]
10	**1e**	$[P_{444ME}][NTf_2]$	0	5	**2e**	97
11	**1f**	$[P_{444ME}][NTf_2]$	0	5	**2f**	94
12	**1g**	$[P_{444ME}][NTf_2]$	0	5	**2g**	99
13	**1h**	$[P_{444ME}][NTf_2]$	25	10	**2h**	91
14	**1i**	$[P_{444ME}][NTf_2]$	25	10	**2i**	51

[a]The reaction was carried out in a mixed solvent (IL and THF = 5:1). See details in the Experimental section.
[b]Isolated yield.
[c]Result using recycled IL (five times).
[d]1,3,5-Trimethylbenzene was detected by GC-MS analysis as a major by-product.
1a: R=H, **1b**: R=4-Me, **1c**: R=2-Me, **1d**: R=2,4,6-Me, **1e**: R=4-MeO, **1f**: R=2-MeO, **1g**: R=4-F, **1h**: 2-ThienylMgBr, **1i**: BenzylMgBr

was recorded even when the reaction was conducted in a mixed solvent of $[P_{444ME}][NTf_2]$ and THF (5:1) (entry 1). But, it should be emphasized that the presence of the IL $[P_{444ME}][NTf_2]$ as a major component of the mixed solvent was essential for accelerating the reaction; it required at least 60 min to complete the reaction, even when the reaction was conducted in a pure THF solvent system at 40°C. Optimization of the ratio of ionic liquid showed that the presence of this liquid at more than ca. 70–80% (v/v) versus THF caused no drop in the reaction rate. Therefore, we conducted further experiments using a mixed solvent of IL and THF (5:1) and the results are summarized in Table 1.





Although **2a** was also obtained in excellent yield in the mixed solvent of $[P_{4441}][NTf_2]$ and THF (5:1) (entry 2), isolation of the product was troublesome because $[P_{4441}][NTf_2]$ was very soluble in many organic solvents, such as hexane and ether. On the other hand, easy extraction was accomplished using $[P_{444ME}][NTf_2]$ or [bdmim][NTf_2] as a solvent. The coupling reaction proceeded very rapidly in [bdmim][NTf_2], although a slightly reduced yield of **2a** (90%) was recorded (entry 3). On the contrary, it took at least 1 h under reflux conditions when the reaction was carried out in pure THF, although the chemical yield of **2a** was excellent (90%; entry 4). Only 2% of **2a** was obtained when hexamethylphosphoramide (HMPA) was used as the solvent (entry 5). A very rapid homocoupling reaction of the aryl Grignard reagent has thus been accomplished using the IL solvent system. One of the benefits of using IL as a solvent for organic reactions is that purification of ILs is easily accomplished by a simple method, and it can be used repeatedly. In fact, we obtained the desired product **2a** in quantitative yield even when the reaction was conducted in the recycled $[P_{444ME}][NTf_2]$ (five times; entry 6). Furthermore, the present oxidative homocoupling could be readily scaled up to the reaction of 15.0 mmol of the Grignard reagent **1a** using 1 mol% of the $FeCl_3$ catalyst, which gave 99% yield (1.14 g) of biaryl **2a** without any by-products.

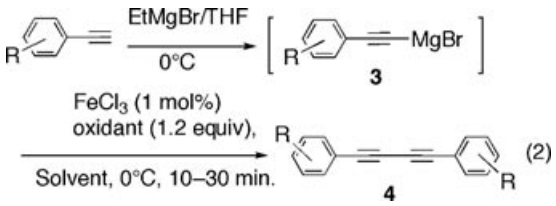
The electric property of the substituent on the benzene ring had no influence on the chemical yield of the products. The desired coupling products **2b** or **2e** were obtained in almost quantitative yields for substrate **1b** (entry 7) or **1e** (entry 10), which have the electron-donating methyl or methoxy group, respectively. Substrate **1g** that has electron-withdrawing fluorine on the phenyl group also provided the coupling product **2g** in 99% yield (entry 12).

On the other hand, steric bulkiness of the substituent affected the reaction greatly. It was found

that 25°C was required to complete the reaction when *o*-tolyl MgBr (**1c**) was used as the substrate, and the desired biaryl compound **2c** was obtained in 86% yield (entry 8), although the acceleration obtained still compared to that in the ether solvent because 12 h under reflux conditions was required to complete the same reaction when the reaction was carried out with ether as the solvent [11b]. Introduction of an electron-donating group is effective to improve the reaction rate, and a very rapid coupling was again accomplished when *o*-methoxyphenyl MgBr (**1f**) was employed for the reaction (entry 11).

The reaction of the 2,4,6-trimethylphenyl Grignard reagent (**1d**) proceeded very slowly, and no reaction took place at 0°C; homocoupling product **2d** was obtained in 18% yield when the reaction was performed at 25°C for 30 min (entry 9). It was confirmed that 1,3,5-trimethylbenezene was formed by GC-MS analysis as a major by-product of this reaction. Unfortunately, no improvement in the chemical yield of **2d** was achieved when the reaction was carried out at more than 40°C; the reaction resulted only in production of 1,3,5-trimethylbenzene because IL $[P_{444ME}][NTf_2]$ has an acidic proton. Furthermore, it was found that the Grignard reagent gradually lost its activity when the reaction was prolonged more than 30 min at room temperature (rt). Therefore, the highest temperature of the present reaction might be below 40°C and the reaction should be completed in 30 min.

It was applicable to use the reaction for a thionyl Grignard reagent **1h** and benzyl Grignard reagent **1i**, and the desired coupling product **2h** and **2i** was obtained in 91% and 51%, respectively (entries 13 and 14). Although there are several limitations, a simple and quick homocoupling reaction of the aryl Grignard reaction using $FeCl_3$ a catalyst has thus been accomplished in the phosphonium IL solvent system.



As mentioned before, Hayashi proposed that the key step might be the reduction step of iron(III) cation by the aryl Grignard reagent or a transmetallation step on the iron as illustrated in Fig. 1 [11b]. We assume that Hayashi's idea might be supported by the fact that the coupling reaction of more electron-rich **1f** proceeded more rapidly than that of **1c**, because it is expected that both reduction and transmetallation take place more easily using the electron-rich Grignard reagent. Since the reaction mixture turned black after addition of the Grignard reagent, iron nanoparticles may be produced under the reaction conditions and this may contribute to completing the coupling reaction. To the best of our knowledge, there is no report of the production of iron (0) nanoparticles in ILs. However, the formation of several transition metal nanoparticles in ILs has been reported in [22]. We have not yet, however, succeeded in obtaining any evidence for this possibility.

Homocoupling Reaction of Alkynyl Grignard Reagents

It is well known that the homocoupling reaction of alkynyl Grignard reagents is catalyzed by palladium [23], copper [24], or manganese [12b,25], whereas we recognize that there is no example of iron-catalyzed homocoupling of this reagent. We tested the reaction using 2-phenylethynyl magnesium bromide (**3a**) as a model substrate in the presence of 1 mol% of $FeCl_3$ as the catalyst using 1,2-dichloroethane (DCE) or 1,2-diiodoethane (DIE) as an oxidant in THF or ether. However, as anticipated, no desired product was obtained when the reaction was conducted in these solvents (entry 1, Table 2). To our delight, we discovered that the desired coupling product was obtained in 30% yield when the reaction was carried out in a mixed solvent of IL and THF using DCE as an oxidant (entry 2). Like the reaction of aryl Grignard reagents, IL was essential to realize the reaction because no desired product **4a** was obtained when the reaction was carried out in a pure THF or Et_2O solvent system (entry 1). After attempting the optimization of the ratio of IL and THF, we succeeded in obtaining **4a** in a mixed solvent of IL and THF that included at least ca. 60% (v/v) of $[P_{444ME}][NTf_2]$. Furthermore, a choice of the oxidant was also important; chemical yield of **4a** was increased to 55% (entry 3) when DIE was used instead of DCE (entry 2) as an oxidant. Among several oxidants such as iodomethane, 1,2-dichloroisobutane, 1,2-dibromoethane, and dry air, DIE gave the best result. Furthermore, a reduced chemical yield (40%) was recorded when the reaction was carried out in [bdmim][NTf_2] and THF (2:1) (entry 4). For the catalyst, $FeCl_3$ gave the best result (55%) (entry 3), and $Fe(BF_4)_2{\cdot}6H_2O$ afforded the second best (51%) (entry 5) whereas reduced chemical yield of the product was recorded when $Fe(ClO_4)_3 \cdot nH_2O$ (20%), $Fe(acac)_3$ (40%), $FeCl_2$ (39%), $FeBr_2$ (44%), FeI_2 (44%), or $Fe(acac)_2$ (33%) was used as the catalyst.

TABLE 2 Iron Salt-Catalyzed Homo Coupling of Alkynyl Grignard Reagents **3**

Entry	*Substrate* ***3***	*Fe Salt (1 mol%)*	*Oxidant*	*Solvent* [a]	*Product* ***4***	*Yield (%)*[b]
1	**3a**	$FeCl_3$	DCE	THF or Et_2O	**4a**	0
2	**3a**	$FeCl_3$	DCE	$[P_{444ME}][NTf_2]$	**4a**	30
3	**3a**	$FeCl_3$	DIE	$[P_{444ME}][NTf_2]$	**4a**	55
4	**3a**	$FeCl_3$	DIE	$[bdmim][NTf_2]$	**4a**	40
5	**3a**	$Fe(BF_4)_2{\cdot}6H_2O$	DIE	$[P_{444ME}][NTf_2]$	**4a**	51
6	**3b**	$FeCl_3$	DIE	$[P_{444ME}][NTf_2]$	**4b**	52
7	**3c**	$FeCl_3$	DIE	$[P_{444ME}][NTf_2]$	**4c**	80
8	**3d**	$FeCl_3$	DIE	$[P_{444ME}][NTf_2]$	**4d**	46
9	**3e**	$FeCl_3$	DIE	$[P_{444ME}][NTf_2]$	**4e**	37
10	**3f**	$FeCl_3$	DIE	$[P_{444ME}][NTf_2]$	**4f**	35

[a]The reaction was carried out in a mixed solvent of IL and THF (2:1). See details in the experimental section.
[b]Isolated yield.

Increased addition of the amount of $FeCl_3$ caused a significant reduction in the yield due to formation of a large amount of polymerized compound; **4a** was obtained in only 8% when the reaction was performed in the presence of 20% of $FeCl_3$

On the basis of these results, we conducted the homocoupling reaction of various types of alkynyl Grignard reagents using DIE as an oxidant in a mixed solvent, $[P_{444ME}][NTf_2]$ and THF (2:1), in the presence of 1 mol% of $FeCl_3$ (see entries 6–10 in Table 2). Comparing the reaction of **3b,** which has the electron-donating methoxy group on the benzene ring (entry 6) and that of **3c,** which has an electron-withdrawing trifluoromethyl group (entry 7). Compound **3c** gave a better result, and diyne **4c** was obtained in 80% yield. This was assumed to be due to the stable nature of **4c** against the acid-catalyzed polymerization because **4b** was easily polymerized when it was stored under atmospheric conditions. It should be noted that the coupling product **4d** or **4f** was also obtained using the present reaction system, although the chemical yields were insufficient (entries 9 and 10).

We have established a very rapid iron-catalyzed homocoupling reaction of aryl and alkynyl Grignard reagents using a phosphonium IL solvent system. The reaction was completed in less than 5 min at 0°C using only 1 mol% of economical $FeCl_3$ as the catalyst. We further established an iron-catalyzed homocoupling reaction of the alkynyl Grignard reaction using this liquid solvent system. It should also be noted that IL was essential for realizing the coupling reaction because no reaction took place in a pure THF or ether solvent system. To the best of our knowledge, this is the first example of the iron-catalyzed homocoupling reaction of the alkynyl Grignard reagent.

Recently, development of quick reactions has become a very important task in many stages of organic synthesis, as mentioned in the Introduction. Further investigation of the scope and limitations of this reaction will make it even more valuable.

EXPERIMENTAL

General Procedures

Reagents and solvents were purchased from common commercial sources and were used as received or purified by distillation from appropriate drying agents. Reactions requiring anhydrous conditions were run under an atmosphere of dry argon. Wako gel C-300 and Wako gel B5F were used for flash column chromatography and thin-layer

chromatography (TLC), respectively. NMR spectra were recorded on JEOL MH-500 (500 MHz for ^{1}H and 125 MHz for ^{13}C) spectrometers, and chemical shifts are expressed in ppm downfield from tetramethylsilane (TMS) in $CDCl_3$ as an internal reference. IR spectra were obtained on a Shimadzu FTIR-8000 spectrometer. GC-MS analysis was obtained on a Shimadzu GCMS-QP2010 spectrometer. $[P_{444ME}][NTf_2]$ is now commercially available from Tokyo Chemical Industry (T2564). Water content of the ionic liquids employed was determined by a Karl Fischer moisture titrator. The values are listed as follows: $[bdmim][NTf_2]$: 110 ppm; $[P_{4441}][NTf_2]$ (Nippon Chemical Co., Ltd.): 145 ppm; $[P_{444ME}][NTf_2]$(TCI T2564): 120 ppm; HMPA (Wako): 150 ppm.

Preparation and Purification Method of $[P_{444ME}][NTf_2]$

To an ethanol (20 mL) solution of 1-bromo-2-methoxyethane (4.68 g, 40 mmol), tributylphosphine (7.5 g, 37 mmol) was added and the resulting mixture was stirred for 22 h at 80°C. After being cooled to rt, hexane was added to form the precipitate, which was removed by filtration. The resulting filtrate was evaporated under vacuum to give the bromine salt (12.31 g, 36 mmol) in 97% yield. The salt was dissolved in ethanol (18 mL), and lithium bis(trifluoromethanesulfonyl)imide (11.37 g, 40 mmol) powder was added. Then the mixture was stirred at rt for 17 h to form lithium bromide as the precipitate. The precipitate was removed by filtration, the filtrate was washed with hexane three times, and the solvent was removed using lyophilization. The resulting oil was dissolved in acetone and was treated with active charcoal, and the charcoal was then removed by filtration. The filtrate was passed through active alumina (type II) and dried under vacuum at 50°C for 5 h to give $[P_{444ME}][NTf_2]$ (19.15 g, 35 mmol) as colorless oil in 95% yield. This IL is now commercially available from Tokyo Chemical Industry (T2564): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.979 (9H, t, J = 6.85 Hz), 1.45–1.55 (12H, m), 2.10–2.20 (6H, m), 2.53 (2H, q, J = 5.95 Hz), 3.36 (3H, s), 3.75 (2H, dt, J = 14.2 Hz, J = 5.95 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.00, 19.16 (d, J_{C-P} = 46.7 Hz), 19.98 (d, J_{C-P} = 46.7 Hz), 23.24 (d, J_{C-P} = 4.78 Hz), 23.60 (d, J_{C-P} = 16.2 Hz), 58.82, 65.08 (d, J_{C-P} = 7.64 Hz), 119.80 (q, J_{C-F} = 315.5 Hz); ^{31}P NMR (202.46 MHz, $CDCl_3$) δ 39.08 (d, J_{P-C} = 26.1 Hz); ^{19}F NMR (170.6 MHz, $CDCl_3$, C_6F_6) δ 92.91; IR (neat) 2937, 2878, 1400, 1194, 1057, 738 cm^{-1}.

Purification Method of $[P_{444ME}][NTf_2]$ *for Recyling Use*

The IL was washed with water (five times) and a mixed solvent of hexane and ethyl acetate (5:1), then treated with active charcoal as an acetone solution. After removing the charcoal by filtration, the filtrate was evaporated and dried under vacuum at 60°C for 5 h.

*Synthesis of Biphenyl (***2a***)*

$FeCl_3$(0.9 mg) was placed in a flask under dry nitrogen, and DCE (65.3 mg) and $[P_{444ME}][NTf_2]$ (1.0 mL) were then added. To the resulting mixture, a THF solution of 0.35 mL of PhMgBr (1.57 M, 0.54 mmol) was added at 0°C under argon and this was stirred for 5 min at the same temperature. The reaction mixture was diluted with 3 mL of a mixed solvent (hexane and diethyl ether = 2:1) to give the biphasic layer. Organic layers were collected by decantation, then evaporation and silica gel thin layer chromatography (TLC) to give **2a** (0.27 mmol, 42.0 mg) in quantitative yield. Using the same method, biaryls **2b**–**2i** were obtained in the yields listed in Table 1.

Biphenyl (**2a**): mp = 66–68°C. *Rf* = 0.49 (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (2 H, t, J = 7.3 Hz), 7.43 (4H, dd, J_1 = 7.3 Hz, J_2 = 7.3 Hz), 7.59 (4 H, d, J = 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 127.1, 127.2, 128.7, 141.2; IR (KBr) 3030, 1944, 1880, 1575, 1480, 1338, 1171, 1083, 902, 745, 704 cm^{-1}.

1-(4-Methylphenyl)-4-methylbenzene (**2b**): mp = 120–122°C; *Rf* = 0.48 (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (6H, s), 7.22 (4H, d, J = 8.0 Hz), 7.47 (4H, d, J = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1, 126.8, 129.4, 136.7, 138.2; IR (KBr) 3027, 2917, 1502, 1114, 1006, 836, 804, 725, 549, 509 cm^{-1}.

1-(2-Methylphenyl)-2-methybenzene (**2c**), CAS Registry Number: 605-39-0: mp = 18°C; *Rf* = 0.52 (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.05 (6H, s), 7.10 (2H, d, J = 7.0 Hz), 7.20–7.27 (6H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.9, 125.6, 127.2, 129.4, 129.9, 135.9, 141.7; IR (neat) 3059, 3019, 2922, 1478, 1458, 1379, 1125, 1009, 754, 729, 625, 457 cm^{-1}.

1-*(2,4,6-Trimethylphenyl)-2,4,6-trimethylbenzene* (**2d**), CAS Registry Number: 50431-97-5: mp = 100–101°C; *Rf* = 0.78 (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.86 (12H, s), 2.33 (6H, s), 6.93 (4H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.8, 21.1, 128.2, 135.5, 136.0, 137.0; IR (KBr) 2916, 2853, 1611, 1474, 1437, 1375, 1005, 853, 596, 530 cm^{-1}.

1-(4-Methoxyphenyl)-4-methoxybenzene (**2e**), CAS Registry Number: 2132-80-1: mp = 173–175°C; *Rf* = 0.56 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84 (6H, s), 6.96 (4H, d, J =

9.0 Hz), 7.47 (4H, d, $J = 9.0$ Hz);^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 114.1, 127.7, 133.5, 158.7; IR (KBr) 1614, 1506, 1276, 1250, 1178, 1040, 1015, 825, 805 cm^{-1}.

1-(2-Methoxyphenyl)-2-methoxybenzene (**2f**), CAS Registry Number: 4877-93-4: mp = 153–155°C; $Rf = 0.39$ (hexane/CH_2Cl_2 = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (6H, s), 6.98 (2H, d, $J = 8.0$ Hz), 7.01 (2H, t, $J = 7.0$ Hz), 7.25 (4H, dd, $J_1 = 8.0$ Hz, $J_2 = 2.0$ Hz), 7.33 (4H, dt,$J_1 = 2.0$ Hz, $J_2 = 7.0$ Hz);^{13}C NMR (125 MHz, $CDCl_3$) δ 55.7, 111.1, 120.3, 127.8, 128.6, 131.4, 157.0; IR (KBr) 1588, 1506, 1429, 1310, 1281, 1255, 1240, 1220, 1168, 1112, 1061, 1025, 999, 933, 764 cm^{-1}.

1-(4-Fluorophenyl)4-fluorobenzene (**2g**), CAS Registry Number: 398-23-2: mp = 88–89°C; Rf = 0.63 (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (4H, t, $J = 9$ Hz), 7.49 (4H, dd, $J = 9$ Hz, 5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 115.66 (d, $J_{C-CF} = 21.0$ Hz), 128.54 (d, $J_{C-CCF} = 8.6$ Hz), 136.38 (d, $J_{C-CCCF} = 2.8$ Hz), 162.41 (d, J_{CF} = 245.8 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ 45.95; IR (KBr) 3073, 1890, 1603, 1501, 1322, 1235, 1112, 825 cm^{-1}.

2,2'-Bithiophene (**2h**), CAS Registry Number: 492-97-7: mp = 31–33°C; $Rf = 0.42$ (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (2 H, dd, $J_1 = 5.0$ Hz, $J_2 = 3.6$ Hz), 7.10 (2H, dd, $J_1 = 3.6$ Hz, $J_2 = 1.3$ Hz), 7.14 (2H, dd, $J_1 = 5.0$ Hz, $J_2 = 1.3$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 123.7, 124.3, 127.7, 137.4; IR (KBr) 3091, 3065, 1527, 1417, 1323, 1209, 1050, 828, 817, 700 cm^{-1}.

*Synthesis of 1,4-Diphenylbuta-1,3-diyne (**4a**)*

To a THF (0.4 mL) solution of 3-phenylethyne (51.1 mg, 0.50 mmol) was added 0.37 mL of ether solution of ethylmagnesium bromide (1.48 M, 0.55 mmol) at 0°C under dry nitrogen and the mixture was stirred for 1 h at the same temperature. The resulting solution was added to the mixture of 1.5 mL of $[P_{444ME}][NTf_2]$, $FeCl_3$(0.9 mg), and DIE (169.1 mg, 0.60 mmol) using a cannula and the resulting mixture was stirred at 0°C for 20 min under dry nitrogen. The reaction was quenched by addition of 3.0 mL of a mixed solvent (hexane and ether 2:1) to give the biphasic layer. Organic layers were collected by decantation five times, then by evaporation and silica gel TLC to give **4a** (28 mg, 0.14 mmol) in 55% yield.

1,4-Diphenylbuta-1,3-diyne (**4a**), CAS Registry Number 59751-58-5: mp = 86–88°C; Rf = 0.31 (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.40 (6H, m), 7.52 (4H, d, $J = 6.87$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 73.9, 81.5, 121.8, 128.4, 129.2, 132.5; IR (KBr) 3050, 2924, 1551, 1067, 1024, 914, 756, 687, 527, 463 cm^{-1}.

1,4-*Bis(4-methoxyphenyl)buta-1,3-diyne* (**4b**), CAS Registry Number: 22779-05-1: mp = 142–144°C; Rf = 0.41 (hexane/CH_2Cl_2 = 6/1);^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (6H, s), 6.85 (2H, d, J = 8.8 Hz), 7.46 (2H, d, $J = 8.8$ Hz);^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 72.9, 81.2, 114.0, 114.1, 134.0, 160.2; IR (KBr) 2974, 2841, 1503, 1439, 1292, 1246, 1169, 1022, 831, 691, 538 cm^{-1}.

1,4-*Bis(4-(trifluoromethyl)phenyl)buta-1,3-diyne* (**4c**), CAS Registry Number: 151362-06-0: mp = 166–168°C; $Rf = 0.57$ (hexane);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (2H, d, $J = 8.5$ Hz), 7.65 (2H, d, $J = 8.5$ Hz);^{13}C NMR (125 MHz, $CDCl_3$) δ 75.6, 81.0, 123.7 (q, $J_{CF} = 272.5$ Hz), 124.8, 125.4 (q, J_{C-CCF} = 3.9 Hz), 131.4 (q, $J_{C-CF} = 32.7$ Hz), 132.8;^{19}F NMR (470 MHz, $CDCl_3$) δ 98.68; IR (KBr) 2963, 1560, 1508, 1408, 1316, 1177, 1132, 1065, 839, 733, 594, 521 cm^{-1}.

1,4-*Dio-tolylbuta-1,3-diyne* (**4d**), CAS Registry Number: 136053-56-0: mp = 80–82°C; Rf = 0.52 (hexane);^{1}H NMR (400 MHz, $CDCl_3$) δ 2.50 (6H, s), 7.14–7.50 (6H, m), 7.51 (2H, d, $J = 1.5$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.7, 77.5, 81.1, 121.7, 125.6, 129.1, 129.6, 132.9, 141.6; IR (KBr) 3055, 2947, 1477, 1456, 1107, 941, 750, 714, 453 cm^{-1}.

1,4-*Dicyclohexenylbuta-1,3-diyne* (**4e**), CAS Registry Number: 2979-05-7: mp = 60–61°C; Rf = 0.50 (hexane);^{1}H NMR (400 MHz, $CDCl_3$) δ 1.55–1.63 (8H, m), 2.10–2.12 (8H, m), 6.24 (2H, t, J = 1.8 Hz);^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3, 22.1, 25.8, 28.7, 71.5, 82.7, 120.0, 138.1; IR (KBr) 2931, 2860, 2128, 1433, 1334, 1138, 916, 841, 797, 515 cm^{-1}.

1,4-*Bis(trimethylsilyl)buta-1,3-diyne* (**4f**), CAS Registry Number: 4526-07-2: $Rf = 0.68$ (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.19 (18H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ −0.5, 85.9, 88.0; IR (neat) 2971, 2912, 2064, 1408, 1255, 1064, 849, 766, 701 cm^{-1}.

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