

Polymer-Supported-Cobalt-Catalyzed Regioselective Cyclotrimerization of Aryl Alkynes

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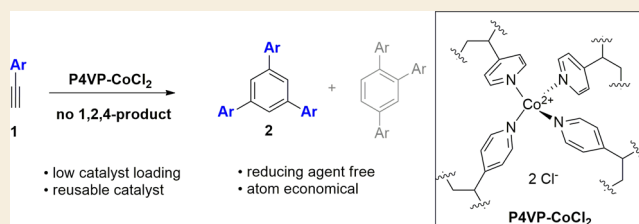
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Supporting Information

ABSTRACT: A convoluted poly(4-vinylpyridine) cobalt(II) (P4VP-CoCl₂) system was developed as a stable and reusable heterogeneous catalyst. The local structure near the Co atom was determined on the basis of experimental data and theoretical calculations. This immobilized cobalt catalyst showed high selectivity and catalytic activity in the [2 + 2 + 2] cyclotrimerization of terminal aryl alkynes. With 0.033 mol % P4VP-CoCl₂, the regioselective formation of 1,3,5-triarylbenzene was realized without 1,2,4-triarylbenzene formation. Further, a multi-gram-scale (11 g) reaction proceeded efficiently. In addition, the polymer-supported catalyst was successfully recovered and used three times. X-ray photoelectron spectroscopy analysis of the recovered catalyst suggested that cobalt was in the +2 oxidation state. The 1,3,5-triarylbenzene derivatives were applied to the synthesis of a molecular beam electron resist and a polycyclic aromatic hydrocarbon.

KEYWORDS: cobalt catalysis, cyclotrimerization, polymer-supported catalyst, regioselective catalyst, reusable catalyst



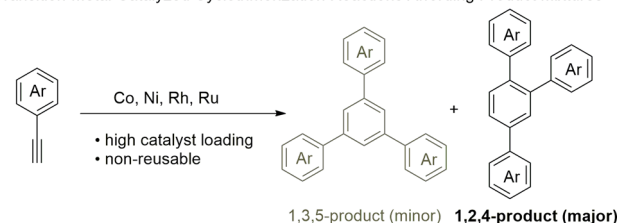
1. INTRODUCTION

Polycyclic aromatic hydrocarbons (PAHs) have long attracted significant research interest because of their potential applicability in nanoparticles, organic semiconductors, and photovoltaics.^{1–18} Symmetric 1,3,5-triarylbenzenes act as key building blocks for the generation of PAHs.¹⁹ Organic light-emitting diodes,^{20–22} dendrimers,^{23,24} and fullerene fragments^{25–28} can also be synthesized from 1,3,5-triarylbenzenes. The common synthesis routes for 1,3,5-triarylbenzenes are multistep Suzuki–Miyaura-type reactions,^{29–33} acid-catalyzed triple condensation reactions of aryl methyl ketones,^{34–39} and transition-metal-catalyzed cyclotrimerization reactions of aryl alkynes.^{40–69} Although several transition metals, including cobalt,^{40–47} nickel,^{48–54,54} rhodium,^{55–57} and ruthenium,^{58,59} are known to catalyze cyclotrimerization reactions, the selective formation of 1,3,5-triarylbenzene has rarely been achieved.^{70–74} The transition-metal-catalyzed cyclotrimerization of alkynes usually generates a mixture of 1,2,4-triarylbenzene as a major product and 1,3,5-triarylbenzene as a minor product (Scheme 1a).^{40–69} Additionally, these reactions typically demand external reducing agents and solvents, resulting in unwanted chemical waste while reducing the atom efficiency of the reaction. These transition-metal-catalyzed reactions also demand high catalyst loadings, and the catalysts are not usually recoverable and reusable.

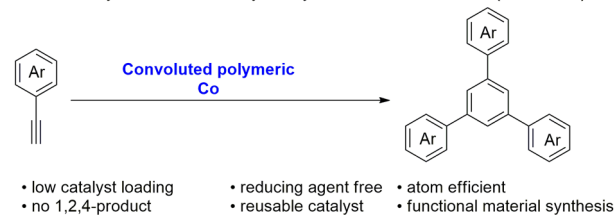
Because steric repulsion between a bulky ligand and an aryl acetylene could suppress the formation of 1,2,4-triarylbenzene,^{43,44} we assumed that a polymer-supported catalyst might generate the desired 1,3,5-triarylbenzenes with very high

Scheme 1. Representative Examples of Transition-Metal-Catalyzed Cyclotrimerization

a) Transition-Metal-Catalyzed Cyclotrimerization Reactions Affording Product Mixtures



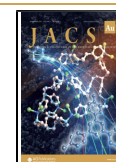
b) Convoluted-Polymeric-Cobalt-Catalyzed Cyclotrimerization Reaction (This Work)



selectivity. Polymers like poly(4-vinylpyridine) (P4VP) are advantageous because in addition to being bulky, they enable

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heterogeneous catalysis^{75–80} and thus catalyst reuse. Although homogeneous cobalt catalysis for cyclotrimerization has been reported,^{40–47} to the best of our knowledge, polymer-supported cobalt^{81–84} has not yet been applied to this reaction. Herein, we report 1,3,5-selective cyclotrimerization using a reusable, stable, heterogeneous, and convoluted polymeric cobalt(II) catalyst under external reducing agent-free conditions (Scheme 1b).

2. RESULTS AND DISCUSSION

Preparation and Structural Analysis for Convoluted Cobalt Catalyst

To prepare the convoluted polymeric cobalt catalyst, a methanol solution of commercially available non-cross-linked

Scheme 2. Synthesis and Calculated Model Structure of P4VP-Supported Cobalt Complex II

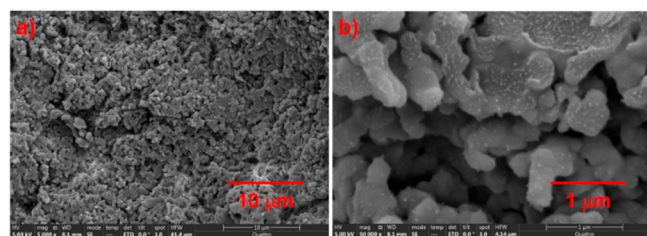
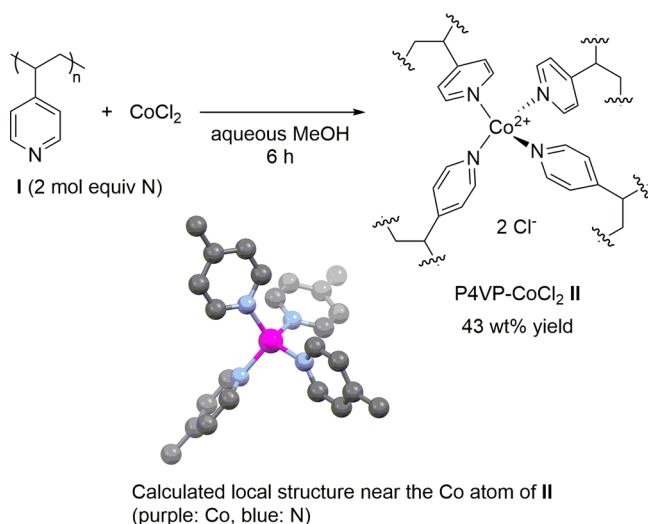


Figure 1. SEM Image of P4VP-CoCl₂ II.

P4VP (I; MW ~ 160 000) was treated with an aqueous solution of CoCl₂ for 6 h at room temperature. Consequently, molecular convolution produced P4VP-CoCl₂ (II) as a blue precipitate (Scheme 2), which was insoluble in water, methanol, 1,4-dioxane, hexane, and ethyl acetate. On the basis of X-ray absorption near edge structure (XANES) and extended X-ray absorption fine structure (EXAFS) data, elemental analysis, and density functional theory (DFT) calculations, the local structure near the Co atom of II was proposed, as shown in Scheme 2 (see Figures S1 and S2 for details). Scanning electron microscopy (SEM) analysis of the synthesized cobalt complex revealed that the catalyst was porous (Figure 1) and it had a regular distribution of cobalt (for details; see Figure S3).

Table 1. Cyclotrimerization of 1a Using P4VP-CoCl₂^a

entry	deviation from standard conditions	yield of 2a (%)	yield of 3a (%)
1	none	69 (68 ^b)	0
2	without base	64	0
3	zinc (1 mol equiv)	63	0
4	0.015 mol % P4VP-CoCl ₂ (150 mol ppm Co)	59	0
5	0.066 mol % P4VP-CoCl ₂ (660 mol ppm Co)	68	0
6	in toluene (0.5 mL)	40	0
7	in xylene (0.5 mL)	66	0
8	in DMF (0.5 mL)	trace	0
9	in the absence of Co	0	0
10	CoCl ₂ (0.3 mol % Co)	trace	9
11	CoCl ₂ (0.3 mol % Co) and pyridine (1.3 mol %)	4	7
12	CpCo(CO) ₂ (0.3 mol % Co) and pyridine (1.3 mol %)	15	21
13	(PPh ₃) ₃ CoCl (0.3 mol % Co) and pyridine (1.3 mol %)	1	0
14	CoCl ₂ (0.3 mol % of Co) and 4- <i>t</i> -Bu-pyridine (1.3 mol %)	16	20
15	CoCl ₂ (0.3 mol % of Co) and 4- <i>i</i> -Pr-pyridine (1.3 mol %)	19	24

^aYield determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. ^bIsolated yield.

Reaction Optimization

With P4VP-CoCl₂ II in hand as a heterogeneous Co catalyst, the cyclotrimerization of phenylacetylene (1a) was investigated (Table 1). Pleasingly, when the reaction of 1a was carried out with 0.033 mol % of II (330 mol ppm of Co) in the presence of *N,N*-diisopropylethylamine (DIPEA, Hünig's base) at 150 °C for 24 h under neat conditions, the regioselective cyclization proceeded selectively to produce 1,3,5-triphenylbenzene (2a) in 68% yield, and no 1,2,4-triphenylbenzene (3a) was detected (entry 1, Table 1). Although the reaction proceeded well without base (entry 2), the catalyst was not reusable (for details, see the Supporting Information, Section 12). Zn as a reducing agent did not improve the reactivity and slightly reduced the product yield (entry 3). When 0.015 mol % of II (150 mol ppm of Co) was used, the reaction still proceeded to afford 2a in 59% yield (entry 4). The increased catalyst loading (0.066 mol % or 660 mol ppm of Co) was unable to increase the reaction yield (entry 5). The reaction in xylene afforded 2a in 66% yield, whereas those in toluene (40% yield) and DMF (trace) were sluggish (entries 6–8). In the absence of metals, no desired product was obtained (entry 9). A homogeneous cobalt catalyst (CoCl₂) without a ligand provided only a trace amount of 2a (entry 10), whereas the yield improved slightly in the presence of pyridine as a ligand (entry 11). The reaction using other homogeneous Co catalysts, including CpCo(CO)₂ and (PPh₃)₃CoCl, produced mixtures of 1,3,5- and 1,2,4-triphenylbenzene (2a and 3a) in yields up to 15% and 21%, respectively (entries 12 and 13). The reaction with more electron-donating 4-*t*-butyl-pyridine as a ligand gave 16% of 1,3,5-triphenylbenzene (2a) and 20% of

Table 2. Substrate Scope for Cyclotrimerization^a

entry	substrate 1 (Ar)	yield of 2 (%)
1	Ph, 1a	68
2	4-MeC ₆ H ₄ , 1b	84
3	3-MeC ₆ H ₄ , 1c	77
4	2-MeC ₆ H ₄ , 1d	67
5	4-MeOC ₆ H ₄ , 1e	86
6	4-BuC ₆ H ₄ , 1f	79
7	4-BrC ₆ H ₄ , 1g	66 ^b
8	4-ClC ₆ H ₄ , 1h	61 ^b
9	4-FC ₆ H ₄ , 1i	53
10	4-CF ₃ C ₆ H ₄ , 1j	42
11	4-EtO ₂ CC ₆ H ₄ , 1k	46
12	4-MeCOC ₆ H ₄ , 1l	39 ^b
13	4-HOC ₆ H ₄ , 1m	71 ^b
14	4-PhC ₆ H ₄ , 1n	49 ^b
15	2-PhC ₆ H ₄ , 1o	42 ^b
16	3-Py, 1p	0 ^b
17	1-naphthyl, 1q	41
18	1-octyne (1r)	0
19	(triisopropylsilyl)acetylene (1s)	0
20	1,2-diphenylethyne (1t)	0 ^b

^aReaction conditions: **1** (1 mol equiv., 5 mmol), P4VP-CoCl₂ (0.033 mol %, 330 mol ppm of Co), DIPEA (6.5 mol %), 150 °C, 24 h, N₂ atmosphere. Isolated yield. ^bOne-half a milliliter of xylene was added.

Table 3. Application of Recovered Catalyst

entry	no. of run	catalyst recovery yield (%)	yield of 2b (%)
1	fresh	98	84
2	1st	95	80
3	2nd	97	72

1,2,4-triphenylbenzene (**3a**), whereas that of 4-*i*-propylpyridine as a monomeric unit of P4VP afforded 19% 1,3,5-triphenylbenzene (**2a**) and 24% 1,2,4-triphenylbenzene (**3a**) (entries 14 and 15). These experimental data suggest that molecular convolution of the metal-cross-linked 3D Co species is important for the 1,3,5-selectivity.

Substrate Scope

Using the optimized reaction conditions, the substrate scope for cyclotrimerization was investigated. All the reactions selectively produced 1,3,5-triarylbenzene products (Table 2). For example, *p*-, *m*-, and *o*-methyl-substituted phenyl acetylenes **1b–d** were readily converted to 1,3,5-tris(methyl phenyl)benzenes **2b–d** in 84, 77, and 67% yield, respectively (entries 2–4). Substrates bearing electron-donating groups, such as *p*-methoxy (**1e**) and *p*-butyl (**1f**), were converted to the desired C₃-symmetric cyclotrimerized products in 86 and 79% yields, respectively (entries 5 and 6). Halogen-containing aryl alkynes 1-bromo-4-ethynylbenzene (**1g**), 1-chloro-4-ethynylbenzene (**1h**), and 1-ethynyl-4-fluorobenzene (**1i**) furnished the desired cycloaddition products in 66, 61, and

Scheme 3. Multigram-Scale Reaction and Application of Cyclotrimerized Products

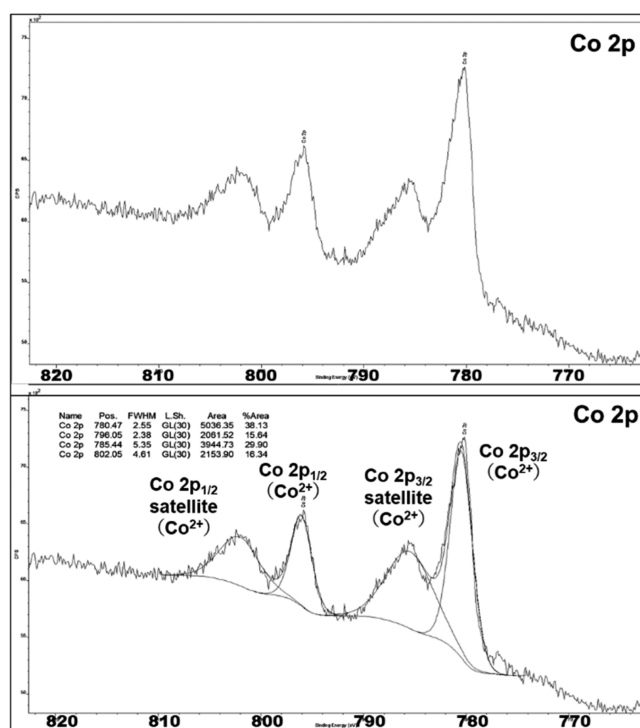
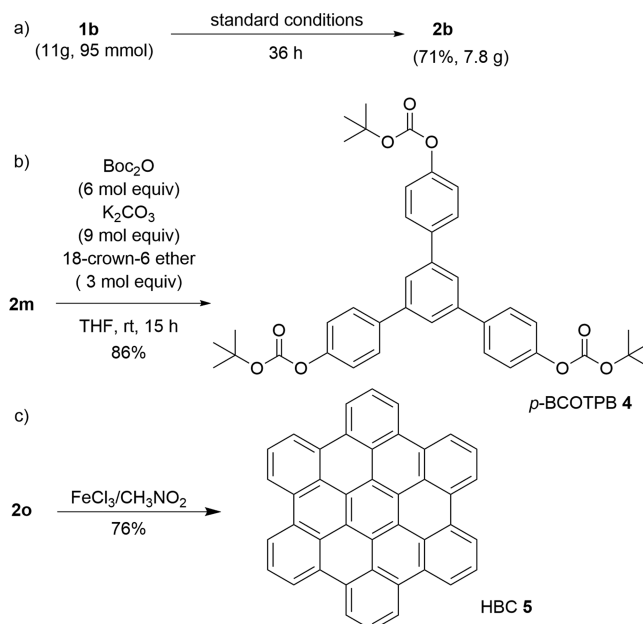
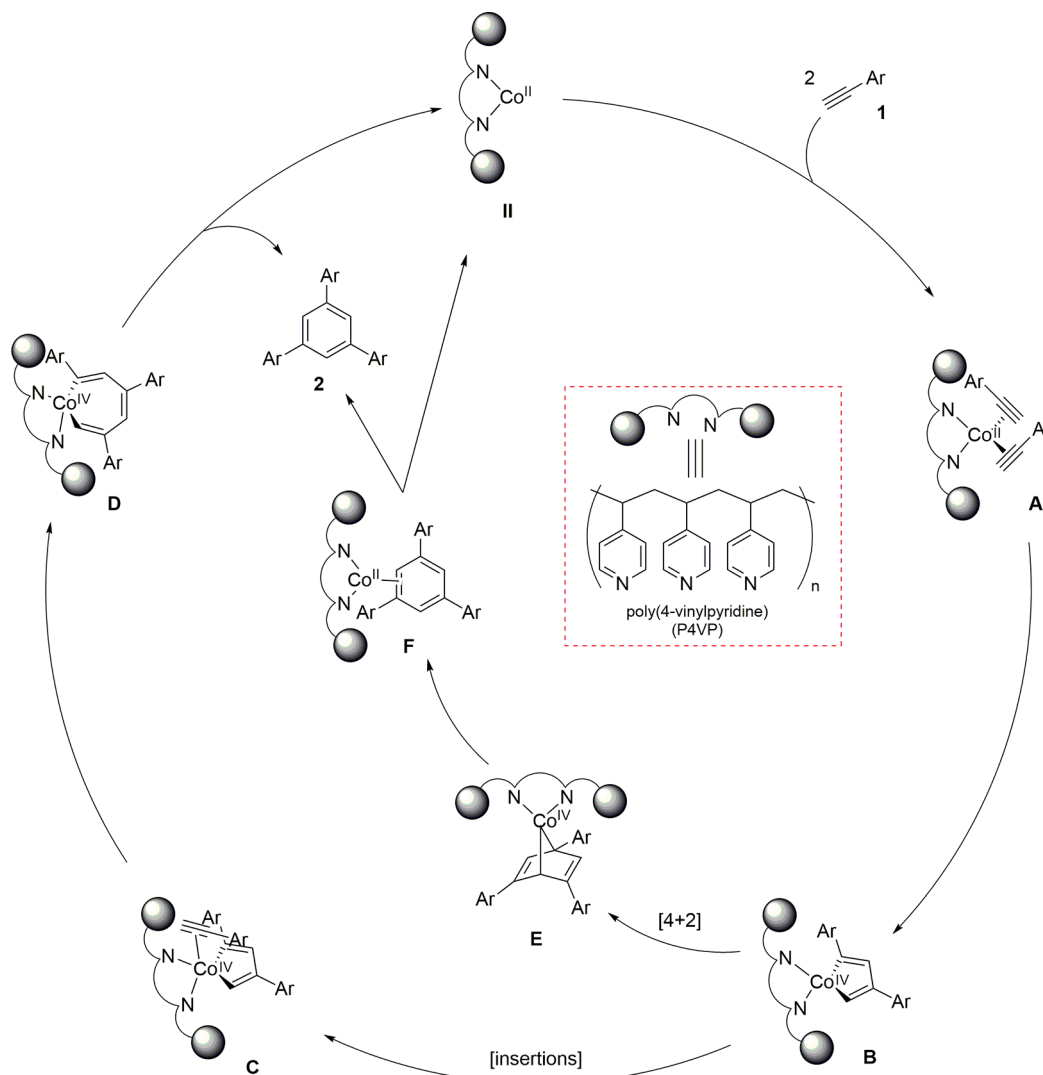


Figure 2. XPS spectra of cobalt 2p orbital of P4VP-Co before (top) and after (bottom) the reaction.

53% yield, respectively (entries 7–9). The reaction also afforded the desired product in the presence of electron-withdrawing groups (entries 10–12) with lower yields. The lower yield is due to several byproduct formations (for details, see the Supporting Information, Section S15). Product **2k** has been used to synthesize the core of self-assembled dendritic supermolecules.^{85,86} Interestingly, unprotected 4-ethynyl phenol (**1m**) was readily converted to desired product **2m** in 71% yield (entry 13). The reactions of 4-ethynyl-1,1'-biphenyl (**1n**) and 2-ethynyl-1,1'-biphenyl (**1o**) proceeded to afford the

Scheme 4. Speculative Catalytic Pathway



corresponding 1,3,5-tris(biphenyl)benzenes in 49 and 42% yield, respectively (entries 14 and 15). Although the reaction did not tolerate 3-ethynylpyridine (**1p**), 1-ethynynaphthalene (**1q**) produced 1,3,5-tri(1-naphthyl)benzene (**2q**) in 41% yield (entries 16 and 17). The reaction with aliphatic alkynes such as 1-octyne (**1r**) and (triisopropylsilyl)acetylene (**1s**) did not proceed under the optimized reaction conditions (entries 18 and 19). The reaction with internal alkyne such as 1,2-diphenylethyne (**1t**) was also not able to furnish the desired cyclotrimerized product (entry 20).

Catalyst Reusability

To our delight, the cyclotrimerization reaction using recovered cobalt catalyst proceeded well (Table 3; for details, see the Supporting Information, Section 9). After the reaction with a fresh catalyst (**II**), the catalyst was recovered from the reaction mixture with 98% yield (entry 1). The reaction with the recovered catalyst provided 80% yield of desired C₃-symmetric triarylbenzene (**2b**) whereas the catalyst can be recovered again with 95% yield (entry 2). Similarly, a third trial provided 72% yield of **2b** with 97% catalyst recovery (entry 3).

Cobalt Contamination Test from Isolated Product

The inductively coupled plasma-mass spectrometry (ICP-MS) analysis of 1,3,5-triphenylbenzene (**2a**) showed only 0.03 ppm cobalt contamination in the product (for details, see the Supporting Information, Section 11). This low amount of Co contamination in the products meets the criteria of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use.⁸⁷ The hot filtration test suggested the heterogeneous nature of the catalytic system (for details, see the Supporting Information, Section 9.3).

Application of Cyclotrimerization Product

The reaction of **1b** also proceeded successfully on a multigram scale (11 g, 95 mmol), yielding 7.8 g (71%) of **2b** (Scheme 3a). To demonstrate the synthetic applications of the obtained products, we synthesized functional materials. The reaction of **2m** with di-*t*-butyl dicarbonate afforded 1,3,5-tris(4-*t*-butoxycarbonyloxyphenyl)benzene (*p*-BCOTPB, **4**) (Scheme 3b). *p*-BCOTPB is an electron beam molecular resist with high sensitivity and high resolution.⁸⁸ Furthermore, product **2o** was converted to a PAH (hexa-peri-hexabenzocoronene; HBC, **5**) after reaction with FeCl₃ in nitromethane (Scheme 3c); HBC is an organic semiconductor.¹⁹

Speculative Catalytic Pathway

We believe there are two plausible pathways for this transformation. One is the Co(I)/Co(III) catalytic pathway,^{44,45} where Co(I) is generated via a disproportionation reaction,⁸⁹ and the other is Co(II)/Co(IV) catalysis.^{90–92} A disproportionation reaction should generate a mixture of Co(I) and Co(III) species. However, the X-ray photoelectron spectrum of the recovered catalyst was similar to that of the P4VP-CoCl₂ catalyst before the reaction, indicating that the recovered catalyst contains only Co(II) (Figure 2; for details, see the Supporting Information, Section S13). Therefore, the cyclotrimerization reaction likely proceed via a Co(II)/Co(IV) pathway, where a high reaction temperature assists in generating the Co(IV) species. As shown in Scheme 4, two equivalents of arylacetylene **1** coordinate to the cobalt(II) species to produce intermediate **A**. Oxidative cyclization proceeds to produce the corresponding five-membered cobalta(IV)-cycle intermediate (**B**). Coordination of another equivalent of **1** (**C**) should proceed via least steric repulsion (Figure S5), which is the critical step for 1,3,5-regioselectivity. Insertion affords seven-membered cobaltacycle intermediate **D**. Finally, the reductive elimination of **D** generates desired C₃-symmetric cycloaddition product **2** and cobalt(II) catalyst **II**. Alternatively, a [4 + 2] cycloaddition of aryl acetylene (**1**) with intermediate **B** could result the formation of intermediate **E**. Reductive elimination from **E** generates the final product **2** via intermediate **F**. Additionally, the fact that the reaction is described only for terminal alkynes leaves some room for consideration of other mechanistic options, namely, those involving vinylidene complex intermediates.^{93,94}

3. CONCLUSION

In conclusion, we developed P4VP-CoCl₂ as a bench-stable convoluted polymeric cobalt catalyst, which showed high catalytic activity for [2 + 2 + 2] cycloaddition and produced 1,3,5-regioselective cyclotrimerized products. The reaction proceeded smoothly using 0.033 mol % of catalyst (330 mol ppm of Co), with little Co leaching. Moreover, the catalyst was recoverable and reusable, and the reaction could be scaled up to the multigram scale. Electron beam molecular resist *p*-BCOTPB and organic semiconductor HBC were successfully synthesized from the cyclotrimerized products. Detailed mechanistic investigations are currently ongoing in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/jacsau.1c00360>.

Experimental details for catalyst preparation, cyclotrimerization reaction procedure, and analytical data (¹H NMR, ¹³C NMR, and ¹⁹F-NMR spectra, XAFS data, XPS spectra, SEM images, elemental analysis results, and melting points) (PDF)

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Author Contributions

The manuscript was written through the contributions of all the authors. All authors have approved the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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